CLR4-DOC-0001-EN-1.0

HDClarity 4.0 Annotated CRF

Documentation

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1 Preamble

The purpose of this document is to provide the annotated view of the HDClarity 4.0 eCRF (*electronic Case Report Form*). The annotated view shows all forms, variables and its variable names used within the study. The forms and variables are described in detail within the CRF requirements [2] and data dictionary [3] of the study.

2 Visit Form Schedule

Forms are CRF entry screens that are displayed to data entry personnel and show how data is entered in the eCRF. The visit form schedule defines the assignment of forms to visit types:

eCRF Form	Screening Y0	Screening Y1-Y3	(Partial) Sampling Y0-Y3	(Partial) Repeat Sampling Y0	Phone Contact Y0-Y3	Repeat Phone Contact Y0-Y3	Events	End
Enrollment (Enrollment into HDClarity)	✓							
Eligibility Check (Eligibility Check)		✓	✓	✓				
Safety Lab Exam (Safety Laboratory Examination)	✓	✓						
Checklist (Visit Checklist)	✓	✓	✓	✓				
Motor (UHDRS® Motor/Diagnostic Confidence)			✓	✓				
CSF (CSF Collection)			(✓)	(✓)				
CSF Quality (CSF Quality)			(✓)	(✓)				

eCRF Form	Screening Y0	Screening Y1-Y3	(Partial) Sampling Y0-Y3	(Partial) Repeat Sampling Y0	Phone Contact Y0-Y3	Repeat Phone Contact Y0-Y3	Events	End
Blood Processing (Blood Processing)			(✓)	(✓)				
Phone Contact (Phone Contact Sampling)					✓	✓		
AE Log (Adverse Event Log)							✓	
SAE (Serious Adverse Event)							(✓)	
End (Premature End)								✓
Monitoring SCR (Monitoring Screening Visit)	✓	✓						
Monitoring SPL (Monitoring Sampling Visit)			✓	✓				
Monitoring (S)AE (Monitoring Serious and Adverse Events)							✓	

eCRF Form	Screening Y0	Screening Y1-Y3	(Partial) Sampling Y0-Y3	(Partial) Repeat Sampling Y0	Phone Contact Y0-Y3	Repeat Phone Contact Y0-Y3	Events	End
Monitoring Event (Monitoring Event Form)	✓	✓	✓	✓	✓	✓	✓	

Table 1: Visit Form Schedule

Note: Forms represented in brackets are either optional or supplemental.

3 eCRF Forms

3.1 Enrollment (Enrollment into HDClarity)

General

Date of visit: svstdtc

Local Participant Classification

Related Items:

Disease burden score at time of screening visit: dbs

HDClarity classification at time of screening visit: ---- hdcat

early pre-manifest HD 1
late pre-manifest HD 2
early HD 3
moderate HD 4
advanced HD 5
healthy control 6
juvenile manifest HD 7
incomplete penetrance HD 8
uncategorized 9

Enrollment into HDClarity

Version of study protocol: ---- protocol

Version 4.0 4

Participant is capable of providing informed consent or has a legal representative: yes 1 no 0 ics1

IC procedures were completed and documented: yes 1 no 0 ics2

Date of informed consent: mon/dd/yyyy rfstdtc

Signed by: sgntr

participant 1
legal representative 2
parent/guardian 3

Is there a local CAG report available that specifies exact allele repeat lengths: ---- ics3

yes 1
no 0
not required 2

Enroll-HD core assessment completed within 90 days from screening: ---- ics4

yes 1
no 0

Enroll-HD Core Assessments Status:

Inclusion Criteria

Either 21-75 years of age (manifest), or 18-75 years of age (incomplete penetrance, premanifest and controls), or ≥11 years of age (JHD), inclusive, at the time of consent: yes 1 no 0 ic1

Capable of complying with study procedures, including fasting, blood sampling and lumbar puncture: yes 1 no 0 ic2

Results of the safety laboratory examinations within 10% of the normal limits: yes 1 no 0 ic3

C-reactive protein (CRP) screening blood test results within >2X of upper limit of normal: yes 1 no 0 ic4

Negative urine pregnancy test available: yes 1 no 0 ic5

Has the PI confirmed that the participant is post-menopausal or is not sexually active:	yes 1 no 0	ic5_1

Exclusion Criteria

Use of investigational drugs or participation in a clinical drug trial within 30 days prior to annual Sampling Visit:	yes 1 no 0	ec1
Current intoxication, drug or alcohol abuse or dependence:	yes 1 no 0	ec2
If using medications or nutraceuticals, the use of inappropriate (e.g., non-prescribed) dosages within 30 days prior to the annual Sampling visit:	yes 1 no 0	ec3
Significant medical, neurological or psychiatric co-morbidity likely, in the judgment of the Investigator, to impair participant's ability to complete study procedures, or likely to reduce the utility of the sample and data for the study of HD:	yes 1 no 0	ec4
Needle phobia:	yes 1 no 0	ec5
Frequent headache:	yes 1 no 0	ec6
Significant lower spinal deformity or major surgery at lumbar spine:	yes 1 no 0	ec7
Antiplatelet or anticoagulant therapy within the past 14 days prior to annual Sampling Visit, including but not limited to: aspirin (>81mg), clopidogrel, dipyridamole, warfarin, dabigatran, rivaroxaban and apixaban:	yes 1 no 0	ec8
Clotting or bruising disorder:	yes 1 no 0	ec9
Predictable non-compliance as assessed by investigator:	yes 1 no 0	ec10
Inability or unwillingness to undertake any experimental procedure:	yes 1 no 0	ec11
Any other reason that, in the clinical judgment of the Site Principal Investigator, it is felt that lumbar puncture performed per this protocol and associated manuals is unsafe without brain imaging:	yes 1 no 0	ec12
General physical examination discloses any reason to suspect spinal deformity or abnormal bleeding tendency, e.g. easy bruising, petechial rash:	yes 1 no 0	ec13
History or physical examination reveals any reason to suspect new focal neurological lesion, e.g. new headache, optic disc swelling, asymmetric focal long tract signs:	yes 1 no 0	ec17
Lumbar puncture procedure performed for any reason in the previous 30 days:	yes 1 no 0	ec14
Any SAE deemed related to the LP procedure or blood patch necessitated after LP:	yes 1 no 0	ec15
Any other complication or experience during or after any previous lumbar puncture that, in the clinical judgement of the Site Principal Investigator, is likely to pose an unacceptable risk for future lumbar puncture:	yes 1 no 0	ec16

Eligibility

Did the participant pass the eligibility criteria? ---- (yes 1, no 0) elgbl

Waiver

Has the CI granted a waiver for all unmet criteria? yes 1 no 0 wvr

Please comment: wvr_cmt

3.2 Eligibility Check (Eligibility Check Screening Y1-Y3)

General

Date of visit: svstdtc

Eligibility Check

Confirmation of consent: ○ yes 1 ○ no 0 ics

Confirmation of Inclusion Criteria

Either 21-75 years of age (manifest), or 18-75 years of age (incomplete penetrance, premanifest and controls), or ≥11 years of age (JHD), inclusive, at the time of consent:	○ yes 1 ○ no 0	ic1
Capable of complying with study procedures, including fasting, blood sampling and lumbar puncture:	○ yes 1 ○ no 0	ic2
Results of the safety laboratory examinations within 10% of the normal limits:	○ yes 1 ○ no 0	ic3
C-reactive protein (CRP) screening blood test results within >2X of upper limit of normal:	○ yes 1 ○ no 0	ic4
Negative urine pregnancy test available?	○ yes 1 ○ no 0	ic5
Has the PI confirmed that the participant is post-menopausal or is not sexually active:	○ yes 1 ○ no 0	ic5_1
Compliance with instructions to fast:	○ yes 1 ○ no 0	ic6

