Collaborative Review of CDISC QRS Instruments

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2021 Virtual PharmaSUG

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Disclaimer

The views and opinions presented here represent those of the speakers and should not be considered to represent advice or guidance on behalf of the U.S. Food and Drug Administration.

Acknowledgements

Outline

- **Motivation**
  - For FDA Involvement in this Collaboration with CDISC
  - For this PharmaSUG Session
- **CDISC QRS Instrument Supplements Overview/Update**
  - Steve Kopko, CDISC SME, External Consultant CDISC
  - Dana Booth, CDISC Standards Project Manager, CDISC
- **FDA/CDISC QRS Subteam Review Activities**
  - Establishing Priorities for the FDA Review of QRS Supplements
  - FDA QRS Draft Supplement Review Experience
- **Q & A**

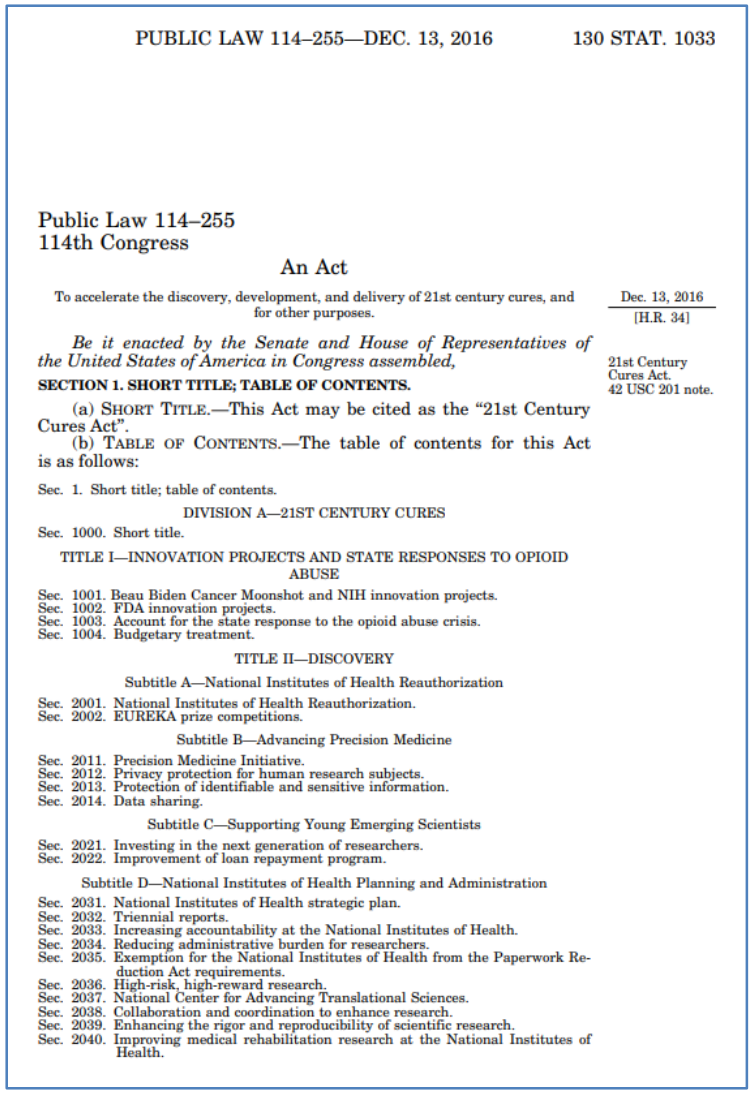
Motivation – For This 2021 PharmaSUG Session

- Transparency
- Publicity for FDA Initiatives and CDISC-QRS Data Standards
- Information Sharing / Education (Yours and Ours)
- A Better understanding Our Regulatory World
- Continuous Improvement of Regulatory Science/Drug Development
- Invitation for You to Collaborate/Volunteer

Motivation: For FDA Involvement in This Collaboration

- The Cures Act /Patient-Focused Drug Development (PFDD)
- PDUFA VI Goals
  - Clinical Outcome Assessments (COAs)
  - "Enhancing the Capacity to Support Analysis Data Standards for Product Development and Review"
- Requirements for Electronic Submission of CDISC-standardized Clinical Trials Data --745A(a) of the FD&C Act & Binding Guidance

The 21st Century Cures Act (December, 2016)



PUBLIC LAW 114–255—DEC. 13, 2016 130 STAT. 1033

Public Law 114–255
114th Congress

An Act

To accelerate the discovery, development, and delivery of 21st century cures, and for other purposes.

Dec. 13, 2016
[H.R. 34]

Be it enacted by the Senate and House of Representatives of the United States of America in Congress assembled,

21st Century Cures Act.
42 USC 201 note.

SECTION 1. SHORT TITLE; TABLE OF CONTENTS.

(a) SHORT TITLE.—This Act may be cited as the "21st Century Cures Act".

(b) TABLE OF CONTENTS.—The table of contents for this Act is as follows:

https://www.congress.gov/114/plaws/publ255/PLAW-114publ255.pdf

"The **Cures Act** further recognizes the significance of the **patient** experience surrounding regulatory decisions and expands on the concept of **Patient-Focused Drug Development** by laying out a framework for its application, guidance and evaluation within FDA."

https://www.nsf.org/knowledge-library/regulatory-radar-21st-century-cures-act-patient-focused-drug-development

Patient-Focused Drug Development (PFDD) and PDUFA VI Goals

CDER Patient-Focused Drug Development

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What is Patient-Focused Drug Development?

Patient-focused drug development (PFDD) is a systematic approach to help ensure that patients' experiences, perspectives, needs, and priorities are captured and meaningfully incorporated into drug development and evaluation. As experts in what it is like to live with their condition, patients are uniquely positioned to inform the understanding of the therapeutic context for drug development and evaluation.

