

Standard implementation:

Battling through the adversity of a pandemic

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The Speakers



Vicky Poulsen

Standards Specialist, Novo Nordisk A/S

Joined Novo Nordisk A/S in 2015 after being a SAS consultant for a decade in the public health sector. She started down the path of CDISC implementation shortly after and continues to work with SDTM implementation in her present position.

Vicky holds an MPhil in Geographic Information Systems and Network Analysis from the University of Hong Kong.



Ana Calduch Arques

Standards Developer, Novo Nordisk A/S

Joined Novo Nordisk A/S in 2019 after working as Research Assistant at the University of Copenhagen. She started with standard CRF development and system implementation. Currently, she continues supporting trials in end-to-end traceability from CRF to SDTM.

Ana holds a MSc in Biotechnology from the University of Copenhagen.

Introduction

Initial Steps to Track COVID-19 Related Deviations

End-to-end Approach

Key Take Away Messages

The Onset of COVID-19 Disruption



CDISC Guidance

Upon the release of CDISC's **Guidance for Ongoing Studies Disrupted by COVID-19 Pandemic**, the need to

- Clearly identify those participants who were impacted by COVID-19 and indicate those missing data solely due to COVID-19
- Generate an overall COVID-19 summary that addresses its impact on the clinical study

became apparent to NN



Guidance for Ongoing Studies Disrupted by COVID-19 Pandemic

Version 1.0

Notes to Readers

This document is based on SDTM v1.7 and SDTMIG v3.3.

Revision History

Date	Version
2020-04-21	1.0

Initial Steps to Track COVID-19 Related Deviations

As study level mitigation, missing data could be documented in:

1. Using form level comments in EDC system
2. A new eCRF or updating an existing one
3. Protocol deviations: "COVID-19" should be added in the beginning of the title

New trials

Date of Visit (DoV)		[VISIT_DATE_DOV] - Non-repeating
Trial ID: NNXXXX-XXXX		
Integration		
* Date of visit	Req☑/Req☑/Req☑ (2020-2030)	
* Contact type	☐ Site visit ☐ Telephone contact ☐ Visit entered in error ☐ Remote contact due to COVID-19 situation ☐ Visit missed due to COVID-19 situation	

DOMAIN	SVGRPID	VISITNUM	VISIT
SV	SITE VISIT	70	VISIT 7 (WEEK 20)
SV	SITE VISIT	80	VISIT 8 (WEEK 26)
SV	VISIT MISSED DUE TO COVID-19 SITUATION	90	VISIT 9 (WEEK 39)
SV	VISIT MISSED DUE TO COVID-19 SITUATION	100	VISIT 10 (WEEK 52)
SV	VISIT MISSED DUE TO COVID-19 SITUATION	110	VISIT 11 (WEEK 65)
SV	REMOTE CONTACT DUE TO COVID-19 SITUATION	120	VISIT 12 (WEEK 78)

