INTERNATIONAL COUNCIL FOR HARMONISATION OF TECHNICAL REQUIREMENTS FOR PHARMACEUTICALS FOR HUMAN USE

ICH HARMONISED GUIDELINE

CLINICAL ELECTRONIC STRUCTURED HARMONISED PROTOCOL

(CeSHarP)

M11 TECHNICAL SPECIFICATION

Step 3 Experts Draft

At Step 2 of the ICH Process, a consensus draft text or guideline, agreed by the appropriate ICH Expert Working Group, is transmitted by the ICH Assembly to the regulatory authorities of the ICH regions for internal and external consultation, according to national or regional procedures.

M11 Technical Specification
Document History

Code	History	Date
M11	Endorsement by the Members of the ICH Assembly under Step 2 and release for public consultation (document dated day/month/year)	day/month/year

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TECHNICAL SPECIFICATION

The purpose of this document is to serve as a technical representation of the ICH M11 protocol template. This Technical Specification (TS) is aligned with the latest version of the ICH M11 Guideline and protocol template, but with flexibility in addressing data exchange needs per ICH and those of regional authorities.

NOTE: <, preamble goes here >

DEFINITION OF TABLE ELEMENTS

Term (Variable)	Term (variable) is the verbatim term from the Template.
Data Type	Data type is a classification that specifies which type of value a variable has.
Data (D), Value (V) or Heading (H)	Specifies the type of the Data as Heading, Data or Value. Selections: • Heading: section heading including table heading, non-numbered title. • Data: Content such as text, image, equation, table • Value: if there is a pick list for the data
Definition	Definition is the meaning of the ICH M11 Data Elements.
User Guidance	User guidance is directly from the instructions of the template.
Conformance	Rules and actions in accordance with the Template conventions and general instructions which characterize how the Headers, data element or Text content will conform
Cardinality	Common cardinalities include one to one, one to many, and many to many. An example of Cardinality is the numerical relationship between rows of one table and rows in another.
Relationship content from ToC representing the protocol hierarchy	Relationship content from ToC representing the protocol hierarchy is relationship to the template Table of Contents.
Value	Indicates the value of a specific data element or heading. Specifies the actual value or value range of specific data (e.g. Value may be from the ICH M11 Valid Value List. For numbered heading, the number will NOT be included here. .
Business rules	**Value Allowed:** Is a value allowed If the header is required, the value will be No. If there is universal text, the Value will be No. **Relationship:** What is the relationship? Identify relationship for the element including the relationship to the TOC. For TOC, numbers are listed Lower to Higher. For Tables elements, there may be a row or a column heading as a a relationship. Other Relationships are also defined, for example an Amendment number to a Protocol Identifier. **Concept:** Identify the Concept for Headings expect to see Heading and for other elements expect reference to controlled terminology or detailed information.
Repeating and/or Reuse Rules	Instructions on how components are repeated and/or reused within the protocol. Is this component repeated? Is this component reused? Is this component repeated/reused in other sections of the document? Repeating is defined as replication of the data element for new content. Reuse is defined as using verbatim content in more than one data element location in the protocol.

10 APPENDIX 1: DETAILED DESCRIPTIONS OF INFORMATION COMPONENTS

11 TITLE PAGE

Term (Variable)	Sponsor Confidentiality Statement:
Data Type	Text
Data (D), Value (V) or Heading (H)	H
Definition	Heading
User Guidance	N/A
Conformance	Optional
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	Title Page
Value	Sponsor Confidentiality Statement:
Business rules	**Value Allowed**: No **Relationship**: Table row heading **Concept**: Heading
Repeating and/or Reuse Rules	No

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Term (Variable)	<Sponsor Confidentiality Statement>
Data Type	Text
Data (D), Value (V) or Heading (H)	D
Definition	C181236 For review purpose, see definition of the controlled terminology below: A written message within the study protocol that asserts a statement of non-disclosure, such that information contained within the protocol document may only be shared with authorized parties.
User Guidance	Insert the Sponsor's confidentiality statement, if applicable, otherwise delete.
Conformance	Optional
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	Title Page
Value	Text
Business rules	**Value Allowed**: Yes **Relationship**: Heading **Concept**: C181236
Repeating and/or Reuse Rules	No

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Term (Variable)	Full Title:
Data Type	Text
Data (D), Value (V) or Heading (H)	H
Definition	Heading
User Guidance	N/A
Conformance	Required
Cardinality	One to one

Relationship content from ToC representing the protocol hierarchy	Title Page
Value	Full Title:
Business rules	**Value Allowed**: No **Relationship**: Table row heading **Concept**: Heading
Repeating and/or Reuse Rules	No

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Term (Variable)	<Full Title>
Data Type	Text
Data (D), Value (V) or Heading (H)	D
Definition	C132346 For review purpose, see definition of the controlled terminology below: The formal descriptive name for the protocol sufficient to describe key elements of the study, aimed at a scientific audience.
User Guidance	The protocol should have a descriptive title that identifies the scientific aspects of the trial sufficiently to ensure it is immediately evident what the trial is investigating and on whom, and to allow retrieval from literature or internet searches.
Conformance	Required
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	Title page
Value	Text
Business rules	**Value Allowed**: Yes **Relationship**: Heading; Sponsor Protocol Identifier **Concept**: C132346
Repeating and/or Reuse Rules	No

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Term (Variable)	Trial Acronym:
Data Type	Text
Data (D), Value (V) or Heading (H)	H
Definition	Heading
User Guidance	N/A
Conformance	Optional
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	Title Page
Value	Trial Acronym:
Business rules	**Value Allowed**: No **Relationship**: Table row heading **Concept**: Heading
Repeating and/or Reuse Rules	No

16

Term (Variable)	<Trial Acronym>

Data Type	Text
Data (D), Value (V) or Heading (H)	D
Definition	C94108 For review purpose, see definition of the controlled terminology below: Acronym or abbreviation used publicly to identify the clinical trial.
User Guidance	Acronym or abbreviation used publicly to identify the clinical trial. Delete this line from the table if not applicable.
Conformance	Optional
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	Title Page
Value	Text
Business rules	**Value Allowed**: Yes **Relationship**: Heading; Protocol Identifier **Concept**: C94108
Repeating and/or Reuse Rules	No

17

Term (Variable)	Sponsor Protocol Identifier:
Data Type	Text
Data (D), Value (V) or Heading (H)	H
Definition	Heading
User Guidance	N/A
Conformance	Required
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	Title Page
Value	Sponsor Protocol Identifier:
Business rules	**Value Allowed**: No **Relationship**: Table row heading **Concept**: Heading
Repeating and/or Reuse Rules	No

18

Term (Variable)	<Sponsor Protocol Identifier>
Data Type	Text
Data (D), Value (V) or Heading (H)	D
Definition	C132351 For review purpose, see definition of the controlled terminology below: A unique code assigned by the Sponsor that identifies a specific protocol.
User Guidance	A unique alphanumeric identifier for the trial, designated by the Sponsor.
Conformance	Required
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	Title page
Value	Text
Business rules	**Value Allowed**: Yes

	Relationship: Heading **Concept**: C132351 Note: Must have at least One Character May not be space(null)
Repeating and/or Reuse Rules	No

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Term (Variable)	Original Protocol:
Data Type	Text
Data (D), Value (V) or Heading (H)	H
Definition	Heading
User Guidance	N/A
Conformance	Required
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	Title Page
Value	Original Protocol:
Business rules	**Value Allowed**: No **Relationship**: Table row heading **Concept**: Heading
Repeating and/or Reuse Rules	No

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Term (Variable)	[Original Protocol Indicator]
Data Type	Valid Value
Data (D), Value (V) or Heading (H)	V
Definition	CNEW For review purpose, see definition of the controlled terminology below An indication as to whether the protocol document reflects the original version of the protocol.
User Guidance	N/A
Conformance	Required
Cardinality	One to one; One to Sponsor Protocol Identifier
Relationship content from ToC representing the protocol hierarchy	Title page
Value	Yes (C49488), No(C49487)
Business rules	**Value Allowed**: Yes **Relationship**: Heading; Sponsor Protocol Identifier **Concept**: CNEW
Repeating and/or Reuse Rules	No

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NCI C-Code	M11 Preferred Term	Draft Definition
C66742	NY	A term that is used to indicate a question with permissible values of yes/no/unknown/not applicable.
C49487	No	The non-affirmative response to a question.
C49488	Yes	The affirmative response to a question.

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Term (Variable)	Version Number:

Data Type	Text
Data (D), Value (V) or Heading (H)	H
Definition	Heading
User Guidance	N/A
Conformance	Optional
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	Title Page
Value	Version Number:
Business rules	**Value Allowed**: No **Relationship**: Table row heading **Concept**: Heading
Repeating and/or Reuse Rules	No

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Term (Variable)	<Version Number>
Data Type	Text
Data (D), Value (V) or Heading (H)	D
Definition	C181232 For review purpose, see definition of the controlled terminology below: A string of numerals that uniquely identifies a specific version of a study protocol.
User Guidance	For use by the Sponsor at their discretion.
Conformance	Optional
Cardinality	One to one, Protocol Identifier
Relationship content from ToC representing the protocol hierarchy	Title Page
Value	Number
Business rules	**Value Allowed**: Yes **Relationship**: Heading, Sponsor Protocol Identifier **Concept**: C181232
Repeating and/or Reuse Rules	No

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Term (Variable)	Version Date:
Data Type	Text
Data (D), Value (V) or Heading (H)	H
Definition	Heading
User Guidance	N/A
Conformance	Optional
Cardinality	One to one; One to Version Number
Relationship content from ToC representing the protocol hierarchy	Title Page
Value	Version Date:
Business rules	**Value Allowed**: No **Relationship**: Table row heading **Concept**: Heading

Repeating and/or Reuse Rules	No

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Term (Variable)	<Version Date>
Data Type	Date
Data (D), Value (V) or Heading (H)	D
Definition	C93813 For review purpose, see definition of the controlled terminology below The date on which the document is versioned.
User Guidance	For use by the Sponsor at their discretion.
Conformance	Optional
Cardinality	One to one; one to Version Number
Relationship content from ToC representing the protocol hierarchy	Title page
Value	Date Format
Business rules	**Value Allowed**: Yes **Relationship**: Heading; Version number; Sponsor Protocol Identifier **Concept**: C93813
Repeating and/or Reuse Rules	No

26

Term (Variable)	{Amendment Identifier:}
Data Type	Text
Data (D), Value (V) or Heading (H)	H
Definition	Heading
User Guidance	N/A
Conformance	Conditional: when there is an amendment
Cardinality	One to one; One to Sponsor Protocol Identifier
Relationship content from ToC representing the protocol hierarchy	Title page
Value	Amendment Identifier:
Business rules	**Value Allowed**: Yes if Original Protocol = No; blank if Original Protocol = Yes **Relationship**: Table Row Heading, Sponsor Protocol Identifier **Concept**: CNEW
Repeating and/or Reuse Rules	Yes, reuse to/from table for document history

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Term (Variable)	{Amendment Identifier}
Data Type	Text
Data (D), Value (V) or Heading (H)	D
Definition	CNEW For review purpose, see definition of the controlled terminology below A sequence of characters used to uniquely identify a protocol amendment.
User Guidance	Enter the amendment identifier (e.g. amendment number). If this is the original instance of the protocol, delete the row or enter “Not applicable”
Conformance	Conditional: when there is an amendment
Cardinality	One to one; One to Protocol Identifier if not original

Relationship content from ToC representing the protocol hierarchy	Title Page
Value	Text
Business rules	**Value Allowed**: Yes if Original Protocol = No; blank if Original Protocol = Yes **Relationship**: Heading, Sponsor Protocol Identifier **Concept**: CNEW
Repeating and/or Reuse Rules	Yes, repeatable for Table for Document History

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Term (Variable)	{Amendment Scope:}
Data Type	Text
Data (D), Value (V) or Heading (H)	H
Definition	Heading
User Guidance	N/A
Conformance	Required
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	Title Page
Value	Amendment Scope:
Business rules	**Value Allowed**: No **Relationship**: Table row heading **Concept**: Heading
Repeating and/or Reuse Rules	No

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Term (Variable)	{[Amendment Scope]}
Data Type	Valid Value
Data (D), Value (V) or Heading (H)	V
Definition	CNEW For review purpose, see definition of the controlled terminology below A description as to whether the amendment scope applies globally across the trial.
User Guidance	Leave blank for original protocol. If this is the original instance of the protocol, delete the row or enter "Not applicable". If an amendment applies to all sites in the trial, enter “global” and delete the Country, Region and Site Identifier fields. If amending a single-country study, enter “global”.
Conformance	Conditional: when there is an amendment
Cardinality	One to one, One to Amendment Identifier
Relationship content from ToC representing the protocol hierarchy	Title page
Value	Blank; Global (C68846), Not Global (CNEW)
Business rules	**Value Allowed**: Yes; Blank if Original Protocol Indicator = Yes

	Relationship: Heading, Amendment Identifier, Sponsor Protocol Identifier **Concept**: CNEW
Repeating and/or Reuse Rules	No

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NCI C-Code	M11 Preferred Term	Draft Definition
CNEW	Amendment Scope Response	A terminology value set relevant to the responses for the protocol amendment scope within the ICH M11 Protocol model.
C68846	Global	Covering or affecting the whole of a system.
CNEW	Not Global	Covering or affecting a portion of the system.

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Term (Variable)	{[Country Identifier] or [Region Identifier] or <Site Identifier>}
Data Type	Valid Value
Data (D), Value (V) or Heading (H)	V
Definition	C20108 CNEW CNEW For review purpose, see definition of the controlled terminology below C20108 A sequence of characters used to identify and/or name the country. CNEW A sequence of characters used to identify and/or name the region CNEW A sequence of characters used to identify and/or name the study site.
User Guidance	Leave blank for original protocol. If the amendment does not apply to all sites in the trial, select "Not Global" and utilise one of the identifiers based on amendment scope.
Conformance	Conditional: when not global
Cardinality	One to one; Many to Amendment Scope; One to Amendment Identifier; One to Sponsor Protocol Identifier
Relationship content from ToC representing the protocol hierarchy	Title Page
Value	Country specific: [Country Identifier] (ISO 3166 Country Codes, Alpha 3; ISO 3166 Country Codes, Alpha 2) or Region Specific: [Region Identifier] or Site specific: [Site Identifier] (Text) Site Identifier Text Condition Blank for Original Protocol Indicator = yes
Business rules	**Value Allowed**: Yes **Relationship**: Heading, Amendment Scope, Amendment Identifier, Sponsor Protocol Identifier **Concept**: C20108, CNEW, CNEW
Repeating and/or Reuse Rules	Yes, repeatable in 12.2 country/region-specific differences

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Term (Variable)	Sponsor's Investigational Product Code(s):

Data Type	Text
Data (D), Value (V) or Heading (H)	H
Definition	Heading
User Guidance	N/A
Conformance	Optional
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	Title Page
Value	Sponsor's Investigational Product Code(s):
Business rules	Value Allowed: No Relationship: Table row heading Concept: Heading
Repeating and/or Reuse Rules	Yes, repeatable for each Investigational compound

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Term (Variable)	<Sponsor's Investigational Product Code(s)>
Data Type	Text
Data (D), Value (V) or Heading (H)	D
Definition	CNEW For review purpose, see definition of the controlled terminology below: A symbol or combination of symbols that are assigned by the Sponsor to uniquely identify an experimental intervention.
User Guidance	Enter the Sponsor's unique identifier for investigational compound(s) in the trial. Add fields as needed.
Conformance	Optional: if there is Sponsor Investigational Product Code
Cardinality	One to one, Many to Sponsor Protocol Identifier
Relationship content from ToC representing the protocol hierarchy	Title Page
Value	Text
Business rules	**Value Allowed**: Yes **Relationship**: Heading, Sponsor Protocol Identifier **Concept**: CNEW
Repeating and/or Reuse Rules	Yes, repeatable for each Investigational compound Yes, repeatable in 1.1.2 under Intervention

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Term (Variable)	Investigational Product Name(s):
Data Type	Text
Data (D), Value (V) or Heading (H)	H
Definition	Heading
User Guidance	N/A
Conformance	Optional
Cardinality	One to one, Many to Sponsor Protocol Identifier
Relationship content from ToC representing the protocol hierarchy	Title Page
Value	Investigational Product Name(s):
Business rules	**Value Allowed**: No **Relationship**: Table row heading

	Concept: Heading
Repeating and/or Reuse Rules	No

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Term (Variable)	<Nonproprietary Name(s)>
Data Type	Text
Data (D), Value (V) or Heading (H)	D
Definition	C97054 For review purpose, see definition of the controlled terminology below Drug name that is not protected by a trademark, usually descriptive of its chemical structure.
User Guidance	Omit nonproprietary name fields if a nonproprietary name has not yet been assigned.
Conformance	Optional; Blank
Cardinality	One to many; Many to Sponsor Investigational Product Code(s); Many to Sponsor Protocol Identifier
Relationship content from ToC representing the protocol hierarchy	Title Page
Value	Text for example WHO INN, USAN, JAN, XEVMPD
Business rules	**Value Allowed**: Yes **Relationship**: Heading, Sponsor Protocol Identifier **Concept**: C97054
Repeating and/or Reuse Rules	Yes, repeatable for each nonproprietary name Yes, repeatable in 1.1,2 under intervention

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Term (Variable)	<Proprietary Name(s)>
Data Type	Text
Data (D), Value (V) or Heading (H)	D
Definition	C71898 For review purpose, see definition of the controlled terminology below A commercial name granted by a naming authority for use in marketing an experimental intervention.
User Guidance	Omit proprietary name fields if not yet established.
Conformance	Optional; Blank
Cardinality	One to many; Many to Sponsor Investigational Product Code(s); Many to Sponsor Protocol Identifier
Relationship content from ToC representing the protocol hierarchy	Title Page
Value	Text
Business rules	**Value Allowed**: Yes **Relationship**: Heading; Protocol Identifier; Sponsor Investigational Product Code(s) **Concept**: C71898
Repeating and/or Reuse Rules	Yes, repeatable for each proprietary name

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Term (Variable)	Trial Phase:
Data Type	Text

Data (D), Value (V) or Heading (H)	H
Definition	Heading
User Guidance	N/A
Conformance	Required
Cardinality	One to one; One to Sponsor Protocol Identifier
Relationship content from ToC representing the protocol hierarchy	Title Page
Value	Trial Phase:
Business rules	**Value Allowed**: No **Relationship**: Table row heading; Sponsor Protocol Identifier **Concept**: Heading
Repeating and/or Reuse Rules	No

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Term (Variable)	[Trial Phase]
Data Type	Valid Value
Data (D), Value (V) or Heading (H)	V
Definition	C48281 For review purpose, see definition of the controlled terminology below A step in the clinical research and development of a therapy from initial clinical trials to post-approval studies.
User Guidance	For trials combining investigational drugs or vaccines with devices, classify according to the phase of drug development.
Conformance	Required
Cardinality	One to one; One to Sponsor Protocol Identifier
Relationship content from ToC representing the protocol hierarchy	Title Page
Value	Early Phase 1 (C54721); Phase 1(C15600); Phase 1/Phase 2 (C15693) Phase 1/Phase 2/Phase 3 (C198366); Phase 1/Phase 3(C198367); Phase 2(C15601); Phase 2/Phase 3(C15694); Phase2/Phase 3/Phase 4(CNEW); Phase 3(C15602); Phase 3/Phase 4 (CNEW); Phase 4 (C15603)))
Business rules	**Value Allowed**: Yes **Relationship**: Heading; Sponsor Protocol Identifier **Concept**: C48281
Repeating and/or Reuse Rules	No

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NCI C-Code	M11 Preferred Term	Draft Definition
C66737	TPHASE	A terminology codelist relevant to the phase, or stage, of the clinical trial.
C54721	Early Phase 1	First-in-human trials, in a small number of subjects, that are conducted before Phase 1 trials and are intended to assess new candidate therapeutic and imaging agents. The study agent is administered at a low dose for a limited time, and there is no therapeutic or diagnostic intent.
C15600	Phase 1	The initial introduction of an investigational new drug into humans. Phase 1 studies are typically closely monitored and may be conducted in patients or normal volunteer subjects.
C15693	Phase 1/Phase 2	A class of clinical study that combines elements characteristic of traditional Phase 1 and Phase 2 trials. See also Phase I, Phase II.

C198366	Phase 1/Phase 2/Phase 3	A study that begins as a Phase 1 study and transitions into Phases 2 and 3 based upon successful completion of each previous portion.
C198367	Phase 1/Phase 3	A study that begins as a Phase 1 study and transitions into a Phase 3 study upon successful completion of the Phase I portion.
CNEW	Phase 2/Phase 3/Phase 4	A study that begins as a Phase 2 study and transitions into Phases 3 and 4 based upon successful completion of each previous portion.
C15601	Phase 2	Phase that includes the controlled clinical trials conducted to evaluate the safety and efficacy of the drug in a limited number of patients with the disease or condition under study. Objectives can be dose-ranging (dose-response, frequency of dosing), type of patients, or numerous other characteristics of safety and efficacy.
C15694	Phase 2/Phase 3	A class of clinical study that combines elements characteristic of traditional Phase 2 and Phase 3 trials.
CNEW	Phase 3/Phase 4	A class of clinical study that combines elements characteristic of traditional Phase 3 and Phase 4 trials.
C15602	Phase 3	Phase that includes the controlled clinical trials intended to confirm safety and effectiveness, evaluate the overall benefit-risk relationship, and to provide substantial evidence for regulatory approval and labeling.
C15603	Phase 4	Post-approval studies to delineate additional information about the drug's risks, benefits, and optimal use that may be requested by regulatory authorities in conjunction with marketing approval.

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Term (Variable)	Short Title
Data Type	Text
Data (D), Value (V) or Heading (H)	H
Definition	Heading
User Guidance	N/A
Conformance	Optional
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	Title Page
Value	Short Title:
Business rules	**Value Allowed**: No **Relationship**: Table row heading **Concept**: Heading
Repeating and/or Reuse Rules	No

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Term (Variable)	<Trial Short Title>
Data Type	Text

Data (D), Value (V) or Heading (H)	D
Definition	C132345 For review purpose, see definition of the controlled terminology below The short descriptive name for the protocol.
User Guidance	Short title should convey in plain language what the trial is about and should be suitable for use as "Brief Title" or "Title in Plain Language" in global clinical trial registries. It can also be suitable for use with informed consents and ethics committee submissions.
Conformance	Optional
Cardinality	One to one, One to Sponsor Protocol identifier
Relationship content from ToC representing the protocol hierarchy	Title Page
Value	Text
Business rules	**Value Allowed**: Yes **Relationship**: Heading, Sponsor Protocol Identifier **Concept**: C132345
Repeating and/or Reuse Rules	No

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Term (Variable)	Sponsor Name and Address:
Data Type	Text
Data (D), Value (V) or Heading (H)	H
Definition	Heading
User Guidance	N/A
Conformance	Required
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	Title Page
Value	Sponsor Name and Address:
Business rules	**Value Allowed**: No **Relationship**: Table row heading **Concept**: Heading
Repeating and/or Reuse Rules	No

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Term (Variable)	<Sponsor Name>
Data Type	Text
Data (D), Value (V) or Heading (H)	D
Definition	C70793 For review purpose, see definition of the controlled terminology below An individual, company, institution, or organisation that takes responsibility for the initiation, management, and/or financing of a clinical study. [After ICH E6, WHO, 21 CFR 50.3 (e), and after IDMP]
User Guidance	Provide the legal name of the individual or pharmaceutical or medical device company, governmental agency, academic institution, private organisation, or other organisation who takes primary responsibility for and initiates a clinical investigation. If more than one Sponsor, list the Primary Sponsor in this field.
Conformance	Required

Cardinality	One to one; One to Sponsor Protocol Identifier
Relationship content from ToC representing the protocol hierarchy	Title Page
Value	Text
Business rules	**Value Allowed**: Yes **Relationship**: Heading; Sponsor Protocol Identifier **Concept**: C70793
Repeating and/or Reuse Rules	No

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Term (Variable)	<Sponsor Legal Address>
Data Type	Text
Data (D), Value (V) or Heading (H)	D
Definition	CNEW For review purpose, see definition of the controlled terminology below The legally registered address of the trial Sponsor.
User Guidance	Provide the legal name of the individual or pharmaceutical or medical device company, governmental agency, academic institution, private organisation, or other organisation who takes primary responsibility for and initiates a clinical investigation. If more than one Sponsor, list the Primary Sponsor in this field.
Conformance	Required
Cardinality	One to one, One to Sponsor Name
Relationship content from ToC representing the protocol hierarchy	Title Page
Value	Text
Business rules	**Value Allowed**: Yes **Relationship**: Heading, Sponsor Name **Concept**: CNEW
Repeating and/or Reuse Rules	No

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Term (Variable)	Co-Sponsor Name and Address:
Data Type	Text
Data (D), Value (V) or Heading (H)	H
Definition	Heading
User Guidance	N/A
Conformance	Optional
Cardinality	One to one, One to Sponsor Name, One to Sponsor Protocol Identifier
Relationship content from ToC representing the protocol hierarchy	Title Page
Value	Co-Sponsor Name and Address:
Business rules	**Value Allowed**: No **Relationship**: Heading, Sponsor Name, Sponsor Protocol Identifier **Concept**: Heading
Repeating and/or Reuse Rules	No

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Term (Variable)	<Co-Sponsor Name>

Data Type	Text
Data (D), Value (V) or Heading (H)	D
Definition	CNEW For review purpose, see definition of the controlled terminology below The literal identifier (i.e. distinctive designation) of the trial co-Sponsor.
User Guidance	Provide the legal name of the individual or pharmaceutical or medical device company, governmental agency, academic institution, private organisation, or other organisation who takes primary responsibility for and initiates a clinical investigation. If more than one Sponsor, list the Primary Sponsor in this field.
Conformance	Optional
Cardinality	One to one, One to Co-Sponsor Name, One to Sponsor Name; One to Sponsor Protocol Identifier
Relationship content from ToC representing the protocol hierarchy	Title Page
Value	Text
Business rules	**Value Allowed**: Yes **Relationship**: Heading, Co-Sponsor Name, Sponsor Name, Sponsor Protocol Identifier **Concept**: CNEW
Repeating and/or Reuse Rules	No

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Term (Variable)	<Co-Sponsor Legal Address>
Data Type	Text
Data (D), Value (V) or Heading (H)	D
Definition	CNEW For review purpose, see definition of the controlled terminology below The legally registered address of the trial co-sponsor.
User Guidance	Provide the legal name of the individual or pharmaceutical or medical device company, governmental agency, academic institution, private organisation, or other organisation who takes primary responsibility for and initiates a clinical investigation. If more than one Sponsor, list the Primary Sponsor in this field.
Conformance	Optional
Cardinality	One to one; One to Heading; One to Co-Sponsor Name
Relationship content from ToC representing the protocol hierarchy	Title Page
Value	Text
Business rules	**Value Allowed**: Yes **Relationship**: Heading, Co- Sponsor Name **Concept**: CNEW
Repeating and/or Reuse Rules	No

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Term (Variable)	Local Sponsor Name and Address:
Data Type	Text
Data (D), Value (V) or Heading (H)	H
Definition	Heading
User Guidance	N/A

Conformance	Optional
Cardinality	One to one; One to Sponsor Name and Address; One to Protocol Sponsor Identifier
Relationship content from ToC representing the protocol hierarchy	Title Page
Value	Local Sponsor Name and Address:
Business rules	**Value Allowed**: No **Relationship**: Heading Sponsor Name and Address **Concept**: Heading
Repeating and/or Reuse Rules	No

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Term (Variable)	<Local Sponsor Name>
Data Type	Text
Data (D), Value (V) or Heading (H)	D
Definition	CNEW For review purpose, see definition of the controlled terminology below The literal identifier (i.e. distinctive designation) of the sponsor's legal representative at a geographical region within which the sponsor has no legal presence.
User Guidance	In some countries, the clinical trial Sponsor may be the local affiliate company (or designee). In such cases, indicate this in the Local Sponsor Name and Address Field.
Conformance	Optional
Cardinality	One to one; One to Sponsor Name and Address; Many to Sponsor Name
Relationship content from ToC representing the protocol hierarchy	Title Page
Value	Text
Business rules	**Value Allowed**: Yes **Relationship**: Heading, Sponsor Name and Address; Sponsor Name; Country **Concept**: CNEW
Repeating and/or Reuse Rules	Yes, repeatable for each Local Sponsor Name

52

Term (Variable)	<Local Sponsor Address>
Data Type	Text
Data (D), Value (V) or Heading (H)	D
Definition	CNEW For review purpose, see definition of the controlled terminology below The legally registered address of the sponsor's legal representative at a geographical region within which the sponsor has no legal presence.
User Guidance	In some countries, the clinical trial Sponsor may be the local affiliate company (or designee). In such cases, indicate this in the Sponsor Local Name and Address Field.
Conformance	Optional
Cardinality	One to one; One to Local Sponsor; One to Country
Relationship content from ToC representing the protocol hierarchy	Title page

Value	Text
Business rules	**Value Allowed**: Yes **Relationship**: Heading, Local Sponsor, Country **Concept**: CNEW
Repeating and/or Reuse Rules	No

53

Term (Variable)	Device Manufacturer Name and Address:
Data Type	Text
Data (D), Value (V) or Heading (H)	H
Definition	Heading
User Guidance	N/A
Conformance	Optional
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	Title Page
Value	Device Manufacturer Name and Address:
Business rules	**Value Allowed**: No **Relationship**: Table row heading **Concept**: Heading
Repeating and/or Reuse Rules	No

54

Term (Variable)	<Device Manufacturer Name>
Data Type	Text
Data (D), Value (V) or Heading (H)	D
Definition	CNEW For review purpose, see definition of the controlled terminology below The organisation defined as being responsible for creating the device as stated on the package in which the product is supplied.
User Guidance	Manufacturer name and address information is required only for protocols that include investigational device(s) and should not be included for other protocols. Include the manufacturer address only if the manufacturer is different than the Sponsor listed above. Add additional fields as needed if multiple investigational devices will be used in the trial. Delete this line if not applicable.
Conformance	Optional
Cardinality	One to one; One to Sponsor Protocol Identifier; One to Sponsor Name
Relationship content from ToC representing the protocol hierarchy	Title Page
Value	Text
Business rules	**Value Allowed**: Yes **Relationship**: Heading; Sponsor Protocol Identifier; Sponsor Name **Concept**: CNEW
Repeating and/or Reuse Rules	Yes, repeatable for each device manufacturers

55

Term (Variable)	<Device Manufacturer Address>
Data Type	Text

Data (D), Value (V) or Heading (H)	D
Definition	CNEW For review purpose, see definition of the controlled terminology below The legally registered address of the device manufacturer.
User Guidance	Manufacturer name and address information is required only for protocols that include investigational device(s) and should not be included for other protocols. Include the manufacturer address only if the manufacturer is different than the Sponsor listed above. Add additional fields as needed if multiple investigational devices will be used in the trial. Delete this line if not applicable.
Conformance	Optional
Cardinality	One to One; One to Device Manufacturer Name
Relationship content from ToC representing the protocol hierarchy	Title Page
Value	Text
Business rules	**Value Allowed**: Yes **Relationship**: Heading; Device Manufacturing Name **Concept**: CNEW
Repeating and/or Reuse Rules	No

56

Term (Variable)	Regulatory or Clinical Trial Identifier(s):
Data Type	Text
Data (D), Value (V) or Heading (H)	H
Definition	Heading
User Guidance	N/A
Conformance	Required
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	Title Page
Value	Regulatory or Clinical Trial Identifier(s):
Business rules	**Value Allowed**: No **Relationship**: Table row heading **Concept**: Heading
Repeating and/or Reuse Rules	No

57

Term (Variable)	<EU CT Number>
Data Type	Text
Data (D), Value (V) or Heading (H)	D
Definition	CNEW For review purpose, see definition of the controlled terminology below A sequence of characters used to identify a clinical trial, as assigned by the Clinical Trials Information System (CTIS) of the European Medicines Agency.
User Guidance	Include all numbers that are applicable for the trial and available at the time of protocol or amendment finalisation. Delete prompts for numbers not available at the time of document finalisation. Delete unused fields. Add fields for “other” if more than one is needed.

Conformance	Optional
Cardinality	One to one; One to Sponsor Protocol Identifier
Relationship content from ToC representing the protocol hierarchy	Title Page
Value	Text
Business rules	**Value Allowed**: Yes; EU CT number: yyyy-5xxxxx-xx with YYYY corresponding to a year i.e. 2024 and x being an integer **Relationship**: Heading; Sponsor Protocol Identifier **Concept**: CNEW
Repeating and/or Reuse Rules	No

58

Term (Variable)	<FDA IND Number>
Data Type	Text
Data (D), Value (V) or Heading (H)	D
Definition	CNEW For review purpose, see definition of the controlled terminology below A sequence of characters used to identify a clinical trial under an Investigational New Drug (IND) application, as assigned by the US Food and Drug Administration.
User Guidance	Include all numbers that are applicable for the trial and available at the time of protocol or amendment finalisation. Delete prompts for numbers not available at the time of document finalisation. Delete unused fields. Add fields for "other" if more than one is needed.
Conformance	Optional
Cardinality	One to one; One to Sponsor Protocol Identifier;
Relationship content from ToC representing the protocol hierarchy	Title Page
Value	Text
Business rules	**Value Allowed**: Yes **Relationship**: Heading; Sponsor Protocol Identifier **Concept**: CNEW
Repeating and/or Reuse Rules	No

59

Term (Variable)	<IDE Number>
Data Type	Text
Data (D), Value (V) or Heading (H)	D
Definition	CNEW For review purpose, see definition of the controlled terminology below A sequence of characters used to identify a clinical trial under an Investigational Device Exemption (IDE) application, as assigned by the US Food and Drug Administration.
User Guidance	Include all numbers that are applicable for the trial and available at the time of protocol or amendment finalisation. Delete prompts for numbers not available at the time of document finalisation. Delete unused fields. Add fields for "other" if more than one is needed.
Conformance	Optional
Cardinality	One to one; One to Sponsor Protocol Identifier

Relationship content from ToC representing the protocol hierarchy	Title Page
Value	Text
Business rules	**Value Allowed**: Yes **Relationship**: Heading, Sponsor Protocol Identifier **Concept**: CNEW
Repeating and/or Reuse Rules	No

61

Term (Variable)	<jRCT Number>
Data Type	Text
Data (D), Value (V) or Heading (H)	D
Definition	CNEW For review purpose, see definition of the controlled terminology below A sequence of characters used to identify a clinical trial, as assigned by the Japan Registry for Clinical Trials (JRCT) of the Ministry of Health, Labour and Welfare (MHLW) in Japan.
User Guidance	Include all numbers that are applicable for the trial and available at the time of protocol or amendment finalisation. Delete prompts for numbers not available at the time of document finalisation. Delete unused fields. Add fields for "other" if more than one is needed.
Conformance	Optional
Cardinality	One to one; One to Sponsor Protocol Identifier
Relationship content from ToC representing the protocol hierarchy	Title Page
Value	Text
Business rules	**Value Allowed**: Yes **Relationship**: Heading, Sponsor Protocol Identifier **Concept**: CNEW
Repeating and/or Reuse Rules	No

62

Term (Variable)	<NCT Number>
Data Type	Text
Data (D), Value (V) or Heading (H)	D
Definition	CNEW For review purpose, see definition of the controlled terminology below

	A sequence of characters used to identify a clinical trial, as assigned by the protocol registration and results (PRS) system of the US National Library of Medicine.
User Guidance	Include all numbers that are applicable for the trial and available at the time of protocol or amendment finalisation. Delete prompts for numbers not available at the time of document finalisation. Delete unused fields. Add fields for "other" if more than one is needed.
Conformance	Optional
Cardinality	One to one; One to Sponsor Protocol Identifier
Relationship content from ToC representing the protocol hierarchy	Title Page
Value	Text
Business rules	**Value Allowed**: Yes **Relationship**: Heading, Sponsor Protocol Identifier **Concept**: CNEW
Repeating and/or Reuse Rules	No

63

Term (Variable)	<NMPA IND Number>
Data Type	Text
Data (D), Value (V) or Heading (H)	D
Definition	CNEW For review purpose, see definition of the controlled terminology below A sequence of characters used to identify a clinical trial under an Investigational New Drug (IND) application, as assigned by the Chinese National Medicinal Products Administration (NMPA).
User Guidance	Include all numbers that are applicable for the trial and available at the time of protocol or amendment finalisation. Delete prompts for numbers not available at the time of document finalisation. Delete unused fields. Add fields for "other" if more than one is needed.
Conformance	Optional
Cardinality	One to one; One to Sponsor Protocol Identifier
Relationship content from ToC representing the protocol hierarchy	Title Page
Value	Text
Business rules	**Value Allowed**: Yes **Relationship**: Heading; Sponsor Protocol Identifier **Concept**: CNEW
Repeating and/or Reuse Rules	No

64

Term (Variable)	<WHO/UTN Number>
Data Type	Text
Data (D), Value (V) or Heading (H)	D
Definition	CNEW For review purpose, see definition of the controlled terminology below A sequence of characters used to identify a clinical trial, as assigned by the World Health Organisation's International Clinical Trial's Registry Platform (ICTRP).

User Guidance	Include all numbers that are applicable for the trial and available at the time of protocol or amendment finalisation. Delete prompts for numbers not available at the time of document finalisation. Delete unused fields. Add fields for “other” if more than one is needed.
Conformance	Optional
Cardinality	One to one; One to Sponsor Protocol Identifier
Relationship content from ToC representing the protocol hierarchy	Title Page
Value	UTN/WHO: Uxxxx-xxxx-xxxx with X being an integer
Business rules	**Value Allowed**: Yes; **Relationship**: Heading; Sponsor Protocol Identifier; **Concept**: CNEW
Repeating and/or Reuse Rules	No

65

Term (Variable)	<Other Regulatory or Clinical Trial Identifier>
Data Type	Text
Data (D), Value (V) or Heading (H)	D
Definition	CNEW For review purpose, see definition of the controlled terminology below A sequence of characters used to identify a clinical trial, that is different than the one(s) previously specified or mentioned.
User Guidance	Include allidentifiers that are applicable for the trial and available at the time of protocol or amendment finalisation. Delete prompts for identifiersnot available at the time of document finalisation. Delete unused fields. Add fields for “other” if more than one is needed.
Conformance	Optional
Cardinality	One to one; One to Sponsor Protocol Identifier
Relationship content from ToC representing the protocol hierarchy	Title Page
Value	Text
Business rules	**Value Allowed**: Yes **Relationship**: Heading, Sponsor Protocol Identifier**Concept**: CNEW
Repeating and/or Reuse Rules	Yes, repeatable for each regulatory agency identifier

66

Term (Variable)	Sponsor Approval:
Data Type	Text
Data (D), Value (V) or Heading (H)	H
Definition	Heading
User Guidance	N/A
Conformance	Required
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	Title page
Value	Sponsor Approval:
Business rules	**Value Allowed**: No **Relationship**: Table row heading

	Concept: Heading
Repeating and/or Reuse Rules	No

67

Term (Variable)	[<Approval Date> or <State location where Information can be found>]
Data Type	Valid Value
Data (D), Value (V) or Heading (H)	V
Definition	CNEW For review purpose, see definition of the controlled terminology below The date that the sponsor approved the current version of the protocol, or the physical or virtual location of the date on which the sponsor approved the current version of the protocol.
User Guidance	All versions should be uniquely identifiable.
Conformance	Required
Cardinality	One to one; One to Sponsor Protocol Identifier; One to Original Protocol One to Amendment Identifier
Relationship content from ToC representing the protocol hierarchy	Title Page
Value	Sponsor Approval Date (C132352) Location of Sponsor Approval Date (CNEW)
Business rules	**Value Allowed**: Yes **Relationship**: Heading, Sponsor Protocol Identifier, Protocol Amendment **Concept**: CNEW
Repeating and/or Reuse Rules	Yes, reuse to approval date in Section 12.3

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NCI C-Code	M11 Preferred Term	Draft Definition
CNEW	ICH M11 Sponsor Approval Response	A terminology value set relevant to the sponsor approval responses within the ICH M11 Protocol model.
C132352	Sponsor Approval Date	The date that the sponsor approved the current version of the protocol.
CNEW	Location of Sponsor Approval Date	The physical or virtual location of the date on which the sponsor approved the current version of the protocol.

69

Term (Variable)	Sponsor Signatory
Data Type	Text
Data (D), Value (V) or Heading (H)	H
Definition	Heading
User Guidance	N/A
Conformance	Required
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	Title Page
Value	Sponsor Signatory
Business rules	**Value Allowed**: No **Relationship**: Heading **Concept**: Heading

Repeating and/or Reuse Rules	No

70

Term (Variable)	[{<sponsor signature block (name and title of sponsor signatory and signature date)>} or {This protocol was approved via <describe method>}]
Data Type	Valid Value
Data (D), Value (V) or Heading (H)	V
Definition	CNEW For review purpose, see definition of the controlled terminology below A block of text containing the name and signature of the sponsor's signatory, along with a signature date, or a statement on behalf of the sponsor that describes the method of protocol approval.
User Guidance	Include either the Sponsor signature or the statement below.
Conformance	Optional
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	Title Page
Value	Sponsor Signature Block (CNEW) OR Sponsor Protocol Approval Statement (CNEW)
Business rules	**Value Allowed**: Yes **Relationship**: Heading **Concept**: CNEW
Repeating and/or Reuse Rules	No

71

NCI C-Code	M11 Preferred Term	Draft Definition
CNEW	ICH M11 Sponsor Signatory Response	A terminology value set relevant to the sponsor signatory responses within the ICH M11 Protocol model.
CNEW	Sponsor Signature Block	A block of text containing the name and signature of the sponsor's signatory, along with the signature date.
CNEW	Sponsor Protocol Approval Statement	A statement that the protocol was approved by a method as described. This protocol was approved via <describe method>

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Term (Variable)	<Describe Method>
Data Type	Text
Data (D), Value (V) or Heading (H)	D
Definition	CNEW For review purpose, see definition of the controlled terminology below The narrative text describing the technique used to approve the protocol.
User Guidance	Include either the Sponsor signature or the statement below.
Conformance	Conditional if Sponsor Protocol Approval Statement
Cardinality	One to Sponsor Protocol Approval Statement
Relationship content from ToC representing the protocol hierarchy	Title Page
Value	Text
Business rules	**Value Allowed**: Yes **Relationship**: Sponsor Protocol Approval Statement

	Concept: CNEW
Repeating and/or Reuse Rules	No

73

Term (Variable)	Medical Expert Contact:
Data Type	Text
Data (D), Value (V) or Heading (H)	H
Definition	Heading
User Guidance	N/A
Conformance	Optional
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	Title Page
Value	Medical Expert Contact:
Business rules	**Value Allowed**: No **Relationship**: Heading **Concept**: Heading
Repeating and/or Reuse Rules	No

74

Term (Variable)	<contact information for Medical Expert (as designated by sponsor) or state location where information can be found>
Data Type	Text
Data (D), Value (V) or Heading (H)	D
Definition	CNEW For review purpose, see definition of the controlled terminology below The contact information for the sponsor's representative who can advise on specific trial-related medical questions or problems.
User Guidance	N/A
Conformance	Optional
Cardinality	One to one; One to Sponsor Protocol Identifier
Relationship content from ToC representing the protocol hierarchy	Title Page
Value	Text
Business rules	**Value Allowed**: Yes **Relationship**: Medical Expert Contact Response **Concept**: CNEW
Repeating and/or Reuse Rules	No

75

Term (Variable)	Amendment Details
Data Type	Text
Data (D), Value (V) or Heading (H)	H
Definition	Heading
User Guidance	N/A
Conformance	Required
Cardinality	One to one

Relationship content from ToC representing the protocol hierarchy	Amendment Details
Value	Amendment Details
Business rules	**Value Allowed**: No **Relationship**: Heading **Concept**: Heading
Repeating and/or Reuse Rules	No

76

Term (Variable)	Amendment Details
Data Type	Valid Value
Data (D), Value (V) or Heading (H)	V
Definition	CNEW For review purpose, see definition of the controlled terminology below A written message within the study protocol that describes the amendment details, especially as to whether the protocol has been amended previously.
User Guidance	Choose the applicable statement below. For an original protocol that has not been amended, retain the first sentence below and delete the remainder of this entire section. {Not applicable. This protocol has not been amended.} Or include the below as applicable. {This protocol has been amended previously. Details of prior amendments are presented in Section 12.3 Prior Protocol Amendment(s).}
Conformance	Required
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	Amendment Details
Value	Not applicable. This protocol has not been amended. (CNEW)Or This is the first protocol amendment (CNEW) OR This protocol has been amended previously. Details of prior amendments are presented in Section 12.3 Prior Protocol Amendment(s). (CNEW)
Business rules	**Value Allowed**: Yes **Relationship**: Heading **Concept**: CNEW
Repeating and/or Reuse Rules	No

77

NCI C-Code	**M11 Preferred Term**	**Draft Definition**
CNEW	ICH M11 Amendment Details Statement Response	A terminology value set relevant to the amendment details statement responses within the ICH M11 Protocol model.
CNEW	Not applicable. This protocol has not been amended.	Not applicable. This protocol has not been amended.

CNEW	This protocol has been amended previously. Details of prior amendments are presented in Prior Protocol Amendment(s).	This protocol has been amended previously. Details of prior amendments are presented in Prior Protocol Amendment(s).

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Data Element Name	Template Location	NCI C-code	M11 Preferred Term	Synonym(s)	Draft Definition
Amendment Details; Prior Protocol Amendment(s)	Amendment Details	CNEW	Not applicable. This protocol has not been amended.		Not applicable. This protocol has not been amended.
Amendment Details; Prior Protocol Amendment(s)	Amendment Details; 12.3 Prior Protocol Amendments	CNEW	Not applicable. This is the first protocol amendment.		Not applicable. This is the first protocol amendment.
Amendment Details; Prior Protocol Amendment(s)	Amendment Details; 12.3 Prior Protocol Amendments	CNEW	This protocol has been amended previously. Details of prior amendments are presented in Prior Protocol Amendment(s).		This protocol has been amended previously. Details of prior amendments are presented in Prior Protocol Amendment(s).

79

Term (Variable)	{Current Amendment}
Data Type	Text
Data (D), Value (V) or Heading (H)	H
Definition	Heading
User Guidance	N/A
Conformance	Conditional: If Protocol is Original = No
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	Amendment Details
Value	Current Amendment
Business rules	**Value Allowed**: No **Relationship**: Heading **Concept**: Heading
Repeating and/or Reuse Rules	No

80

Term (Variable)	The table below describes the current amendment
Data Type	Text
Data (D), Value (V) or Heading (H)	D
Definition	N/A
User Guidance	N/A

Conformance	Optional
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	Amendment Details
Value	Universal Text
Business rules	**Value Allowed**: No **Relationship**: Current Amendment **Concept**: Required text
Repeating and/or Reuse Rules	No

81

Term (Variable)	Approximate <(#/%)> Enrolled at Time of Sponsor Approval:
Data Type	Text
Data (D), Value (V) or Heading (H)	H
Definition	Heading
User Guidance	N/A
Conformance	Optional
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	Amendment Details
Value	Approximate # enrolled at Time of Sponsor Approval or Approximate % enrolled at Time of Sponsor Approval
Business rules	**Value Allowed**: No **Relationship**: Table row heading **Concept**: Heading
Repeating and/or Reuse Rules	No

82

Term (Variable)	Approximately <#/%> enrolled <Globally/Locally/by Cohort>
Data Type	Text
Data (D), Value (V) or Heading (H)	D
Definition	C68846 CNEW For review purpose, see definition of the controlled terminology below The numeric value (expressed as an absolute value or percentage) for the estimated number of participants enrolled at the time of the protocol amendment.
User Guidance	Enter the approximate number or percentage of participants enrolled as a percentage of the expected total. If the number of expected participants is changing as a result of the current amendment, use the updated number of expected participants to estimate the current per cent of enrollment. Estimates are adequate, as precise enrollment figures will likely be changing while an amendment is being prepared. • For a global or single-country amendment, provide the estimated total enrollment at the time of the Sponsor approved the amendment. • For global amendments providing (or consolidating) only country/region-specific requirements, list approximate local enrollment (total or percentage) at the time of the amendment and select "locally".

	• If consolidating a series of local amendments, the status of all the relevant locations can be listed For a country/regional amendment, provide the estimated local or regional enrollment at the time the Sponsor approved the amendment.
Conformance	Optional
Cardinality	One to one; One to amendment number
Relationship content from ToC representing the protocol hierarchy	Amendment Details
Value	Approximate <#/%> enrolled <Globally/Locally/by Cohort>
Business rules	**Value Allowed**: Yes **Relationship**: Statement **Concept**: C68846, CNEW
Repeating and/or Reuse Rules	Yes, reuse to Section 12.3

83

Term (Variable)	Number or %
Data Type	Number
Data (D), Value (V) or Heading (H)	D
Definition	CNEW For review purpose, see definition of the controlled terminology below The numeric value (expressed as an absolute value or percentage) for the estimated number of participants enrolled at the time of the protocol amendment.
User Guidance	Enter the approximate number or percentage of participants enrolled as a percentage of the expected total. If the number of expected participants is changing as a result of the current amendment, use the updated number of expected participants to estimate the current per cent of enrollment. Estimates are adequate, as precise enrollment figures will likely be changing while an amendment is being prepared. • For a global or single-country amendment, provide the estimated total enrollment at the time of the Sponsor approved the amendment. • For global amendments providing (or consolidating) only country/region-specific requirements, list approximate local enrollment (total or percentage) at the time of the amendment and select "locally". • If consolidating a series of local amendments, the status of all the relevant locations can be listed For a country/regional amendment, provide the estimated local or regional enrollment at the time the Sponsor approved the amendment.
Conformance	Conditional: if Original Protocol =No
Cardinality	One to Amendment Number
Relationship content from ToC representing the protocol hierarchy	Amendment Details
Value	Integer for Number or one decimal point for percent
Business rules	**Value Allowed**: Yes **Relationship**: Table Row Heading, Statement **Concept**: CNEW
Repeating and/or Reuse Rules	Yes, reuse to section 12.3

84

Term (Variable)	Amendment Scope Enrolment Description
Data Type	Valid Value

Data (D), Value (V) or Heading (H)	V or D
Definition	CNEW For review purpose, see definition of the controlled terminology below The enrollment description as to whether the amendment scope applies globally, locally, or per cohort across the trial.
User Guidance	Enter the approximate number or percentage of participants enrolled as a percentage of the expected total. If the number of expected participants is changing as a result of the current amendment, use the updated number of expected participants to estimate the current per cent of enrollment. Estimates are adequate, as precise enrollment figures will likely be changing while an amendment is being prepared. • For a global or single-country amendment, provide the estimated total enrollment at the time of the Sponsor approved the amendment. • For global amendments providing (or consolidating) only country/region-specific requirements, list approximate local enrollment (total or percentage) at the time of the amendment and select "locally". • If consolidating a series of local amendments, the status of all the relevant locations can be listed For a country/regional amendment, provide the estimated local or regional enrollment at the time the Sponsor approved the amendment.
Conformance	Conditional: if Original Protocol =No
Cardinality	One to Amendment Number
Relationship content from ToC representing the protocol hierarchy	Amendment Details
Value	Globally (C68846), Locally (CNEW), Cohort (CNEW)
Business rules	**Value Allowed**: Yes **Relationship**: Statement **Concept**: CNEW
Repeating and/or Reuse Rules	Yes, reuse to section 12.3

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NCI C-Code	M11 Preferred Term	Draft Definition
CNEW	Approximate Enrolled At Time of Sponsor Approval Scope	A terminology value set relevant to the responses for the approximate enrollment at time of sponsor approval scope within the ICH M11 Protocol model.
C68846	Globally	Covering or affecting the whole of a system.
CNEW	Locally	Covering or affecting a portion of the system.
CNEW	Cohort	Covering or affecting a cohort of individuals.

86

Term (Variable)	{Reason(s) for Amendment:}
Data Type	Text
Data (D), Value (V) or Heading (H)	H
Definition	Heading
User Guidance	N/A
Conformance	Conditional : If Original Protocol = No
Cardinality	One to one; Amendment Number
Relationship content from ToC representing the protocol hierarchy	Amendment Details

Value	Reason(s) for Amendment:
Business rules	**Value Allowed**: No **Relationship**: Table row heading **Concept**: Heading
Repeating and/or Reuse Rules	No

87

Term (Variable)	Primary:
Data Type	Text
Data (D), Value (V) or Heading (H)	H
Definition	Heading
User Guidance	N/A
Conformance	Conditional: If Original Protocol = No
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	Amendment Details
Value	Primary:
Business rules	**Value Allowed**: No **Relationship**: Table Column Heading **Concept**: Heading
Repeating and/or Reuse Rules	No

88

Term (Variable)	{[Primary Reason for Amendment]}
Data Type	Valid Value
Data (D), Value (V) or Heading (H)	V
Definition	CNEW For review purpose, see definition of the controlled terminology below The rationale of greatest importance for the protocol amendment.
User Guidance	Choose from the available categories as the primary reason and secondary reason(s) for the amendment. Select the closest match among the choices. Changes to primary estimand, endpoints, or related measures should be listed as a change of strategy. If none of the choices apply, choose "other" and provide a description. If no secondary reason, indicate "not applicable" for the secondary reason.
Conformance	Conditional : if the protocol is=No
Cardinality	One to Amendment Details
Relationship content from ToC representing the protocol hierarchy	Amendment Details
Value	• Regulatory agency request to amend (CNEW) • New regulatory guidance (CNEW) • IRB/IEC feedback (CNEW) • New safety information available (CNEW) • Manufacturing change (NEW) • IMP addition (CNEW) • Change in strategy (CNEW) • Change in standard of care (CNEW) • New data available (other than safety data) (CNEW) • Investigator/site feedback (CNEW)

	• Recruitment difficulty (CNEW) • Inconsistency and/or error in the protocol (CNEW) • Protocol design error (CNEW) • Other(C17649) • Not applicable(C48660)
Business rules	**Value Allowed**: Yes **Relationship**: Heading, Sponsor Protocol Identifier, Protocol Amendment **Concept**: CNEW
Repeating and/or Reuse Rules	Yes, Multiple values can be selected except when it is Original Protocol

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NCI C-Code	M11 Preferred Term	Draft Definition
CNEW	Reason for Amendment Response	A terminology value set relevant to the primary reason for amendment responses within the ICH M11 Protocol model.
CNEW	Regulatory Agency Request To Amend	A regulatory agency has expressed a need for a change(s) to, or formal clarification of, the protocol.
CNEW	New Regulatory Guidance	A regulatory agency has published a guidance document that necessitates a change(s) to, or formal clarification of, the protocol.
CNEW	IRB/IEC Feedback	Feedback from the institutional review board or independent ethics committee necessitates a change(s) to, or formal clarification of, the protocol.
CNEW	New Safety Information Available	Previously unavailable safety data becomes available, which necessitates a change(s) to, or formal clarification of, the protocol.
CNEW	Manufacturing Change	A change to manufacturing processes of the study agents necessitates a change(s) to, or formal clarification of, the protocol.
CNEW	IMP Addition	The addition of an investigational medicinal product to a clinical trial design necessitates a change(s) to, or formal clarification of, the protocol.
CNEW	Change In Strategy	A change in the study purpose or intent of the scientific plan necessitates a change(s) to, or formal clarification of, the protocol.
CNEW	Change In Standard Of Care	A change in the standard of care necessitates a change(s) to, or formal clarification of, the protocol.
CNEW	New Data Available (Other Than Safety Data)	Previously unavailable data (other than safety data) becomes available, which necessitates a change(s) to, or formal clarification of, the protocol.
CNEW	Investigator/Site Feedback	Feedback from the investigator or study site necessitates a change(s) to, or formal clarification of, the protocol.
CNEW	Recruitment Difficulty	Challenges with participant recruitment necessitates a change(s) to, or formal clarification of, the protocol.
CNEW	Inconsistency And/Or Error In The Protocol	An error or inconsistency in the protocol necessitates a change(s) to, or formal clarification of, the protocol.
CNEW	Protocol Design Error	A protocol design error necessitates a change(s) to, or formal clarification of, a document.
C17649	Other	Different than the one(s) previously specified or mentioned.
C48660	Not Applicable	Determination of a value is not relevant in the current context.