The primary goal of patient-focused drug development is to better incorporate the patient's voice in drug development and evaluation, including but not limited to:

- Facilitating and advancing use of systematic approaches to collecting and utilizing robust and meaningful patient and caregiver input to more consistently inform drug development and regulatory decision-making
- Encouraging identification and use of approaches and best practices to facilitate patient enrollment and minimizing the burden of patient participation in clinical trials
- Enhancing understanding and appropriate use of methods to capture information on patient preferences and the potential acceptability of tradeoffs between treatment benefit and risk outcomes
- Identifying the information that is most important to patients related to treatment benefits, risks, and burden, and how to best communicate the information to support their decision making.

https://www.fda.gov/drugs/development-approval-process-drugs/cder-patient-focused-drug-development

PDUFA REAUTHORIZATION PERFORMANCE GOALS AND PROCEDURES FISCAL YEARS 2018 THROUGH 2022

J. ENHANCING REGULATORY DECISION TOOLS TO SUPPORT DRUG DEVELOPMENT AND REVIEW

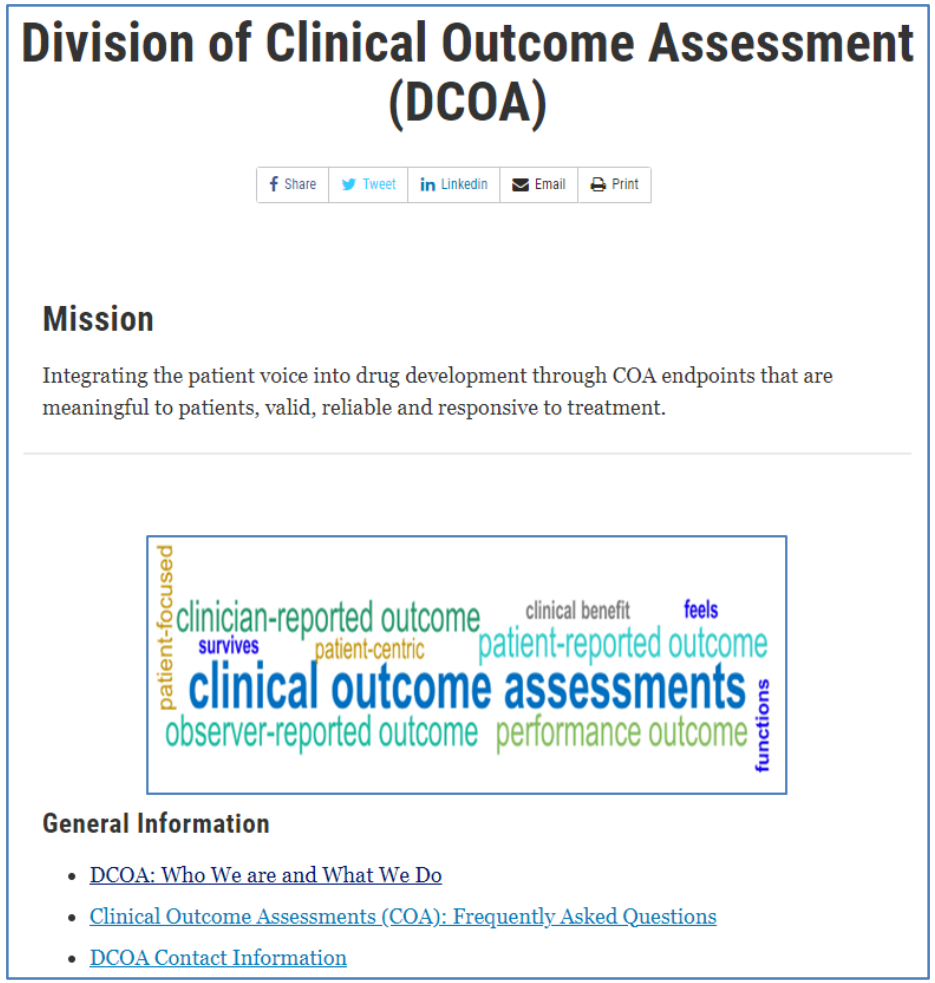
1. Enhancing the Incorporation of the Patient's Voice in Drug Development and Decision-Making

To facilitate the advancement and use of systematic approaches to collect and utilize robust and meaningful patient and caregiver input that can more consistently inform drug development and, as appropriate, regulatory decision making, FDA will conduct the following activities during PDUFA VI:

a. FDA will strengthen the staff capacity to facilitate development and use of patient-focused methods to inform drug development and regulatory decisions…clinical, statistical, psychometric, and health outcomes research expertise, will be integrated into review teams ….where the sponsor intends to use patient input or clinical outcome assessment (COAs) such as patient-reported outcomes (PROs) as part of the development program. …

https://www.fda.gov/media/99140/download

COAs at CDER



Division of Clinical Outcome Assessment (DCOA)

Share Tweet Linkedin Email Print

Mission

Integrating the patient voice into drug development through COA endpoints that are meaningful to patients, valid, reliable and responsive to treatment.

General Information

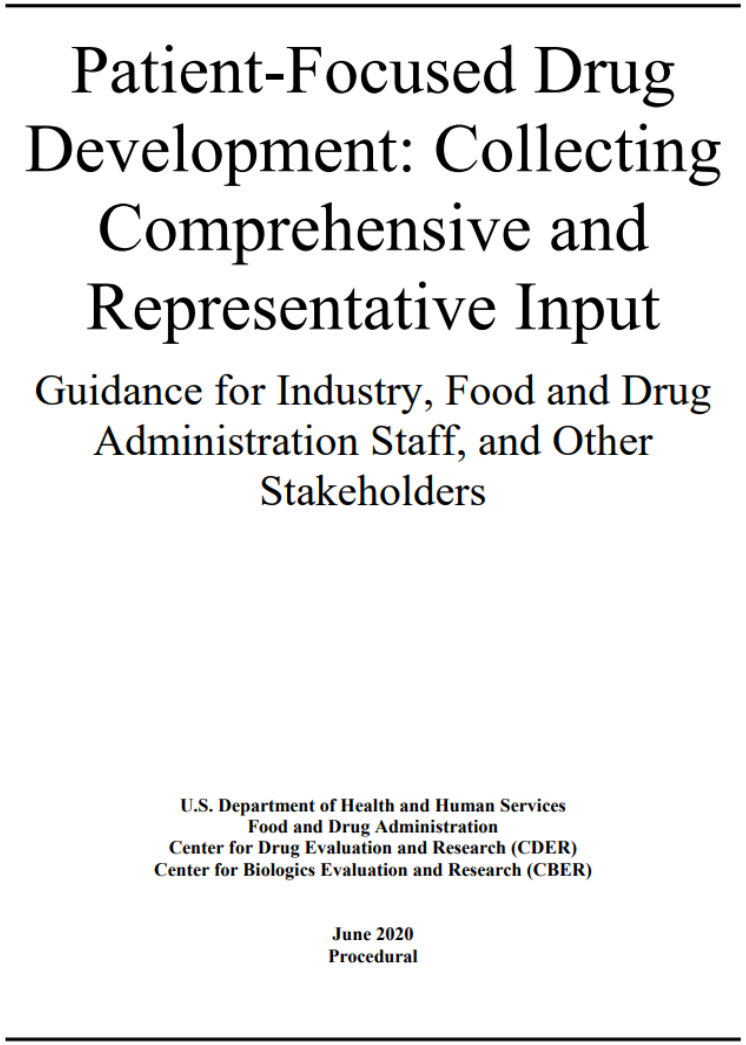
- DCOA: Who We are and What We Do
- Clinical Outcome Assessments (COA): Frequently Asked Questions
- DCOA Contact Information

