

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

ICH HARMONISED GUIDELINE

**CLINICAL ELECTRONIC STRUCTURED HARMONISED PROTOCOL**

**(**CeSHarP**)**

**M11 TECHNICAL SPECIFICATION**

Draft version

Endorsed on

*Currently under public consultation*

*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**

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| --- | --- | --- |
| **Code** | **History** | **Date** |
|  |  |  |
| M11 | Endorsement by the Members of the ICH Assembly under *Step 2* and release for public consultation (document dated 6 September 2022).  *Minor editorial changes made pre-publication (document dated 14 October 2022).* | 27 September 2022 |

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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:

Definition of Table Elements

|  |  |
| --- | --- |
| Term (Variable) | Term (variable) is the verbatim term from the Template |
| Data Type | A data type is a classification that specifies which type of value a variable has. |
| Data (D), Value (V) or Header (H) | Identifies the content of the Data type as Header or Data element or Value |
| Definition | A definition is the meaning of the Data Type |
| User Guidance | The user guidance is directly from the instructions of the template. |
| Conformance | Rules and actions for this data type in accordance with some specified standard or authority |
| 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 to the template Table of Contents. |
| Relationship (reference to high level conceptual model) | Relationship to the Conceptual Models.  This will be blank |
| Value | Valid Values |
| Business rules | ValueAllowed**:** Is a value allowed?  Relationship**:** What is the relationship?  Concept**:** Identify the Concept |
| Duplicate field in other sections | In what sections is the value used in the template |

The template uses the typefaces described in the table below to distinguish between their intended use and applicability. For reference the Table appears below

| **Type of Text (Applicability)** | **Typeface Details** | **Description (Intended Use)** |
| --- | --- | --- |
| Universal text | Black Times New Roman font | Text that should appear in all protocols |
| Instructional text | Red Calibri font  (Delete for final document) | Text that provides instructions, but which should not appear in a final protocol |
| Optional text | Blue Arial font  Restyle to Black Times New Roman for final document | Text (including optional headings) that may be modified, deleted, or replaced according to the specific aspects of the trial |
| Conditional required text | {braces} in the prevailing typeface | Text that is required if applicable to study. In some cases, a choice between options of required text. |
| Controlled terminology | [Square brackets] in the prevailing typeface with grey shading  Populate field from available choices, or with free text if indicated; remove brackets and restyle text to match other text in the final document | Brackets with grey shading are used to indicate variable text modelled as a field in the electronic manifestation of the protocols |
| Text insertion point | <Chevrons> in the prevailing typeface | Chevrons are used to indicate where to insert text. Any text within chevrons is intended to be replaced by applicable content. |

Appendix 1: Detailed Descriptions of Information Components

Title Page

|  |  |
| --- | --- |
| Term (Variable) | Sponsor Confidentiality Statement |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | H |
| Definition | Heading |
| User Guidance | None |
| Conformance | Optional Text |
| Cardinality | One |
| Relationship content from ToC representing the protocol hierarchy | Title Page |
| Relationship (reference to high level conceptual model) |  |
| Value | Sponsor Confidentiality Statement: |
| Business rules | Value Allowed: No  Relationship: Table row heading  Concept: Header, Identifier |
| Duplicate field in other sections | No |

|  |  |
| --- | --- |
| Term (Variable) | <Sponsor Confidentiality Statement> |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | D |
| Definition | See C1811236  For review context C181123 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 a sponsor confidentiality statement, if applicable, otherwise delete. |
| Conformance | Optional Text |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | Title page |
| Relationship (reference to high level conceptual model) |  |
| Value | Text |
| Business rules | Value Allowed: Yes  Relationship: Heading  Concept: Data Element C181236 |
| Duplicate field in other sections | No |

|  |  |
| --- | --- |
| Term (Variable) | Full Title |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | H |
| Definition | Heading |
| User Guidance | None |
| Conformance | Required |
| Cardinality | One |
| Relationship content from ToC representing the protocol hierarchy | Title Page |
| Relationship (reference to high level conceptual model) |  |
| Value | Full Title: |
| Business rules | Value Allowed: No  Relationship: Table row heading  Concept: Header, Identifier |
| Duplicate field in other sections | No |

|  |  |
| --- | --- |
| Term (Variable) | <Full Title> |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | D |
| Definition | See CNew  For review context CNEW  An extensive descriptive name of the clinical trial that is intended for medical professionals, written using medical and scientific language. |
| 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; Protocol Identifier |
| Relationship content from ToC representing the protocol hierarchy | Title page |
| Relationship (reference to high level conceptual model) |  |
| Value | Text  600 ct.gov  UTF 8 - Special |
| Business rules | Value Allowed: Yes  Relationship: Heading; Protocol Identifier  Concept: Data Element Cnew |
| Duplicate field in other sections | No |

|  |  |
| --- | --- |
| Term (Variable) | Trial Acronym: |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | H |
| Definition | Heading |
| User Guidance | Not applicable |
| Conformance | Optional |
| Cardinality | One to One |
| Relationship content from ToC representing the protocol hierarchy | Title Page |
| Relationship (reference to high level conceptual model) |  |
| Value | Trial Acronym: |
| Business rules | Value Allowed: No  Relationship: Table row heading  Concept: Header, Identifier |
| Duplicate field in other sections | No |