Ongoing trials

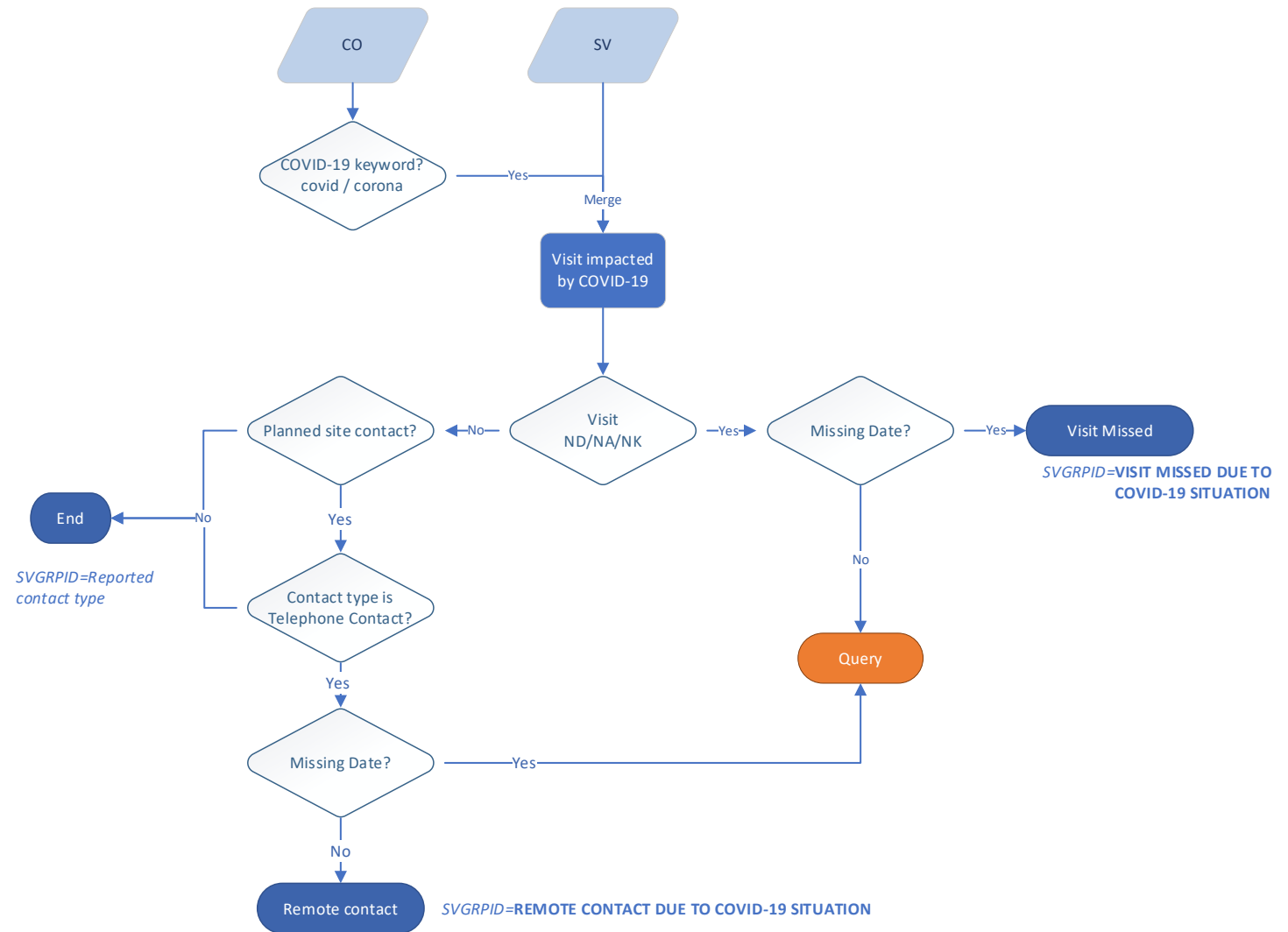
DOMAIN	COREF	COVAL	VISITNUM	VISIT
CO	EDC_FORM_COMMENT-VISIT_DATE_DOV	.	22	PHONE VISIT 3
CO	EDC_FORM_COMMENT-VISIT_DATE_DOV	-	61	PHONE VISIT...
CO	EDC_FORM_COMMENT-VISIT_DATE_DOV	:	40	VISIT 8 (WEEK...
CO	EDC_FORM_COMMENT-VISIT_DATE_DOV	Visit has to be done 1 day later because of holidays, so titration w...	43	PHONE VISIT...
CO	EDC_FORM_COMMENT-VISIT_DATE_DOV	Treatment discontinuation on 03-JUL-2019 -> patient was later con...	61	PHONE VISIT...
CO	EDC_FORM_COMMENT-VISIT_DATE_DOV	patient out of study	62	VISIT 21 (WEE...
CO	EDC_FORM_COMMENT-VISIT_DATE_DOV	patient out of study	63	PHONE VISIT...
CO	EDC_FORM_COMMENT-VISIT_DATE_DOV	patient out of study	64	PHONE VISIT...
CO	EDC_FORM_COMMENT-VISIT_DATE_DOV	DUE TO COVID-19 situation	90	VISIT 36 (WEE...
CO	EDC_FORM_COMMENT-VISIT_DATE_DOV	Visit was not performed, as patient withdraw consent to participate...	1000	TREATMENT...
CO	EDC_FORM_COMMENT-VISIT_DATE_DOV	Due to COVID-19 situation.	65	VISIT 24 (WEE...
CO	EDC_FORM_COMMENT-VISIT_DATE_DOV	Visit changed to telephone contact due to COVID-19 situation	80	VISIT 33 (WEE...
CO	EDC_FORM_COMMENT-VISIT_DATE_DOV	Visit out of visit window due to COVID-19 situation	90	VISIT 36 (WEE...
CO	EDC_FORM_COMMENT-VISIT_DATE_DOV	Due to COVID-19 situation	999	FOLLOW-UP
CO	EDC_FORM_COMMENT-VISIT_DATE_DOV	Visit changed to telephone contact due to COVID-19 situation	80	VISIT 33 (WEE...
CO	EDC_FORM_COMMENT-VISIT_DATE_DOV	Visit out of visit window due to COVID-19 situation	90	VISIT 36 (WEE...