Mission

Integrating the patient voice into drug development through COA endpoints that are meaningful to patients, valid, reliable and responsive to treatment

https://www.fda.gov/about-fda/center-drug-evaluation-and-research-cder/division-clinical-outcome-assessment-dcoa

Patient-Focused Drug Development: Collecting Comprehensive and Representative Input


Patient-Focused Drug Development: Collecting Comprehensive and Representative Input

Guidance for Industry, Food and Drug Administration Staff, and Other Stakeholders

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)
Center for Biologics Evaluation and Research (CBER)

June 2020
Procedural

https://www.fda.gov/media/139088/download

H. Data Standards

External stakeholders should use appropriate data standards when collecting, managing, and reporting patient experience data. When planning a study (including the design of case report forms, data management systems, and data analysis plans), you should determine which FDA-supported standards to use. See Appendix 1. Standards and Requirements Pertaining to Submission of Data for some data standards resources.

While compliance with these standards may not be required for studies other than those conducted to support a regulatory medical product application (e.g., an Investigational New Drug (IND), New Drug Application (NDA) or Biologics License Application (BLA)) or medical product labeling language, we encourage researchers to, at a minimum, bear these standards in mind, because patient experience data that are ultimately intended for use in clinical trials would be subject to the applicable standards.

A PDUFA VI Goal for Office of Biostatistics (OB) -- "Enhancing the Capacity to Support Analysis Data Standards for Product Development and Review"

- Support pre- and post-submission discussion of standardized datasets and programs
- Maintain the knowledge of and engage in collaborations about standards models (including CDISC SDTM, ADaM, CDASH and SEND)
- Assist with FDA development and updating of therapeutic area user guides (TAUGs)
- Convene a public workshop to advance the development and application of data standards
- Collaborate with external stakeholders

745A(a) of the FD&C Act & Binding Guidance – Requiring the Submission of Standardized Data

Section 745A(a) of the Federal Food, Drug, and Cosmetic Act (FD&C Act), added by section 1136 of the Food and Drug Administration Safety and Innovation Act (FDASIA) (Public Law 112-144), requires that submissions under section 505(b), (i), or (j) of the FD&C Act2 and submissions under section 351(a) or (k) of the Public Health Service Act (PHS Act)3 be submitted in electronic format specified by the Food and Drug Administration (FDA or the Agency) …

- To comply with the GGP regulations and make sure that regulated entities and the public understand that guidance documents are nonbinding, FDA guidances ordinarily contain standard language explaining that guidances should be viewed only as recommendations unless specific regulatory or statutory requirements are cited.
- FDA is not including this standard language in this guidance because it is not an accurate description of the effects of this guidance.
- Insofar as this guidance specifies the format for electronic submissions, or provides for exemptions pursuant to section 745A(a) of the FD&C Act, it will have binding effect.

https://www.fda.gov/regulatory-information/search-fda-guidance-documents/providing-regulatory-submissions-electronic-format-submissions-under-section-745aa-federal-food-drug

Outline

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  - Establishing Priorities for the FDA Review of QRS Draft Supplements
  - FDA QRS Draft Supplement Review Experience
- **Q & A**

CDISC Questionnaires, Ratings, and Scales (QRS) Instrument Supplements Overview

Presenters: Steve Kopko, CDISC SME, External Consultant CDISC

Dana Booth, CDISC Standards Project Manager, CDISC

PharmaSUG 25 May 2021

CDISC Disclaimer

CDISC specifies how to structure the data that has been collected in a database, not what should be collected or how to conduct clinical assessments or protocols. CDISC disclaims any liability for your use of this material.

CDISC Introduction (https://www.cdisc.org/)

What we do:

- Create Clarity.
- In the ever-evolving and complex clinical research landscape, CDISC provides critical clarity. We develop and advance data standards of the highest quality to transform incompatible formats, inconsistent methodologies, and diverse perspectives into a powerful framework for generating clinical research data that is as accessible as it is illuminating..

CDISC Introduction (https://www.cdisc.org/)

How we do it:

- Individual Contributions.
- Collective Power.