|  |  |
| --- | --- |
| Term (Variable) | <Trial Acronym> |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | D |
| Definition | See CNEW  For review context CNEW:  Acronym or abbreviation used publicly to identify the clinical trial. |
| User Guidance | Acronym or abbreviation used publicly to identify the clinical trial, if any. Delete this line from the table if not applicable. |
| Conformance | Optional |
| Cardinality | One to One; one to Protocol Identifier |
| Relationship content from ToC representing the protocol hierarchy | Title Page |
| Relationship (reference to high level conceptual model) |  |
| Value | Text |
| Business rules | Value Allowed: Yes  Relationship: Heading; Protocol Identifier  Concept: Data Element CNEW |
| Duplicate field in other sections | No |

|  |  |
| --- | --- |
| Term (Variable) | **Sponsor Protocol Identifier:** |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | H |
| Definition | Heading |
| User Guidance | Not applicable |
| Conformance | Required |
| Cardinality | One to One |
| Relationship content from ToC representing the protocol hierarchy | Title Page |
| Relationship (reference to high level conceptual model) |  |
| Value | Sponsor Protocol Identifier |
| Business rules | Value Allowed: No  Relationship: Table row heading  Concept: Header, Identifier |
| Duplicate field in other sections | No |

|  |  |
| --- | --- |
| Term (Variable) | <Enter Sponsor Protocol Identifier> |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | D |
| Definition | See C132351  Review for Context C132351 A unique code assigned by the sponsor that identifies a specific protocol. (CDISC) |
| User Guidance | A unique alphanumeric identifier for the trial, designated by the Sponsor, is a standard part of trial data, and should be included for most trials. |
| Conformance | Required |
| Cardinality | One to one; Uniquely identify all related data elements |
| Relationship content from ToC representing the protocol hierarchy | Title page |
| Relationship (reference to high level conceptual model) |  |
| Value | Text |
| Business rules | Value Allowed: Yes  Relationship: Heading  Concept: Data element C132351  Note: May not be blank (null) |
| Duplicate field in other sections | No |

|  |  |
| --- | --- |
| Term (Variable) | Original Protocol: |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | H |
| Definition | Heading |
| User Guidance | Not applicable |
| Conformance | Required |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | Title Page |
| Relationship (reference to high level conceptual model) |  |
| Value | Original Protocol: |
| Business rules | Value Allowed: No  Relationship: Table row heading  Concept: Header, Identifier |
| Duplicate field in other sections | No |

|  |  |
| --- | --- |
| Term (Variable) | NY |
| Data Type | Valid Value |
| Data (D), Value (V) or Header (H) | V |
| Definition | See C66742  For review context C66742 A term that is used to indicate a question with permissible values of yes/no/unknown/not applicable. |
| User Guidance | Not applicable |
| Conformance | Required |
| Cardinality | One to One, Protoco Identifier |
| Relationship content from ToC representing the protocol hierarchy | Title page |
| Relationship (reference to high level conceptual model) | Original Protocol Yes Not Original Protocol No (aka amendment) |
| Value | Yes, No |
| Business rules | **Value** **Allowed**: Yes  **Relationship**: Heading Original Protocol; Protocol Identifier  **Concept**: C66742 |
| Duplicate field in other sections | No |

|  |  |
| --- | --- |
| Term (Variable) | Version Number: |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | H |
| Definition | Heading |
| User Guidance | Not applicable |
| Conformance | Optional |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | Title Page |
| Relationship (reference to high level conceptual model) |  |
| Value | Version Number: |
| Business rules | Value Allowed: no  Relationship: Table row heading  Concept: Header, Identifier |
| Duplicate field in other sections | No |

|  |  |
| --- | --- |
| Term (Variable) | <Version Number> |
| Data Type | Number |
| Data (D), Value (V) or Header (H) | D |
| Definition | See C181232  For Context C181232 A string of numerals that uniquely identifies a specific version of a study protocol. |
| User Guidance | An optional field for use by the sponsor at their discretion. |
| Conformance | Optional |
| Cardinality | One to One |
| Relationship content from ToC representing the protocol hierarchy | Title page |
| Relationship (reference to high level conceptual model) |  |
| Value | 10 Integer |
| Business rules | Value Allowed: Yes  Relationship: Version Number; Protocol Identifier  Concept: C181232 |
| Duplicate field in other sections | No |

|  |  |
| --- | --- |
| Term (Variable) | Version Date: |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | H |
| Definition | Heading |
| User Guidance | Not applicable |
| Conformance | Optional |
| Cardinality | One to One , One to Version Number |
| Relationship content from ToC representing the protocol hierarchy | Title Page |
| Relationship (reference to high level conceptual model) |  |
| Value | Version Date: |
| Business rules | Value Allowed: no  Relationship: Table row heading  Concept: Header, Identifier |
| Duplicate field in other sections | No |