Identify and Report Visits Impacted by COVID-19

using form level comments

A programmatic approach has been implemented to identify and report visits impacted by COVID-19

- 💣 Mis-interpretation of comments: presence of COVID-19 keywords can have opposite meaning e.g. not due to COVID-19 situation
- 💣 Mis-representation of results: mis-spelling of COVID-19 keywords e.g. COVOD-19
- 💣 Results need to be verified with manual QC



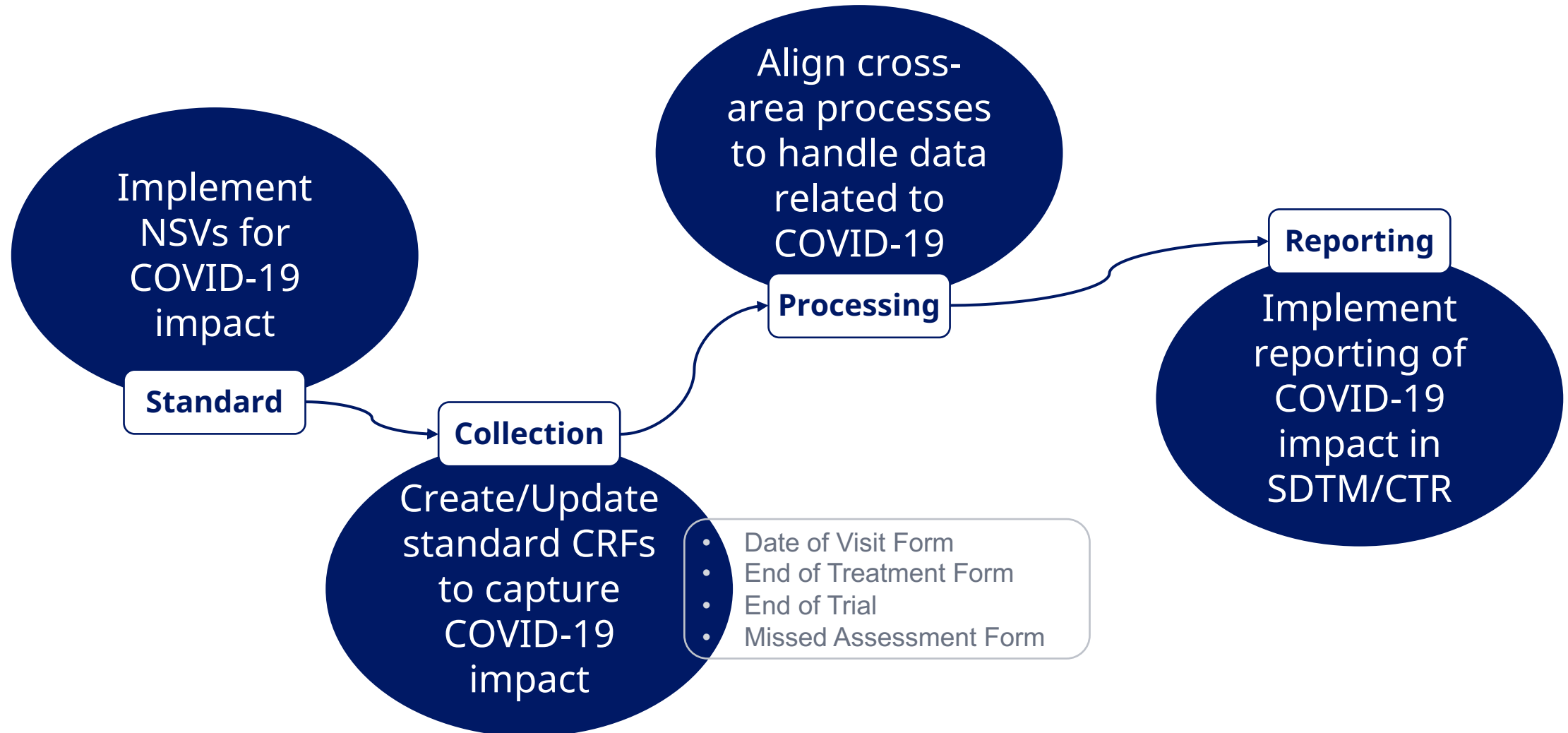
Submission Requirements

Reviewer's comments confirm the need to

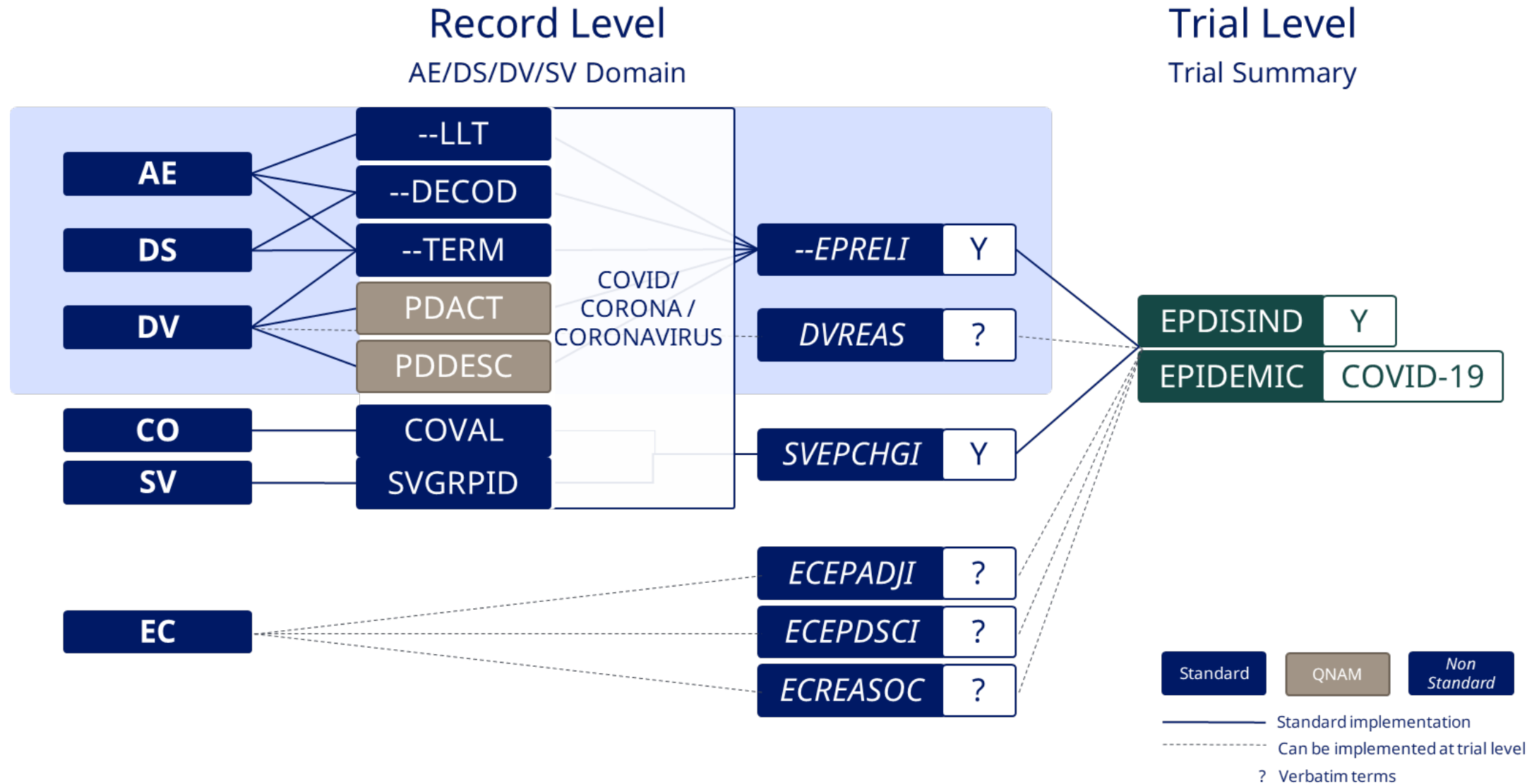
- Clearly identify those participants who were impacted by COVID-19 and indicate those missing data solely due to COVID-19
- Generate an overall COVID-19 summary that addresses its impact on the clinical study