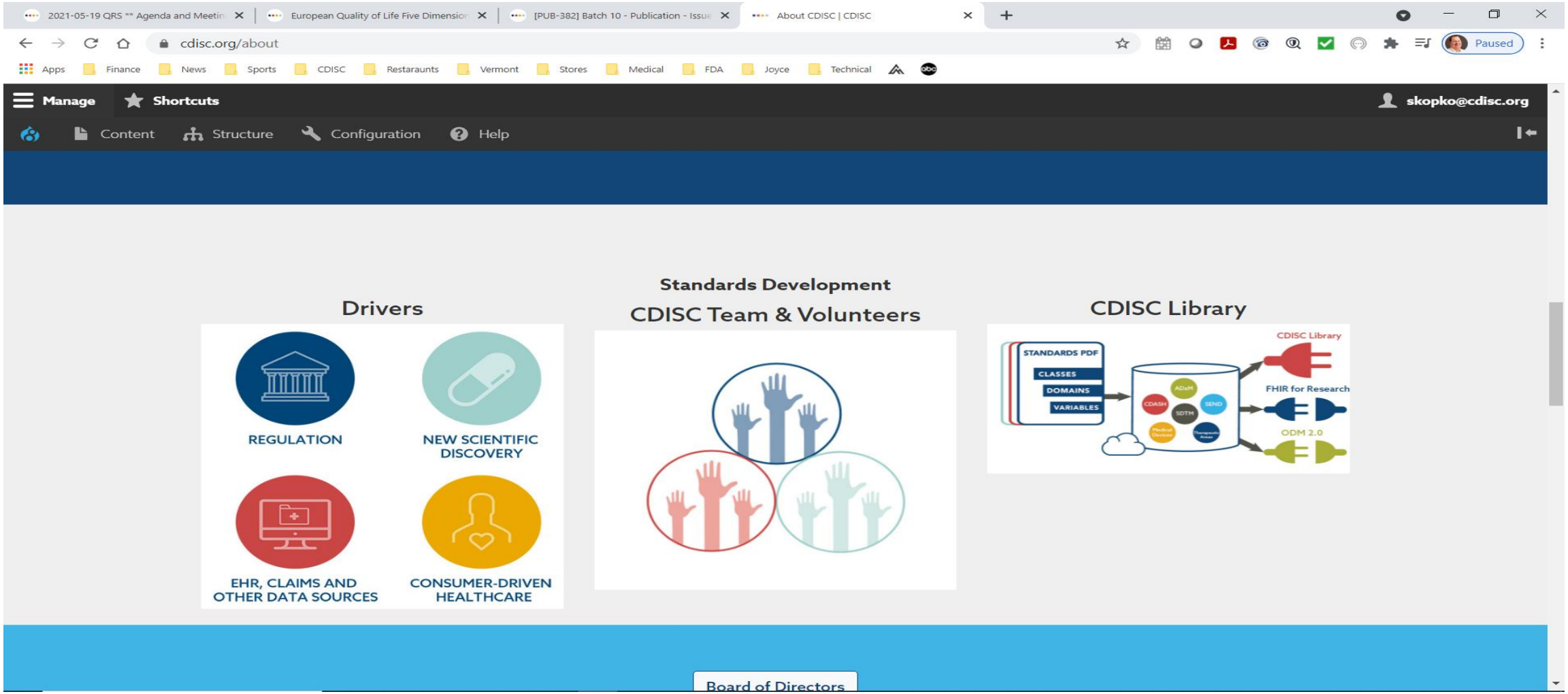
- CDISC convenes a global community of research experts representing a range of experiences and backgrounds. Each brings a vision, we bring the blueprint. They develop the data, we develop the platform. They provide the insights, we provide the focus. With everyone contributing their unique strengths, we're able to harness our collective power to drive more meaningful clinical research.

CDISC Introduction (https://www.cdisc.org/)

Why we do it:

- To Amplify Data's Impact.
- CDISC is driven by the belief that the true measure of data is the impact it has, but for far too long, its full potential wasn’t being realized. So, we enable the accessibility, interoperability, and reusability of data, helping the entire field of clinical research tap into—and amplify—its full value. From greater efficiency to unprecedented discoveries, we make it possible to turn information into invaluable impact for clinical research and global health.

CDISC Introduction (https://www.cdisc.org/)



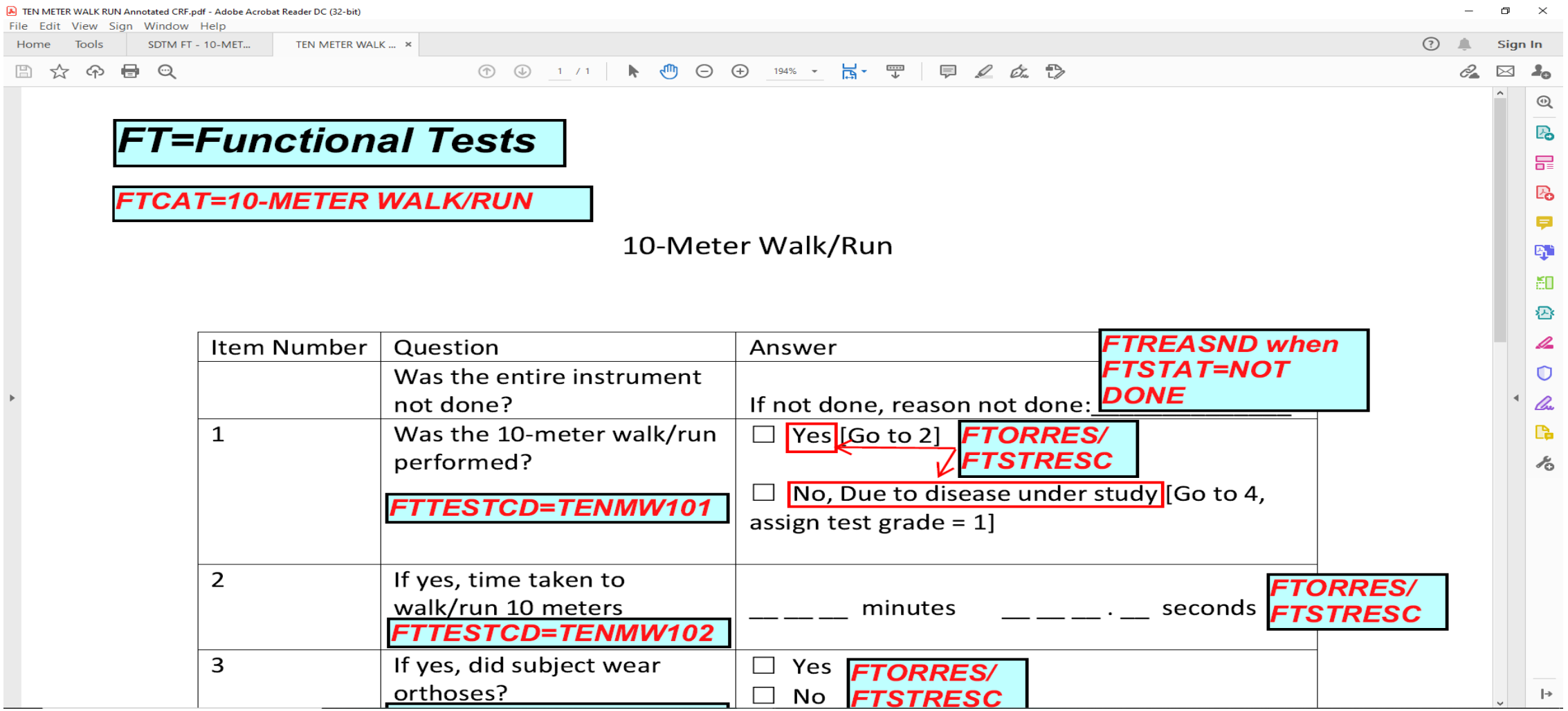
Agenda

- CDISC Questionnaires, Ratings, and Scales (QRS) Overview
  - What is a CDISC QRS instrument supplement?
    - Supplement to Study Data Tabulation Model Implementation Guide (SDTMIG)
    - Supplement to Analysis Data Model Implementation Guide (ADaMIG)
  - CDISC COP-001- Standards Development Addendum for QRS Supplements
    - CDISC High Level Instrument Supplement Development Process
  - QRS subteam's Home and Development WIKI Pages
  - QRS Data Representation
    - SDTMIG QRS Supplements
  - FDA Clinical Outcome Assessment (COA) Instruments
  - CDISC Publication of QRS Supplements
  - QRS subteam Activities

What is included in a QRS Instrument Supplement?