|  |  |
| --- | --- |
| Term (Variable) | <Version Date> |
| Data Type | Date |
| Data (D), Value (V) or Header (H) | D |
| Definition | See C93813  For Context C93813 The date on which the document is versioned. |
| User Guidance | An optional field for use by the sponsor at their discretion. |
| Conformance | Optional |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | Title page |
| Relationship (reference to high level conceptual model) |  |
| Value | Date Format DD MMM YYYY where DD is 2N MMM is 3A and Year is 4N |
| Business rules | Value Allowed: DD MMM YYYY  Relationship: Version Date  Concept: C93813 |
| Duplicate field in other sections | No |

|  |  |
| --- | --- |
| Term (Variable) | Amendment Identifier |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | H |
| Definition | Heading |
| User Guidance | One |
| Conformance | Required |
| Cardinality | One to One |
| Relationship content from ToC representing the protocol hierarchy | Title page |
| Relationship (reference to high level conceptual model) |  |
| Value | Amendment Identifier |
| Business rules | Value Allowed: No  Relationship: Table row heading  Concept: Header, Identifier |
| Duplicate field in other sections | No |

|  |  |
| --- | --- |
| Term (Variable) | {[Amendment Identifier]} |
| Data Type | AN OR BLANK |
| Data (D), Value (V) or Header (H) | D |
| Definition | CNEW  For Context CNEW A sequence of characters used to uniquely identifies a protocol amendment. |
| User Guidance | Enter the amendment identifier (e.g., amendment number). If this is the original instance of the protocol, leave blank. |
| Conformance | Conditional |
| Cardinality | One to One, One to Protocol Identifier if not original |
| Relationship content from ToC representing the protocol hierarchy | Title page |
| Relationship (reference to high level conceptual model) |  |
| Value | 10AN or blank if Original Protocol = Yes |
| Business rules | Value Allowed: Yes  Relationship: Header, Protocol Identifier  Concept: CNEW |
| Duplicate field in other sections | No |

|  |  |
| --- | --- |
| Term (Variable) | Amendment Scope |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | H |
| Definition | Heading |
| User Guidance | CNEW |
| Conformance | Required |
| Cardinality | One to One; One to Amendment Identifier |
| Relationship content from ToC representing the protocol hierarchy | Title Page |
| Relationship (reference to high level conceptual model) |  |
| Value | Amendment Scope |
| Business rules | Value Allowed: No  Relationship: Table row heading  Concept: Header, Identifier |
| Duplicate field in other sections | No |

|  |  |
| --- | --- |
| Term (Variable) | {[Amendment Scope]} |
| Data Type | Valid Value List |
| Data (D), Value (V) or Header (H) | D |
| Definition | See CNEW  For Context CNEW: A description as to whether the amendment scope applies globally across the trial. |
| User Guidance | Leave blank for original protocol.  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 Required when there is an amendments |
| Cardinality | One to One; One to Amendment Identifier |
| Relationship content from ToC representing the protocol hierarchy | Title page |
| Relationship (reference to high level conceptual model) |  |
| Value | Blank; Global, Not Global |
| Business rules | Value Allowed: Yes  Relationship: Header; Amendment Identifier  Concept: CNEW |
| Duplicate field in other sections | No |

|  |  |
| --- | --- |
| Term (Variable) | {[Country Identifier] or [Region Identifier] or <Enter Site Identifier>} |
| Data Type | Pick list |
| Data (D), Value (V) or Header (H) | D |
| Definition | C20108  CNEW  For Context C20108 A sequence of characters used to identify and/or name the country.  For Context CNEW A sequence of characters used to identify and/or name the region  For Context 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 utilize one of the identifiers based on amendment scope.. |
| Conformance | Conditionally Required when Not Global |
| Cardinality | One to One; many to Amendment Scope; One to Amendment Identifier; One to Protocol Identifier |
| Relationship content from ToC representing the protocol hierarchy | Title page |
| Relationship (reference to high level conceptual model) |  |
| Value | ISO 3166 for country  ISO 3166 for and region Text Condition Blank for Original Protocol = yes |
| Business rules | Value Allowed: Yes  Relationship: Header, Amendment Scope; Amendment Identifier  Concept: C20108, CNEW, CNEW |
| Duplicate field in other sections | Repeatable for list of Country, Region, Site |

|  |  |
| --- | --- |
| Term (Variable) | Compound Code(s) |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | H |
| Definition | Heading |
| User Guidance | Not applicable |
| Conformance | Optional |
| Cardinality | One to One |
| Relationship content from ToC representing the protocol hierarchy | Title Page |
| Relationship (reference to high level conceptual model) |  |
| Value | Compound Code |
| Business rules | Value Allowed: No  Relationship: Table row heading  Concept: Header |
| Duplicate field in other sections | No  REPEAT in OVERALL desiceion |