Confirmation of Exclusion Criteria

Current use of investigational drugs or participation in a clinical drug trial within 30 days prior to annual Sampling Visit:	○ yes 1 ○ no 0	ec1
Current intoxication, drug or alcohol abuse or dependence:	○ yes 1 ○ no 0	ec2
If using medications or nutraceuticals, the use of inappropriate (e.g., non-prescribed) dosages within 30 days prior to the annual Sampling Visit:	○ yes 1 ○ no 0	ec3
Significant medical, neurological or psychiatric co-morbidity likely, in the judgment of the Investigator, to impair participant's ability to complete study procedures, or likely to reduce the utility of the sample and data for the study of HD:	○ yes 1 ○ no 0	ec4
Needle phobia:	○ yes 1 ○ no 0	ec5
Frequent headache:	○ yes 1 ○ no 0	ec6
Significant lower spinal deformity or major surgery at lumbar spine:	○ yes 1 ○ no 0	ec7
Antiplatelet or anticoagulant therapy within the past 14 days prior to annual Sampling Visit, including but not limited to: aspirin (>81mg), clopidogrel, dipyridamole, warfarin, dabigatran, rivaroxaban and apixaban:	○ yes 1 ○ no 0	ec8
Clotting or bruising disorder:	○ yes 1 ○ no 0	ec9
Predictable non-compliance as assessed by investigator:	○ yes 1 ○ no 0	ec10
Inability or unwillingness to undertake any experimental procedure:	○ yes 1 ○ no 0	ec11
Any other reason that, in the clinical judgment of the Site Principal Investigator, it is felt that lumbar puncture performed per this protocol and associated manuals is unsafe without brain imaging:	○ yes 1 ○ no 0	ec12
General physical examination discloses any reason to suspect spinal deformity or abnormal bleeding tendency, e.g. easy bruising, petechial rash:	○ yes 1 ○ no 0	ec13
History or physical examination reveals any reason to suspect new focal neurological lesion, e.g. new headache, optic disc swelling, asymmetric focal long tract signs:	○ yes 1 ○ no 0	ec17

Lumbar puncture procedure performed for any reason in the previous 30 days:	○ yes 1 ○ no 0	ec14
Any SAE deemed related to the LP procedure or blood patch necessitated after LP:	○ yes 1 ○ no 0	ec15
Any other complication or experience during or after any previous lumbar puncture that, in the clinical judgement of the Site Principal Investigator, is likely to pose an unacceptable risk for future lumbar puncture:	○ yes 1 ○ no 0	ec16

Additional Information

Use of any anti-inflammatory medication within the past 14 days:	○ yes 1 ○ no 0	ainf1
Use of any dietary supplements containing tryptophan, leucine, niacin or niacinamide in the past 14 days:	○ yes 1 ○ no 0	ainf2
Use of any antidepressant medication within the past 30 days:	○ yes 1 ○ no 0	ainf3
Use of any antipsychotic medication within the past 30 days:	○ yes 1 ○ no 0	ainf4

Eligibility

Did the participant pass the eligibility criteria? ---- elgbl
yes 1
no 0

Has the CI granted a waiver for all unmet criteria? ○ yes 1 ○ no 0 wvr

Please comment: wvr_cmt

Options

Please select one of the following options:
○ cancel this annual cycle but keep participant enrolled 2
○ cancel this annual cycle and end participation 3
wvrno

3.3 Eligibility Check (Eligibility Check Sampling Y0-Y3/Repeat Sampling Y0)

General

Date of visit: svstdtc

Eligibility Check

Confirmation of consent: yes 1 no 0 ics

Confirmation of Inclusion Criteria

Either 21-75 years of age (manifest), or 18-75 years of age (incomplete penetrance, premanifest and controls), or ≥11 years of age (JHD), inclusive, at the time of consent: yes 1 no 0 ic1

Capable of complying with study procedures, including fasting, blood sampling and lumbar puncture: yes 1 no 0 ic2

Negative urine pregnancy test available? yes 1 no 0 ic5

Has the PI confirmed that the participant is post-menopausal or is not sexually active: yes 1 no 0 ic5_1

Compliance with instructions to fast: yes 1 no 0 ic6

Confirmation of Exclusion Criteria

Current use of investigational drugs or participation in a clinical drug trial within 30 days prior to annual Sampling Visit: yes 1 no 0 ec1

Current intoxication, drug or alcohol abuse or dependence: yes 1 no 0 ec2

If using medications or nutraceuticals, the use of inappropriate (e.g., non-prescribed) dosages within 30 days prior to the annual Sampling Visit: yes 1 no 0 ec3

Significant medical, neurological or psychiatric co-morbidity likely, in the judgment of the Investigator, to impair participant's ability to complete study procedures, or likely to reduce the utility of the sample and data for the study of HD: yes 1 no 0 ec4

Needle phobia: yes 1 no 0 ec5

Frequent headache: yes 1 no 0 ec6

Significant lower spinal deformity or major surgery at lumbar spine: yes 1 no 0 ec7

Antiplatelet or anticoagulant therapy within the past 14 days prior to annual Sampling Visit, including but not limited to: aspirin (>81mg), clopidogrel, dipyridamole, warfarin, dabigatran, rivaroxaban and apixaban: yes 1 no 0 ec8

Clotting or bruising disorder: yes 1 no 0 ec9

Predictable non-compliance as assessed by investigator: yes 1 no 0 ec10

Inability or unwillingness to undertake any experimental procedure: yes 1 no 0 ec11

Any other reason that, in the clinical judgment of the Site Principal Investigator, it is felt that lumbar puncture performed per this protocol and associated manuals is unsafe without brain imaging: yes 1 no 0 ec12

General physical examination discloses any reason to suspect spinal deformity or abnormal bleeding tendency, e.g. easy bruising, petechial rash: yes 1 no 0 ec13

History or physical examination reveals any reason to suspect new focal neurological lesion, e.g. new headache, optic disc swelling, asymmetric focal long tract signs: yes 1 no 0 ec17

Lumbar puncture procedure performed for any reason in the previous 30 days: yes 1 no 0 ec14

Any SAE deemed related to the LP procedure or blood patch necessitated after LP: ○ yes 1 ○ no 0 ec15

Any other complication or experience during or after any previous lumbar puncture that, in the clinical judgement of the Site Principal Investigator, is likely to pose an unacceptable risk for future lumbar puncture: ○ yes 1 ○ no 0 ec16

Additional Information

Use of any anti-inflammatory medication within the past 14 days: ○ yes 1 ○ no 0 ainf1

Use of any dietary supplements containing tryptophan, leucine, niacin or niacinamide in the past 14 days: ○ yes 1 ○ no 0 ainf2

Use of any antidepressant medication within the past 30 days: ○ yes 1 ○ no 0 ainf3

Use of any antipsychotic medication within the past 30 days: ○ yes 1 ○ no 0 ainf4

Eligibility

Did the participant pass the eligibility criteria? [---- ▾] elgbl
yes 1
no 0

Has the CI granted a waiver for all unmet criteria? ○ yes 1 ○ no 0 wvr

Please comment: [ ] wvr_cmt

Options

Please select one of the following options: wvrno
○ cancel visit and reschedule a new Sampling Visit 1
○ cancel this annual cycle but keep participant enrolled 2
○ cancel this annual cycle and end participation 3

3.4 Safety Lab Exam (Safety Laboratory Examination)

Laboratory Examinations for Safety - Screening

15 ml of venous blood drawn for evaluation by the local laboratory: ○ yes 1 ○ no 0 lbsmpl1

Date of blood draw: dd.mon.yyyy lbdat1

Results of laboratory examinations for safety:

	Actual:	Lower limit:	Upper limit:	Unit:
White Cell Count:	wbcres1	wbclo1	wbchi1	wbcu1 µl 1 K/cu mm 4 L 5 10E3/µl 10 10E9/l 11 other 88
Neutrophil Count:	ncres1	nclo1	nchi1	ncu1 µl 1 K/cu mm 4 L 5 10E3/µl 10 10E9/l 11 other 88
Lymphocyte Count:	lcres1	lclo1	lchi1	lcu1 µl 1 K/cu mm 4 L 5 10E3/µl 10 10E9/l 11 other 88
Hemoglobin (Hb):	hbres1	hblo1	hbhi1	hbu1 g/dl 2 g/l 3 other 88
Platelets:	pltres1	pltlo1	plthi1	pltu1 µl 1 K/cu mm 4 L 5 10E3/µl 10 10E9/l 11 other 88
Prothrombin Time (PT):	ptres1	ptlo1	pthi1	ptu1 seconds 9 other 88
Activated Partial Thromboplastin time (APTT):	apttres1	apttlo1	aptthi1	apttu1 seconds 9 other 88
CRP:	crpres1	crplo1	crphi1	crpu1 mg/dl 6 mg/l 7 nmol/l 8 other 88

Safety lab result: ---- lbres1
passed 1
failed 2

Laboratory Examinations for Safety - Rescreening

Second blood draw for rescreening: ○ yes 1 ○ no 0 lbsmpl2

Date of blood draw: dd.mon.yyyy lbdat2

Results of laboratory examinations for safety:

	Actual:	Lower limit:	Upper limit:	Unit:
White Cell Count:	wbcres2	wbclo2	wbchi2	wbcu2 µl 1 K/cu mm 4 L 5 10E3/µl 10 10E9/l 11 other 88
Neutrophil Count:	ncres2	nclo2	nchi2	ncu2 µl 1 K/cu mm 4 L 5 10E3/µl 10 10E9/l 11 other 88
Lymphocyte Count:	lcres2	lclo2	lchi2	lcu2 µl 1 K/cu mm 4 L 5 10E3/µl 10 10E9/l 11 other 88
Hemoglobin (Hb):	hbres2	hblo2	hbhi2	hbu2 g/dl 2 g/l 3 other 88
Platelets:	pltres2	pltlo2	plthi2	pltu2 µl 1 K/cu mm 4 L 5 10E3/µl 10 10E9/l 11 other 88
Prothrombin Time (PT):	ptres2	ptlo2	pthi2	ptu2 seconds 9 other 88
Activated Partial Thromboplastin time (APTT):	apttres2	apttlo2	aptthi2	apttu2 seconds 9 other 88
CRP:	crpres2	crplo2	crphi2	crpu2 mg/dl 6 mg/l 7 nmol/l 8 other 88

Safety lab result: lbres2

passed 1
failed 2

3.5 Checklist (Visit Checklist)

Have the following forms been completed for this visit?

Comorbid:	○ yes 1 ○ no 0	vc2
Pharmacotherapy:	○ yes 1 ○ no 0	vc3
Nutritional Supplements:	○ yes 1 ○ no 0	vc4
Non-Pharmacotherapy:	○ yes 1 ○ no 0	vc5
Weight at last Enroll-HD visit:	Weight: ____ kg weight_enr ____ lbs weightenr_2	
Is there a weight difference of ±3 kg or 6.5 lbs since the last Enroll-HD visit:	○ yes 1 ○ no 0	weightupd
	Weight: ____ kg weight ____ lbs weight_2	

3.6 Motor (UHDRS® Motor/Diagnostic Confidence)

General

Assessment date:	mon/dd/yyyy	qsdtc
Rater code:		raterid
Motor score (TMS):		motscore
Motor score (TMS) incomplete:		miscore

Motor Assessment

Ocular pursuit:

Horizontal:	Vertical:	
○	○	0 = complete (normal)
○	○	1 = jerky movement
○	○	2 = interrupted pursuits/full range
○	○	3 = incomplete range
○ oculargh	○ ocularv	4 = cannot pursue

Saccade initiation:

Horizontal:	Vertical:	
○	○	0 = normal
○	○	1 = increased latency only
○	○	2 = suppressible blinks or head movements to initiate
○	○	3 = unsuppressible head movements
○ sacinith	○ sacinitv	4 = cannot initiate saccades

Saccade velocity:

Horizontal:	Vertical:	
○	○	0 = normal
○	○	1 = mild slowing
○	○	2 = moderate slowing
○	○	3 = severely slow, full range
○ sacvelh	○ sacvelv	4 = incomplete range

Dysarthria:

○ 0 = normal 0
○ 1 = unclear, no need to repeat 1
○ 2 = must repeat to be understood 2
○ 3 = mostly incomprehensible 3
○ 4 = anarthria 4

dysarth

Tongue protrusion:

○ 0 = can hold tongue fully protruded for 10 sec 0
○ 1 = cannot keep fully protruded for 10 sec 1
○ 2 = cannot keep fully protruded for 5 sec 2
○ 3 = cannot fully protrude tongue 3
○ 4 = cannot protrude tongue beyond lips 4

tongue

Finger taps:

Right:	Left:	
○	○	0 = normal (≥15/5 sec.)
○	○	1 = mild slowing, reduction in amplitude (11-14/5 sec.)
○	○	2 = moderately impaired (7-10/5 sec.)
○	○	3 = severely impaired (3-6/5 sec.)
○ fingtapr	○ fingtapl	4 = can barely perform task (0-2/5 sec.)

Pronate/supinate-hands:

Right:	Left:	
○	○	0 = normal
○	○	1 = mild slowing and/or irregular
○	○	2 = moderate slowing and irregular
○	○	3 = severe slowing and irregular
○ prosupr	○ prosupl	4 = cannot perform

Luria: luria

- ○ 0 = ≥4 in 10 sec, no cue 0
- ○ 1 = <4 in 10 sec, no cue 1
- ○ 2 = ≥4 in 10 sec with cues 2
- ○ 3 = <4 in 10 sec with cues 3
- ○ 4 = cannot perform 4

Rigidity-arms:

Right:	Left:	
○	○	0 = absent
○	○	1 = slight or present only with activation
○	○	2 = mild to moderate
○	○	3 = severe, full range of motion
○ rigarmr	○ rigarml	4 = severe with limited range

Bradykinesia-body: brady

- ○ 0 = normal 0
- ○ 1 = minimally slow (?normal) 1
- ○ 2 = mildly but clearly slow 2
- ○ 3 = moderately slow, some hesitation 3
- ○ 4 = markedly slow, long delays in initiation 4

Maximal dystonia:

Trunk:	RUE:	LUE:	RLE:	LLE:	
○	○	○	○	○	0 = absent
○	○	○	○	○	1 = slight/intermittent
○	○	○	○	○	2 = mild/common or moderate/intermittent
○	○	○	○	○	3 = moderate/common
○ dysttrnk	○ dystrue	○ dystlue	○ dystrle	○ dystlle	4 = marked/prolonged

Maximal chorea:

Face:	BOL:	Trunk:	RUE:	LUE:	RLE:	LLE:	
○	○	○	○	○	○	○	0 = absent
○	○	○	○	○	○	○	1 = slight/intermittent
○	○	○	○	○	○	○	2 = mild/common or moderate/intermittent
○	○	○	○	○	○	○	3 = moderate/common
○ chorface	○ chorbol	○ chortrnk	○ chorrue	○ chorlue	○ chorrle	○ chorlle	4 = marked/prolonged

Gait: gait

- ○ 0 = normal gait, narrow base 0
- ○ 1 = wide base and/or slow 1
- ○ 2 = wide base and walks with difficulty 2
- ○ 3 = walks only with assistance 3
- ○ 4 = cannot attempt 4

Tandem walking: tandem

- ○ 0 = normal for 10 steps 0
- ○ 1 = 1 to 3 deviations from straight line 1
- ○ 2 = >3 deviations 2
- ○ 3 = cannot complete 3
- ○ 4 = cannot attempt 4