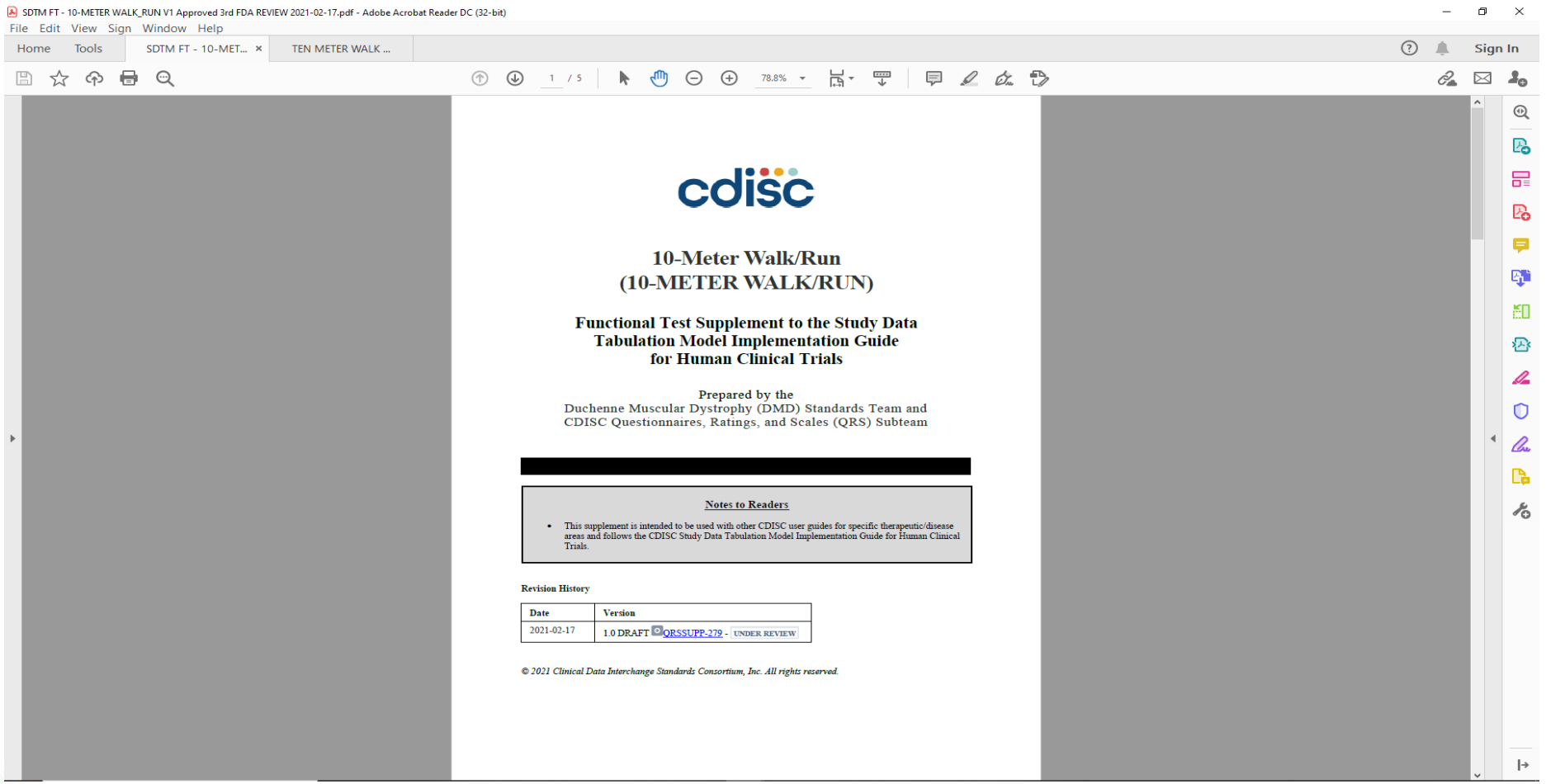
- **QRS supplements to the SDTMIG include:**
  - Instrument-specific Controlled Terminology;
  - An SDTM example illustrating the use;
  - Applicable supplemental qualifiers and item-level mapping instructions for the results;
  - Assumptions for implementing the instrument in SDTM;
- **ADQRS supplements to the ADaMIG (To be discussed in the future):**
  - Describe how to structure the instrument analysis dataset based on data structures described in the ADaMIG;
  - Sample analysis descriptions;
  - Scoring for the statistical analysis plan;
  - Data checks;
  - Examples of analysis dataset metadata, analysis variable metadata, and value-level metadata;
  - Example of the final analysis dataset to be used for analysis and regulatory submission;

Sample SDTMIG QRS Instrument Annotated CRF



Sample SDTMIG QRS Instrument Supplement

Adobe Acrobat Document



CDISC Operating Procedure: COP-001 Standards Development

- Addendum for QRS SDTMIG Supplements

- The development of QRS SDTMIG Supplement packages follows the CDISC Standards Development process outlined in COP-001.