|  |  |
| --- | --- |
| Term (Variable) | <Enter Compound Code(s)> |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | D |
| Definition | See CNEW  For context CNEW 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 |
| Cardinality | One to One; Many to Protocol Identifier |
| Relationship content from ToC representing the protocol hierarchy | Title Page |
| Relationship (reference to high level conceptual model) |  |
| Value | AN |
| Business rules | Value Allowed:Yes  Relationship: Header;Protocol Identifier  Concept: CNEW |
| Duplicate field in other sections | Repeatable |

|  |  |
| --- | --- |
| Term (Variable) | Compound Name(s) |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | H |
| Definition | Heading |
| User Guidance | Not applicable |
| Conformance | Optional |
| Cardinality | One to One ; Many to Protocol Identifier |
| Relationship content from ToC representing the protocol hierarchy | Title Page |
| Relationship (reference to high level conceptual model) |  |
| Value | Compound Name(s) |
| Business rules | Value Allowed: No  Relationship: Table row headers  Concept: Header |
| Duplicate field in other sections | No |

|  |  |
| --- | --- |
| Term (Variable) | <Enter Nonproprietary Name(s)> |
| Data Type | Valid Value List of Generics |
| Data (D), Value (V) or Header (H) | V |
| Definition | See C97054 For Context C97054 Drug name that is not protected by a trademark, usually descriptive of its chemical structure. (ICH E2B) |
| User Guidance | Delete this line from the table if a nonproprietary name has not yet been assigned. Omit proprietary name fields if not yet established. |
| Conformance | Optional; conditional |
| Cardinality | Many to Protocol Identifier |
| Relationship content from ToC representing the protocol hierarchy | Title Page |
| Relationship (reference to high level conceptual model) |  |
| Value | 300AN Valid Value list for Generics Use for example WHO INN, USAN, JAN, XEVMPD |
| Business rules | Value Allowed:yes  Relationship: Header, Protocol Identifier  Concept: C97054 |
| Duplicate field in other sections | Repeatable for each non-proprietary name |

|  |  |
| --- | --- |
| Term (Variable) | <Enter Proprietary Name(s)> |
| Data Type | text |
| Data (D), Value (V) or Header (H) | D |
| Definition | See C71898  For context C71898 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 / Conditional |
| Cardinality | One to Protocol Identifier |
| Relationship content from ToC representing the protocol hierarchy | Title Page |
| Relationship (reference to high level conceptual model) |  |
| Value | 300 A/N |
| Business rules | Value Allowed: n/a  Relationship: Header; Protocol Identifier  Concept: C71898 |
| Duplicate field in other sections | Repeatable for each proprietary name |

|  |  |
| --- | --- |
| Term (Variable) | Trial Phase |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | H |
| Definition | Heading |
| User Guidance | Not applicable |
| Conformance | Required |
| Cardinality | One to Protocol Identifier |
| Relationship content from ToC representing the protocol hierarchy | Title Page |
| Relationship (reference to high level conceptual model) |  |
| Value | Trial phase |
| Business rules | Value Allowed: No  Relationship: Table row heading  Concept: Header |
| Duplicate field in other sections | No |

|  |  |
| --- | --- |
| Term (Variable) | Trial Phase |
| Data Type | Valid Value List |
| Data (D), Value (V) or Header (H) | V |
| Definition | See C48281  For context C48281 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 Protocol Identifier |
| Relationship content from ToC representing the protocol hierarchy | Title Page |
| Relationship (reference to high level conceptual model) |  |
| Value | Early Phase 1; Phase 1;Phase 1/Phase 2;Phase 1/Phase 2/Phase 3;Phase 1/Phase 3;Phase 2; Phase 2/Phase 3;Phase2/Phase 3/Phase 4;Phase 3;Phase 3/Phase 4; Phase 4; Other |
| Business rules | Value Allowed: yes  Relationship: Header; Protocol Identifier  Concept: C48281 |
| Duplicate field in other sections | No |

|  |  |
| --- | --- |
| Term (Variable) | {<Enter Description of Trial Phase Other>} |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | D |
| Definition | See CNEW  For context CNEW A narrative representation of the trial phase that is different than the one(s) previously specified or mentioned. |
| User Guidance | For trials combining investigational drugs or vaccines with devices, classify according to the phase of drug development. |
| Conformance | Conditional when Trial Phase = Other |
| Cardinality | One to one; One to Protocol Identifier |
| Relationship content from ToC representing the protocol hierarchy | Title Page |
| Relationship (reference to high level conceptual model) |  |
| Value | Text |
| Business rules | Value Allowed: yes  Relationship: Trial Phase = Other ; Protocol Identifier  Concept: NEW |
| Duplicate field in other sections | No |

|  |  |
| --- | --- |
| Term (Variable) | **Short Title:** |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | H |
| Definition | Heading |
| User Guidance | Not applicable |
| Conformance | Optional |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | Title Page |
| Relationship (reference to high level conceptual model) |  |
| Value | Short Title |
| Business rules | Value Allowed: No  Relationship: Table row heading  Concept: Heading |
| Duplicate field in other sections | No |