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Term (Variable)	Other
Data Type	Text
Data (D), Value (V) or Heading (H)	H
Definition	Heading
User Guidance	N/A
Conformance	Required

Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	Amendment Details
Value	Other:
Business rules	**Value Allowed**: No **Relationship**: Selection of Other **Concept**: Heading
Repeating and/or Reuse Rules	No

91

Term (Variable)	Other description
Data Type	Text
Data (D), Value (V) or Heading (H)	D
Definition	C17649 For review purpose, see definition of the controlled terminology below Different than the one(s) previously specified or mentioned.
User Guidance	Choose from the available categories the primary reason and secondary reason(s) for the amendment. Select the closest match among the choices. Changes to primary estimand, endpoints, or related measures should be listed as a change of strategy. If none of the choices apply, choose "other" and provide a description. If no secondary reason, indicate "Not applicable" for the secondary reason.
Conformance	Conditional : if Other is selected as a Valid Value
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	Amendment Details
Value	Text
Business rules	**Value Allowed**: Yes **Relationship**: Heading, Primary reason, Sponsor Protocol Identifier, Protocol Amendment **Concept**:C17649
Repeating and/or Reuse Rules	No

92

Term (Variable)	Secondary:
Data Type	Text
Data (D), Value (V) or Heading (H)	H
Definition	Heading
User Guidance	N/A
Conformance	Conditional
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	Amendment Details
Value	Secondary:
Business rules	**Value Allowed**: No **Relationship**: Table Column Heading **Concept**: Heading
Repeating and/or Reuse Rules	No

93

Term (Variable)	{[Secondary Reason for Amendment] }
Data Type	Valid Value
Data (D), Value (V) or Heading (H)	V
Definition	CNEW For review purpose, see definition of the controlled terminology below Additional rationale for the protocol amendment that is not considered the primary rationale.
User Guidance	Choose from the available categories as the primary reason and secondary reason(s) for the amendment. Select the closest match among the choices. Changes to primary estimand, endpoints, or related measures should be listed as a change of strategy. If none of the choices apply, choose "other" and provide a description. If no secondary reason, indicate "not applicable" for the secondary reason.
Conformance	Conditional If Protocol Original = No
Cardinality	One to one; One to Protocol Identifier; One to Amendment Identifier
Relationship content from ToC representing the protocol hierarchy	Amendment Details
Value	• Regulatory agency request to amend (CNEW) • New regulatory guidance (CNEW) • IRB/IEC feedback (CNEW) • New safety information available (CNEW) • Manufacturing change (CNEW) • IMP addition (CNEW) • Change in strategy (CNEW) • Change in standard of care (CNEW) • New data available (other than safety data) (CNEW) • Investigator/site feedback (CNEW) • Recruitment difficulty (CNEW) • Inconsistency and/or error in the protocol (CNEW) • Protocol design error (CNEW) • Other(C17649) • Not applicable(C48660)
Business rules	**Value Allowed**: Yes **Relationship**: Heading, Sponsor Protocol Identifier, Protocol Amendment **Concept**: CNEW
Repeating and/or Reuse Rules	Yes, Multiple accepted except for the Original

94

NCI C-Code	M11 Preferred Term	Draft Definition
CNEW	Reason for Amendment Response	A terminology value set relevant to the secondary reason for amendment responses within the ICH M11 Protocol model.
CNEW	Regulatory Agency Request To Amend	A regulatory agency has expressed a need for a change(s) to, or formal clarification of, the protocol.
CNEW	New Regulatory Guidance	A regulatory agency has published a guidance document that necessitates a change(s) to, or formal clarification of, the protocol.
CNEW	IRB/IEC Feedback	Feedback from the institutional review board or independent ethics committee necessitates a change(s) to, or formal clarification of, the protocol.

CNEW	New Safety Information Available	Previously unavailable safety data becomes available, which necessitates a change(s) to, or formal clarification of, the protocol.
CNEW	Manufacturing Change	A change to manufacturing processes of the study agents necessitates a change(s) to, or formal clarification of, the protocol.
CNEW	IMP Addition	The addition of an investigational medicinal product to a clinical trial design necessitates a change(s) to, or formal clarification of, the protocol.
CNEW	Change In Strategy	A change in the study purpose or intent of the scientific plan necessitates a change(s) to, or formal clarification of, the protocol.
CNEW	Change In Standard Of Care	A change in the standard of care necessitates a change(s) to, or formal clarification of, the protocol.
CNEW	New Data Available (Other Than Safety Data)	Previously unavailable data (other than safety data) becomes available, which necessitates a change(s) to, or formal clarification of, the protocol.
CNEW	Investigator/Site Feedback	Feedback from the investigator or study site necessitates a change(s) to, or formal clarification of, the protocol.
CNEW	Recruitment Difficulty	Challenges with participant recruitment necessitates a change(s) to, or formal clarification of, the protocol.
CNEW	Inconsistency And/Or Error In The Protocol	An error or inconsistency in the protocol necessitates a change(s) to, or formal clarification of, the protocol.
CNEW	Protocol Design Error	A protocol design error necessitates a change(s) to, or formal clarification of, a document.
C17649	Other	Different than the one(s) previously specified or mentioned.
C48660	Not Applicable	Determination of a value is not relevant in the current context.

95

Term (Variable)	Other
Data Type	Text
Data (D), Value (V) or Heading (H)	H
Definition	Heading
User Guidance	N/A
Conformance	Conditional
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	Amendment Details
Value	Other:
Business rules	**Value Allowed**: No **Relationship**: Selection of Other **Concept**: Heading
Repeating and/or Reuse Rules	No

96

Term (Variable)	Other description
Data Type	Text
Data (D), Value (V) or Heading (H)	D
Definition	C17649 For review purpose, see definition of the controlled terminology below Different than the one(s) previously specified or mentioned.

User Guidance	Choose from the available categories as the primary reason and secondary reason(s) for the amendment. Select the closest match among the choices. Changes to primary estimand, endpoints, or related measures should be listed as a change of strategy. If none of the choices apply, choose "other" and provide a description. If no secondary reason, indicate "not applicable" for the secondary reason.
Conformance	Conditional if Other is selected as a Valid Value
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	Amendment Details
Value	Text
Business rules	**Value Allowed**: Yes **Relationship**: Heading, Secondary reason, Protocol Identifier, Protocol Amendment **Concept**:C17649
Repeating and/or Reuse Rules	No

97

Term (Variable)	{Amendment Summary:}
Data Type	Text
Data (D), Value (V) or Heading (H)	H
Definition	Heading
User Guidance	N/A
Conformance	Conditional: if original protocol =no
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	Amendment Details
Value	Amendment Summary:
Business rules	**Value Allowed**: No **Relationship**: Amendment details, Amendment Identifier **Concept**: Heading
Repeating and/or Reuse Rules	No

98

Term (Variable)	{<Amendment Summary>}
Data Type	Text
Data (D), Value (V) or Heading (H)	D
Definition	CNEW For review purpose, see definition of the controlled terminology below A short narrative representation describing the changes introduced in the current version of the protocol.
User Guidance	Describe key changes briefly. Changes which are included in the amendment but unrelated to the key changes do not need to be described here.
Conformance	Conditional: if there is an amendment
Cardinality	One to Amendment identifier
Relationship content from ToC representing the protocol hierarchy	Amendment Details
Value	Text

Business rules	**Value Allowed**: Yes **Relationship**: Amendment Details; Amendment Identifier, Sponsor Protocol Identifier **Concept**: CNEW
Repeating and/or Reuse Rules	No

99

Term (Variable)	{Is this amendment likely to have a substantial impact on the safety or rights of the participants?}
Data Type	Text
Data (D), Value (V) or Heading (H)	H
Definition	Heading
User Guidance	N/A
Conformance	Conditional: if there is an amendment
Cardinality	One to one amendment identifier
Relationship content from ToC representing the protocol hierarchy	Amendment Details
Value	Is this amendment likely to have a substantial impact on the safety or rights of the participants?
Business rules	**Value Allowed**: No **Relationship**: Amendment Details **Concept**: Heading
Repeating and/or Reuse Rules	No

100

Term (Variable)	[Yes/No]
Data Type	Valid Value
Data (D), Value (V) or Heading (H)	V
Definition	CNEW For review purpose, see definition of the controlled terminology below An indication as to whether the amendment likely to have a substantial impact on the safety or rights of the participants.
User Guidance	N/A
Conformance	Conditional If there is an amendment
Cardinality	One to one; One to Amendment Identifier; One to Sponsor Protocol Identifier
Relationship content from ToC representing the protocol hierarchy	Amendment Details
Value	Yes (C49488), No (C49487)
Business rules	**Value Allowed**: Yes **Relationship**: Amendment Details, Amendment Identifier, Sponsor Protocol Identifier **Concept**: CNEW
Repeating and/or Reuse Rules	No

101

NCI C-Code	M11 Preferred Term	Draft Definition
C66742	NY	A term that is used to indicate a question with permissible values of yes/no/unknown/not applicable.

C49487	No	The non-affirmative response to a question.
C49488	Yes	The affirmative response to a question.

102

Term (Variable)	{If yes, briefly explain}
Data Type	Text
Data (D), Value (V) or Heading (H)	D
Definition	CNEW For review purpose, see definition of the controlled terminology below A short descriptive account of any substantial impacts on the safety or rights of the participants due to the protocol amendment.
User Guidance	Briefly Explain Substantial Impact On Safety
Conformance	Conditional: if there is an amendment and If the "Is this amendment likely to have a substantial impact on the safety or rights of the participants? " is yes
Cardinality	One to one Amendment Identifier, Is this amendment likely to have a substantial impact on the safety or rights of the participants? Response when Yes
Relationship content from ToC representing the protocol hierarchy	Amendment Details
Value	Text
Business rules	**Value Allowed**: Yes **Relationship**: Amendment Details, Amendment Identifier, Sponsor Protocol Identifier When the value is yes there is a text response for explanation **Concept**: CNEW
Repeating and/or Reuse Rules	No

103

Term (Variable)	{Is this amendment likely to have a substantial impact on the reliability and robustness of the data generated in the clinical trial?}
Data Type	Text
Data (D), Value (V) or Heading (H)	H
Definition	Heading
User Guidance	N/A
Conformance	Conditional: If there is an amendment
Cardinality	One to amendment details, One to amendment identifier, Sponsor Protocol Identifier
Relationship content from ToC representing the protocol hierarchy	Amendment Details
Value	Is this amendment likely to have a substantial impact on the reliability and robustness of the data generated in the clinical trial?
Business rules	**Value Allowed**: No **Relationship**: Amendment Details, Sponsor Protocol Identifier **Concept**: Heading
Repeating and/or Reuse Rules	No

104

Term (Variable)	[Yes/No]
Data Type	Valid Value

Data (D), Value (V) or Heading (H)	V
Definition	CNEW For review purpose, see definition of the controlled terminology below An indication as to whether the amendment likely to have a substantial impact on the reliability and robustness of the data generated in the clinical trial.
User Guidance	N/A
Conformance	Conditional : if there is an amendment
Cardinality	One to one; One to Amendment Identifier; One to Sponsor Protocol Identifier
Relationship content from ToC representing the protocol hierarchy	Amendment Details
Value	Yes (C49488), No (C49487)
Business rules	**Value Allowed**: Yes **Relationship**: Amendment Details, Amendment Identifier, Sponsor Protocol Identifier **Concept**: CNEW
Repeating and/or Reuse Rules	No

105

NCI C-Code	M11 Preferred Term	Draft Definition
C66742	NY	A term that is used to indicate a question with permissible values of yes/no/unknown/not applicable.
C49487	No	The non-affirmative response to a question.
C49488	Yes	The affirmative response to a question.

106

Term (Variable)	{If yes, briefly explain}
Data Type	Text
Data (D), Value (V) or Heading (H)	D
Definition	CNEW For review purpose, see definition of the controlled terminology below A short descriptive account of any substantial impacts on the reliability and robustness of the data generated in the clinical trial due to the protocol amendment.
User Guidance	Briefly Explain Substantial Impact on Data
Conformance	Conditional: if there is an amendment and if the answer to "Is this amendment likely to have a substantial impact on the reliability and robustness of the data generated in the clinical trial?" is yes
Cardinality	One to amendment identifier
Relationship content from ToC representing the protocol hierarchy	Amendment Details
Value	Text
Business rules	**Value Allowed**: Yes **Relationship**: Amendment Details, Amendment Identifier, Sponsor Protocol Identifier When the value is yes there is a text response for explanation **Concept**: CNEW

Repeating and/or Reuse Rules	No

107

Term (Variable)	{Overview of Changes in the Current Amendment:}
Data Type	Text
Data (D), Value (V) or Heading (H)	H
Definition	Heading
User Guidance	Instructions for the Overview of Changes: • If an Overview of Changes already exists from a prior amendment, move it to Section 12.3 Prior Protocol Amendment(s), and populate a clean overview table for the current amendment. • List the changes that apply to the current amendment. Provide a brief description of the change(s) and a concise scientific rationale for specific changes (e.g., change to inclusion/exclusion criteria). • If the same change affects multiple parts of the protocol, it is acceptable to list multiple locations in the right column. • Table can be sorted in any order preferred by the sponsor. • Minor edits such as clarifications and corrections to typographical errors do not need to be itemised in this table. • The changes in the table do not need to be detailed in revision marks, as these can be provided in a separate supporting document. Tabular presentation is common but not required. The page can be changed to landscape orientation if necessary.
Conformance	Conditional : If there is an amendment
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	Amendment Details
Value	Overview of Changes in the Current Amendment:
Business rules	**Value Allowed**: No **Relationship**: Amendment Details **Concept**: Heading
Repeating and/or Reuse Rules	No

108

Term (Variable)	{Description of Change}
Data Type	Text
Data (D), Value (V) or Heading (H)	H
Definition	Heading
User Guidance	N/A
Conformance	Conditional: if there is an amendment
Cardinality	One to many
Relationship content from ToC representing the protocol hierarchy	Amendment Details
Value	Description of Change
Business rules	**Value Allowed**: No **Relationship**: Table Column Heading, Amendment Details **Concept**: Heading
Repeating and/or Reuse Rules	No

109

Term (Variable)	<Description of Change>
Data Type	Text
Data (D), Value (V) or Heading (H)	D
Definition	CNEW For review purpose, see definition of the controlled terminology belowA narrative representation of the change introduced in the current version of the protocol.
User Guidance	N/A
Conformance	Conditional: if there is an amendment
Cardinality	One to many
Relationship content from ToC representing the protocol hierarchy	Amendment Details
Value	Text
Business rules	**Value Allowed**: Yes **Relationship**: Table Column Heading and Row; Amendment Details; Column Heading, Row Heading **Concept**: CNEW
Repeating and/or Reuse Rules	Yes, repeatable for every description of change in the amendment

110

Term (Variable)	{Brief Rationale for Change}
Data Type	Text
Data (D), Value (V) or Heading (H)	H
Definition	Heading
User Guidance	N/A
Conformance	Conditional: if there is an amendment
Cardinality	One to many
Relationship content from ToC representing the protocol hierarchy	Amendment Details
Value	Brief Rationale for Change
Business rules	**Value Allowed**: No **Relationship**: Table Column Heading **Concept**: Heading
Repeating and/or Reuse Rules	No

111

Term (Variable)	<Brief Rationale for Change>
Data Type	Text
Data (D), Value (V) or Heading (H)	D
Definition	CNEW For review purpose, see definition of the controlled terminology below The brief reason for the change introduced in the current version of the protocol.
User Guidance	N/A
Conformance	Conditional: if there is an amendment
Cardinality	One to many

Relationship content from ToC representing the protocol hierarchy	Amendment Details
Value	Text
Business rules	**Value Allowed**: Yes **Relationship**: Amendment Details; Table Column Heading Row; Description of change; Section # and Name **Concept**: CNEW
Repeating and/or Reuse Rules	Yes, repeatable for each description of change in the amendment

112

Term (Variable)	{Section # and Name}
Data Type	Text
Data (D), Value (V) or Heading (H)	H
Definition	Heading
User Guidance	N/A
Conformance	Conditional: if there is an amendment
Cardinality	One to many
Relationship content from ToC representing the protocol hierarchy	Amendment Details
Value	Section # and Name
Business rules	**Value Allowed**: No **Relationship**: Amendment Details; Description of Change; Brief Rationale for Change; Table Heading Row **Concept**: Heading
Repeating and/or Reuse Rules	No

113

Term (Variable)	<Section # and Name of Change>
Data Type	Valid Value
Data (D), Value (V) or Heading (H)	V
Definition	CNEW For review purpose, see definition of the controlled terminology below The protocol section number and name containing the change introduced in the current version of the protocol.
User Guidance	N/A
Conformance	Conditional: if there is an amendment
Cardinality	One to many Row description of change Description of Change, Rational for Amendment Change
Relationship content from ToC representing the protocol hierarchy	Amendment Details; Description of Change; Brief Rationale for Change; Table Column Heading
Value	
Business rules	**Value Allowed**: Yes **Relationship**: Amendment Details, Brief Rational; Change description; table **Concept**: CNEW
Repeating and/or Reuse Rules	Yes, repeatable for each description of change in the amendment

114

NCI C-Code	M11 Preferred Term	Draft Definition
CNEW	ICH M11 Protocol Number and Name Response	A terminology value set relevant to the protocol number and name responses within the ICH M11 Protocol model.

115

Term (Variable)	Table of Contents
Data Type	Text
Data (D), Value (V) or Heading (H)	H
Definition	Heading
User Guidance	N/A
Conformance	Required
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	Table of Contents
Value	Table of Contents
Business rules	**Value Allowed**: No **Relationship**: N/A **Concept**: N/A
Repeating and/or Reuse Rules	No

116

Term (Variable)	Table of Contents
Data Type	Word Generated Table of Contents
Data (D), Value (V) or Heading (H)	D
Definition	N/A
User Guidance	N/A
Conformance	Generated
Cardinality	N/A
Relationship content from ToC representing the protocol hierarchy	Table of Contents
Value	Text
Business rules	**Value Allowed**: Yes **Relationship**: N/A **Concept**: N/A
Repeating and/or Reuse Rules	No

117 # 1 PROTOCOL SUMMARY

Term (Variable)	1 PROTOCOL SUMMARY
Data Type	Text
Data (D), Value (V) or Heading (H)	H
Definition	Heading
User Guidance	No text is intended here (Heading only)
Conformance	Required
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	1

Value	PROTOCOL SUMMARY
Business rules	**Value Allowed**: No **Relationship**: Table of Contents **Concept**: Heading
Repeating and/or Reuse Rules	No

1.1 Protocol Synopsis

Term (Variable)	1.1 Protocol Synopsis
Data Type	Text
Data (D), Value (V) or Heading (H)	H
Definition	Heading
User Guidance	The protocol synopsis is a short summary of the key points of the trial. In order to keep the synopsis brief, cross references to full details in the main body of the protocol are acceptable. No text is intended here (heading only).
Conformance	Required
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	1.1
Value	Protocol Synopsis
Business rules	**Value Allowed**: No **Relationship**:1 PROTOCOL SUMMARY and Table of Contents **Concept**: Heading
Repeating and/or Reuse Rules	No

1.1.1 Primary and Secondary Objectives and Estimands

Term (Variable)	1.1.1 Primary and Secondary Objectives and Estimands
Data Type	Text
Data (D), Value (V) or Heading (H)	H
Definition	Heading
User Guidance	Summarise the primary and secondary objectives and any associated estimands in natural, nontechnical (layperson) language. For trials intended to estimate a treatment effect or test a hypothesis related to a treatment effect, include the primary and secondary objectives and any associated estimands using a nontechnical summary describing the objective and treatment effect of interest (estimand). For other types of trials not intended to estimate a treatment effect or test a hypothesis related to a treatment effect, define trial objectives and describe additional information relevant to the clinical question(s) of interest (e.g., the endpoint(s) associated with each objective). For trials with numerous objectives in which the description of objectives will exceed half a page, consider including the most important objectives and estimands in the synopsis and refer to Section 3 Trial Objectives and Associated Estimands, which covers the objectives and estimands in technical detail. For considerations on estimands, refer to ICH E9(R1).
Conformance	Required

Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	1.1.1
Value	Primary and Secondary Objectives and Estimands
Business rules	**Value Allowed**: No **Relationship**: 1.1 Protocol Synopsis, 1 PROTOCOL SUMMARY and Table of Contents **Concept**: Heading
Repeating and/or Reuse Rules	No

122

Term (Variable)	<Primary and Secondary Objectives and Estimands>
Data Type	Text
Data (D), Value (V) or Heading (H)	D
Definition	CNEW For review purpose, see definition of the controlled terminology below A descriptive summary of the primary and secondary objectives and their associated estimands related to the trial.
User Guidance	Summarise the primary and secondary objectives and any associated estimands in natural, nontechnical (layperson) language. For trials intended to estimate a treatment effect or test a hypothesis related to a treatment effect, include the primary and secondary objectives and any associated estimands using a nontechnical summary describing the objective and treatment effect of interest (estimand). For other types of trials not intended to estimate a treatment effect or test a hypothesis related to a treatment effect, define trial objectives and describe additional information relevant to the clinical question(s) of interest (e.g., the endpoint(s) associated with each objective). For trials with numerous objectives in which the description of objectives will exceed half a page, consider including the most important objectives and estimands in the synopsis and refer to Section 3 Trial Objectives and Associated Estimands, which covers the objectives and estimands in technical detail. For considerations on estimands, refer to ICH E9(R1).
Conformance	Required
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	1.1.1
Value	Text
Business rules	**Value Allowed**: Yes **Relationship**: 1.1.1 Primary and Secondary Objectives and Estimands **Concept**: CNEW
Repeating and/or Reuse Rules	Yes, Reuse <Primary Objective> and <Endpoint> for each Primary Objective from section 3.1, reuse <Secondary Objective> and <Endpoint> for each Secondary Objective from section 3.2.

123

124 ### 1.1.2 Overall Design

Term (Variable)	1.1.2 Overall Design
Data Type	Text

Data (D), Value (V) or Heading (H)	H
Definition	Heading
User Guidance	N/A
Conformance	Required
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	1.1.2
Value	Overall Design
Business rules	**Value Allowed**: No **Relationship**: 1.1 Protocol Synopsis, 1 PROTOCOL SUMMARY and Table of Contents **Concept**: Heading
Repeating and/or Reuse Rules	No

125

Term (Variable)	Key aspects of the trial design are summarised below.
Data Type	Universal Text
Data (D), Value (V) or Heading (H)	H
Definition	N/A
User Guidance	N/A
Conformance	Required
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	1.1.2
Value	Key aspects of the trial design are summarised below.
Business rules	**Value Allowed**: No **Relationship**: 1.1.2 Overall Design, 1.1 Protocol Synopsis, 1 PROTOCOL SUMMARY and Table of Contents **Concept**: Required sentence
Repeating and/or Reuse Rules	No

126

Term (Variable)	Intervention
Data Type	Text
Data (D), Value (V) or Heading (H)	H
Definition	Heading
User Guidance	N/A
Conformance	Required
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	1.1.2
Value	Intervention:
Business rules	**Value Allowed**: No **Relationship**: Table Cell title **Concept**: Heading
Repeating and/or Reuse Rules	No

127

Term (Variable)	[Sponsor's Investigational Product Code(s)]
Data Type	Text
Data (D), Value (V) or Heading (H)	D
Definition	CNEW
User Guidance	N/A
Conformance	Optional Required Either Sponsor Investigational Product Code or Nonproprietary Name
Cardinality	One to one; One to Heading One to Protocol Identifier
Relationship content from ToC representing the protocol hierarchy	1.1.2
Value	Text
Business rules	**Value Allowed**: Yes **Relationship**: Row title; Sponsor Protocol Identifier **Concept**:
Repeating and/or Reuse Rules	Yes, repeatable from Title Page Sponsor Investigational Product Code(s) yes, reuse for each Investigational Product

128

Term (Variable)	[NonProprietary Name(s)]
Data Type	Text
Data (D), Value (V) or Heading (H)	D
Definition	CNEW
User Guidance	N/A
Conformance	Optional Required Either Sponsor Investigational Product Code or Nonproprietary Name
Cardinality	One to one; One to Heading One to Protocol Identifier
Relationship content from ToC representing the protocol hierarchy	1.1.2
Value	Text
Business rules	**Value Allowed**: Yes **Relationship**: Row title; Sponsor Protocol Identifier **Concept**:
Repeating and/or Reuse Rules	Yes, repeatable from Title Page Nonproprietary Name(s) Yes, reuse for each Investigational Product

130

Term (Variable)	Intervention Model
Data Type	Text
Data (D), Value (V) or Heading (H)	H
Definition	Heading
User Guidance	N/A
Conformance	Required
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	1.1.2
Value	Intervention Model:
Business rules	**Value Allowed**: No **Relationship**: Table Cell title

	Concept: Heading
Repeating and/or Reuse Rules	No

131

Term (Variable)	[Intervention Model]
Data Type	Valid Value
Data (D), Value (V) or Heading (H)	V
Definition	C98746 For review purpose, see definition of the controlled terminology below The overall design configuration for assigning intervention to participants.
User Guidance	N/A
Conformance	Required
Cardinality	One to one; One to Heading One to Sponsor Protocol Identifier
Relationship content from ToC representing the protocol hierarchy	1.1.2
Value	Single group (C82640), parallel group (C82639), cross-over (C82637), factorial(C82638), sequential (C142568), other(C17649)
Business rules	**Value Allowed**: Yes **Relationship**: Row title; Sponsor Protocol Identifier **Concept**: C98746
Repeating and/or Reuse Rules	No

132

NCI C-Code	M11 Preferred Term	Draft Definition
C99076	INTMODEL	A terminology codelist relevant to the trial design developed to compare treatment groups.
C82637	Cross-over	Participants receive one of two or more alternative intervention(s) during the initial epoch of the study and receive other intervention(s) during the subsequent epoch(s) of the study.
C82638	Factorial	Two or more interventions, each alone or in combination, are evaluated in parallel against a control group. This study design allows for the comparison of active drug to placebo, presence of drug-drug interactions, and comparison of active drugs against each other.
C82639	Parallel Group	Participants are assigned to one of two or more treatment groups in parallel for the duration of the study.
C142568	Sequential	Groups of participants are assigned to receive interventions based on prior milestones being reached in the study.
C82640	Single Group	All trial participants are assigned to a single treatment group for the duration of the study.
C17649	Other	Different than the one(s) previously specified or mentioned.

133

Term (Variable)	Population Type
Data Type	Text
Data (D), Value (V) or Heading (H)	H
Definition	Heading
User Guidance	N/A
Conformance	Required
Cardinality	One to one

Relationship content from ToC representing the protocol hierarchy	1.1.2
Value	Population Type:
Business rules	**Value Allowed**: No **Relationship**: Table Cell title **Concept**: Heading
Repeating and/or Reuse Rules	No

134

Term (Variable)	[Population Type]
Data Type	Valid Value
Data (D), Value (V) or Heading (H)	V
Definition	CNEW For review purpose, see definition of the controlled terminology below A characterisation or classification of the trial population.
User Guidance	N/A
Conformance	Required
Cardinality	One to one; One to Heading; One to Sponsor Protocol Identifier
Relationship content from ToC representing the protocol hierarchy	1.1.2
Value	With Disease (CNEW); Without Disease (CNEW)
Business rules	**Value Allowed**: Yes **Relationship**: Row Title; Sponsor Protocol Identifier **Concept**: CNEW
Repeating and/or Reuse Rules	No

135

NCI C-Code	M11 Preferred Term	Draft Definition
CNEW	Population Type Response	A terminology value set relevant to the study population type responses within the ICH M11 Protocol model.
CNEW	With Disease	An indication that the individual or group of individuals has been diagnosed with the disease of interest or under study.
CNEW	Without Disease	An indication that the individual or group of individuals has not been diagnosed with the disease of interest or under study.

136

Term (Variable)	Control Type
Data Type	Text
Data (D), Value (V) or Heading (H)	H
Definition	Heading
User Guidance	N/A
Conformance	Required
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	1.1.2
Value	Control Type:
Business rules	**Value Allowed**: No **Relationship**: Table Row title

	Concept: Heading
Repeating and/or Reuse Rules	No

137

Term (Variable)	[Control Type]
Data Type	Valid Value
Data (D), Value (V) or Heading (H)	V
Definition	C49647 For review purpose, see definition of the controlled terminology below A characterisation or classification of the comparator against which the study intervention is evaluated.
User Guidance	Control method (for example, placebo, active comparator, low dose, historical, standard of care, sham procedure, or none [uncontrolled])
Conformance	Required
Cardinality	One to one; One to Heading; One to Sponsor Protocol Identifier
Relationship content from ToC representing the protocol hierarchy	1.1.2
Value	Placebo (C49648), active comparator(C49649), Dose Response(C120841); Different Dose or Regimen (CNEW), External (CNEW), sham procedure(C184727), or No Control(C28280)
Business rules	**Value Allowed**: Yes **Relationship**: Row Title; Sponsor Protocol Identifier **Concept**: C49647
Repeating and/or Reuse Rules	No

138

NCI C-Code	M11 Preferred Term	Draft Definition
C66785	TCNTRL	A terminology codelist relevant to a comparator against which the study treatment is evaluated.
C49649	Active Comparator	A type of control, which has a demonstrated effect, administered as a comparator to subjects in a clinical trial.
C120841	Dose Response	A type of control using different doses or regimens of the same treatment across the treatment arms.
C28280	No Control	A clinical study that lacks a comparison (i.e., a control) group.
C49648	Placebo	An inactive, identical-appearing drug or treatment that does not contain the test product.
CNEW	Different Dose or Regimen	A type of control that comprises a different dose or dosage regimen in comparison to the investigational intervention dose or dosage regimen.
CNEW	External	The use of external control data as a control arm for those studies where ethical concerns and/or underserved disease indications may make it difficult to enroll subjects/participants.
C184727	Sham Procedure	A type of negative control in which a procedure is performed that mimics the procedure under study but does not include investigational processes or components.

139

Term (Variable)	Population Diagnosis or Condition
Data Type	Text
Data (D), Value (V) or Heading (H)	H
Definition	Heading
User Guidance	N/A

Conformance	Required
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	1.1.2
Value	Population Diagnosis or Condition:
Business rules	**Value Allowed**: No **Relationship**: Table cell title **Concept**: N/A
Repeating and/or Reuse Rules	No

140

Term (Variable)	[Population Diagnosis or Condition]
Data Type	Valid Value or Text
Data (D), Value (V) or Heading (H)	V or D
Definition	C112038 For review purpose, see definition of the controlled terminology below A textual description of the condition, disease or disorder that the clinical trial is intended to investigate or address.
User Guidance	MedDRA Preferred Term(s) or indicate "other" and describe.
Conformance	Required
Cardinality	One to one; One to Heading; One to Sponsor Protocol Identifier
Relationship content from ToC representing the protocol hierarchy	1.1.2
Value	Use examples MedDRA PT or SNOMED CT: "acute lung injury," or a specific biomarker profile); indicate "N/A – Healthy" for studies in healthy volunteers
Business rules	**Value Allowed**: Yes **Relationship**: Row Title Heading; Sponsor Protocol Identifier **Concept**: C112038
Repeating and/or Reuse Rules	Yes, repeatable for each population diagnosis or condition

141

Term (Variable)	Control Description
Data Type	Text
Data (D), Value (V) or Heading (H)	H
Definition	Heading
User Guidance	N/A
Conformance	Required
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	1.1.2
Value	Control Description:
Business rules	**Value Allowed**: No **Relationship**: Table Cell title; Sponsor Protocol Identifier **Concept**: Heading
Repeating and/or Reuse Rules	No

142

Term (Variable)	{[Nonproprietary name] or [INN] or <Enter "Not applicable">}
Data Type	Text
Data (D), Value (V) or Heading (H)	D
Definition	CNEW For review purpose, see definition of the controlled terminology below A narrative representation of the comparator against which the study intervention is evaluated.
User Guidance	Further clarification: • Control description - if active comparator or low dose, pick nonproprietary name or International Nonproprietary Name, indicate "Not applicable" if not applicable
Conformance	Conditional : if there is a nonproprietary name or INN or Not applicable
Cardinality	One to many
Relationship content from ToC representing the protocol hierarchy	1.1.2
Value	[Nonproprietary name] or [INN] or <Enter "N/A">
Business rules	**Value Allowed**: Yes **Relationship**: Row title; Sponsor Protocol Identifier **Concept**: CNEW
Repeating and/or Reuse Rules	No

143

Term (Variable)	[Nonproprietary name]
Data Type	Valid Value
Data (D), Value (V) or Heading (H)	V
Definition	C97054 For review purpose, see definition of the controlled terminology below Drug name that is not protected by a trademark, usually descriptive of its chemical structure. (ICH E2B)
User Guidance	Further clarification: • Control description - if active comparator or low dose, pick nonproprietary name or International Nonproprietary Name, indicate "Not applicable" if not applicable
Conformance	Conditional: if there is a Nonproprietary name
Cardinality	One to many
Relationship content from ToC representing the protocol hierarchy	1.1.2
Value	Use for example WHO INN, USAN, JAN, XEVMPD
Business rules	**Value Allowed**: Yes **Relationship**: Row title; Control Description; Sponsor Protocol Identifier **Concept**: C97054
Repeating and/or Reuse Rules	Yes, repeatable for each nonproprietary name used as control

144

Term (Variable)	or [INN] or
Data Type	Valid Value
Data (D), Value (V) or Heading (H)	V

Definition	C142585 For review purpose, see definition of the controlled terminology below A unique name that is globally recognised and public property, which identifies pharmaceutical substances or active pharmaceutical ingredients. (After WHO)
User Guidance	Further clarification: • Control description - if active comparator or low dose, pick nonproprietary name or International Nonproprietary Name, indicate "Not applicable" if not applicable
Conformance	Conditional: if there is an INN
Cardinality	One to many
Relationship content from ToC representing the protocol hierarchy	1.1.2
Value	or use for example WHO INN, USAN, JAN, XEVMPD
Business rules	**Value Allowed**: Yes **Relationship**: Row title; Control Description; Protocol Identifier **Concept**: C142585
Repeating and/or Reuse Rules	Yes, repeatable for each INN used as control

145

Term (Variable)	<"Not applicable">
Data Type	Text
Data (D), Value (V) or Heading (H)	D
Definition	Verbatim Text
User Guidance	Further clarification: • Control description - if active comparator or low dose, pick nonproprietary name or International Nonproprietary Name, indicate "Not applicable" if not applicable
Conformance	Conditional: if there is no nonproprietary name and INN
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	1.1.2
Value	N/A
Business rules	**Value Allowed**: Yes, cannot have not applicable if Nonproprietary or INN are completed **Relationship**: Row title; Control Description; Protocol Identifier **Concept**: Verbatim Text
Repeating and/or Reuse Rules	No

146

Term (Variable)	Population Age
Data Type	Text
Data (D), Value (V) or Heading (H)	H
Definition	Heading
User Guidance	N/A
Conformance	Required
Cardinality	One to two
Relationship content from ToC representing the protocol hierarchy	1.1.2

Value	Population Age:
Business rules	**Value Allowed**: No **Relationship**: Row Table cell title **Concept**: Heading
Repeating and/or Reuse Rules	No

147

Term (Variable)	Minimum
Data Type	Text
Data (D), Value (V) or Heading (H)	H
Definition	Heading
User Guidance	N/A
Conformance	Required
Cardinality	One to two; One to Sponsor Protocol Identifier
Relationship content from ToC representing the protocol hierarchy	1.1.2
Value	Minimum:
Business rules	**Value Allowed**: No **Relationship**: Population Age; Sponsor Protocol Identifier **Concept**: Heading
Repeating and/or Reuse Rules	No

148

Term (Variable)	<Minimum age>
Data Type	Number
Data (D), Value (V) or Heading (H)	D
Definition	C49693 For review purpose, see definition of the controlled terminology below The anticipated minimum age of the participants to be entered in a clinical trial.
User Guidance	Population age range - For trials in which multiple age ranges may be eligible (for example, a younger cohort and an older cohort), indicate the minimum and maximum ages for the trial overall, with an additional comment for any excluded age ranges.
Conformance	Required
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	1.1.2
Value	Integer
Business rules	**Value Allowed**: Yes **Relationship**: population age, Minimum; minimum unit of age **Concept**:C49693
Repeating and/or Reuse Rules	No

149

Term (Variable)	[units of minimum age]
Data Type	Valid Value
Data (D), Value (V) or Heading (H)	V
Definition	C50400

	For review purpose, see definition of the controlled terminology below Those units of time that are routinely used to express the age of a person.
User Guidance	Population age range - For trials in which multiple age ranges may be eligible (for example, a younger cohort and an older cohort), indicate the minimum and maximum ages for the trial overall, with an additional comment for any excluded age ranges.
Conformance	Required
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	1.1.2
Value	hour (C25529), day (C25301), weeks (C29844), months (C29846), years (C29848)
Business rules	**Value Allowed**: Yes **Relationship**: Population age; Minimum, Numeric Minimum **Concept**: C50400
Repeating and/or Reuse Rules	No

150

NCI C-Code	M11 Preferred Term	Draft Definition
CNEW	ICH M11 Units of Time	A terminology value set relevant to units of time within the ICH M11 Protocol model.
C25301	DAYS	A unit of measurement of time equal to 24 hours.
C25529	HOURS	A unit of measurement of time equal to 60 minutes.
C29846	MONTHS	One of the 12 divisions of a year as determined by a calendar. It corresponds to the unit of time of approximately to one cycle of the moon's phases, about 30 days or 4 weeks.
C29844	WEEKS	Any period of seven consecutive days.
C29848	YEARS	The period of time that it takes for Earth to make a complete revolution around the sun, approximately 365 days; a specific one year period.

151

Term (Variable)	Maximum
Data Type	Text
Data (D), Value (V) or Heading (H)	H
Definition	Heading
User Guidance	N/A
Conformance	Required
Cardinality	One to two; One to Sponsor Protocol Identifier
Relationship content from ToC representing the protocol hierarchy	1.1.2
Value	Maximum:
Business rules	**Value Allowed**: No **Relationship**: Population Age; Sponsor Protocol Identifier **Concept**: Heading
Repeating and/or Reuse Rules	No

152

Term (Variable)	<maximum age>
Data Type	Number

TextData (D), Value (V) or Heading (H)	D
Definition	C49694 For review purpose, see definition of the controlled terminology below The anticipated maximum age of the participants to be entered in a clinical trial
User Guidance	Population age range - For trials in which multiple age ranges may be eligible (for example, a younger cohort and an older cohort), indicate the minimum and maximum ages for the trial overall, with an additional comment for any excluded age ranges.
Conformance	Required
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	1.1.2
Value	Integer
Business rules	**Value Allowed**: Yes **Relationship**: population age, Maximum Age; Maximum unit of age **Concept**:C49694
Repeating and/or Reuse Rules	No

153

Term (Variable)	[units of maximum age]
Data Type	Valid Value
Data (D), Value (V) or Heading (H)	V
Definition	C50400 For review purpose, see definition of the controlled terminology below Those units of time that are routinely used to express the age of a person.
User Guidance	Population age range - For trials in which multiple age ranges may be eligible (for example, a younger cohort and an older cohort), indicate the minimum and maximum ages for the trial overall, with an additional comment for any excluded age ranges.
Conformance	Required
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	1.1.2
Value	hour (C25529), day (C25301), weeks (C29844), months (C29846), years (C29848)
Business rules	**Value Allowed**: Yes **Relationship**: Population Age; Maximum, Numeric Maximum **Concept**: C50400
Repeating and/or Reuse Rules	No

154

NCI C-Code	M11 Preferred Term	Draft Definition
CNEW	ICH M11 Units of Time	A terminology value set relevant to units of time within the ICH M11 Protocol model.
C25301	DAYS	A unit of measurement of time equal to 24 hours.
C25529	HOURS	A unit of measurement of time equal to 60 minutes.

C29846	MONTHS	One of the 12 divisions of a year as determined by a calendar. It corresponds to the unit of time of approximately to one cycle of the moon's phases, about 30 days or 4 weeks.
C29844	WEEKS	Any period of seven consecutive days.
C29848	YEARS	The period of time that it takes for Earth to make a complete revolution around the sun, approximately 365 days; a specific one year period.

155

Term (Variable)	Intervention Assignment Method
Data Type	Text
Data (D), Value (V) or Heading (H)	H
Definition	Heading
User Guidance	N/A
Conformance	Required
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	1.1.2
Value	Intervention Assignment Method:
Business rules	**Value Allowed**: No **Relationship**: Row Table cell Title **Concept**: Heading
Repeating and/or Reuse Rules	No

156

Term (Variable)	[Intervention Assignment Method]
Data Type	Valid Value
Data (D), Value (V) or Heading (H)	V
Definition	CNEW For review purpose, see definition of the controlled terminology below The process used to assign trial participants to a trial intervention or trial arm.
User Guidance	Intervention assignment method - Do NOT state block size.
Conformance	Required
Cardinality	One to one: One toSponsor Protocol Identifier
Relationship content from ToC representing the protocol hierarchy	1.1.2
Value	Randomisation (C25196), Stratification (C25689), Stratified Randomisation (CNEW), Other (C17649) or Not Applicable (C48660)
Business rules	**Value Allowed**: Yes **Relationship**: Row title identifier; Sponsor Protocol Identifiers **Concept**: CNEW
Repeating and/or Reuse Rules	No

157

NCI C-Code	M11 Preferred Term	Draft Definition
CNEW	Trial Intervention Assignment Method Response	A terminology value set relevant to the trial intervention assignment method responses within the ICH M11 Protocol model.
C25196	Randomisation	The process of assigning trial subjects to treatment or control groups using an element of chance to determine

		the assignments in order to reduce bias. NOTE: Unequal randomization is used to allocate subjects into groups at a differential rate; for example, three subjects may be assigned to a treatment group for every one assigned to the control group.
C25689	Stratification	Grouping defined by important prognostic factors measured at baseline.
CNEW	Stratified Randomisation	The process of grouping trial participants into strata according to important prognostic factors and then assigning participants within each stratum to different treatment or control groups using an element of chance and in order to reduce bias.

158

Term (Variable)	Site Distribution and Geographic Scope
Data Type	Text
Data (D), Value (V) or Heading (H)	H
Definition	Heading
User Guidance	N/A
Conformance	Required
Cardinality	One to two
Relationship content from ToC representing the protocol hierarchy	1.1.2
Value	Site Distribution and Geographic Scope:
Business rules	**Value Allowed**: No **Relationship**: Row title Heading; Site distribution; Site Geographic scope **Concept**: Heading
Repeating and/or Reuse Rules	No

159

Term (Variable)	[Site Distribution]
Data Type	Valid Value
Data (D), Value (V) or Heading (H)	V
Definition	CNEW For review purpose, see definition of the controlled terminology below An indication as to whether the occurrence applies to a single or multiple trial sites.
User Guidance	N/A
Conformance	Required
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	1.1.2
Value	single-centre (CNEW), multi-centre(CNEW)
Business rules	**Value Allowed**: Yes **Relationship**: Row Title heading; Sponsor Protocol Identifier **Concept**: CNEW
Repeating and/or Reuse Rules	No

160

NCI C-Code	M11 Preferred Term	Draft Definition

CNEW	Trial Site Distribution Response	A terminology value set relevant to the trial site distribution responses within the ICH M11 Protocol model.
CNEW	Single-Centre	A clinical study that is conducted at a single study site.
CNEW	Multicentre	A clinical trial conducted according to a single protocol but at more than one site, and therefore, carried out by more than one investigator.

161

Term (Variable)	[Site geographic scope]
Data Type	Valid Value
Data (D), Value (V) or Heading (H)	V
Definition	CNEW For review purpose, see definition of the controlled terminology below An indication as to whether the trial is taking place in one or more countries.
User Guidance	N/A
Conformance	Required
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	1.1.2
Value	Single Country (CNEW), Multiple Countries (CNEW)
Business rules	**Value Allowed**: Yes **Relationship**: Row Title Heading, Sponsor Protocol Identifier **Concept**: CNEW
Repeating and/or Reuse Rules	No

162

NCI C-Code	M11 Preferred Term	Draft Definition
CNEW	Trial Site Geographic Scope Response	A terminology value set relevant to the trial site geographic scope responses within the ICH M11 Protocol model.
CNEW	Single Country	Of, or pertaining to, an occurrence in one country.
CNEW	Multiple Countries	Of, or pertaining to, an occurrence in more than one country.

163

Term (Variable)	Adaptive Trial Design:
Data Type	Text
Data (D), Value (V) or Heading (H)	H
Definition	Heading
User Guidance	N/A
Conformance	Required
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	1.1.2
Value	Adaptive Trial Design:
Business rules	**Value Allowed**: No **Relationship**: Table row heading **Concept**: Heading
Repeating and/or Reuse Rules	No

164

Term (Variable)	[Adaptative Trial Design Indicator]
Data Type	Valid Value

Data (D), Value (V) or Heading (H)	V
Definition	CNEW For review purpose, see definition of the controlled terminology below An indication as to whether the clinical trial uses an adaptive kind of trial design, that is a clinical trial design that allows for prospectively planned modifications to one or more aspects of the design based on accumulating data from subjects in the trial.
User Guidance	N/A
Conformance	Required
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	1.1.2
Value	Yes (C49488), No(C49487)
Business rules	**Value Allowed**: Yes **Relationship**: Heading; Sponsor Protocol Identifier **Concept**: CNEW
Repeating and/or Reuse Rules	No

165

Term (Variable)	Master Protocol:
Data Type	Text
Data (D), Value (V) or Heading (H)	H
Definition	Heading
User Guidance	N/A
Conformance	Required
Cardinality	One to One
Relationship content from ToC representing the protocol hierarchy	1.1.2
Value	Master Protocol:
Business rules	**Value Allowed**: No **Relationship**: Table row heading **Concept**: Heading
Repeating and/or Reuse Rules	No

166

Term (Variable)	[Master Protocol Indicator]
Data Type	Valid Value
Data (D), Value (V) or Heading (H)	V
Definition	CNEW For review purpose, see definition of the controlled terminology below An indication as to whether this is a master protocol.
User Guidance	N/A
Conformance	Required
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	1.1.2
Value	Yes (C49488), No(C49487)

Business rules	**Value Allowed**: Yes **Relationship**: Heading Master Protocol Indicator; Sponsor Protocol Identifier **Concept**: CNEW
Repeating and/or Reuse Rules	No

167

NCI C-Code	M11 Preferred Term	Draft Definition
C66742	NY	A term that is used to indicate a question with permissible values of yes/no/unknown/not applicable.
C49487	No	The non-affirmative response to a question.
C49488	Yes	The affirmative response to a question.

168

Term (Variable)	Drug/Device Combination Product Indicator:
Data Type	Text
Data (D), Value (V) or Heading (H)	H
Definition	Heading
User Guidance	N/A
Conformance	Required
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	1.1.2
Value	Drug/Device Combination Product Indicator:
Business rules	**Value Allowed**: No **Relationship**: Table row heading **Concept**: Heading
Repeating and/or Reuse Rules	No

169

Term (Variable)	[Drug/Device Combination Product Indicator]
Data Type	Valid Value
Data (D), Value (V) or Heading (H)	V
Definition	CNEW For review purpose, see definition of the controlled terminology below An indication as to whether the clinical trial is testing a drug device combination product.
User Guidance	N/A
Conformance	Required
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	1.1.2
Value	Yes (C49488), No(C49487)
Business rules	**Value Allowed**: Yes **Relationship**: Heading Drug/Device Combination Product; Sponsor Protocol Identifier **Concept**: CNEW
Repeating and/or Reuse Rules	No

170

NCI C-Code	M11 Preferred Term	Draft Definition
C66742	NY	A term that is used to indicate a question with permissible values of yes/no/unknown/not applicable.
C49487	No	The non-affirmative response to a question.
C49488	Yes	The affirmative response to a question.

171

Term (Variable)	Number of Arms
Data Type	Text
Data (D), Value (V) or Heading (H)	H
Definition	Heading
User Guidance	N/A
Conformance	Required
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	1.1.2
Value	Number of Arms:
Business rules	**Value Allowed**: No **Relationship**: 1.1.2 Heading. Overall Design, 1.1 Protocol Synopsis, 1 PROTOCOL SUMMARY and Table of Contents **Concept**: Heading
Repeating and/or Reuse Rules	No

172

Term (Variable)	[Number of Arms]
Data Type	Number
Data (D), Value (V) or Heading (H)	D
Definition	C98771 For review purpose, see definition of the controlled terminology below The planned number of intervention groups.
User Guidance	Enter the numeric value for the number of arms in the trial. For trials with a different number of arms in different periods, populate this field based on the period with the greatest number of arms.
Conformance	Required
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	1.1.2
Value	Integer
Business rules	**Value Allowed**: Yes **Relationship**: Number of Arms, Heading; Sponsor Protocol Identifier **Concept**: C98771
Repeating and/or Reuse Rules	No

173

Term (Variable)	Trial Blind Schema
Data Type	Text
Data (D), Value (V) or Heading (H)	H
Definition	Heading

User Guidance	N/A
Conformance	Required
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	1.1.2
Value	Trial Blind Schema:
Business rules	**Value Allowed:** No **Relationship:** 1.1.2 Overall Design, 1.1 Protocol Synopsis, 1 PROTOCOL SUMMARY and Table of Contents Heading; Overall Design **Concept**: Heading
Repeating and/or Reuse Rules	No

174

Term (Variable)	[Trial Blind Schema]
Data Type	Valid Value
Data (D), Value (V) or Heading (H)	V
Definition	C49658 For review purpose, see definition of the controlled terminology below The type of experimental design used to describe the level of awareness of the study subjects and/ or study personnel as it relates to the respective intervention(s) or assessments being observed, received or administered.
User Guidance	For designs in which these details may differ in one or more trial periods, answer according to the portion of the trial in which the highest number of blinded roles occurs. Additional details can be provided in Section 6.8.3 of the protocol.
Conformance	Required
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	1.1.2
Value	Double Blind (C15228), Observer Blind (C187674), Open Label (C49659), Single Blind (C28233)
Business rules	**Value Allowed**: Yes **Relationship**: Trial Blind Schema, Heading; Protocol Sponsor Identifier **Concept**: C49658
Repeating and/or Reuse Rules	No

175

NCI C-Code	M11 Preferred Term	Draft Definition
C66735	TBLIND	A terminology codelist relevant to the type of blinding for the trial.
C15228	Double Blind	A study in which neither the subject nor the study personnel interacting with the subject or data during the study knows what intervention a subject is receiving.
C187674	Observer Blind	A study in which the study personnel who measure, record, or assess the subject do not know which intervention the subject is receiving or, in the context of observational studies, do not know the external factors to which a subject has been exposed.
C49659	Open Label	A study in which subjects and study personnel know which intervention each subject is receiving.
C28233	Single Blind	A study in which one party, either the subject or study personnel, does not know which intervention is administered to the subject.

176

Term (Variable)	Blinded roles:
Data Type	Text
Data (D), Value (V) or Heading (H)	H
Definition	Heading
User Guidance	N/A
Conformance	Required
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	1.1.2
Value	**Blinded roles:** The following roles indicated will not be made aware of the treatment group assignment during the trial:
Business rules	**Value Allowed**: No **Relationship**: 1.1.2 Heading; Overall Design , 1.1 Protocol Synopsis, 1 PROTOCOL SUMMARY and Table of Contents **Concept**: Heading
Repeating and/or Reuse Rules	No

177

Term (Variable)	[Blinded roles]
Data Type	Valid Value
Data (D), Value (V) or Heading (H)	V
Definition	CNEW For review purpose, see definition of the controlled terminology below An identifying designation assigned to a blinded individual within a clinical trial that corresponds with their function
User Guidance	"Not applicable (No blinding)" indicates an open label trial.
Conformance	Required
Cardinality	One to many
Relationship content from ToC representing the protocol hierarchy	1.1.2
Value	Participant (C142710), Care Provider (C17445), Investigator (C25936), Outcomes Assessor (CNEW), Sponsor (C70793) Not Applicable (C48660)
Business rules	**Value Allowed**: Yes, Multiple roles can be selected **Relationship**: Blinded Roles; Sponsor Protocol Identifier **Concept**: CNEW
Repeating and/or Reuse Rules	No

178

NCI C-Code	M11 Preferred Term	Draft Definition
CNEW	Trial Blinding Role	A terminology value set relevant to the trial blinding roles within the ICH M11 Protocol model.
C142710	Participant	A member of the clinical study population from whom data are being collected.
C17445	Care Provider	The primary person in charge of the care of a patient, usually a family member or a designated health care professional.
C25936	Investigator	A person responsible for the conduct of the clinical trial at a trial site. If a trial is conducted by a team of individuals at the trial site, the

		investigator is the responsible leader of the team and may be called the principal investigator.
CNEW	Outcomes Assessor	The individual who evaluates the outcome(s) of interest.
C70793	Sponsor	An individual, company, institution, or organization that takes responsibility for the initiation, management, and/or financing of a clinical study.
C48660	Not Applicable	Determination of a value is not relevant in the current context.

179

Term (Variable)	Number of participants:
Data Type	Text
Data (D), Value (V) or Heading (H)	H
Definition	Heading
User Guidance	N/A
Conformance	Required
Cardinality	One to many
Relationship content from ToC representing the protocol hierarchy	1.1.2
Value	Number of Participants:
Business rules	**Value Allowed**: No **Relationship**: 1.1.2 Overall Design , 1.1 Protocol Synopsis, 1 PROTOCOL SUMMARY and Table of Contents **Concept**: Heading
Repeating and/or Reuse Rules	No

180

Term (Variable)	[Target/Maximum]
Data Type	Valid Value
Data (D), Value (V) or Heading (H)	V
Definition	CNEW For review purpose, see definition of the controlled terminology below A characterisation or classification of the trial participant numbers as to whether the numbers reflect a target or maximum.
User Guidance	State the expected number of participants to be assigned to trial intervention/enrolled. Indicate whether the number provided is the target or maximum number of individuals to be randomly assigned to trial intervention/enrolled.
Conformance	Required
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	1.1.2
Value	A (choose Target/Maximum) of
Business rules	**Value Allowed**: Universal Text and Yes **Relationship**: Heading; Sponsor Protocol Identifier **Concept**: CNEW
Repeating and/or Reuse Rules	No

181

Term (Variable)	<Number of Participants>
Data Type	Number

Data (D), Value (V) or Heading (H)	D
Definition	C49692 For review purpose, see definition of the controlled terminology below The planned number of participant be entered in a clinical trial.
User Guidance	State the expected number of participants to be assigned to trial intervention/enrolled. Indicate whether the number provided is the target or maximum number of individuals to be randomly assigned to trial intervention/enrolled
Conformance	Required
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	1.1.2
Value	Integer; <Number of Participants> participants will be
Business rules	**Value Allowed**: Yes and Universal Text **Relationship**: beheading; Sponsor Protocol Identifiers **Concept**: C49692
Repeating and/or Reuse Rules	No

182

Term (Variable)	[randomly assigned to trial intervention/ enrolled]
Data Type	Valid Value
Data (D), Value (V) or Heading (H)	V
Definition	CNEW For review purpose, see definition of the controlled terminology below The target or maximum number of participants who have been randomly assigned to the trial intervention or enrolled in the trial.
User Guidance	State the expected number of participants to be assigned to trial intervention/enrolled. Indicate whether the number provided is the target or maximum number of individuals to be randomly assigned to trial intervention/enrolled
Conformance	Required
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	1.1.2
Value	randomly assigned to trial intervention/enrolled
Business rules	**Value Allowed**: Universal Text **Relationship**: Heading; Sponsor Protocol Identifier **Concept**: CNEW
Repeating and/or Reuse Rules	No

183

Term (Variable)	Duration
Data Type	Text
Data (D), Value (V) or Heading (H)	H
Definition	Heading
User Guidance	N/A
Conformance	Required
Cardinality	One to one

Relationship content from ToC representing the protocol hierarchy	1.1.2
Value	Duration:
Business rules	Value Allowed: No Relationship: 1.1.2 Overall Design, 1.1 Protocol Synopsis, 1 PROTOCOL SUMMARY and Table of Contents Concept: Heading
Repeating and/or Reuse Rules	No

184

Term (Variable)	Total planned duration of trial intervention for each participant:
Data Type	Universal Text
Data (D), Value (V) or Heading (H)	H
Definition	Heading
User Guidance	Select one of the two options for total planned duration of trial intervention and trial participation for each participant. Note that the total duration of trial participation should include any washout and any follow-up periods in which the participant is not receiving trial intervention. When duration will vary, provide a short explanation (e.g., “event-driven” or “adaptive design”
Conformance	Required
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	1.1.2
Value	Total planned duration of trial intervention for each participant:
Business rules	**Value Allowed**: No **Relationship**: Duration **Concept**: Heading
Repeating and/or Reuse Rules	No

185

Term (Variable)	{<total planned duration of trial intervention> [total planned duration of trial unit of time]}
Data Type	Integer, Valid value
Data (D), Value (V) or Heading (H)	D, V
Definition	Total planned duration of trial intervention CNEW Total planned duration of trial Unit of time: CNEW For review purpose, see definition of the controlled terminology below • Number: The numeric value for the planned duration of trial intervention. • Unit of time: The unit of time associated with the numeric value for the planned duration of trial intervention.
User Guidance	Select one of the two options for total planned duration of trial intervention and trial participation for each participant. Note that the total duration of trial participation should include any washout and any follow-up periods in which the participant is not receiving trial intervention. When duration will vary, provide a short explanation (e.g., “event-driven” or “adaptive design”
Conformance	Conditional: when Planned Duration of trial Intervention Number and unit of time
Cardinality	One to one

Relationship content from ToC representing the protocol hierarchy	1.1.2
Value	total planned duration of trial intervention Integer total planned duration of time unit of time days (C25301), hours (25529), months (C29846), weeks (C29844), years (C29848)
Business rules	**Value Allowed**: Yes **Relationship**: Total duration of trial intervention for each participant: **Concept**: CNEW, CNEW
Repeating and/or Reuse Rules	No

186

NCI C-Code	M11 Preferred Term	Draft Definition
CNEW	ICH M11 Units of Time	A terminology value set relevant to units of time within the ICH M11 Protocol model.
C25301	DAYS	A unit of measurement of time equal to 24 hours.
C25529	HOURS	A unit of measurement of time equal to 60 minutes.
C29846	MONTHS	One of the 12 divisions of a year as determined by a calendar. It corresponds to the unit of time of approximately to one cycle of the moon's phases, about 30 days or 4 weeks.
C29844	WEEKS	Any period of seven consecutive days.
C29848	YEARS	The period of time that it takes for Earth to make a complete revolution around the sun, approximately 365 days; a specific one year period.