Retropulsion pull test: retropls

- ○ 0 = normal 0
- ○ 1 = recovers spontaneously 1
- ○ 2 = would fall if not caught 2
- ○ 3 = tends to fall spontaneously 3
- ○ 4 = cannot stand 4

Diagnostic Confidence

Diagnostic confidence level (DCL):	○ 0 = normal (no abnormalities) 0 ○ 1 = non-specific motor abnormalities (less than 50 % confidence) 1 ○ 2 = motor abnormalities that may be signs of HD (50 - 89 % confidence) 2 ○ 3 = motor abnormalities that are likely signs of HD (90 - 98 % confidence) 3 ○ 4 = motor abnormalities that are unequivocal signs of HD (≥ 99 % confidence) 4	diagconf

3.7 CSF (CSF Collection)

CSF Collection

LAB-ID: labid

Kit ID: kitid

Date and time CSF collection procedure is started: mon/dd/yyyy time: hh:mm time zone: csfpdtc

Total volume of CSF obtained: ml lblpvol

Total volume of usable CSF obtained: ml lblpvolu

Is this a partial sampling visit? yes 1 no 0 csfpartial

Time CSF collection procedure is completed: hh:mm lblpetim

Number of LP attempts: 1 1 2 2 3 3 lblpcnt

LP Attempt #1

Investigator ID: invid1

Lumbar space used for lumbar puncture (LP): L4/5 space 1 L3/4 space 2 other 3 lpsp1

Please enter used lumbar space: lpsp1spc

Initial participant posture:

Lateral decubitus: yes 1 no 0 ipp1ld

Upright: yes 1 no 0 ipp1up

Was patient transferred to lateral decubitus position before CSF collection: yes 1 no 0 ipp1upt

Local anaesthesia (2% lidocaine) used: yes 1 no 0 lplca1

Volume of lidocaine used: ml lplca1v

Why lidocaine was not used:

- Allergy 1
- Other Contraindications 2
- Patient Request 3
- Investigator Preference 4
- Other 5

lplca1r

Number of needle passes to obtain CSF: 1 1 2 2 3 3 4 4 5 5 lpnnp1

Was the first ml of CSF blood contaminated? ○ yes 1 ○ no 0 lp1bc1

Was the second ml of CSF blood contaminated? ○ yes 1 ○ no 0 lp1bc2

Was the third ml of CSF blood contaminated? ○ yes 1 ○ no 0 lp1bc3

LP Attempt #2

Investigator ID: [ ] invid2

Lumbar space used for lumbar puncture (LP): ○ L4/5 space 1 ○ L3/4 space 2 ○ other 3 lpsp2

Please enter used lumbar space: [ ] lpsp2spc

Initial participant posture:

Lateral decubitus: ○ yes 1 ○ no 0 ipp2ld

Upright: ○ yes 1 ○ no 0 ipp2up

Was patient transferred to lateral decubitus position before CSF collection: ○ yes 1 ○ no 0 ipp2upt

Local anaesthesia (2% lidocaine) used: ○ yes 1 ○ no 0 lplca2

Volume of lidocaine used: [ ] ml lplca2v

Why lidocaine was not used: lplca2r
- ○ Allergy 1
- ○ Other Contraindications 2
- ○ Patient Request 3
- ○ Investigator Preference 4
- ○ Other 5

Number of needle passes to obtain CSF: ○ 1 1 ○ 2 2 ○ 3 3 ○ 4 4 ○ 5 5 lpnnp2

Was the first ml of CSF blood contaminated? ○ yes 1 ○ no 0 lp2bc1

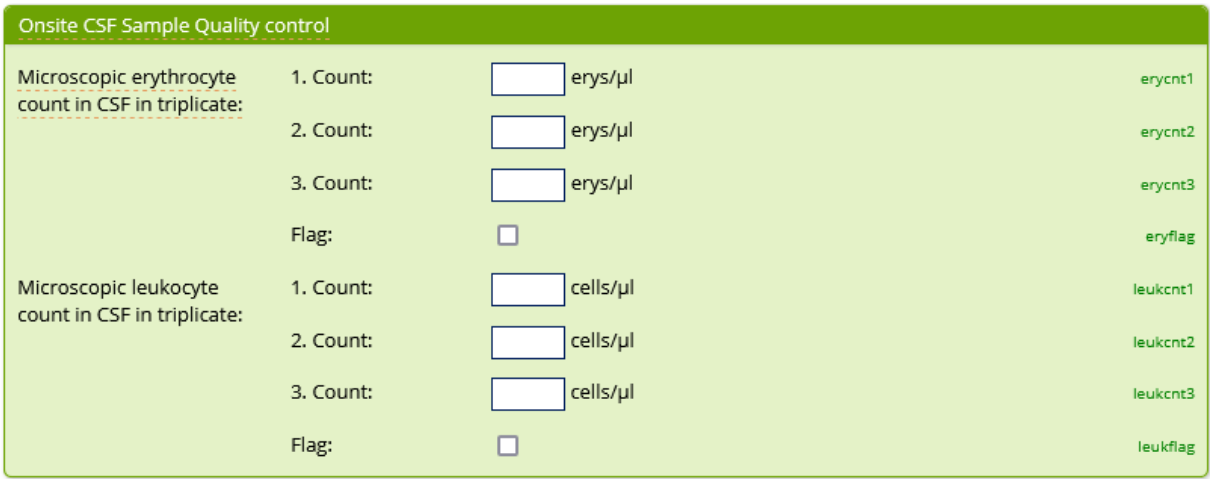
Was the second ml of CSF blood contaminated? ○ yes 1 ○ no 0 lp2bc2

Was the third ml of CSF blood contaminated? ○ yes 1 ○ no 0 lp2bc3

CSF Processing

Time CSF processing is started:	hh:mm		csfstim
Time CSF processing is completed:	hh:mm		csfctim
CSF Tube Rack ID:			csfrkid
CSF aliquot:	Tube ID:		csfaid
	Quantity:		csfaqty
Cells from CSF:	Tube ID:		csfcid
	Quantity:		csfcqty
Comments/Notable deviations for CSF collection/processing:			csfcmt

3.8 CSF Quality (CSF Quality)



3.9 Blood Processing (Blood Processing)

General

LAB-ID:			labid
Kit ID:			kitid
When did the participant last eat or drink anything (except water)?	dd.mon.yyyy time: hh:mm		fastdtc
Date and time of blood draw:	dd.mon.yyyy time: hh:mm		lbdtc
Lithium Heparin Collection Tube:	Tube ID:		lhtid
	Quantity:		lhqty
Serum Collection Tube:	Tube ID:		sstid
	Quantity:		sstqty

Blood Processing

Serum:	Tube ID:		sertid
	Quantity of aliquots:		seraqty
	Tube rack ID:		sertrid
	Time serum processing is started:	hh:mm	serstim
	Time serum processing is completed:	hh:mm	serctim
Plasma:	Total volume (ml) of plasma transferred to 50 ml tube:	ml	plsmtotvol
	Tube ID:		plsmtid
	Quantity of aliquots:		plsmaqty
	Tube rack ID:		plsmtrid
	Time plasma processing is started:	hh:mm	plsmstim
	Time plasma processing is completed:	hh:mm	plsmctim
	Comments/Notable deviations for blood collection/processing:		plsmcmt

On site Sample Storage

Date and time CSF samples are stored on site:	dd.mon.yyyy	time: hh:mm	time zone:		
Date and time blood-derived samples are stored on site:	dd.mon.yyyy	time: hh:mm	time zone:		

3.10 Phone Contact (Phone Contact Sampling)

Phone Contact

Did the participant receive phone contact from the site after the sampling visit? ○ yes 1 ○ no 0 pc1