|  |  |
| --- | --- |
| Term (Variable) | <Enter Trial Short Title |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | D |
| Definition | See C132345  For Context C132345 The short descriptive name for the protocol. |
| User Guidance | Short title should convey in plain language what the trial is about and is 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 Protocol identifier |
| Relationship content from ToC representing the protocol hierarchy | Title page |
| Relationship (reference to high level conceptual model) |  |
| Value | 300AN |
| Business rules | Value Allowed: yes  Relationship: Heading; Protocol Identifier  Concept: C132345 |
| Duplicate field in other sections | No |

|  |  |
| --- | --- |
| Term (Variable) | Sponsor Name and Address |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | H |
| Definition | Heading |
| User Guidance | Not applicable |
| Conformance | Required |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | Title page |
| Relationship (reference to high level conceptual model) |  |
| Value | Sponsor Name and Address |
| Business rules | Value Allowed:No  Relationship Table row heading  Concept: Header |
| Duplicate field in other sections | No |

|  |  |
| --- | --- |
| Term (Variable) | <Enter Sponsor Name> |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | D |
| Definition | See C70793  For Context C70793 An individual, company, institution, or organization 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 Heading; One to Protocol Identifier |
| Relationship content from ToC representing the protocol hierarchy | Title Page |
| Relationship (reference to high level conceptual model) |  |
| Value | AN |
| Business rules | Value Allowed:Yes  Relationship: Heading; Protocol Identifier  Concept: C70983 |
| Duplicate field in other sections | No |

|  |  |
| --- | --- |
| Term (Variable) | Sponsor Legal Address |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | D |
| Definition | See CNEW  For context CNEW 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 Heading; One to Sponsor Name; One to Protocol Identifier |
| Relationship content from ToC representing the protocol hierarchy | Title Page |
| Relationship (reference to high level conceptual model) |  |
| Value | Text |
| Business rules | Value Allowed: Yes  Relationship: Heading, Sponsor Name, Protocol Identifier  Concept: CNEW |
| Duplicate field in other sections | No |

|  |  |
| --- | --- |
| Term (Variable) | <Enter Co- Sponsor Name> |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | D |
| Definition | See CNEW  For Context CNEW 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 Heading; One to Sponsor Name; One to Protocol Identifier |
| Relationship content from ToC representing the protocol hierarchy | Title Page |
| Relationship (reference to high level conceptual model) |  |
| Value | Text |
| Business rules | Value Allowed:Yes  Relationship: Heading; Sponsor Name; Protocol Identifier  Concept: CNEW |
| Duplicate field in other sections | No |

|  |  |
| --- | --- |
| Term (Variable) | <Enter Co-Sponsor Legal Address> |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | D |
| Definition | See CNEW  For context CNEW 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 Heading; One to Co-Sponsor Name; |
| Relationship content from ToC representing the protocol hierarchy | Title Page |
| Relationship (reference to high level conceptual model) |  |
| Value | Text |
| Business rules | Value Allowed: Yes  Relationship: Heading, Co- Sponsor Name  Concept: CNEW |
| Duplicate field in other sections | No |

|  |  |
| --- | --- |
| Term (Variable) | Local Sponsor Name and Address: |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | H |
| Definition | Heading |
| User Guidance | Not applicable |
| Conformance | Optional |
| Cardinality | One to Sponsor Name and Address |
| Relationship content from ToC representing the protocol hierarchy | Title Page |
| Relationship (reference to high level conceptual model) |  |
| Value | Local Sponsor Name and Address: |
| Business rules | Value Allowed: No  Relationship: Heading Sponsor Name and Address;  Concept: Header |
| Duplicate field in other sections | No |

|  |  |
| --- | --- |
| Term (Variable) | <Enter Sponsor Local Name> |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | D |
| Definition | See CNEW  For Context CNEW 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 in the Sponsor Local Name and Address Field. |
| Conformance | Optional |
| Cardinality | One to Heading; One to Sponsor Name and Address; many to Sponsor Name ; Many to Protocol Identifier |
| Relationship content from ToC representing the protocol hierarchy | Title page |
| Relationship (reference to high level conceptual model) |  |
| Value | Text |
| Business rules | Value Allowed: yes  Relationship:Heading, Sponsor Name and Address; Sponsor; Country; Protocol Identifier  Concept: CNEW |
| Duplicate field in other sections | Yes for each Local sponsor |

|  |  |
| --- | --- |
| Term (Variable) | <Enter Sponsor Local Address> |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | D |
| Definition | See CNEW  For Context CNEW 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 in the Sponsor Local Name and Address Field. |
| Conformance | Optional |
| Cardinality | One to Local Sponsor; Country |
| Relationship content from ToC representing the protocol hierarchy | Title page |
| Relationship (reference to high level conceptual model) |  |
| Value | Text |
| Business rules | Value Allowed: Yes  Relationship: Heading; country; Local Sponsor  Concept: CNEW |
| Duplicate field in other sections | No |

|  |  |
| --- | --- |
| Term (Variable) | Manufacturer Name and Address |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | H |
| Definition | Heading |
| User Guidance | Not applicable |
| Conformance | Optional |
| Cardinality | One to One |
| Relationship content from ToC representing the protocol hierarchy | Title Page |
| Relationship (reference to high level conceptual model) |  |
| Value | Manufacturer Name and Address |
| Business rules | Value Allowed:No  Relationship: Table row heading  Concept: Header |
| Duplicate field in other sections | No |