187

Term (Variable)	{<alternate description of planned duration of trial intervention if duration will vary>}
Data Type	Text
Data (D), Value (V) or Heading (H)	D
Definition	CNEW For review purpose, see definition of the controlled terminology below An alternative textual narrative for the planned duration of trial intervention.
User Guidance	Select one of the two options for total planned duration of trial intervention and trial participation for each participant. Note that the total duration of trial participation should include any washout and any follow-up periods in which the participant is not receiving trial intervention. When duration will vary, provide a short explanation (e.g., “event-driven” or “adaptive design”
Conformance	Conditional: when an alternate description for planned duration of trial Intervention if the duration varies
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	1.1.2
Value	text
Business rules	**Value Allowed**: Yes **Relationship**: Total duration of trial intervention for each participant: **Concept**: CNEW
Repeating and/or Reuse Rules	No

188

Term (Variable)	Total planned duration of trial participation for each participant:
Data Type	Universal Text

Data (D), Value (V) or Heading (H)	H
Definition	Heading
User Guidance	Select one of the two options for total planned duration of trial intervention and trial participation for each participant. Note that the total duration of trial participation should include any washout and any follow-up periods in which the participant is not receiving trial intervention. When duration will vary, provide a short explanation (e.g., “event-driven” or “adaptive design”
Conformance	Required
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	1.1.2
Value	Total planned duration of trial participation for each participant:
Business rules	**Value Allowed**: No **Relationship**: Duration **Concept**: Heading
Repeating and/or Reuse Rules	No

189

Term (Variable)	{<total planned duration of trial participation> [Total planned duration of trial participation unit of time]}
Data Type	Integer, Valid value
Data (D), Value (V) or Heading (H)	D, V
Definition	Total planned duration of trial participation: CNEW Total planned duration of trial participation Unit of time: CNEW For review purpose, see definition of the controlled terminology below • Number: The numeric value for the planned duration of trial participation. • Unit of time: The unit of time associated with the numeric value for the planned duration of trial participation.
User Guidance	Select one of the two options for total planned duration of trial intervention and trial participation for each participant. Note that the total duration of trial participation should include any washout and any follow-up periods in which the participant is not receiving trial intervention. When duration will vary, provide a short explanation (e.g., “event-driven” or “adaptive design”
Conformance	Conditional: when planned duration of trial participation number and unit of time
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	1.1.2
Value	total planned duration of trial participation : Integer total planned duration of trial participation unit of time: days (C25301), hours (25529), months (C29846), weeks (C29844), years (C29848)
Business rules	**Value Allowed**: Yes **Relationship**: Total duration of trial participation for each participant: **Concept**: CNEW, CNEW
Repeating and/or Reuse Rules	No

190

NCI C-Code	M11 Preferred Term	Draft Definition

CNEW	ICH M11 Units of Time	A terminology value set relevant to units of time within the ICH M11 Protocol model.
C25301	DAYS	A unit of measurement of time equal to 24 hours.
C25529	HOURS	A unit of measurement of time equal to 60 minutes.
C29846	MONTHS	One of the 12 divisions of a year as determined by a calendar. It corresponds to the unit of time of approximately to one cycle of the moon's phases, about 30 days or 4 weeks.
C29844	WEEKS	Any period of seven consecutive days.
C29848	YEARS	The period of time that it takes for Earth to make a complete revolution around the sun, approximately 365 days; a specific one year period.

191

Term (Variable)	{<alternate description of planned duration of trial participation if duration will vary>}
Data Type	Text
Data (D), Value (V) or Heading (H)	D
Definition	CNEW For review purpose, see definition of the controlled terminology below An alternative narrative for the planned duration of trial participation.
User Guidance	Select one of the two options for total planned duration of trial intervention and trial participation for each participant. Note that the total duration of trial participation should include any washout and any follow-up periods in which the participant is not receiving trial intervention. When duration will vary, provide a short explanation (e.g., “event-driven” or “adaptive design”
Conformance	Conditional: when an alternate description for planned duration of trial participation if duration will vary
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	1.1.2
Value	Text
Business rules	**Value Allowed**: Yes **Relationship**: Total duration of planned duration of trial participation if duration will vary: **Concept**: CNEW
Repeating and/or Reuse Rules	No

192

Term (Variable)	<Additional Description of Duration>
Data Type	Text
Data (D), Value (V) or Heading (H)	D
Definition	CNEW For review purpose, see definition of the controlled terminology below A narrative clarifying information regarding the length of time an individual usage of trial intervention or planned time in a trial.
User Guidance	If necessary, include any clarifications or cross-references to details in the main body of the protocol in the optional field below.
Conformance	Optional
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	1.1.2

Value	Text
Business rules	**Value Allowed**: Yes **Relationship**: Duration **Concept**: CNEW
Repeating and/or Reuse Rules	No

193

Term (Variable)	Committees:
Data Type	Text
Data (D), Value (V) or Heading (H)	H
Definition	Heading
User Guidance	N/A
Conformance	Required
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	1.1.2
Value	Committees:
Business rules	**Value Allowed**: No **Relationship**: 1.1.2 Overall Design, 1.1 Protocol Synopsis, 1 PROTOCOL SUMMARY and Table of Contents **Concept**: Heading
Repeating and/or Reuse Rules	No

194

Term (Variable)	Independent Committees:
Data Type	Text
Data (D), Value (V) or Heading (H)	H
Definition	Heading
User Guidance	N/A
Conformance	Required
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	1.1.2
Value	Independent Committees:
Business rules	**Value Allowed**: No **Relationship**: Committees; 1.1.2 Overall Design, 1.1 Protocol Synopsis, 1 PROTOCOL SUMMARY and Table of Contents **Concept**: Heading
Repeating and/or Reuse Rules	No

195

Term (Variable)	<Independent Committees>
Data Type	Valid Value
Data (D), Value (V) or Heading (H)	V
Definition	CNEW For review purpose, see definition of the controlled terminology below An independent group of experts that has oversight over, and conducts periodic review of, specific trial activities.

User Guidance	Indicate whether any committee(s) will be reviewing data while the trial is ongoing, and the type of committee. Common examples include Data Monitoring Committee, Dose Escalation Committee, or Endpoint Adjudication Committee; describe others, if applicable. List independent committees in the space indicated. Other committees may be included in the separate space provided. Committees listed here should be fully described in Section 11.4.
Conformance	Required
Cardinality	One to many
Relationship content from ToC representing the protocol hierarchy	1.1.2
Value	Independent Data Monitoring Committee(C142578), Dose Escalation Committee(C78726), Endpoint Adjudication Committee(C78726), other (C17649), none(C41132)
Business rules	**Value Allowed**: Yes, More than one committee can be selected **Relationship**: Independent Committees **Concept**: CNEW
Repeating and/or Reuse Rules	No

196

NCI C-Code	M11 Preferred Term	Draft Definition
CNEW	Independent Committee Name Response	A terminology value set relevant to the independent committee name responses within the ICH M11 Protocol model.
C142578	Independent Data Monitoring Committee	A committee established by the sponsor to assess at intervals the progress of a clinical trial, safety data, and critical efficacy variables and recommend to the sponsor whether to continue, modify, or terminate the trial.
CNEW	Dose Escalation Committee	A type of safety monitoring committee that monitors dose escalation activities in first-in-human trials.
C78726	Endpoint Adjudication Committee	An external committee whose purpose is to evaluate study data and decide whether a study endpoint or other criterion has been met.
C17649	Other	Different than the one(s) previously specified or mentioned.
C41132	None	No person or thing, nobody, not any.

197

Term (Variable)	Other Committees:
Data Type	Text
Data (D), Value (V) or Heading (H)	H
Definition	Heading
User Guidance	N/A
Conformance	Optional
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	1.1.2
Value	Other Committees:
Business rules	**Value Allowed**: No **Relationship**: Committees, 1.1.2 Overall Design, 1.1 Protocol Synopsis, 1 PROTOCOL SUMMARY and Table of Contents **Concept**: Heading

Repeating and/or Reuse Rules	No

198

Term (Variable)	<Other Committees>
Data Type	Text
Data (D), Value (V) or Heading (H)	D
Definition	CNEW For review purpose, see definition of the controlled terminology below A committee that is different than the one(s) previously specified or mentioned.
User Guidance	Delete “Other Committees” if not applicable.
Conformance	Optional
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	1.1.2
Value	Text
Business rules	**Value Allowed**: Yes **Relationship**: Other Committees **Concept**: CNEW
Repeating and/or Reuse Rules	No

199

200 1.2 Trial Schema

Term (Variable)	1.2 Trial Schema
Data Type	Text
Data (D), Value (V) or Heading (H)	H
Definition	Heading
User Guidance	The purpose of this section is to provide a visual depiction of the trial design, orienting users of the protocol to the key features of the trial design. The schema depicts the trial arms, the flow of individual participants through the progression of trial period(s)/epochs (such as screening, washout/run-in, intervention, and key milestones [e.g., randomisation, cross-over, end of treatment]). For complex trials, additional schemas may be added to describe activities or trial periods in greater detail.
Conformance	Required
Cardinality	One to many
Relationship content from ToC representing the protocol hierarchy	1.2
Value	Trial Schema
Business rules	**Value Allowed**: No **Relationship**: 1 PROTOCOL SUMMARY and Table of Contents; **Concept**: Heading
Repeating and/or Reuse Rules	No

201

Term (Variable)	<Trial Schema>
Data Type	Image; Text
Data (D), Value (V) or Heading (H)	D

Definition	C93682 For review purpose, see definition of the controlled terminology below A diagram that outlines the decision points (e.g. randomisation, response evaluation) that define the different paths a participant could take through the trial.
User Guidance	The purpose of this section is to provide a visual depiction of the trial design, orienting users of the protocol to the key features of the design. The schema depicts the trial arms, the flow of individual participants through the progression of trial period(s)/epochs (such as screening, washout/run-in, intervention, and key milestones [e.g., randomisation, cross-over, end of treatment, end of study, post-treatment follow-up]). For complex trials, additional schemas may be added to describe activities or trial periods in greater detail.
Conformance	Required
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	1.2
Value	Image; Text
Business rules	**Value Allowed**: Yes **Relationship**: 1.2 Trial Schema **Concept**: C93682
Repeating and/or Reuse Rules	Yes, repeatable within Section

202

Term (Variable)	<Schema Notes>
Data Type	Text
Data (D), Value (V) or Heading (H)	D
Definition	CNEW For review purpose, see definition of the controlled terminology below A brief written record describing the trial schematic.
User Guidance	The purpose of this section is to provide a visual depiction of the trial design, orienting users of the protocol to the key features of the design. The schema depicts the trial arms, the flow of individual participants through the progression of trial period(s)/epochs (such as screening, washout/run-in, intervention, and key milestones [e.g., randomisation, cross-over, end of treatment, end of study, post-treatment follow-up]). For complex trials, additional schemas may be added to describe activities or trial periods in greater detail.
Conformance	Optional
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	1.2
Value	Text
Business rules	**Value Allowed**: Yes **Relationship**: 1.2 Trial Schema **Concept**: CNEW
Repeating and/or Reuse Rules	Yes, repeatable and aligned with appropriate schema

203

204 ## 1.3 Schedule of Activities

Term (Variable)	1.3 Schedule of Activities

Data Type	Text
Data (D), Value (V) or Heading (H)	H
Definition	Heading
User Guidance	The schedule of activities must capture the procedures that will be accomplished at each trial visit, and all contact with trial participants, e.g., telephone contacts. This includes any tests that are used for eligibility, participant randomisation or stratification, or decisions on trial intervention discontinuation. Allowable windows should be stated for all visits and procedures. A tabular format is recommended. When applicable for studies with extensive sampling (e.g., serial PK sampling) a separate table may be added.
Conformance	Required
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	1.3
Value	Schedule of Activities
Business rules	**Value Allowed**: No **Relationship**: 1 PROTOCOL SUMMARY and Table of Contents **Concept**: Heading
Repeating and/or Reuse Rules	No

205

Term (Variable)	<Schedule of Activities>
Data Type	Table; Text; Image
Data (D), Value (V) or Heading (H)	D
Definition	CNEW For review purpose, see definition of the controlled terminology below A standardised representation of planned clinical trial activities including interventions (e.g. administering drug, surgery) and study administrative activities (e.g. obtaining informed consent, distributing clinical trial material and diaries, randomisation) as well as assessments.
User Guidance	The schedule of activities must capture the procedures that will be accomplished at each trial visit, and all contact with participants, e.g., telephone contacts. This includes any tests that are used for eligibility, participant randomisation or stratification, or decisions on trial intervention discontinuation. Allowable windows should be stated for all visits and procedures. A tabular format is recommended. When applicable for studies with extensive sampling, e.g., serial PK sampling, a separate table may be added
Conformance	Required
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	1.3
Value	Table; text; Image
Business rules	**Value Allowed**: Yes **Relationship**: 1.3 Schedule of Activities **Concept**: CNEW
Repeating and/or Reuse Rules	Yes, repeatable for each Schedule of Activity if needed

206

207 # 2 INTRODUCTION

Term (Variable)	2 INTRODUCTION
Data Type	Text
Data (D), Value (V) or Heading (H)	H
Definition	Heading
User Guidance	No text is intended here (Heading only).
Conformance	Required
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	2
Value	INTRODUCTION
Business rules	**Value Allowed**: No **Relationship**: Table of Contents **Concept**: Heading
Repeating and/or Reuse Rules	No

208

209 ## 2.1 Purpose of Trial

Term (Variable)	2.1 Purpose of Trial
Data Type	Text
Data (D), Value (V) or Heading (H)	H
Definition	Heading
User Guidance	N/A
Conformance	Required
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	2.1
Value	Purpose of Trial
Business rules	**Value Allowed**: No **Relationship**: 2 INTRODUCTION and Table of Contents **Concept**: Heading
Repeating and/or Reuse Rules	No

210

Term (Variable)	<Purpose of Trial>
Data Type	Text
Data (D), Value (V) or Heading (H)	D
Definition	C146997 For review purpose, see definition of the controlled terminology below The overall rationale, reason, or intention of the clinical trial.
User Guidance	
Conformance	Required
Cardinality	One to one

Relationship content from ToC representing the protocol hierarchy	2.1
Value	Text
Business rules	**Value Allowed**: Yes **Relationship**: 2.1 Purpose of Trial **Concept**: C146997
Repeating and/or Reuse Rules	No

211

212 ## 2.2 Assessment of Risks and Benefits

Term (Variable)	2.2 Assessment of Risks and Benefits
Data Type	Text
Data (D), Value (V) or Heading (H)	H
Definition	Heading
User Guidance	Include an assessment of known and potential risks and benefits, if any, as a result of participating in the trial from the perspective of an individual participant, including the basis of the risk (e.g., nonclinical trials or prior clinical trials). This section may be structured under one single heading 2.2 Assessment of Risks and Benefits, or if applicable under 3 subheadings as 2.2.1 Risk Summary and Mitigation Strategy, 2.2.2 Benefit Assessment and 2.2.3 Overall Risk-Benefit Assessment
Conformance	Required
Cardinality	One to many
Relationship content from ToC representing the protocol hierarchy	2.2
Value	Assessment of Risks and Benefits
Business rules	**Value Allowed**: No **Relationship**: 2 INTRODUCTION and Table of Contents **Concept**: Heading
Repeating and/or Reuse Rules	No

213

216 ### 2.2.1 Risk Summary and Mitigation Strategy

Term (Variable)	2.2.1 Risk Summary and Mitigation Strategy
Data Type	Text

Data (D), Value (V) or Heading (H)	H
Definition	Heading
User Guidance	N/A
Conformance	Optional
Cardinality	One to many
Relationship content from ToC representing the protocol hierarchy	2.2.1
Value	Risk Summary and Mitigation Strategy
Business rules	**Value Allowed**: No **Relationship**: 2.2 Assessment of Risks and Benefits, 2 INTRODUCTION and Table of Contents **Concept**: Heading
Repeating and/or Reuse Rules	No

217

Term (Variable)	<Trial-specific Intervention Risks and Mitigations>
Data Type	Text
Data (D), Value (V) or Heading (H)	D
Definition	CNEW For review purpose, see definition of the controlled terminology below A description of the potential risks associated with the trial interventions and mitigation strategies to be employed within the trial.
User Guidance	Trial Intervention – Describe risks related to trial-specific treatments and interventions. For the protocol, focus on the relevant key risks for THIS trial. Provide a brief description of strategies to mitigate identified risks or provide a cross-reference to the relevant protocol section.
Conformance	Optional
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	2.2.1
Value	Text
Business rules	**Value Allowed**: Yes **Relationship**: 2.2.1 Risk Summary and Mitigation Strategy **Concept**: CNEW
Repeating and/or Reuse Rules	No

218

Term (Variable)	<Trial-specific Procedure Risks and Mitigations>
Data Type	Text
Data (D), Value (V) or Heading (H)	D
Definition	CNEW For review purpose, see definition of the controlled terminology below A description of the potential risks associated with the trial procedures and mitigation strategies to be employed within the trial.
User Guidance	
Conformance	Optional
Cardinality	One to one

Relationship content from ToC representing the protocol hierarchy	2.2.1
Value	Text
Business rules	**Value Allowed**: Yes **Relationship**: 2.2.1 Risk Summary and Mitigation Strategy **Concept**: CNEW
Repeating and/or Reuse Rules	No

Term (Variable)	<Trial-specific Other Risks and Mitigations>
Data Type	Text
Data (D), Value (V) or Heading (H)	D
Definition	CNEW For review purpose, see definition of the controlled terminology below A description of the potential risks associated with other trial-related agents and mitigation strategies to be employed within the trial.
User Guidance	
Conformance	Optional
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	2.2.1
Value	Text
Business rules	**Value Allowed**: Yes **Relationship**: 2.2.1 Risk Summary and Mitigation Strategy **Concept**: CNEW
Repeating and/or Reuse Rules	No

2.2.2 Benefit Summary

Term (Variable)	2.2.2 Benefit Summary
Data Type	Text
Data (D), Value (V) or Heading (H)	H
Definition	Heading
User Guidance	N/A
Conformance	Optional
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	2.2.2
Value	Benefit Summary
Business rules	**Value Allowed**: No **Relationship**: 2.2 Assessment of Risks and Benefits, 2 INTRODUCTION and Table of Contents **Concept**: Heading
Repeating and/or Reuse Rules	No

Term (Variable)	<Benefit Summary>

Data Type	Text
Data (D), Value (V) or Heading (H)	D
Definition	CNEW For review purpose, see definition of the controlled terminology below A short textual description containing the potential physical, psychological, social, legal, and other benefits to the trial participant.
User Guidance	The benefit summary should describe any physical, psychological, social, or any other potential benefits to individual participants as a result of participating in the trial, addressing immediate potential benefits and/or long-range potential benefits. Clearly state if no benefits to an individual participant can be anticipated, or if potential benefits are unknown. For early clinical trials such as Phase 1 or trials in healthy participants, benefits for an individual participant (other than those of altruism) are expected to be minimal. Benefits to society in general may also be included but should be described separately from the individual participant perspective.
Conformance	Optional
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	2.2.2
Value	Text
Business rules	**Value Allowed**: Yes **Relationship**: 2.2.2 Benefit Summary **Concept**: CNEW
Repeating and/or Reuse Rules	No

223

224 ### 2.2.3 Overall Risk-Benefit Assessment

Term (Variable)	2.2.3 Overall Risk-Benefit Assessment
Data Type	Text
Data (D), Value (V) or Heading (H)	H
Definition	Heading
User Guidance	N/A
Conformance	Optional
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	2.2.3
Value	Overall Risk-Benefit Assessment
Business rules	**Value Allowed**: No **Relationship**: 2.2 Assessment of Risks and Benefits, 2 INTRODUCTION and Table of Contents **Concept**: Heading
Repeating and/or Reuse Rules	No

225

Term (Variable)	<Overall Risk-Benefit Assessment>
Data Type	Text
Data (D), Value (V) or Heading (H)	D

Definition	CNEW For review purpose, see definition of the controlled terminology below A short textual description containing the risks and benefits associated with participation in the trial.
User Guidance	Provide a succinct, concluding statement on the perceived balance between risks that have been identified from cumulative safety data, protocol procedures, and anticipated efficacy/benefits within the context of the proposed trial.
Conformance	Required
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	2.2.3
Value	Text
Business rules	**Value Allowed**: Yes **Relationship**: 2.2.3 Overall Risk-Benefit Assessment OR 2.2 Assessment of Risks and Benefits (when the Optional Level 3 subheading (2.2.3) is not used) If the Optional Level 3 subheadings (2.2.1, 2.2.2, 2.2.3) are not used, the user guidance below Section 2.2 applies. **Concept**: CNEW
Repeating and/or Reuse Rules	No

3 TRIAL OBJECTIVES AND ASSOCIATED ESTIMANDS

Term (Variable)	3 TRIAL OBJECTIVES AND ASSOCIATED ESTIMANDS
Data Type	Text
Data (D), Value (V) or Heading (H)	H
Definition	Heading
User Guidance	In this section, precisely define each trial objective and refine each trial objective into a precise clinical question of interest by defining the associated estimand. For considerations on estimands, see ICH E9(R1). Ensure alignment with every other section of the protocol. Include additional level 3 Headings (e.g. add a new level 3 Heading for each secondary objective) as needed. If there is more than one objective in a category (e.g., more than one secondary objective), number each objective consecutively as the level 3 heading (e.g., Secondary Objective 1, Secondary Objective 2, etc.). No text is intended here (Heading only).
Conformance	Required
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	3
Value	TRIAL OBJECTIVES AND ASSOCIATED ESTIMANDS
Business rules	**Value Allowed**: No **Relationship**: Table of Contents **Concept**: Heading
Repeating and/or Reuse Rules	No

3.1 Primary Objective(s) and Associated Estimand(s)

Term (Variable)	3.1 Primary Objective(s) and Associated Estimand(s)
Data Type	Text
Data (D), Value (V) or Heading (H)	H
Definition	Heading
User Guidance	No text is intended here (Heading only)
Conformance	Required
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	3.1
Value	Primary Objective(s) and Associated Estimand(s)
Business rules	**Value Allowed**: No **Relationship**: 3 TRIAL OBJECTIVES AND ASSOCIATED ESTIMANDS and Table of Contents **Concept**: Heading
Repeating and/or Reuse Rules	No

3.1.1 Primary Objective

Term (Variable)	3.1.X Primary Objective X
Data Type	Text
Data (D), Value (V) or Heading (H)	H
Definition	Heading
User Guidance	For all trials, precisely state each primary trial objective by providing a meaningful and concise description of the treatment effect of interest using natural, non-technical language for clear understanding of sponsors, investigators, clinical site personnel, trial participants, ethics committees, and regulators. For trials intended to estimate a treatment effect or test a hypothesis related to a treatment effect, use the table to precisely describe the associated estimand(s). This includes specification of the target population, the treatment condition(s), the endpoint (or variable) and the population-level summary. Precise specifications of treatment, population, and variable are likely to address many of the key intercurrent events. Other key intercurrent events not already addressed in the clinical question of interest by the aforementioned attributes should be described with their associated strategies. For other types of trials not intended to estimate a treatment effect or test a hypothesis related to a treatment effect, describe additional information relevant to the clinical question(s) of interest (at a minimum, present the endpoint(s) associated with each objective). For these trials, including the table is not required.
Conformance	Required
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	3.1.X where X is a unique number for each primary objective
Value	Primary Objective X: X is a unique number for each primary objective
Business rules	**Value Allowed**: No

	Relationship: 3.1 Primary Objective and Associated Estimand(s), 3. TRIAL OBJECTIVES AND ASSOCIATED ESTIMAND and Table of Contents **Concept**: Heading
Repeating and/or Reuse Rules	Yes, repeatable for each numbered primary objective. Yes, reuse to the table in Section 1.1.1.for each primary objective

232

Term (Variable)	<Primary Objective>
Data Type	Text
Data (D), Value (V) or Heading (H)	D
Definition	C85826 For review purpose, see definition of the controlled terminology below The principle reason for performing a study in terms of the scientific questions to be answered by the analysis of data collected during the study.
User Guidance	N/A
Conformance	Required
Cardinality	One to One, One to Table of Contents Number 3.1.X, One to Estimand Characteristics Table, Primary Objective X, Protocol Identifier
Relationship content from ToC representing the protocol hierarchy	3.1.X: X is a unique number for each primary objective.
Value	Text and unique integer which is same as Level 3 number for the section.
Business rules	**Value Allowed**: Yes **Relationship**: 3.1.X Primary Objective **Concept**: C85826
Repeating and/or Reuse Rules	Yes, repeatable for each numbered primary objective. Yes, reuse to the table in Section 1.1.1.for each primary objective

233

Term (Variable)	< Table of Estimand Characteristics including Endpoint at a minimum>
Data Type	Text
Data (D), Value (V) or Heading (H)	D
Definition	N/A
User Guidance	N/A
Conformance	Required
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	3.1.X: X is a unique number for each primary objective
Value	Estimand Characteristics
Business rules	**Value Allowed**: **Yes** **Relationship**: 3.1.1 Primary Objective **Concept**: Heading
Repeating and/or Reuse Rules	Yes, repeatable for each numbered primary objective. Yes, reuse to the table in Section 1.1.1.for each primary objective

234

Term (Variable)	Estimand Characteristics
Data Type	Text
Data (D), Value (V) or Heading (H)	H
Definition	Table Column Heading
User Guidance	N/A
Conformance	Required

Cardinality	One to many
Relationship content from ToC representing the protocol hierarchy	3.1.X
Value	Estimand Characteristic
Business rules	**Value Allowed**: No **Relationship**: 3.1 Primary Objective(s) and associated Estimand(s); Table column Heading; Description, Population, Treatment, Endpoint, Population-Level Summary, Other Intercurrent Event **Concept**: Heading
Repeating and/or Reuse Rules	Yes, repeatable for each numbered primary objective Yes, reuse to the table in Section 1.1.1.for each primary objective

235

Term (Variable)	Description
Data Type	Text
Data (D), Value (V) or Heading (H)	H
Definition	Table Column Heading
User Guidance	N/A
Conformance	Required
Cardinality	One to many rows
Relationship content from ToC representing the protocol hierarchy	3.1.X
Value	Description
Business rules	**Value Allowed**: No **Relationship**: 3.1 Primary Objective(s) and associated Estimand(s); Table column Heading; Estimand Characteristics, Population, Treatment, Endpoint, Population-Level, Other Intercurrent Event, Strategy **Concept**: Heading
Repeating and/or Reuse Rules	Yes, repeatable for each numbered primary objective Yes, reuse to the table in Section 1.1.1.for each primary objective

236

Term (Variable)	{Population}
Data Type	Text
Data (D), Value (V) or Heading (H)	H
Definition	Heading
User Guidance	N/A
Conformance	Conditional: If there is a population as estimand characteristic
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	3.1.X
Value	{Population}
Business rules	**Value Allowed**: No **Relationship**: Row Heading, Estimand Characteristics **Concept**: Heading
Repeating and/or Reuse Rules	Yes, repeatable for each numbered primary objective

237

Term (Variable)	{<Population>}
Data Type	Text

Data (D), Value (V) or Heading (H)	D
Definition	C70833 For review purpose, see definition of the controlled terminology below The population of patients targeted by the clinical question. This will be represented by the entire trial population, a subgroup defined by a particular characteristic measured at baseline, or a principal stratum defined by the occurrence (or non-occurrence, depending on context) of a specific intercurrent event.
User Guidance	List of key characteristics, such as demographic characteristics (e.g. age, sex) and clinical characteristics (e.g. prior therapies, symptoms, severity, biomarker status)
Conformance	Conditional: If there is a population as estimand characteristic
Cardinality	One to Row Heading, One to Primary Objective Table, Primary Objective X, Protocol Identifier
Relationship content from ToC representing the protocol hierarchy	3.1.X
Value	Text
Business rules	**Value Allowed**: Yes **Relationship**: Row Heading, Description **Concept**: C70833
Repeating and/or Reuse Rules	Yes, repeatable for each numbered primary objective

238

Term (Variable)	{Treatment}
Data Type	Text
Data (D), Value (V) or Heading (H)	H
Definition	Heading
User Guidance	N/A
Conformance	Conditional: If there is a treatment as estimand characteristic
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	3.1.X
Value	{Treatment}
Business rules	**Value Allowed**: No **Relationship**: Row Heading, Estimand Characteristics **Concept**: Heading
Repeating and/or Reuse Rules	Yes, repeatable for each numbered primary objective

239

Term (Variable)	{<Treatment>}
Data Type	Text
Data (D), Value (V) or Heading (H)	D
Definition	C49236 For review purpose, see definition of the controlled terminology below

	The treatment condition of interest and, as appropriate, the alternative treatment condition to which comparison will be made (referred to as "treatment" through the remainder of this document). These might be individual interventions, combinations of interventions administered concurrently, e.g. as add-on to standard of care, or might consist of an overall regimen involving a complex sequence of interventions.
User Guidance	List of key aspects of treatment regimens in each study group, including at least investigational agents, dosage, and administration route
Conformance	Conditional: If there is a treatment as estimand characteristic
Cardinality	One to Row Heading, One to Primary Objective Table, Project Identifier
Relationship content from ToC representing the protocol hierarchy	3.1.X
Value	Text
Business rules	**Value Allowed**: Yes **Relationship**: Row Heading, Description **Concept:** C49236
Repeating and/or Reuse Rules	Yes, repeatable for each numbered primary objective

240

Term (Variable)	Endpoint
Data Type	Text
Data (D), Value (V) or Heading (H)	H
Definition	Heading
User Guidance	N/A
Conformance	Required
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	3.1.X
Value	Endpoint
Business rules	**Value Allowed**: No **Relationship**: Row Heading, Estimand Characteristics **Concept**: Heading
Repeating and/or Reuse Rules	Yes, repeatable for each numbered primary objective

241

Term (Variable)	{< Endpoint >}
Data Type	Text
Data (D), Value (V) or Heading (H)	D
Definition	C25212 For review purpose, see definition of the controlled terminology below The variable to be obtained for each patient that is required to address the clinical question. The specification of the variable might include whether the patient experiences an intercurrent event
User Guidance	List of key characteristics, such as demographic characteristics (e.g. age, sex) and clinical characteristics (e.g. prior therapies, symptoms, severity, biomarker status))
Conformance	Required
Cardinality	One to Row Heading, One to Primary Objective Table, Project Identifier

Relationship content from ToC representing the protocol hierarchy	3.1.X
Value	Text
Business rules	**Value Allowed**: Yes **Relationship**: Row Heading, Description **Concept**: C25212
Repeating and/or Reuse Rules	Yes, repeatable for each numbered primary objective

242

Term (Variable)	{Population-Level Summary}
Data Type	Text
Data (D), Value (V) or Heading (H)	H
Definition	Heading
User Guidance	N/A
Conformance	Conditional: If there is a population -level summary as estimand characteristic
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	3.1.X
Value	{Population-Level Summary}
Business rules	**Value Allowed**: No **Relationship**: Row Heading, Estimand Characteristics **Concept**: Heading
Repeating and/or Reuse Rules	Yes, repeatable for each numbered primary objective

243

Term (Variable)	{<Population-Level Summary>}
Data Type	Text
Data (D), Value (V) or Heading (H)	D
Definition	C188853 For review purpose, see definition of the controlled terminology below The variable to be obtained for each patient that is required to address the clinical question. The specification of the variable might include whether the patient experiences an intercurrent event
User Guidance	Description of the population-level summary (e.g., mean difference, relative risk)
Conformance	Conditional: If there is a population-level summary as estimand
Cardinality	One to Row Heading, One to Primary Objective Table, Project Identifier
Relationship content from ToC representing the protocol hierarchy	3.1.X
Value	Text
Business rules	**Value Allowed**: Yes **Relationship**: Row Heading, Description **Concept**: C188853
Repeating and/or Reuse Rules	Yes, repeatable for each numbered primary objective

244

Term (Variable)	**{Other Intercurrent Event}**
Data Type	Text

Data (D), Value (V) or Heading (H)	H
Definition	Table Column Heading
User Guidance	N/A
Conformance	Conditional: If there is one or more other intercurrent events as estimand characteristic.
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	3.1.X
Value	Intercurrent Event
Business rules	**Value Allowed**: No **Relationship**: Row Heading, Estimand Characteristics **Concept**: Heading
Repeating and/or Reuse Rules	Yes, repeatable for each numbered primary objective

245

Term (Variable)	{Strategy}
Data Type	Text
Data (D), Value (V) or Heading (H)	H
Definition	Table Column Heading
User Guidance	N/A
Conformance	Conditional: If there is one or more other intercurrent events as estimand characteristic.
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	3.1.X
Value	Strategy
Business rules	**Value Allowed**: No **Relationship**: Table column Heading, Other Intercurrent Event, Description **Concept**: Heading
Repeating and/or Reuse Rules	Yes, repeatable for each numbered primary objective

246

Term (Variable)	{Description of Intercurrent Event}
Data Type	Text
Data (D), Value (V) or Heading (H)	D
Definition	C188853 For review purpose, see definition of the controlled terminology below A textual description of the planned strategy to address intercurrent events.
User Guidance	Enter Description of Intercurrent Event
Conformance	Conditional: If there is one or more other intercurrent events as estimand characteristic.
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	3.1.X
Value	Text
Business rules	**Value Allowed**: Yes **Relationship**: Row Heading, Estimand Characteristics

	Concept: C188853
Repeating and/or Reuse Rules	Yes, repeatable for each intercurrent event

Term (Variable)	{Intercurrent Event 1 Strategy}
Data Type	Text
Data (D), Value (V) or Heading (H)	D
Definition	C188857 For review purpose, see definition of the controlled terminology below A textual description of the planned strategy to address intercurrent events.
User Guidance	Description of the strategy to address the intercurrent event (e.g. a treatment policy strategy); cross-reference the justification in Section 4. If there is >1 intercurrent event for an objective, add additional intercurrent event rows
Conformance	Conditional: If there is one or more other intercurrent events as estimand characteristic.
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	3.1.X
Value	Text
Business rules	**Value Allowed**: Yes **Relationship**: Row Heading, Strategy, Description **Concept**: C188857
Repeating and/or Reuse Rules	Yes, repeatable for each intercurrent event

3.2 Secondary Objective(s) and Associated Estimand(s)

Term (Variable)	3.2 Secondary Objective(s) and Associated Estimand(s)
Data Type	Text
Data (D), Value (V) or Heading (H)	H
Definition	Heading
User Guidance	N/A
Conformance	Required
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	3.2
Value	Secondary Objective(s) and Associated Estimand(s)
Business rules	**Value Allowed**: No **Relationship**: 3 Trial Objectives and Associated Estimand(s) and Table of Contents **Concept**: Heading
Repeating and/or Reuse Rules	No

3.2.1 Secondary Objective X

Term (Variable)	{3.2 X Secondary Objective X}
Data Type	Text

Data (D), Value (V) or Heading (H)	H
Definition	Heading
User Guidance	Describe the secondary objective(s) and associated estimand(s) as outlined in Section 3.1. Use the same approach as above and consider including a table for a precise estimand description.
Conformance	Conditional: when there are Secondary Objective Heading for each secondary requirement
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	3.2.X where X is a unique Secondary objective
Value	Secondary Objective X
Business rules	**Value Allowed**: No **Relationship**: 3.2 Secondary Objective and Associated Endpoints, 3 Trial Objectives and Associated Estimand(s) and Table of Contents **Concept**: Heading
Repeating and/or Reuse Rules	Yes, repeatable for each numbered secondary objective.

252

Term (Variable)	<Secondary Objective X>
Data Type	Text
Data (D), Value (V) or Heading (H)	D
Definition	C85827 For review purpose, see definition of the controlled terminology below The secondary reason for performing a study in terms of the scientific questions to be answered by the analysis of data collected during the study.
User Guidance	N/A
Conformance	Required
Cardinality	One to one; Table of Contents Number 3.2.X, One to Estimand Characteristic Table, Secondary Objective X, Protocol Identifier
Relationship content from ToC representing the protocol hierarchy	3.2.X
Value	Text and unique integer which is same as Level 3 number for the section.
Business rules	**Value Allowed**: Yes **Relationship**: 3.2.X Secondary Objective, Estimand Characteristics table **Concept**: C85827
Repeating and/or Reuse Rules	Yes, repeatable for each numbered secondary objective.

253

Term (Variable)	Secondary Objective Number
Data Type	Number
Data (D), Value (V) or Heading (H)	D
Definition	N/A
User Guidance	
Conformance	Optional
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	3.2.X

Value	an integer, unique number
Business rules	**Value Allowed**: Yes **Relationship**: 3.2.X Secondary Objective **Concept**: Sequential number
Repeating and/or Reuse Rules	Yes, repeatable for each numbered secondary objective.

254

Term (Variable)	{If a Secondary Objective has been entered: <Enter Table of Estimand Characteristics including Endpoint at a minimum>}
Data Type	Text
Data (D), Value (V) or Heading (H)	D
Definition	N/A
User Guidance	{If a Secondary Objective has been entered: <Enter Table of Estimand Characteristics>} including Endpoint at a minimum}
Conformance	Conditional: either Enter Table of Estimand Characteristics or details of the characteristics relevant to objective
Cardinality	One to many rows
Relationship content from ToC representing the protocol hierarchy	3.2.X
Value	Estimand Characteristics
Business rules	**Value Allowed**: No **Relationship**: 3 3.2 Secondary Objective(s) and associated Estimand(s) **Concept**: Heading
Repeating and/or Reuse Rules	Yes, repeatable for each numbered secondary objective.

255

Term (Variable)	{Estimand Characteristics}
Data Type	Text
Data (D), Value (V) or Heading (H)	H
Definition	Table Column Heading
User Guidance	N/A
Conformance	Conditional: if there is a secondary objective
Cardinality	One to many rows
Relationship content from ToC representing the protocol hierarchy	3.2.X
Value	Estimand Characteristics
Business rules	**Value Allowed**: No **Relationship**: 3.2 Secondary Objective(s) and associated Estimand(s); Table column Heading; Description, Population, Treatment, Endpoint, Population-Level Summary, Intercurrent Event **Concept**: Heading
Repeating and/or Reuse Rules	Yes, repeatable for each numbered secondary objective.

256

Term (Variable)	{Description}
Data Type	Text
Data (D), Value (V) or Heading (H)	H
Definition	Table Column Heading

User Guidance	N/A
Conformance	Conditional
Cardinality	One to many rows
Relationship content from ToC representing the protocol hierarchy	3.2.X
Value	Description
Business rules	**Value Allowed**: No **Relationship**: 3 3.2 Secondary Objective(s) and associated Estimand(s); Table column Heading; Estimand Characteristics, Population, Treatment, Endpoint, Population-Leve Summary, Other Intercurrent Event, Strategy **Concept**: Heading
Repeating and/or Reuse Rules	Yes, repeatable for each numbered secondary objective.

257

Term (Variable)	{Population}
Data Type	Text
Data (D), Value (V) or Heading (H)	H
Definition	Heading
User Guidance	N/A
Conformance	Conditional: If there is a population
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	3.2.X
Value	{Population}
Business rules	**Value Allowed**: No **Relationship**: Row Heading, Estimand Characteristics **Concept**: Heading
Repeating and/or Reuse Rules	Yes, repeatable for each numbered secondary objective.

258

Term (Variable)	{<Population>}
Data Type	Text
Data (D), Value (V) or Heading (H)	D
Definition	C70833 For review purpose, see definition of the controlled terminology below The population of patients targeted by the clinical question. This will be represented by the entire trial population, a subgroup defined by a particular characteristic measured at baseline, or a principal stratum defined by the occurrence (or non-occurrence, depending on context) of a specific intercurrent event.
User Guidance	List of key characteristics, such as demographic characteristics (e.g. age, sex) and clinical characteristics (e.g. prior therapies, symptoms, severity, biomarker status)
Conformance	Conditional: If there is a population for Secondary
Cardinality	One to Row Heading, One to Secondary Objective Table, Secondary Objective X, Protocol Identifier
Relationship content from ToC representing the protocol hierarchy	3.2.X

Value	Text
Business rules	**Value Allowed**: Yes **Relationship**: Row Heading, Description; Estimand Characteristics, **Concept:** C70833
Repeating and/or Reuse Rules	Yes, repeatable for each numbered secondary objective.

259

Term (Variable)	{Treatment}
Data Type	Text
Data (D), Value (V) or Heading (H)	H
Definition	Heading
User Guidance	N/A
Conformance	Conditional: If there is a population
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	3.2.X
Value	{Treatment}
Business rules	**Value Allowed**: No **Relationship**: Row Heading, Estimand Characteristics **Concept**: Heading
Repeating and/or Reuse Rules	Yes, repeatable for each numbered secondary objective.

260

Term (Variable)	{<Treatment>}
Data Type	Text
Data (D), Value (V) or Heading (H)	D
Definition	C49236 For review purpose, see definition of the controlled terminology below The treatment condition of interest and, as appropriate, the alternative treatment condition to which comparison will be made (referred to as "treatment" through the remainder of this document). These might be individual interventions, combinations of interventions administered concurrently, e.g. as add-on to standard of care, or might consist of an overall regimen involving a complex sequence of interventions.
User Guidance	List of key aspects of treatment regimens in each study group, including at least investigational agents, dosage, and administration route
Conformance	Conditional: If there is a population for Secondary
Cardinality	One to Row Heading, One to Secondary Objective Table, Project Identifier
Relationship content from ToC representing the protocol hierarchy	3.2.X
Value	Text
Business rules	**Value Allowed**: Yes **Relationship**: Row Heading, Description; Estimand Characteristics, **Concept: C49236**
Repeating and/or Reuse Rules	Yes, repeatable for each numbered secondary objective.

261

Term (Variable)	{Endpoint}
Data Type	Text

Data (D), Value (V) or Heading (H)	H
Definition	Heading
User Guidance	N/A
Conformance	Conditional: if there is a secondary Objective
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	3.2.X
Value	Endpoint
Business rules	**Value Allowed**: No **Relationship**: Row Heading, Description, Estimand Characteristics **Concept**: Heading
Repeating and/or Reuse Rules	Yes, repeatable for each numbered secondary objective.

262

Term (Variable)	{< Endpoint >}
Data Type	Text
Data (D), Value (V) or Heading (H)	D
Definition	C25212 For review purpose, see definition of the controlled terminology below The variable to be obtained for each patient that is required to address the clinical question. The specification of the variable might include whether the patient experiences an intercurrent event
User Guidance	List of key characteristics, such as demographic characteristics (e.g. age, sex) and clinical characteristics (e.g. prior therapies, symptoms, severity, biomarker status)
Conformance	Required
Cardinality	One to Row Heading, One to Secondary Objective Table, Project Identifier
Relationship content from ToC representing the protocol hierarchy	3.2.X
Value	Text
Business rules	**Value Allowed**: Yes **Relationship**: Row Heading, Description; Table Estimand Characteristics, Secondary (1…n) Estimand; **Concept**: C25212
Repeating and/or Reuse Rules	Yes, repeatable for each numbered secondary objective.

263

Term (Variable)	{Population-Level Summary}
Data Type	Text
Data (D), Value (V) or Heading (H)	H
Definition	Heading
User Guidance	N/A
Conformance	Conditional: If there is a population -Level Summary
Cardinality	One to
Relationship content from ToC representing the protocol hierarchy	3.2.X
Value	{Population-Level Summary}

Business rules	**Value Allowed**: No **Relationship**: Row Heading, Estimand Characteristics **Concept**: Heading
Repeating and/or Reuse Rules	Yes, repeatable for each numbered secondary objective.

264

Term (Variable)	{<Population-Level Summary>}
Data Type	Text
Data (D), Value (V) or Heading (H)	D
Definition	C188853 For review purpose, see definition of the controlled terminology below The variable to be obtained for each patient that is required to address the clinical question. The specification of the variable might include whether the patient experiences an intercurrent event
User Guidance	List of key characteristics, such as demographic characteristics (e.g. age, sex) and clinical characteristics (e.g. prior therapies, symptoms, severity, biomarker status)
Conformance	Conditional: If there is a population for Secondary
Cardinality	One to Row Heading, One to Secondary Objective Table, Project Identifier
Relationship content from ToC representing the protocol hierarchy	3.2.X
Value	Text
Business rules	**Value Allowed**: Yes **Relationship**: Row Heading, Description; Table estimand Characteristics, Secondary (1…n) Estimand; Protocol Identifier **Concept**: C188853
Repeating and/or Reuse Rules	Yes, repeatable for each numbered secondary objective.

265

Term (Variable)	{Other Intercurrent Event}
Data Type	Text
Data (D), Value (V) or Heading (H)	H
Definition	Table Column Heading
User Guidance	N/A
Conformance	Conditional: If there is one or more other intercurrent events
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	3.2.X
Value	Intercurrent Event
Business rules	**Value Allowed**: No **Relationship**: 3 3.2 Secondary Objective(s) and associated Estimand(s); Table column Heading **Concept**: Heading
Repeating and/or Reuse Rules	Yes, repeatable for each numbered secondary objective.

266

Term (Variable)	{Strategy}
Data Type	Text

Data (D), Value (V) or Heading (H)	H
Definition	Table Column Heading
User Guidance	N/A
Conformance	Conditional: If there is one or more other intercurrent events
Cardinality	One to many rows
Relationship content from ToC representing the protocol hierarchy	3.2.X
Value	Strategy
Business rules	**Value Allowed**: No **Relationship**: Table column Heading; Other Intercurrent Event (1…n) **Concept**: Heading
Repeating and/or Reuse Rules	Yes, repeatable for each numbered secondary objective.

267

Term (Variable)	{Description of Intercurrent Event}
Data Type	Text
Data (D), Value (V) or Heading (H)	H
Definition	C188853 For review purpose, see definition of the controlled terminology below A textual description of the planned strategy to address intercurrent events.
User Guidance	Enter Description of Intercurrent Event
Conformance	Conditional: If there is one or more other intercurrent events.
Cardinality	One to one or as many intercurrent event as available
Relationship content from ToC representing the protocol hierarchy	3.2.X
Value	Text
Business rules	**Value Allowed**: No **Relationship**: Row Heading, Estimand Characteristics, Protocol Identifier **Concept**: C188853
Repeating and/or Reuse Rules	Yes, repeatable for each intercurrent event

268

Term (Variable)	{Intercurrent Event Strategy}
Data Type	Text
Data (D), Value (V) or Heading (H)	D
Definition	C188857 For review purpose, see definition of the controlled terminology below A textual description of the planned strategy to address intercurrent events.
User Guidance	Description of the strategy to address the intercurrent event (e.g. a treatment policy strategy); cross-reference the justification in Section 4. If there is >1 intercurrent event for an objective, add additional intercurrent event rows
Conformance	Conditional: If there is one or more other intercurrent events.
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	3.2.X
Value	Text
Business rules	**Value Allowed**: Yes

	Relationship: Row Heading Intercurrent Event, Description **Concept**: C188857
Repeating and/or Reuse Rules	Yes, repeatable for each intercurrent event

3.3 Exploratory Objective(s)

Term (Variable)	3.3 Exploratory Objective(s)
Data Type	Text
Data (D), Value (V) or Heading (H)	H
Definition	Heading
User Guidance	For all trials, precisely state each Exploratory trial objective by providing a meaningful and concise description of the treatment effect of interest using natural, non-technical language for clear understanding of sponsors, investigators, clinical site personnel, trial participants, ethics committees, and regulators. No text is intended here (Heading only)
Conformance	Required
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	3.3
Value	Exploratory Objective(s)
Business rules	**Value Allowed**: No **Relationship**: TRIAL OBJECTIVES AND ENDPOINT and Table of Contents **Concept**: Heading
Repeating and/or Reuse Rules	No

3.3.1 Exploratory Objective

Term (Variable)	3.3.1 Exploratory Objective
Data Type	Text
Data (D), Value (V) or Heading (H)	H
Definition	Heading
User Guidance	N/A
Conformance	Conditional: when there are exploratory Objective Heading for each exploratory requirement
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	3.3.X where X is a unique Exploratory objective
Value	3.3.1
Business rules	**Value Allowed**: No **Relationship**: 3.3 Exploratory Objective(s), 3 TRIAL OBJECTIVES AND ASSOCIATED ESTIMANDS and Table of Contents **Concept**: Heading
Repeating and/or Reuse Rules	Yes, repeatable for each numbered exploratory objective.

Term (Variable)	<Exploratory Objective>

Data Type	Text
Data (D), Value (V) or Heading (H)	D
Definition	C163559 For review purpose, see definition of the controlled terminology below The exploratory reason for performing a study in terms of the scientific questions to be answered by the analysis of data collected during the study.
User Guidance	State each exploratory objective. This should generally include documentation of associated exploratory endpoints. It may be helpful in some cases to describe precise estimands to provide clarity on what is being estimated.
Conformance	Conditional: if an exploratory objective is part of the trial
Cardinality	One to Table of Contents Number 3.3.X, One to Estimand Characteristic Table, Exploratory Objective X, Protocol Identifier
Relationship content from ToC representing the protocol hierarchy	3.3.X
Value	Text
Business rules	**Value Allowed**: Yes **Relationship**: 3.3.X Exploratory Objective(s) **Concept**: C163559
Repeating and/or Reuse Rules	Yes, repeatable for each numbered exploratory objective.

273

Term (Variable)	{If an Exploratory Objective has been entered: <Enter Table of Estimand Characteristics> including Endpoint at a minimum}
Data Type	Text
Data (D), Value (V) or Heading (H)	D
Definition	N/A
User Guidance	{If an Exploratory Objective has been entered: <Table of Estimand Characteristics> including Endpoint at a minimum}
Conformance	Conditional: either Enter Table of Estimand Characteristics or details of the characteristics relevant to objective
Cardinality	One to many
Relationship content from ToC representing the protocol hierarchy	3.3.X
Value	Text
Business rules	**Value Allowed**: Yes **Relationship**: 3.3.3 Exploratory Objective(s) and associated Estimand(s);Table column Heading; Description, Population, Treatment, Endpoint, Population-Level, Intercurrent Event (1…n) **Concept**: Heading
Repeating and/or Reuse Rules	Yes, repeatable for each numbered exploratory objective.

274

Term (Variable)	Estimand Characteristics
Data Type	Text
Data (D), Value (V) or Heading (H)	H
Definition	Table Column Heading
User Guidance	N/A
Conformance	Conditional: if there is exploratory endpoint(s).

Cardinality	One to many rows
Relationship content from ToC representing the protocol hierarchy	3.3.X
Value	Estimand Characteristics
Business rules	**Value Allowed**: No **Relationship**: 3 3.X Exploratory Objective; Table Column Heading; Description, Population, Treatment, Endpoint, Population-Level, Intercurrent Event **Concept**: Heading
Repeating and/or Reuse Rules	Yes, repeatable for each numbered exploratory objective.

275

Term (Variable)	Description
Data Type	Text
Data (D), Value (V) or Heading (H)	H
Definition	Table Column Heading
User Guidance	N/A
Conformance	Required
Cardinality	One to many rows
Relationship content from ToC representing the protocol hierarchy	3.3.X
Value	Description
Business rules	**Value Allowed**: No **Relationship**: 3 3.X Exploratory Objective Table Column Heading; Estimand Characteristic, Population, Treatment, Endpoint, Population-Level, Intercurrent Event (1…n), Strategy **Concept**: Heading
Repeating and/or Reuse Rules	Yes, repeatable for each numbered exploratory objective.

276

Term (Variable)	{Population}
Data Type	Text
Data (D), Value (V) or Heading (H)	H
Definition	Heading
User Guidance	N/A
Conformance	Conditional: If there is a population as estimand
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	3.3.X
Value	Population
Business rules	**Value Allowed**: No **Relationship**: Row Heading, Estimand Characteristics **Concept**: Heading
Repeating and/or Reuse Rules	Yes, repeatable for each numbered exploratory objective.

277

Term (Variable)	{<Population>}

Data Type	Text
Data (D), Value (V) or Heading (H)	D
Definition	C70833 For review purpose, see definition of the controlled terminology below The population of patients targeted by the clinical question. This will be represented by the entire trial population, a subgroup defined by a particular characteristic measured at baseline, or a principal stratum defined by the occurrence (or non-occurrence, depending on context) of a specific intercurrent event.
User Guidance	List of key characteristics, such as demographic characteristics (e.g. age, sex) and clinical characteristics (e.g. prior therapies, symptoms, severity, biomarker status)
Conformance	Conditional: If there is a population as estimand characteristic
Cardinality	One to Row Heading, One to Exploratory Objective Table, Exploratory Objective X, Protocol Identifier
Relationship content from ToC representing the protocol hierarchy	3.3.X
Value	Text
Business rules	**Value Allowed**: Yes **Relationship**: Row Heading, Description; Table Estimand Characteristics, Exploratory (1…n) Estimand **Concept**: C70833
Repeating and/or Reuse Rules	Yes, repeatable for each numbered exploratory objective.

278

Term (Variable)	{Treatment}
Data Type	Text
Data (D), Value (V) or Heading (H)	H
Definition	Heading
User Guidance	N/A
Conformance	Conditional: If there is a treatment as estimand.
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	3.3.X
Value	{Treatment}
Business rules	**Value Allowed**: No **Relationship**: Row Heading, Estimand Characteristics **Concept**: Heading
Repeating and/or Reuse Rules	Yes, repeatable for each numbered exploratory objective.

279

Term (Variable)	{<Treatment>}
Data Type	Text
Data (D), Value (V) or Heading (H)	D

Definition	C49236 For review purpose, see definition of the controlled terminology below The treatment condition of interest and, as appropriate, the alternative treatment condition to which comparison will be made (referred to as "treatment" through the remainder of this document). These might be individual interventions, combinations of interventions administered concurrently, e.g. as add-on to standard of care, or might consist of an overall regimen involving a complex sequence of interventions.
User Guidance	List of key aspects of treatment regimens in each study group, including at least investigational agents, dosage, and administration route
Conformance	Conditional: If there is a treatment as estimand
Cardinality	One to Row Heading, One to Exploratory Objective Table, Project Identifier
Relationship content from ToC representing the protocol hierarchy	3.3.X
Value	Text
Business rules	**Value Allowed**: Yes **Relationship**: Row Heading, Description; Table Estimand Characteristics, Exploratory (1…n) Estimand; Protocol Identifier **Concept: C49236**
Repeating and/or Reuse Rules	Yes, repeatable for each numbered exploratory objective.