Events related to COVID-19	
Discontinuation of treatment	DS
Individual level	
Site level	
Supply disruption	
Withdrawal from trial	
Individual level	
Site level (e.g., site closure)	
COVID-19 positive	AE/CM/HO
Hospitalized	
Treatment for COVID-19 – e.g., medication 1	
Treatment for COVID-19 – e.g., medication 2	
Missed primary endpoint ascertainment	Events/ Findings/ Interventions
Individual level	
Site level	
Missed key secondary endpoint ascertainment	
Individual level	
Site level	
Use of alternative endpoint ascertainment	SV
Remote visit	
Out-of-window	

End-to-end Approach



Implementation of NSVs for COVID-19 Impacts



Deviations from Planned Visits

Participant misses visit or does not attend the visit as per the contact mode specified in the protocol

Date of Visit (DoV)			SV=Subject Visits		[VISIT DATE DOV] - Non-repeating
Study ID: NNXXXX-XXXX					Integration
*	Date of visit	Req✓/Req✓/Req✓ (2020-2030)	SVSTDTC	SVENDTC	
*	Contact type	☐ Site visit ☐ Telephone contact ☐ Visit entered in error ☐ Remote video contact ☐ Off-site visit ☐ Visit missed	SVCNTMOD		
*	Was the visit impacted by COVID-19? <i>Tick 'Yes' if the contact type was changed, the visit date was rescheduled outside the visit window or missed due to COVID-19 situation.</i>	☐ Yes ☐ No	SVEPCHGI		

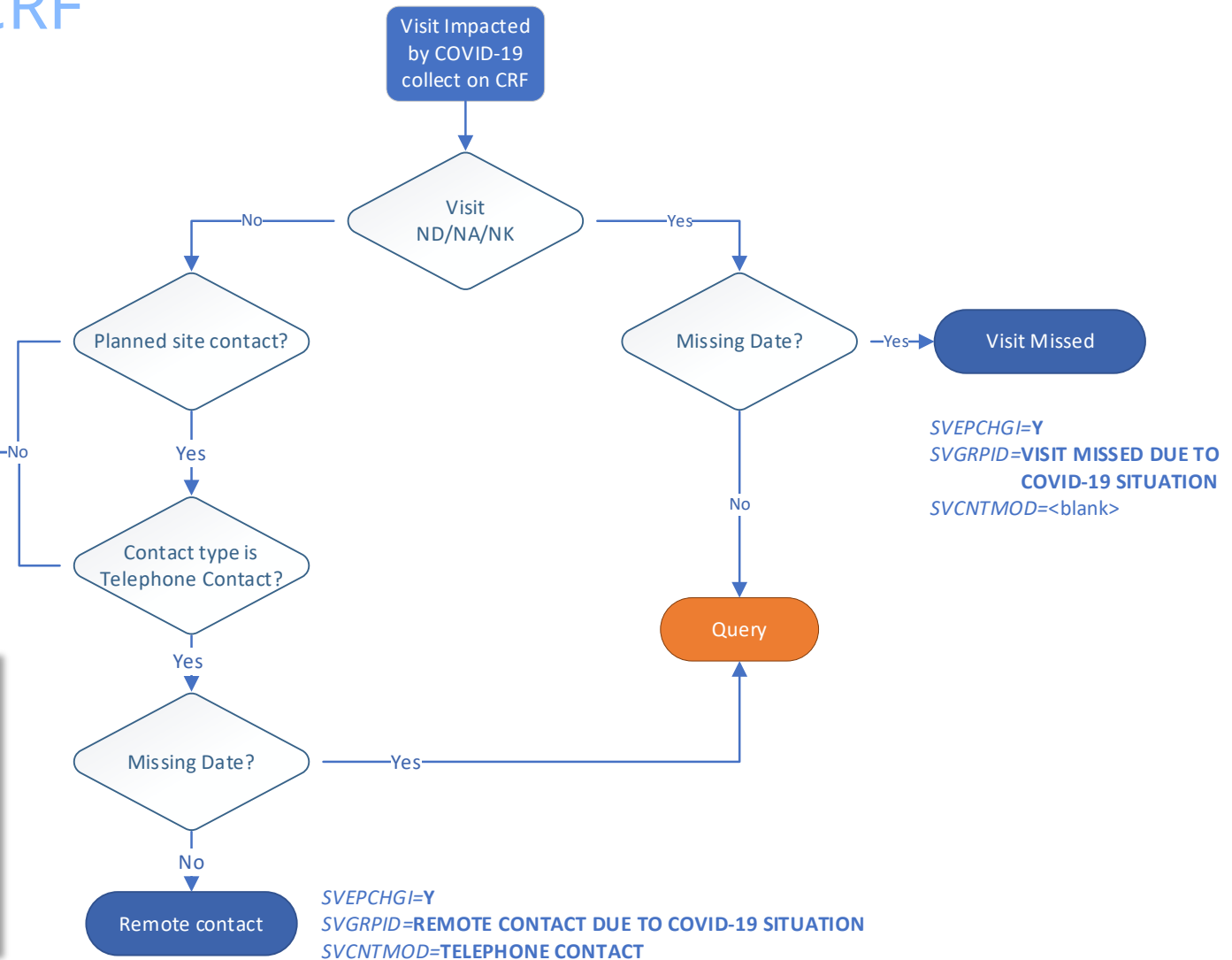
DOMAIN	SVGRPID	VISITNUM	VISIT	SVCNTMOD	SVEPCHGI
SV	SITE VISIT	10	VISIT 1 (UP TO -3w)	SITE VISIT	
SV	SITE VISIT	20	VISIT 2 (WEEK 0)	SITE VISIT	
SV	REMOTE CONTACT DUE TO COVID-19 SITUATION	30	VISIT 3 (WEEK 4)	REMOTE AUDIO	Y
SV	SITE VISIT	40	VISIT 4 (WEEK 8)	SITE VISIT	
SV	VISIT MISSED DUE TO COVID-19 SITUATION	50	VISIT 5 (WEEK 12)		Y
SV	SITE VISIT	60	VISIT 6 (WEEK 16)	SITE VISIT	
SV	SITE VISIT	70	VISIT 7 (WEEK 20)	SITE VISIT	
SV	SITE VISIT	80	VISIT 8 (WEEK 26)	SITE VISIT	
SV	REMOTE CONTACT DUE TO COVID-19 SITUATION	90	VISIT 9 (WEEK 39)	REMOTE AUDIO	Y
SV	SITE VISIT	100	VISIT 10 (WEEK 52)	SITE VISIT	