Date of contact: pc11

Time of contact: hh:mm pc12

Reason: pc10
- ○ unable to contact participant after multiple attempts 1
- ○ participant withdrew consent to be contacted 2
- ○ contact was not attempted 3

Were there any adverse events? ○ yes 1 ○ no 0 pc2

Repeat Sampling Visit

Is this participant interested in attending a repeat sampling visit? ○ yes 1 ○ no 0 pc3

3.11 AE Log (Adverse Event Log)

3.12 SAE (Serious Adverse Event)

General

Date of serious adverse event report: dd.mon.yyyy aedat

Serious Adverse Event

Serious Adverse Events reported in the AE log

AE number: aenum

Start date of serious adverse event: dd.mon.yyyy aestdat

Is the serious adverse event ongoing: yes 1 no 0 aeongo

Stop date of serious adverse event: dd.mon.yyyy aeendat

Was this an expected serious adverse event: yes 1 no 0 aeexp

Brief description of participant:

Sex: ---- sex
female f
male m

Age: age

SAE verbatim term: aeterm

Brief description of the nature of the serious adverse event: aetermbd

Category (outcome) of the serious adverse event:

Death: yes 1 no 0 aesdth

Disability/incapacity: yes 1 no 0 aesdisab

Life-threatening: yes 1 no 0 aeslife

Congenital anomaly/birth defect: yes 1 no 0 aescong

Hospitalization-initial or prolonged: yes 1 no 0 aeshosp

Required intervention to prevent permanent impairment: yes 1 no 0 aesinter

None of the above: yes 1 no 0 aesnone

Outcome: aeout
- resolved; no sequelae 1
- ongoing; no treatment 2
- ongoing; undergoing treatment 3
- residual effects present; no treatment 4
- residual effects present; undergoing treatment 5
- death 6
- unknown 7

Describe any medical, behavioral, or other interventions taken as a result of this SAE:		aerelnst
Status of this report:	Final report: ☐	aerver
Was the participant withdrawn from the research due to this SAE:	○ yes 1 ○ no 0	aedis

SAE Notification

Date of notification:		aenotdat

3.13 End (Premature End)

General

Assessment date: dsdtc

End of Study

Specify primary reason for participant's premature discontinuation from study: dsterm
- ○ event or intercurrent illness of a nature requiring withdrawal 1
- ○ request of primary care physician, site investigator 2
- ○ participant's request (includes carer/spouse/authorized representative's request) 3
- ○ lost to follow up 4
- ○ institutionalized (will not be followed further) 5
- ○ specific adverse event 7
- ○ other 6

Please specify the reason for the participant's request: dsreas
- ○ unable to travel 1
- ○ participant unwilling to continue 2
- ○ participant moved away from the study site 3

Please specify: termoth

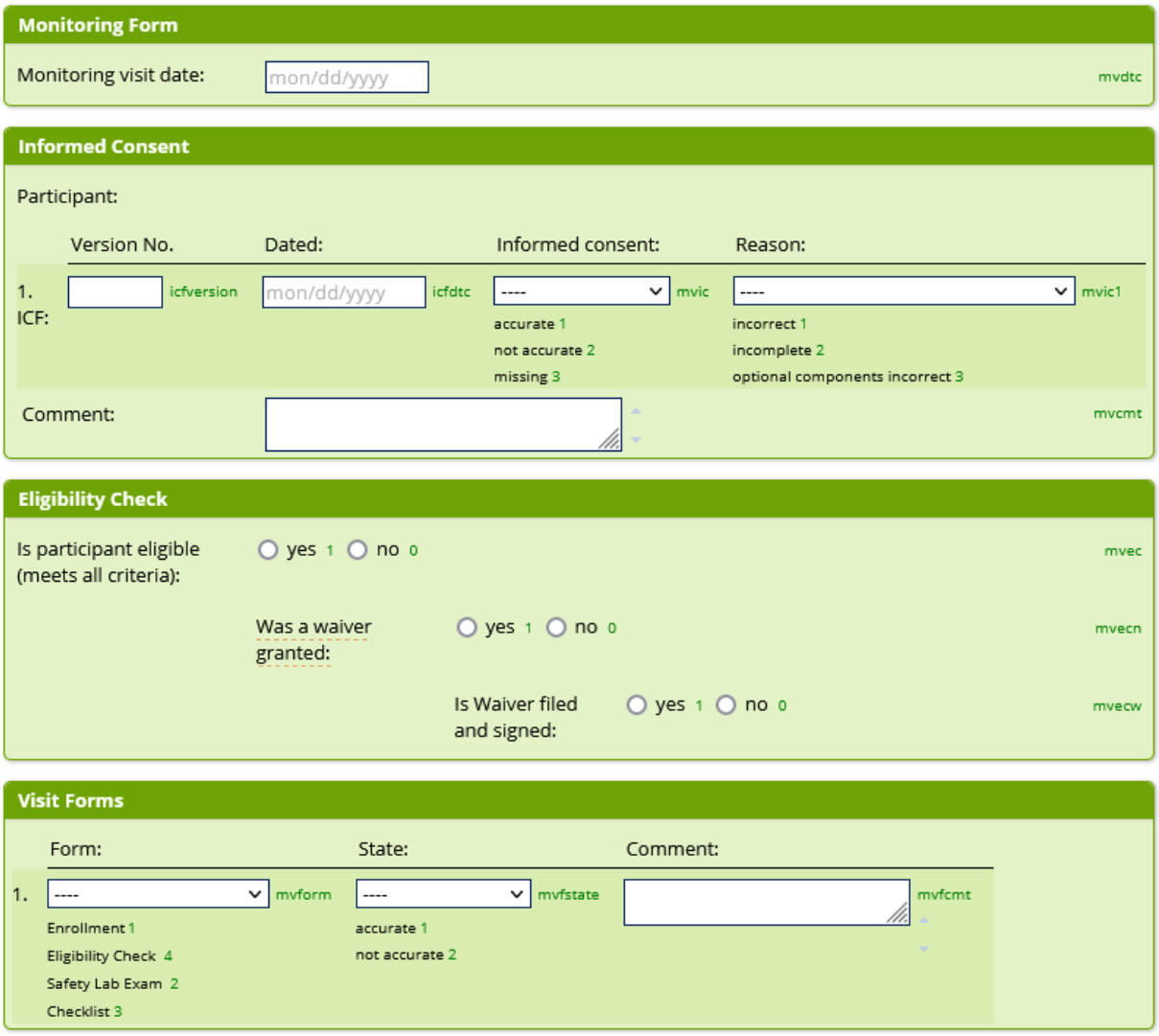
List of Adverse Events

AE number: aenum

Did the participant request the removal of data: dsrdt
- ○ yes 1
- ○ no 0

4 Monitoring Report Forms

4.1 Monitoring SCR (Monitoring Screening Visit)



Monitoring Form

Monitoring visit date: mon/dd/yyyy mvdtc

Informed Consent

Participant:

	Version No.	Dated:	Informed consent:	Reason:
1. ICF:	icfversion	mon/dd/yyyy icfdtc	---- mvic accurate 1 not accurate 2 missing 3	---- mvic1 incorrect 1 incomplete 2 optional components incorrect 3