COP-001 Standards Development Addendum for QRS SDTMIG Supplements

https://www.cdisc.org/about/bylaws

- CDISC standards development stages specifically address the differences for QRS development for each stage.
- Stage 0: Scoping and Planning
- Stage 1: Development of Biomedical Concepts (NA)
- Stage 2: Development of Draft Standards
- Stage 3a: Internal Review
- Stage 3b: Public Review
- Stage 3c: Publication
- Stage 4: Standard Maintenance

QRS subteam WIKI home page

- SDS Questionnaires, Ratings and Scales (QRS) Subteam Home
  - Calendar
  - QRS subteam meeting notes
  - QRS Issues
  - QRS Shared Files
  - QRS Webinars

SDTMIG QRS Supplements WIKI Development Environment

CDISC WIKI: SDS QRS Supplements Home

- Calendar – SDS QRS meeting and events information
- QRS Training – new volunteer training information
- QRS Maker – CDISC application to develop instrument specific metadata needed for a QRS supplement and the CDISC Library
- QRS Supplement Best Practices – documented decisions on how best to handle the specifics in developing QRS supplements
- QRS template documents used in the supplement development process
  - QRS Supplement Template
  - QRS Review Process Documents
- Supplements under Development

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SDTMIG QRS Supplements WIKI Development Environment

CDISC WIKI: SDS QRS Supplements Home

- Team Review – supplements under QRS subteam TR
- Internal Review – supplements under wider CDISC IR
- Public Review – supplements under CDISC PR
- Published / Archive – source files archived for published QRS supplements
- File lists – subteam shared files used in the development/review process

QRS Data Representation

- SDTMIG QRS Supplements Concept and Domain
  - Functional Test (FT)
  - Questionnaires (QS)
  - Clinical Classifications (RS)

CDISC Definitions QS/FT/RS Domains

Functional Test (FT)

- Functional Test instruments are stored in the Functional Tests (FT) domain and are named, standalone task-based evaluations, designed to provide an assessment of mobility, dexterity, and/or cognitive ability. A Functional Test is not a subjective assessment of how the subject generally performs a task. Rather, it is an objective measurement of the performance of the task by the subject in a specific instance. Functional Tests have documented methods for administration and analysis and require a subject to perform specific activities that are evaluated and recorded. Most often, Functional Tests are direct, quantitative measurements.

PDFPlus Document

CDISC Definitions QS/FT/RS Domains

Questionnaires (QS)

- Questionnaire instruments are stored in the Questionnaires (QS) domain and are named, standalone instruments designed to provide an assessment of a concept. Questionnaires often have a defined standard structure, format, and content; consist of conceptually related items that are typically scored; and usually document methods for administration and analysis. Questionnaires consist of defined questions with a defined set of potential answers. Most often, the primary purpose of questionnaires is to generate quantitative statistic to assess a qualitative concept.

Adobe Acrobat Document

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CDISC Definitions QS/FT/RS Domains

Clinical Classifications (RS)

- Named instruments whose output is an ordinal or categorical score that serves as a surrogate for, or ranking of, disease status, or other physiological or biological status. Usually, the instrument will be published in a professional journal or on a website.

- Clinical Classifications are based on a trained healthcare professional's observation of a subject's health condition or status with input from associated clinical records review. Clinical Classifications may be based solely on objective data from clinical records or may involve a clinical judgment or interpretation of the directly observable signs, behaviors, or other physical manifestations related to a condition or subject status. These physical manifestations may be findings that are typically represented in other SDTM domains, such as labs, vital signs, or clinical events. Therefore, Clinical Classifications may be composite scores based on diverse inputs. This assessment method differs from a more traditional question-and-answer interview commonly seen in questionnaires.

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How does the FDA Clinical Outcome Assessment (COA) program relate to CDISC QRS supplements?

- The FDA discusses the need for outcome measures that are defined as part of the Drug Development Tools Qualification Program for Clinical Outcome Assessment (COA) instruments.

- CDISC QRS Instrument Supplements assist in structuring the COA data so that it is collected and reported in a standardized format.

FDA Clinical Outcome Assessment (COA) definitions

http://www.fda.gov/Drugs/DevelopmentApprovalProcess/DrugDevelopmentToolsQualificationProgram/ucm370262.htm

CDISC Domain	FDA Outcome	FDA Definition
QS - Questionnaire RS – Clinical Classification	Clinician-reported outcome (ClinRO)	A ClinRO is based on a report that comes from a trained health-care professional after observation of a patient's health condition. A ClinRO measure involves a clinical judgment or interpretation of the observable signs, behaviors, or other physical manifestations thought to be related to a disease or condition. ClinRO measures cannot directly assess symptoms that are known only to the patient (e.g., pain intensity).
QS - Questionnaire	Concept of interest (COI)	The thing measured by an assessment (e.g., pain intensity).
QS – Questionnaire RS – Clinical Classification	Observer-reported outcome (ObsRO)	An ObsRO is a measurement based on an observation by someone other than the patient or a health professional. This may be a parent, spouse, or other non-clinical caregiver who is in a position to regularly observe and report on a specific aspect of the patient's health. An ObsRO measure does not include medical judgment or interpretation. Generally, ObsROs are reported by a parent, caregiver, or someone who observes the patient in daily life. For patients who cannot respond for themselves (e.g., infants or cognitively impaired), we encourage observer reports that include only those events or behaviors that can be observed. For example, in the assessment of a child's functioning in the classroom, the teacher is the most appropriate observer. Examples of ObsROs include a parent report of a child's vomiting episodes or a report of wincing thought to be the result of pain in patients who are unable to report for themselves.

FDA Clinical Outcome Assessment (COA) definitions

CDISC Domain	FDA Outcome	FDA Definition
QS - Questionnaire	Patient-reported outcome (PRO)	A PRO is a measurement based on a report that comes from the patient (i.e., study subject) about the status of a patient's health condition without amendment or interpretation of the patient's report by a clinician or anyone else. A PRO can be measured by self-report or by interview, provided that the interviewer records only the patient's response. Symptoms or other unobservable concepts known only to the patient (e.g., pain severity or nausea) can only be measured by PRO measures. PROs can also assess the patient perspective on functioning or activities that may also be observable by others.
FT – Functional Test	Performance outcome (PerfO)	A PerfO is a measurement based on a task(s) performed by a patient according to instructions that is administered by a health care professional. Performance outcomes require patient cooperation and motivation. These include measures of gait speed (e.g., timed 25 foot walk test), memory recall, or other cognitive testing (e.g., digit symbol substitution test).

