Electronic Health Records and Clinical Data Interchange Standards

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IPPCR – February 23, 2016
Disclaimer

This presentation reflects the views of the author and should not be construed to represent FDA’s views or policies.
Acknowledgements

Becky Kush, CDISC

Chuck Cooper, (formerly FDA/CDER)

Ron Fitzmartin, FDA/CDER

Shannon Labout, CDISC

Lilliam Rosario, FDA/OTS
Science, Statistics and Experimental Design

Science is concerned with understanding variability in nature

Statistics is concerned with making decisions about nature in the presence of variability

Experimental design is concerned with reducing and controlling variability in ways which make statistical theory applicable to decisions about nature.
Data Transparency

Patients and their physicians depend on clinical trials for reliable evidence on what therapies are effective and safe.

Responsible sharing of the data gleaned from clinical trials will increase the validity and extent of this evidence.
My Assumptions – What You Have Already Learned in this IPPCR Course

Good Clinical Research Practice

Design

Conduct

Statistical Analysis

Legal and Ethical Principles

Data Management

Drug Development

FDA Product Regulation
Steve’s Black Box Warning

FDA/CDER-Centric -- There are regulation/guidance differences between Centers at FDA

FDA regulation/guidance codifies Good Research Practice

Primary focus: Confirmatory (Phase III) Trials

A CDER statistical reviewer perspective

If you feel that your clinical research will contribute to the development of marketed medical products ... please pay special attention

Good clinical research practice is a global concern
Outline

Substantial Evidence and FDA/CDER Review of Confirmatory (Phase 3) Clinical Trials

CDISC Data Standards

New CDER/CBER Requirements

CDISC Basics

Using eHealth Records in Clinical Research for Drug Development
FDA Mission

FDA is responsible for protecting the public health by assuring the safety, efficacy and security of human and veterinary drugs, biological products, medical devices, our nation’s food supply, cosmetics, and products that emit radiation.

FDA is responsible for advancing the public health by helping to speed innovations that make medicines more effective, safer, and more affordable and by helping the public get the accurate, science-based information they need to use medicines and foods to maintain and improve their health.
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NDA/BLA Review at CDER
(Center for Drug Evaluation and Research)
CDER

Almost all clinical research associated with New Drug Applications (NDAs) and Biologics License Applications (BLAs) are reviewed by CDER

Within CDER -- Primary offices for planning and review of clinical trials

Office of New Drugs (OND)
We Worry About Bias That Will Affect Our Decisions –
Due Decision Diligence (DDD)

Bias is a preconceived personal preference or inclination that influences the way in which a
measurement
analysis
assessment
or procedure
...is performed or reported
Always a Risk-Benefit Decision
We Worry About Bias
We Worry About Bias
Substantial Evidence / Adequate and Well-Controlled Studies

The Food and Drug Administration considers these characteristics in determining whether an investigation is adequate and well-controlled for purposes of section 505 of the act.

Reports of adequate and well-controlled investigations provide the primary basis for determining whether there is "substantial evidence" to support the claims of effectiveness for new drugs.
ICH E9 – Confirmatory Trials
FDA’s “Gold Standard” for Approval

NDA/BLA

Two adequate and well-controlled, confirmatory clinical trials (AWCCCT)

Pre-specified endpoint(s), sample size & analysis

Two-sided, p-value < 0.05

Clinical benefit
21st Century Review of NDAs/BLAs
The Call from a CDER Reviewer
Review Tools:

OCS/CSC JumpStart Service

Provides a recommended sequence for using the outputs

Allows reviewer to follow a safety signal from a high-level to the specific patient details with complementary tools
OCS/CSC JumpStart Service

Starts a review by performing many standard analyses and identifying key information
Required Submission of CDISC Standardized Data Standards
The New Call from a CDER Reviewer
CDISC
Clinical Data Interchange Standards Consortium

What is CDISC?

Submission Data Standards to CDER

Developing Ebola TAs
What is CDISC?
www.cdisc.org
CDISC Vision and Mission
CDISC Standards ...