Comment: mvcmt

Eligibility Check

Is participant eligible (meets all criteria): yes 1 no 0 mvec

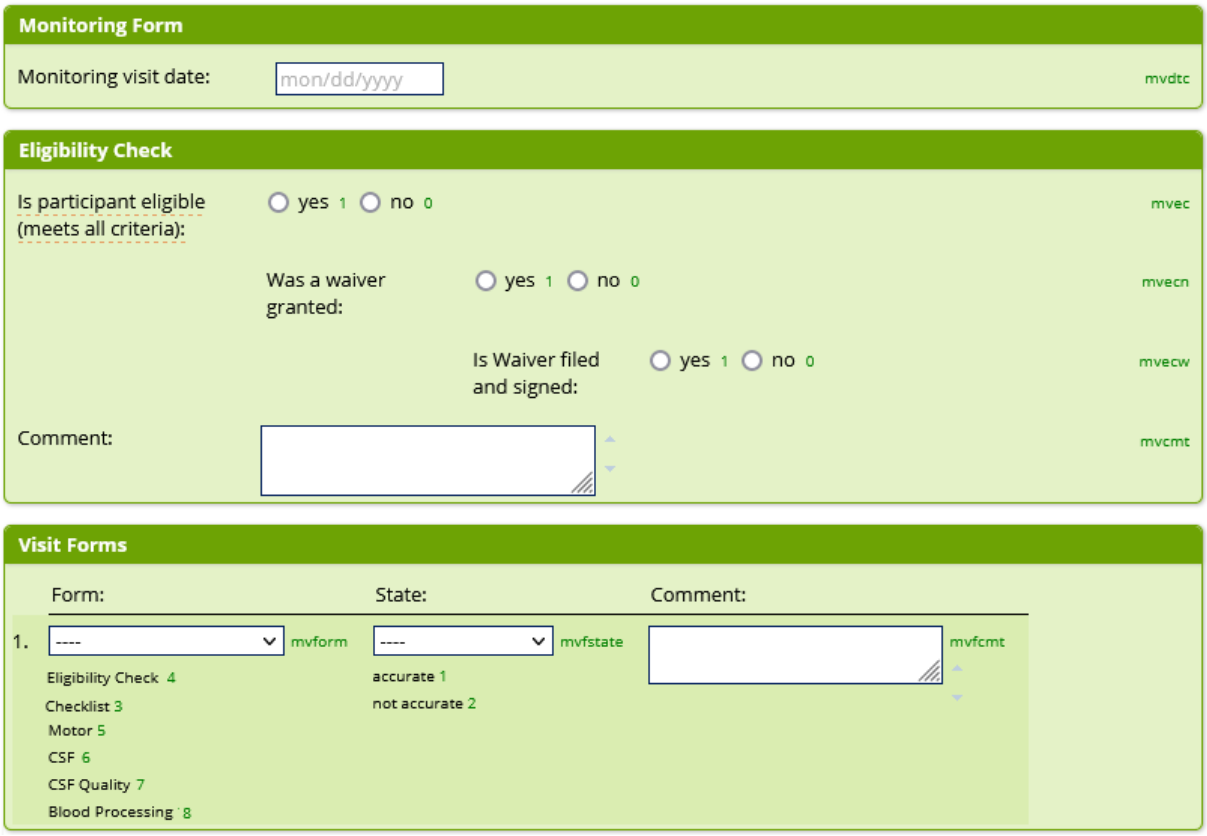
Was a waiver granted: yes 1 no 0 mvecn

Is Waiver filed and signed: yes 1 no 0 mvecw

Visit Forms

	Form:	State:	Comment:
1.	---- mvform Enrollment 1 Eligibility Check 4 Safety Lab Exam 2 Checklist 3	---- mvfstate accurate 1 not accurate 2	mvfcmt

4.2 Monitoring SPL (Monitoring Sampling Visit)



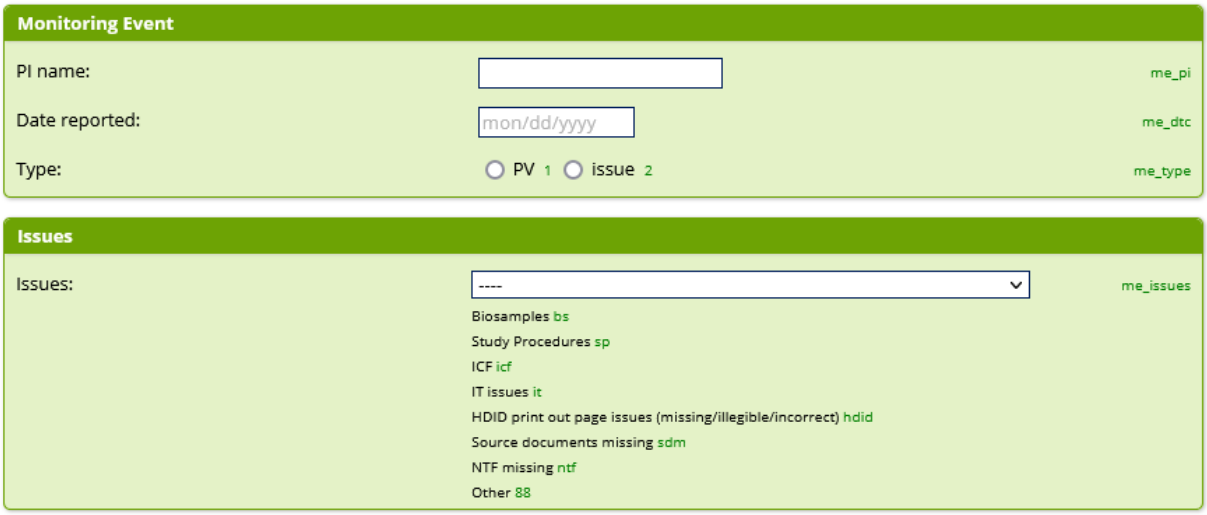
4.3 Monitoring (S)AE (Monitoring Serious and Adverse Events)

