

The Computational Science Symposium

September 21st–23rd

Panel Discussion: COVID-19 Lessons from
Agility in a Pandemic

PHUSE CSS

CDISC COVID-19 User Guide Lessons Learned

Peter Van Reusel, CDISC





NBC

5 March

News from March 2020



1,5 d.



Like



Comment



CNN

8 March

Coronavirus: 169 confirmed cases in Belgium



CNN

15 March

What you need to know about the covid-19 testing in the U.S.



2,8 d.

2,1 d. Comments

1,9 d. Shared



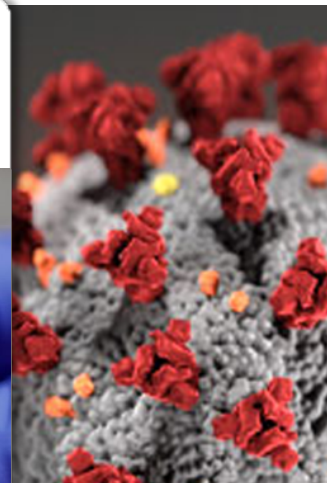
Like



Comment



Share



1,6 d. Shared



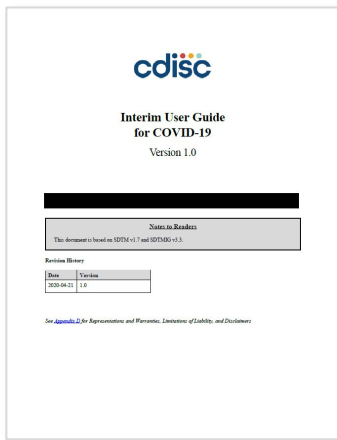
Share



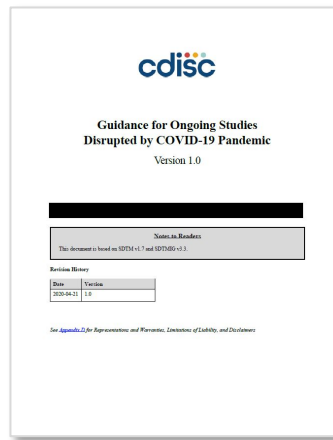
CDISC COVID-19 Project Overview

- CDISC convened a Task Force in Late March 2020
 - *Industry stakeholders*
 - *Regulatory*
 - *Academia*
 - *Key CDISC data standards staff*
- Development did not follow formal Standards Development Process (CDISC COP-001)
- Three sets of documents published on CDISC Website on 21 April 2020
 - *CDISC Interim User Guide for COVID-19*
 - *Guidance for Ongoing Studies Disrupted by the COVID-19 Pandemic*
 - *Resources for Public Health Researchers*
- COVID-19 Controlled Terminology posted 08 May 2020 – an additional publication from NCI-EVS
 - <https://www.cdisc.org/standards/therapeutic-areas/covid-19>

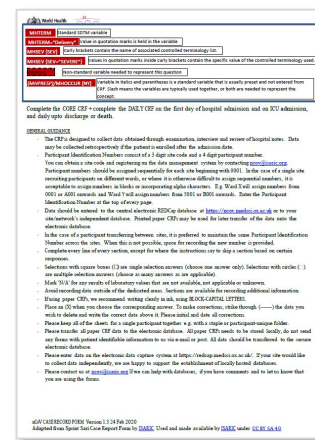
What is included in the COVID-19 materials produced by CDISC?



COVID-19 Interim
User Guide



COVID-19 Guidance for
Ongoing Studies
Disrupted by the COVID-19
Pandemic



Resources for Public Health
Researchers

COVID-19 Interim User Guide Topics

- Risk Factors
 - Pre-existing Medical Conditions
 - Personal Protective Equipment (PPE)
 - Travel
 - Contacts
 - Substance Use
 - Exposure to Animals
- Onset of Disease
- Signs and Symptoms
- Laboratory Test Results
- Diagnostics and Virology
 - Virus Identification
 - Antibody Testing
 - SARS-CoV-2 Viral Load
- Vital Signs and Urine Output
- Concomitant Medications
- Respiratory Findings
 - Imaging
 - Pulmonary Function Tests
- Cardiac Events/Findings
- Hospitalization
- Procedures
 - Assisted Ventilation and Oxygen Treatments
 - Renal Treatment
- Vaccines
- Questionnaires, Ratings, and Scales

Example from COVID-19 Interim User Guide

6.1 Virus Identification

Identification of viruses from a collected sample is represented in the Microbiology Specimen (MB) domain.