Report Visits Impacted by COVID-19

based on data collected on CRF

Eliminates uncertainties
associated with programmatic
derivation

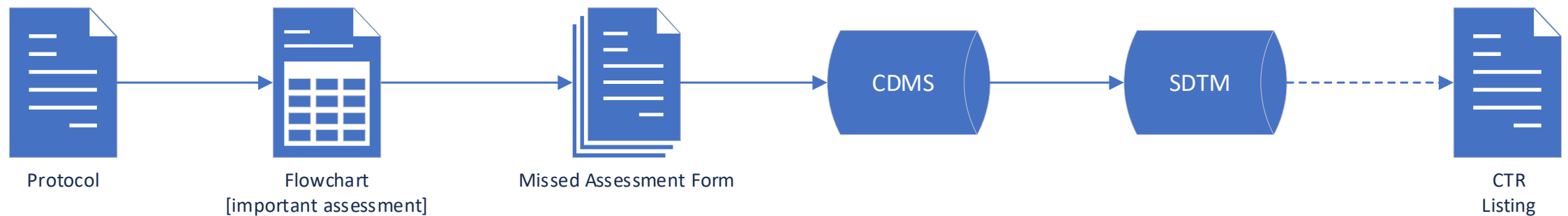
DOMAIN	SVGRPID	VISITNUM	VISIT	SVCNTMOD	SVEPCHGI
SV	SITE VISIT	10	VISIT 1 (UP TO -3w)	SITE VISIT	
SV	SITE VISIT	20	VISIT 2 (WEEK 0)	SITE VISIT	
SV	REMOTE CONTACT DUE TO COVID-19 SITUATION	30	VISIT 3 (WEEK 4)	REMOTE AUDIO	Y
SV	SITE VISIT	40	VISIT 4 (WEEK 8)	SITE VISIT	
SV	VISIT MISSED DUE TO COVID-19 SITUATION	50	VISIT 5 (WEEK 12)		Y
SV	SITE VISIT	60	VISIT 6 (WEEK 16)	SITE VISIT	
SV	SITE VISIT	70	VISIT 7 (WEEK 20)	SITE VISIT	
SV	SITE VISIT	80	VISIT 8 (WEEK 26)	SITE VISIT	
SV	REMOTE CONTACT DUE TO COVID-19 SITUATION	90	VISIT 9 (WEEK 39)	REMOTE AUDIO	Y
SV	SITE VISIT	100	VISIT 10 (WEEK 52)	SITE VISIT	



Deviations from Planned Important Assessments

Important Assessments:

- Assessment(s) for Primary and key Secondary Endpoints, as a minimum
- In alignment with protocol deviations categorisation



Specify Planned Important Assessments

Specify Planned Important Assessments in Flowchart with input from Biostat

	A	B	C	D	E	F	G	H	I	J	K	L	M	N
1		Information	Screening	Pre treatment period	Randomisation			Time	Period				End of treatment	End of trial
2	Visit	V0	V1	V2	V3	V4	P5	V6	P7	V8	V9	V10	V11	V12
3	Timing of Visit (Weeks)				0	1	2	4	8	12	26	39	52	57
4	Visit Window (Days)				±0	±3	±3	±3	±3	±7	±7	±7	±7	±7
43	Kidney biopsy													
44	Kidney biopsy ^b			X									X	
45	SAFETY													
46	Adverse Event													
48	Adverse Event				X	X	X	X	X	X	X	X	X	X
67	Vital Signs													
68	Blood Pressure													
69	Systolic Blood Pressure		X		X	X		X		X	X	X	X	X
70	Diastolic Blood Pressure		X		X	X		X		X	X	X	X	X
71	Pulse		X		X	X		X		X	X	X	X	X
74	Laboratory Assessments													
106	Normalised Kidney Injury Molecule-1			X									X	
107	Kidney perfusion measurement			X									X	
109	Kidney Injury Molecule-1			X									X	
110	Albumin/Creatinine Ratio		X		X	X		X		X	X	X	X	X
111														
112	Information													
113	^b [important assessment]													
114														

Edit all Intervention

EFFICACY > Kidney biopsy > Kidney Biopsy Performed

Common Protocol attributes

Unblinding Assessment: ☐

Visit Related: ☒ **Planned Important Assessment**

Planned Group: Kidney biopsy

Planned Sub Group:

Planned Reference ID:

Primary Assessment:

Assessment Note: [important assessment]

Reset

Protocol

Capture Missed Planned Important Assessments

Specify Planned Important Assessments in Flowchart with **input from Biostat**

Fill out *Missed Assessment due to COVID-19* Form Template

Specific assessment: *HBA1C_BLOOD*

Specific assessment: *BODY_WEIGHT*

V1, Vn

Missed Assessment due to COVID-19 (Missd Assmnt COVID-19) – [MISSD_ASSMNT] - Non-repeating

Study ID: NNXXXX-XXXX

PR=Procedures **LB=Laboratory Test Results** **VS=Vital Signs** Integration

Were any of the below assessments not done? ☐ Yes ☐ No **NOT SUBMITTED**

	Domain [Hidden]	Assessment	Status	REASND
1.a	VS	Body weight	☐ Not done	☐ COVID-19
1.b	LB	HbA1c	☐ Not done	☐ COVID-19
1.c	PR	Kidney biopsy	☐ Not done	☐ COVID-19

Grouped assessments: *KIDNEY_BIOPSY_PERFORMED*

Kidney biopsy

Kidney biopsy^b

SAFETY

Adverse Event

Adverse Event

Vital Signs

Blood Pressure

Systolic Blood Pressure

Diastolic Blood Pressure

Pulse

Laboratory Assessments

Normalised Kidney Injury Molecule-1

Kidney perfusion measurement

Kidney Injury Molecule-1

Albumin/Creatinine Ratio

Protocol

CRF

Report Missed Planned Important Assessments

Specify Planned Important Assessments in Flowchart with **input from Biostat**

Fill out *Missed Assessment due to COVID-19* Form Template

Map result to SDTM according to Flowchart

Protocol

CRF

SDTM

⚠	USUBJID	Ⓜ	VISITNUM	⚠	SVCNTMOD	⚠	SVGRPID	⚠	VIS_TYPE	⚠	ASSM1	⚠	ASSM2
	12		65		REMOTE AUDIO		REMOTE CONTACT DUE TO COVID-19 SITUATION		SITE VISIT		HBA1C		WEIGHT
	14		72		REMOTE AUDIO		REMOTE CONTACT DUE TO COVID-19 SITUATION		SITE VISIT		HBA1C		WEIGHT