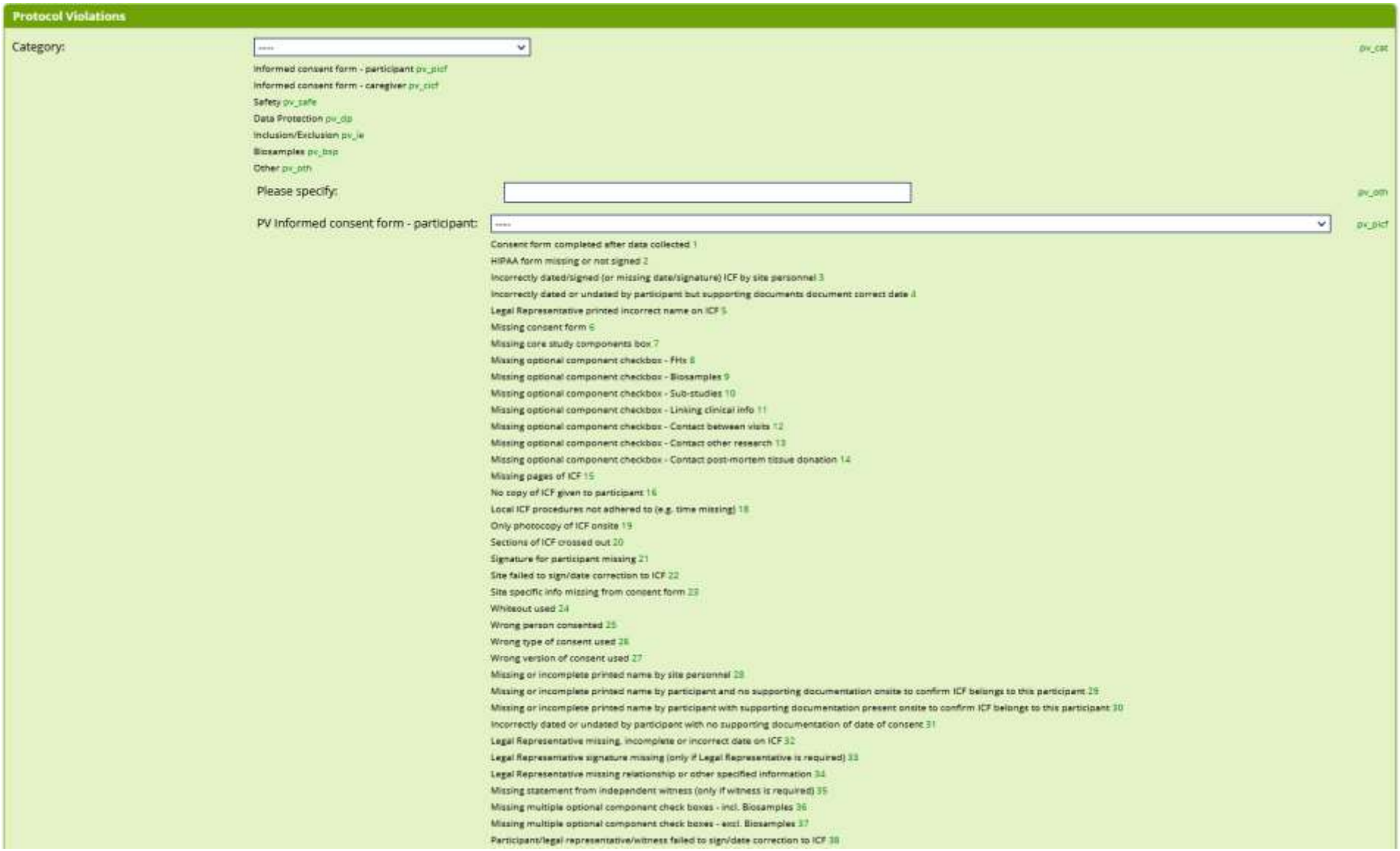
Monitoring Form

Monitoring visit date:	dd.mon.yyyy	mvdtc
Is the AE log complete, up to date and accurate:	yes 1 no 0	mvaecmp
Were all AEs reported within 24hrs:	yes 1 no 0	mvaerep
Are any AEs classified as SAEs:	yes 1 no 0	mvsae
Comment:		mvcmt

5 Monitoring Event Forms

5.1 Monitoring Event (Monitoring Event Form)





Protocol Violations

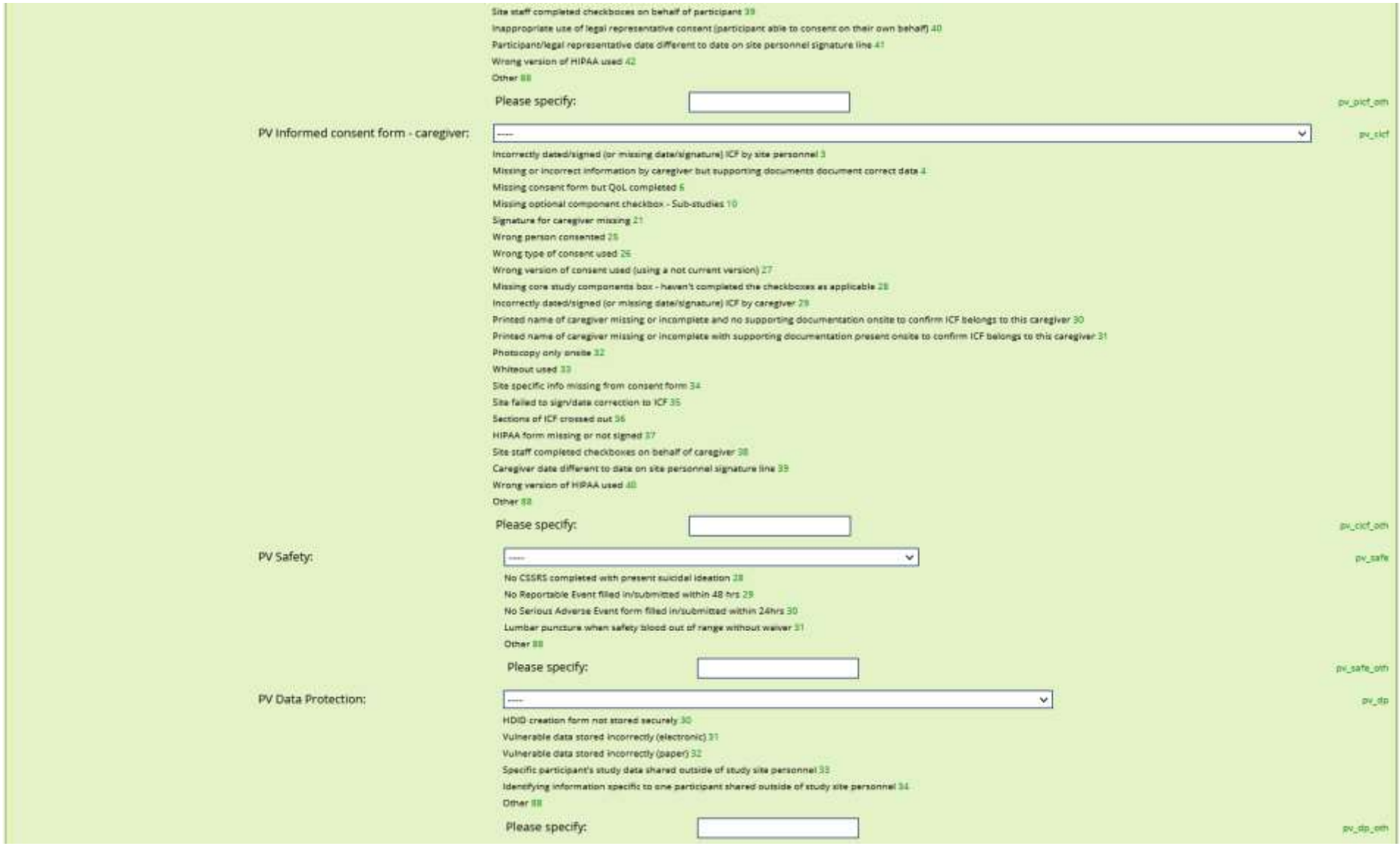
Category: ---- pv_cat

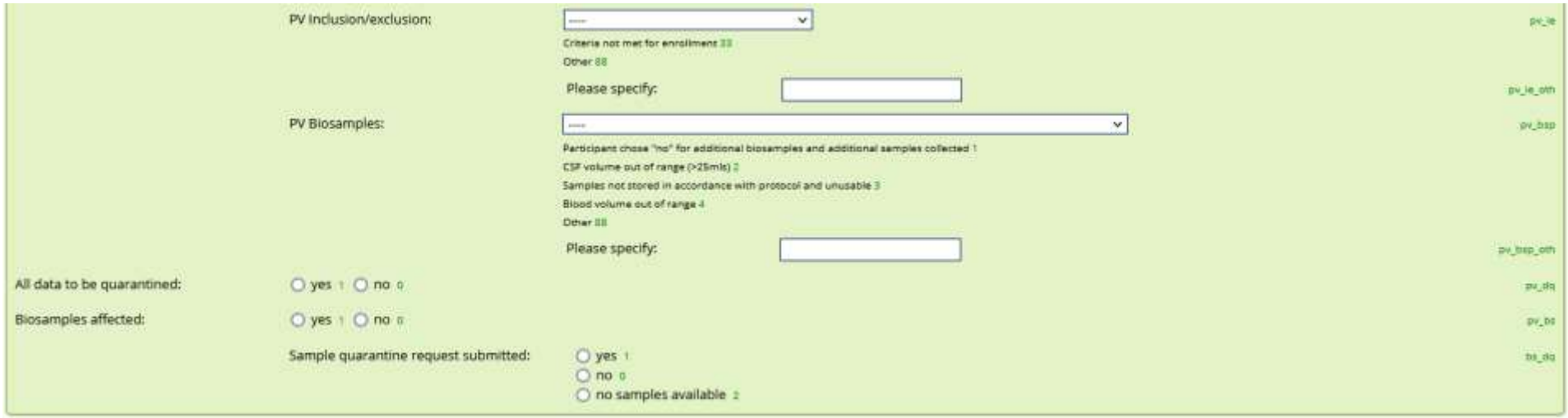
Informed consent form - participant pv_picf
Informed consent form - caregiver pv_cicf
Safety pv_safe
Data Protection pv_dp
Inclusion/Exclusion pv_ie
Biosamples pv_bsp
Other pv_oth