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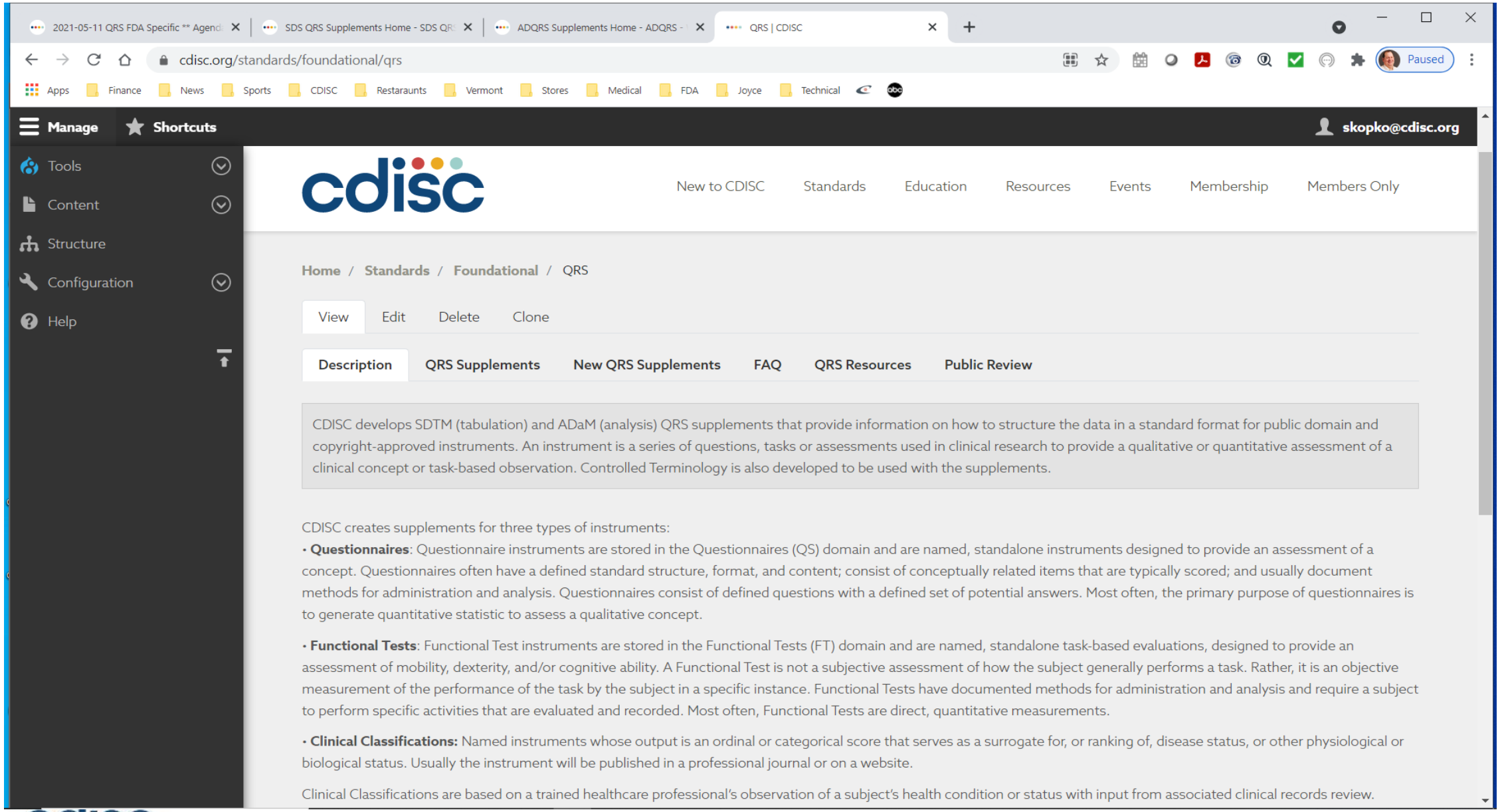
How the CDISC QRS supplements correlate with the FDA COA program

CDISC SDTM QRS Supplements		FDA COA		
	ClinRO	ObsRO	PRO	PerfO
Questionnaires	X	X	X	
Functional tests				X
Clinical Classifications	X	X		

CDISC Publication of QRS Supplements

What you need to know about CDISC Published QRS Supplements

Publication: CDISC QRS Webpage



Publication: CDISC QRS Webpage

QRS Supplements and New QRS Supplements Tables

SDTM Domain/ADaM Dataset		Permission		Search by Name	
SDTM Domain/ADaM Dataset		Permission			
FT		Public Domain			
RS		Granted			
QS		Denied			
		Author Permission Required			
		No response received			
		Pending			

QRS Name	Short Name (--CAT)	SDTM Domain/ADaM Dataset	Permission	Version	Release Date
12-Item Multiple Sclerosis Walking Scale	MSWS-12	QS	No Response Received		
6 Minute Walk Test	SIX MINUTE WALK	FT	Public Domain	v 1.0	21-May-14
Abnormal Involuntary Movement Scale	AIMS	QS	Public Domain	v 1.0	22-May-13
Acute Physiology and Chronic Health Evaluation II	APACHE II	RS	Public Domain	v 1.0	29-Jun-16

Published QRS supplements on CDISC QRS Webpage

QRS Supplement Type	Public Domain	Granted	Author Permission Required:	Denied	No response received	Pending	Total Supplements
Questionnaires	33	90	2	2	3	0	130
Functional Tests	3	7	1	1	0	0	12
Clinical Classifications	23	9	0	0	0	0	32
Total	59	106	3	3	3	0	174

QRS Subteam Activities

- Core subteam members and sponsor volunteers are implementing QS/FT/RS Supplements based on resource availability
  - Priority are Supplements required for TA User Guides and FDA priority instruments.
  - TA Projects identify supplement implementers to expedite the process

Acute Kidney Injury	Duchenne Muscular Dystrophy	Pancreatic Cancer
Alzheimer's	Dyslipidemia	Parkinson's Disease
Asthma	Ebola	Polycystic Kidney Disease
Breast Cancer	Heart Failure	Post Traumatic Stress Disorder
Cardiovascular	Hepatitis C	Prostate Cancer
CDAD	HIV	Psoriasis
Colorectal Cancer	Huntington's Disease	QT Studies
COPD	Influenza	Rare Diseases
COVID-19	Kidney Transplant	Rheumatoid Arthritis
Crohn's Disease	Lung Cancer	Schizophrenia
Diabetes	Major Depressive Disorder	Traditional Chinese Medicine - Acupuncture
Diabetes Type 1 - Exercise and Nutrition	Malaria	Traditional Chinese Medicine - Coronary Artery Disease-Angina
Diabetes Type 1 - Pediatrics and Devices	Multiple Sclerosis	Traumatic Brain Injury
Diabetes Type 1 - Screening, Staging and Monitoring of Pre-clinical Type 1 Diabetes	Nutrition	Tuberculosis
Diabetic Kidney Disease	Pain	Vaccines
		Virology