Example 1

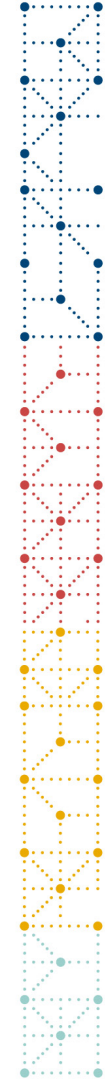
This example shows the results of tests to detect SARS-CoV-2, the virus that causes COVID-19, in 2 different subjects.

Row 1: Shows a subject who tested positive for SARS-CoV-2 by quantitative reverse transcriptase polymerase chain reaction (PCR) of an endotracheal fluid specimen.

Row 2: Shows a subject who tested negative for SARS-CoV-2 by quantitative reverse transcriptase PCR of a throat swab specimen.

mb.xpt

Row	STUDYID	DOMAIN	USUBJID	MBSEQ	MBREFID	MBGPRID	MBTESTCD	MBTEST	MBTSTDTL	MBORRES	MBSTRESC	MBSPEC	MBLOC	MBMETHOD	VISITNUM	VISIT	MBDTC
1	ABC	MB	ABC-01-601	1	60101	1	SARSCOV2	Severe Acute Resp Syndrome Coronavirus 2	DETECTION	POSITIVE	POSITIVE	ENDOTRACHEAL FLUID		QUANTITATIVE REVERSE TRANSCRIPTASE POLYMERASE CHAIN REACTION	1	SCREENING	2020-03-27T14:15
2	ABC	MB	ABC-01-722	2	72201	1	SARSCOV2	Severe Acute Resp Syndrome Coronavirus 2	DETECTION	NEGATIVE	NEGATIVE	SWABBED MATERIAL	THROAT	QUANTITATIVE REVERSE TRANSCRIPTASE POLYMERASE CHAIN REACTION	1	SCREENING	2011-04-01T10:00



Guidance for Ongoing Studies Disrupted by the COVID-19 Pandemic

- Developed by a separate team, but worked on the same wiki space for transparency
 - Listing of COVID-19 Related Impacts as Part of CSR
 - Relationships to COVID-19
 - Protocol Deviations
 - Disposition
 - Missed Visits
 - Missed Assessments
 - Changes to Drug Accountability
 - Changes to Adverse Event Data Collection
 - Changes in Exposure
 - Transfer to Another Site
 - Trial Summary to Provide Pandemic Relationship

Example from Ongoing Studies Disrupted by COVID-19

4 Protocol Deviations

COVID-19 disruptions may lead to protocol deviations at the site level. The SDTMIG DV domain represents deviations at the subject level, but does not provide a mechanism for representing deviations using a site identifier. In addition, a deviation at the site level might not affect all subjects at that site (e.g., subjects who have completed the study, future subjects). A site-level deviation can be represented in DV in 2 ways, as illustrated by the following examples.

Example 1

In this example, when a protocol deviation that affected subjects occurred at a site, the sponsor determined which subjects were affected by the deviation and recorded the deviation for each subject at the site. The sponsor used DVCAT = "SITE DEVIATION" to identify site-level deviations.

Rows 1, 2, 4, 8: Show subjects who were affected by a site shutdown due to a flooded basement, a problem not related to COVID-19.

Rows 3, 5-7, 9: Show subjects were affected when all transportation in the country was down due to COVID-19.

dv.xpt

Row	STUDYID	DOMAIN	USUBJID	DVSEQ	DVREFID	DVSPID	DVTERM	DVDECOD	DVCAT	DVSCAT	EPOCH	DVSTDT	DVENDTC	DVREAS	DVEPRELI
1	CVD-3	DV	300	1			Site shut down		SITE DEVIATION		TREATMENT	2020-02-17	2020-02-20	Flooded basement	
2	CVD-3	DV	301	1			Site shut down		SITE DEVIATION		TREATMENT	2020-02-17	2020-02-20	Flooded basement	
3	CVD-3	DV	301	2			Site shut down		SITE DEVIATION		TREATMENT	2020-04-06	2020-04-18	All transportation in country down due to COVID-19.	Y
4	CVD-3	DV	303	1			Site shut down		SITE DEVIATION		TREATMENT	2020-02-17	2020-02-20	Flooded basement	
5	CVD-3	DV	306	1			Site shut down		SITE DEVIATION		TREATMENT	2020-04-06	2020-04-18	All transportation in country down due to COVID-19.	Y
6	CVD-3	DV	307	1			Site shut down		SITE DEVIATION		TREATMENT	2020-04-06	2020-04-18	All transportation in country down due to COVID-19.	Y
7	CVD-3	DV	309	1			Site shut down		SITE DEVIATION		TREATMENT	2020-04-06	2020-04-18	All transportation in country down due to COVID-19.	Y
8	CVD-3	DV	312	1			Site shut down		SITE DEVIATION		TREATMENT	2020-02-17	2020-02-20	Flooded basement	
9	CVD-3	DV	312	2			Site shut down		SITE DEVIATION		TREATMENT	2020-04-06	2020-04-18	All transportation in country down due to COVID-19.	Y