280

Term (Variable)	Endpoint
Data Type	Text
Data (D), Value (V) or Heading (H)	H
Definition	Heading
User Guidance	N/A
Conformance	Conditional: if there is exploratory endpoint(s).
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	3.3.X
Value	Endpoint
Business rules	**Value Allowed**: No **Relationship**: Row Heading, Estimand Characteristics **Concept**: Heading
Repeating and/or Reuse Rules	Yes, repeatable for each numbered exploratory objective.

281

Term (Variable)	Endpoint
Data Type	Text
Data (D), Value (V) or Heading (H)	D
Definition	C25212 For review purpose, see definition of the controlled terminology below The variable to be obtained for each patient that is required to address the clinical question. The specification of the variable might include whether the patient experiences an intercurrent event
User Guidance	List of key characteristics, such as demographic characteristics (e.g. age, sex) and clinical characteristics (e.g. prior therapies, symptoms, severity, biomarker status)

Conformance	Conditional: if there is exploratory endpoint(s).
Cardinality	One to Row Heading, One to Exploratory Objective Table, Project Identifier
Relationship content from ToC representing the protocol hierarchy	3.3.X
Value	Text
Business rules	**Value Allowed**: Yes **Relationship**: Row Heading, Description; Table Estimand Characteristics, Exploratory (1…n) Estimand **Concept**: C25212
Repeating and/or Reuse Rules	Yes, repeatable for each numbered exploratory objective.

282

Term (Variable)	{Population-Level Summary}
Data Type	Text
Data (D), Value (V) or Heading (H)	H
Definition	Heading
User Guidance	N/A
Conformance	Conditional: If there is a population -level summary
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	3.3.X
Value	Population-Level Summary
Business rules	**Value Allowed**: No **Relationship**: Row Heading, Estimand Characteristics **Concept**: Heading
Repeating and/or Reuse Rules	Yes, repeatable for each numbered exploratory objective.

283

Term (Variable)	{<Population-Level Summary>}
Data Type	Text
Data (D), Value (V) or Heading (H)	D
Definition	C188853 For review purpose, see definition of the controlled terminology below A synopsis of the clinical endpoint of interest within the analysis target study population.
User Guidance	List of key characteristics, such as demographic characteristics (e.g. age, sex) and clinical characteristics (e.g. prior therapies, symptoms, severity, biomarker status)
Conformance	Conditional: If there is a population -level summary
Cardinality	One to Row Heading, One to Exploratory Objective Table, Project Identifier
Relationship content from ToC representing the protocol hierarchy	3.3.X
Value	Text
Business rules	**Value Allowed**: **Yes** **Relationship**: Row Heading, Description; Table Estimand Characteristics, Exploratory (1…n) Estimand **Concept**: C188857

Repeating and/or Reuse Rules	Yes, repeatable for each numbered exploratory objective.

284

Term (Variable)	{Other Intercurrent Event}
Data Type	Text
Data (D), Value (V) or Heading (H)	H
Definition	Table Column Heading
User Guidance	N/A
Conformance	Conditional: If there is one or more other intercurrent event as estimand charactristic.
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	3.3.X
Value	Other Intercurrent Event
Business rules	**Value Allowed**: No **Relationship**: 3 3.3 Exploratory Objective(s) and associated Estimand(s); Table column Heading, Estimand Characteristic **Concept**: Heading
Repeating and/or Reuse Rules	Yes, repeatable for each numbered exploratory objective.

285

Term (Variable)	{Strategy}
Data Type	Text
Data (D), Value (V) or Heading (H)	H
Definition	Table Column Heading
User Guidance	N/A
Conformance	Conditional: If there is one or more other intercurrent event as estimand.
Cardinality	One to many rows
Relationship content from ToC representing the protocol hierarchy	3.3.X
Value	Strategy
Business rules	**Value Allowed**: No **Relationship**: Table Column Heading; Estimand Characteristics, Other Intercurrent Event **Concept**: Heading
Repeating and/or Reuse Rules	Yes, repeatable for each numbered exploratory objective.

286

Term (Variable)	{Description of Intercurrent Event}
Data Type	Text
Data (D), Value (V) or Heading (H)	D
Definition	C188853 For review purpose, see definition of the controlled terminology below A textual description of the planned strategy to address intercurrent events.
User Guidance	Enter Description of Intercurrent Event
Conformance	Conditional: If there is one or more other intercurrent events as estimand charactristic.

Cardinality	One to one or as many intercurrent event as available
Relationship content from ToC representing the protocol hierarchy	3.3.X
Value	Text
Business rules	**Value Allowed**: Yes **Relationship**: Row Heading, Estimand Characteristics **Concept**: C188853
Repeating and/or Reuse Rules	Yes, repeatable for each intercurrent event

Term (Variable)	{<Intercurrent Event # Strategy>}
Data Type	Text
Data (D), Value (V) or Heading (H)	D
Definition	C188857 For review purpose, see definition of the controlled terminology below A textual description of the planned strategy to address intercurrent events.
User Guidance	Description of the strategy to address the intercurrent event (e.g. a treatment policy strategy); cross-reference the justification in Section 4. If there is >1 intercurrent event for an objective, add additional intercurrent event rows
Conformance	Conditional: If there is one or more other intercurrent events as estimand charactristic.
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	3.3.X
Value	Text
Business rules	**Value Allowed**: Yes **Relationship**: Row Heading; Strategy, Description **Concept**: C188857
Repeating and/or Reuse Rules	Yes, repeatable for each intercurrent event

4 TRIAL DESIGN

Term (Variable)	4 TRIAL DESIGN
Data Type	Text
Data (D), Value (V) or Heading (H)	H
Definition	Heading
User Guidance	In the subsections below, describe the trial design with specific mention, as applicable, of the components of an adequate and well-controlled trial and reflect the principles of Quality by Design. The description of the design should be concise and consistent with Section 1.1 Protocol Synopsis and Section 1.2 Trial Schema. The trial design should align with objectives/estimand(s) described in Section 3 Trial Objectives and Associated Estimands. This section is intended to provide a description for the important aspects of the trial design and rationale for its key attributes. Operational details needed to implement the trial design should be covered in more detail in subsequent sections.
Conformance	Required
Cardinality	One to one

Relationship content from ToC representing the protocol hierarchy	4
Value	TRIAL DESIGN
Business rules	**Value Allowed**: No **Relationship**: Table of Contents **Concept**: Heading
Repeating and/or Reuse Rules	No

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291 ## 4.1 Description of Trial Design

Term (Variable)	4.1 Description of Trial Design
Data Type	Text
Data (D), Value (V) or Heading (H)	H
Definition	Heading
User Guidance	N/A
Conformance	Required
Cardinality	One to many
Relationship content from ToC representing the protocol hierarchy	4.1
Value	Description of Trial Design
Business rules	**Value Allowed**: No **Relationship**: 4 TRIAL DESIGN and Table of Contents **Concept**: Heading
Repeating and/or Reuse Rules	No

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294

Term (Variable)	<Overall Description of Trial Design and Description of Intervention Model>
Data Type	Text
Data (D), Value (V) or Heading (H)	D
Definition	CNEW For review purpose, see definition of the controlled terminology below A narrative representation of the trial duration.
User Guidance	Describe the overall trial design and intervention model (e.g., single group, parallel group, cross-over, factorial, sequential), the expected number of participants, and the control method (e.g., placebo, active comparator, low dose, external, standard of care, sham procedure, or none [uncontrolled]). If there are any key aspects of the investigational trial intervention that inform the selection of the intervention model, this should be described. If applicable, indicate other design characteristics (e.g., superiority, noninferiority, dose escalation, or equivalence). If the trial will have an adaptive or novel design (e.g., the trial will be conducted under a master protocol), provide a summary of these design aspects. If applicable, describe within-trial transition rules, e.g., transitions involving cohorts or trial parts. Dose escalation or dose-ranging details should also be described.
Conformance	Optional
Cardinality	One to one

Relationship content from ToC representing the protocol hierarchy	4.1
Value	Text
Business rules	**Value Allowed**: Yes **Relationship**: 4.1 Description of Trial Design **Concept**: CNEW
Repeating and/or Reuse Rules	No

295

Term (Variable)	<Description of Trial Duration>
Data Type	Text
Data (D), Value (V) or Heading (H)	D
Definition	
User Guidance	Describe the trial duration with reference to Section 1.2 Trial Schema. Explain what the overall duration for an individual participant is anticipated to be and why, including the sequence and duration of trial periods (e.g., screening, run-in, randomisation, treatment [fixed dose/titration], follow-up/washout periods). Where applicable, include discussion of sentinel dosing (or lack thereof), dose escalation, and cohort expansion. If dose modification decisions are dependent upon review by a committee, include details in Section 11.4 Committees.
Conformance	Optional
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	4.1
Value	Text
Business rules	**Value Allowed**: Yes **Relationship**: 4.1 Description of Trial Design **Concept**: CNEW
Repeating and/or Reuse Rules	No

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297

Term (Variable)	<Method of Assignment to Trial Intervention>
Data Type	Text
Data (D), Value (V) or Heading (H)	D
Definition	CNEW For review purpose, see definition of the controlled terminology below The technique used to assign trial participants to a trial intervention or trial arm.
User Guidance	State the method of assignment to trial intervention the level and method of blinding that will be used with reference to Section 6.7 Investigational Trial Intervention Assignment, Randomisation and Blinding.
Conformance	Optional
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	4.1
Value	Text
Business rules	**Value Allowed**: Yes **Relationship**: 4.1 Description of Trial Design **Concept**: CNEW

Repeating and/or Reuse Rules	No

298

Term (Variable)	<Description of Level and Method of Blinding>
Data Type	Text
Data (D), Value (V) or Heading (H)	D
Definition	CNEW For review purpose, see definition of the controlled terminology below A description of the level of awareness of the study participants and/or personnel to the respective intervention(s) or assessments being observed, received or administered
User Guidance	N/A
Conformance	Optional
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	4.1
Value	Text
Business rules	**Value Allowed**: Yes **Relationship**: 4.1 Description of Trial Design **Concept**: CNEW
Repeating and/or Reuse Rules	No

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300

Term (Variable)	<Additional Description of Trial Design>
Data Type	Text
Data (D), Value (V) or Heading (H)	D
Definition	CNEW For review purpose, see definition of the controlled terminology below An extra or further textual representation of the trial design.
User Guidance	Describe any other important aspects of the design, e.g.: • geographic scope of trial (e.g., single-centre, multi-centre, or multi-centre and multi-national) • use of decentralised processes, tools, or features in the trial; • planned use of a Data Monitoring Committee, or similar review group and cross reference Section 11.4 Committees, for details; • hether an interim analysis is planned and, if so, refer to details in Section 10.9 Interim Analyses • any planned extension trial, long-term follow-up/registry, planned future use of samples or data, or post-trial sample analysis or other data-related activities
Conformance	Optional
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	4.1
Value	Text
Business rules	**Value Allowed**: Yes **Relationship**: 4.1 Description of Trial Design **Concept**: CNEW

Repeating and/or Reuse Rules	No

4.1.1 Stakeholder Input into Design

Term (Variable)	4.1.1 Stakeholder Input into Design
Data Type	Text
Data (D), Value (V) or Heading (H)	H
Definition	Heading
User Guidance	N/A
Conformance	Optional
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	4.1.1
Value	Stakeholder Input into Design
Business rules	**Value Allowed**: No **Relationship**: 4.1.1 Stakeholder Input into Design, 4.1 Description of Trial Design, 4 TRIAL DESIGN and Table of Contents **Concept**: Heading
Repeating and/or Reuse Rules	No

Term (Variable)	<Stakeholder Input into Design>
Data Type	Text
Data (D), Value (V) or Heading (H)	D
Definition	CNEW For review purpose, see definition of the controlled terminology below The textual representation of the way in which trial stakeholders were consulted when determining the trial design.
User Guidance	If applicable, describe any stakeholder (e.g., patient, healthcare professional and patient advocacy groups) involvement in the design of the trial and any suggestions implemented.
Conformance	Optional
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	4.1.1
Value	Text
Business rules	**Value Allowed**: Yes **Relationship**: 4.1.1 Stakeholder Input into Design **Concept**: CNEW
Repeating and/or Reuse Rules	No

4.2 Rationale for Trial Design

Term (Variable)	4.2 Rationale for Trial Design
Data Type	Text
Data (D), Value (V) or Heading (H)	H

Definition	Heading
User Guidance	N/A
Conformance	Required
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	4.2
Value	Rationale for Trial Design
Business rules	**Value Allowed**: No **Relationship**: 4 TRIAL DESIGN and Table of Contents **Concept**: Heading
Repeating and/or Reuse Rules	No

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Term (Variable)	<Overall Rationale for Trial Design>
Data Type	Text
Data (D), Value (V) or Heading (H)	D
Definition	CNEW For review purpose, see definition of the controlled terminology below Trial design considerations that are different than the one(s) previously specified or mentioned.
User Guidance	N/A
Conformance	Conditional: If Level 3 subheadings are not used
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	4.2
Value	Text
Business rules	**Value Allowed**: Yes **Relationship**: 4.2 Rationale for Trial Design **Concept**: CNEW
Repeating and/or Reuse Rules	No

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308 ### 4.2.1 Rationale for Estimand(s)

Term (Variable)	4.2.1 Rationale for Estimand(s)
Data Type	Text
Data (D), Value (V) or Heading (H)	H
Definition	Heading
User Guidance	N/A
Conformance	Conditional: when<Overall Rationale for Trial Design> is not used
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	4.2.1
Value	Rationale for Estimand(s)
Business rules	**Value Allowed**: No **Relationship**: 4.2 Rationale for Trial Design, 4 TRIAL DESIGN and Table of Contents **Concept**: Heading

Repeating and/or Reuse Rules	No

309

Term (Variable)	<Rationale for Estimand(s)>
Data Type	Text
Data (D), Value (V) or Heading (H)	D
Definition	CNEW For review purpose, see definition of the controlled terminology below An explanation as to the scientific reasons for the choice of the trial estimand features.
User Guidance	When estimands are associated with the Primary and Secondary Objectives described in Section 3 Trial Objectives and Associated Estimands, provide a rationale for the estimand not described elsewhere in the document. This should include a rationale that the selected endpoint(s) are clinically relevant and provide a reliable and valid measurement of the intended intervention effect. It should also include a rationale for the selected strategies for handling intercurrent events.
Conformance	Conditional: when<Overall Rationale for Trial Design> is not used
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	4.2.1
Value	Text
Business rules	**Value Allowed**: Yes **Relationship**: 4.2.1 Rationale for Estimand(s) **Concept**: CNEW
Repeating and/or Reuse Rules	No

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311 ### 4.2.2 Rationale for Intervention Model

Term (Variable)	4.2.2 Rationale for Intervention Model
Data Type	Text
Data (D), Value (V) or Heading (H)	H
Definition	Heading
User Guidance	N/A
Conformance	Conditional: when <Overall Rationale for Trial Design> is not used
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	4.2.2
Value	Rationale for Intervention Model
Business rules	**Value Allowed**: No **Relationship**: 4.2 Rationale for Trial Design, 4 TRIAL DESIGN and Table of Contents **Concept**: Heading
Repeating and/or Reuse Rules	No

312

Term (Variable)	<Rationale for Trial Intervention Model>
Data Type	Text

Data (D), Value (V) or Heading (H)	D
Definition	CNEW For review purpose, see definition of the controlled terminology below An explanation as to the scientific reasons for why the intervention model was chosen for the trial.
User Guidance	Provide a rationale for the trial intervention model described in Section 4.1 Description of Trial Design with a cross-reference to Section 6.2 Rationale for Investigational Intervention Dose and Regimen. Rationale for choice of comparator, if applicable, should be described separately in Section 4.2.5 Rationale for Control Type. A rationale for the choice of trial population should be described separately in Section 5.1 Description of Trial Population and Rationale.
Conformance	Conditional: when <Overall Rationale for Trial Design> is not used
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	4.2.2
Value	Text
Business rules	**Value Allowed**: Yes **Relationship**: 4.2.2 Rational for Intervention Model **Concept**: CNEW
Repeating and/or Reuse Rules	No

4.2.3 Rationale for Control Type

Term (Variable)	4.2.3 Rationale for Control Type
Data Type	Text
Data (D), Value (V) or Heading (H)	H
Definition	Heading
User Guidance	N/A
Conformance	Conditional: when <Overall Rationale for Trial Design> is not used
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	4.2.3
Value	Rationale for Control Type
Business rules	**Value Allowed**: No **Relationship**: 4.2 Rationale for Trial Design, 4 TRIAL DESIGN and Table of Contents **Concept**: Heading
Repeating and/or Reuse Rules	No

Term (Variable)	<Rationale for Control Type>
Data Type	Text
Data (D), Value (V) or Heading (H)	D
Definition	CNEW For review purpose, see definition of the controlled terminology below

	An explanation as to the scientific reasons for the choice of the control types used in the trial.
User Guidance	If applicable, provide a rationale for the type and choice of control selected for the trial (e.g., placebo, active drug, combination, external). Describe any known or potential problems associated with the control group selected in light of the specific disease and intervention(s) being studied. If comparators will differ by region, describe. The rationale for dose/dose regimen is explained in Section 6.2 Rationale for Investigational Trial Intervention Dose and Regimen.
Conformance	Conditional: when <Overall Rationale for Trial Design> is not used
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	4.2.3
Value	Text
Business rules	**Value Allowed**: Yes **Relationship**: 4.2.3 Rational for Control Type **Concept**: CNEW
Repeating and/or Reuse Rules	No

316

317 ### 4.2.4 Rationale for Trial Duration

Term (Variable)	4.2.4 Rationale for Trial Duration
Data Type	Text
Data (D), Value (V) or Heading (H)	H
Definition	Heading
User Guidance	N/A
Conformance	Conditional: when <Overall Rationale for Trial Design> is not used
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	4.2.4
Value	Rationale for Trial Duration
Business rules	**Value Allowed**: No **Relationship**: 4.2 Rationale for Trial Design, 4 TRIAL DESIGN and Table of Contents **Concept**: Heading
Repeating and/or Reuse Rules	No

318

Term (Variable)	<Rationale for Duration>
Data Type	Text
Data (D), Value (V) or Heading (H)	D
Definition	CNEW For review purpose, see definition of the controlled terminology below An explanation as to the scientific reasons for the trial duration.
User Guidance	Provide a rationale that the trial duration is appropriate for a reliable and relevant evaluation of the trial intervention per the trial objective(s).
Conformance	Conditional: when <Overall Rationale for Trial Design> is not used
Cardinality	One to one

Relationship content from ToC representing the protocol hierarchy	4.2.4
Value	Text
Business rules	**Value Allowed**: Yes **Relationship**: 4.2.4 Rationale for Duration **Concept**: CNEW
Repeating and/or Reuse Rules	No

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322 ### 4.2.5 Rationale for Adaptive or Novel Trial Design

Term (Variable)	4.2.5 Rationale for Adaptive or Novel Trial Design
Data Type	Text
Data (D), Value (V) or Heading (H)	H
Definition	Heading
User Guidance	N/A
Conformance	Conditional: when <Overall Rationale for Trial Design> is not used
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	4.2.5
Value	Rationale for Adaptive or Novel Design
Business rules	**Value Allowed**: No **Relationship**: 4.2 Rationale for Trial Design, 4 TRIAL DESIGN and Table of Contents **Concept**: Heading
Repeating and/or Reuse Rules	No

323

Term (Variable)	<Rationale for Adaptive or Novel Trial Design>
Data Type	Text
Data (D), Value (V) or Heading (H)	D
Definition	CNEW For review purpose, see definition of the controlled terminology below An explanation as to the scientific reasons for why an adaptive or novel trial design was chosen for the trial.
User Guidance	If applicable, provide a rationale for the use of an adaptive or novel design.
Conformance	Conditional: when <Overall Rationale for Trial Design> is not used
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	4.2.5
Value	Text
Business rules	**Value Allowed**: Yes **Relationship**: 4.2.5 Rational for Adoptive or Novel Trial Design **Concept**: CNEW
Repeating and/or Reuse Rules	No

4.2.6 Rationale for Interim Analysis

Term (Variable)	4.2.6 Rationale for Interim Analysis
Data Type	Text
Data (D), Value (V) or Heading (H)	H
Definition	Heading
User Guidance	N/A
Conformance	Conditional: when <Overall Rationale for Trial Design> is not used
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	4.2.6
Value	Rationale for Interim Analysis
Business rules	**Value Allowed**: No **Relationship**: 4.2 Rationale for Trial Design, 4 TRIAL DESIGN and Table of Contents **Concept**: Heading
Repeating and/or Reuse Rules	No

Term (Variable)	<Rationale for Interim Analysis>
Data Type	Text
Data (D), Value (V) or Heading (H)	D
Definition	CNEW For review purpose, see definition of the controlled terminology below An explanation for the analysis comparing intervention groups at any time before the formal completion of the trial, usually before recruitment is complete.
User Guidance	If applicable, provide a rationale for any interim analysis planned with respect to its purpose (e.g., stopping the trial early for efficacy or futility) and timing.
Conformance	Conditional: when<Overall Rationale for Trial Design> is not used
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	4.2.6
Value	Text
Business rules	**Value Allowed**: Yes **Relationship**: 4.2.6 Rational for Interim Analysis **Concept**: CNEW
Repeating and/or Reuse Rules	No

4.2.7 Rationale for Other Trial Design Aspects

Term (Variable)	4.2.7 Rationale for Other Trial Design Aspects
Data Type	Text
Data (D), Value (V) or Heading (H)	H
Definition	Heading
User Guidance	N/A
Conformance	Conditional: when<Overall Rationale for Trial Design> is not used

Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	4.2.7
Value	Rationale for Other Trial Design Aspects
Business rules	**Value Allowed**: No **Relationship**: 4.2 Rationale for Trial Design, 4 TRIAL DESIGN and Table of Contents **Concept**: Heading
Repeating and/or Reuse Rules	No

Term (Variable)	<Rationale for Other Trial Design Aspects>
Data Type	Text
Data (D), Value (V) or Heading (H)	D
Definition	CNEW For review purpose, see definition of the controlled terminology below An explanation as to the scientific reasons for additional trial design considerations that are different than the one(s) previously specified or mentioned.
User Guidance	Discuss rationale for any additional aspects of the design not addressed above.
Conformance	Conditional: when <Overall Rationale for Trial Design> is not used
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	4.2.7
Value	Text
Business rules	**Value Allowed**: Yes **Relationship**: 4.2.7 Rational for Other Trial Design Aspects **Concept**: CNEW
Repeating and/or Reuse Rules	No

4.3 Trial Stopping Rules

Term (Variable)	4.3 Trial Stopping Rules
Data Type	Text
Data (D), Value (V) or Heading (H)	H
Definition	Heading
User Guidance	N/A
Conformance	Required
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	4.3
Value	Trial Stopping Rules
Business rules	**Value Allowed**: No **Relationship**: 4 TRIAL DESIGN and Table for Content **Concept**: Heading
Repeating and/or Reuse Rules	No

Term (Variable)	<Trial Stopping Rules>

Data Type	Text
Data (D), Value (V) or Heading (H)	D
Definition	C142698 For review purpose, see definition of the controlled terminology below A criterion that, when met by the accumulating data, indicates that the trial can or should be stopped early to avoid putting participants at risk unnecessarily or because the intervention effect is so great that further data collection is unnecessary.
User Guidance	If applicable, describe any trial-specific stopping rules, including guidance on when the trial should be stopped for efficacy or safety reasons, when a cohort or dose escalation should be terminated, and/or when a given treatment arm should be terminated. If applicable, describe any rules that may result in a temporary pause of dosing and/or enrollment into the trial and criteria for restarting enrollment. Ensure that the trial stopping rules are aligned with the specifications that are described in Section 10.9 for Interim Analyses.
Conformance	Required
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	4.3
Value	Text
Business rules	**Value Allowed**: Yes **Relationship**: 4.3 Trial Stopping Rules **Concept**: C142698
Repeating and/or Reuse Rules	No

4.4 Start of Trial and End of Trial

Term (Variable)	4.4 Start of Trial and End of Trial
Data Type	Text
Data (D), Value (V) or Heading (H)	H
Definition	Heading
User Guidance	N/A
Conformance	Required
Cardinality	One to many
Relationship content from ToC representing the protocol hierarchy	4.4
Value	Start of Trial and End of Trial
Business rules	**Value Allowed**: No **Relationship**: 4 TRIAL DESIGN and Table of Contents **Concept**: Heading
Repeating and/or Reuse Rules	No

Term (Variable)	<Start of Trial>
Data Type	Text
Data (D), Value (V) or Heading (H)	D
Definition	CNEW For review purpose, see definition of the controlled terminology below

	A textual description containing a concise explanation, any local regulatory requirements and considerations, extensions, follow-up, and analysis for the trial start.
User Guidance	Define key timepoints in the trial, including trial start and end definitions. (e.g., a key timepoint definition for start of trial might be when the informed consent is signed by the first participant and a key timepoint definition for end of trial might be when participants are no longer being examined or the last participant's last trial assessment has occurred). Consider local regulatory requirements for these and other definitions (e.g., the first act of recruitment). If appropriate, provide a cross-reference to Section 11.11 Early Site Closure.
Conformance	Required
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	4.4
Value	Text
Business rules	**Value Allowed**: Yes **Relationship**: 4.4 Start of Trial and End of Trial **Concept**: CNEW
Repeating and/or Reuse Rules	No

340

Term (Variable)	<End of Trial>
Data Type	Text
Data (D), Value (V) or Heading (H)	D
Definition	CNEW For review purpose, see definition of the controlled terminology below A textual description containing a concise explanation, any local regulatory requirements and considerations, extensions, follow-up, and analysis for the trial end.
User Guidance	Define key timepoints in the trial, including trial start and end definitions. (e.g., a key timepoint definition for start of trial might be when the informed consent is signed by the first participant and a key timepoint definition for end of trial might be when participants are no longer being examined or the last participant's last trial assessment has occurred). If applicable, consider local regulatory requirements for these and other definitions (e.g., the first act of recruitment). If appropriate, provide a cross-reference to Section 11.10 Early Site Closure.
Conformance	Required
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	4.4
Value	Text
Business rules	**Value Allowed**: Yes **Relationship**: 4.4 Start of Trial **Concept**: CNEW
Repeating and/or Reuse Rules	No

341

342 ## 4.5 Access to Trial Intervention After End of Trial

Term (Variable)	4.5 Access to Trial Intervention After End of Trial
Data Type	Text

Data (D), Value (V) or Heading (H)	H
Definition	Heading
User Guidance	N/A
Conformance	Required
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	4.5
Value	Access to Trial Intervention After End of Trial
Business rules	**Value Allowed**: No **Relationship**: 4 TRIAL DESIGN and Table of Contents **Concept**: Heading
Repeating and/or Reuse Rules	No

Term (Variable)	<Access to Trial Intervention after End of Trial>
Data Type	Text
Data (D), Value (V) or Heading (H)	D
Definition	CNEW For review purpose, see definition of the controlled terminology below A textual representation containing information about whether and how trial participants have access to the trial interventions after the trial ends.
User Guidance	If applicable, describe any possibilities for access to trial intervention, if any, beyond completion of the trial. Planned extension trials, if described in Section 4.1 Description of Trial Design do not need to be repeated in this section.
Conformance	Required
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	4.5
Value	Text
Business rules	**Value Allowed**: Yes **Relationship**: 4.5 Access to Trial Intervention After End of Trial **Concept**: CNEW
Repeating and/or Reuse Rules	No

5 TRIAL POPULATION

Term (Variable)	5 TRIAL POPULATION
Data Type	Text
Data (D), Value (V) or Heading (H)	H
Definition	Heading
User Guidance	No text is intended here (Heading only). List the criteria necessary for participation in the trial. Ensure that each criterion can be easily assessed definitively and answered with yes/no responses. • Criteria should be written to avoid protocol waivers or exemptions. • If participants require screening, distinguish between screening vs enrolling participants.

	• If measures to enrich the trial population for pre-specified subgroups of interest are used, these should be described.
Conformance	Required
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	5
Value	TRIAL POPULATION
Business rules	**Value Allowed**: No **Relationship**: Table of contents **Concept**: Heading
Repeating and/or Reuse Rules	No

346

347 5.1 Description of Trial Population and Rationale

Term (Variable)	5.1 Description of Trial Population and Rationale
Data Type	Text
Data (D), Value (V) or Heading (H)	H
Definition	Heading
User Guidance	N/A
Conformance	Required
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	5.1
Value	Description of Trial Population and Rationale
Business rules	**Value Allowed**: No **Relationship**: 5 TRIAL POPULATION and Table of Contents **Concept**: Heading
Repeating and/or Reuse Rules	No

348

Term (Variable)	<Description of Trial Population and Rationale>
Data Type	Text
Data (D), Value (V) or Heading (H)	D
Definition	CNEW A narrative representation of the rationale for selection of trial population describing how the selected population can meet the trial objectives and how the enrolment criteria reflect the targeted populations.
User Guidance	Describe the population selected (e.g., healthy participants, adult participants, paediatric participants) and how the enrollment criteria reflect the populations that are likely to use the drug if approved. Specify the population age range (e.g., ≤3 months, ≥18 to ≤80 years old) including the time point at which qualification for age criteria is determined (e.g., at time of screening vs randomisation for paediatric trials). Specify any key diagnostic criteria for the population (e.g., "acute lung injury", or a specific biomarker profile). If applicable, describe similar conditions or diseases and their differential diagnosis. Provide a rationale for the trial population ensuring that the population selected is well defined and clinically recognisable. Describe how the selected population can

	meet the trial objectives and how the enrollment criteria reflect the population of interest. If the population targeted by a clinical question is based on a subset of the entire trial population, e.g., defined by a particular characteristic measured at baseline (e.g. a specific biomarker), this subset should be justified in this section. Justify whether the trial intervention is to be evaluated in paediatric participants, in adults unable to consent for themselves, other vulnerable participant populations, or those that may respond to the trial intervention differently (e.g., elderly, hepatic or renally impaired, or immunocompromised participants).
Conformance	Required
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	5.1
Value	Text
Business rules	**Value Allowed**: Yes **Relationship**: 5.1 Description of Trial Population and Rationale **Concept**: CNEW
Repeating and/or Reuse Rules	No

Term (Variable)	Prospective approval of protocol deviations to recruitment and enrollment criteria, also known as protocol waivers or exemptions, is not permitted.
Data Type	Text
Data (D), Value (V) or Heading (H)	V
Definition	Universal Text
User Guidance	N/A
Conformance	Required
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	5.1
Value	Prospective approval of protocol deviations to recruitment and enrollment criteria, also known as protocol waivers or exemptions, is not permitted.
Business rules	**Value Allowed**: No **Relationship**: 5.1 Description of Trial Population and Rationale **Concept**: Universal text
Repeating and/or Reuse Rules	No

5.2 Inclusion Criteria

Term (Variable)	5.2 Inclusion Criteria
Data Type	Text
Data (D), Value (V) or Heading (H)	H
Definition	Heading
User Guidance	
Conformance	Required
Cardinality	One to many

Relationship content from ToC representing the protocol hierarchy	5.2
Value	5.2 Inclusion Criteria
Business rules	**Value Allowed**: No **Relationship**: 5 TRIAL POPULATION and Table of Contents **Concept**: Heading
Repeating and/or Reuse Rules	No

352

Term (Variable)	To be eligible to participate in this trial, an individual must meet all the following criteria:
Data Type	Text
Data (D), Value (V) or Heading (H)	V
Definition	Universal text
User Guidance	N/A
Conformance	Required
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	5.2
Value	To be eligible to participate in this trial, an individual must meet all the following criteria:
Business rules	**Value Allowed**: No **Relationship**: 5.2 Inclusion Criteria **Concept**: Universal text
Repeating and/or Reuse Rules	No

353

Term (Variable)	<#>
Data Type	Number
Data (D), Value (V) or Heading (H)	D
Definition	N/A
User Guidance	Add criteria as needed. Consider numbering the criteria sequentially.
Conformance	Optional
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	5.2
Value	# is an integer <criterion identifier> unique number and not replaceable
Business rules	**Value Allowed**: Yes **Relationship**: 5.2 Inclusion Criteria **Concept**: Sequential number
Repeating and/or Reuse Rules	Yes, repeatable for each inclusion criterion

354

Term (Variable)	<Inclusion Criterion>
Data Type	Text
Data (D), Value (V) or Heading (H)	D

Definition	C25532 For review purpose, see definition of the controlled terminology below The criteria in a protocol that prospective subjects must meet to be eligible for participation in a study.
User Guidance	Add criteria as needed. Consider numbering the criteria sequentially
Conformance	Required
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	5.2
Value	Text
Business rules	**Value Allowed**: Yes **Relationship**: to Number #, 5.2 Inclusion Criteria **Concept**: C25532
Repeating and/or Reuse Rules	Yes, number consecutively, repeatable for each inclusion criteria, if deleted do not replace, do not duplicate

355

356 ## 5.3 Exclusion Criteria

Term (Variable)	5.3 Exclusion Criteria
Data Type	Text
Data (D), Value (V) or Heading (H)	H
Definition	Heading
User Guidance	Exclusion criteria are characteristics that make an individual ineligible for participation.
Conformance	Required
Cardinality	One to many
Relationship content from ToC representing the protocol hierarchy	5.3
Value	Exclusion Criteria
Business rules	**Value Allowed**: No **Relationship**: 5 TRIAL POPULATION and Table of Contents **Concept**: Heading
Repeating and/or Reuse Rules	No

357

Term (Variable)	An individual who meets any of the following criteria will be excluded from participation in this trial:
Data Type	Text
Data (D), Value (V) or Heading (H)	V
Definition	Universal text
User Guidance	N/A
Conformance	Required
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	5.3
Value	An individual who meets any of the following criteria will be excluded from participation in this trial:

Business rules	**Value Allowed**: No **Relationship**: 5.3 Exclusion Criteria, 5 TRIAL POPULATION and Table of Contents **Concept:** Universal text
Repeating and/or Reuse Rules	No

358

Term (Variable)	<#>
Data Type	Number
Data (D), Value (V) or Heading (H)	D
Definition	N/A
User Guidance	
Conformance	Required
Cardinality	One to many
Relationship content from ToC representing the protocol hierarchy	5.3
Value	# is an identifier <criterion identifier> unique number and not replaceable
Business rules	**Value Allowed**: Yes **Relationship**: 5.3 Exclusion Criteria **Concept**: Sequential number
Repeating and/or Reuse Rules	Yes. number consecutively, repeatable for each exclusion criteria, if deleted do not replace, do not duplicate

359

Term (Variable)	<Exclusion Criterion>
Data Type	Text
Data (D), Value (V) or Heading (H)	D
Definition	C25370 For review purpose, see definition of the controlled terminology below List of characteristics in a protocol, any one of which excludes a potential subject from participation in a study. (CDISC glossary)
User Guidance	Add criteria as needed. Consider numbering the criteria sequentially
Conformance	Required
Cardinality	One to many
Relationship content from ToC representing the protocol hierarchy	5.3
Value	Text
Business rules	**Value Allowed**: Yes **Relationship**: to Number #, 5.3 Exclusion Criteria **Concept**: C25370
Repeating and/or Reuse Rules	Yes, repeatable for each exclusion criterion, if deleted do not replace, do not duplicate

360

361 ## 5.4 Contraception

Term (Variable)	5.4 Contraception
Data Type	Text
Data (D), Value (V) or Heading (H)	H

Definition	Heading
User Guidance	
Conformance	Required
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	5.4
Value	Contraception
Business rules	**Value Allowed**: No **Relationship**: 5 TRIAL POPULATION and Table of Contents **Concept**: Heading
Repeating and/or Reuse Rules	No

362

363 ### 5.4.1 Definitions Related to Childbearing Potential

Term (Variable)	5.4.1 Definitions Related to Childbearing Potential
Data Type	Text
Data (D), Value (V) or Heading (H)	H
Definition	Heading
User Guidance	N/A
Conformance	Required
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	5.4.1
Value	Definitions Related to Childbearing Potential
Business rules	**Value Allowed**: No **Relationship**: 5.4 Contraception, 5 TRIAL POPULATION and Table of Contents **Concept**: Heading
Repeating and/or Reuse Rules	No

364

Term (Variable)	<Definitions Related to Childbearing Potential>
Data Type	Text
Data (D), Value (V) or Heading (H)	D
Definition	CNEW For review purpose, see definition of the controlled terminology below A concise explanation of the meaning of participants of childbearing potential and non-childbearing potential within the context of a trial, or state not applicable.
User Guidance	Specify the definitions of: ●
Conformance	Required
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	5.4.1
Value	Text
Business rules	**Value Allowed**: Yes **Relationship**: 5.4.1 Definitions Related to Childbearing Potential **Concept**: CNEW

Repeating and/or Reuse Rules	No

365

366 ### 5.4.2 Contraception Requirements

Term (Variable)	5.4.2 Contraception Requirements
Data Type	Text
Data (D), Value (V) or Heading (H)	H
Definition	Heading
User Guidance	N/A
Conformance	Required
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	5.4
Value	Contraception Requirements
Business rules	**Value Allowed**: No **Relationship**: 5.4 Contraception, 5 TRIAL POPULATION and Table of Contents **Concept**: Heading
Repeating and/or Reuse Rules	No

367

Term (Variable)	<Contraception Requirements>
Data Type	Text
Data (D), Value (V) or Heading (H)	D
Definition	CNEW For review purpose, see definition of the controlled terminology below A description of the requirements for the prevention of conception or impregnation by the use of devices or drugs or surgery within a context of a trial l, or state not applicable.
User Guidance	Specify the: •
Conformance	Required
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	5.4
Value	Text
Business rules	**Value Allowed**: Yes **Relationship**: 5.4.2 Contraception requirements **Concept**: CNEW
Repeating and/or Reuse Rules	No

368

369 ## 5.5 Lifestyle Restrictions

Term (Variable)	5.5 Lifestyle Restrictions
Data Type	Text
Data (D), Value (V) or Heading (H)	H

Definition	Heading
User Guidance	N/A
Conformance	Required
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	5.5
Value	Lifestyle Restrictions
Business rules	**Value Allowed**: No **Relationship**: 5 TRIAL POPULATION and Table of Contents **Concept**: Heading
Repeating and/or Reuse Rules	No

370

Term (Variable)	{<Lifestyle Restrictions>}
Data Type	Text
Data (D), Value (V) or Heading (H)	D
Definition	CNEW For review purpose, see definition of the controlled terminology below A description of the restrictions related to trial participant lifestyle such as diet, substance intake, and physical or other daily activities.
User Guidance	In the following subsections, describe any restrictions during the trial pertaining to lifestyle and/or diet, intake of caffeine, alcohol, or tobacco, or physical and other activities. If not applicable, include a statement that no restrictions are required.
Conformance	Conditional: If Level 3 subheadings are not used
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	5.5
Value	Text
Business rules	**Value Allowed**: Yes **Relationship**: 5.5 Lifestyle Restrictions **Concept**: CNEW
Repeating and/or Reuse Rules	No

371

372 ### 5.5.1 Meals and Dietary Restrictions

Term (Variable)	5.5.1 Meals and Dietary Restrictions
Data Type	Text
Data (D), Value (V) or Heading (H)	H
Definition	Heading
User Guidance	N/A
Conformance	Optional
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	5.5.1
Value	Meals and Dietary Restrictions
Business rules	**Value Allowed**: No

	Relationship: 5.5 Lifestyle Restrictions, 5 TRIAL POPULATION and Table of Contents **Concept**: Heading
Repeating and/or Reuse Rules	No

373

Term (Variable)	<Meals and Dietary Restrictions>
Data Type	Text
Data (D), Value (V) or Heading (H)	D
Definition	CNEW For review purpose, see definition of the controlled terminology below A description of the restrictions related to participant diet during the trial.
User Guidance	
Conformance	Optional
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	5.5.1
Value	Text
Business rules	**Value Allowed**: Yes **Relationship**: 5.5.1 Meals and Dietary Restrictions **Concept**: CNEW
Repeating and/or Reuse Rules	No

374

375 ### 5.5.2 Caffeine, Alcohol, Tobacco, and Other Restrictions

Term (Variable)	5.5.2 Caffeine, Alcohol, Tobacco, and Other Restrictions
Data Type	Text
Data (D), Value (V) or Heading (H)	H
Definition	Heading
User Guidance	N/A
Conformance	Optional
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	5.5.2
Value	Caffeine, Alcohol, Tobacco, and Other Restrictions
Business rules	**Value Allowed**: No **Relationship**: 5.5 Lifestyle Restrictions, 5 TRIAL POPULATION and Table of Contents **Concept**: Heading
Repeating and/or Reuse Rules	No

376

Term (Variable)	<Caffeine, Alcohol, Tobacco, and Other Restrictions>
Data Type	Text
Data (D), Value (V) or Heading (H)	D
Definition	CNEW

	For review purpose, see definition of the controlled terminology below A textual description of the restrictions related to participant intake of caffeine, alcohol, tobacco, and other habit-forming substances during the trial.
User Guidance	If applicable, describe any restrictions on the intake of caffeine, alcohol, tobacco, or other restrictions.
Conformance	Optional
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	5.5.2
Value	Text
Business rules	**Value Allowed**: Yes **Relationship**: 5.2.2 Caffeine, Alcohol, Tobacco, and Other Restrictions **Concept**: CNEW
Repeating and/or Reuse Rules	No

377

378 ### 5.5.3 Physical Activity Restrictions

Term (Variable)	5.5.3 Physical Activity Restrictions
Data Type	Text
Data (D), Value (V) or Heading (H)	H
Definition	Heading
User Guidance	N/A
Conformance	Optional
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	5.5.3
Value	Physical Activity Restrictions
Business rules	**Value Allowed**: No **Relationship**: 5.5 Lifestyle Restrictions, 5 TRIAL POPULATION and Table of Contents **Concept**: Heading
Repeating and/or Reuse Rules	No

379

Term (Variable)	<Physical Activity Restrictions>
Data Type	Text
Data (D), Value (V) or Heading (H)	D
Definition	C17708 For review purpose, see definition of the controlled terminology below Any form of exercise or movement. Physical activity may include planned activity such as walking, running, basketball, or other sports. Physical activity may also include other daily activities such as household chores, yard work, walking the dog, etc.
User Guidance	If applicable, describe any restrictions on activity (e.g., in first-in-human trials, activity may be restricted by ensuring participants remain in bed for 4 to 6 hours after dosing).
Conformance	Optional

Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	5.5.3
Value	Text
Business rules	**Value Allowed**: Yes **Relationship**: 5.5.3 Physical Activity Restrictions **Concept**: C17708
Repeating and/or Reuse Rules	No

380

381 ### 5.5.4 Other Activity Restrictions

Term (Variable)	5.5.4 Other Activity Restrictions
Data Type	Text
Data (D), Value (V) or Heading (H)	H
Definition	Heading
User Guidance	N/A
Conformance	Optional
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	5.5.4
Value	Other Activity Restrictions
Business rules	**Value Allowed**: No **Relationship**: 5.5 Lifestyle Restrictions, 5 TRIAL POPULATION and Table of Contents **Concept**: Heading
Repeating and/or Reuse Rules	No

382

Term (Variable)	<Other Activity Restrictions>
Data Type	Text
Data (D), Value (V) or Heading (H)	D
Definition	CNEW For review purpose, see definition of the controlled terminology below An activity that is different than the one(s) previously specified or mentioned.
User Guidance	If applicable, describe restrictions on any other activity (e.g., blood or tissue donation, driving, heavy machinery use, or sun exposure).
Conformance	Optional
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	5.5.4
Value	Text
Business rules	**Value Allowed**: Yes **Relationship**: 5.5.4 Other Activity Restrictions **Concept**: CNEW
Repeating and/or Reuse Rules	No

5.6 Screen Failure and Rescreening

Term (Variable)	5.6 Screen Failure and Rescreening
Data Type	Text
Data (D), Value (V) or Heading (H)	H
Definition	Heading
User Guidance	N/A
Conformance	Required
Cardinality	One to many
Relationship content from ToC representing the protocol hierarchy	5.6
Value	Screen Failure and Rescreening
Business rules	**Value Allowed**: No **Relationship**: 5 TRIAL POPULATION and Table of Contents **Concept**: Heading
Repeating and/or Reuse Rules	No

Term (Variable)	<Screen Failure>
Data Type	Text
Data (D), Value (V) or Heading (H)	D
Definition	C49628 For review purpose, see definition of the controlled terminology below The potential subject who does not meet eligibility (inclusion/exclusion) criteria during the screening period.
User Guidance	Describe screen failure and indicate how screen failure will be handled in the trial, including conditions and criteria upon which rescreening is acceptable. If applicable, indicate the circumstances and time window under which a repeat procedure is allowed for screen failure relating to specific inclusion/exclusion criteria for the trial.
Conformance	Required
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	5.6
Value	Text
Business rules	**Value Allowed**: Yes **Relationship**: 5.6 Screen Failure and Rescreening **Concept**: C49628
Repeating and/or Reuse Rules	No

Term (Variable)	<Rescreening>
Data Type	Text
Data (D), Value (V) or Heading (H)	D
Definition	CNEW For review purpose, see definition of the controlled terminology below

	The process of active consideration of subjects for enrolment in a trial, for those potential subjects who have failed a prior screening attempt.
User Guidance	Describe screen failure and indicate how screen failure will be handled in the trial, including conditions and criteria upon which rescreening is acceptable. If applicable, indicate the circumstances and time window under which a repeat procedure is allowed for screen failure relating to specific inclusion/exclusion criteria for the trial.
Conformance	Required
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	5.6
Value	Text
Business rules	**Value Allowed**: Yes **Relationship**: 5.6 Screen Failure and Rescreening **Concept**: CNEW
Repeating and/or Reuse Rules	No

6 TRIAL INTERVENTION AND CONCOMITANT THERAPY

Term (Variable)	6 TRIAL INTERVENTION AND CONCOMITANT THERAPY
Data Type	Text
Data (D), Value (V) or Heading (H)	H
Definition	Heading
User Guidance	N/A
Conformance	Required
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	6
Value	TRIAL INTERVENTION AND CONCOMITANT THERAPY
Business rules	**Value Allowed**: No **Relationship**: Table of Contents **Concept**: Heading
Repeating and/or Reuse Rules	No

Term (Variable)	<Description of the overview of trial interventions or a heading for the optional table below>
Data Type	Text
Data (D), Value (V) or Heading (H)	D
Definition	CNEW
User Guidance	Trial interventions are all pre-specified, investigational and non-investigational medicinal products, medical devices or other interventions intended for the participants during the trial. The investigational trial intervention is the product used in the trial as part of trial objectives. Description of investigational trial intervention is provided in Section 6.1. Other trial interventions that are not part of trial objectives (not an investigational role in this trial) are described in Section 6.9 Description of Non-investigational trial interventions. Any regional requirements should be noted in the appropriate subsections.

	Provide an overview of investigational and non-investigational trial interventions. Classify the trial intervention as IMP, NIMP/AxMP designations based on study design and local legislation. Consider the optional table below
Conformance	Required
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	6
Value	Text
Business rules	**Value Allowed**: Yes **Relationship**: 6 TRIAL INTERVENTION AND CONCOMITANT THERAPY **Concept**: CNEW
Repeating and/or Reuse Rules	No

390

Term (Variable)	Arm Name
Data Type	Text
Data (D), Value (V) or Heading (H)	H
Definition	Table Column Heading
User Guidance	N/A
Conformance	Optional: if the table used
Cardinality	One to many
Relationship content from ToC representing the protocol hierarchy	6
Value	Arm Name
Business rules	**Value Allowed**: No **Relationship**: Optional Table Heading **Concept**: Heading
Repeating and/or Reuse Rules	No

391

Term (Variable)	Arm Type
Data Type	Text
Data (D), Value (V) or Heading (H)	H
Definition	Table Column Heading
User Guidance	N/A
Conformance	Optional: if the table used
Cardinality	One to many
Relationship content from ToC representing the protocol hierarchy	6
Value	Arm Type
Business rules	**Value Allowed**: No **Relationship**: Optional Table Heading **Concept**: Heading
Repeating and/or Reuse Rules	No

392

Term (Variable)	Intervention Name
Data Type	Text

Data (D), Value (V) or Heading (H)	H
Definition	Table Column Heading
User Guidance	N/A
Conformance	Optional if the table used
Cardinality	One to many
Relationship content from ToC representing the protocol hierarchy	6
Value	Intervention Name
Business rules	**Value Allowed**: No **Relationship**: Optional Table Heading **Concept**: Heading
Repeating and/or Reuse Rules	No

393

Term (Variable)	Intervention Type
Data Type	Text
Data (D), Value (V) or Heading (H)	H
Definition	Table Column Heading
User Guidance	N/A
Conformance	Optional: if the table used
Cardinality	One to many
Relationship content from ToC representing the protocol hierarchy	6
Value	Intervention Type
Business rules	**Value Allowed**: No **Relationship**: Optional Table Heading **Concept**: Heading
Repeating and/or Reuse Rules	No

394

Term (Variable)	Pharmaceutical Dose Form
Data Type	Text
Data (D), Value (V) or Heading (H)	H
Definition	Table Column Heading
User Guidance	N/A
Conformance	Optional: if the table used
Cardinality	One to many
Relationship content from ToC representing the protocol hierarchy	6
Value	Pharmaceutical Dose Form
Business rules	**Value Allowed**: No **Relationship**: Optional Table Heading **Concept**: Heading
Repeating and/or Reuse Rules	No

395

Term (Variable)	Dosage Strength(s)

Data Type	Text
Data (D), Value (V) or Heading (H)	H
Definition	Table Column Heading
User Guidance	N/A
Conformance	Optional: if the table used
Cardinality	One to many
Relationship content from ToC representing the protocol hierarchy	6
Value	Dosage Strength(s)
Business rules	**Value Allowed**: No **Relationship**: Optional Table Heading **Concept**: Heading
Repeating and/or Reuse Rules	No

396

Term (Variable)	Dosage Level(s)
Data Type	Text
Data (D), Value (V) or Heading (H)	H
Definition	Table Column Heading
User Guidance	N/A
Conformance	Optional: if the table used
Cardinality	One to many
Relationship content from ToC representing the protocol hierarchy	6
Value	Dosage Level(s)
Business rules	**Value Allowed**: No **Relationship**: Optional Table Heading **Concept**: Heading
Repeating and/or Reuse Rules	No

397

Term (Variable)	Route of Administration
Data Type	Text
Data (D), Value (V) or Heading (H)	H
Definition	Table Column Heading
User Guidance	N/A
Conformance	Optional: if the table used
Cardinality	One to many
Relationship content from ToC representing the protocol hierarchy	6
Value	Route of Administration
Business rules	**Value Allowed**: No **Relationship**: Optional Table Heading **Concept**: Heading
Repeating and/or Reuse Rules	No

398

Term (Variable)	Regimen/Treatment Period/Vaccination Regimen
Data Type	Text
Data (D), Value (V) or Heading (H)	H
Definition	Table Column Heading
User Guidance	N/A
Conformance	Optional: if the table used
Cardinality	One to many
Relationship content from ToC representing the protocol hierarchy	6
Value	Regimen/Treatment Period/Vaccination Regimen
Business rules	**Value Allowed**: No **Relationship**: Optional Table Heading **Concept**: Heading
Repeating and/or Reuse Rules	No

399

Term (Variable)	Use
Data Type	Text
Data (D), Value (V) or Heading (H)	H
Definition	Table Column Heading
User Guidance	N/A
Conformance	Optional: if the table used
Cardinality	One to many
Relationship content from ToC representing the protocol hierarchy	6
Value	Use
Business rules	**Value Allowed**: No **Relationship**: Optional Table Heading **Concept**: Heading
Repeating and/or Reuse Rules	No

400

Term (Variable)	IMP/NIMP
Data Type	Text
Data (D), Value (V) or Heading (H)	H
Definition	Table Column Heading
User Guidance	N/A
Conformance	Optional: if the table used
Cardinality	One to many
Relationship content from ToC representing the protocol hierarchy	6
Value	IMP/NIMP
Business rules	**Value Allowed**: No **Relationship**: Optional Table Heading **Concept**: Heading
Repeating and/or Reuse Rules	No

401

Term (Variable)	Sourcing
Data Type	Text
Data (D), Value (V) or Heading (H)	H
Definition	Table Column Heading
User Guidance	N/A
Conformance	Optional: if the table used
Cardinality	One to many
Relationship content from ToC representing the protocol hierarchy	6
Value	Sourcing
Business rules	**Value Allowed**: No **Relationship**: Optional Table Heading **Concept**: Heading
Repeating and/or Reuse Rules	No

402

Term (Variable)	<Arm Name>
Data Type	Text
Data (D), Value (V) or Heading (H)	D
Definition	C93729 For review purpose, see definition of the controlled terminology below The literal identifier (i.e. distinctive designation) for the arm.
User Guidance	N/A
Conformance	Optional: if the table used
Cardinality	One to many; one to interventions for arm name
Relationship content from ToC representing the protocol hierarchy	6
Value	Text
Business rules	**Value Allowed**: Yes **Relationship**: arm name **Concept**: C93729
Repeating and/or Reuse Rules	Yes, repeatable for each arm name and intervention and use combination

403

Term (Variable)	<Arm Type>
Data Type	Valid Value
Data (D), Value (V) or Heading (H)	V
Definition	C172457 For review purpose, see definition of the controlled terminology below A characterization or classification of the study arm.
User Guidance	N/A
Conformance	Optional: if the table used
Cardinality	One to each arm name
Relationship content from ToC representing the protocol hierarchy	6

Value	Experimental Arm(C174266), Active Comparator Arm(C174267), Placebo Comparator Arm (C174268, Sham Comparator Arm (C174269), No Intervention Arm (C174270), Control Arm(C174226)
Business rules	**Value Allowed**: Yes **Relationship**: arm name and arm type **Concept**: C172457
Repeating and/or Reuse Rules	Yes, repeatable for each arm name

404

NCI C-Code	M11 Preferred Term	Draft Definition
C174222	Study Arm Type Value Set Terminology	The terminology relevant to the identification of the kind of arm.
C174267	Active Comparator Arm	An arm describing the active comparator.
C174226	Control Arm	An arm describing the intervention or treatment plan for a group of participants in the study receiving a control. The control may comprise a non-investigational product (active control) or regimen, placebo, or no treatment.
C174266	Experimental Arm	An arm describing the intervention or treatment plan for a group of participants in the study receiving test product(s).
C174270	No Intervention Arm	A study arm without an intervention or treatment.
C174268	Placebo Comparator Arm	An arm describing the placebo comparator.
C174269	Sham Comparator Arm	An arm describing the sham comparator.

405

Term (Variable)	<Intervention Name>
Data Type	Text
Data (D), Value (V) or Heading (H)	D
Definition	C177930 For review purpose, see definition of the controlled terminology below The literal identifier (i.e. distinctive designation) for the study intervention.
User Guidance	N/A
Conformance	Optional: if the table used
Cardinality	One to arm name and arm type
Relationship content from ToC representing the protocol hierarchy	6
Value	Nonproprietary name or Sponsor Investigational Product Code
Business rules	**Value Allowed**: Yes **Relationship**: Arm name and intervention name, **Concept:** C177930
Repeating and/or Reuse Rules	Yes, repeatable for each arm name and arm type

406

Term (Variable)	<Intervention Type>
Data Type	Valid Value
Data (D), Value (V) or Heading (H)	V
Definition	C98747 For review purpose, see definition of the controlled terminology below The kind of product or procedure studied in a trial.