QRS Subteam Activities

- QRS Co-Leads
  - Dana Booth
  - Diane Corey
  - Steve Kopko
- 42 subteam members
  - Volunteer to implement QRS supplements
  - Participate in CDISC QRS domain related topics
  - Provide Collaborative Consensus Decisions on QRS issues

SDTMIG QRS Supplements Status May 2001

❖QRS Publication updates

❖January CDISC Internal Review - QRS 3 supplements completed February 11

- ❖ COWAT, HCS, SES-CD V1

❖February Public Review - QRS 8 supplements completed March 5

- ❖ AIMS, ADSD V1.0, ANSD V1.0, DRS, ECOG, KPS SCALE, KFSS, IBDQ

❖March Public Review - QRS 7 supplements to complete by April 9

- ❖ COVI, DRRI-2, DISEASE STEPS, FAQ, GMSS VERSION TYPE 1 DIABETES, KDIGO AKI, PDDS

❖March CDISC Internal Review - QRS 3 supplements to be scheduled

- ❖ CDAI V1, IPAQ-LF SELF-ADMINISTERED VERSION, FACT-C

SDTMIG QRS Supplements Status May 2001

❖QRS Publication updates (cont.)

❖Publication QRS supplement Requests in process

- ❖ FDA Internal Review - 10-METER WALK/RUN, NSCLC-SAQ V1.0, SMDDS V1.0, ADSD V1.0 and ANSD V1.0
- ❖ CDISC Copyediting Request in Process for FDA Internal Review - BPRS 1988 VERSION,CDRS-R, HAMD 17, EDSS
- ❖ Awaiting CDISC Copyediting Request in Process for FDA Internal Review - EORTC QLQ-C30 V3.0, EORTC QLQ-C15-PAL V1.0

QRS Subteam Activities

- CDISC QRS activities in process:
  - CDISC QRS Office Hours Webinars
  - CDISC QRS Partnership with Mapi Research Trust (MRT) (ongoing)
  - QRS domain (FT, QS, RS) document updates to the draft SDTMIG V3.4 (completed)
  - QRS Webpage updates (completed)
  - QRS --EVAL and –EVALID Variables Recommendation
  - Draft QRS Reference (QX) Domain – in process
  - QRS Logically Skipped Items and QRS Missing Data representation in review with FDA

QRS Subteam Activities

❖CDISC QRS activities in process:

- ❖Draft QRS Supplements TAUG/COA cross-reference table under development with FDA

- ❖Draft Functional Assessment of Chronic Illness Therapy (FACIT) Library in QRS CT development
  - ❖ FACT allows sponsors to select from the item bank to create their own instruments
  - ❖ CDISC to create QRS CT for each FACIT item in the library to ensure consistency within and across sponsors for each item
  - ❖ FACIT continues to develop specific individual instruments using the items from the item bank for additional therapeutic areas/disease indications

- ❖Prepare QRS supplements information in the CDISC Library

- ❖CDISC QRS Supplement Request Form

- ❖CDISC COP 001 Standards Development
  - ❖ Provides the capability for sponsors to volunteer to develop QRS Instrument Supplements under QRS Subteam guidance

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Establishing Priorities for the FDA Review of QRS Draft Supplements

- CDER Office of New Drugs is primarily responsible determining FDA QRS Supplement Priorities
  - New Drug Divisions (Reorganization from 19 to 27 Clinical Review Divisions)
  - https://www.fda.gov/about-fda/center-drug-evaluation-and-research-cder/office-new-drugs
- FDA priorities incorporate thoughts and perspectives of FDA clinical reviewers and external stakeholders (patient groups, industry, NIH, Critical Path Institute, etc.), taking into account the information/evidence needed to develop new medical products.
- Assessment/scoping of FDA priorities is done on both a regular and as-needed basis.
- FDA only reviews QRS supplements that are described in our priority list.

FDA QRS Draft Supplement Review Process – Initial Submission

- The CDISC QRS Subteam drafts a CDISC QRS Supplement document for a given instrument (i.e., the annotated CRF, controlled terminology and supplement document).
- The QRS Subteam submits a draft supplement review package, including an annotated CRF, a draft supplement and references in a request (or "Ask") for FDA review that is sent to the Office of Strategic Programs (OSP) in Center for Drug Evaluation and Research (CDER) using the e-mail address established for this work (COADataStandards@fda.hhs.gov)
- This draft review package is uploaded to the COA Data Standards SharePoint site and the OB QRS Review Team is notified.

FDA QRS Draft Supplement Review Process – FDA Review

- In the initial review of the QRS Draft Supplement Package, the OB QRS Review Team reviews the submitted documents, assesses completeness, and identifies any need for SME input.
- If required, internal/external SMEs are identified/notified and requested to provide input regarding specific review questions/comments.
- Following a process in which the Review Team collects/flags, coalesces and reconciles comments and issues the final review document is submitted to the OSP for posting to the COA Data Standards SharePoint Site and transmittal to the CDISC QRS Subteam.
- In subsequent review cycles, the CDISC QRS Subteam includes an Excel spreadsheet describing Jira issues and responses to FDA questions/comments in the review package submitted to the Agency.

FDA QRS Draft Supplement Review Process – Purpose

- Accuracy and Consistency
  - Is the information provided in the draft supplement, supporting references and annotated CRF accurate and internally consistent?
- Utility
  - Consider whether the information provided is sufficient to make it possible for industry programmers/data managers and FDA reviewers to understand how the observations generated by the instrument have been recorded, organized/structured and submitted.

FDA QRS Draft Supplement Review Process – Finalizing

- The FDA review of QRS Draft Supplements is completed when the Review Team note to CDISC that there are no additional comments.
- Published QRS Supplements that have gone through FDA review include the following comment in Section 1.1. Representations and Warranties, Limitations of Liability, and Disclaimers --

Although the United States Food and Drug Administration has provided input with regard to this supplement, this input does not constitute US FDA endorsement of any particular instrument.

THANK YOU

THE CDISC QRS Subteam

WANTS YOU !!!

Q&A