Streamline research processes and enable data sharing/aggregation

Support all types of research from protocol through analysis and reporting

Include link to healthcare through EHRs
Do you need Data Standards?
Do you need Data Standards?
Do you need CDISC?
Do you need CDISC?
CDISC Data Standards
in the Clinical Research Process
CDISC – End to End
(quality, speed, provenance)

CDISC Data Standards for Submission to CDER
Study Data Tabulation Model (SDTM)

Analysis Data Model (ADaM)

Therapeutic Area (TA) Standards

Study Data Tabulation Model (SDTM)
Basic Concepts of SDTM
Value of SDTM

Study #1 – demog.xpt

Study #1 – DM.xpt

SDTM Logically Organizes Data
Analysis Data Model (ADaM)
Basic Concepts of ADaM
Value of ADaM
OCS/CSC JumpStart Service

Starts a review by performing many standard analyses and identifying key information
CDASH – Data Collection

Ebola virus Disease Case Study - Global Harmonization to Increase Power and Accelerate Outcomes in Clinical Research Data

Facilitator: Shannon Labout

Vice President Education

CDISC
A Case Study: A Randomized, Controlled Trial To Evaluate Ebola Therapies
Dionne L. Price, Ph.D.
Director, Division of Biometrics IV
OB/OTS/CDER/FDA
Setting the Stage and Understanding the Challenges of Ebolavirus Disease Clinical Research

Laura Merson, Clinical Trialist, Oxford University

Consulting Expert to CDISC Ebolavirus Therapeutic Area standards development team
Leveraging CDISC standards to support Ebola research

Maura Kush, Pharmastat consultant

Co-lead of CDISC Ebolavirus Therapeutic Area standards development team
Leveraging CDISC Standards to Support Ebola Research

Efforts to standardize data collection and reporting began last October

Started to annotate CRFs we received from the Oxford University Clinical Research Unit (OUCRU) using CDASH and SDTM variables:

EVD CORE CRF (World Health Organization)

RAPIDE BCV (Chimerix)

Plasma Convalescence

Ended up with a finalized four-page CRF the WHO shortened to only collect the most important, pertinent information
Development of an EVD-specific Standard

Project Team includes representatives from Oxford, CDISC teams, government, and pharma

Face-to-face meetings at CDISC Interchange Conferences in November 2014 (Washington, DC) and May 2015 (Basel, Switzerland)

Following the CDISC Standards Development Process (COP-001) for TA standards

Expanding CDISC Standards

Most variables and terms can be taken from the existing SDTMIG and TAUGs (TB/Virology/Hepatitis C)

Epidemiological data presents an opportunity for growth

TB TAUG contains some ‘contact investigation’ criteria, controlled terms in SC domain:

CNTCINV, CTRYDDTC, CTRYDEXP, EDLEVEL, EMPJOB, JOBCLAS, NATORIG, PRICON, RISKPOP, RISKSOC, SETCON, SRCCSINV, TYPCON

Terms may need to be added

Discussion in Basel of a new ‘Contact Investigation’ domain, or a set of implementation rules to assist the collection and reporting of epidemiological data
What’s next?

Broadening use of CDISC standards from the traditional clinical trial setting to outbreak and public health situations

For Ebola, this includes:

Names, surnames, addresses using GPS coordinates

Death occurring pre-‘exposure’ or pre-‘admission’

Contact investigation information

Friends/family (names and addresses using GPS coordinates), healthcare workers, animals

Missing information

Ensuring broad public review of the EVD draft standard will ensure that it will be useful for research on future outbreaks of EVD and related viruses
“Real World Data”
Rob Califf and Rachel Sherman, FDA 12/10/2015

Networked systems, electronic health records, electronic insurance claims databases, social media, patient registries, and smartphones and other personal devices together comprise an immense new set of sources for data about health and healthcare.

... these “real-world” sources can provide data about patients in the setting of their environments—whether at home or at work—and in the social context of their lives
“Electronic health records: new opportunities for clinical research”

... emerging research infrastructures are being developed to ensure that EHRs can be used for secondary purposes such as clinical research, including the design and execution of clinical trials for new medicines.

...EHR systems should be able to exchange information through the use of recently published international standards for their interoperability and clinically validated information structures (such as archetypes and international health terminologies), to ensure consistent and more complete recording and sharing of data for various patient groups.

Electronic Health Records (EHRs)

Digital versions of a medical chart

Real-time, patient-centered records
EHR in Clinical Research

EHR – EDC - eSource

eCRF

Use of remote data capture (RDC) is increasing

Oracle Clinical, Clintrial, Macro, Rave, eClinical Suite

Electronic CRFs
What can EHRs do?

Make patient information easier to find

Automate providers' workflows

Provide evidence-based tools

Support changes in insurance requirements
EHR vs EMR

Electronic Medical Record

Medical and treatment history of patients in one practice

Electronic Health Record

Information can be shared

Information from all clinicians involved
FR Notice: CDER Promoting EHRs

Source Data Capture from Electronic Health Records (EHRs)


Proposed Demonstration Solutions
In Conclusion

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