User Guidance	N/A
Conformance	Optional: if the table used
Cardinality	One to each intervention name
Relationship content from ToC representing the protocol hierarchy	6
Value	Drug (C1909), Device (C16830), Biologic (C307), Vaccine (C923), Non-Surgical Procedure (CNEW), Surgery (C15329), Radiation (C15313), Behavioral (C15184), Genetic (C15238), Dietary Supplement (C1505), Combination Product (C54696), Diagnostic Test (C18020)
Business rules	**Value Allowed**: Yes **Relationship**: arm name, arm type and Intervention name, **Concept**: C98747
Repeating and/or Reuse Rules	Yes, repeatable for each arm name and arm type combination

407

NCI C-Code	M11 Preferred Term	Draft Definition
C99078	INTTYPE	A terminology codelist relevant to the kind of product or procedure studied in a trial.
C15184	Behavioral	A technique used to change the behavior of a subject (e.g., psychotherapy, lifestyle counseling, or hypnosis).
C307	Biologic	A product of biological origin applicable to the prevention, treatment, or cure of a disease or condition, for example: virus, therapeutic serum, toxin, antitoxin, vaccine, blood, blood component or derivative, allergenic product, or analogous product.
C923	Vaccine	A medicinal product inducing immunity against disease, most often to prevent occurrence of a disease, (e.g., a preventative vaccine against infectious disease), but also to treat a disease, (e.g., a therapeutic vaccine against cancer).
C54696	Combination Product	A product composed of two or more different types of medical products (i.e., a combination of a drug, device, and/or biological product with one another and are referred to as "constituent parts" of the combination product).
C16830	Device	Any instrument, apparatus, implement, machine, appliance, implant, reagent for in vitro use, software, material or other similar or related article, intended by the manufacturer to be used, alone or in combination for, one or more specific medical purpose(s).
C1505	Dietary Supplement	Preparations containing ingredient(s) intended to supplement the diet.
C1909	Drug	An active natural, synthetic or semi-synthetic ingredient including endogenous body substance that is intended to furnish pharmacological activity or other direct effect in the diagnosis, cure, mitigation, treatment, or prevention of disease or to affect the structure or any function of the human body, but does not include intermediates used in the synthesis of such ingredient.
C15238	Genetic	Introduction of genetic material into cells in order to correct or treat an inherited or acquired disease.
C15329	Surgery	A diagnostic or treatment procedure performed by manual and/or instrumental means, often involving an incision and the removal or replacement of a diseased organ or tissue; of or relating to or involving or used in surgery or requiring or amenable to treatment by surgery.
CNEW	Non-Surgical Procedure	A medical procedure that produces an effect, or that is intended to alter the course of a disease in a patient or population, which is not considered a surgical procedure.
C15313	Radiation	Use of targeted or whole body radiation to treat a disease.

C18020	Diagnostic Test	Any procedure or test to diagnose a disease or disorder.

408

Term (Variable)	<Pharmaceutical Dose Formulation>
Data Type	Valid Value
Data (D), Value (V) or Heading (H)	V
Definition	C42636 For review purpose, see definition of the controlled terminology below Physical characteristics of a drug product, (e.g. tablet, capsule, or solution) that contains a drug substance, generally-but not necessarily-in association with one or more other ingredients
User Guidance	N/A
Conformance	Optional: if the table used
Cardinality	One to each arm name, arm type and intervention combination
Relationship content from ToC representing the protocol hierarchy	6
Value	Use IDMP (e.g., EDQM, CDISC)
Business rules	**Value Allowed**: Yes **Relationship**: arm name and dosage formulation **Concept**: C42636
Repeating and/or Reuse Rules	Yes, repeatable for each intervention and dosage formulation

409

Term (Variable)	<Dosage Strength(s)>
Data Type	Text
Data (D), Value (V) or Heading (H)	D
Definition	CNEW For review purpose, see definition of the controlled terminology below The strength of a drug product, which indicates the amount of each active ingredient in a given dosage form, measured in units of volume or concentration.
User Guidance	N/A
Conformance	Optional: if the table used
Cardinality	One to each dosage formulation
Relationship content from ToC representing the protocol hierarchy	Trial Intervention and Concomitant Therapy
Value	Text
Business rules	**Value Allowed**: Yes **Relationship**: arm name and dose strength, 6 Trial Intervention and Concomitant Therapy **Concept**: CNEW
Repeating and/or Reuse Rules	Yes, repeatable for each intervention and formulation per arm name and arm type

410

Term (Variable)	<Dosage Level(s)>
Data Type	Text
Data (D), Value (V) or Heading (H)	D
Definition	C94394

	For review purpose, see definition of the controlled terminology below Specified quantity of a medicine, to be taken at one time or at stated intervals. [ISO 11615:2012 Health Informatics]
User Guidance	N/A
Conformance	Optional: if the table used
Cardinality	One to each intervention and dosage formulation
Relationship content from ToC representing the protocol hierarchy	6
Value	Text
Business rules	**Value Allowed**: Yes **Relationship**: arm name and dose level **Concept**: C94394
Repeating and/or Reuse Rules	Yes, repeatable for each intervention, dose formulation, dosage strength and dosage level per arm

411

Term (Variable)	<Route of Administration>
Data Type	Valid Value
Data (D), Value (V) or Heading (H)	V
Definition	C38114 For review purpose, see definition of the controlled terminology below Path by which the pharmaceutical product is taken into or makes contact with the body.
User Guidance	N/A
Conformance	Optional: if the table used
Cardinality	One to each intervention and dosage formulation
Relationship content from ToC representing the protocol hierarchy	6
Value	Use IDMP (e.g. EDQM, CDISC)
Business rules	**Value Allowed**: Yes **Relationship**: arm name and route of administration **Concept**: C38114
Repeating and/or Reuse Rules	Yes, repeatable for each intervention. Dose formulation, per arm name

412

Term (Variable)	{<Regimen/Treatment Period/Vaccination regimen>}
Data Type	Text
Data (D), Value (V) or Heading (H)	D
Definition	CNEW For review purpose, see definition of the controlled terminology below A textual description of the schedule and periodicity of a treatment or vaccination regimen.
User Guidance	N/A
Conformance	Optional: if the table used
Cardinality	One to each intervention, dose formulation, dosage strength per arm
Relationship content from ToC representing the protocol hierarchy	6
Value	Regimen/Treatment Period
Business rules	**Value Allowed**: Yes

	Relationship: arm name and regimen/treatment period/vaccine regimen, **Concept**: CNEW
Repeating and/or Reuse Rules	Yes, repeatable for each arm name

413

Term (Variable)	<Use>
Data Type	Valid Value
Data (D), Value (V) or Heading (H)	V
Definition	CNEW For review purpose, see definition of the controlled terminology below The reason or intention for the use of the trial intervention within the trial arm.
User Guidance	N/A
Conformance	Optional: if the table used
Cardinality	One to each intervention
Relationship content from ToC representing the protocol hierarchy	6
Value	Experimental Intervention(C41161), Placebo(C753), Rescue Medicine(C165835), Background treatment(C165822), Challenge Agent(C158128), Diagnostic(C18020), Additional Required treatment (CNEW)
Business rules	**Value Allowed**: Yes **Relationship**: arm name and use, **Concept**: CNEW
Repeating and/or Reuse Rules	Yes, repeatable for each intervention per arm

414

NCI C-Code	M11 Preferred Term	Draft Definition
CNEW	Intervention Use Response	A terminology value set relevant to the intervention use responses within the ICH M11 Protocol model.
C41161	Experimental Intervention	The drug, device, therapy, procedure, or process under investigation in a clinical study that is believed to have an effect on outcomes of interest in a study (e.g., health-related quality of life, efficacy, safety, pharmacoeconomics
C753	Placebo	A pharmaceutical preparation that does not contain the investigational agent and is generally prepared to be physically indistinguishable from the preparation containing the investigational product.
C165835	Rescue Medicine	Medicinal products identified in the protocol as those that may be administered to subjects when the efficacy of the investigational medicinal product (IMP) is not satisfactory, the effect of the IMP is too great and is likely to cause a hazard to the patient, or to manage an emergency situation.
C165822	Background Treatment	Medicinal products that are administered to each clinical trial subject, regardless of randomization group, a) to treat the indication which is the object of the study, or b) required in the protocol as part of standard care for a condition that is not the indication under investigation, and is relevant for the clinical trial design.
C158128	Challenge Agent	A non-investigational medicinal product (NIMP) given to trial subjects to produce a physiological response that is necessary before the pharmacological action of the investigational medicinal product can be assessed.
C18020	Diagnostic	Any procedure or test to diagnose a disease or disorder.

CNEW	Additional Required Treatment	A medicinal product that must be administered along with the experimental treatment (e.g., drug studies wherein opioid blockers are administered to prevent overdose).

415

Term (Variable)	<IMP/NIMP>
Data Type	Valid value
Data (D), Value (V) or Heading (H)	V
Definition	CNEW For review purpose, see definition of the controlled terminology below An indication as to whether the investigational intervention is an investigational medicinal product or an auxiliary medicinal product.
User Guidance	N/A
Conformance	Optional: if the table used
Cardinality	One to each intervention
Relationship content from ToC representing the protocol hierarchy	6
Value	IMP(CNEW), NIMP(C156473)
Business rules	**Value Allowed**: Yes **Relationship**: One per each intervention **Concept**: CNEW
Repeating and/or Reuse Rules	Yes, repeatable for each intervention per arm

416

NCI C-Code	M11 Preferred Term	Draft Definition
CNEW	ICH M11 Investigational Medicinal Product Indicator Response	A terminology value set relevant to the investigational medicinal product indicator responses within the ICH M11 Protocol model.
CNEW	IMP	A medicinal product which is being tested or used as a reference, including as a placebo, in a clinical trial.
C156473	NIMP (AxMP)	A medicinal product that is related to the specific needs of the clinical trial as described in the protocol, but not as an investigational medicinal product.

417

Term (Variable)	<Sourcing>
Data Type	Valid Value
Data (D), Value (V) or Heading (H)	V
Definition	CNEW CNEW For review purpose, see definition of the controlled terminology below An indication as to whether the investigational intervention is sourced from a local or central vendor.
User Guidance	N/A
Conformance	Optional: if the table used
Cardinality	One to many
Relationship content from ToC representing the protocol hierarchy	6
Value	Centrally Sourced (CNEW); Locally Sourced (CNEW)

Business rules	**Value Allowed**: Yes **Relationship**: One per each Intervention **Concept**: CNEW
Repeating and/or Reuse Rules	Yes, repeatable for each intervention per arm name

418

NCI C-Code	M11 Preferred Term	Draft Definition
CNEW	ICH M11 Investigational Intervention Sourcing Response	A terminology value set relevant to the investigational intervention source responses within the ICH M11 Protocol model.
CNEW	Centrally Sourced	An indication that the entity is obtained from a central vendor.
CNEW	Locally Sourced	An indication that the entity is obtained from a local vendor.

419

420 ## 6.1 Description of Investigational Trial Intervention

Term (Variable)	6.1 Description of Investigational Trial Intervention
Data Type	Text
Data (D), Value (V) or Heading (H)	H
Definition	Heading
User Guidance	N/A
Conformance	Required
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	6.1
Value	Description of Investigational Trial Intervention
Business rules	**Value Allowed**: No **Relationship**: 6 TRIAL INTERVENTION AND CONCOMITANT THERAPY and Table of Contents **Concept**: Heading
Repeating and/or Reuse Rules	No

421

Term (Variable)	<Description of Investigational Trial Intervention>
Data Type	Text
Data (D), Value (V) or Heading (H)	D
Definition	CNEW For review purpose, see definition of the controlled terminology below A narrative representation of the investigational trial intervention.
User Guidance	Describe the investigational trial intervention to be administered in each arm of the trial and for each period of the trial including route and mode of administration, dose, dosage regimen, duration of intervention, use, packaging and labelling. Refer to approved regional labelling, as appropriate. For drug/device combination products, include details on the configuration and use of the device and device manufacturer. A device user manual may be referenced in this section.
Conformance	Required
Cardinality	One to one

Relationship content from ToC representing the protocol hierarchy	6.1
Value	Text
Business rules	**Value Allowed**: Yes **Relationship**: 6.1 Description of Investigational Trial Intervention **Concept**: CNEW
Repeating and/or Reuse Rules	No

Term (Variable)	<Additional Text, if Needed>
Data Type	Text
Data (D), Value (V) or Heading (H)	D
Definition	CNEW For review purpose, see definition of the controlled terminology below Extra or further descriptive text that is optionally added as needed.
User Guidance	N/A
Conformance	Optional
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	6.1
Value	Text
Business rules	**Value Allowed**: Yes **Relationship**: 6.1 Description of Investigational Trial Intervention **Concept**: CNEW
Repeating and/or Reuse Rules	No

6.2 Rationale for Investigational Trial Intervention Dose and Regimen

Term (Variable)	6.2 Rationale for Investigational Trial Intervention Dose and Regimen
Data Type	Text
Data (D), Value (V) or Heading (H)	H
Definition	Heading
User Guidance	N/A
Conformance	Required
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	6.2
Value	Rationale for Investigational Trial Intervention Dose and Regimen
Business rules	**Value Allowed**: No **Relationship**: 6 TRIAL INTERVENTION AND CONCOMITANT THERAPY and Table of Contents **Concept**: Heading
Repeating and/or Reuse Rules	No

Term (Variable)	<Rationale for Investigational Trial Intervention Dose and Regimen>
Data Type	Text

Data (D), Value (V) or Heading (H)	D
Definition	CNEW For review purpose, see definition of the controlled terminology below An explanation as to the scientific reasons for the choice of the trial intervention dose and dose regimen.
User Guidance	Provide a rationale for the selection of the dose(s) or dose range, pharmaceutical dose form, the route of administration, and dosing regimen of the investigational trial intervention, as applicable. This rationale should include relevant results from previous nonclinical studies and clinical trials that support selection of the dose and regimen. Discuss impact of differences in study population characteristics (for example, age, sex and/or race) which could lead to differences in pharmacokinetics and pharmacodynamics in this study as compared to previous studies. If applicable, justify any differences in dose regimen or therapeutic use relative to approved labelling. Describe prior trials and other information that support the dose and/or dose regimen of the investigational intervention. Include a rationale for prospective dose adjustments incorporated in the trial, if any.
Conformance	Required
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	6.2
Value	Text
Business rules	**Value Allowed**: Yes **Relationship**: 6.2 Rationale for Investigational Trial Intervention Dose and Regimen **Concept**: CNEW
Repeating and/or Reuse Rules	No

6.3 Investigational Trial Intervention Administration

Term (Variable)	6.3 Investigational Trial Intervention Administration
Data Type	Text
Data (D), Value (V) or Heading (H)	H
Definition	Heading
User Guidance	N/A
Conformance	Required
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	6.3
Value	Investigational Trial Intervention Administration
Business rules	**Value Allowed**: No **Relationship**: 6 TRIAL INTERVENTION AND CONCOMITANT THERAPY and Table of Contents **Concept**: Heading
Repeating and/or Reuse Rules	No

Term (Variable)	<Investigational Trial Intervention Administration>

Data Type	Text
Data (D), Value (V) or Heading (H)	D
Definition	CNEW For review purpose, see definition of the controlled terminology below An explanation as to the scientific reasons for the choice of the trial intervention dose and dose regimen.
User Guidance	Describe the detailed procedures for administration of each participant's dose of each investigational trial intervention. This may include the timing of dosing (for example, time of day, interval), the duration (for example, the length of time participants will be administered the investigational trial intervention), and the timing of dosing relative to meals. Include any specific instructions to trial participants about when or how to prepare and take the dose(s) and how delayed or missed doses should be handled. Dose escalation or cohort expansion as part of the overall design should be covered in Section 4.1 Description of Trial Design.
Conformance	Required
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	6.3
Value	Text
Business rules	**Value Allowed**: Yes **Relationship**: 6.3 Investigational Trial Intervention Administration **Concept**: CNEW
Repeating and/or Reuse Rules	No

6.4 Investigational Trial Intervention Dose Modification

Term (Variable)	6.4 Investigational Trial Intervention Dose Modification
Data Type	Text
Data (D), Value (V) or Heading (H)	H
Definition	Heading
User Guidance	N/A
Conformance	Required
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	6.4
Value	Investigational Trial Intervention Dose Modification
Business rules	**Value Allowed**: No **Relationship**: 6 TRIAL INTERVENTION AND CONCOMITANT THERAPY and Table of Contents **Concept**: Heading
Repeating and/or Reuse Rules	No

Term (Variable)	<Investigational Trial Intervention Dose Modification>
Data Type	Text
Data (D), Value (V) or Heading (H)	D

Definition	CNEW For review purpose, see definition of the controlled terminology below A change, alteration, or adjustment to the dose of a investigational trial intervention.
User Guidance	For each participant, describe any dose modifications allowed, including conditions for such dose modifications, particularly regarding failure to respond or safety concerns. State any minimum period required before a participant's dose might be raised to the next higher dose or dose range. Include whether it is permissible to start and stop treatment and how dose reductions (if permitted) are to be managed. Information on stopping investigational trial intervention for participants due to safety/other reasons should be detailed in Section 7 Participant Discontinuation of Trial Intervention and Discontinuation or Withdrawal from Trial.
Conformance	Required
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	6.4
Value	Text
Business rules	**Value Allowed**: Yes **Relationship**: 6.4 Investigational Trial Intervention Dose Modification **Concept**: CNEW
Repeating and/or Reuse Rules	No

6.5 Management of Investigational Trial Intervention Overdose

Term (Variable)	6.5 Management of Investigational Trial Intervention Overdose
Data Type	Text
Data (D), Value (V) or Heading (H)	H
Definition	Heading
User Guidance	N/A
Conformance	Required
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	6.5
Value	Management of Investigational Trial Intervention Overdose
Business rules	**Value Allowed**: No **Relationship**: 6 TRIAL INTERVENTION AND CONCOMITANT THERAPY and Table of Contents **Concept**: Heading
Repeating and/or Reuse Rules	No

Term (Variable)	<Management of Investigational Trial Intervention Overdose>
Data Type	Text
Data (D), Value (V) or Heading (H)	D

Definition	CNEW For review purpose, see definition of the controlled terminology below A description of how a potential investigational trial intervention overdose will be handled.
User Guidance	Describe what is meant by investigational trial intervention overdose. Provide any available information on managing the overdose and ensure it is consistent with the Investigator's Brochure or product labelling. Cross-references these documents as applicable.
Conformance	Required
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	6.5
Value	Text
Business rules	**Value Allowed**: Yes **Relationship**: 6.5 Management of Investigational Trial Intervention Overdose **Concept**: CNEW
Repeating and/or Reuse Rules	No

6.6 Preparation, Storage, Handling and Accountability of Investigational Trial Intervention

Term (Variable)	6.6 Preparation, Storage, Handling and Accountability of Investigational Trial Intervention
Data Type	Text
Data (D), Value (V) or Heading (H)	H
Definition	Heading
User Guidance	N/A
Conformance	Required
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	6.6
Value	Preparation, Storage, Handling and Accountability of Investigational Trial Intervention
Business rules	**Value Allowed**: No **Relationship**: 6 TRIAL INTERVENTION AND CONCOMITANT THERAPY and Table of Contents **Concept**: Heading
Repeating and/or Reuse Rules	No

6.6.1 Preparation of Investigational Trial Intervention

Term (Variable)	6.6.1 Preparation of Investigational Trial Intervention
Data Type	Text
Data (D), Value (V) or Heading (H)	H
Definition	Heading
User Guidance	N/A

Conformance	Required
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	6.6.1
Value	Preparation of Investigational Trial Intervention
Business rules	**Value Allowed**: No **Relationship**: 6.6 Preparation, Storage, Handling and Accountability of Investigational Trial Intervention, 6 TRIAL INTERVENTION AND CONCOMITANT THERAPY and Table of Contents **Concept**: Heading
Repeating and/or Reuse Rules	No

Term (Variable)	<Preparation of Investigational Trial Intervention>
Data Type	Text
Data (D), Value (V) or Heading (H)	D
Definition	C176274 For review purpose, see definition of the controlled terminology below The way in which the investigational trial intervention is prepared for use or administration to the study participant.
User Guidance	Describe any preparation of the investigational trial intervention, and when necessary, by whom. When applicable, describe the maximum hold time once thawed/mixed before administration. Include thawing, diluting, mixing, and reconstitution/preparation instructions. For drug/device combination products, include any relevant assembly or use instructions and reference the package insert that is provided separately. If the instructions are lengthy or complicated, it is acceptable to reference the package insert (if applicable) or include instructions in a separate document(s) provided to the site (for example, a pharmacy manual). If the latter, reference the separate documents.
Conformance	Required
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	6.6.1
Value	Text
Business rules	**Value Allowed**: Yes **Relationship**: 6.6.1 Preparation of Investigational Trial Intervention **Concept**: C176274
Repeating and/or Reuse Rules	No

6.6.2 Storage and Handling of Investigational Trial Intervention

Term (Variable)	6.6.2 Storage and Handling of Investigational Trial Intervention
Data Type	Text
Data (D), Value (V) or Heading (H)	H
Definition	Heading
User Guidance	N/A
Conformance	Required

Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	6.6.2
Value	Storage and Handling of Investigational Trial Intervention
Business rules	**Value Allowed**: No **Relationship**: 6.6 Preparation, Storage, Handling and Accountability of Investigational Trial Intervention, 6 TRIAL INTERVENTION AND CONCOMITANT THERAPY and Table of Contents **Concept**: Heading
Repeating and/or Reuse Rules	No

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Term (Variable)	<Storage and Handling of Investigational Trial Intervention>
Data Type	Text
Data (D), Value (V) or Heading (H)	D
Definition	C115525 For review purpose, see definition of the controlled terminology below The safe handling, storage, distribution, and return of unused investigational trial intervention.
User Guidance	Describe storage and handling requirements (for example, protection from light, temperature, humidity) for the investigational trial intervention(s). For trials in which multi-dose vials are utilised, provide additional information regarding stability and expiration time after initial use (for example, the seal is broken). State how the investigational trial intervention(s) will be provided to the Investigator. If applicable, describe the kits, packaging, or other material of the investigational trial intervention for blinding purposes. If the instructions are lengthy or complicated, it is acceptable to reference the package insert (if applicable) or include instructions in a separate document(s) provided to the site (for example, a pharmacy manual). If the latter, reference the separate documents.
Conformance	Required
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	6.6.2
Value	Text
Business rules	**Value Allowed**: Yes **Relationship**: 6.6.2 Storage and Handling of Investigational Trial Intervention **Concept**: C115525
Repeating and/or Reuse Rules	No

444

445 6.6.3 Accountability of Trial Intervention

Term (Variable)	6.6.3 Accountability of Trial Intervention
Data Type	Text
Data (D), Value (V) or Heading (H)	H
Definition	Heading
User Guidance	N/A
Conformance	Required

Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	6.6.3
Value	Accountability of Trial Intervention
Business rules	**Value Allowed**: No **Relationship**: 6.6 Preparation, Storage, Handling and Accountability of Investigational Trial Intervention, 6 TRIAL INTERVENTION AND CONCOMITANT THERAPY and Table of Contents **Concept**: Heading
Repeating and/or Reuse Rules	No

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Term (Variable)	<Accountability of Investigational Trial Intervention>
Data Type	Text
Data (D), Value (V) or Heading (H)	D
Definition	C176267 For review purpose, see definition of the controlled terminology below The act or process for documenting the storage, inventory tracking, and disposition of the investigational trial intervention.
User Guidance	Describe the method by which the accountability will be achieved, including trial intervention will be distributed and related details, including: • how and by whom the trial intervention will be distributed • participation of a drug repository or pharmacy, if applicable, • plans for disposal or return of unused product • if applicable, plans for reconciliation of investigational trial intervention
Conformance	Required
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	6.6.3
Value	Text
Business rules	**Value Allowed**: Yes **Relationship**: 6.6.3 Accountability of Trial Intervention **Concept**: C176267
Repeating and/or Reuse Rules	No

447

448 6.7 Investigational Trial Intervention Assignment, Randomisation and Blinding

Term (Variable)	6.7 Investigational Trial Intervention Assignment, Randomisation and Blinding
Data Type	Text
Data (D), Value (V) or Heading (H)	H
Definition	Heading
User Guidance	N/A
Conformance	Required
Cardinality	One to many
Relationship content from ToC representing the protocol hierarchy	6.7
Value	Investigational Trial Intervention Assignment, Randomisation and Blinding

Business rules	**Value Allowed**: No **Relationship**: 6 TRIAL INTERVENTION AND CONCOMITANT THERAPY and Table of Contents **Concept**: Heading
Repeating and/or Reuse Rules	No

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450 6.7.1 Participant Assignment to Investigational Trial Intervention

Term (Variable)	6.7.1 Participant Assignment to Investigational Trial Intervention
Data Type	Text
Data (D), Value (V) or Heading (H)	H
Definition	Heading
User Guidance	N/A
Conformance	Required
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	6.7.1
Value	Participant Assignment to Investigational Trial Intervention
Business rules	**Value Allowed**: No **Relationship**: 6.7 Investigational Trial Intervention Assignment, Randomisation and Blinding, 6 TRIAL INTERVENTION AND CONCOMITANT THERAPY and Table of Contents **Concept**: Heading
Repeating and/or Reuse Rules	No

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Term (Variable)	<Participant Assignment to Investigational Trial Intervention>
Data Type	Text
Data (D), Value (V) or Heading (H)	D
Definition	CNEW For review purpose, see definition of the controlled terminology below The technique used to assign trial participants to a trial arm.
User Guidance	Describe the method of assigning participants to investigational trial intervention without being so specific that blinding or randomisation might be compromised. If assignment to investigational trial intervention is by randomisation, describe when randomisation occurs relative to screening. State that at enrollment, participant identification codes should be assigned. If adaptive randomisation or other methods of covariate balancing/minimisation are employed, include a cross-reference to the methods of analysis in Section 10 Statistical Considerations. As applicable, details regarding the implementation of procedures to minimise bias should be described.
Conformance	Required
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	6.7.1
Value	Text
Business rules	**Value Allowed**: Yes

	Relationship: 6.7.1 Participant Assignment to Investigational Trial Intervention **Concept**: CNEW
Repeating and/or Reuse Rules	No

6.7.2 Randomisation

Term (Variable)	6.7.2 {Randomisation}
Data Type	Text
Data (D), Value (V) or Heading (H)	H
Definition	Heading
User Guidance	N/A
Conformance	Conditional: when randomised trial
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	6.7.2
Value	Randomisation
Business rules	**Value Allowed**: No **Relationship**: 6.7 Investigational Trial Intervention Assignment, Randomisation and Blinding, 6 TRIAL INTERVENTION AND CONCOMITANT THERAPY and Table of Contents **Concept**: Heading
Repeating and/or Reuse Rules	No

Term (Variable)	{<Randomisation>}
Data Type	Text
Data (D), Value (V) or Heading (H)	D
Definition	C25196 For review purpose, see definition of the controlled terminology below The process of assigning trial subjects to treatment or control groups using an element of chance to determine the assignments in order to reduce bias. [ICH E6 1.48]
User Guidance	Describe the randomisation procedures (for example, central randomisation procedures), the method used to generate the randomisation schedule (for example, computer generated), the source of the randomisation schedule (for example, sponsor, investigator, or other), and whether IxRS will be used. To maintain the integrity of the blinding, do not include the block size.
Conformance	Conditional: when randomised trial
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	6.7.2
Value	Text
Business rules	**Value Allowed**: Yes **Relationship**: 6.7.2 Randomisation **Concept**: C25196
Repeating and/or Reuse Rules	No

6.7.3 Measures to Maintain Blinding

Term (Variable)	6.7.3 {Measures to Maintain Blinding}
Data Type	Text
Data (D), Value (V) or Heading (H)	H
Definition	Heading
User Guidance	N/A
Conformance	Conditional: when blind trial
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	6.7.3
Value	Blinding
Business rules	**Value Allowed**: No **Relationship**: 6.7 Investigational Trial Intervention Assignment, Randomisation and Blinding, 6 TRIAL INTERVENTION AND CONCOMITANT THERAPY and Table of Contents **Concept**: Heading
Repeating and/or Reuse Rules	No

Term (Variable)	{<Measures to Maintain Blinding>}
Data Type	Text
Data (D), Value (V) or Heading (H)	D
Definition	C189349 For review purpose, see definition of the controlled terminology below The methodology used for enacting trial blinding.
User Guidance	Describe efforts to ensure that the investigational trial intervention(s) are as indistinguishable as possible. Plans for the maintenance of randomisation codes and appropriate blinding for the trial should be described. Procedures for planned (e.g. Interim Analysis), and unintentional (e.g. breach of procedure) breaking of randomisation codes should be provided. For unplanned but intentional actions (e.g. safety events), refer to Section 6.7.4 Emergency Unblinding at the Site. If the trial allows for some investigators or other designated staff to remain unblinded (for example, to allow them to adjust investigational trial intervention), the means of maintaining the blinding for other investigators or staff should be explained. Measures to prevent unblinding by laboratory measurements or while performing study assessments, if used, should be described.
Conformance	Conditional: when blind trial
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	6.7.3
Value	Text
Business rules	**Value Allowed**: Yes **Relationship**: 6.7.3 Blinding **Concept**: C189349
Repeating and/or Reuse Rules	No

6.7.4 Emergency Unblinding at the Site

Term (Variable)	6.7.4 Emergency Unblinding at the Site
Data Type	Text
Data (D), Value (V) or Heading (H)	H
Definition	Heading
User Guidance	N/A
Conformance	Conditional: when blind trial
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	6.7.4
Value	Emergency Unblinding at the Site
Business rules	**Value Allowed**: No **Relationship**: 6.7 Investigational Trial Intervention Assignment, Randomisation and Blinding, 6 TRIAL INTERVENTION AND CONCOMITANT THERAPY and Table of Contents **Concept**: Heading
Repeating and/or Reuse Rules	No

Term (Variable)	{<Emergency Unblinding at the Site>}
Data Type	Text
Data (D), Value (V) or Heading (H)	D
Definition	CNEW For review purpose, see definition of the controlled terminology below A description of the methodology used for unblinding of the trial treatment in the case of a sudden unforeseen crisis that requires immediate medical care of the participant.
User Guidance	Describe the criteria for breaking the trial blind or participant code. Describe the circumstances in which the blinding would be broken for an individual or for all participants and who has responsibility. Include the procedure for emergency unblinding such as via IxRS or code envelopes as well as documentation of unblinding. Indicate to whom the intentional and unplanned unblinding should be reported.
Conformance	Conditional: when blind trial
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	6.7.4
Value	Text
Business rules	**Value Allowed**: Yes **Relationship**: 6.7.4 Emergency Unblinding at the Site **Concept**: CNEW
Repeating and/or Reuse Rules	No

6.8 Investigational Trial Intervention Adherence

Term (Variable)	6.8 Investigational Trial Intervention Adherence

Data Type	Text
Data (D), Value (V) or Heading (H)	H
Definition	Heading
User Guidance	N/A
Conformance	Required
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	6.8
Value	Investigational Trial Intervention Compliance
Business rules	**Value Allowed**: No **Relationship:** 6 TRIAL INTERVENTION AND CONCOMITANT THERAPY and Table of Contents **Concept:** Heading
Repeating and/or Reuse Rules	No

Term (Variable)	<Investigational Trial Intervention Adherence>
Data Type	Text
Data (D), Value (V) or Heading (H)	D
Definition	CNEW For review purpose, see definition of the controlled terminology below A textual description of the measures taken to ensure trial intervention compliance, including mandatory documentation to be filled out and the source data that will be used to document investigational trial intervention compliance.
User Guidance	Describe the measures to monitor and document participants' compliance with investigational intervention (e.g. study intervention accountability records, diary cards, or investigational intervention concentration measurements). List what documents are mandatory to complete (for example, participant drug log) and what source data/records will be used to document investigational intervention compliance.
Conformance	Required
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	6.8
Value	Text
Business rules	**Value Allowed**: Yes **Relationship**: 6.8 Investigational Trial Intervention Adherence **Concept**: CNEW
Repeating and/or Reuse Rules	No

6.9 Description of Noninvestigational Trial Intervention

Term (Variable)	6.9 Description of Noninvestigational Trial Intervention
Data Type	Text
Data (D), Value (V) or Heading (H)	H
Definition	Heading
User Guidance	N/A

Conformance	Required
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	6.9
Value	Description of Non-Investigational Trial Intervention
Business rules	**Value Allowed**: No **Relationship:** 6 TRIAL INTERVENTION AND CONCOMITANT THERAPY and Table of Contents **Concept:** Heading
Repeating and/or Reuse Rules	No

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Term (Variable)	<Description of Noninvestigational Trial Intervention>
Data Type	Text
Data (D), Value (V) or Heading (H)	D
Definition	CNEW For review purpose, see definition of the controlled terminology below A narrative representation of the non-investigational trial intervention
User Guidance	As stated in Section 6, non-investigational interventions are products used in the trial but are not part of trial objectives and hence, are not investigational trial interventions. The non-investigational trial intervention(s) may be described concisely in a table or in the following sections as applicable.
Conformance	Required
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	6.9
Value	Text
Business rules	**Value Allowed**: Yes **Relationship**: 6.9 Description of Noninvestigational Trial Intervention **Concept**: CNEW
Repeating and/or Reuse Rules	No

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468 ### 6.9.1 Background Intervention

Term (Variable)	6.9.1 {Background Trial Intervention}
Data Type	Text
Data (D), Value (V) or Heading (H)	H
Definition	Heading
User Guidance	N/A
Conformance	Conditional: when any background interventions are defined
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	6.9.1
Value	Background Trial Intervention
Business rules	**Value Allowed**: No

	Relationship: 6.9 Description of Noninvestigational Trial Intervention, 6 TRIAL INTERVENTION AND CONCOMITANT THERAPY and Table of Contents **Concept:** Heading
Repeating and/or Reuse Rules	No

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Term (Variable)	{<Background Trial Intervention>}
Data Type	Text
Data (D), Value (V) or Heading (H)	D
Definition	C165822 For review purpose, see definition of the controlled terminology below Medicinal products that are administered to each clinical trial subject, regardless of randomization group, a) to treat the indication which is the object of the study, or b) required in the protocol as part of standard care for a condition that is not the indication under investigation, and is relevant for the clinical trial design. [After Recommendations from the expert group on clinical trials for the implementation of Regulation (EU) No 536/2014' dd 28 June 2017]
User Guidance	Describe permitted background intervention(s), including administration and any conditions for use.
Conformance	Conditional: when any background interventions are defined
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	6.9.1
Value	Text
Business rules	**Value Allowed**: Yes **Relationship**: 6.9.1 Background Trial Intervention **Concept**: C165822
Repeating and/or Reuse Rules	No

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471 ### 6.9.2 Rescue Therapy

Term (Variable)	6.9.2 {Rescue Therapy}
Data Type	Text
Data (D), Value (V) or Heading (H)	H
Definition	Heading
User Guidance	N/A
Conformance	Conditional: when any rescue therapies are defined
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	6.9.2
Value	Rescue Therapy
Business rules	**Value Allowed**: No **Relationship:** 6.9 Description of Noninvestigational Trial Intervention, 6 TRIAL INTERVENTION AND CONCOMITANT THERAPY and Table of Contents **Concept:** Heading
Repeating and/or Reuse Rules	No

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Term (Variable)	{<Rescue Therapy>}
Data Type	Text
Data (D), Value (V) or Heading (H)	D
Definition	C165835 For review purpose, see definition of the controlled terminology below Medicinal products identified in the protocol as those that may be administered to subjects when the efficacy of the investigational medicinal product (IMP) is not satisfactory, the effect of the IMP is too great and is likely to cause a hazard to the patient, or to manage an emergency situation. [After EU-CTR Recommendations from the expert group on clinical trials for the implementation of Regulation (EU) No 536/2014' dd 28 June 2017]
User Guidance	List all permitted rescue medications, treatments, and/or procedures, including any relevant instructions about administration and any conditions for use. If administration of rescue therapy leads to the temporary discontinuation of trial intervention or a participant's withdrawal from the trial, refer to Section 7 Participant Discontinuation of Trial Intervention and Withdrawal from Trial.
Conformance	Conditional: when any rescue therapies are defined
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	6.9.2
Value	Text
Business rules	**Value Allowed**: Yes **Relationship**: 6.9.2 Rescue Therapy **Concept**: C165835
Repeating and/or Reuse Rules	No

6.9.3 Other Noninvestigational Intervention

Term (Variable)	6.9.3 {Other Noninvestigational Intervention}
Data Type	Text
Data (D), Value (V) or Heading (H)	H
Definition	Heading
User Guidance	N/A
Conformance	Conditional: when any other noninvestigational interventions are defined
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	6.9.3
Value	Other Non-investigational Intervention
Business rules	**Value Allowed**: No **Relationship:** 6.9 Description of Noninvestigational Trial Intervention, 6 TRIAL INTERVENTION AND CONCOMITANT THERAPY and Table of Contents **Concept:** Heading
Repeating and/or Reuse Rules	No

Term (Variable)	{<Other Noninvestigational Intervention>}
Data Type	Text

Data (D), Value (V) or Heading (H)	D
Definition	CNEW For review purpose, see definition of the controlled terminology below A non-investigational trial therapy that is different than the one(s) previously specified or mentioned.
User Guidance	If applicable, describe the use of any other non-investigational intervention, for example, challenge agents or diagnostics.
Conformance	Conditional: when any other non-investigational interventions are defined
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	6.9.3
Value	Text
Business rules	**Value Allowed**: Yes **Relationship**: 6.9.3 Other Noninvestigational Intervention **Concept**: CNEW
Repeating and/or Reuse Rules	No

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477 ## 6.10 Concomitant Therapy

Term (Variable)	6.10 Concomitant Therapy
Data Type	Text
Data (D), Value (V) or Heading (H)	H
Definition	Heading
User Guidance	N/A
Conformance	Required
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	6.10
Value	Concomitant Therapy
Business rules	**Value Allowed**: No **Relationship:** 6 TRIAL INTERVENTION AND CONCOMITANT THERAPY and Table of Contents **Concept:** Heading
Repeating and/or Reuse Rules	No

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Term (Variable)	<Concomitant Therapy>
Data Type	Text
Data (D), Value (V) or Heading (H)	D
Definition	C53630 For review purpose, see definition of the controlled terminology below Any pharmaceutical agent, other than the trial interventions, that is administered to or used by the subject prior to or during a specified time period.
User Guidance	Describe the concomitant medications, supplements, complementary and alternative therapies, treatments, and/or procedures which are prohibited or permitted during the trial and include details about when the information will be collected (for example, screening, all visits).

	This section should be consistent with the medication restrictions in the inclusion/exclusion criteria. When appropriate to separate the content, subheadings may be used.
Conformance	Required
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	6.10
Value	Text
Business rules	**Value Allowed**: Yes **Relationship**: 6.10 Concomitant Therapy **Concept**: C53630
Repeating and/or Reuse Rules	No

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480 ### 6.10.1 Prohibited Concomitant Therapy

Term (Variable)	6.10.1 {Prohibited Concomitant Therapy}
Data Type	Text
Data (D), Value (V) or Heading (H)	H
Definition	Heading
User Guidance	N/A
Conformance	Conditional: when any prohibited concomitant therapies are defined
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	6.10.1
Value	Prohibited Concomitant Therapy
Business rules	**Value Allowed**: No **Relationship:** 6.10 Concomitant Therapy, 6 TRIAL INTERVENTION AND CONCOMITANT THERAPY and Table of Contents **Concept:** Heading
Repeating and/or Reuse Rules	No

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Term (Variable)	{<Prohibited Concomitant Therapy>}
Data Type	Text
Data (D), Value (V) or Heading (H)	D
Definition	CNEW For review purpose, see definition of the controlled terminology below Concomitant therapy that is banned from use in the trial.
User Guidance	If applicable, describe any prohibited concomitant therapy.
Conformance	Conditional: when any prohibited concomitant therapies are defined
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	6.10.1
Value	Text
Business rules	**Value Allowed**: Yes **Relationship**: 6.10.1 Prohibited Concomitant Therapy **Concept**: CNEW

Repeating and/or Reuse Rules	No

6.10.2 Permitted Concomitant Therapy

Term (Variable)	6.10.2 Permitted Concomitant Therapy
Data Type	Text
Data (D), Value (V) or Heading (H)	H
Definition	Heading
User Guidance	N/A
Conformance	Conditional: when any permitted concomitant therapies are defined
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	6.10.2
Value	Permitted Concomitant Therapy
Business rules	**Value Allowed**: No **Relationship:** 6.10 Concomitant Therapy, 6 TRIAL INTERVENTION AND CONCOMITANT THERAPY and Table of Contents **Concept:** Heading
Repeating and/or Reuse Rules	No

Term (Variable)	{<Permitted Concomitant Therapy>}
Data Type	Text
Data (D), Value (V) or Heading (H)	D
Definition	CNEW For review purpose, see definition of the controlled terminology below Concomitant therapy that is approved for use in the trial.
User Guidance	If applicable, describe any permitted concomitant therapy.
Conformance	Conditional: when any permitted concomitant therapies are defined
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	6.10.2
Value	Text
Business rules	**Value Allowed**: Yes **Relationship**: 6.10.2 Permitted Concomitant Therapy **Concept**: CNEW
Repeating and/or Reuse Rules	No

7 PARTICIPANT DISCONTINUATION OF TRIAL INTERVENTION AND DISCONTINUATION OR WITHDRAWAL FROM TRIAL

Term (Variable)	7 PARTICIPANT DISCONTINUATION OF TRIAL INTERVENTION AND DISCONTINUATION OR WITHDRAWAL FROM TRIAL
Data Type	Text
Data (D), Value (V) or Heading (H)	H

Definition	Heading
User Guidance	This section must align with the intercurrent events, and their handling strategies introduced in Section 3 Trial Objectives and Associated Estimands, and the investigational trial intervention described in Section 6 Trial Intervention and Concomitant Therapy. No text is intended here (heading only).
Conformance	Required
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	7
Value	PARTICIPANT DISCONTINUATION OF TRIAL INTERVENTION AND DISCONTINUATION OR WITHDRAWAL FROM TRIAL
Business rules	**Value Allowed**: No **Relationship**: Table of Contents **Concept**: Heading
Repeating and/or Reuse Rules	No

7.1 Discontinuation of Trial Intervention for Individual Participants

Term (Variable)	7.1 Discontinuation of Trial Intervention for Individual Participants
Data Type	Text
Data (D), Value (V) or Heading (H)	H
Definition	Heading
User Guidance	No text is intended here (heading only).
Conformance	Required
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	7.1
Value	Discontinuation of Trial Intervention for Individual Participants
Business rules	**Value Allowed**: No **Relationship**: 7 PARTICIPANT DISCONTINUATION OF TRIAL INTERVENTION AND DISCONTINUATION OR WITHDRAWAL FROM TRIAL and Table of Contents **Concept**: Heading
Repeating and/or Reuse Rules	No

7.1.1 Permanent Discontinuation of Trial Intervention

Term (Variable)	7.1.1 Permanent Discontinuation of Trial Intervention
Data Type	Text
Data (D), Value (V) or Heading (H)	H
Definition	Heading
User Guidance	N/A
Conformance	Required
Cardinality	One to one

Relationship content from ToC representing the protocol hierarchy	7.1.1
Value	Permanent Discontinuation of Trial Intervention
Business rules	**Value Allowed**: No **Relationship**: 7.1 Discontinuation of Trial Intervention for Individual Participants, 7 PARTICIPANT DISCONTINUATION OF TRIAL INTERVENTION AND DISCONTINUATION OR WITHDRAWAL FROM TRIAL and Table of Contents **Concept**: Heading
Repeating and/or Reuse Rules	No

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Term (Variable)	<Permanent Discontinuation of Trial Intervention>
Data Type	Text
Data (D), Value (V) or Heading (H)	D
Definition	CNEW For review purpose, see definition of the controlled terminology below The requirements that must be met in order to permanently discontinue the administration of trial intervention.
User Guidance	Describe: • the criteria for discontinuation of a participant from any trial intervention, carefully evaluating which are appropriate for the trial population and therapy being studied. • how participants who discontinue trial intervention will be followed after discontinuation. Depending on the chosen intercurrent event handling strategy, it will be important to continue to follow and ascertain outcomes in participants who discontinue treatment through the end of the trial to prevent missing data in important analyses. Refer to the Section 1.3 Schedule of Activities for assessments to be performed at the time of and following discontinuation of trial intervention. • the process for collecting and recording the detailed reasons for discontinuing trial intervention if not described elsewhere.
Conformance	Required
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	7.1.1
Value	Text
Business rules	**Value Allowed**: Yes **Relationship**: 7.1.1 Permanent Discontinuation of Trial Intervention **Concept**: CNEW
Repeating and/or Reuse Rules	No

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494 ### 7.1.2 Temporary Discontinuation of Trial Intervention

Term (Variable)	7.1.2 Temporary Discontinuation of Trial Intervention
Data Type	Text
Data (D), Value (V) or Heading (H)	H
Definition	Heading

User Guidance	N/A
Conformance	Required
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	7.1.2
Value	Temporary Discontinuation of Trial Intervention
Business rules	**Value Allowed**: No **Relationship**: 7.1 Discontinuation of Trial Intervention for Individual Participants, 7 PARTICIPANT DISCONTINUATION OF TRIAL INTERVENTION AND DISCONTINUATION OR WITHDRAWAL FROM TRIAL and Table of Contents **Concept**: Heading
Repeating and/or Reuse Rules	No

Term (Variable)	<Temporary Discontinuation of Trial Intervention>
Data Type	Text
Data (D), Value (V) or Heading (H)	D
Definition	CNEW For review purpose, see definition of the controlled terminology below The requirements that must be met in order to temporarily discontinue the administration of trial intervention.
User Guidance	Describe: • the criteria for temporary discontinuation or interruption of trial intervention for an individual participant • what to do and which restrictions still apply if the participant has to temporarily discontinue or interrupt trial intervention • whether the participant will continue in the trial • which assessments will be performed for the stated duration of the trial Details of any rechallenge or restart after a safety-related event should be included in Section 7.1.3 Rechallenge.
Conformance	Required
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	7.1.2
Value	Text
Business rules	**Value Allowed**: Yes **Relationship**: 7.1.2 Temporary Discontinuation of Trial Intervention **Concept**: CNEW
Repeating and/or Reuse Rules	No

7.1.3 Rechallenge

Term (Variable)	7.1.3 Rechallenge
Data Type	Text
Data (D), Value (V) or Heading (H)	H
Definition	Heading
User Guidance	N/A

Conformance	Required
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	7.1.3
Value	Rechallenge
Business rules	**Value Allowed**: No **Relationship**: 7.1 Discontinuation of Trial Intervention for Individual Participants, 7 PARTICIPANT DISCONTINUATION OF TRIAL INTERVENTION AND DISCONTINUATION OR WITHDRAWAL FROM TRIAL and Table of Contents **Concept**: Heading
Repeating and/or Reuse Rules	No

498

Term (Variable)	<Rechallenge>
Data Type	Text
Data (D), Value (V) or Heading (H)	D
Definition	CNEW For review purpose, see definition of the controlled terminology below The requirements that must be met in order to reintroduce previously withdrawn or temporarily discontinued medical intervention in the same patient.
User Guidance	Describe the criteria for rechallenge/restarting trial intervention, how and when to perform rechallenge, number of rechallenges allowed during the trial, and whether all, or specify which, assessments will be performed for the stated duration of the trial. If rechallenge is not allowed, state this.
Conformance	Required
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	7.1.3
Value	Text
Business rules	**Value Allowed**: Yes **Relationship**: 7.1.3 Rechallenge **Concept**: CNEW
Repeating and/or Reuse Rules	No

499

500 ## 7.2 Participant Discontinuation or Withdrawal from the Trial

Term (Variable)	7.2 Participant Discontinuation or Withdrawal from the Trial
Data Type	Text
Data (D), Value (V) or Heading (H)	H
Definition	Heading
User Guidance	N/A
Conformance	Required
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	7.2

Value	Participant Discontinuation or Withdrawal from the Trial
Business rules	**Value Allowed**: No **Relationship**: 7 PARTICIPANT DISCONTINUATION OF TRIAL INTERVENTION AND DISCONTINUATION OR WITHDRAWAL FROM TRIAL and Table of Contents **Concept**: Heading
Repeating and/or Reuse Rules	No

501

Term (Variable)	<Participant Discontinuation or Withdrawal from Trial>
Data Type	Text
Data (D), Value (V) or Heading (H)	D
Definition	CNEW For review purpose, see definition of the controlled terminology below The rationale for why the participant either discontinued or withdrawal from the trial.
User Guidance	Describe the criteria for participant discontinuation or withdrawal from the trial. Describe the reason for withdrawal and the type of data to be collected for the final assessments with reference to the schedule of activities for the participant's end of study visit unless provided in another section. In many cases, the only reason for a participant being considered withdrawn from the trial should be a participant's withdrawal of consent to continue to participate in the trial. All other participants, including those who discontinue treatment, should remain in the trial and continue to be followed to prevent missing data in important analyses. Refer to Section 10 Statistical Considerations for the data that must be collected for the trial estimands.
Conformance	Required
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	7.2
Value	Text
Business rules	**Value Allowed**: Yes **Relationship**: 7.2 Participants Discontinuation or Withdrawal from the Trial **Concept**: CNEW
Repeating and/or Reuse Rules	No

502

503 ## 7.3 Management of Loss to Follow-Up

Term (Variable)	7.3 Management of Loss to Follow-Up
Data Type	Text
Data (D), Value (V) or Heading (H)	H
Definition	Heading
User Guidance	N/A
Conformance	Required
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	7.3
Value	Management of Loss to Follow-Up

Business rules	**Value Allowed**: No **Relationship**: 7 PARTICIPANT DISCONTINUATION OF TRIAL INTERVENTION AND DISCONTINUATION OR WITHDRAWAL FROM TRIAL and Table of Contents **Concept**: Heading
Repeating and/or Reuse Rules	No

504

Term (Variable)	<Management of Loss to Follow-Up>
Data Type	Text
Data (D), Value (V) or Heading (H)	D
Definition	CNEW For review purpose, see definition of the controlled terminology below The mitigation strategies to be employed for the loss or lack of continuation of a participant to follow-up, including the frequency by which follow-up occurs.
User Guidance	Describe how the trial will define how participants are lost to follow-up. In general, participants should be considered lost to follow-up only if they cannot be reached despite multiple attempts to contact. Also describe approaches that will be used to minimise loss to follow-up, such as multiple, diverse methods to remain in contact with participants (e.g., telephone calls, texts, and emails to the participant) and how contacts will be recorded.
Conformance	Required
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	7.3
Value	Text
Business rules	**Value Allowed**: Yes **Relationship**: 7.3 Management of Loss to Follow-up **Concept**: CNEW
Repeating and/or Reuse Rules	No

505

506 # 8 TRIAL ASSESSMENTS AND PROCEDURES

Term (Variable)	8 TRIAL ASSESSMENTS AND PROCEDURES
Data Type	Text
Data (D), Value (V) or Heading (H)	H
Definition	Heading
User Guidance	In this section: • Describe the assessments and procedures required during each phase of the trial that are relevant to the stated endpoints and related intercurrent events (e.g., surgery or use of rescue therapy). Provide details that are not already presented in the SoA, taking care not to duplicate information. • Ensure alignment with every other section of the protocol. In particular, this section must align with: o the intercurrent events and associated strategies for handling them described in Section 3 Trial Objectives and Associated Estimands o trial intervention and therapies outlined in Section 6 Trial Intervention and Concomitant Therapy

	○ discontinuation and withdrawal procedures in Section 7 Participant Discontinuation of Trial Intervention and Discontinuation or Withdrawal From Trial ○ the statistical analysis that is defined in Section 10 Statistical Considerations • Reference the literature for the validation of scales/instruments/questionnaires/assays. • Instructions or protocols for specialised tests and scales/instruments/questionnaires/assays may be presented in an appendix or a separate document and cross referenced. • If the trial includes qualitative interviews, describe these evaluations. • Include minimums and limits for procedures (e.g., number of imaging procedures/biopsies, radiation exposure, etc.) if appropriate to the trial. No text is intended here (heading only).
Conformance	Required
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	8
Value	TRIAL ASSESSMENTS AND PROCEDURES
Business rules	**Value Allowed**: No **Relationship**: Table of Contents **Concept**: Heading
Repeating and/or Reuse Rules	No

8.1 Trial Assessments and Procedures Considerations

Term (Variable)	8.1 Trial Assessments and Procedures Considerations
Data Type	Text
Data (D), Value (V) or Heading (H)	H
Definition	Heading
User Guidance	N/A
Conformance	Required
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	8.1
Value	Trial Assessments and Procedures Considerations
Business rules	**Value Allowed**: No **Relationship**: 8 TRIAL ASSESSMENTS AND PROCEDURES and Table of Contents **Concept**: Heading
Repeating and/or Reuse Rules	No

Term (Variable)	<Trial Assessments and Procedures Considerations>
Data Type	Text
Data (D), Value (V) or Heading (H)	D

Definition	CNEW For review purpose, see definition of the controlled terminology below A description of general considerations applicable across trial assessments and procedures.
User Guidance	Describe general considerations applicable across trial assessments and procedures.
Conformance	Required
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	8.1
Value	Text
Business rules	**Value Allowed**: Yes **Relationship**: 8.1 Trial Assessments and Procedures Considerations **Concept**: CNEW
Repeating and/or Reuse Rules	No

8.2 Screening/Baseline Assessments and Procedures

Term (Variable)	8.2 Screening/Baseline Assessments and Procedures
Data Type	Text
Data (D), Value (V) or Heading (H)	H
Definition	Heading
User Guidance	N/A
Conformance	Required
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	8.2
Value	Screening/Baseline Assessments and Procedures
Business rules	**Value Allowed**: No **Relationship**: 8 TRIAL ASSESSMENTS AND PROCEDURES and Table of Contents **Concept**: Heading
Repeating and/or Reuse Rules	No

Term (Variable)	<Screening Assessments and Procedures>
Data Type	Text
Data (D), Value (V) or Heading (H)	D
Definition	CNEW For review purpose, see definition of the controlled terminology below Trial assessments and procedures related to the screening epoch of the trial.
User Guidance	Describe any assessments and procedures that are unique to screening/baseline (e.g., collection of data on participant characteristics, assessments/procedures performed for the purpose of determining eligibility or for stratification) in this section. Describe screening and baseline assessments and procedures separately when screening and baseline are different or performed at different visits.