|  |  |
| --- | --- |
| Term (Variable) | <Enter Device Manufacturer Name> |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | D |
| Definition | See CNEW  For context CNEW The organization 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 from the table if not applicable.. |
| Conformance | Optional |
| Cardinality | One to Heading; One Protocol Identifier; One to Sponsor |
| Relationship content from ToC representing the protocol hierarchy | Title Page |
| Relationship (reference to high level conceptual model) |  |
| Value | Text |
| Business rules | Value Allowed: yes  Relationship: Heading; Protocol Identifier; Sponsor  Concept: CNEW |
| Duplicate field in other sections | Repeatable |

|  |  |
| --- | --- |
| Term (Variable) | <Enter Device Manufacturer Address> |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | D |
| Definition | See CNEW  For Context CNEW 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 from the table if not applicable. |
| Conformance | Optional |
| Cardinality | One to Device Manufacturer Name |
| Relationship content from ToC representing the protocol hierarchy | Title Page |
| Relationship (reference to high level conceptual model) |  |
| Value | Text |
| Business rules | Value Allowed: yes  Relationship: Heading; device manufacturing Name  Concept: CNEW |
| Duplicate field in other sections | No |

|  |  |
| --- | --- |
| Term (Variable) | Regulatory Agency Identifier Number(s) |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | H |
| Definition | Heading |
| 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 | Required |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | Title Page |
| Relationship (reference to high level conceptual model) |  |
| Value | Regulatory Agency Identifier Number(s): |
| Business rules | Value Allowed: No  Relationship: Table row heading  Concept: Header |
| Duplicate field in other sections | No |

|  |  |
| --- | --- |
| Term (Variable) | <EU CT Number> |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | D |
| Definition | See CNEW  For context CNEW 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 / Conditional |
| Cardinality | One to One; One to Heading; One to Protocol Identifier; One to Sponsor Name |
| Relationship content from ToC representing the protocol hierarchy | Title Page |
| Relationship (reference to high level conceptual model) |  |
| Value | Text |
| Business rules | Value Allowed: yes  Relationship: Heading; Protocol Identifier; Sponsor Name  Concept:CNEW |
| Duplicate field in other sections | No |

|  |  |
| --- | --- |
| Term (Variable) | <FDA IDE Number> |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | D |
| Definition | See CNEW  For context CNEW 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 / Conditional |
| Cardinality | One to One; One to Heading; One to Protocol Identifier; One to Sponsor Name |
| Relationship content from ToC representing the protocol hierarchy | Title Page |
| Relationship (reference to high level conceptual model) |  |
| Value | Text |
| Business rules | Value Allowed: n/a  Relationship: Heading; Protocol Identifier; Sponsor Name  Concept:CNEW |
| Duplicate field in other sections | No |

|  |  |
| --- | --- |
| Term (Variable) | <FDA IND Number> |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | D |
| Definition | See CNEW  For context CNEW 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 / Conditional |
| Cardinality | One to One; Onte to Heading; One to Protocol Identifier; One to Sponsor Name |
| Relationship content from ToC representing the protocol hierarchy | Title page |
| Relationship (reference to high level conceptual model) |  |
| Value | Text |
| Business rules | Value Allowed: Yes  Relationship: Heading; Protocol Identifier; Sponsor Name  Concept: CNEW |
| Duplicate field in other sections | No |

|  |  |
| --- | --- |
| Term (Variable) | <jRCT Number> |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | D |
| Definition | See CNEW  For context CNEW 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, Labor 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 / Conditional |
| Cardinality | One to One; Onte to Heading; One to Protocol Identifier; One to Sponsor Name |
| Relationship content from ToC representing the protocol hierarchy | Title Page |
| Relationship (reference to high level conceptual model) |  |
| Value | Text |
| Business rules | Value Allowed: Yes  Relationship: Heading; Protocol Identifier; Sponsor Name  Concept:CNEW |
| Duplicate field in other sections |  |

|  |  |
| --- | --- |
| Term (Variable) | <NCT Number> |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | D |
| Definition | See CNEW  For Context CNEW 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 / Conditional |
| Cardinality | One to One; Onte to Heading; One to Protocol Identifier; One to Sponsor Name |
| Relationship content from ToC representing the protocol hierarchy | Title Page |
| Relationship (reference to high level conceptual model) |  |
| Value | Text |
| Business rules | Value Allowed: yes  Relationship: Heading; Protocol Identifier; Sponsor Name  Concept: CNEW |
| Duplicate field in other sections | No |

|  |  |
| --- | --- |
| Term (Variable) | <NMPA IND Number> |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | D |
| Definition | See CNEW  For Context CNEW 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 / Conditional |
| Cardinality | One to One; One to protocol Identifier; One to Sponsor Name |
| Relationship content from ToC representing the protocol hierarchy | Title Page |
| Relationship (reference to high level conceptual model) |  |
| Value | Text |
| Business rules | Value Allowed: n/a  Relationship: Heading; Protocol Identifier; Sponsor Name  Concept:CNEW |
| Duplicate field in other sections | No |