DV NSV Metadata

Variable	Label	Type	Codelist	Role	Origin	Comment
DVREAS	Reason for Deviation	text	DVCODES	Non-standard Record Qualifier	CRF	DVCODES is a sponsor-defined codelist.
DVEPRELI	Epi/Pandemic Related Indicator	text	NY	Non-standard Record Qualifier	CRF	

Resources for Public Health Researchers

- Novel Coronavirus (nCoV) Acute Respiratory Infection Clinical Characterisation Data Tool
 - Developed by the World Health Organization (WHO) and the International Severe Acute Respiratory and Emerging Infection Consortium (ISARIC)
 - Data tool is being used as the foundation for many COVID-19 research studies globally by more than 40 countries
- SDTM and CDASH Annotations and Excel Mapping File created by CDISC team published on CDISC website

CORE CASE RECORD FORM

DEMOGRAPHICS	
Clinical centre name:	DM.SITEID Country: DM.COUNTRY {ISO-3166-1 Alpha-3}
Enrolment date: [D][D]/[M][M]/[2][0][Y][Y]	DM.RFICDTC
Ethnic group (check all that apply): ☐ Arab ☐ Black ☐ East Asian ☐ South Asian ☐ West Asian ☐ Latin American ☐ White ☐ Aboriginal/First Nations ☐ Other: _____ ☐ Unknown RACE {RACE} RACE1, RACE2, etc. {RACEC}	
Employed as a Healthcare Worker?	☐ YES ☐ NO ☐ N/A ERTESTCD {ERTESTCD} ERORRES
Employed in a microbiology laboratory?	☐ YES ☐ NO ☐ N/A ERTESTCD {ERTESTCD} ERORRES
Sex at Birth:	☐ Male ☐ Female ☐ Not specified SCTESTCD {SCTESTCD} SCORRES
Estimated Age [][][]years OR [][][]months	AGE AGEU {AGEU}
Pregnant?	☐ YES ☐ NO ☐ Unknown ☐ N/A If YES: Gestational weeks assessment: [][] weeks
MHTERM	(MHPRESP)/MHOCCUR {NY} RPTTESTCD {RPTTESTCD}=“Estimated Gestational Age” on mother’s ID
	RPORRES RPORRESU {AGEU}

ISARIC/WHO Core CRF Excel Mapping File

CRF Item	Domain	SDTM Variable	SDTM Value	CDASH Variable If Different from SDTM	Notes
Was pathogen testing done during this illness episode?	MBTESTCD	MBALL	MBPERF		
	MBTEST	Microbiology Data			
	MBORRES	Y		If MBPERF is yes, question not mapped; proceed to subsequent questions	
		N		If MBPERF is No, Map test, set MBSTAT=NOT DONE	
		N/A		DO NOT MAP	
Influenza	MBTESTCD	HAEMINF		CRF does not specify antigen/antibody/RNA, but the term shown here exists as CT	
	MBTEST	Haemophilus influenzae		CRF does not specify antigen/antibody/RNA, but the term shown here exists as CT	
	MBTSTDTL	DETECTION			
	MBORRES	POSITIVE		Corresponds to result of "YES-Confirmed" on CRF	
		PRESUMPTIVE		Corresponds to result of "YES-Probable" on CRF	
		NEGATIVE		Corresponds to result of "No" on CRF	
If yes (influenza):	MBTESTCD	MCORGIDN			
	MBTEST	Microbial Organism Identification			
	MBORRES	INFLUENZA A VIRUS SUBTYPE H3N2		New term request for microorganism codelist	
		INFLUENZA A VIRUS SUBTYPE H1N1 2009		New term request for microorganism codelist; existing term doesn't differentiate 2009 from other H1N1s. Note CRF reads "A/H1N1pdm09"	
		INFLUENZA A VIRUS SUBTYPE H7N9		New term request for microorganism codelist	
		INFLUENZA A VIRUS SUBTYPE H5N1		Term already exists	
		INFLUENZA A VIRUS		Term already exists	
		INFLUENZA B VIRUS		Term already exists	
		(Other specified influenza type)		See microorganism codelist. If specific term not available, new terminology would have to be requested	
Coronavirus	MBTESTCD	CRONAVIR		New term request; existing term CORONAVIRIDAE exists for non-specified CoV in the <i>microorganism</i> codelist, but NOT in the <i>MBTEST/CD</i> codelists	
	MBTEST	Coronavirus		New term request (see noted above)	
	MBTSTDTL	DETECTION			
	MBORRES	POSITIVE		Corresponds to result of "YES-Confirmed" on CRF	
		PRESUMPTIVE		Corresponds to result of "YES-Probable" on CRF	
		NEGATIVE		Corresponds to result of "No" on CRF	
If yes (coronavirus):	MBTESTCD	MCORGIDN			
	MBTEST	Microbial Organism Identification			
	MBORRES	SARS-CoV-2		SARS-CoV-2 is Currently under review in CT p42. Note the CRF says "Novel CoV".	
		MERS-CoV		MERS-CoV would have to be a new term request for Microorganism Codelist	
		{Other specified CoV}		Terminology would have to be requested.	
RSV	MBTESTCD	RSV		CRF doesn't specify antigen/antibody/RNA	
	MBTEST	Respiratory Syncytial Virus		CRF doesn't specify antigen/antibody/RNA	
	MBTSTDTL	DETECTION			