Conformance	Required
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	8.2
Value	Text
Business rules	**Value Allowed**: Yes **Relationship**: 8.2 Screening/Baseline Assessments and Procedures **Concept**: CNEW
Repeating and/or Reuse Rules	No

513

Term (Variable)	{<Baseline Assessments and Procedures>}
Data Type	Text
Data (D), Value (V) or Heading (H)	D
Definition	CNEW For review purpose, see definition of the controlled terminology below Trial assessments and procedures related to the baseline epoch of the trial.
User Guidance	Describe any assessments and procedures that are unique to screening/baseline (e.g., collection of data on participant characteristics, assessments/procedures performed for the purpose of determining eligibility or for stratification) in this section. Describe screening and baseline assessments and procedures separately when screening and baseline are different or performed at different visits.
Conformance	Conditional: when the Baseline Assessments and Procedures are different from Screening
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	8.2
Value	Text
Business rules	**Value Allowed**: Yes **Relationship**: 8.2 Screening/Baseline Assessments and Procedures **Concept**: CNEW
Repeating and/or Reuse Rules	No

514

515 ## 8.3 Efficacy Assessments and Procedures

Term (Variable)	8.3 Efficacy Assessments and Procedures
Data Type	Text
Data (D), Value (V) or Heading (H)	H
Definition	Heading
User Guidance	N/A
Conformance	Required
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	8.3
Value	Efficacy Assessments and Procedures

Business rules	**Value Allowed**: No **Relationship**: 8 TRIAL ASSESSMENTS AND PROCEDURES and Table of Contents **Concept**: Heading
Repeating and/or Reuse Rules	No

516

Term (Variable)	<Efficacy Assessments and Procedures>
Data Type	Text
Data (D), Value (V) or Heading (H)	D
Definition	CNEW For review purpose, see definition of the controlled terminology below Trial assessments and procedures related to trial intervention efficacy.
User Guidance	Describe efficacy assessments and procedures in this section. Cross reference Section 8.7 Immunogenicity Assessments if immunogenicity assessments are used in efficacy determination.
Conformance	Required
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	8.3
Value	Text
Business rules	**Value Allowed**: Yes **Relationship**: 8.3 Efficacy Assessments and Procedures **Concept**: CNEW
Repeating and/or Reuse Rules	No

517

518 ## 8.4 Safety Assessments and Procedures

Term (Variable)	8.4 Safety Assessments and Procedures
Data Type	Text
Data (D), Value (V) or Heading (H)	H
Definition	Heading
User Guidance	N/A
Conformance	Required
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	8.4
Value	Safety Assessments and Procedures
Business rules	**Value Allowed**: No **Relationship**: 8 TRIAL ASSESSMENTS AND PROCEDURES and Table of Contents **Concept**: Heading
Repeating and/or Reuse Rules	No

519

Term (Variable)	<Safety Assessments and Procedures>
Data Type	Text

Data (D), Value (V) or Heading (H)	D
Definition	CNEW For review purpose, see definition of the controlled terminology below A description of the assessments and procedures related to participant safety within the trial.
User Guidance	Describe safety assessments and procedures utilizing the following subsections as applicable. Add level 3 headings as needed. • Identify any noninvestigator party responsible for evaluation of laboratory or other safety assessments (e.g., Sponsor or external Independent Data Monitoring Committee; cross refer to Section 11.4 Committees for details as applicable). • Include guidelines for the medical management of relevant laboratory or other safety assessment abnormalities.
Conformance	Required
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	8.4
Value	Text
Business rules	**Value Allowed**: Yes **Relationship**: 8.4 Safety Assessments and Procedures **Concept**: CNEW
Repeating and/or Reuse Rules	No

520

521 ### 8.4.1 {Physical Examination}

Term (Variable)	8.4.1 {Physical Examination}
Data Type	Text
Data (D), Value (V) or Heading (H)	H
Definition	Heading
User Guidance	N/A
Conformance	Conditional: when Physical Exams are required
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	8.4.1
Value	Physical Examination
Business rules	**Value Allowed**: No **Relationship**: 8.4 Safety Assessment and Procedures, 8 TRIAL ASSESSMENTS AND PROCEDURES and Table of Contents **Concept**: Heading
Repeating and/or Reuse Rules	No

522

Term (Variable)	{<Physical Examination>}
Data Type	Text

Data (D), Value (V) or Heading (H)	D
Definition	C20989 For review purpose, see definition of the controlled terminology below The procedures for a systemic evaluation of the body and its functions using visual inspection, palpation, percussion and auscultation.
User Guidance	Include any specific instructions for the collection and interpretation of physical examinations.
Conformance	Conditional: when Physical Exams are required
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	8.4.1
Value	Text
Business rules	**Value Allowed**: Yes **Relationship**: 8.4.1 Physical Examination **Concept**: C20989
Repeating and/or Reuse Rules	No

523

524 **8.4.2 {Vital Signs}**

Term (Variable)	8.4.2{Vital Signs}
Data Type	Text
Data (D), Value (V) or Heading (H)	H
Definition	Heading
User Guidance	N/A
Conformance	Conditional: when Vital Signs are required
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	8.4.2
Value	Vital Signs
Business rules	**Value Allowed**: No **Relationship**: 8.4 Safety Assessments and Procedures, 8 TRIAL ASSESSMENTS AND PROCEDURES and Table of Contents **Concept**: Heading
Repeating and/or Reuse Rules	No

525

Term (Variable)	{<Vital Signs>}
Data Type	Text
Data (D), Value (V) or Heading (H)	D
Definition	C154628 For review purpose, see definition of the controlled terminology below The procedures for measurements of the body's basic functions that provide insight into the health status of the person.
User Guidance	Include any specific instructions for the collection and interpretation of vital signs.
Conformance	Conditional: when Vital Signs are required
Cardinality	One to one

Relationship content from ToC representing the protocol hierarchy	8.4.2
Value	Text
Business rules	**Value Allowed**: Yes **Relationship**: 8.4.2 Vital Signs **Concept**: C154628
Repeating and/or Reuse Rules	No

526

527 **8.4.3 {Electrocardiograms}**

Term (Variable)	8.4.3{Electrocardiograms}
Data Type	Text
Data (D), Value (V) or Heading (H)	H
Definition	Heading
User Guidance	N/A
Conformance	Conditional: when Electrocardiograms are required
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	8.4.3
Value	Electrocardiograms
Business rules	**Value Allowed**: No **Relationship**: 8.4 Safety Assessments and Procedures, 8 TRIAL ASSESSMENTS AND PROCEDURES and Table of Contents **Concept**: Heading
Repeating and/or Reuse Rules	No

528

Term (Variable)	{<Electrocardiograms>}
Data Type	Text
Data (D), Value (V) or Heading (H)	D
Definition	C168186 For review purpose, see definition of the controlled terminology below The procedures for the recordings produced by the variations in electrical potential caused by electrical activity of the heart muscle and detected at the body surface, as a method for studying the action of the heart muscle.
User Guidance	Include any specific instructions for the collection, interpretation, and archiving of ECGs.
Conformance	Conditional: when Electrocardiograms are required
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	8.4.3
Value	Text
Business rules	**Value Allowed**: Yes **Relationship**: 8.4.3 Electrocardiograms **Concept**: C168186
Repeating and/or Reuse Rules	No

8.4.4 {Clinical Laboratory Assessments}

Term (Variable)	8.4.4 {Clinical Laboratory Assessments}
Data Type	Text
Data (D), Value (V) or Heading (H)	H
Definition	Heading
User Guidance	N/A
Conformance	Conditional: when Clinical Laboratory Assessments are required
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	8.4.4
Value	Clinical Laboratory Assessments
Business rules	**Value Allowed**: No **Relationship**: 8.4 Safety Assessments and Procedures, 8 TRIAL ASSESSMENTS AND PROCEDURES and Table of Contents **Concept**: Heading
Repeating and/or Reuse Rules	No

Term (Variable)	{<Clinical Safety Laboratory Assessments>}
Data Type	Text
Data (D), Value (V) or Heading (H)	D
Definition	CNEW For review purpose, see definition of the controlled terminology below Trial-related laboratory assessments and procedures related to participant safety.
User Guidance	Describe any specific instructions for the collection and interpretation of clinical laboratory assessments, including: • type of laboratory (central/local/hybrid) • acceptability of additional tests deemed necessary by the investigator or local regulations • instructions for situations in which central laboratory results are not available in time for trial intervention and/or response evaluation, or in the event of a severe disruption (e.g., a pandemic or natural disaster) • treatment algorithms for results out of normal range • cross reference Section 12.1 Clinical Laboratory Tests for laboratory assessment panels
Conformance	Conditional: when Clinical Laboratory Assessments are required
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	8.4.4
Value	Text
Business rules	**Value Allowed**: Yes **Relationship**: 8.4.4 Clinical Laboratory Assessments **Concept**: CNEW
Repeating and/or Reuse Rules	No

8.4.5 {Pregnancy Testing}

Term (Variable)	8.4.5 {Pregnancy Testing}
Data Type	Text
Data (D), Value (V) or Heading (H)	H
Definition	Heading
User Guidance	N/A
Conformance	Conditional: when Pregnancy Testing is required
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	8.4.5
Value	Pregnancy Testing
Business rules	**Value Allowed**: No **Relationship**: 8.4 Safety Assessments and Procedures, 8 TRIAL ASSESSMENTS AND PROCEDURES and Table of Contents **Concept**: Heading
Repeating and/or Reuse Rules	No

Term (Variable)	{<Pregnancy Testing>}
Data Type	Text
Data (D), Value (V) or Heading (H)	D
Definition	C92949 For review purpose, see definition of the controlled terminology below Any examination performed to assess if a female is gravid.
User Guidance	Include any specific instructions for the collection and interpretation of pregnancy testing.
Conformance	Conditional: when Pregnancy Testing is required
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	8.4.5
Value	Text
Business rules	**Value Allowed**: Yes **Relationship**: 8.4.5 Pregnancy Testing **Concept**: C92949
Repeating and/or Reuse Rules	No

8.4.6 {Suicidal Ideation and Behaviour Risk Monitoring}

Term (Variable)	8.4.6 {Suicidal Ideation and Behaviour Risk Monitoring}
Data Type	Text
Data (D), Value (V) or Heading (H)	H
Definition	Heading
User Guidance	N/A
Conformance	Conditional: when Suicidal Ideation and Behaviour Risk Monitoring are required

Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	8.4.6
Value	Suicidal Ideation and Behaviour Risk Monitoring
Business rules	**Value Allowed**: No **Relationship**: 8.4 Safety Assessments and Procedures, 8 TRIAL ASSESSMENTS AND PROCEDURES and Table of Contents **Concept**: Heading
Repeating and/or Reuse Rules	No

536

Term (Variable)	{<Suicidal Ideation and Behaviour Risk Monitoring>}
Data Type	Text
Data (D), Value (V) or Heading (H)	D
Definition	CNEW For review purpose, see definition of the controlled terminology below A description of data collection procedures and analysis related to suicidal ideation and behaviour risk monitoring.
User Guidance	If the trial meets any of the criteria requiring suicidal ideation and behaviour risk monitoring by the guidance/guideline in each region, include justification for the need for suicidal ideation and behaviour risk monitoring in the study and add any specific instructions for the collection and interpretation of the assessment. In case this is an AESI in the study, justification should also be provided in Section 9.2.4 Adverse Events of Special Interest.
Conformance	Conditional: when Suicidal Ideation and Behaviour Risk Monitoring are required
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	8.4.6
Value	Text
Business rules	**Value Allowed**: Yes **Relationship**: 8.4.6 Suicidal Ideation and Behaviour Risk Monitoring **Concept**: CNEW
Repeating and/or Reuse Rules	No

537

538 ## 8.5 Pharmacokinetics

Term (Variable)	8.5 Pharmacokinetics
Data Type	Text
Data (D), Value (V) or Heading (H)	H
Definition	Heading
User Guidance	N/A
Conformance	Required
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	8.5
Value	Pharmacokinetics
Business rules	**Value Allowed**: No

	Relationship: 8 TRIAL ASSESSMENTS AND PROCEDURES and Table of Contents **Concept**: Heading
Repeating and/or Reuse Rules	No

539

Term (Variable)	<Pharmacokinetics>
Data Type	Text
Data (D), Value (V) or Heading (H)	D
Definition	CNEW For review purpose, see definition of the controlled terminology below A narrative description containing information about the collection, use, and retention of biospecimens, and their use in pharmacokinetic assessments within the trial.
User Guidance	Include any specific instructions for the collection and assay of samples and interpretation of PK assessments. • Describe the biological samples collected, the handling of samples, and the assay method. o Specific sample collection and processing instructions can be described in an appendix or a separate document and cross referenced. • Describe the retention time for the samples (ensuring alignment with the ICF). • Indicate the types of analyses for each sample. • Define the PK parameters to be calculated and the calculation methods.
Conformance	Required
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	8.5
Value	Text
Business rules	**Value Allowed**: Yes **Relationship**: 8.5 Pharmacokinetics **Concept**: CNEW
Repeating and/or Reuse Rules	No

540

541 ## 8.6 Biomarkers

Term (Variable)	8.6 Biomarkers
Data Type	Text
Data (D), Value (V) or Heading (H)	H
Definition	Heading
User Guidance	Include any specific instructions for the collection of samples and interpretation of biomarkers in the subsections below as applicable. Safety biomarkers should be included in Section 8.4 Safety Assessments and Procedures and immunogenicity markers in Section 8.7 Immunogenicity Assessments. No text is intended here (heading only).

Conformance	Required
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	8.6
Value	Biomarkers
Business rules	**Value Allowed**: No **Relationship**: 8 TRIAL ASSESSMENTS AND PROCEDURES and Table of Contents **Concept**: Heading
Repeating and/or Reuse Rules	No

542

543 ### 8.6.1 Genetics and Pharmacogenomics

Term (Variable)	8.6.1 Genetics and Pharmacogenomics
Data Type	Text
Data (D), Value (V) or Heading (H)	H
Definition	Heading
User Guidance	N/A
Conformance	Required
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	8.6.1
Value	Genetics and Pharmacogenomics
Business rules	**Value Allowed**: No **Relationship**: 8.6 Biomarkers, 8 TRIAL ASSESSMENTS AND PROCEDURES and Table of Contents **Concept**: Heading
Repeating and/or Reuse Rules	No

544

Term (Variable)	<Genetics and Pharmacogenomics>
Data Type	Text
Data (D), Value (V) or Heading (H)	D
Definition	CNEW For review purpose, see definition of the controlled terminology below A narrative description containing information about the collection, use, and retention of biospecimens, and their use in genetic and pharmacogenomic biomarker assessments within the trial.
User Guidance	Include any specific instructions for the collection and assay of samples for genetic and/or pharmacogenomic analysis. • Describe the biological samples that will be collected (e.g., tissue, serum, plasma), handling of samples, and the assay method. o Specific sample collection and processing instructions can be described in an appendix or a separate document and cross referenced. • Describe the retention time for the samples (ensuring alignment with the ICF).

	• Indicate the types of analyses that may be studied for each sample.
Conformance	Required
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	8.6.1
Value	Text
Business rules	**Value Allowed**: Yes **Relationship**: 8.6.1 Genetics and Pharmacogenomics **Concept**: CNEW
Repeating and/or Reuse Rules	No

545

546 ### 8.6.2 Pharmacodynamic Biomarkers

Term (Variable)	8.6.2 Pharmacodynamic Biomarkers
Data Type	Text
Data (D), Value (V) or Heading (H)	H
Definition	Heading
User Guidance	N/A
Conformance	Required
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	8.6.2
Value	Pharmacodynamic Biomarkers
Business rules	**Value Allowed**: No **Relationship**: 8.6 Biomarkers, 8 TRIAL ASSESSMENTS AND PROCEDURES and Table of Contents **Concept**: Heading
Repeating and/or Reuse Rules	No

547

Term (Variable)	<Pharmacodynamic Biomarkers>
Data Type	Text
Data (D), Value (V) or Heading (H)	D
Definition	CNEW For review purpose, see definition of the controlled terminology below A narrative description containing information about the collection, use, and retention of biospecimens, and their use in pharmacodynamic biomarker assessments within the trial.
User Guidance	Include any specific instructions for the collection of samples and assessment of pharmacodynamic biomarkers. • Describe the biological samples that will be collected (e.g., tissue, serum, plasma). ○ Specific sample collection and processing instructions can be described in an appendix or a separate document and cross referenced.

	• Describe the retention time for the samples (ensuring alignment with the ICF). • Indicate the types of biomarkers that will be studied for each sample. • Specify whether each sample is optional or required. Required samples must be based on a protocol objective.
Conformance	Required
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	8.6.2
Value	Text
Business rules	**Value Allowed**: Yes **Relationship**: 8.6.2 Pharmacodynamic Biomarkers **Concept**: CNEW
Repeating and/or Reuse Rules	No

548

549 ### 8.6.3 {Other Biomarkers}

Term (Variable)	8.6.3 {Other Biomarkers}
Data Type	Text
Data (D), Value (V) or Heading (H)	H
Definition	Heading
User Guidance	N/A
Conformance	Conditional: when Other Biomarkers are required
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	8.6.3
Value	Other Biomarkers
Business rules	**Value Allowed**: No **Relationship**: 8.6 Biomarkers, 8 TRIAL ASSESSMENTS AND PROCEDURES and Table of Contents **Concept**: Heading
Repeating and/or Reuse Rules	No

550

Term (Variable)	{<Other Biomarkers>}
Data Type	Text
Data (D), Value (V) or Heading (H)	D
Definition	CNEW For review purpose, see definition of the controlled terminology below A narrative description containing information about the collection, use, and retention of biospecimens, and their use in other biomarker assessments within the trial.
User Guidance	Include any specific instructions for the collection of samples and assessment of other biomarkers. • Describe the biological samples that will be collected (e.g., tissue, serum, plasma).

	○ Specific sample collection and processing instructions can be described in an appendix or a separate document and cross referenced. • Describe the retention time for the samples (ensuring alignment with the ICF). • Indicate the types of biomarkers that will be studied for each sample. • Specify whether each sample is optional or required. Required samples must be based on a protocol objective.
Conformance	Conditional: when Other Biomarkers are required
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	8.6.3
Value	Text
Business rules	**Value Allowed**: Yes **Relationship**: 8.6.3 Other Biomarkers **Concept**: CNEW
Repeating and/or Reuse Rules	No

551

552 ## 8.7 Immunogenicity Assessments

Term (Variable)	8.7 Immunogenicity Assessments
Data Type	Text
Data (D), Value (V) or Heading (H)	H
Definition	Heading
User Guidance	N/A
Conformance	Required
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	8.7
Value	Immunogenicity Assessments
Business rules	**Value Allowed**: No **Relationship**: 8 TRIAL ASSESSMENTS AND PROCEDURES and Table of Contents **Concept**: Heading
Repeating and/or Reuse Rules	No

553

Term (Variable)	<Immunogenicity Assessments>
Data Type	Text
Data (D), Value (V) or Heading (H)	D
Definition	CNEW For review purpose, see definition of the controlled terminology below A narrative description containing information about the collection, use, and retention of biospecimens, and their use in immunogenicity assessments within the trial.

User Guidance	Include any specific instructions for the collection of samples and interpretation of immunogenicity. If immunogenicity assessments are included within Efficacy Assessments or Safety Assessments, cross reference to that section. • Describe the biological samples that will be collected (e.g., tissue, serum, plasma). o Specific sample collection and processing instructions can be described in an appendix or a separate document and cross referenced. • Describe the retention time for the samples (ensuring alignment with the ICF). • Indicate the types of biomarkers that will be studied for each sample. • Specify whether each sample is optional or required. Required samples must be based on a protocol objective.
Conformance	Required
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	8.7
Value	Text
Business rules	**Value Allowed**: Yes **Relationship**: 8.7 Immunogenicity Assessments **Concept**: CNEW
Repeating and/or Reuse Rules	No

8.8 Medical Resource Utilisation and Health Economics

Term (Variable)	8.8 Medical Resource Utilisation and Health Economics
Data Type	Text
Data (D), Value (V) or Heading (H)	H
Definition	Heading
User Guidance	N/A
Conformance	Required
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	8.8
Value	Medical Resource Utilisation and Health Economics
Business rules	**Value Allowed**: No **Relationship**: 8 TRIAL ASSESSMENTS AND PROCEDURES and Table of Contents **Concept**: Heading
Repeating and/or Reuse Rules	No

Term (Variable)	<Medical Resource Utilisation and Health Economics>
Data Type	Text
Data (D), Value (V) or Heading (H)	D
Definition	CNEW

	For review purpose, see definition of the controlled terminology below A narrative description containing information about medical resource utilization and the health outcome measures, collection method and participant burden.
User Guidance	This section does not apply to COAs. Include this section only for any value evidence and outcomes assessments not included in either the efficacy or safety sections. Describe the health outcome measures, collection method (e.g., diary, physician interview), and participant burden.
Conformance	Required
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	8.8
Value	Text
Business rules	**Value Allowed**: Yes **Relationship**: 8.8 Medical Resource Utilisation and Health Economics **Concept**: CNEW
Repeating and/or Reuse Rules	No

9 ADVERSE EVENTS, SERIOUS ADVERSE EVENTS, PRODUCT COMPLAINTS, PREGNANCY AND POSTPARTUM INFORMATION, AND SPECIAL SAFETY SITUATIONS

Term (Variable)	9 ADVERSE EVENTS, SERIOUS ADVERSE EVENTS, PRODUCT COMPLAINTS, PREGNANCY AND POSTPARTUM INFORMATION, AND SPECIAL SAFETY SITUATIONS
Data Type	Text
Data (D), Value (V) or Heading (H)	H
Definition	Heading
User Guidance	N/A
Conformance	Required
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	9
Value	ADVERSE EVENTS, SERIOUS ADVERSE EVENTS, PRODUCT COMPLAINTS, PREGNANCY AND POSTPARTUM INFORMATION, AND SPECIAL SAFETY SITUATIONS
Business rules	**Value Allowed**: No **Relationship**: Table of Contents **Concept**: Heading
Repeating and/or Reuse Rules	No

9.1 Definitions

Term (Variable)	9.1 Definitions
Data Type	Text
Data (D), Value (V) or Heading (H)	H

Definition	Heading
User Guidance	No text is intended here (heading only).
Conformance	Required
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	9.1
Value	Definitions
Business rules	**Value Allowed**: No **Relationship**: 9 ADVERSE EVENTS, SERIOUS ADVERSE EVENTS, PRODUCT COMPLAINTS, PREGNANCY AND POSTPARTUM INFORMATION, AND SPECIAL SAFETY SITUATIONS and Table of Contents **Concept**: Heading
Repeating and/or Reuse Rules	No

563

564 ### 9.1.1 Definitions of Adverse Events

Term (Variable)	9.1.1 Definitions of Adverse Events
Data Type	Text
Data (D), Value (V) or Heading (H)	H
Definition	Heading
User Guidance	N/A
Conformance	Required
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	9.1.1
Value	Definitions of Adverse Events
Business rules	**Value Allowed**: No **Relationship**: 9.1 Definitions, 9 ADVERSE EVENTS, SERIOUS ADVERSE EVENTS, PRODUCT COMPLAINTS, PREGNANCY AND POSTPARTUM INFORMATION, AND SPECIAL SAFETY SITUATIONS and Table of Contents **Concept**: Heading
Repeating and/or Reuse Rules	No

565

Term (Variable)	<Definitions of Adverse Events>
Data Type	Text
Data (D), Value (V) or Heading (H)	D
Definition	CNEW For review purpose, see definition of the controlled terminology below A concise explanation of the meaning of adverse events within the context of the trial.
User Guidance	Specify the AE definitions, including: • any relevant regional AE requirements • any events that meet and do not meet the AE definition • any trial-specific AE clarifications

	• if applicable, any clarifications on the AE and SAE definitions for efficacy trials (e.g., lack of efficacy or failure of pharmacological actions reporting)
Conformance	Required
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	9.1.1
Value	Text
Business rules	**Value Allowed**: Yes **Relationship**: 9.1.1 Definitions of Adverse Events **Concept**: CNEW
Repeating and/or Reuse Rules	No

566

567 ### 9.1.2 Definitions of Serious Adverse Events

Term (Variable)	9.1.2 Definitions of Serious Adverse Events
Data Type	Text
Data (D), Value (V) or Heading (H)	H
Definition	Heading
User Guidance	N/A
Conformance	Required
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	9.1.2
Value	Definitions of Serious Adverse Events
Business rules	**Value Allowed**: No **Relationship**: 9.1 Definitions, 9 ADVERSE EVENTS, SERIOUS ADVERSE EVENTS, PRODUCT COMPLAINTS, PREGNANCY AND POSTPARTUM INFORMATION, AND SPECIAL SAFETY SITUATIONS and Table of Contents **Concept**: Heading
Repeating and/or Reuse Rules	No

568

Term (Variable)	<Definitions of Serious Adverse Events>
Data Type	Text
Data (D), Value (V) or Heading (H)	D
Definition	CNEW For review purpose, see definition of the controlled terminology below A concise explanation of the meaning of serious adverse events within the context of the trial.
User Guidance	Specify the SAE definitions, including: • any relevant regional SAE requirements • any events that meet and do not meet the SAE definition • any trial-specific SAE clarifications
Conformance	Required
Cardinality	One to one

Relationship content from ToC representing the protocol hierarchy	9.1.2
Value	Text
Business rules	**Value Allowed**: Yes **Relationship**: 9.1.2 Definitions of Serious Adverse Events **Concept**: CNEW
Repeating and/or Reuse Rules	No

569

570 ### 9.1.3 Definitions of Product Complaints

Term (Variable)	9.1.3 Definition of Product Complaints
Data Type	Text
Data (D), Value (V) or Heading (H)	H
Definition	Heading
User Guidance	N/A
Conformance	Required
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	9.1.3
Value	Definition of Product Complaints
Business rules	**Value Allowed**: No **Relationship**: 9.1 Definitions, 9 ADVERSE EVENTS, SERIOUS ADVERSE EVENTS, PRODUCT COMPLAINTS, PREGNANCY AND POSTPARTUM INFORMATION, AND SPECIAL SAFETY SITUATIONS and Table of Contents **Concept**: Heading
Repeating and/or Reuse Rules	No

571

Term (Variable)	<Definition of Product Complaints>
Data Type	Text
Data (D), Value (V) or Heading (H)	D
Definition	
User Guidance	Specify the definition of product complaints in the context of the trial.
Conformance	Required
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	9.1.3
Value	Text
Business rules	**Value Allowed**: Yes **Relationship**: 9.1.3 Definition of Product Complaints **Concept**: CNEW
Repeating and/or Reuse Rules	No

572

9.1.3.1 {Definition of Medical Device Product Complaints}

Term (Variable)	9.1.3.1 {Definition of Medical Device Product Complaints}
Data Type	Text
Data (D), Value (V) or Heading (H)	H
Definition	Heading
User Guidance	N/A
Conformance	Conditional: when there is Medical Device Product Complaints
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	9.1.3.1
Value	{Definition of Medical Device Product Complaints}
Business rules	**Value Allowed**: No **Relationship**: 9.1.3 Definition of Product Complaints, 9.1 Definitions, 9 ADVERSE EVENTS, SERIOUS ADVERSE EVENTS, PRODUCT COMPLAINTS, PREGNANCY AND POSTPARTUM INFORMATION, AND SPECIAL SAFETY SITUATIONS and Table of Contents **Concept**: Heading
Repeating and/or Reuse Rules	No

Term (Variable)	{<Definition of Medical Device Product Complaints>}
Data Type	Text
Data (D), Value (V) or Heading (H)	D
Definition	CNEW For review purpose, see definition of the controlled terminology below A concise explanation of the meaning of medical device product complaints within the context of the trial.
User Guidance	N/A
Conformance	Conditional: when there is Medical Device Product Complaints
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	9.1.3.1
Value	Text
Business rules	**Value Allowed**: Yes **Relationship**: 9.1.3.1 Definition of Medical Device Product Complaints **Concept**: CNEW
Repeating and/or Reuse Rules	No

9.2 Timing and Procedures for Collection and Reporting

Term (Variable)	9.2 Timing and Procedures for Collection and Reporting
Data Type	Text
Data (D), Value (V) or Heading (H)	H

Definition	Heading
User Guidance	N/A
Conformance	Required
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	9.2
Value	Timing and Procedures for Collection and Reporting
Business rules	**Value Allowed**: No **Relationship**: 9 ADVERSE EVENTS, SERIOUS ADVERSE EVENTS, PRODUCT COMPLAINTS, PREGNANCY AND POSTPARTUM INFORMATION, AND SPECIAL SAFETY SITUATIONS and Table of Contents **Concept**: Heading
Repeating and/or Reuse Rules	No

578

Term (Variable)	This table describes the timing and procedures for collecting events.
Data Type	Universal Text
Data (D), Value (V) or Heading (H)	H
Definition	CNEW For review purpose, see definition of the controlled terminology below A table containing the timing and procedures for collection and reporting of adverse events, serious adverse events, medical device product complaints, and pregnancy and postpartum information.
User Guidance	Specify timing and procedures for collection and reporting of AEs, SAEs, product complaints (including medical device product complaints if applicable) and pregnancy and postpartum information in the sections below. This information may be summarized in a tabular format as shown in the example table below.
Conformance	Optional
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	9.2
Value	This table describes the timing and procedures for collecting events.
Business rules	**Value Allowed**: No **Relationship**: 9.2 Timing and Procedures for Collection and Reporting **Concept**: Universal Text
Repeating and/or Reuse Rules	No

579
580

Term (Variable)	Event Type
Data Type	Text
Data (D), Value (V) or Heading (H)	H
Definition	Table Column Heading
User Guidance	N/A
Conformance	Optional: If the table is used.
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	9.2

Value	Event Type
Business rules	**Value Allowed**: No **Relationship**: Table Column Heading **Concept**: Heading
Repeating and/or Reuse Rules	No

581

Term (Variable)	<Event Type>
Data Type	Valid Value
Data (D), Value (V) or Heading (H)	V
Definition	CNEW For review purpose, see definition of the controlled terminology below A categorization or classification of trial-related safety events, such as adverse events, serious adverse events, product complaints, medical device product complaints, and pregnancy and postpartum events.
User Guidance	N/A
Conformance	Optional if the table is used
Cardinality	One to many
Relationship content from ToC representing the protocol hierarchy	9.2
Value	Adverse Event (C41331), Serious Adverse Event(C41335), Trial Intervention Complaint (CNEW), Medical Device Product Complaint (C54026), Pregnancy Event (C25742), Lactation Event (CNEW), Post-Partum Event (CNEW), Reportable Adverse Event of Special Interest (CNEW), Not Reportable Adverse Event of Special Interest (CNEW)
Business rules	**Value Allowed**: Yes **Relationship**: Event Type **Concept**: CNEW
Repeating and/or Reuse Rules	Yes, repeatable for each event type

582

NCI C-Code	M11 Preferred Term	Draft Definition
CNEW	ICH M11 Event Type Response	A terminology value set relevant to the safety event type responses within the ICH M11 Protocol model.
C41331	Adverse Event	Any untoward medical occurrence in a patient or clinical investigation subject administered a pharmaceutical product and which does not necessarily have to have a causal relationship with this treatment.
C41335	Serious Adverse Event	Any untoward medical occurrence that at any dose: results in death, is life-threatening, requires inpatient hospitalization or prolongation of existing hospitalization, results in persistent or significant disability/ incapacity, or is a congenital anomaly/ birth defect.
CNEW	Trial Intervention Complaint	Any concern about the safety and/or quality of any trial-related interventions.
C54026	Medical Device Product Complaint	Any concern about the safety, quality, and/or performance of a trial-related drug-device combination.
C25742	Pregnancy Event	Any event that occurs when the participant is pregnant.
CNEW	Lactation Event	Any event that occurs when the participant is lactating.
CNEW	Post-Partum Event	Any event that occurs when the participant is in the stages of recovery post pregnancy and birth event.

CNEW	Reportable Adverse Event of Special Interest	An adverse event of special interest (serious or non-serious) is one of scientific and medical concern specific to the sponsor's product or programme, for which ongoing monitoring and rapid communication by the investigator to the sponsor could be appropriate, and which is deemed to be reportable to the appropriate regulatory authority.
CNEW	Not Reportable Adverse Event of Special Interest	An adverse event of special interest (serious or non-serious) is one of scientific and medical concern specific to the sponsor's product or programme, for which ongoing monitoring and rapid communication by the investigator to the sponsor could be appropriate, and which is deemed to be not reportable to the appropriate regulatory authority.

583

Term (Variable)	Situational Scope
Data Type	Text
Data (D), Value (V) or Heading (H)	H
Definition	Table Column Heading
User Guidance	N/A
Conformance	Optional if table used
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	9.2
Value	Situational Scope
Business rules	**Value Allowed**: No **Relationship**: Table Column Heading **Concept**: Heading
Repeating and/or Reuse Rules	No

584

Term (Variable)	<Situational Scope>
Data Type	Text
Data (D), Value (V) or Heading (H)	D
Definition	CNEW For review purpose, see definition of the controlled terminology below A description of the specific circumstances and context in which safety events are collected and monitored.
User Guidance	N/A
Conformance	Optional if table used
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	9.2
Value	Text
Business rules	**Value Allowed**: Yes **Relationship**: Event Type, Situational Scope **Concept**: CNEW
Repeating and/or Reuse Rules	Yes, repeatable for each event type

585

Term (Variable)	Reportable Period Start
Data Type	Text

Data (D), Value (V) or Heading (H)	H
Definition	Table Column Heading
User Guidance	N/A
Conformance	Optional if table used
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	9.2
Value	Reportable Period Start
Business rules	**Value Allowed**: No **Relationship**: Table Column Heading **Concept**: Heading
Repeating and/or Reuse Rules	No

586

Term (Variable)	<Reportable Period Start>
Data Type	Text
Data (D), Value (V) or Heading (H)	D
Definition	CNEW For review purpose, see definition of the controlled terminology below The date on which reporting will begin for trial related events such as adverse events, serious adverse events, product complaints, medical device product complaints, and pregnancy and postpartum events.
User Guidance	N/A
Conformance	Optional if table used
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	9.2
Value	Text
Business rules	**Value Allowed**: Yes **Relationship**: Event Type, Situational Scope **Concept**: CNEW
Repeating and/or Reuse Rules	Yes, repeatable for each event type and situational scope

587

Term (Variable)	Reportable Period End
Data Type	Text
Data (D), Value (V) or Heading (H)	H
Definition	Table Column Heading
User Guidance	N/A
Conformance	Optional if table used
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	9.2
Value	Reportable Period End
Business rules	**Value Allowed**: No **Relationship**: Table Column Heading **Concept**: Heading

Repeating and/or Reuse Rules	No

588

Term (Variable)	<Reportable Period End>
Data Type	Text
Data (D), Value (V) or Heading (H)	D
Definition	CNEW For review purpose, see definition of the controlled terminology below The date on which reporting will cease for trial related events such as adverse events, serious adverse events, product complaints, medical device product complaints, and pregnancy and postpartum events.
User Guidance	N/A
Conformance	Optional if table used
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	9.2
Value	Text
Business rules	**Value Allowed**: Yes **Relationship**: Event Type, Situational Scope, Reportable Period Start **Concept**: CNEW
Repeating and/or Reuse Rules	Yes, repeatable for each event type, situation scope, reportable period start

589

Term (Variable)	Timing for Reporting to Sponsor or Designee
Data Type	Text
Data (D), Value (V) or Heading (H)	H
Definition	Table Column Heading
User Guidance	N/A
Conformance	Optional if table used
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	9.2
Value	Timing for Reporting to Sponsor or Designee
Business rules	**Value Allowed**: No **Relationship**: Table Column Heading **Concept**: Heading
Repeating and/or Reuse Rules	No

590

Term (Variable)	<Timing for Reporting to Sponsor or Designee>
Data Type	Text
Data (D), Value (V) or Heading (H)	D
Definition	CNEW For review purpose, see definition of the controlled terminology below A description of the timing window between trial related events and their reporting to the sponsor or designee.
User Guidance	N/A
Conformance	Optional if table used

Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	9.2
Value	Text
Business rules	**Value Allowed**: Yes **Relationship**: Event Type, Situational Scope **Concept**: CNEW
Repeating and/or Reuse Rules	Yes, repeatable for each event type and situational scope

591

Term (Variable)	Method for Reporting
Data Type	Text
Data (D), Value (V) or Heading (H)	H
Definition	Table Column Heading
User Guidance	N/A
Conformance	Optional if table used
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	9.2
Value	Method for Reporting
Business rules	**Value Allowed**: No **Relationship**: Table Column Heading **Concept**: Heading
Repeating and/or Reuse Rules	No

592

Term (Variable)	<Method for Reporting>
Data Type	Text
Data (D), Value (V) or Heading (H)	D
Definition	CNEW For review purpose, see definition of the controlled terminology below A description of the technique by which trial related events, such as adverse events, serious adverse events, product complaints, medical device product complaints, and pregnancy and postpartum events, are reported to the sponsor and/or regulatory authority.
User Guidance	N/A
Conformance	Optional if used
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	9.2
Value	Text
Business rules	**Value Allowed**: Yes **Relationship**: Event Type, Situational Scope **Concept**: CNEW
Repeating and/or Reuse Rules	Yes, repeatable for each event type and situational scope

593

Term (Variable)	Back-up Method for Reporting
Data Type	Text
Data (D), Value (V) or Heading (H)	H
Definition	Table Column Heading
User Guidance	N/A
Conformance	Optional if table is used
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	9.2
Value	Back-up Method for Reporting
Business rules	**Value Allowed**: No **Relationship**: Table Column Heading **Concept**: Heading
Repeating and/or Reuse Rules	No

Term (Variable)	<Back-up Method for Reporting>
Data Type	Text
Data (D), Value (V) or Heading (H)	D
Definition	CNEW For review purpose, see definition of the controlled terminology below A description of alternative techniques by which trial related events, such as adverse events, serious adverse events, product complaints, medical device product complaints, and pregnancy and postpartum events, are reported to the sponsor and/or regulatory authority.
User Guidance	N/A
Conformance	Optional if table is used
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	9.2
Value	Text
Business rules	**Value Allowed**: Yes **Relationship**: Event Type, Situational Scope **Concept**: CNEW
Repeating and/or Reuse Rules	Yes, repeatable for each event type and situational scope

9.2.1 Timing

Term (Variable)	9.2.1 Timing
Data Type	Text
Data (D), Value (V) or Heading (H)	H
Definition	Heading
User Guidance	N/A
Conformance	Required
Cardinality	One to one

Relationship content from ToC representing the protocol hierarchy	9.2.1
Value	Timing
Business rules	**Value Allowed**: No **Relationship**: 9.2 Timing and Procedures for Collection and Reporting, 9 ADVERSE EVENTS, SERIOUS ADVERSE EVENTS, PRODUCT COMPLAINTS, PREGNANCY AND POSTPARTUM INFORMATION, AND SPECIAL SAFETY SITUATIONS and Table of Contents **Concept**: Heading
Repeating and/or Reuse Rules	No

597

Term (Variable)	<Event Collection and Reporting Timing>
Data Type	Text
Data (D), Value (V) or Heading (H)	D
Definition	CNEW For review purpose, see definition of the controlled terminology below A description of the timing window between trial related events and their reporting to the sponsor or designee.
User Guidance	Specify timing for collection and reporting, including: • start and end dates for collection and reporting • frequency of collection and reporting • cross reference to the Schedule of Assessments as appropriate
Conformance	Required
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	9.2.1
Value	Text
Business rules	**Value Allowed**: Yes **Relationship**: 9.2.1 Timing **Concept**: CNEW
Repeating and/or Reuse Rules	No

598

599 ### 9.2.2 Collection Procedures

Term (Variable)	9.2.2 Collection Procedures
Data Type	Text
Data (D), Value (V) or Heading (H)	H
Definition	Heading
User Guidance	Specify procedures for collection and recording of AEs, SAEs, product complaints (including medical device product complaints if applicable) and pregnancy and postpartum information in the sections below.
Conformance	Required
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	9.2.2

Value	Collection Procedures
Business rules	**Value Allowed**: No **Relationship**: 9.2 Timing and Procedures for Collection and Reporting, 9 ADVERSE EVENTS, SERIOUS ADVERSE EVENTS, PRODUCT COMPLAINTS, PREGNANCY AND POSTPARTUM INFORMATION, AND SPECIAL SAFETY SITUATIONS and Table of Contents **Concept**: Heading
Repeating and/or Reuse Rules	No

600

Term (Variable)	Identification
Data Type	Text
Data (D), Value (V) or Heading (H)	H
Definition	Heading
User Guidance	N/A
Conformance	Required
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	9.2.2
Value	Identification
Business rules	**Value Allowed**: No **Relationship**: 9.2.2 Collection Procedures, 9.2 Timing and Procedures for Collection and Reporting, 9 ADVERSE EVENTS, SERIOUS ADVERSE EVENTS, PRODUCT COMPLAINTS, PREGNANCY AND POSTPARTUM INFORMATION, AND SPECIAL SAFETY SITUATIONS and Table of Contents **Concept**: Heading
Repeating and/or Reuse Rules	No

601

Term (Variable)	<Identification>
Data Type	Text
Data (D), Value (V) or Heading (H)	D
Definition	CNEW For review purpose, see definition of the controlled terminology below A summary of the identification, recording, assessments of severity and causality, and follow-up of adverse events, serious adverse events, pregnancy and postpartum events, and medical device product complaints.
User Guidance	Specify how information will be identified (e.g., spontaneous reporting, solicited questions).
Conformance	Required
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	9.2.2
Value	Text
Business rules	**Value Allowed**: Yes **Relationship**: Identification and 9.2.2 Collection Procedures **Concept**: CNEW
Repeating and/or Reuse Rules	No

602
603
604

Term (Variable)	Severity
Data Type	Text
Data (D), Value (V) or Heading (H)	H
Definition	Heading
User Guidance	N/A
Conformance	Required
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	9.2.2
Value	Severity
Business rules	**Value Allowed**: No **Relationship**: 9.2.2 Collection Procedures, 9.2 Timing and Procedures for Collection and Reporting, 9 ADVERSE EVENTS, SERIOUS ADVERSE EVENTS, PRODUCT COMPLAINTS, PREGNANCY AND POSTPARTUM INFORMATION, AND SPECIAL SAFETY SITUATIONS and Table of Contents **Concept**: Heading
Repeating and/or Reuse Rules	No

605

Term (Variable)	<Severity>
Data Type	Text
Data (D), Value (V) or Heading (H)	D
Definition	C25676 For review purpose, see definition of the controlled terminology below The evaluation of the intensity (severity) of an event.
User Guidance	Specify the intensity rating categories/scale.
Conformance	Required
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	9.2.2
Value	Text
Business rules	**Value Allowed**: Yes **Relationship**: Severity and 9.2.2 Collection Procedures **Concept**: C25676
Repeating and/or Reuse Rules	No

606

Term (Variable)	Causality
Data Type	Text
Data (D), Value (V) or Heading (H)	H
Definition	Heading
User Guidance	N/A
Conformance	Required
Cardinality	One to one

Relationship content from ToC representing the protocol hierarchy	9.2.2
Value	Causality
Business rules	**Value Allowed**: No **Relationship**: 9.2.2 Collection Procedures, 9.2 Timing and Procedures for Collection and Reporting, 9 ADVERSE EVENTS, SERIOUS ADVERSE EVENTS, PRODUCT COMPLAINTS, PREGNANCY AND POSTPARTUM INFORMATION, AND SPECIAL SAFETY SITUATIONS and Table of Contents **Concept**: Heading
Repeating and/or Reuse Rules	No

607

Term (Variable)	<Causality>
Data Type	Text
Data (D), Value (V) or Heading (H)	D
Definition	C82552 For review purpose, see definition of the controlled terminology below The evaluation of the degree of causality (attributability) between a trial intervention and an event.
User Guidance	Specify: • the causality categories/scale • procedures for assessing causality
Conformance	Required
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	9.2.2
Value	Text
Business rules	**Value Allowed**: Yes **Relationship**: Causality and 9.2.2 Collection Procedures **Concept**: C82552
Repeating and/or Reuse Rules	No

608

Term (Variable)	Recording
Data Type	Text
Data (D), Value (V) or Heading (H)	H
Definition	Heading
User Guidance	N/A
Conformance	Required
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	9.2.2
Value	Recording
Business rules	**Value Allowed**: No **Relationship**: 9.2.2 Collection Procedures, 9.2 Timing and Procedures for Collection and Reporting, 9 ADVERSE EVENTS, SERIOUS ADVERSE EVENTS, PRODUCT COMPLAINTS, PREGNANCY AND POSTPARTUM INFORMATION, AND SPECIAL SAFETY SITUATIONS and Table of Contents

	Concept: Heading
Repeating and/or Reuse Rules	No

609

Term (Variable)	<Recording>
Data Type	Text
Data (D), Value (V) or Heading (H)	D
Definition	CNEW For review purpose, see definition of the controlled terminology below A description for the procedures used to document an event.
User Guidance	Specify procedures for recording.
Conformance	Required
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	9.2.2
Value	Text
Business rules	**Value Allowed**: Yes **Relationship**: Recording and 9.2.2 Collection Procedures **Concept**: CNEW
Repeating and/or Reuse Rules	No

610

Term (Variable)	Follow-up
Data Type	Text
Data (D), Value (V) or Heading (H)	H
Definition	Heading
User Guidance	N/A
Conformance	Required
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	9.2.2
Value	Follow-up
Business rules	**Value Allowed**: No **Relationship**: 9.2.2 Collection Procedures, 9.2 Timing and Procedures for Collection and Reporting, 9 ADVERSE EVENTS, SERIOUS ADVERSE EVENTS, PRODUCT COMPLAINTS, PREGNANCY AND POSTPARTUM INFORMATION, AND SPECIAL SAFETY SITUATIONS and Table of Contents **Concept**: Heading
Repeating and/or Reuse Rules	No

611

Term (Variable)	<Follow-up>
Data Type	Text
Data (D), Value (V) or Heading (H)	D
Definition	CNEW For review purpose, see definition of the controlled terminology below A description of the procedures for follow-up, including the assessment tools that will be used to monitor an event and the duration of follow-up.

User Guidance	Specify the procedures for follow-up. Include the assessment tools that will be used to monitor the events and the duration of follow-up after appearance of the events.
Conformance	Required
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	9.2.2
Value	Text
Business rules	**Value Allowed**: Yes **Relationship**: Follow-up and 9.2.2 Collection Procedures **Concept**: CNEW
Repeating and/or Reuse Rules	No

612

613 ### 9.2.3 Reporting

Term (Variable)	9.2.3 Reporting
Data Type	Text
Data (D), Value (V) or Heading (H)	H
Definition	Heading
User Guidance	N/A
Conformance	Required
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	9.2.3
Value	Reporting
Business rules	**Value Allowed**: No **Relationship**: 9.2 Timing and Procedures for Collection and Reporting, 9 ADVERSE EVENTS, SERIOUS ADVERSE EVENTS, PRODUCT COMPLAINTS, PREGNANCY AND POSTPARTUM INFORMATION, AND SPECIAL SAFETY SITUATIONS and Table of Contents **Concept**: Heading
Repeating and/or Reuse Rules	No

614

Term (Variable)	<Reporting>
Data Type	Text
Data (D), Value (V) or Heading (H)	D
Definition	CNEW For review purpose, see definition of the controlled terminology below A description of the method and timelines for reporting an event to the sponsor.
User Guidance	Specify the reporting method (e.g., an electronic data collection tool or a paper CRF), backup reporting method if applicable and reporting timeline to the Sponsor.
Conformance	Required
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	9.2.3
Value	Text
Business rules	**Value Allowed**: Yes

	Relationship: 9.2.3 Reporting **Concept**: CNEW
Repeating and/or Reuse Rules	No

615

616 ### 9.2.3.1 Regulatory Reporting Requirements

Term (Variable)	9.2.3.1 Regulatory Reporting Requirements
Data Type	Text
Data (D), Value (V) or Heading (H)	H
Definition	Heading
User Guidance	N/A
Conformance	Required
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	9.2.3.1
Value	Regulatory Reporting Requirements
Business rules	**Value Allowed**: No **Relationship**: 9.2.3 Reporting, 9.2 Timing and Procedures for Collection and Reporting, 9 ADVERSE EVENTS, SERIOUS ADVERSE EVENTS, PRODUCT COMPLAINTS, PREGNANCY AND POSTPARTUM INFORMATION, AND SPECIAL SAFETY SITUATIONS and Table of Contents **Concept**: Heading
Repeating and/or Reuse Rules	No

617

Term (Variable)	<Regulatory Reporting Requirements>
Data Type	Text
Data (D), Value (V) or Heading (H)	D
Definition	CNEW For review purpose, see definition of the controlled terminology below A description of the requirements for the sponsor/designee to report a serious adverse event, including the criteria for reporting, to the relevant regulatory authority.
User Guidance	Specify: • the investigators' responsibilities for reporting to the Sponsor (and to Ethics Committees, where required), specifying timing of reporting to allow the Sponsor to meet their responsibilities • the Sponsor's legal/regulatory responsibilities to report to regulatory authorities, ethics committees, and investigators • serious and unexpected adverse reaction reporting
Conformance	Required
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	9.2.3.1
Value	Text
Business rules	**Value Allowed**: Yes

	Relationship: 9.2.3.1 Regulatory Reporting Requirements **Concept**: CNEW
Repeating and/or Reuse Rules	No

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619 ### 9.2.4 Adverse Events of Special Interest

Term (Variable)	9.2.4 Adverse Events of Special Interest
Data Type	Text
Data (D), Value (V) or Heading (H)	H
Definition	Heading
User Guidance	N/A
Conformance	Required
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	9.2.4
Value	Adverse Events of Special Interest
Business rules	**Value Allowed**: No **Relationship**: 9.2 Timing and Procedures for Collection and Reporting, 9 ADVERSE EVENTS, SERIOUS ADVERSE EVENTS, PRODUCT COMPLAINTS, PREGNANCY AND POSTPARTUM INFORMATION, AND SPECIAL SAFETY SITUATIONS and Table of Contents **Concept**: Heading
Repeating and/or Reuse Rules	No

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Term (Variable)	<Adverse Events of Special Interest or state "Not applicable">
Data Type	Text
Data (D), Value (V) or Heading (H)	D
Definition	CNEW For review purpose, see definition of the controlled terminology below A description of the processes and procedures used to define, measure, confirm, and report the occurrence of adverse events that are of special interest to the specific trial, or state not applicable.
User Guidance	Specify any AESI: • any event (serious or nonserious) of scientific and medical concern relative to the trial intervention, for which ongoing monitoring and rapid communication by the investigator to the sponsor can be appropriate • other events that merit reporting to the Sponsor, trial leadership, IRB, and regulatory agencies Include the following for each AESI: • the definition • the approach for ascertaining information • if applicable, any approach to confirm or adjudicate the occurrence
Conformance	Required
Cardinality	One to one

Relationship content from ToC representing the protocol hierarchy	9.2.4
Value	Text
Business rules	**Value Allowed**: Yes **Relationship**: 9.2.4 Adverse Events of Special Interest **Concept**: CNEW
Repeating and/or Reuse Rules	No

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622 ### 9.2.5 Disease-related Events or Outcomes Not Qualifying as AEs or SAEs

623

Term (Variable)	9.2.5 Disease-related Events or Outcomes Not Qualifying as AEs or SAEs
Data Type	Text
Data (D), Value (V) or Heading (H)	H
Definition	Heading
User Guidance	N/A
Conformance	Required
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	9.2.5
Value	Disease-related Events or Outcomes Not Qualifying as AEs or SAEs
Business rules	**Value Allowed**: No **Relationship**: 9.2 Timing and Procedures for Collection and Reporting, 9 ADVERSE EVENTS, SERIOUS ADVERSE EVENTS, PRODUCT COMPLAINTS, PREGNANCY AND POSTPARTUM INFORMATION, AND SPECIAL SAFETY SITUATIONS and Table of Contents **Concept**: Heading
Repeating and/or Reuse Rules	No

624

Term (Variable)	<Disease-related Events or Outcomes Not Qualifying as AEs or SAEs>
Data Type	Text
Data (D), Value (V) or Heading (H)	D
Definition	CNEW For review purpose, see definition of the controlled terminology below A description of events or outcomes related to the trial disease indication but not qualifying as adverse events or serious adverse events within the trial, or state not applicable.
User Guidance	Specify any DREs, DROs, or both that will **not** be reported as AEs or SAEs (e.g., seizures in anticonvulsant trials) or state "Not applicable."
Conformance	Required
Cardinality	One to one

Relationship content from ToC representing the protocol hierarchy	9.2.5
Value	Text
Business rules	**Value Allowed**: Yes **Relationship**: 9.2.5 Disease-related Events or Outcomes Not Qualifying as AEs or SAEs **Concept**: CNEW
Repeating and/or Reuse Rules	No

9.3 Pregnancy and Postpartum Information

Term (Variable)	9.3 Pregnancy and Postpartum Information
Data Type	Text
Data (D), Value (V) or Heading (H)	H
Definition	Heading
User Guidance	While pregnancy itself is not considered to be an AE or SAE, if negative or consequential outcome occurs in the participant or child/foetus, it will be reported as an AE or SAE. Refer to Section 9.2 Timing and Procedures for Collection and Reporting for AE and SAE related procedures as applicable. If the negative event meets the seriousness criteria, then this is considered an SAE (e.g., spontaneous abortion, foetal death, stillbirth, congenital anomalies, ectopic pregnancy, or pre-eclampsia) and reported per Section 9.2.3 Reporting. No text is intended here (heading only).
Conformance	Required
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	9.3
Value	Pregnancy and Postpartum Information
Business rules	**Value Allowed**: No **Relationship**: 9 ADVERSE EVENTS, SERIOUS ADVERSE EVENTS, PRODUCT COMPLAINTS, PREGNANCY AND POSTPARTUM INFORMATION, AND SPECIAL SAFETY SITUATIONS and Table of Contents **Concept**: Heading
Repeating and/or Reuse Rules	No

9.3.1 {Participants Who Become Pregnant During the Trial}

Term (Variable)	9.3.1 {Participants Who Become Pregnant During the Trial}
Data Type	Text
Data (D), Value (V) or Heading (H)	H
Definition	Heading
User Guidance	N/A
Conformance	Conditional: when collecting pregnancy data for a trial participant who becomes pregnant during the trial.
Cardinality	One to one

Relationship content from ToC representing the protocol hierarchy	9.3.1
Value	Participants Who Become Pregnant During the Trial
Business rules	**Value Allowed**: No **Relationship**: 9.3 Pregnancy and Postpartum Information, 9 ADVERSE EVENTS, SERIOUS ADVERSE EVENTS, PRODUCT COMPLAINTS, PREGNANCY AND POSTPARTUM INFORMATION, AND SPECIAL SAFETY SITUATIONS and Table of Contents **Concept**: Heading
Repeating and/or Reuse Rules	No

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Term (Variable)	{<Participants Who Become Pregnant During the Trial>}
Data Type	Text
Data (D), Value (V) or Heading (H)	D
Definition	CNEW For review purpose, see definition of the controlled terminology below A description of the processes and procedures used to collect pregnancy data for a trial participant who becomes pregnant while the participant is in the trial, as well as data collection about the child.
User Guidance	Specify: • the assessments to be performed • type and duration of monitoring • whether participants who become pregnant during the trial may continue with trial intervention or must be discontinued from trial intervention (refer to Section 7 Participant Discontinuation of Trial Intervention and Discontinuation or Withdrawal from Trial as applicable) • any trial modifications that need to be made for participants who become pregnant • what information will be collected about a participant who becomes pregnant during the trial (e.g., recording and reporting to the Sponsor, postpartum follow-up, trial intervention discontinuation or continuation, or trial withdrawal) For postpartum follow-up, include the time period (e.g., initial child development) with the justification. If exposure to trial intervention during breastfeeding is applicable, specify: • the assessments to be performed • type and duration of monitoring • what information will be collected for both the participant and child
Conformance	Conditional: when collecting pregnancy data for a trial participant who becomes pregnant during the trial.
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	9.3.1
Value	Text
Business rules	**Value Allowed**: Yes **Relationship**: 9.3.1 Participants Who Become Pregnant During the Trial

	Concept: CNEW
Repeating and/or Reuse Rules	No

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631 ### 9.3.2 {Participants Whose Partners Become Pregnant During the Trial}

Term (Variable)	9.3.2 {Participants Whose Partners Become Pregnant During the Trial}
Data Type	Text
Data (D), Value (V) or Heading (H)	H
Definition	Heading
User Guidance	N/A
Conformance	Conditional: when collecting pregnancy data for the partner of a trial participant who becomes pregnant during the trial.
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	9.3.2
Value	Participants Whose Partners Become Pregnant During the Trial
Business rules	**Value Allowed**: No **Relationship**: 9.3 Pregnancy and Postpartum Information, 9 ADVERSE EVENTS, SERIOUS ADVERSE EVENTS, PRODUCT COMPLAINTS, PREGNANCY AND POSTPARTUM INFORMATION, AND SPECIAL SAFETY SITUATIONS and Table of Contents **Concept**: Heading
Repeating and/or Reuse Rules	No

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Term (Variable)	{<Participants Whose Partners Become Pregnant During the Trial>}
Data Type	Text
Data (D), Value (V) or Heading (H)	D
Definition	CNEW For review purpose, see definition of the controlled terminology below A description of the processes and procedures used to collect pregnancy data for a trial participant's partner, who becomes pregnant while the participant is in the trial.
User Guidance	Specify: • if the investigator will attempt to collect pregnancy information about a participant's partner, who becomes pregnant during the specified period in the trial • whether the participant whose partner becomes pregnant should be discontinued from trial intervention (refer to Section 7 Participant Discontinuation of Trial Intervention and Discontinuation or Withdrawal from Trial as applicable) • the assessments to be performed, type and duration of monitoring, and the information to be collected
Conformance	Conditional: when collecting pregnancy data for the partner of a trial participant who becomes pregnant during the trial.

Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	9.3.2
Value	Text
Business rules	Value Allowed: Yes Relationship: 9.3.2 Participants Whose Partners Become Pregnant During the Trial Concept: CNEW
Repeating and/or Reuse Rules	No

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634 ## 9.4 Special Safety Situations

Term (Variable)	9.4 Special Safety Situations
Data Type	Text
Data (D), Value (V) or Heading (H)	H
Definition	Heading
User Guidance	N/A
Conformance	Required
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	9.4
Value	Special Safety Situations
Business rules	**Value Allowed**: No **Relationship**: 9 ADVERSE EVENTS, SERIOUS ADVERSE EVENTS, PRODUCT COMPLAINTS, PREGNANCY AND POSTPARTUM INFORMATION, AND SPECIAL SAFETY SITUATIONS and Table of Contents **Concept**: Heading
Repeating and/or Reuse Rules	No

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Term (Variable)	<Special Safety Situations>
Data Type	Text
Data (D), Value (V) or Heading (H)	D
Definition	CNEW For review purpose, see definition of the controlled terminology below A characterization or classification of those trial specific situations that are associated with the trial intervention(s) and require regulatory reporting, but that do not qualify as an adverse event or serious adverse event for the given trial.
User Guidance	Specify special safety situations associated with the trial intervention(s) that do not qualify as an AE or SAE, but require regulatory reporting. Examples include: • misuse or abuse • off-label use (if applicable) • medication error (prescription or dispensing error) • occupational exposure • use outside of what is foreseen in the protocol

	• unintended exposure of embryo, foetus, or child via meterial exposure (pregnancy or breastfeeding) or via paternal exposure (semen) • lack of therapeutic efficacy; this is not applicable for studies that measure efficacy as a study endpoint • suspected transmission of an infectious agent; this is only applicable for injected or biologic medicinal products • product complaint, including falsified or counterfeit products • suspected drug-food or drug-drug interaction
Conformance	Required
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	9.4
Value	Text
Business rules	**Value Allowed**: Yes **Relationship**: 9.4 Special Safety Situations **Concept**: CNEW
Repeating and/or Reuse Rules	No

10 STATISTICAL CONSIDERATIONS

Term (Variable)	10 STATISTICAL CONSIDERATIONS
Data Type	Text
Data (D), Value (V) or Heading (H)	H
Definition	Heading
User Guidance	Ensure that the data analysis complies with ICH E9 Guideline and ICH E9(R1) Guideline. In general, all relevant data collected in the trial should be considered in this section. No text is intended here (Heading only)
Conformance	Required
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	10
Value	STATISTICAL CONSIDERATIONS
Business rules	**Value Allowed**: **No** **Relationship**: Table of Contents **Concept**: Heading
Repeating and/or Reuse Rules	No

10.1 General Considerations

Term (Variable)	10.1 General Considerations
Data Type	Text
Data (D), Value (V) or Heading (H)	H

Definition	Heading
User Guidance	N/A
Conformance	Required
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	10.1
Value	General Considerations
Business rules	**Value Allowed**: No **Relationship**:10 STATISTICAL CONSIDERATIONS and Table of Contents **Concept**: Heading
Repeating and/or Reuse Rules	No

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Term (Variable)	<General Considerations>
Data Type	Text
Data (D), Value (V) or Heading (H)	D
Definition	C164387 For review purpose, see definition of the controlled terminology below Careful thought or deliberation related to the planned conduct of statistical analyses within the context of the trial.
User Guidance	Provide statements relevant to statistical considerations in general. For example, this might include statements indicating whether there is a separate statistical analysis plan, which general summary statistics will be provided, and when the analyses will be conducted (e.g. "The analysis will be conducted on all participant data at the time the trial ends.").
Conformance	Required
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	10.1
Value	Text
Business rules	**Value Allowed**: Yes **Relationship**: 10.1 General Considerations, 10 STATISTICAL CONSIDERATIONS and Table of Contents **Concept**: C164387
Repeating and/or Reuse Rules	No

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642 ## 10.2 Analysis Sets

Term (Variable)	10.2 Analysis Sets
Data Type	Text
Data (D), Value (V) or Heading (H)	H
Definition	Heading
User Guidance	N/A
Conformance	Required
Cardinality	One to One
Relationship content from ToC representing the protocol hierarchy	10.2

Value	Analysis Sets
Business rules	**Value Allowed**: No **Relationship**: 10 STATISTICAL CONSIDERATIONS and Table of Contents **Concept**: Heading
Repeating and/or Reuse Rules	No

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Term (Variable)	<Analysis Sets>
Data Type	Text
Data (D), Value (V) or Heading (H)	D
Definition	CNEW For review purpose, see definition of the controlled terminology below A description of the set of participants whose data are to be included in the analyses.
User Guidance	Describe analysis sets to be considered at the trial level, i.e. the set of participants whose data are to be included in the analyses. For each analysis described in Section 10, it should be clear which analysis set should be used.
Conformance	Required
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	10.2
Value	Text
Business rules	**Value Allowed**: Yes **Relationship**: 10.2 Analysis Sets, 10 STATISTICAL CONSIDERATIONS and Table of Contents **Concept**: CNEW
Repeating and/or Reuse Rules	No

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645 10.3 Analyses of Demographics and Other Baseline Variables

Term (Variable)	10.3 Analyses of Demographics and Other Baseline Variables
Data Type	Text
Data (D), Value (V) or Heading (H)	H
Definition	Heading
User Guidance	N/A
Conformance	Required
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	10.3
Value	Analyses of Demographics and Other Baseline Variables
Business rules	**Value Allowed**: No **Relationship**: 10 STATISTICAL CONSIDERATIONS and Table of Contents **Concept**: Heading
Repeating and/or Reuse Rules	No

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Term (Variable)	<Analyses of Demographics and Other Baseline Variables>
Data Type	Text

Data (D), Value (V) or Heading (H)	D
Definition	CNEW For review purpose, see definition of the controlled terminology below A textual description of analyses relevant to variables at baseline, for example demographics, related to the trial.
User Guidance	Describe the summary statistics that will be used to describe the distribution of demographic and other relevant variables at baseline. Specify the timing of the measurement of the variables (e.g., at inclusion in the trial; before, or at randomisation). Relevant variables include but are not limited to: stratification variables specified in Section 6.7 Investigational Trial Intervention Assignment, Randomisation and Blinding, covariates for the statistical models specified in Section 10.4 Analyses Associated with the Primary Objective(s), other suspected predictive or prognostic variables, and variables used for planned subgroup analyses.
Conformance	Required
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	10.3
Value	Text
Business rules	**Value Allowed**: Yes **Relationship**: 10.3 Analyses of Demographics and Other Baseline Variables, 10 STATISTICAL CONSIDERATIONS and Table of Contents **Concept**: CNEW
Repeating and/or Reuse Rules	No

10.4 Analyses Associated with Primary Objective(s)

Term (Variable)	10.4 Analyses Associated with Primary Objective(s)
Data Type	Text
Data (D), Value (V) or Heading (H)	H
Definition	Heading
User Guidance	N/A
Conformance	Required
Cardinality	One to many
Relationship content from ToC representing the protocol hierarchy	10.4
Value	Analyses Associated with Primary Objective(s)
Business rules	**Value Allowed**: No **Relationship**: 10 STATISTICAL CONSIDERATIONS and Table of Contents **Concept**: Heading
Repeating and/or Reuse Rules	No

10.4.1 Primary Objective X

Term (Variable)	10.4.X Primary Objective X
Data Type	Text

Data (D), Value (V) or Heading (H)	H
Definition	Heading
User Guidance	No text is intended here (heading only).
Conformance	Collection for only one primary objective 10.4.1, 10.4.2, 10.4.3, 10.4.4, 10.4.5| For more than one primary objective repeat the collection as level 4 headings where X is = to the number of Primary objectives
Cardinality	One to many
Relationship content from ToC representing the protocol hierarchy	10.4.X
Value	Primary Objective X. If more than one primary objective, add sequential unique number for each objective.
Business rules	**Value Allowed**: No **Relationship**: 3.1.X Primary Objective(s), 10.4 Analyses Associated with Primary Objective(s), 10 STATISTICAL CONSIDERATIONS and Table of Contents **Concept**: Heading
Repeating and/or Reuse Rules	Yes, repeatable for each objective.

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652 #### 10.4.1.1 Statistical Analysis Method

Term (Variable)	10.4.X.1 Statistical Analysis Method
Data Type	Text
Data (D), Value (V) or Heading (H)	H
Definition	Heading
User Guidance	N/A
Conformance	Required
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	10.4.X.1
Value	Statistical Analysis Method
Business rules	**Value Allowed**: No **Relationship**: 10.4.X Primary Objective X. 10.4 Analyses Associated with Primary Objective(s), 10 STATISTICAL CONSIDERATIONS and Table of Contents **Concept**: Heading
Repeating and/or Reuse Rules	Yes, repeatable for each objective as a series of level 4 sections (10.4.X.1, 10.4.X.2, 10.4.X.3, 10.4.X.4, 10.4.X.5).

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Term (Variable)	<Statistical Method of Analysis>
Data Type	Text
Data (D), Value (V) or Heading (H)	D
Definition	CNEW For review purpose, see definition of the controlled terminology below A textual description of the statistical model, hypothesis, and methods of analyses for each objective within the trial.

User Guidance	Describe the statistical analysis methods that will be used to evaluate the primary objective(s) and associated estimand(s) in Section 3.1. Ensure that the statistical hypothesis/model/analysis (and corresponding assumptions) is aligned with the primary estimand(s). If there is more than one primary objective, present each objective as a level 3 heading and present each subsequent heading in Section 10.4 as a level 4 heading. For each objective, state the null and alternative hypotheses, including the pre-planned type 1 error rate, or alternative criteria for evaluating whether the objective has been met, and relevant operating characteristics if appropriate. Describe the statistical model used and the factors that will be included (covariates and interactions) and any rules for handling these factors (for example, pooling of centres). If modelling and simulation methods are to be used, please describe the model (inputs and outputs), the underlying assumptions, and the method of model fitting.
Conformance	Required
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	10.4.X.1
Value	Text
Business rules	**Value Allowed**: Yes **Relationship**: 10.4.X.1 Statistical Analysis Method **Concept**: CNEW
Repeating and/or Reuse Rules	Yes, repeatable for each objective as a series of level 4 sections (10.4.X.1, 10.4.X.2, 10.4.X.3, 10.4.X.4, 10.4.X.5).

10.4.1.2 Handling of Data in Relation to Primary Estimand(s)

Term (Variable)	10.4.X.2 Handling of Data in relation to Primary Estimand(s)
Data Type	Text
Data (D), Value (V) or Heading (H)	H
Definition	Heading
User Guidance	N/A
Conformance	Required
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	10.4.X.2
Value	Handling of Data in relation to Primary Estimand(s)
Business rules	**Value Allowed**: No X may be a number for the collection **Relationship**: 10.4.X Primary Objective(s), 10.4 Analyses Associated with Primary Objective(s), 10 STATISTICAL CONSIDERATIONS and Table of Contents **Concept**: Heading
Repeating and/or Reuse Rules	Yes, repeatable for each objective as a series of level 4 sections (10.4.X.1, 10.4.X.2, 10.4.X.3, 10.4.X.4, 10.4.X.5).

Term (Variable)	<Handling of Data in Relation to Primary Estimand(s)>
Data Type	Text
Data (D), Value (V) or Heading (H)	D
Definition	CNEW

	For review purpose, see definition of the controlled terminology below A textual description of how data will be handled for the statistical analysis in line with the primary estimand.
User Guidance	For each intercurrent event of the primary estimand(s) (Section 3.1, Estimand(s) for the Primary Objective(s)), explain how data will be handled for the statistical analysis in line with the primary estimand. The handling of intercurrent events in statistical analysis should be aligned with the specific estimand strategies being used. This section should describe with more detail the rationale and handling of the data rather than repeating the guidance from the preceding sections.
Conformance	Required
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	10.4.X.2 Handling of Data in relation to Primary Estimand(s)
Value	Text
Business rules	**Value Allowed**: Yes **Relationship**: 10.4.X.2 Handling of Data in relation to Primary Estimand(s) **Concept**: CNEW
Repeating and/or Reuse Rules	Yes, repeatable for each objective as a series of level 4 sections (10.4.X.1, 10.4.X.2, 10.4.X.3, 10.4.X.4, 10.4.X.5).

10.4.1.3 Handling of Missing Data in Relation to Primary Estimand(s)

Term (Variable)	10.4.X.3 Handling of Missing Data in Relation to Primary Estimand(s)
Data Type	Text
Data (D), Value (V) or Heading (H)	H
Definition	Heading
User Guidance	N/A
Conformance	Required
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	10.4.X.3
Value	Handling of Missing Data in Relation to Primary Estimand(s)
Business rules	**Value Allowed**: No **Relationship**: 10.4.X Primary Objective(s), 10.4 Analyses Associated with Primary Objective(s), 10 STATISTICAL CONSIDERATIONS and Table of Contents **Concept**: Heading
Repeating and/or Reuse Rules	No

Term (Variable)	<Handling of Missing Data in Relation to Primary Estimand>
Data Type	Text
Data (D), Value (V) or Heading (H)	D
Definition	CNEW For review purpose, see definition of the controlled terminology below A textual description of how missing data associated with the primary estimand will be handled, including the rationale for the approach.

User Guidance	Describe how missing data will be addressed (e.g., imputation method and model), state the underlying assumptions, and provide a rationale for the approach.
Conformance	Required
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	10.4.X.3
Value	Text
Business rules	**Value Allowed**: Yes **Relationship**: 10.4.X.3 Handling of Missing Data **Concept**: CNEW
Repeating and/or Reuse Rules	Yes, repeatable for each objective as a series of level 4 sections (10.4.X.1, 10.4.X.2, 10.4.X.3, 10.4.X.4, 10.4.X.5).

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661 ### 10.4.1.4 Sensitivity Analysis

Term (Variable)	10.4.X.4 Sensitivity Analysis
Data Type	Text
Data (D), Value (V) or Heading (H)	H
Definition	Heading
User Guidance	N/A
Conformance	Conditional: when there is Sensitivity Analysis for a primary objective
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	10.4.X.4
Value	Sensitivity Analysis
Business rules	**Value Allowed**: No **Relationship**: 10.4.X Primary Objective(s), 10.4 Analyses Associated with Primary Objective(s), 10 STATISTICAL CONSIDERATIONS and Table of Contents **Concept**: Heading
Repeating and/or Reuse Rules	Yes, repeatable for each objective as a series of level 4 sections (10.4.X.1, 10.4.X.2, 10.4.X.3, 10.4.X.4, 10.4.X.5).

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Term (Variable)	{<Sensitivity Analysis>}
Data Type	Text
Data (D), Value (V) or Heading (H)	D
Definition	CNEW For review purpose, see definition of the controlled terminology below A textual description of the series of analyses conducted to explore the robustness of inferences from the main estimator to deviations from its underlying modelling assumptions and limitations in the data.
User Guidance	Describe sensitivity analyses. Sensitivity analyses are a series of analyses conducted with the intent to explore the robustness of inferences from the main estimator to deviations from its underlying modelling assumptions and limitations in the data.
Conformance	Conditional: when there is Sensitivity Analysis for a primary objective
Cardinality	One to many

Relationship content from ToC representing the protocol hierarchy	10.4.X.4
Value	Text
Business rules	**Value Allowed** Yes **Relationship**: 10.4.X.4 Sensitivity Analysis **Concept**: CNEW
Repeating and/or Reuse Rules	Yes, repeatable for each objective as a series of level 4 sections (10.4.X.1, 10.4.X.2, 10.4.X.3, 10.4.X.4, 10.4.X.5).

663

664 ### 10.4.1.5 Supplementary Analysis

Term (Variable)	10.4.X.5 Supplementary Analysis
Data Type	Text
Data (D), Value (V) or Heading (H)	H
Definition	Heading
User Guidance	N/A
Conformance	Conditional: when there is Supplementary Analysis for a primary objective
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	10.4.X.5
Value	Supplementary Analysis
Business rules	**Value Allowed**: No **Relationship**: 10.4.X Primary Objective(s), 10.4 Analyses Associated with the Primary Objective(s), 10 STATISTICAL CONSIDERATIONS and Table of Contents **Concept**: Heading
Repeating and/or Reuse Rules	Yes, repeatable for each objective as a series of level 4 sections (10.4.X.1, 10.4.X.2, 10.4.X.3, 10.4.X.4, 10.4.X.5).

665

Term (Variable)	{<Supplementary Analysis>}
Data Type	Text
Data (D), Value (V) or Heading (H)	D
Definition	CNEW For review purpose, see definition of the controlled terminology below A textual description of the analyses that are conducted in addition to the main and sensitivity analysis with the intent to provide additional insights into the understanding of the treatment effect.
User Guidance	Describe any supplementary analysis if applicable. Supplementary analyses are conducted in addition to the main and sensitivity analysis with the intent to provide additional insights into the understanding of the treatment effect.
Conformance	Conditional: when there is Supplementary Analysis for a primary objective
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	10.4.X.5
Value	Text
Business rules	**Value Allowed**: Yes **Relationship**: 10.4.X.5 Supplementary Analysis

	Concept: CNEW
Repeating and/or Reuse Rules	Yes, repeatable for each objective as a series of level 4 sections (10.4.X.1, 10.4.X.2, 10.4.X.3, 10.4.X.4, 10.4.X.5).

666

667 ## 10.5 Analysis Associated with the Secondary Objective(s)

Term (Variable)	10.5 Analyses Associated with the Secondary Objective(s)
Data Type	Text
Data (D), Value (V) or Heading (H)	H
Definition	Heading
User Guidance	Describe the statistical analysis methods in alignment with the secondary objectives and associated estimands in Section 3.2 Secondary Objective(s) and Associated Estimands. Use the same section structure as Section 10.4 Analyses Associated with the Primary Objective(s). No text is intended here (heading only) unless there is no secondary objective, in which case indicate "Not applicable."
Conformance	Required
Cardinality	One to many
Relationship content from ToC representing the protocol hierarchy	10.5
Value	Analyses Associated with Secondary Objective(s)
Business rules	**Value Allowed**: No **Relationship**: 10 STATISTICAL CONSIDERATIONS and Table of Contents **Concept**: Heading
Repeating and/or Reuse Rules	No

669

670 ### 10.5.1 {Secondary Objective}

Term (Variable)	10.5.X Secondary Objective
Data Type	Text
Data (D), Value (V) or Heading (H)	H
Definition	Data
User Guidance	N/A
Conformance	Conditional: secondary objective 10.5.1, 10.5.2, 10.5.3, 10.5.4, 10.5.5 For more than one secondary objective repeat the collection as level 4 headings where X is = to the number of secondary objectives
Cardinality	One to many
Relationship content from ToC representing the protocol hierarchy	10.5.X
Value	Secondary Objective X. If more than one secondary objective, add sequential unique number for each objective.
Business rules	**Value Allowed**: No **Relationship**: 10.5 Analyses Associated with Secondary Objective(s), 10 STATISTICAL CONSIDERATIONS and Table of Contents **Concept**: Heading

Repeating and/or Reuse Rules	Yes, repeatable for each objective.

671

672 **10.5.1.1 Statistical Analysis Method**

Term (Variable)	{10.5.X.1 Statistical Analysis Method}
Data Type	Text
Data (D), Value (V) or Heading (H)	H
Definition	Heading
User Guidance	N/A
Conformance	Conditional: when there is Secondary Objective
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	10.5.X.1
Value	Statistical Analysis Method
Business rules	**Value Allowed**: No **Relationship**: 10.5.X Secondary Objective, 10.5 Analyses Associated with Secondary Objective(s), 10 STATISTICAL CONSIDERATIONS and Table of Contents **Concept**: Heading
Repeating and/or Reuse Rules	Yes, repeatable for each objective as a series of Level 4 sections (10.5.X.1, 10.5.X.2, 10.5.X.3, 10.5.X.4, 10.5.X.5).

673

Term (Variable)	{<Statistical Method of Analysis>}
Data Type	Text
Data (D), Value (V) or Heading (H)	D
Definition	CNEW For review purpose, see definition of the controlled terminology below A textual description of the statistical model, hypothesis, and methods of analyses for each objective within the trial.
User Guidance	Describe the statistical analysis methods that will be used to evaluate the Secondary objective(s) and associated estimand(s) in Section 3.2. Ensure that the statistical hypothesis/model/analysis (and corresponding assumptions) is aligned with the Secondary estimand(s). If there is more than one Secondary objective, present each objective as a level 3 heading and present each subsequent heading in Section 10.5 as a level 4 heading. For each objective, state the null and alternative hypotheses, including the pre-planned type 1 error rate, or alternative criteria for evaluating whether the objective has been met, and relevant operating characteristics if appropriate. Describe the statistical model used and the factors that will be included (covariates and interactions) and any rules for handling these factors (for example, pooling of centres). If modelling and simulation methods are to be used, please describe the model (inputs and outputs), the underlying assumptions, and the method of model fitting.
Conformance	Conditional: when there is Secondary estimand
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	10.5.X.1

Value	Text
Business rules	**Value Allowed**: Yes **Relationship**: 10.5.X.1 Statistical Analysis Method **Concept**: CNEW
Repeating and/or Reuse Rules	Yes, repeatable for each objective as a series of level 4 sections (10.5.X.1, 10.5.X.2, 10.5.X.3, 10.5.X.4, 10.5.X.5).

674

675 ### 10.5.1.2 Handling of Data in Relation to Secondary Estimand(s)

Term (Variable)	{10.5.X.2 Handling of Data in Relation to Secondary Estimand(s)}
Data Type	Text
Data (D), Value (V) or Heading (H)	H
Definition	Heading
User Guidance	N/A
Conformance	Conditional: when there is Secondary estimand
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	10.5.X.2
Value	Statistical Method of Analysis
Business rules	**Value Allowed**: No **Relationship**: 10.5.X Secondary Objective, 10.5 Analyses Associated with Secondary Objective(s), 10 STATISTICAL CONSIDERATIONS and Table of Contents **Concept**: Heading
Repeating and/or Reuse Rules	Yes, repeatable for each objective as a series of Level 4 sections (10.5.X.1, 10.5.X.2, 10.5.X.3, 10.5.X.4, 10.5.X.5).

676

Term (Variable)	{<Handling of Data in Relation to Secondary Estimand(s)>}
Data Type	Text
Data (D), Value (V) or Heading (H)	D
Definition	CNEW For review purpose, see definition of the controlled terminology below A textual description of how data will be handled for the statistical analysis in line with the Secondary estimand.
User Guidance	For each intercurrent event of the Secondary estimand(s) (Section 3.1, Estimand(s) for the Secondary Objective(s)), explain how data will be handled for the statistical analysis in line with the Secondary estimand. The handling of intercurrent events in statistical analysis should be aligned with the specific estimand strategies being used. This section should describe with more detail the rationale and handling of the data rather than repeating the guidance from the preceding sections.
Conformance	Conditional: when there is Secondary estimand
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	10.5.X.2
Value	Text
Business rules	**Value Allowed**: Yes **Relationship**:10.5.X.2 Handling of Data in relation to Secondary Estimand(s)

	Concept: CNEW
Repeating and/or Reuse Rules	Yes, repeatable for each objective as a series of level 4 sections (10.5.X.1, 10.5.X.2, 10.5.X.3, 10.5.X.4, 10.5.X.5).

677

678 ### 10.5.1.3 Handling of Missing Data in Relation to Secondary Estimand(s)

Term (Variable)	{10.5.1.3 Handling of Missing Data in Relation to Secondary Estimand(s)}
Data Type	Text
Data (D), Value (V) or Heading (H)	H
Definition	Heading
User Guidance	N/A
Conformance	Conditional: when there is Secondary estimand
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	10.5.X.3
Value	Handling of Missing Data in Relation to Secondary Estimand(s)
Business rules	**Value Allowed**: No **Relationship**: 10.5.X Secondary Objective, 10.5 Analysis Associated with the Secondary Objective(s), 10 STATISTICAL CONSIDERATIONS and Table of Contents **Concept**: Heading
Repeating and/or Reuse Rules	Yes, repeatable for each objective as a series of level 4 sections (10.5.X.1, 10.5.X.2, 10.5.X.3, 10.5.X.4, 10.5.X.5).

679

Term (Variable)	{<Handling of Missing Data in Relation to Secondary Estimand(s)>}
Data Type	Text
Data (D), Value (V) or Heading (H)	D
Definition	CNEW For review purpose, see definition of the controlled terminology below A textual description of how missing data associated with the Secondary estimand will be handled, including the rationale for the approach.
User Guidance	Describe how missing data will be addressed (e.g., imputation method and model), state the underlying assumptions, and provide a rationale for the approach.
Conformance	Conditional: when there is Secondary estimand
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	10.5.X.3
Value	Text
Business rules	**Value Allowed**: Yes **Relationship**: 10.5.X.3 Handling of Missing Data in Relation to Secondary Estimand(s) **Concept**: CNEW
Repeating and/or Reuse Rules	Yes, repeatable for each objective as a series of level 4 sections (10.5.X.1, 10.5.X.2, 10.5.X.3, 10.5.X.4, 10.5.X.5).

680

681 ### 10.5.1.4 Sensitivity Analysis

Term (Variable)	{10.5.X.4 Sensitivity Analysis}

Data Type	Text
Data (D), Value (V) or Heading (H)	H
Definition	Heading
User Guidance	N/A
Conformance	Conditional: when there is Sensitivity Analysis for a Secondary objective
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	10.5.X.4
Value	Sensitivity Analysis
Business rules	**Value Allowed**: No **Relationship**: 10.5.X Secondary Objective, 10.5 Analysis Associated with the Secondary Objective(s), 10 STATISTICAL CONSIDERATIONS and Table of Contents **Concept**: Heading
Repeating and/or Reuse Rules	Yes, repeatable for each objective as a series of level 4 sections (10.5.X.1, 10.5.X.2, 10.5.X.3, 10.5.X.4, 10.5.X.5).

682

Term (Variable)	{<Sensitivity Analysis>}
Data Type	Text
Data (D), Value (V) or Heading (H)	D
Definition	CNEW For review purpose, see definition of the controlled terminology below A textual description of the series of analyses conducted to explore the robustness of inferences from the main estimator to deviations from its underlying modelling assumptions and limitations in the data.
User Guidance	Describe any supplementary analysis, if applicable. Supplementary analyses are conducted in addition to the main and sensitivity analysis with the intent to provide additional insights into the understanding of the treatment effect.
Conformance	Conditional: when there is Seconday Objective and sensitivity Analysis for a Secondary objective
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	10.5.X.4
Value	Text
Business rules	**Value Allowed** Yes **Relationship**: 10.5.X.4 Sensitivity Analysis **Concept**: CNEW
Repeating and/or Reuse Rules	Yes, repeatable for each objective as a series of level 4 sections (10.5.X.1, 10.5.X.2, 10.5.X.3, 10.5.X.4, 10.5.X.5).

683

684 ### 10.5.1.5 Supplementary Analysis

Term (Variable)	{10.5.X.5 Supplementary Analysis}
Data Type	Text
Data (D), Value (V) or Heading (H)	H
Definition	Heading
User Guidance	N/A

Conformance	Conditional: when there is a Supplementary Analysis for a Secondary objective
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	10.5.X.5
Value	Supplementary Analysis
Business rules	**Value Allowed**: No **Relationship**: 10.5.X Secondary Objective, 10.5 Analysis Associated with the Secondary Objective(s), 10 STATISTICAL CONSIDERATIONS and Table of Contents **Concept**: Heading
Repeating and/or Reuse Rules	Yes, repeatable for each objective.

685

Term (Variable)	{<Supplementary Analysis>}
Data Type	Text
Data (D), Value (V) or Heading (H)	D
Definition	CNEW For review purpose, see definition of the controlled terminology below A textual description of the analyses that are conducted in addition to the main and sensitivity analysis with the intent to provide additional insights into the understanding of the treatment effect.
User Guidance	Describe any supplementary analysis if applicable. Supplementary analyses are conducted in addition to the main and sensitivity analysis with the intent to provide additional insights into the understanding of the treatment effect.
Conformance	Conditional: when there Supplementary Analysis for a Secondary objective
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	10.5.X.5
Value	Text
Business rules	**Value Allowed**: Yes **Relationship**: 10.5.X.5 Supplementary Analysis **Concept**: CNEW
Repeating and/or Reuse Rules	Yes, repeatable for each objective as a series of level 4 sections (10.5.X.1, 10.5.X.2, 10.5.X.3, 10.5.X.4, 10.5.X.5).

686

687 10.6 Analyses Associated with Exploratory Objective(s)

Term (Variable)	10.6 Analyses Associated with Exploratory Objective(s)
Data Type	Text
Data (D), Value (V) or Heading (H)	H
Definition	Heading
User Guidance	N/A
Conformance	Required
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	10.6
Value	Analyses of Exploratory Endpoint(s)
Business rules	**Value Allowed**: No

	Relationship: 10 STATISTICAL CONSIDERATIONS and Table of Contents **Concept**: Heading
Repeating and/or Reuse Rules	No

688

Term (Variable)	<Analysis Associated with Exploratory Objectives(s)>
Data Type	Text
Data (D), Value (V) or Heading (H)	D
Definition	CNEW For review purpose, see definition of the controlled terminology below A textual description of the statistical model, hypothesis, and methods of analyses for each exploratory objective within the trial.
User Guidance	Describe any exploratory analyses, if applicable. Additional subsections could be created to describe the analyses, as needed. If there is no exploratory objective, indicate "not applicable"
Conformance	Required
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	10.6
Value	Text
Business rules	**Value Allowed**: Yes **Relationship**: 10.6 Analysis Associated with the Exploratory Objective(s), **Concept**: CNEW
Repeating and/or Reuse Rules	No

689

690 ## 10.7 Safety Analyses

Term (Variable)	10.7 Safety Analyses
Data Type	Text
Data (D), Value (V) or Heading (H)	H
Definition	Heading
User Guidance	N/A
Conformance	Required
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	10.7
Value	Safety Analysis
Business rules	**Value Allowed**: No **Relationship**: 10 STATISTICAL CONSIDERATIONS and Table of Contents **Concept**: Heading
Repeating and/or Reuse Rules	No

691

Term (Variable)	<Safety Analyses>
Data Type	Text
Data (D), Value (V) or Heading (H)	D
Definition	CNEW

	For review purpose, see definition of the controlled terminology below A textual description of the analyses of relevant safety variables, including adverse events of special interest.
User Guidance	If safety is a primary and/or secondary objective, describe the corresponding safety analyses in the appropriate section above (Section 10.4 Analyses Associated with the Primary Objective(s) or Section 10.5 Analyses Associated with the Secondary Objective[s]). In this section, describe statistical methods that will be used to analyse relevant safety outcomes, including any AESI. This should typically include specification of a measure to estimate risk within treatment arms, a measure to compare risks across treatment arms, and a measure of statistical uncertainty around the comparison such as a confidence interval.
Conformance	Required
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	10.7
Value	Text
Business rules	**Value Allowed**: Yes **Relationship**: 10.7 Safety Analyses **Concept**: CNEW
Repeating and/or Reuse Rules	No

10.8 Other Analyses

Term (Variable)	10.8 Other Analyses
Data Type	Text
Data (D), Value (V) or Heading (H)	H
Definition	Heading
User Guidance	N/A
Conformance	Required
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	10.8
Value	Other Analyses
Business rules	**Value Allowed**: No **Relationship**: 10 STATISTICAL CONSIDERATIONS and Table of Contents **Concept**: Heading
Repeating and/or Reuse Rules	No

Term (Variable)	<Other Analyses>
Data Type	Text
Data (D), Value (V) or Heading (H)	D
Definition	CNEW For review purpose, see definition of the controlled terminology below A textual description of the analyses that are different than the one(s) previously specified or mentioned.
User Guidance	Describe other analyses not included in Sections 10.3-10.8, such as subgroup analyses.

Conformance	Required
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	10.8
Value	Text
Business rules	**Value Allowed**Yes **Relationship**: 10.8 Other Analyses,**Concept**: CNEW
Repeating and/or Reuse Rules	No

10.9 Interim Analyses

Term (Variable)	10.9 Interim Analyses
Data Type	Text
Data (D), Value (V) or Heading (H)	H
Definition	Heading
User Guidance	N/A
Conformance	Required
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	10.9
Value	Interim Analyses
Business rules	**Value Allowed**: No **Relationship**: 10 STATISTICAL CONSIDERATIONS and Table of Contents **Concept**: Heading
Repeating and/or Reuse Rules	No

Term (Variable)	<Interim Analyses>
Data Type	Text
Data (D), Value (V) or Heading (H)	D
Definition	C142582 For review purpose, see definition of the controlled terminology below A textual description of any analysis intended to compare treatment arms with respect to efficacy or safety at any time prior to the formal completion of a trial.
User Guidance	Describe any interim analysis and criteria for stopping or adapting the trial. Ensure alignment with Section 4.3. The description should include, but is not limited to, the following: • Any planned interim analysis, even if it is only to be performed at the request of an oversight body (for example, DMC). • The purpose of the interim analysis, including whether the interim analysis may be used for stopping and/or for other trial adaptations such as sample size re-estimation, alteration to the proportion of participants allocated to each trial group, or changes to eligibility criteria. • The applied statistical method, for example, group sequential test and spending function (for example, O'Brien-Fleming), as applicable. • The party(ies) responsible for performing and reviewing the results of the analyses (e.g. adaptation committee, DMC, independent statistician). • When the analyses will be conducted (timing and/or triggers).

	• The decision criteria—statistical or other—that will be adopted to judge the interim results as part of a guideline for early stopping or other adaptations. • Who will see the outcome data while the trial is ongoing. • Whether these individuals will remain blinded to trial groups. • How the integrity of the trial implementation will be protected (for example, maintaining blinding) when decisions are made after interim analyses (e.g. a decision to continue the trial or implement a specific adaptation). • Who has the ultimate authority to stop or modify the trial, for example, investigator, principal investigator, DMC, or Sponsor.
Conformance	Required
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	10.9
Value	Text
Business rules	**Value Allowed**: Yes **Relationship**: 10.9 Interim Analyses **Concept**: C142582
Repeating and/or Reuse Rules	Yes, repeatable for each interim

10.10 Multiplicity Adjustments

Term (Variable)	10.10 Multiplicity Adjustments
Data Type	Text
Data (D), Value (V) or Heading (H)	H
Definition	Heading
User Guidance	N/A
Conformance	Required
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	10.10
Value	Multiplicity Adjustments
Business rules	**Value Allowed**: No **Relationship**: 10 STATISTICAL CONSIDERATIONS and Table of Contents **Concept**: Heading
Repeating and/or Reuse Rules	No

Term (Variable)	<Multiplicity Adjustments>
Data Type	Text
Data (D), Value (V) or Heading (H)	D
Definition	CNEW For review purpose, see definition of the controlled terminology below A textual description of the statistical adjustments needed to limit the probability of false positive findings in trials where there are multple simultaneous hypotheses.

User Guidance	Multiple testing procedures may be needed to limit the probability of false positive findings in a trial. Reasons for carrying out multiple statistical tests include - but are not restricted to - multiple endpoints, multiple treatment groups, multiple hypotheses, subgroups, different statistical methods, etc. Describe any approaches to multiplicity control for the trial. This description might go beyond the analysis of primary objectives. Specify the statistical approach to control the overall type I error rate as well as the (adjusted) significance levels to test specific hypotheses, as applicable. Clarify whether the tests/confidence intervals are one- or two-sided. State the circumstances under which a study will be considered to have met its primary objective(s). For example, in a study with two primary efficacy endpoints, this section should state whether the study would be expected to provide evidence on at least one or on both of the endpoints in order to confirm the efficacy of the treatment. For some statistical approaches it might be helpful to include a graphical depiction, as visualisation will be helpful for understanding, coupled with the clinical translation of the mathematical choices. Details regarding Interim Analyses should be provided in section 10.9.
Conformance	Required
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	10.10
Value	Text
Business rules	**Value Allowed**: Yes **Relationship**:10.10 Multiplicity Adjustments **Concept**: CNEW
Repeating and/or Reuse Rules	No

10.11 Sample Size Determination

Term (Variable)	10.11 Sample Size Determination
Data Type	Text
Data (D), Value (V) or Heading (H)	H
Definition	Heading
User Guidance	N/A
Conformance	Required
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	10.11
Value	Sample Size Determination
Business rules	**Value Allowed**: No **Relationship**: 10 STATISTICAL CONSIDERATIONS and Table of Contents **Concept**: Heading
Repeating and/or Reuse Rules	No

Term (Variable)	<Sample Size Determination>
Data Type	Text

Data (D), Value (V) or Heading (H)	D
Definition	C115467 For review purpose, see definition of the controlled terminology below A statistical calculation to determine the number of subjects required for the primary analysis, which should be large enough to provide a reliable answer to the questions addressed and should be determined by the primary objective of the trial. If the sample size is determined on some other basis, then this should be made clear and justified.
User Guidance	This section should detail the methods used for the determination of the sample size. The sample size calculation should be aligned with the primary estimand and the primary analysis, otherwise a justification is needed. Details of sample size calculation should include all relevant information to enable reproduction of the sample size, for example: • referencing of any prior studies on which assumptions were based, • significance level (including information on the choice of one- or two-sided level), • power, • assumed treatment effect and variability, • impact of dropout rate and intercurrent events on sample size calculation, • precision of estimator/length of confidence interval Any assumptions made should be stated and justified. Further analysis of how deviations from the assumptions will affect the sample size should be included. If complex simulations were used to calculate the sample size, consider including details in a separate simulation report as an appendix to the protocol. If the planned sample size is not derived statistically, then this should be explicitly stated along with a rationale for the intended sample size (for example, exploratory nature of pilot trials; pragmatic considerations for trials in rare diseases).
Conformance	Required
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	10.11
Value	Text
Business rules	**Value Allowed**: Yes **Relationship**: 10.11 Sample Size Determination, **Concept**: C115467
Repeating and/or Reuse Rules	No

11 TRIAL OVERSIGHT AND OTHER GENERAL CONSIDERATIONS

Term (Variable)	11 TRIAL OVERSIGHT AND OTHER GENERAL CONSIDERATIONS
Data Type	Text
Data (D), Value (V) or Heading (H)	H
Definition	Heading
User Guidance	No text is intended here (heading only).
Conformance	Required
Cardinality	One to one

Relationship content from ToC representing the protocol hierarchy	11
Value	TRIAL OVERSIGHT AND OTHER GENERAL CONSIDERATIONS
Business rules	**Value Allowed**: No **Relationship**: Table of Contents **Concept**: Heading
Repeating and/or Reuse Rules	No

706

707 11.1 Regulatory and Ethical Considerations

Term (Variable)	11.1 Regulatory and Ethical Considerations
Data Type	Text
Data (D), Value (V) or Heading (H)	H
Definition	Heading
User Guidance	N/A
Conformance	Required
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	11.1
Value	Regulatory and Ethical Considerations
Business rules	**Value Allowed**: No **Relationship**: 11 TRIAL OVERSIGHT AND OTHER GENERAL CONSIDERATIONS and Table of Contents **Concept**: Heading
Repeating and/or Reuse Rules	No

708

Term (Variable)	<Regulatory and Ethical Considerations>
Data Type	Text
Data (D), Value (V) or Heading (H)	D
Definition	CNEW For review purpose, see definition of the controlled terminology below Careful thought or deliberation related to the regulatory and ethical aspects of the trial.
User Guidance	Provide a high-level statement on the prevailing ethical, legal, and regulatory guidelines that will be applied throughout the trial. This trial will be conducted in accordance with the protocol and with the following: • Ethical principles that have their origin in the Declaration of Helsinki for medical research involving human subjects • Consensus ethical principles derived from international guidelines including the Declaration of Helsinki and the Council for International Organisations of Medical Sciences (CIOMS) International Ethical Guidelines • ICH Good Clinical Practice (GCP) Guidelines • Applicable laws and regulations
Conformance	Required
Cardinality	One to one

Relationship content from ToC representing the protocol hierarchy	11.1
Value	Text
Business rules	**Value Allowed**: Yes **Relationship**: 11.1 Regulatory and Ethical Considerations **Concept**: CNEW
Repeating and/or Reuse Rules	No

11.2 Trial oversight

Term (Variable)	11.2 Trial Oversight
Data Type	Text
Data (D), Value (V) or Heading (H)	H
Definition	Heading
User Guidance	N/A
Conformance	Required
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	11.2
Value	Trial Oversight
Business rules	**Value Allowed**: No **Relationship**: 11 TRIAL OVERSIGHT AND OTHER GENERAL CONSIDERATIONS and Table of Contents **Concept**: Heading
Repeating and/or Reuse Rules	No

Term (Variable)	{<Trial Oversight>}
Data Type	Text
Data (D), Value (V) or Heading (H)	D
Definition	CNEW For review purpose, see definition of the controlled terminology below A description of the planned processes and procedures to govern and conduct a clinical trial in order to protect the rights, safety and welfare of the trial participants.
User Guidance	Concisely summarize the trial oversight listing the investigator and sponsor responsibilities not covered in other sections of the protocol which are essential for the operations of the trial, specifying the ones related to quality assurance. if not using below optional subheadings
Conformance	Conditional: if not using the optional subheadings Level 3 (11.2.1, 11.2.2)
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	11.2
Value	Text
Business rules	**Value Allowed**: Yes **Relationship**: 11.2 Trial Oversight

	Concept: CNEW
Repeating and/or Reuse Rules	No

11.2.1 Investigator Responsibilities

Term (Variable)	11.2.1 Investigator Responsibilities
Data Type	Text
Data (D), Value (V) or Heading (H)	H
Definition	Heading
User Guidance	N/A
Conformance	Optional
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	11.2.1
Value	Investigator Responsibilities
Business rules	**Value Allowed**: No **Relationship**: 11.2 Trial Oversight, 11 TRIAL OVERSIGHT AND OTHER GENERAL CONSIDERATIONS and Table of Contents **Concept**: Heading
Repeating and/or Reuse Rules	No

Term (Variable)	<Investigator Responsibilities>
Data Type	Text
Data (D), Value (V) or Heading (H)	D
Definition	CNEW For review purpose, see definition of the controlled terminology below A description of the obligations of the investigator with respect to the trial.
User Guidance	Describe the investigator duties, including the oversight of duties delegated to a third party that may impact the trial conduct at sites, if applicable and if not addressed elsewhere.
Conformance	Optional
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	11.2.1
Value	Text
Business rules	**Value Allowed**: Yes **Relationship**: 11.2.1 Investigator Responsibilities **Concept**: CNEW
Repeating and/or Reuse Rules	No

11.2.2 Sponsor Responsibilities

Term (Variable)	11.2.2 Sponsor Responsibilities
Data Type	Text

Data (D), Value (V) or Heading (H)	H
Definition	Heading
User Guidance	N/A
Conformance	Optional
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	11.2.2
Value	Sponsor Responsibilities
Business rules	**Value Allowed**: No **Relationship**: 11.2 Trial Oversight, 11 TRIAL OVERSIGHT AND OTHER GENERAL CONSIDERATIONS and Table of Contents **Concept**: Heading
Repeating and/or Reuse Rules	No

717

Term (Variable)	<Sponsor Responsibilities>
Data Type	Text
Data (D), Value (V) or Heading (H)	D
Definition	CNEW For review purpose, see definition of the controlled terminology below A description of the obligations of the sponsor with respect to the trial.
User Guidance	Describe the sponsor duties, including those to be transferred to a third party that may impact the investigators sites, if applicable.
Conformance	Optional
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	11.2.2
Value	Text
Business rules	**Value Allowed**: Yes **Relationship**: 11.2.2 Sponsor Responsibilities **Concept**: CNEW
Repeating and/or Reuse Rules	No

718

719 11.3 Informed Consent Process

Term (Variable)	11.3 Informed Consent Process
Data Type	Text
Data (D), Value (V) or Heading (H)	H
Definition	Heading
User Guidance	N/A
Conformance	Required
Cardinality	One to many
Relationship content from ToC representing the protocol hierarchy	11.3

Value	Informed Consent Process
Business rules	**Value Allowed**: No **Relationship**: 11 TRIAL OVERSIGHT AND OTHER GENERAL CONSIDERATIONS and Table of Contents **Concept**: Heading
Repeating and/or Reuse Rules	No

720

Term (Variable)	<Description of Informed Consent Process>
Data Type	Text
Data (D), Value (V) or Heading (H)	D
Definition	C184390 For review purpose, see definition of the controlled terminology below The procedure by which informed consent is obtained and documented by means of a written, signed, and dated informed consent form. This process may include obtaining assent from participants with legally authorised representatives. (ICH GCP)
User Guidance	Specify the key elements of the informed consent process, including any special needs and how these are addressed (e.g., assent, capacity, legally acceptable representative, adolescents who may reach age of majority during the trial, pregnant participants and pregnant partners of participants).
Conformance	Required
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	11.3
Value	Text
Business rules	**Value Allowed**: Yes **Relationship**: 11.3 Informed Consent Process **Concept**: C184390
Repeating and/or Reuse Rules	No

721

Term (Variable)	<Description of Assent Process>
Data Type	Text
Data (D), Value (V) or Heading (H)	D
Definition	CNEW For review purpose, see definition of the controlled terminology below A description of the assent process for those individuals unable to give informed consent on their own behalf, to participate in the trial.
User Guidance	N/A
Conformance	Optional
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	11.3
Value	Text
Business rules	**Value Allowed**: Yes **Relationship**: 11.3 Informed Consent Process **Concept**: CNEW

Repeating and/or Reuse Rules	No

722

Term (Variable)	<Description of Emergency Consent Process>
Data Type	Text
Data (D), Value (V) or Heading (H)	D
Definition	CNEW For review purpose, see definition of the controlled terminology below A type of informed consent process that may occur during an emergency situation in which the participant or their legally authorised representative is not available to give consent.
User Guidance	If enrollment in the trial may occur during an emergency in which the participant or their legally acceptable representative is not able or available to give consent, describe the consent process.
Conformance	Optional
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	11.3
Value	Text
Business rules	**Value Allowed**: Yes **Relationship**: 11.3 Informed Consent Process **Concept**: CNEW
Repeating and/or Reuse Rules	No

723

724 ### 11.3.1 {Informed Consent for Rescreening}

Term (Variable)	11.3.1 {Informed Consent for Rescreening}
Data Type	Text
Data (D), Value (V) or Heading (H)	H
Definition	Heading
User Guidance	N/A
Conformance	Conditional
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	11.3.1
Value	Informed Consent for Rescreening
Business rules	**Value Allowed**: No **Relationship**: 11.3 Informed Consent Process, 11 TRIAL OVERSIGHT AND OTHER GENERAL CONSIDERATIONS and Table of Contents **Concept**: Heading
Repeating and/or Reuse Rules	No

725

Term (Variable)	{<Informed Consent for Rescreening>}
Data Type	Text
Data (D), Value (V) or Heading (H)	D

Definition	CNEW For review purpose, see definition of the controlled terminology below A description of the consent requirements for participants in the event of screen failure and rescreening.
User Guidance	If participants can be rescreened as described in Section 5.6, state whether the participant needs to complete a new consent. Screen failure and rescreening should be clearly defined in the protocol, with cross-reference to those definitions.
Conformance	Conditional
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	11.3.1
Value	Text
Business rules	**Value Allowed**: Yes **Relationship**: 11.3.1 Informed Consent for Rescreening **Concept**: CNEW
Repeating and/or Reuse Rules	No

726

727 ### 11.3.2 {Informed Consent for Use of Remaining Samples in Exploratory Research}

Term (Variable)	11.3.2 {Informed Consent for Use of Remaining Samples in Exploratory Research}
Data Type	Text
Data (D), Value (V) or Heading (H)	H
Definition	Heading
User Guidance	N/A
Conformance	Conditional
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	11.3.2
Value	Informed Consent for Use of Remaining Samples in Exploratory Research
Business rules	**Value Allowed**: No **Relationship**: 11.3 Informed Consent Process, 11 TRIAL OVERSIGHT AND OTHER GENERAL CONSIDERATION and Table of Contents **Concept**: Heading
Repeating and/or Reuse Rules	No

728

Term (Variable)	{<Informed Consent for Use of Remaining Samples in Exploratory Research>}
Data Type	Text
Data (D), Value (V) or Heading (H)	D
Definition	CNEW For review purpose, see definition of the controlled terminology below A description of the consent requirements for exploratory research using the remainder of mandatory samples. If applicable, this may include text in the original consent that address the use of remaining samples or additional text.

User Guidance	If participants will be asked to consent to optional exploratory research using the remainder of mandatory samples, describe the use of remaining samples for optional exploratory research. If any exploratory research is planned and additional written consent regarding the use of remaining samples for exploratory research will be obtained, describe the consent process.
Conformance	Conditional
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	11.3.2
Value	Text
Business rules	**Value Allowed**: Yes **Relationship**: 11.3.2 Informed Consent for Use of Remaining Samples in Exploratory Research **Concept**: CNEW
Repeating and/or Reuse Rules	No

729

730 ## 11.4 Committees

Term (Variable)	11.4 Committees
Data Type	Text
Data (D), Value (V) or Heading (H)	H
Definition	Heading
User Guidance	N/A
Conformance	Required
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	11.4
Value	Committees
Business rules	**Value Allowed**: No **Relationship**: 11 TRIAL OVERSIGHT AND OTHER GENERAL CONSIDERATIONS and Table of Contents **Concept**: Heading
Repeating and/or Reuse Rules	No

731

Term (Variable)	<Committees>
Data Type	Text
Data (D), Value (V) or Heading (H)	D
Definition	CNEW For review purpose, see definition of the controlled terminology below A description of the type and administrative structure of any committee associated with the trial.
User Guidance	Briefly describe the administrative structure of committees that will be reviewing data while the trial is ongoing, and the type of committee (e.g., Dose Escalation Committee, Data Monitoring Committee or Data Safety Monitoring Board). Note that specific details may be required depending on local law or regulation. If

	applicable, Committee Charters may be cross-referenced. If no committees are applicable, state "Not applicable."
Conformance	Required
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	11.4
Value	Text
Business rules	**Value Allowed**: Yes **Relationship**: 11.4 Committees **Concept**: CNEW
Repeating and/or Reuse Rules	No

732

733 ## 11.5 Insurance and indemnity

Term (Variable)	11.5 Insurance and Indemnity
Data Type	Text
Data (D), Value (V) or Heading (H)	H
Definition	Heading
User Guidance	N/A
Conformance	Required
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	11.5
Value	Insurance and Indemnity
Business rules	**Value Allowed**: No **Relationship**: 11 TRIAL OVERSIGHT AND OTHER GENERAL CONSIDERATIONS and Table of Contents **Concept**: Heading
Repeating and/or Reuse Rules	No

734

Term (Variable)	<Insurance and Indemnity>
Data Type	Text
Data (D), Value (V) or Heading (H)	D
Definition	CNEW For review purpose, see definition of the controlled terminology below A concise summary of the arrangements for participants insurance and indemnity as required by the applicable regulatory body.
User Guidance	Concisely summarize the arrangements for participants insurance and indemnity if not addressed in a separate agreement, if required by the applicable regulatory requirements.
Conformance	Required
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	11.5
Value	Text

Business rules	**Value Allowed**: Yes **Relationship**: 11.5 Insurance and Indemnity **Concept**: CNEW
Repeating and/or Reuse Rules	No

735

736 ## 11.6 Risk-Based Quality Management

Term (Variable)	11.6 Risk-Based Quality Management
Data Type	Text
Data (D), Value (V) or Heading (H)	H
Definition	Heading
User Guidance	N/A
Conformance	Required
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	11.6
Value	Risk-Based Quality Management
Business rules	**Value Allowed**: No **Relationship**: 11 TRIAL OVERSIGHT AND OTHER GENERAL CONSIDERATIONS and Table of Contents **Concept**: Heading
Repeating and/or Reuse Rules	No

737

Term (Variable)	<Risk-Based Quality Management>
Data Type	Text
Data (D), Value (V) or Heading (H)	D
Definition	CNEW For review purpose, see definition of the controlled terminology below A description of how potential risks and critical to quality factors associated with the trial will be identified and handled.
User Guidance	Describe the identified critical to quality factors, associated risks and risk mitigation strategies in the trial or refer to a separate document where this is described.
Conformance	Required
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	11.6
Value	Text
Business rules	**Value Allowed**: Yes **Relationship**: 11.6 Risk-Based Quality Management **Concept**: CNEW
Repeating and/or Reuse Rules	No

738

11.7 Data Governance

Term (Variable)	11.7 Data Governance
Data Type	Text
Data (D), Value (V) or Heading (H)	H
Definition	Heading
User Guidance	N/A
Conformance	Required
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	11.7
Value	Data Governance
Business rules	**Value Allowed**: No **Relationship**: 11 TRIAL OVERSIGHT AND OTHER GENERAL CONSIDERATIONS and Table of Contents **Concept**: Heading
Repeating and/or Reuse Rules	No

Term (Variable)	<Data Governance>
Data Type	Text
Data (D), Value (V) or Heading (H)	D
Definition	CNEW For review purpose, see definition of the controlled terminology below A description of the key processes to ensure data integrity, traceability and security, in order to enable accurate collection, reporting, monitoring, transfer, retention, access and publication.
User Guidance	Describe the key processes for critical trial integrity, traceability and security including a summary of the monitoring approaches enabling accurate collection, reporting, monitoring, transfer, retention, and access if not addressed in separate agreement(s).
Conformance	Required
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	11.7
Value	Text
Business rules	**Value Allowed**: Yes **Relationship**: 11.7 Data Governance **Concept**: CNEW
Repeating and/or Reuse Rules	No

11.8 Data Protection

Term (Variable)	11.8 Data Protection
Data Type	Text
Data (D), Value (V) or Heading (H)	H

Definition	Heading
User Guidance	N/A
Conformance	Required
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	11.8
Value	Data Protection
Business rules	**Value Allowed**: No **Relationship**: 11 TRIAL OVERSIGHT AND OTHER GENERAL CONSIDERATIONS and Table of Contents **Concept**: Heading
Repeating and/or Reuse Rules	No

743

Term (Variable)	<Data Protection>
Data Type	Text
Data (D), Value (V) or Heading (H)	D
Definition	CNEW For review purpose, see definition of the controlled terminology below A description of the measures taken to protect the privacy and confidentiality of person information of trial participants in accordance with applicable regulatory requirements on personal data protection and any measures that should be taken in case of a data security breach.
User Guidance	Describe the measures to protect the privacy and confidentiality of personal information of trial participants in accordance with applicable regulatory requirements on personal data protection and any measures that should be taken in case of a data security breach.
Conformance	Required
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	11.8
Value	Text
Business rules	**Value Allowed**: Yes **Relationship**: 11.8 Data Protection **Concept**: CNEW
Repeating and/or Reuse Rules	No

744

745 11.9 Source Data

Term (Variable)	11.9 Source Data
Data Type	Text
Data (D), Value (V) or Heading (H)	H
Definition	Heading
User Guidance	N/A
Conformance	Required
Cardinality	One to many

Relationship content from ToC representing the protocol hierarchy	11.9
Value	Source Data
Business rules	**Value Allowed**: No **Relationship**: 11 TRIAL OVERSIGHT AND OTHER GENERAL CONSIDERATIONS and Table of Contents **Concept**: Heading
Repeating and/or Reuse Rules	No

746

Term (Variable)	<Source Data Introduction>
Data Type	Text
Data (D), Value (V) or Heading (H)	D
Definition	CNEW For review purpose, see definition of the controlled terminology below A description of trial-related source data including the importance of source data maintenance and expectations for data traceability.
User Guidance	Establish the importance of source data and expectation for traceability of transcribed information back to source. Delineate expectations for investigators (e.g., maintain source data at the site, ensure availability of current records) and trial monitors (e.g., verify CRF data relative to source, ensure that safety of participants is being protected and that conduct is in accordance with GCP). Identify what constitutes source data and its origin or provide a reference to the location of this information, if contained in a separate document, such as a monitoring guideline or source data acknowledgement). Describe the provision for direct access to source data and documents enabling clinical trial-related monitoring, audits and regulatory inspections, if not included in separate agreement(s).
Conformance	Required
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	11.9
Value	Text
Business rules	**Value Allowed**: Yes **Relationship**: 11.9 Source Data **Concept**: CNEW
Repeating and/or Reuse Rules	No

747

Term (Variable)	<Investigator Expectations for Source Data>
Data Type	Text
Data (D), Value (V) or Heading (H)	D
Definition	CNEW For review purpose, see definition of the controlled terminology below A description of the obligations of the investigator with respect to maintaining and ensuring availability of the source data.
User Guidance	N/A
Conformance	Required
Cardinality	One to one

Relationship content from ToC representing the protocol hierarchy	11.9
Value	Text
Business rules	**Value Allowed**: Yes **Relationship**: 11.9 Source Data **Concept**: CNEW
Repeating and/or Reuse Rules	No

748

Term (Variable)	<Trial Monitor Expectations for Source Data>
Data Type	Text
Data (D), Value (V) or Heading (H)	D
Definition	CNEW For review purpose, see definition of the controlled terminology below A description of the obligations of the trial monitor with respect to maintaining and ensuring availability of the source data.
User Guidance	N/A
Conformance	Required
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	11.9
Value	Text
Business rules	**Value Allowed**: Yes **Relationship**: 11.9 Source Data **Concept**: CNEW
Repeating and/or Reuse Rules	No

749

Term (Variable)	<Identification of Source Data>
Data Type	Text
Data (D), Value (V) or Heading (H)	D
Definition	C125442 For review purpose, see definition of the controlled terminology below A description of how trial-related source data will be identified.
User Guidance	N/A
Conformance	Required
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	11.9
Value	Text
Business rules	**Value Allowed**: Yes **Relationship**: 11.9 Source Data **Concept**: C125442
Repeating and/or Reuse Rules	No

750

11.10 Protocol Deviations

Term (Variable)	11.10 Protocol Deviations
Data Type	Text
Data (D), Value (V) or Heading (H)	H
Definition	Heading
User Guidance	N/A
Conformance	Required
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	11.10
Value	Protocol Deviations
Business rules	**Value Allowed**: No **Relationship**: 11 TRIAL OVERSIGHT AND OTHER GENERAL CONSIDERATIONS and Table of Contents **Concept**: Heading
Repeating and/or Reuse Rules	No