Please specify: pv_oth

PV Informed consent form - participant: ---- pv_picf

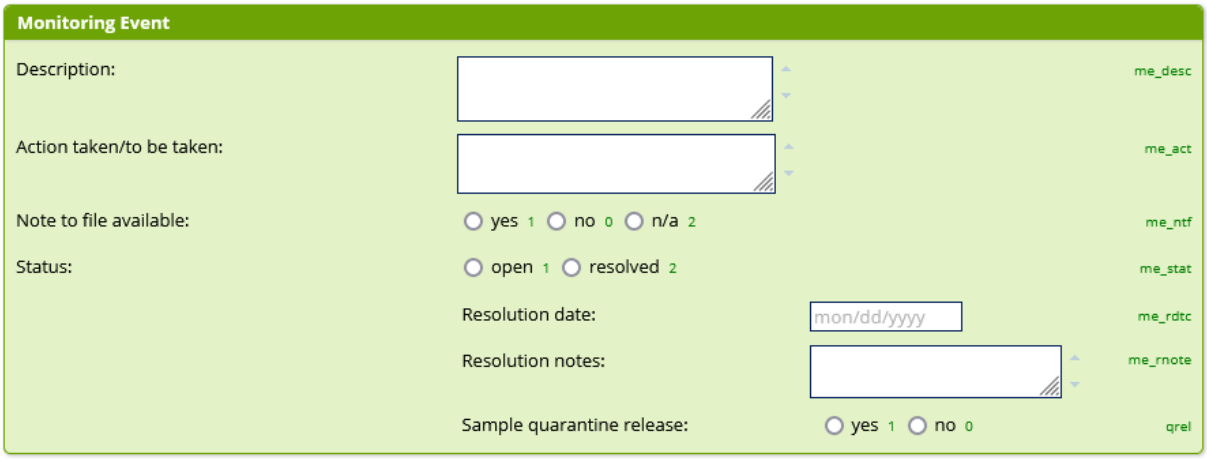
Consent form completed after data collected 1
HIPAA form missing or not signed 2
Incorrectly dated/signed (or missing date/signature) ICF by site personnel 3
Incorrectly dated or undated by participant but supporting documents document correct date 4
Legal Representative printed incorrect name on ICF 5
Missing consent form 6
Missing core study components box 7
Missing optional component checkbox - FHs 8
Missing optional component checkbox - Biosamples 9
Missing optional component checkbox - Sub-studies 10
Missing optional component checkbox - Linking clinical info 11
Missing optional component checkbox - Contact between visits 12
Missing optional component checkbox - Contact other research 13
Missing optional component checkbox - Contact post-mortem tissue donation 14
Missing pages of ICF 15
No copy of ICF given to participant 16
Local ICF procedures not adhered to (e.g. time missing) 18
Only photocopy of ICF onsite 19
Sections of ICF crossed out 20
Signature for participant missing 21
Site failed to sign/date correction to ICF 22
Site specific info missing from consent form 23
Whiteout used 24
Wrong person consented 25
Wrong type of consent used 26
Wrong version of consent used 27
Missing or incomplete printed name by site personnel 28
Missing or incomplete printed name by participant and no supporting documentation onsite to confirm ICF belongs to this participant 29
Missing or incomplete printed name by participant with supporting documentation present onsite to confirm ICF belongs to this participant 30
Incorrectly dated or undated by participant with no supporting documentation of date of consent 31
Legal Representative missing, incomplete or incorrect date on ICF 32
Legal Representative signature missing (only if Legal Representative is required) 33
Legal Representative missing relationship or other specified information 34
Missing statement from independent witness (only if witness is required) 35
Missing multiple optional component check boxes - incl. Biosamples 36
Missing multiple optional component check boxes - excl. Biosamples 37
Participant/legal representative/witness failed to sign/date correction to ICF 38


Site staff completed checkboxes on behalf of participant 39
Inappropriate use of legal representative consent (participant able to consent on their own behalf) 40
Participant/legal representative date different to date on site personnel signature line 41
Wrong version of HIPAA used 42
Other 88
Please specify:
pv_picf_oth
PV Informed consent form - caregiver:
---
pv_cicf
Incorrectly dated/signed (or missing date/signature) ICF by site personnel 3
Missing or incorrect information by caregiver but supporting documents document correct data 4
Missing consent form but QoL completed 6
Missing optional component checkbox - Sub-studies 19
Signature for caregiver missing 21
Wrong person consented 25
Wrong type of consent used 26
Wrong version of consent used (using a not current version) 27
Missing core study components box - haven't completed the checkboxes as applicable 28
Incorrectly dated/signed (or missing date/signature) ICF by caregiver 29
Printed name of caregiver missing or incomplete and no supporting documentation onsite to confirm ICF belongs to this caregiver 30
Printed name of caregiver missing or incomplete with supporting documentation present onsite to confirm ICF belongs to this caregiver 31
Photocopy only onsite 32
Whiteout used 33
Site specific info missing from consent form 34
Site failed to sign/date correction to ICF 35
Sections of ICF crossed out 36
HIPAA form missing or not signed 37
Site staff completed checkboxes on behalf of caregiver 38
Caregiver date different to date on site personnel signature line 39
Wrong version of HIPAA used 40
Other 88
Please specify:
pv_cicf_oth
PV Safety:
---
pv_safe
No CSSRS completed with present suicidal ideation 28
No Reportable Event filled in/submitted within 48 hrs 29
No Serious Adverse Event form filled in/submitted within 24hrs 30
Lumbar puncture when safety blood out of range without waiver 31
Other 88
Please specify:
pv_safe_oth
PV Data Protection:
---
pv_dp
HDID creation form not stored securely 30
Vulnerable data stored incorrectly (electronic) 31
Vulnerable data stored incorrectly (paper) 32
Specific participant's study data shared outside of study site personnel 33
Identifying information specific to one participant shared outside of study site personnel 34
Other 88
Please specify:
pv_dp_oth


PV Inclusion/exclusion:

Criteria not met for enrollment 33
Other 88
pv_ie
Please specify:
pv_ie_oth
PV Biosamples:

Participant chose "no" for additional biosamples and additional samples collected 1
CSF volume out of range (>25mls) 2
Samples not stored in accordance with protocol and unusable 3
Blood volume out of range 4
Other 88
pv_bsp
Please specify:
pv_bsp_oth
All data to be quarantined:
yes 1 no 0
pv_dq
Biosamples affected:
yes 1 no 0
pv_bs
Sample quarantine request submitted:
yes 1
no 0
no samples available 2
bs_dq


Monitoring Event
Description:
me_desc
Action taken/to be taken:
me_act
Note to file available:
yes 1 no 0 n/a 2
me_ntf
Status:
open 1 resolved 2
me_stat
Resolution date:
mon/dd/yyyy
me_rdtc
Resolution notes:
me_rnote
Sample quarantine release:
yes 1 no 0
qrel

References

[1]	CHDI Foundation Inc., *HDClarity 4.0 Data Management Requirements*, CLR4-REQ-0001-EN, Version 1.0, 19-Nov-2021
[2]	CHDI Foundation Inc., *HDClarity 4.0 CRF Requirements*, CLR4-REQ-0002-EN, Version 1.0, 19-Nov-2021
[3]	CHDI Foundation, Inc., *HDClarity 4.0 Data Dictionary*, CLR4-SPC-0001-EN, Version 1.0, 11-Nov-2021

Approval

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Author	Gunter Antoneag	17-Nov-2021	
Review	Torsten Illmann	23-Nov-2021	
Approval	Nicole Piller	23-Nov-2021	

Revision Index

Date	Version	Chapter	Summary of Change(s) and if applicable Reason for Change(s)
23-Nov-2021	1.0	---	Initial Version