Convened a Focused Group of Volunteers

Responsible for:

- Scoping
- Sharing sample CRFs
- Being Dedicated Reviewers
 - Posted new content on a daily basis – asked for feedback within 3 days
 - Wiki was open and transparent
- Initial plan to create one guide for both COVID-19 Studies and Impacts to Ongoing Studies, but quickly realized they needed to be two distinct publications
- Two sets of Volunteer SMEs
 - COVID-19 Interim Guide – volunteers conducting or planning COVID-19 studies
 - Guide for Ongoing Studies – volunteers mainly from existing Foundational Teams





Lessons Learned - Pros

- Can be **flexible** to address rapidly changing public health emergencies
- Can develop draft standards quickly with **dedicated and focused** developers
- Can **release** draft standards **quickly** for implementation
- Not needing to achieve **consensus** allows more rapid development and publication
- Communication turn-around in a **small, dedicated** team is very efficient
- Very **focused** development
- People are **altruistic** and wanted to help



Lessons Learned - Cons

- Scoping is very rapid, so **key concepts** may not be considered
- Difficult to develop an “**end-to-end**” standard (for example, ADaM concepts not developed due to compressed timeline)
- Not a fully consensus-based standard due to lack of **Public Review**
 - Not enough time for regulatory feedback
 - Has lead to inconsistencies between guidance and standards
- Role for **volunteers** is limited
- Development is primarily done by **paid staff**
- Work on other projects is **halted**
- Overtime/weekend work - **unrealistic workload**, not sustainable over a long period of time

Finalizing the COVID-19 Materials

- Posting both the Interim User Guide and Guidance for Ongoing Studies for Public Review
- The ADaM team is developing CDISC ADaM guidance for ongoing studies disrupted by the COVID-19 pandemic
 - Builds from the previously published "CDISC Guidance for Ongoing Studies Disrupted by COVID-19 Pandemic" document
- Address inconsistencies with the FDA's Technical Conformance Guide for Missed and Modified Visits due to the COVID-19 Pandemic

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Some FDA COVID19 Guidances



- Conduct of Clinical Trials of Medical Products during COVID-19 Public Health Emergency (Updated July 2, 2020)
- Development and Licensure of Vaccines to Prevent COVID-19
- Statistical Considerations for Clinical Trials During the COVID-19 Public Health Emergency Guidance for Industry
- COVID-19: Developing Drugs and Biological Products for Treatment or Prevention

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**COVID-19 Lessons from
Agility in a Pandemic**

Rebecca Sudlow



Data sharing during a pandemic ...



- Data sharing of clinical trials has been “business as usual” since 2013 (EFPIA/PhRMA principles published)



- Research environment-wide effort (pharma, academia, regulators)



- Speed is essential (evolving research and understanding)



What's different?

Data Sharing Route	What's different?
Registries & Results Postings	Results posted well ahead of the 1 year deadline.
Publications	Expedited publication of results
Summary Data Sharing	<p>International COVID-19 Data Research Alliance and Workbench: Objective to draw meaningful inferences across a set of Randomised Controlled Trials. Summary level data dictionary developed as a starting point.</p> <p>A dozen pharmaceutical companies of the COVID19 R&D Consortium have committed summary-level data sharing from their trials. Other organizations have also indicated they are interested in partnering.</p>
Datasets Sharing	<p>Vivli.org: Not for profit dataset sharing platform. Positioned as the “go to” platform for COVID-19 data sharing for trials being run by pharma, academia & NGOs.</p> <p>Datacelerate (part of Transcelerate) Historical Trial Data platform. Created COVID-19 data sharing platform for pharma research. Open to non-Transcelerate members researching within the COVID-19 space.</p>

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