Term (Variable)	<Protocol Deviations>
Data Type	Text
Data (D), Value (V) or Heading (H)	D
Definition	CNEW For review purpose, see definition of the controlled terminology below A description of plans for detecting, reviewing, and reporting any deviations from the protocol.
User Guidance	Describe plans for detecting, reviewing, and reporting any deviations from the protocol or include reference to a separate document.
Conformance	Required
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	11.10
Value	Text
Business rules	**Value Allowed**: Yes **Relationship**: 11.10 Protocol Deviations **Concept**: CNEW
Repeating and/or Reuse Rules	No

11.11 Early Site Closure

Term (Variable)	11.11 Early Site Closure
Data Type	Text
Data (D), Value (V) or Heading (H)	H
Definition	Heading
User Guidance	N/A
Conformance	Required

Cardinality	One to many
Relationship content from ToC representing the protocol hierarchy	11.11
Value	Early Site Closure
Business rules	**Value Allowed**: No **Relationship**: 11 TRIAL OVERSIGHT AND OTHER GENERAL CONSIDERATIONS and Table of Contents **Concept**: Heading
Repeating and/or Reuse Rules	No

755

Term (Variable)	<Decision Rights for Site Closure>
Data Type	Text
Data (D), Value (V) or Heading (H)	D
Definition	CNEW For review purpose, see definition of the controlled terminology below A description of the legal principles of entitlement for the sponsor to close a trial site, or for the investigator to initiate the closure of a trial site.
User Guidance	List the sponsor's rights to close a site early. Likewise, list the investigator's rights to initiate early site closure.
Conformance	Required
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	11.11
Value	Text
Business rules	**Value Allowed**: Yes **Relationship**: 11.11 Early Site Closure **Concept**: CNEW
Repeating and/or Reuse Rules	No

756

Term (Variable)	<Criteria for Early Closure>
Data Type	Text
Data (D), Value (V) or Heading (H)	D
Definition	CNEW For review purpose, see definition of the controlled terminology below The requirements that must be met in order to close a trial site prematurely.
User Guidance	List the criteria for early closure of a site by the sponsor or investigator.
Conformance	Required
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	11.11
Value	Text
Business rules	**Value Allowed**: Yes **Relationship**: 11.11 Early Site Closure **Concept**: CNEW

Repeating and/or Reuse Rules	No

757

Term (Variable)	<Responsibilities Following Early Site Closure>
Data Type	Text
Data (D), Value (V) or Heading (H)	D
Definition	CNEW For review purpose, see definition of the controlled terminology below The responsibilities of the sponsor and/or investigator following an unplanned early termination or suspension of the trial at an individual site.
User Guidance	List the responsibilities of the sponsor and investigator following early site closure, such as informing the ethics committee(s), and prompt notification of the participant and their transition to appropriate therapy and/or follow-up.
Conformance	Required
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	11.11
Value	Text
Business rules	**Value Allowed**: Yes **Relationship**: 11.11 Early Site Closure **Concept**: CNEW
Repeating and/or Reuse Rules	No

758

759 11.12 Data Dissemination

Term (Variable)	11.12 Data Dissemination
Data Type	Text
Data (D), Value (V) or Heading (H)	H
Definition	Heading
User Guidance	N/A
Conformance	Required
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	11.12
Value	Data Dissemination
Business rules	**Value Allowed**: No **Relationship**: 11 TRIAL OVERSIGHT AND OTHER GENERAL CONSIDERATIONS and Table of Contents **Concept**: Heading
Repeating and/or Reuse Rules	No

760

Term (Variable)	<Data Dissemination>
Data Type	Text
Data (D), Value (V) or Heading (H)	D
Definition	CNEW For review purpose, see definition of the controlled terminology below

	A description of whether and which public databases the clinical trial, and results if applicable, will be registered.
User Guidance	Describe whether the clinical trial will be registered in public databases, including reporting of results, if applicable.
Conformance	Required
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	11.12
Value	Text
Business rules	**Value Allowed**: Yes **Relationship**: 11.12 Data Dissemination **Concept**: CNEW
Repeating and/or Reuse Rules	No

12 APPENDIX: SUPPORTING DETAILS

Term (Variable)	12 APPENDIX: SUPPORTING DETAILS
Data Type	Text
Data (D), Value (V) or Heading (H)	H
Definition	Heading
User Guidance	No text is intended here (heading only). Additional supporting detail appendices may be added at the end of the existing level 2 headings as needed.
Conformance	Required
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	12
Value	APPENDIX: SUPPORTING DETAILS
Business rules	**Value Allowed**: No **Relationship:** Table of Contents **Concept:** Heading
Repeating and/or Reuse Rules	No

12.1 Clinical Laboratory Tests

Term (Variable)	12.1 Clinical Laboratory Tests
Data Type	Text
Data (D), Value (V) or Heading (H)	H
Definition	Heading
User Guidance	N/A
Conformance	Required
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	12.1
Value	Clinical Laboratory Tests
Business rules	**Value Allowed**: No

	Relationship: 12 APPENDIX: SUPPORTING DETAILS and Table of Contents **Concept:** Heading
Repeating and/or Reuse Rules	No

765

Term (Variable)	<Clinical Laboratory Tests>
Data Type	Text
Data (D), Value (V) or Heading (H)	D
Definition	C25294 For review purpose, see definition of the controlled terminology below Any procedure that involves testing or manipulating a sample of blood, urine, or other body substance in a laboratory setting.
User Guidance	Specify which laboratory parameters should be included in each clinical laboratory assessment panel (e.g., for haematology, chemistry, urinalysis). A tabular presentation for such information is common. If applicable, include equations and references for locally calculated laboratory results. If not applicable, retain heading and enter "Not applicable."
Conformance	Required
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	12.1
Value	Text
Business rules	**Value Allowed**: Yes **Relationship**: 12.1 Clinical Laboratory Tests **Concept**: C25294
Repeating and/or Reuse Rules	No

766

767 12.2 Country/Region-Specific Differences

Term (Variable)	12.2 Country/Region-Specific Differences
Data Type	Text
Data (D), Value (V) or Heading (H)	H
Definition	Heading
User Guidance	N/A
Conformance	Required
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	12.2
Value	Country/Region-Specific Differences
Business rules	**Value Allowed**: No **Relationship:** 12 APPENDIX: SUPPORTING DETAILS and Table of Contents **Concept:** Heading
Repeating and/or Reuse Rules	No

768

Term (Variable)	<Not applicable>
Data Type	Universal Text

Data (D), Value (V) or Heading (H)	D
Definition	
User Guidance	N/A
Conformance	Optional: if there are no Country/Region Specific Differences
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	12.2
Value	Not applicable
Business rules	**Value Allowed**: Yes **Relationship:** 12.2 Country/Region-Specific Differences **Concept:** Universal Text
Repeating and/or Reuse Rules	No

769

Term (Variable)	[Country/Region Identifier]
Data Type	Valid Value
Data (D), Value (V) or Heading (H)	H
Definition	C20108 or CNEW For review purpose, see definition of the controlled terminology below Country: A sequence of characters used to identify and/or name the country. Region: A sequence of characters used to identify and/or name the region.
User Guidance	Although global clinical trial practices are increasingly harmonised, some country/ region-specific differences in requirements do exist (e.g., document retention periods, contraception requirements). Where differences in requirements cannot be reconciled, sponsors should explain how they will document and communicate country/region-specific differences (e.g., by country/region-specific amendments or addenda). An alternative to country/region-specific amendments is to list the specific differences by country or countries in this section, including a reference to the relevant section of the protocol where the differing requirement applies. If not applicable, retain the heading and enter "Not applicable."
Conformance	Optional: if there is Country/Region-specific differences
Cardinality	One to many
Relationship content from ToC representing the protocol hierarchy	12.2
Value	Country Data element ISO 3166 Alpha 2, Region Data element ISO 3166 Alpha 2 or Not applicable
Business rules	**Value Allowed**: Yes **Relationship:** 12.2 Country/Region-Specific Differences **Concept:** C20108, CNEW, Heading, Identifier, ISO 3166 Country Codes, Alpha 2; ISO 3166 Region Codes, Alpha 2
Repeating and/or Reuse Rules	Yes, repeatable for each Country/Region

770

Term (Variable)	<Country/Region-Specific Requirements>
Data Type	Text

Data (D), Value (V) or Heading (H)	D
Definition	CNEW For review purpose, see definition of the controlled terminology below A description of any country or region-specific requirements related to the trial but not related to individual items in the protocol.
User Guidance	Although global clinical trial practices are increasingly harmonised, some country/ region-specific differences in requirements do exist (e.g., document retention periods, contraception requirements). Where differences in requirements cannot be reconciled, sponsors should explain how they will document and communicate country/region-specific differences (e.g., by country/region-specific amendments or addenda). An alternative to country/region-specific amendments is to list the specific differences by country or countries in this section, including a reference to the relevant section of the protocol where the differing requirement applies.
Conformance	Optional If there is Country/Region-specific differences
Cardinality	One to many
Relationship content from ToC representing the protocol hierarchy	12.2
Value	Text
Business rules	**Value Allowed**: Yes **Relationship**: 12.2 Country /Region Identifier ;Country/Region-Specific Differences **Concept**: CNEW
Repeating and/or Reuse Rules	Yes, repeatable for each Country/Region

771

Term (Variable)	<Country/Region-specific Protocol Clarifications>
Data Type	Text
Data (D), Value (V) or Heading (H)	D
Definition	CNEW For review purpose, see definition of the controlled terminology below A description of any country or region-specific clarifications related to a protocol item.
User Guidance	Although global clinical trial practices are increasingly harmonised, some country/ region-specific differences in requirements do exist (e.g., document retention periods, contraception requirements). Where differences in requirements cannot be reconciled, sponsors should explain how they will document and communicate country/region-specific differences (e.g., by country/region-specific amendments or addenda). An alternative to country/region-specific amendments is to list the specific differences by country or countries in this section, including a reference to the relevant section of the protocol where the differing requirement applies.
Conformance	Optional if there is Country/Region-specific differences
Cardinality	One to many
Relationship content from ToC representing the protocol hierarchy	12.2
Value	Text
Business rules	**Value Allowed**: Yes

	Relationship: 12.2 Country /Region Identifier Country/Region-Specific Differences **Concept**: CNEW
Repeating and/or Reuse Rules	Yes, repeatable for each country/region

772

773 ## 12.3 Prior Protocol Amendment(s)

Term (Variable)	12.3 Prior Protocol Amendment(s)
Data Type	Text
Data (D), Value (V) or Heading (H)	H
Definition	Heading
User Guidance	N/A
Conformance	Required
Cardinality	One to many
Relationship content from ToC representing the protocol hierarchy	12.3
Value	Prior Protocol Amendment(s)
Business rules	**Value Allowed**: No **Relationship**: 12 APPENDIX: SUPPORTING DETAILS and Table of Contents **Concept**: Heading
Repeating and/or Reuse Rules	No

774

Term (Variable)	Prior Protocol Amendment(s)
Data Type	Valid Value
Data (D), Value (V) or Heading (H)	V
Definition	CNEW For review purpose, see definition of the controlled terminology below An indication as to whether the protocol has not been amended, is the first protocol amendment, or a statement that the protocol has been amended previously.
User Guidance	Choose the applicable statement below. For an original protocol that has not been amended, retain the first sentence below and delete the remainder of this entire section. {Not applicable. This protocol has not been amended.} Or {Not applicable. This is the first protocol amendment.} Or include the below as applicable. {This protocol has been amended previously. The Protocol Amendment Summary of Changes for the current amendment is located directly before the Table of Contents. Prior amendment(s) to this protocol are listed in the table below, beginning with the most recent.}
Conformance	Required
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	12.3
Value	Not applicable. This protocol has not been amended. (CNEW) Or

	Not applicable. This is the first protocol amendment. (CNEW) Or This protocol has been amended previously. The Protocol Amendment Summary of Changes for the current amendment is located directly before the Table of Contents. Prior amendment(s) to this protocol are listed in the table below, beginning with the most recent. (CNEW)
Business rules	**Value Allowed**: Yes **Relationship**: 12.3 Prior Protocol Amendment(s) **Concept**: CNEW
Repeating and/or Reuse Rules	No

775

NCI C-Code	M11 Preferred Term	Draft Definition
CNEW	ICH M11 Amendment Details Statement Response	A terminology value set relevant to the amendment details statement responses within the ICH M11 Protocol model.
CNEW	Not applicable. This protocol has not been amended.	Not applicable. This protocol has not been amended.
CNEW	Not applicable. This is the first protocol amendment.	Not applicable. This is the first protocol amendment.
CNEW	{This protocol has been amended previously. The Protocol Amendment Summary of Changes for the current amendment is located directly before the Table of Contents. Prior amendment(s) to this protocol are listed in the table below, beginning with the most recent.}	{This protocol has been amended previously. The Protocol Amendment Summary of Changes for the current amendment is located directly before the Table of Contents. Prior amendment(s) to this protocol are listed in the table below, beginning with the most recent.}

776

Term (Variable)	Document
Data Type	Text
Data (D), Value (V) or Heading (H)	H
Definition	Table Column Heading
User Guidance	Previous amendments should appear in reverse chronological order with the most recent at the top (e.g., Amendment 3, 2, 1). Delete lines not needed, add lines as needed. Inclusion of regional-, country-, and site-specific amendments in the table is optional. If included, ensure that the scope is clearly distinguishable from global amendments. If including the column with enrollment numbers, follow the instructions below.

	• For global amendments to international clinical trials or amendments to a single-country trial, list approximate global enrollment total or percentage at the time of the amendment and select “globally”. • For global amendments consolidating only country/region-specific requirements, list approximate local enrollment total or percentage at the time of the amendment and select “locally”. If consolidating a series of local amendments, the status of all the relevant locations can be listed. • For country/region amendments to international clinical trials, list the approximate local enrollment total or percentage at the time of the amendment and select “locally”. • For studies in which enrollment status by cohort is more meaningful, such as for single-site or early-phase studies, listing approximate enrollment by cohort is an option. If multiple cohorts are ongoing at the time of the amendment, the status of all the ongoing cohorts can be listed. • Enter the approximate number or percentage of participants enrolled as a percentage of the expected total.
Conformance	Required
Cardinality	One to many
Relationship content from ToC representing the protocol hierarchy	12.3
Value	Document
Business rules	**Value Allowed**: No **Relationship**: Table Column Heading and 12.3 Prior Protocol Amendment(s) **Concept**: Table Column Heading
Repeating and/or Reuse Rules	No

777

Term (Variable)	Sponsor Approval Date
Data Type	Text
Data (D), Value (V) or Heading (H)	H
Definition	Table Column Heading
User Guidance	Previous amendments should appear in reverse chronological order with the most recent at the top (e.g., Amendment 3, 2, 1). Delete lines not needed, add lines as needed. Inclusion of regional-, country-, and site-specific amendments in the table is optional. If included, ensure that the scope is clearly distinguishable from global amendments. If including the column with enrollment numbers, follow the instructions below. • For global amendments to international clinical trials or amendments to a single-country trial, list approximate global enrollment total or percentage at the time of the amendment and select “globally”. • For global amendments consolidating only country/region-specific requirements, list approximate local enrollment total or percentage at

	the time of the amendment and select "locally". If consolidating a series of local amendments, the status of all the relevant locations can be listed. • For country/region amendments to international clinical trials, list the approximate local enrollment total or percentage at the time of the amendment and select "locally". • For studies in which enrollment status by cohort is more meaningful, such as for single-site or early-phase studies, listing approximate enrollment by cohort is an option. If multiple cohorts are ongoing at the time of the amendment, the status of all the ongoing cohorts can be listed. • Enter the approximate number or percentage of participants enrolled as a percentage of the expected total.
Conformance	Required
Cardinality	One to many
Relationship content from ToC representing the protocol hierarchy	12.3
Value	Sponsor Approval Date
Business rules	**Value Allowed**: No **Relationship**: Table Column Heading and 12.3 Prior Protocol Amendment(s) **Concept**: Table Column Heading
Repeating and/or Reuse Rules	No

778

Term (Variable)	Approximate Enrollment when Sponsor Approved Amendment
Data Type	Text
Data (D), Value (V) or Heading (H)	H
Definition	Table Column Heading
User Guidance	Previous amendments should appear in reverse chronological order with the most recent at the top (e.g., Amendment 3, 2, 1). Delete lines not needed, add lines as needed. Inclusion of regional-, country-, and site-specific amendments in the table is optional. If included, ensure that the scope is clearly distinguishable from global amendments. If including the column with enrollment numbers, follow the instructions below. • For global amendments to international clinical trials or amendments to a single-country trial, list approximate global enrollment total or percentage at the time of the amendment and select "globally". • For global amendments consolidating only country/region-specific requirements, list approximate local enrollment total or percentage at the time of the amendment and select "locally". If consolidating a series of local amendments, the status of all the relevant locations can be listed.

	• For country/region amendments to international clinical trials, list the approximate local enrollment total or percentage at the time of the amendment and select "locally". • For studies in which enrollment status by cohort is more meaningful, such as for single-site or early-phase studies, listing approximate enrollment by cohort is an option. If multiple cohorts are ongoing at the time of the amendment, the status of all the ongoing cohorts can be listed. • Enter the approximate number or percentage of participants enrolled as a percentage of the expected total.
Conformance	Optional if there is an amendment and sponsor chooses to use
Cardinality	One to many
Relationship content from ToC representing the protocol hierarchy	12.3
Value	Approximate Enrollment when Sponsor Approved Amendment
Business rules	**Value Allowed**: No **Relationship**: Table Column Heading and 12.3 Prior Protocol Amendment(s) **Concept**: Table Column Heading
Repeating and/or Reuse Rules	No

779

Term (Variable)	<Amendment Identifier>
Data Type	Text or Universal Text "Original Protocol"
Data (D), Value (V) or Heading (H)	D
Definition	CNEW For review purpose, see definition of the controlled terminology below A sequence of characters used to uniquely identify a protocol amendment.
User Guidance	Previous amendments should appear in reverse chronological order with the most recent at the top (e.g., Amendment 3, 2, 1). Delete lines not needed, add lines as needed. Inclusion of regional-, country-, and site-specific amendments in the table is optional. If included, ensure that the scope is clearly distinguishable from global amendments. If including the column with enrollment numbers, follow the instructions below. • For global amendments to international clinical trials or amendments to a single-country trial, list approximate global enrollment total or percentage at the time of the amendment and select "globally". • For global amendments consolidating only country/region-specific requirements, list approximate local enrollment total or percentage at the time of the amendment and select "locally". If consolidating a series of local amendments, the status of all the relevant locations can be listed. • For country/region amendments to international clinical trials, list the approximate local enrollment total or percentage at the time of the amendment and select "locally".

	• For studies in which enrollment status by cohort is more meaningful, such as for single-site or early-phase studies, listing approximate enrollment by cohort is an option. If multiple cohorts are ongoing at the time of the amendment, the status of all the ongoing cohorts can be listed. • Enter the approximate number or percentage of participants enrolled as a percentage of the expected total.
Conformance	Required
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	12.3
Value	Text or Universal Text "Original Protocol"
Business rules	**Value Allowed**: Yes **Relationship**: Table Column Heading "Document" **Concept**: CNEW
Repeating and/or Reuse Rules	Yes, reuse from the title page

780

Term (Variable)	<Sponsor Approval Date>
Data Type	Date
Data (D), Value (V) or Heading (H)	D
Definition	CNEW For review purpose, see definition of the controlled terminology below The date that the sponsor approved the version of the protocol,
User Guidance	Previous amendments should appear in reverse chronological order with the most recent at the top (e.g., Amendment 3, 2, 1). Delete lines not needed, add lines as needed. Inclusion of regional-, country-, and site-specific amendments in the table is optional. If included, ensure that the scope is clearly distinguishable from global amendments. If including the column with enrollment numbers, follow the instructions below. • For global amendments to international clinical trials or amendments to a single-country trial, list approximate global enrollment total or percentage at the time of the amendment and select "globally". • For global amendments consolidating only country/region-specific requirements, list approximate local enrollment total or percentage at the time of the amendment and select "locally". If consolidating a series of local amendments, the status of all the relevant locations can be listed. • For country/region amendments to international clinical trials, list the approximate local enrollment total or percentage at the time of the amendment and select "locally". • For studies in which enrollment status by cohort is more meaningful, such as for single-site or early-phase studies, listing approximate enrollment by cohort is an option. If multiple cohorts are ongoing at the

	time of the amendment, the status of all the ongoing cohorts can be listed. • Enter the approximate number or percentage of participants enrolled as a percentage of the expected total.
Conformance	Required
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	12.3
Value	Date
Business rules	**Value Allowed**: Yes **Relationship**: Table Column Heading "Document"; "Sponsor Approval Date" **Concept**: CNEW
Repeating and/or Reuse Rules	Yes, reuse from the title page

781

Term (Variable)	<# or %> enrolled <globally/locally/per cohort>
Data Type	Text
Data (D), Value (V) or Heading (H)	D
Definition	CNEW For review purpose, see definition of the controlled terminology below The numeric value for the estimated number of participants enrolled in the trial, expressed as an absolute value or percentage. The numeric value for the estimated number of participants enrolled in the trial, expressed as an absolute value or percentage.
User Guidance	Previous amendments should appear in reverse chronological order with the most recent at the top (e.g., Amendment 3, 2, 1). Delete lines not needed, add lines as needed. Inclusion of regional-, country-, and site-specific amendments in the table is optional. If included, ensure that the scope is clearly distinguishable from global amendments. If including the column with enrollment numbers, follow the instructions below. • For global amendments to international clinical trials or amendments to a single-country trial, list approximate global enrollment total or percentage at the time of the amendment and select "globally". • For global amendments consolidating only country/region-specific requirements, list approximate local enrollment total or percentage at the time of the amendment and select "locally". If consolidating a series of local amendments, the status of all the relevant locations can be listed. • For country/region amendments to international clinical trials, list the approximate local enrollment total or percentage at the time of the amendment and select "locally". • For studies in which enrollment status by cohort is more meaningful, such as for single-site or early-phase studies, listing approximate enrollment by cohort is an option. If multiple cohorts are ongoing at the

	time of the amendment, the status of all the ongoing cohorts can be listed. • Enter the approximate number or percentage of participants enrolled as a percentage of the expected total.
Conformance	Optional: when there is an amendment and sponsor chooses
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	12.3
Value	<# or %> enrolled <globally/locally/per cohort>
Business rules	**Value Allowed**: Yes **Relationship**: Document, Sponsor Approval Date **Concept**: CNEW
Repeating and/or Reuse Rules	Yes, reuse from the title page

782

Term (Variable)	<# or %>
Data Type	Number
Data (D), Value (V) or Heading (H)	D
Definition	CNEW For review purpose, see definition of the controlled terminology below The numeric value (expressed as an absolute value or percentage) for the estimated number of participants enrolled at the time of the protocol amendment.
User Guidance	N/A
Conformance	Optional: if Original Protocol =No
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	Amendment Details
Value	Integer for Number or one decimal point for percent
Business rules	**Value Allowed**: Yes **Relationship**: Document; Sponsor Approval Date" **Concept**: CNEW
Repeating and/or Reuse Rules	Yes, reuse from the title page

783

Term (Variable)	{The Overview of Changes from each prior protocol amendment is {provided below} or <specify alternative location>}.
Data Type	Text
Data (D), Value (V) or Heading (H)	Universal text and V, D
Definition	N/A
User Guidance	Move the Overview of Changes table from the previous amendments to this section in reverse chronological order (most recent first).
Conformance	Conditional: if not original protocol or first amendment
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	12.3
Value	The Overview of Changes from each prior protocol amendment is Choose

	provided below or <specify alternative location>.
Business rules	**Value Allowed**: Yes **Relationship**: 12.3 Prior Protocol Amendment(s) **Concept**: Universal text
Repeating and/or Reuse Rules	No

784

Term (Variable)	<specify alternative location>
Data Type	Text
Data (D), Value (V) or Heading (H)	D
Definition	CNEW For review purpose, see definition of the controlled terminology below the physical or virtual location of the date on which the sponsor approved the current version of the protocol.
User Guidance	N/A
Conformance	Conditional: when a specify alternative location is selected
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	12.3
Value	Text Location where information can be found
Business rules	**Value Allowed**: Yes **Relationship**: Location for previous amendments **Concept**: CNEW
Repeating and/or Reuse Rules	Yes, reuse from the title page.

785

Term (Variable)	{Overview of Changes in Amendment <amendment number> (<date>)}
Data Type	Text
Data (D), Value (V) or Heading (H)	H
Definition	Heading
User Guidance	Move the Overview of Changes table from the previous amendments to this section in reverse chronological order (most recent first).
Conformance	Conditional: when there is an amendment
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	12.3
Value	Overview of Changes in Amendment:
Business rules	**Value Allowed**: No **Relationship**: {The Overview of Changes from each prior protocol amendment is {provided below} or <specify alternative location>}. **Concept**: Heading
Repeating and/or Reuse Rules	Yes, repeatable one table per amendment

786

Term (Variable)	<amendment number>
Data Type	Text

Data (D), Value (V) or Heading (H)	D
Definition	CNEW For review purpose, see definition of the controlled terminology below A sequence of characters used to uniquely identify a protocol amendment
User Guidance	Move the Overview of Changes table from the previous amendments to this section in reverse chronological order (most recent first).
Conformance	Conditional: if amendment
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	12.3
Value	Text
Business rules	**Value Allowed**: Yes **Relationship**: {The Overview of Changes from each prior protocol amendment is {provided below} or <specify alternative location>}. **Concept**: CNEW
Repeating and/or Reuse Rules	Yes, repeatable one table per amendment

787

Term (Variable)	<Sponsor Approval Date>
Data Type	Date
Data (D), Value (V) or Heading (H)	D
Definition	CNEW For review purpose, see definition of the controlled terminology below The date that the sponsor approved the version of the protocol,
User Guidance	Move the Overview of Changes table from the previous amendments to this section in reverse chronological order (most recent first).
Conformance	Conditional: if amendment
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	12.3
Value	Date
Business rules	**Value Allowed**: Yes **Relationship**: {The Overview of Changes from each prior protocol amendment is {provided below} or <specify alternative location>}. **Concept**: CNEW
Repeating and/or Reuse Rules	Yes, repeatable one table per amendment

788

Term (Variable)	{Description of Change}
Data Type	Text
Data (D), Value (V) or Heading (H)	H
Definition	Table Column Heading
User Guidance	N/A
Conformance	Conditional: if there is a previous amendment
Cardinality	One to one

Relationship content from ToC representing the protocol hierarchy	12.3
Value	Description of Change
Business rules	**Value Allowed**: No **Relationship**: Table and 12.3 Prior Protocol Amendment(s) **Concept**: Table Column Heading
Repeating and/or Reuse Rules	No

789

Term (Variable)	<Description of Change>
Data Type	Text
Data (D), Value (V) or Heading (H)	D
Definition	CNEW For review purpose, see definition of the controlled terminology below A narrative representation of the change introduced in the current version of the protocol.
User Guidance	N/A
Conformance	Conditional: if there is a previous amendment. Table optional
Cardinality	Column Heading Row Content
Relationship content from ToC representing the protocol hierarchy	12.3
Value	Text
Business rules	**Value Allowed**: Yes **Relationship**: Table Column Heading "Description of Change" and 12.3 Prior Protocol Amendment(s) **Concept**: CNEW
Repeating and/or Reuse Rules	Yes, repeatable for every description of change

790

Term (Variable)	{Brief Rationale for Change}
Data Type	Text
Data (D), Value (V) or Heading (H)	H
Definition	Table Column Heading
User Guidance	N/A
Conformance	Conditional: if there is a previous amendment
Cardinality	Column Heading Table
Relationship content from ToC representing the protocol hierarchy	12.3
Value	Brief Rationale for Change
Business rules	**Value Allowed**: No **Relationship**: Table and 12.3 Prior Protocol Amendment(s) **Concept**: Table Column Heading
Repeating and/or Reuse Rules	No

791

Term (Variable)	<Brief Rationale for Change>
Data Type	Text
Data (D), Value (V) or Heading (H)	D
Definition	CNEW For review purpose, see definition of the controlled terminology below The brief reason for the change introduced in the current version of the protocol.
User Guidance	N/A
Conformance	Conditional: if there is a previous amendment. Table optional
Cardinality	One to Column Heading Row description of change Section# and Name
Relationship content from ToC representing the protocol hierarchy	12.3
Value	Text
Business rules	**Value Allowed**: Yes **Relationship**: Table Column Heading {Brief Rationale for Change} and description of change <Description of Change> **Concept**: CNEW
Repeating and/or Reuse Rules	Yes, repeatable for every description of change

792

Term (Variable)	{Section # and Name}
Data Type	Text
Data (D), Value (V) or Heading (H)	H
Definition	Table Column Heading
User Guidance	N/A
Conformance	Conditional: if there is a previous amendment
Cardinality	Column Heading Table
Relationship content from ToC representing the protocol hierarchy	12.3
Value	Section # and Name
Business rules	**Value Allowed**: No **Relationship**: Change in Amendment **Concept**: Table Column Heading
Repeating and/or Reuse Rules	No

793

Term (Variable)	<Section # and Name of Change>
Data Type	Valid Value
Data (D), Value (V) or Heading (H)	V
Definition	CNEW For review purpose, see definition of the controlled terminology below The protocol section number and name containing the change introduced in the current version of the protocol.
User Guidance	N/A
Conformance	Conditional: if there is a previous amendment. Table optional

Cardinality	One to Column Heading Row description of change Description of Change, Rational for Amendment Change
Relationship content from ToC representing the protocol hierarchy	12.3
Value	Text
Business rules	**Value Allowed**: Yes **Relationship**: Description of Change **Concept**: CNEW
Repeating and/or Reuse Rules	Yes, repeatable for every Description of Change

794

NCI C-Code	M11 Preferred Term	Draft Definition
CNEW	ICH M11 Protocol Number and Name Response	A terminology value set relevant to the protocol number and name responses within the ICH M11 Protocol model.
CNEW	1 PROTOCOL SUMMARY	Section 1 of the ICH M11 Protocol standard, PROTOCOL SUMMARY.
CNEW	1.1 Protocol Synopsis	Section 1.1 of the ICH M11 Protocol standard, Protocol Synopsis.
CNEW	1.1.1 Primary and Secondary Objectives and Estimands	Section 1.1.1 of the ICH M11 Protocol standard, Primary and Secondary Objectives and Estimands.
CNEW	1.1.2 Overall Design	Section 1.1.2 of the ICH M11 Protocol standard, Overall Design.
CNEW	1.2 Trial Schema	Section 1.2 of the ICH M11 Protocol standard, Trial Schema.
CNEW	1.3 Schedule of Activities	Section 1.3 of the ICH M11 Protocol standard, Schedule of Activities.
CNEW	2 INTRODUCTION	Section 2 of the ICH M11 Protocol standard, INTRODUCTION.
CNEW	2.1 Purpose of Trial	Section 2.1 of the ICH M11 Protocol standard, Purpose of Trial.
CNEW	2.2 Assessment of Risks and Benefits	Section 2.2 of the ICH M11 Protocol standard, Summary of Benefits and Risks.
CNEW	2.2.1 Risk Summary and Mitigation Strategy	Section 2.2.1 of the ICH M11 Protocol standard, Risk Summary and Mitigation Strategy.
CNEW	2.2.2 Benefit Summary	Section 2.2.2 of the ICH M11 Protocol standard, Benefit Summary.
CNEW	2.2.3 Overall Risk-Benefit Assessment	Section 2.2.3 of the ICH M11 Protocol standard, Overall Risk-Benefit Assessment.
CNEW	3 TRIAL OBJECTIVES AND ASSOCIATED ESTIMANDS	Section 3 of the ICH M11 Protocol standard, TRIAL OBJECTIVES AND ASSOCIATED ESTIMANDS.
CNEW	3.1 Primary Objective(s) and Associated Estimand(s)	Section 3.1 of the ICH M11 Protocol standard, Primary Objective(s) and Associated Estimand(s).
CNEW	3.1.1 Primary Objective	Section 3.1.1 of the ICH M11 Protocol standard, Primary Objective.
CNEW	3.2 Secondary Objective(s) and Associated Estimand(s)	Section 3.2 of the ICH M11 Protocol standard, Secondary Objective(s) and Associated Estimand(s).
CNEW	3.3 Exploratory Objective(s)	Section 3.3 of the ICH M11 Protocol standard, Exploratory Objective(s).
CNEW	4 TRIAL DESIGN	Section 4 of the ICH M11 Protocol standard, TRIAL DESIGN.
CNEW	4.1 Description of Trial Design	Section 4.1 of the ICH M11 Protocol standard, Description of Trial Design.
CNEW	4.1.1 Stakeholder Input into Design	Section 4.1.1 of the ICH M11 Protocol standard, Stakeholder Input into Design.

CNEW	4.2 Rationale for Trial Design	Section 4.2 of the ICH M11 Protocol standard, Rationale for Trial Design.
CNEW	4.2.1 Rationale for Intervention Model	Section 4.2.1 of the ICH M11 Protocol standard, Rationale for Intervention Model.
CNEW	4.2.2 Rationale for Duration	Section 4.2.2 of the ICH M11 Protocol standard, Rationale for Duration.
CNEW	4.2.3 Rationale for Estimands	Section 4.2.3 of the ICH M11 Protocol standard, Rationale for Estimands.
CNEW	4.2.4 Rationale for Interim Analysis	Section 4.2.4 of the ICH M11 Protocol standard, Rationale for Interim Analysis.
CNEW	4.2.5 Rationale for Control Type	Section 4.2.5 of the ICH M11 Protocol standard, Rationale for Control Type.
CNEW	4.2.6 Rationale for Adaptive or Novel Trial Design	Section 4.2.6 of the ICH M11 Protocol standard, Rationale for Adaptive or Novel Trial Design.
CNEW	4.2.7 Rationale for Other Trial Design Aspects	Section 4.2.7 of the ICH M11 Protocol standard, Rationale for Other Trial Design Aspects.
CNEW	4.3 Trial Stopping Rules	Section 4.3 of the ICH M11 Protocol standard, Trial Stopping Rules.
CNEW	4.4 Start of Trial and End of Trial	Section 4.4 of the ICH M11 Protocol standard, Start of Trial and End of Trial.
CNEW	4.5 Access to Trial Intervention After End of Trial	Section 4.5 of the ICH M11 Protocol standard, Access to Trial Intervention After End of Trial.
CNEW	5 TRIAL POPULATION	Section 5 of the ICH M11 Protocol standard, TRIAL POPULATION.
CNEW	5.1 Description of Trial Population and Rationale	Section 5.1 of the ICH M11 Protocol standard, Description of Trial Population and Rationale.
CNEW	5.2 Inclusion Criteria	Section 5.2 of the ICH M11 Protocol standard, Inclusion Criteria.
CNEW	5.3 Exclusion Criteria	Section 5.3 of the ICH M11 Protocol standard, Exclusion Criteria.
CNEW	5.4 Contraception	Section 5.4 of the ICH M11 Protocol standard, Contraception.
CNEW	5.4.1 Definitions Related to Childbearing Potential	Section 5.4.1 of the ICH M11 Protocol standard, Definitions Related to Childbearing Potential.
CNEW	5.4.2 Contraception Requirements	Section 5.4.2 of the ICH M11 Protocol standard, Contraception Requirements.
CNEW	5.5 Lifestyle Restrictions	Section 5.5 of the ICH M11 Protocol standard, Lifestyle Restrictions.
CNEW	5.5.1 Meals and Dietary Restrictions	Section 5.5.1 of the ICH M11 Protocol standard, Contraception Requirements.
CNEW	5.5.2 Caffeine, Alcohol, Tobacco, and Other Restrictions	Section 5.5.2 of the ICH M11 Protocol standard, Caffeine, Alcohol, Tobacco, and Other Restrictions.
CNEW	5.5.3 Physical Activity Restrictions	Section 5.5.3 of the ICH M11 Protocol standard, Physical Activity Restrictions.
CNEW	5.5.4 Other Activity Restrictions	Section 5.5.4 of the ICH M11 Protocol standard, Other Activity Restrictions.
CNEW	5.6 Screen Failure and Rescreening	Section 5.6 of the ICH M11 Protocol standard, Screen Failure and Rescreening.
CNEW	6 TRIAL INTERVENTION AND CONCOMITANT THERAPY	Section 6 of the ICH M11 Protocol standard, TRIAL INTERVENTION AND CONCOMITANT THERAPY.
CNEW	6.1 Description of Investigational Trial Intervention	Section 6.1 of the ICH M11 Protocol standard, Overview of Trial Interventions.

CNEW	6.2 Description of Investigational Trial Intervention	Section 6.2 of the ICH M11 Protocol standard, Description of Investigational Trial Intervention.
CNEW	6.3 Rationale for Investigation Trial Intervention Dose and Regimen	Section 6.3 of the ICH M11 Protocol standard, Rationale for Investigation Trial Intervention Dose and Regimen.
CNEW	6.4 Investigational Trial Intervention Administration	Section 6.4 of the ICH M11 Protocol standard, Investigational Trial Intervention Administration.
CNEW	6.5 Investigational Trial Intervention Dose Modification	Section 6.5 of the ICH M11 Protocol standard, Investigational Trial Intervention Dose Modification.
CNEW	6.6 Management of Investigational Trial Intervention Overdose	Section 6.6 of the ICH M11 Protocol standard, Management of Investigational Trial Intervention Overdose.
CNEW	6.7 Preparation, Storage, Handling and Accountability of Investigational Trial Intervention(s)	Section 6.7 of the ICH M11 Protocol standard, Preparation, Storage, Handling and Accountability of Investigational Trial Intervention(s).
CNEW	6.7.1 Preparation of Investigational Trial Intervention(s)	Section 6.7.1 of the ICH M11 Protocol standard, Preparation of Investigational Trial Intervention(s).
CNEW	6.7.2 Storage and Handling of Investigational Trial Intervention	Section 6.7.2 of the ICH M11 Protocol standard, Storage and Handling of Investigational Trial Intervention.
CNEW	6.7.3 Accountability of Investigational Trial Intervention	Section 6.7.3 of the ICH M11 Protocol standard, Accountability of Investigational Trial Intervention.
CNEW	6.8 Investigational Trial Intervention Assignment, Randomisation and Blinding	Section 6.8 of the ICH M11 Protocol standard, Investigational Trial Intervention Assignment, Randomisation and Blinding.
CNEW	6.8.1 Participant Assignment to Investigational Trial Intervention	Section 6.8.1 of the ICH M11 Protocol standard, Participant Assignment to Investigational Trial Intervention.
CNEW	6.8.2 Randomisation	Section 6.8.2 of the ICH M11 Protocol standard, Randomisation.
CNEW	6.8.3 Blinding	Section 6.8.3 of the ICH M11 Protocol standard, Blinding.
CNEW	6.8.4 Emergency Unblinding at the Site	Section 6.8.4 of the ICH M11 Protocol standard, Emergency Unblinding at the Site.
CNEW	6.9 Investigational Trial Intervention Compliance	Section 6.9 of the ICH M11 Protocol standard, Investigational Trial Intervention Compliance.
CNEW	6.10 Description of Non-Investigational Trial Intervention(s)	Section 6.1 of the ICH M11 Protocol standard, Description of Non-Investigational Trial Intervention(s).
CNEW	6.10.1 Background Intervention	Section 6.10.1 of the ICH M11 Protocol standard, Background Intervention.
CNEW	6.10.2 Rescue Therapy	Section 6.10.2 of the ICH M11 Protocol standard, Rescue Therapy.
CNEW	6.10.3 Other Non-investigational Intervention	Section 6.10.3 of the ICH M11 Protocol standard, Other Non-investigational Intervention.

CNEW	6.11 Concomitant Therapy	Section 6.11 of the ICH M11 Protocol standard, Concomitant Therapy.
CNEW	6.11.1 Prohibited Concomitant Therapy	Section 6.11.1 of the ICH M11 Protocol standard, Prohibited Concomitant Therapy.
CNEW	6.11.2 Permitted Concomitant Therapy	Section 6.11.2 of the ICH M11 Protocol standard, Permitted Concomitant Therapy.
CNEW	7 PARTICIPANT DISCONTINUATION OF TRIAL INTERVENTION AND DISCONTINUATION OR WITHDRAWAL FROM TRIAL	Section 7 of the ICH M11 Protocol standard, PARTICIPANT DISCONTINUATION OF TRIAL INTERVENTION AND DISCONTINUATION OR WITHDRAWAL FROM TRIAL.
CNEW	7.1 Discontinuation of Trial Intervention for Individual Participants	Section 7.1 of the ICH M11 Protocol standard, Discontinuation of Trial Intervention for Individual Participants.
CNEW	7.1.1 Permanent Discontinuation of Trial Intervention	Section 7.1.1 of the ICH M11 Protocol standard, Permanent Discontinuation of Trial Intervention.
CNEW	7.1.2 Temporary Discontinuation of Trial Intervention	Section 7.1.2 of the ICH M11 Protocol standard, Temporary Discontinuation of Trial Intervention.
CNEW	7.1.3 Rechallenge	Section 7.1.3 of the ICH M11 Protocol standard, Rechallenge.
CNEW	7.2 Discontinuation or Withdrawal from the Trial	Section 7.2 of the ICH M11 Protocol standard, Discontinuation or Withdrawal from the Trial.
CNEW	7.3 Lost to Follow-Up	Section 7.3 of the ICH M11 Protocol standard, Lost to Follow-Up.
CNEW	8 TRIAL ASSESSMENTS AND PROCEDURES	Section 8 of the ICH M11 Protocol standard, TRIAL ASSESSMENTS AND PROCEDURES.
CNEW	8.1 Trial Assessments and Procedures Considerations	Section 8.1 of the ICH M11 Protocol standard, Trial Assessments and Procedures Considerations.
CNEW	8.2 Screening/Baseline Assessments and Procedures	Section 8.2 of the ICH M11 Protocol standard, Screening/Baseline Assessments and Procedures.
CNEW	8.3 Efficacy Assessments and Procedures	Section 8.3 of the ICH M11 Protocol standard, Efficacy Assessments and Procedures.
CNEW	8.4 Safety Assessments and Procedures	Section 8.4 of the ICH M11 Protocol standard, Safety Assessments and Procedures.
CNEW	8.4.1 Physical Examination	Section 8.4.1 of the ICH M11 Protocol standard, Physical Examination.
CNEW	8.4.2 Vital Signs	Section 8.4.2 of the ICH M11 Protocol standard, Vital Signs.
CNEW	8.4.3 Electrocardiograms	Section 8.4.3 of the ICH M11 Protocol standard, Electrocardiograms.
CNEW	8.4.4 Clinical Laboratory Assessments	Section 8.4.4 of the ICH M11 Protocol standard, Clinical Laboratory Assessments.
CNEW	8.4.5 Pregnancy Testing	Section 8.4.5 of the ICH M11 Protocol standard, Pregnancy Testing.
CNEW	8.4.6 Suicidal Ideation and Behaviour Risk Monitoring	Section 8.4.6 of the ICH M11 Protocol standard, Suicidal Ideation and Behaviour Risk Monitoring.
CNEW	8.5 Pharmacokinetics	Section 8.5 of the ICH M11 Protocol standard, Pharmacokinetics.
CNEW	8.6 Biomarkers	Section 8.6 of the ICH M11 Protocol standard, Biomarkers.
CNEW	8.6.1 Genetics and Pharmacogenomics	Section 8.6.1 of the ICH M11 Protocol standard, Genetics and Pharmacogenomics.

CNEW	8.6.2 Pharmacodynamic Biomarkers	Section 8.6.2 of the ICH M11 Protocol standard, Pharmacodynamic Biomarkers.
CNEW	8.6.3 Other Biomarkers	Section 8.6.3 of the ICH M11 Protocol standard, Other Biomarkers.
CNEW	8.7 Immunogenicity Assessments	Section 8.7 of the ICH M11 Protocol standard, Immunogenicity Assessments.
CNEW	8.8 Medical Resource Utilisation and Health Economics	Section 8.8 of the ICH M11 Protocol standard, Medical Resource Utilisation and Health Economics.
CNEW	9 ADVERSE EVENTS, SERIOUS ADVERSE EVENTS, PRODUCT COMPLAINTS, PREGNANCY AND POSTPARTUM INFORMATION	Section 9 of the ICH M11 Protocol standard, ADVERSE EVENTS, SERIOUS ADVERSE EVENTS, PRODUCT COMPLAINTS, PREGNANCY AND POSTPARTUM INFORMATION.
CNEW	9.1 Definitions	Section 9.1 of the ICH M11 Protocol standard, Definitions.
CNEW	9.1.1 Definitions of Adverse Events	Section 9.1.1 of the ICH M11 Protocol standard, Definitions of Adverse Events.
CNEW	9.1.2 Definitions of Serious Adverse Events	Section 9.1.2 of the ICH M11 Protocol standard, Definitions of Serious Adverse Events.
CNEW	9.1.3 Definition of Medical Device Product Complaints	Section 9.1.3 of the ICH M11 Protocol standard, Definition of Medical Device Product Complaints.
CNEW	9.2 Timing and Mechanism for Collection and Reporting	Section 9.2 of the ICH M11 Protocol standard, Timing and Mechanism for Collection and Reporting.
CNEW	9.3 Identification, Recording and Follow-Up	Section 9.3 of the ICH M11 Protocol standard, Identification, Recording and Follow-Up.
CNEW	9.3.1 Identification	Section 9.3.1 of the ICH M11 Protocol standard, Identification.
CNEW	9.3.2 Severity	Section 9.3.2 of the ICH M11 Protocol standard, Severity.
CNEW	9.3.3 Causality	Section 9.3.3 of the ICH M11 Protocol standard, Causality.
CNEW	9.3.4 Follow-up	Section 9.3.4 of the ICH M11 Protocol standard, Follow-up.
CNEW	9.4 Reporting	Section 9.4 of the ICH M11 Protocol standard, Reporting.
CNEW	9.4.1 Regulatory Reporting Requirements	Section 9.4.1 of the ICH M11 Protocol standard, Regulatory Reporting Requirements.
CNEW	9.4.2 Adverse Events of Special Interest	Section 9.4.2 of the ICH M11 Protocol standard, Adverse Events of Special Interest.
CNEW	9.4.3 Disease-related Events or Outcomes Not Qualifying as AEs or SAEs	Section 9.4.3 of the ICH M11 Protocol standard, Disease-related Events or Outcomes Not Qualifying as AEs or SAEs.
CNEW	9.5 Pregnancy and Postpartum Information	Section 9.5 of the ICH M11 Protocol standard, Pregnancy and Postpartum Information.
CNEW	9.5.1 Participants Who Become Pregnant During the Trial	Section 9.5.1 of the ICH M11 Protocol standard, Participants Who Become Pregnant During the Trial.
CNEW	9.5.2 Participants Whose Partners Become Pregnant	Section 9.5.2 of the ICH M11 Protocol standard, Participants Whose Partners Become Pregnant.
CNEW	10 Statistical Considerations	Section 10 of the ICH M11 Protocol standard, Statistical Considerations.
CNEW	10.1 General Considerations	Section 10.1 of the ICH M11 Protocol standard, General Considerations.
CNEW	10.2 Analysis Sets	Section 10.2 of the ICH M11 Protocol standard, Analysis Sets.

CNEW	10.3 Analyses of Demographics and Other Baseline Variables	Section 10.3 of the ICH M11 Protocol standard, Analyses of Demographics and Other Baseline Variables.
CNEW	10.4 Analyses Associated with the Primary Objective(s)	Section 10.4 of the ICH M11 Protocol standard, Analyses Associated with the Primary Objective(s).
CNEW	10.4.1 Statistical Method of Analysis	Section 10.4.1 of the ICH M11 Protocol standard, Statistical Method of Analysis.
CNEW	10.4.2 Handling of Data in Relation to Primary Estimand(s)	Section 10.4.2 of the ICH M11 Protocol standard, Handling of Data in Relation to Primary Estimand(s).
CNEW	10.4.3 Handling of Missing Data	Section 10.4.3 of the ICH M11 Protocol standard, Handling of Missing Data.
CNEW	10.4.4 Sensitivity Analysis	Section 10.4.4 of the ICH M11 Protocol standard, Sensitivity Analysis.
CNEW	10.4.5 Supplementary Analysis	Section 10.4.5 of the ICH M11 Protocol standard, Supplementary Analysis.
CNEW	10.5 Analysis Associated with the Secondary Objective(s)	Section 10.5 of the ICH M11 Protocol standard, Analysis Associated with the Secondary Objective(s).
CNEW	10.5.1 Statistical Method of Analysis	Section 10.5.1 of the ICH M11 Protocol standard, Statistical Method of Analysis.
CNEW	10.5.2 Handling of Data in Relation to Secondary Estimand(s)	Section 10.5.2 of the ICH M11 Protocol standard, Handling of Data in Relation to Secondary Estimand(s).
CNEW	10.5.3 Handling of Missing Data in Relation to Secondary Estimand(s)	Section 10.5.3 of the ICH M11 Protocol standard, Handling of Missing Data in Relation to Secondary Estimand(s).
CNEW	10.5.4 Sensitivity Analyses	Section 10.5.4 of the ICH M11 Protocol standard, Sensitivity Analyses.
CNEW	10.5.5 Supplementary Analyses	Section 10.5.5 of the ICH M11 Protocol standard, Supplementary Analyses.
CNEW	10.6 Analysis Associated with the Exploratory Objective(s)	Section 10.6 of the ICH M11 Protocol standard, Analysis Associated with the Exploratory Objective(s).
CNEW	10.7 Safety Analyses	Section 10.7 of the ICH M11 Protocol standard, Safety Analyses.
CNEW	10.8 Other Analyses	Section 10.8 of the ICH M11 Protocol standard, Other Analyses.
CNEW	10.9 Interim Analyses	Section 10.9 of the ICH M11 Protocol standard, Interim Analyses.
CNEW	10.10 Multiplicity Adjustments	Section 10.1 of the ICH M11 Protocol standard, Multiplicity Adjustments.
CNEW	10.11 Sample Size Determination	Section 10.11 of the ICH M11 Protocol standard, Sample Size Determination.
CNEW	11 TRIAL OVERSIGHT AND OTHER GENERAL CONSIDERATIONS	Section 11 of the ICH M11 Protocol standard, TRIAL OVERSIGHT AND OTHER GENERAL CONSIDERATIONS.
CNEW	11.1 Regulatory and Ethical Considerations	Section 11.1 of the ICH M11 Protocol standard, Regulatory and Ethical Considerations.
CNEW	11.2 Trial Oversight	Section 11.2 of the ICH M11 Protocol standard, Trial Oversight.
CNEW	11.2.1 Investigator Responsibilities	Section 11.2.1 of the ICH M11 Protocol standard, Investigator Responsibilities.
CNEW	11.2.2 Sponsor Responsibilities	Section 11.2.2 of the ICH M11 Protocol standard, Sponsor Responsibilities.
CNEW	11.3 Informed Consent Process	Section 11.3 of the ICH M11 Protocol standard, Informed Consent Process.

CNEW	11.3.1 Informed Consent for Rescreening	Section 11.3.1 of the ICH M11 Protocol standard, Informed Consent for Rescreening.
CNEW	11.3.2 Informed Consent for Use of Remaining Samples in Exploratory Research	Section 11.3.2 of the ICH M11 Protocol standard, Informed Consent for Use of Remaining Samples in Exploratory Research.
CNEW	11.4 Committees	Section 11.4 of the ICH M11 Protocol standard, Committees.
CNEW	11.5 Insurance and Indemnity	Section 11.5 of the ICH M11 Protocol standard, Insurance and Indemnity.
CNEW	11.6 Risk-Based Quality Management	Section 11.5 of the ICH M11 Protocol standard, Risk Management.
CNEW	11.7 Data Governance	Section 11.7 of the ICH M11 Protocol standard, Data Governance.
CNEW	11.8 Data Protection	Section 11.8 of the ICH M11 Protocol standard, Data Protection
CNEW	11.9 Source Data	Section 11.9 of the ICH M11 Protocol standard, Source Data.
CNEW	11.10 Protocol Deviations	Section 11.10 of the ICH M11 Protocol standard, Protocol Deviations.
CNEW	11.11 Early Site Closure	Section 11.1 of the ICH M11 Protocol standard, Early Site Closure.
CNEW	12 APPENDIX: SUPPORTING DETAILS	Section 12 of the ICH M11 Protocol standard, APPENDIX: SUPPORTING DETAILS.
CNEW	12.1 Clinical Laboratory Tests	Section 12.1 of the ICH M11 Protocol standard, Clinical Laboratory Tests.
CNEW	12.2 Country/Region-Specific Differences	Section 12.2 of the ICH M11 Protocol standard, Country/Region-Specific Differences.
CNEW	12.3 Prior Protocol Amendment(s)	Section 12.3 of the ICH M11 Protocol standard, Prior Protocol Amendment(s).
CNEW	13 APPENDIX: GLOSSARY OF TERMS AND ABBREVIATIONS	Section 13 of the ICH M11 Protocol standard, APPENDIX: GLOSSARY OF TERMS AND ABBREVIATIONS.
CNEW	14 APPENDIX: REFERENCES	Section 14 of the ICH M11 Protocol standard, APPENDIX: REFERENCES.

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Term (Variable)	12.X Additional Appendices
Data Type	Text
Data (D), Value (V) or Heading (H)	H
Definition	Heading
User Guidance	N/A
Conformance	Optional
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	12.X where X is a unique number for each Additional Appendix
Value	Title of Appendix
Business rules	**Value Allowed**: Yes **Relationship**: 12 APPENDIX: SUPPORTING DETAILS and Table of Contents **Concept**: Heading
Repeating and/or Reuse Rules	No

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Term (Variable)	<Enter Appendix>

Data Type	Text
Data (D), Value (V) or Heading (H)	D
Definition	N/A
User Guidance	N/A
Conformance	Optional
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	12 X where X is a unique number for each Additional Appendix
Value	Text
Business rules	**Value Allowed**: Yes **Relationship**: 12.X Additional Appendices **Concept**: CNEW
Repeating and/or Reuse Rules	No

13 APPENDIX: GLOSSARY OF TERMS AND ABBREVIATIONS

Term (Variable)	13 APPENDIX: GLOSSARY OF TERMS AND ABBREVIATIONS
Data Type	Text
Data (D), Value (V) or Heading (H)	H
Definition	Heading
User Guidance	N/A
Conformance	Required
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	13
Value	APPENDIX: GLOSSARY OF TERMS AND ABBREVIATIONS
Business rules	**Value Allowed**: No **Relationship**: Table of Contents **Concept**: Heading
Repeating and/or Reuse Rules	No

Term (Variable)	<Glossary of Terms and Abbreviations>
Data Type	Text
Data (D), Value (V) or Heading (H)	D
Definition	CNEW For review purpose, see definition of the controlled terminology below A collection of abbreviations (a shortened form of a word or phrase) and definitions (a concise explanation of the meaning of a word or phrase or symbol).
User Guidance	Define abbreviations and other terms used in the protocol. A tabular presentation is common and may serve as the definition at first use.
Conformance	Required
Cardinality	One to one

Relationship content from ToC representing the protocol hierarchy	13
Value	Text
Business rules	**Value Allowed**: Yes **Relationship**: 13 APPENDIX: GLOSSARY OF TERMS AND ABBREVIATIONS **Concept**: CNEW
Repeating and/or Reuse Rules	No

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Term (Variable)	14 APPENDIX: REFERENCES
Data Type	Text
Data (D), Value (V) or Heading (H)	H
Definition	Heading
User Guidance	N/A
Conformance	Required
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	14
Value	APPENDIX: REFERENCES
Business rules	**Value Allowed**: No **Relationship**: Table of Contents **Concept**: Heading
Repeating and/or Reuse Rules	No

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Term (Variable)	<References>
Data Type	Text
Data (D), Value (V) or Heading (H)	D
Definition	C184397 For review purpose, see definition of the controlled terminology below The curated list of sources that are cited within the reference section of the document.
User Guidance	References should be listed in a common format that includes all relevant information to identify the source and date published. If not published, this should be clearly indicated.
Conformance	Required
Cardinality	One to one
Relationship content from ToC representing the protocol hierarchy	14
Value	Text
Business rules	**Value Allowed**: Yes **Relationship**: 14 APPENDIX: REFERENCES **Concept**: C184397
Repeating and/or Reuse Rules	No

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