|  |  |
| --- | --- |
| Term (Variable) | <WHO/UTN Number> |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | D |
| Definition | See CNEW  For Context CNEW A sequence of characters used to identify a clinical trial, as assigned by the World Health Organization'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 / Conditional |
| Cardinality |  |
| Relationship content from ToC representing the protocol hierarchy | Title Page |
| Relationship (reference to high level conceptual model) |  |
| Value | Text |
| Business rules | Value Allowed: yes  Relationship: Heading; Protoco Identifier; Sponsor Name  Concept: CNEW |
| Duplicate field in other sections | No |

|  |  |
| --- | --- |
| Term (Variable) | <Other Regulatory Agency Identifier Number> |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | D |
| Definition | See CNEW  For Context CNew A sequence of characters used to identify a clinical trial, that is different than the one(s) previously specified or mentioned. |
| 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 / Conditional |
| Cardinality | One to Protocol Identifier; One to Sponsor Name |
| Relationship content from ToC representing the protocol hierarchy | Title Page |
| Relationship (reference to high level conceptual model) |  |
| Value | Text |
| Business rules | Value Allowed: Yes  Relationship: Heading, Protocol Identifier; Sponsor Name  Concept: CNEW |
| Duplicate field in other sections | Repeatable |

|  |  |
| --- | --- |
| Term (Variable) | Sponsor Approval Date |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | H |
| Definition | Heading |
| User Guidance | Not applicable |
| Conformance | Required / Required |
| Cardinality | One to One |
| Relationship content from ToC representing the protocol hierarchy | Title page |
| Relationship (reference to high level conceptual model) |  |
| Value | Sponsor Approval Date |
| Business rules | Value Allowed:No  Relationship: Table row heading  Concept: Header |
| Duplicate field in other sections | No |

|  |  |
| --- | --- |
| Term (Variable) | <Sponsor Approval Date> |
| Data Type | Valid Value List |
| Data (D), Value (V) or Header (H) | V |
| Definition | See CNEW  For context CNEW he 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. Use the date format (dd/mmm/yyyy, for example 07/JUN/2015) to indicate the date the protocol (or amendment) was approved by the Sponsor. |
| Conformance | Required |
| Cardinality | One to One; One to Protocol Identifier; One to Original Protocol and Amendment |
| Relationship content from ToC representing the protocol hierarchy | Title Page |
| Relationship (reference to high level conceptual model) |  |
| Value | Date or text Location where information of Approval Data can be found |
| Business rules | Value Allowed: Yes  Relationship: Header; Protocol Identifier and Original Protocol and Amendment  Concept: CNEW |
| Duplicate field in other sections | No |

|  |  |
| --- | --- |
| Term (Variable) | Sponsor Signatory: |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | H |
| Definition | Header |
| User Guidance | Not applicable |
| Conformance | required |
| Cardinality | One-to One |
| Relationship content from ToC representing the protocol hierarchy | Title Page |
| Relationship (reference to high level conceptual model) |  |
| Value | Sponsor Signatory |
| Business rules | Value Allowed: No  Relationship:Heading  Concept: Header |
| Duplicate field in other sections | No |

|  |  |
| --- | --- |
| Term (Variable) | <ICH M11 Sponsor Signatory Response> |
| Data Type | Valid Value List |
| Data (D), Value (V) or Header (H) | V |
| Definition | See CNEW  For context CNEW 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 | Required |
| Cardinality | One to One |
| Relationship content from ToC representing the protocol hierarchy | Title Page |
| Relationship (reference to high level conceptual model) |  |
| Value | Sponsor Signature Block or Sponsor Protocol Approval Statement |
| Business rules | Value Allowed: yes  Relationship: Header  Concept: CNEW |
| Duplicate field in other sections | No |

|  |  |
| --- | --- |
| Term (Variable) | <Describe Method> |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | D |
| Definition | See CNEW  For context CNEW 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 |
| Relationship (reference to high level conceptual model) |  |
| Value | AN |
| Business rules | Value Allowed: yes  Relationship: Sponsor Protocol Approval Statement  Concept: CNEW |
| Duplicate field in other sections | No |

|  |  |
| --- | --- |
| Term (Variable) | Medical Expert Contact |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | H |
| Definition | Heading |
| User Guidance | Not applicable |
| Conformance | One to One |
| Cardinality | Requires |
| Relationship content from ToC representing the protocol hierarchy | Title Page |
| Relationship (reference to high level conceptual model) |  |
| Value | Medical Expert Contact: |
| Business rules | Value Allowed: No  Relationship:Heading  Concept: Header |
| Duplicate field in other sections | No |

