An Introduction to CDISC: Part One
“What is CDISC and Why Standards?”

Rebecca Kush, PhD, CDISC
David Handelsman, SAS
Lack of standards make our lives more complicated

- Electrical power

Standards make our lives easier

- ATMs
- Bancomat
- Geldautomat
Health - AP

Pfizer Takes Painkiller Bextra Off Market

Thu Apr 7, 7:48 PM ET

By LAURAN NEERGAARD, AP Medical Writer

WASHINGTON - The blockbuster painkiller Bextra was yanked off the market Thursday, and the government ordered that 19 other popular prescription competitors — from Celebrex to Motrin to high-dose naproxen — carry tough new warnings that they, too, may increase the risk of heart attacks and strokes.

The warnings encompass an entire class of anti-inflammatory medicines called NSAIDs that are the backbone of U.S. pain treatment, not just newer versions of the painkillers initially suspected when the heart concerns made headlines last fall.
Clinical Information Dispersion Today

- Healthcare information is found in:
  - paper medical records
  - disparate databases
  - hospital-based information systems

- Clinical research data exists in:
  - additional databases
  - research notebooks

- Clinical trial data collection:
  - 3-part NCR forms in ~85% of trials
  - multitude of electronic data capture applications
    - eCRF
    - IVRS
    - ePRO
The Move to Standards…

“Faced with rapid changes, the nation’s healthcare system has fallen short of its ability to translate information into knowledge that can be used in practice, and to apply new technology safely and appropriately. The results are exactly what you would expect. Everyone who uses the current system constantly confronts large information gaps, whether it’s at the doctor’s office, on the hospital ward or at government agencies charged with protecting the public health. That goes for the FDA -- we’re no exception.”

Dr. Mark McClellan, former FDA Commissioner
CDISC Interchange, October 2003

“Innovation depends upon standardization.”

Dr. Bob O’Neill, Director, Office of Biostatistics, CDER, FDA
Benefits of Standards: Operational

- Increase efficiencies of performing clinical trials
- Simplify processes among investigators, pharma companies, CROs, vendors, laboratories
- Streamline data collection at investigator sites
- Improve sponsor’s access to data and ability to understand it
- Provide long-term means for electronic data archive
- Facilitate FDA review of submissions
- Improve links between healthcare delivery and clinical research
Benefits of Standards: Scientific

• Facilitate integration of data
  – Across trials, compounds, companies
• Enable assessment of trends and patterns in data
  – Public health benefit
  – Drug development benefit
  – Better guidance for studying disease states
• Allow companies to focus on their potential therapeutic products vs. data issues
• Improve safety monitoring and pharmacovigilance
• Support ad hoc analyses; enhance decision-making capabilities during data review
Standards: Yours, Mine, Ours

• Internal standards are a good first step, but are insufficient
  – Streamline internal processes
  – Little effect of data transfer and interoperability with external organizations
  – CROs are a classic example of the limits of internal standards

• Development and adoption of public standards are the next logical steps
  – Increase data efficiency of all participating organizations
  – Brings a renewed focus to the science of clinical research
Why Are Standards Important?

- Pre-Clinical
  - Animal Studies
    - Up to 10,000
  - Phase I
    - 30-100 Volunteers
    - 10 - 15

- Clinical Development
  - Phase II
    - 200-400 Patients
    - 4 - 8
  - Phase III
    - 3000+ Patients
    - 2 - 3

- Post Marketing
  - Phase IV
  - Approval
  - 10-15 Years elapsed time

# of Compounds
Why Are Standards Important?
Before Standards…

Regulatory Agencies
Corporate Partners
Statistical Programs
After CDISC Standards

EDC (ODM) → Internal CDM System → Internal Data Warehouse (SDS)

Regulatory Agencies
Corporate Partners
Statistical Programs

CDISC
Looking into the future…

What other options exist?