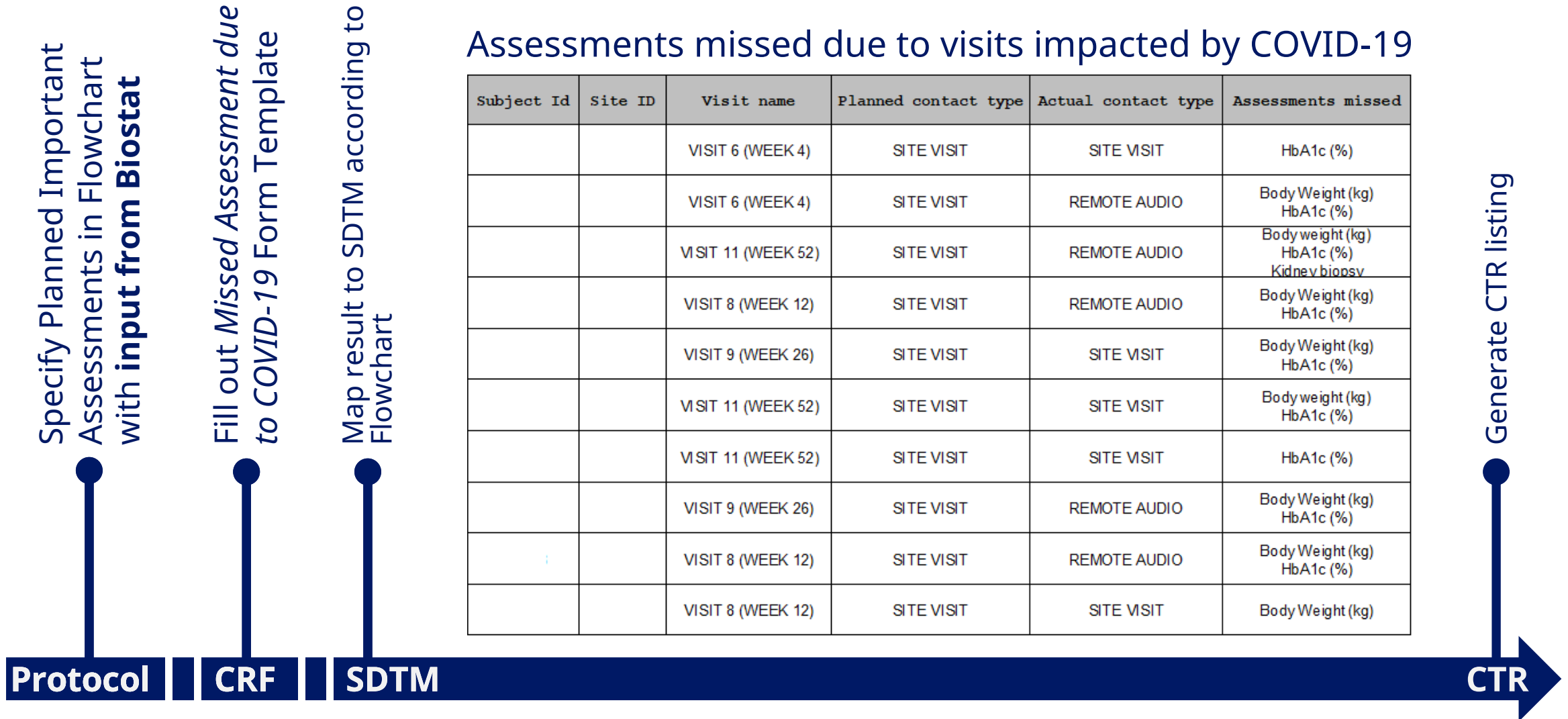
1.b	LB	HbA1c	LBTEST	☐ Not done	LBSTAT=NOT DONE	COVID-19	LBREASND=COVID-19
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⚠	USUBJID	⚠	LBTESTCD	⚠	LBTEST	⚠	LBCAT	⚠	LBSTAT	⚠	LBREASND
	12		HBA1C		Hemoglobin A1C		GLUCOSE METABOLISM		NOT DONE		COVID-19

1.a	VS	Body weight	VSTEST	☐ Not done	VSSTAT=NOT DONE	COVID-19	VSREASND=COVID-19
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⚠	USUBJID	⚠	VSTESTCD	⚠	VSTEST	⚠	VSCAT	⚠	VSSTAT	⚠	VSREASND
	12		WEIGHT		Weight		BODY MEASUREMENT		NOT DONE		COVID-19

Report Missed Planned Important Assessments



Key Take Away Messages

- A corporate strategy is critical to ensure cross-organisation implementation
- It pays off to think end-to-end standard implementation early on instead of relying on ad hoc piecemeal study level quick fixes
- The need to track COVID-19 related deviations reveals disconnected systems and activities, e.g. clinical data in CDMS vs protocol deviations reporting in CTMS