- eSource Data
- Internal Data Warehouse
- Regulatory Agencies
- Corporate Partners
- Statistical Programs
Benefits of Standards – Regulatory View

Before SDTM
- Domains = Yes
- Standard Domain Names = No
- Standard Structure = No
- Standard Variables = No
- Standard Variable Names = No
- Standard Terms = No

After SDTM
- Domains = Yes
- Standard Domain Names = Yes
- Standard Structure = Yes
- Standard Variables = Yes
- Standard Variable Names = Yes
- Standard Terms = not yet, but coming
Benefits of Standards – Regulatory View

“The importance of a standard for the exchange of clinical trial data cannot be overstated. FDA reviewers spend far too much valuable time simply reorganizing large amounts of data submitted in varying formats. Having the data presented in a standard structure will improve FDA’s ability to evaluate the data and help speed new discoveries to the public.” -Lester Crawford, Former Commissioner, FDA
Clinical Data Interchange Standards Consortium: Original Mission Statement

CDISC is an open, multidisciplinary, non-profit organization committed to the development of worldwide industry standards to support the electronic acquisition, exchange, submission and archiving of clinical trials data and metadata for medical and biopharmaceutical product development.

The mission of CDISC is to develop and support global, platform-independent data standards that enable information system interoperability to improve medical research and related areas of healthcare.
Current State of Clinical Data Transfer

- Medical Records
- CRF
- Lab
- Operational Data
- Submission Data
- Submission

CDISC
Clinical Back Office…

EDC Without Standards, courtesy Charles Jaffe, MD, PhD
The Future: Standards to Facilitate Data Flow ....from Source to Reviewers

Sources of electronic data

- ECG
- LAB
- EDC
- CRO

Operational Database

SDS ADaM

eSubmission for Regulatory Review
CDISC

• Formed in 1997 as a volunteer group
• As of 2000, incorporated and funded as non-profit organization
• Now supported by >170 member companies:
  – pharmaceutical companies; biotech companies; CROs/service providers; technology providers
• CDISC Groups now growing in Japan, Europe, India
• Standards developed through consensus-based approach with public reviews; open standards
CDISC Principles

- Lead the development of **standard data models** that improve process efficiency while supporting the scientific nature of clinical research.
- Recognize the ultimate **goal of creating regulatory submissions** that allow for flexibility in scientific content and are easily interpreted, understood, and navigated by regulatory reviewers.
- Acknowledge that the data content, structure and quality of the standard data models are of paramount importance, **independent of implementation strategy and platform**.
CDISC Principles

• Maintain a global, multidisciplinary, cross-functional composition for CDISC and its working groups.
• Work with other professional groups to encourage that there is maximum sharing of information and minimum duplication of efforts.
• Provide educational programs on CDISC standards, models, values and benefits.
• Accomplish the CDISC goals and mission without promoting any individual vendor or organization.
CDISC Structure

CDISC Board of Directors

Industry Advisory Board

CDISC Working and Support Teams

- Operational Data Modeling (ODM)
- Submission Data Standards (SDS)
- Analysis Data Set Modeling (ADaM)
- Laboratory Data (LAB)
- Protocol Representation
- SEND
- Terminology

Board Committees
- Financial Oversight
- Governance
- Nominating
- Scientific
- Technical Support & Guidance

Alliances

- HL7
- Others

CDISC Regional Groups

- Regional CDISC Coordinating Committees (r3C)
  - Regional CDISC Groups
    - Regions, including Europe, Japan, India...

Operations and Infrastructure (OIS)

- Education
- Membership Services
- PR/Communications
- Operations and Financial Management

- Technical Direction; TCC
- Implementation Group Coordination
- Standards Maintenance
- Glossary Group Leadership
Standards

- Definition of **Standard**: An object considered by an authority or by general consent as a basis of comparison; an approved **model**

- Standard data models, metadata models, codes, terminology, content, technology

- Definition of **Model**: A **standard** or example for imitation or comparison

* The Random House Dictionary of the English Language, unabridged version
Data and Metadata: Definitions

• Data
  – representations of facts, concepts, or instructions in a manner suitable for communication, interpretation, or processing by humans or by automated means. [FDA] (Synonym: Information)

• Metadata
  – Data about data

• Metadata Elements
  – The metadata of a study describes the types of study events, forms, item groups, and items that are allowed in the study.
How Important is Metadata?

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Slide developed by David Christiansen, DrPH
In this case $125,000,000: Mars Climate Orbiter

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<th>Mars Orbit Insertion Burn</th>
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Data Interchange: Definition

• Data Interchange
  – the transfer of information between two or more parties. Data interchange is distinguished from data transfer in that the integrity of the contents of the data is maintained. [CDISC]

• CDISC Glossary is available on the website (www.cdisc.org) and in December resource issues of Applied Clinical Trials.
CDISC Approach

• The CDISC models are the products of contributions from numerous organizations, functional groups, and individuals; they do not have a sole source.

• Consensus building
  – Involves different disciplines within the industry
  – Involves ‘consolidating’ existing models, review comments and testing
  – Takes time, but results in widely accepted models
CDISC Standards Development Process
(COP-001)

Stage I: Standard Definition/Team Initiation

Need for Specific Standard(s) Identified (any stakeholder)

Proposal to Board of Directors (via OIS)

Review per strategy, budget priorities

Team Leader ID And Team Formation (multidisciplinary) (OIS)

Not Approved

Working Plan (timelines, deliverables communication mech., resources req’d) (Team)

Stage II: Standards Development/Review/V 1.0 Release

Consensus (Initial) Version

Proposal to Board of Directors (via OIS)

Review per strategy, budget priorities

Team Leader ID And Team Formation (multidisciplinary) (OIS)

Not Approved

Working Plan (timelines, deliverables communication mech., resources req’d) (Team)

Harmonized Version

TCC Review

External Focused Review

Review Version

Public Review

Released (Production) Version 1.0

Stage III: Education & Support

Respond To Comments And Questions

Educational Programs (EDU, OIS)

Comments addressed

Comments to address by team

Stage IV: Standards Update & Maintenance

Annual Review of Released Version (comments, chg reqsts, tests, plans) (Team)

Working Plan (timelines, deliverables, communication mech., resources req’d) (Team)

Consensus (Revised) Version

TCC Review

Optional

Ex Focused Review

Harmonized Version

Public Review as needed

New Released (Production) Version

Note: Occasional bug fix releases may be issued as needed with team review only.
Scope of CDISC Models

**Data Sources**
- Site CRFs
- Laboratories
- Contract Research Organizations
- Development Partners

**Operational Database**
- Study Data
- Audit Trail
- Metadata

**Submission Data**
- CRT/Domain Datasets
- Analysis Datasets
- Metadata

ODM = Operational Data Model
LAB = Laboratory Data Model
SDM = Submission Data Model
ADaM = Analysis Data Models
Evolution of CDISC Standards:
Started with the end in mind…

Data Sources
• Site CRFs
• Laboratories
• Contract Research Organizations
• Development Partners

Operational Data Interchange & Archive: ODM, LAB

Operational Database
• Study Data
• Audit Trail
• Metadata

Submission Data Interchange & Archive: SDS, ADaM SEND

Submission Data
• CRT/Domain Datasets
• Analysis Datasets
• Metadata

ODM = Operational Data Model/Std
LAB = Laboratory Data Model/Std
SDS = Submission Domain Standards
ADaM = Analysis Data Models
SEND = Standards for the Exchange of Non-Clinical Data
<table>
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<tr>
<th>Standard</th>
<th>Description</th>
<th>Implementation Release Version</th>
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<tbody>
<tr>
<td>Study Data Tabulation Model (SDTM), including SEND for non-clinical (animal) data</td>
<td>Content Model - regulatory submission of case report tabulations (CRT) and non-clinical (animal) data</td>
<td>July 2004</td>
</tr>
<tr>
<td>Operational Data Model (ODM)</td>
<td>XML-based Transport Standard – acquisition, exchange and archive</td>
<td>Mid-2001</td>
</tr>
<tr>
<td>Clinical Laboratory Model (LAB)</td>
<td>Content Model - exchange of laboratory data between labs and sponsors/CROs</td>
<td>Mid-2002</td>
</tr>
<tr>
<td>Analysis Dataset Model</td>
<td>Content Model - General Considerations Document and Examples of Datasets</td>
<td>Late 2004</td>
</tr>
<tr>
<td>Case Report Tabulation (CRT) Data Definition Specification (Define.xml)</td>
<td>Transport Standard - Describes how to create data description doc (metadata) for submission in ODM XML standard.</td>
<td>Late 2004</td>
</tr>
<tr>
<td>Structured Clinical Trial Protocol (SCTP)</td>
<td>Machine- and Human-readable model that enables exchange of protocol information amongst stakeholders.</td>
<td>In progress</td>
</tr>
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</table>
FDA has endorsed the standards by including them as specifications in FDA Guidance.

FDA News

FOR IMMEDIATE RELEASE
P04-73
July 21, 2004

FDA Announces Standard Format That Drug Sponsors Can Use to Submit Human Drug Clinical Trial Data

The Food and Drug Administration (FDA) today announced a standard format, called the Study Data Tabulation Model (SDTM) developed by the Clinical Data Interchange Standards Consortium (CDISC), that sponsors of human drug clinical trials can use to submit data to the agency. It is expected that this step will lead to greater efficiencies in clinical research and FDA reviews of New Drug Applications (NDAs).

SDTM and define.xml: Specifications for FDA implementation of the ICH eCommon Technical Document.
Speaking of health benefits/opportunities to be realized from making more effective use of IT….

• “I think that CDISC will be a big part of moving FDA onto an electronic information architecture where we can realize all of these opportunities. I think this will have a profound and positive impact on our drug review process, allowing us to design trials that can be less expensive and still tell us more about the risks and benefits of a new medical product. And I think that the most significant and perhaps enduring legacy to your efforts could be the very immediate and significant impact it has on improving the lives of patients.”

-Mark McClellan, MD, PhD, FDA Commissioner, September 2003
CDISC Teams and Projects - 2005

- Single Source
- eSource Data Interchange
- HL7-CDISC Harmonization; BRIDG Model
- Metadata – end-to-end consistency LAB and AE scenarios
- eDCI HL7 V3
- Define.xml
- Terminology (Codelists)
- NIH Roadmap CV, TB Stds
- PRG ODM LAB SDS SEND ADaM

Maintenance, Member Relations, Education and Implementation Groups, Glossary
The mission of CDISC is to develop and support global, platform-independent data standards that enable information system interoperability to improve medical research and related areas of healthcare.
What's New

SEND Review Version 1.5: The Standard for Exchange of Nondclinical Data (SEND) Models have been prepared by the SEND Consortium to guide the organization, structure, and format for non-clinical data submitted to the FDA. The focus of the SEND Consortium has been on data collected from animal Toxicology studies. SEND is intended to facilitate transfer of nondclinical data from sponsor to the FDA and subsequent loading into the FDA repository. Please submit comments on this review version through our public Discussion Forum by 31-August-2004. Click here for SEND V1.5 Review Version.
Knowing is not enough; we must apply.
Willing is not enough; we must do.

- Goethe-

To the gracious supporters who ‘apply’ and ‘do’....

THANK YOU!
Rebecca Kush
rkush@cdisc.org
Information and Contacts

• For standards and information, see www.cdisc.org
• eNewsletters available via e-mail; contact Shirley Williams swilliams@cdisc.org or sign up on the CDISC website.
• Technical questions: Julie Evans jevans@cdisc.org or Public Discussion Forum
• Education and Membership: Frank Newby fnewby@cdisc.org
• Rebecca Kush: rkush@cdisc.org