|  |  |
| --- | --- |
| Term (Variable) | <Medical Expert Contact Response> |
| Data Type | Valid Value List |
| Data (D), Value (V) or Header (H) | V |
| Definition | See CNEW  For Context The response for the contact methods for the sponsor representative who has medical authority for the evaluation of the safety aspects of a clinical trial. |
| User Guidance | Enter contact information for Medical Expert (as designated by sponsor) orstate location where information can be found |
| Conformance | required |
| Cardinality | One to tone |
| Relationship content from ToC representing the protocol hierarchy | Title Page |
| Relationship (reference to high level conceptual model) | o |
| Value | Text  Enter contact information for the Medical Expert (as designated by sponsor) orstate location where information can be found |
| Business rules | Value Allowed: yes  Relationship: Medical expert Contact Response  Concept: CNEW |
| Duplicate field in other sections | No |

|  |  |
| --- | --- |
| Term (Variable) | SAE reporting Method: |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | H |
| Definition | Heading |
| User Guidance | Not applicable |
| Conformance | One to One |
| Cardinality | Required |
| Relationship content from ToC representing the protocol hierarchy | Title Page |
| Relationship (reference to high level conceptual model) |  |
| Value | SAE Reporting Method |
| Business rules | Value Allowed: No  Relationship:Heading  Concept: Header |
| Duplicate field in other sections | No |

|  |  |
| --- | --- |
| Term (Variable) | Report Serious Adverse Events to the sponsor <Enter SAE reporting method(s)> Refer to Section 9.4 for detailed reporting instructions. |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | H |
| Definition | Required Text |
| User Guidance | Report Serious Adverse Events to the sponsor <Enter SAE reporting method(s)> Refer to Section 9.4 for detailed reporting instructions. |
| Conformance | Required |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | Title Pages |
| Relationship (reference to high level conceptual model) |  |
| Value | Report Serious Adverse Events to the sponsor <Enter SAE reporting method(s)> Refer to Section 9.4 for detailed reporting instructions. |
| Business rules | Value Allowed: No  Relationship: Header  Concept: Required Text |
| Duplicate field in other sections | No |

|  |  |
| --- | --- |
| Term (Variable) | <SAE Reporting Method(s)> |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | Data |
| Definition | See CNEW  For Context CNEW The methodologies used to report serious adverse events within 24 hours. |
| User Guidance | Enter SAE Reporting Method |
| Conformance | One |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | Title Page |
| Relationship (reference to high level conceptual model) |  |
| Value | Text AN |
| Business rules | Value Allowed:yes  Relationship: Header  Concept:CNEW |
| Duplicate field in other sections | No |

|  |  |
| --- | --- |
| Term (Variable) | Amendment Details |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | H |
| Definition | Heading |
| User Guidance | Not Applicable |
| Conformance | Required |
| Cardinality | One to One |
| Relationship content from ToC representing the protocol hierarchy | Amendment Details |
| Relationship (reference to high level conceptual model) |  |
| Value | Amendment Details |
| Business rules | Value Allowed: No  Relationship: Heading  Concept: Header |
| Duplicate field in other sections | No |

|  |  |
| --- | --- |
| Term (Variable) | Amendment Details |
| Data Type | Valid Value List |
| Data (D), Value (V) or Header (H) | V |
| Definition | See CNEW  For Context 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 Prior Protocol Amendment(s).} |
| Conformance | Required |
| Cardinality | One to One |
| Relationship content from ToC representing the protocol hierarchy | Amendment Details |
| Relationship (reference to high level conceptual model) |  |
| Value | Not applicable. This protocol has not been amended. Or This protocol has been amended previously. Details of prior amendments are presented in Prior Protocol Amendment(s). |
| Business rules | Value Allowed: Yes  Relationship: Heading  Concept: CNEW |
| Duplicate field in other sections | No |

|  |  |
| --- | --- |
| Term (Variable) | {Current Amendment}  The table below describes the current amendment |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | H |
| Definition | Heading |
| User Guidance | Not Applicable |
| Conformance | Conditionally Required Condition if Protocol is Original=Yes |
| Cardinality | One to One |
| Relationship content from ToC representing the protocol hierarchy | Amendment Details |
| Relationship (reference to high level conceptual model) |  |
| Value | Current Amendment  The table below describes the current amendment |
| Business rules | Value Allowed: No  Relationship: Heading  Concept: Header |
| Duplicate field in other sections | No |

|  |  |
| --- | --- |
| Term (Variable) | Approximate <(#/%)> enrolled at time of Sponsor Approval |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | H |
| Definition | Heading |
| User Guidance | Not applicable |
| Conformance | Required if Original Protocol =Yes |
| Cardinality | One to Amendment Number |
| Relationship content from ToC representing the protocol hierarchy | Amendment Details |
| Relationship (reference to high level conceptual model) |  |
| Value | Approximate <(#/%> enrolled |
| Business rules | Value Allowed:No  Relationship: Table Row Header  Concept: Header |
| Duplicate field in other sections | No |

|  |  |
| --- | --- |
| Term (Variable) | Number or % |
| Data Type | For number integer for % is integer or 1 character decimal |
| Data (D), Value (V) or Header (H) | D |
| Definition | See CNEW  For context CNEW 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 percent 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 (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 | Required if Original Protocol =No |
| Cardinality | One to Amendment Number |
| Relationship content from ToC representing the protocol hierarchy | Amendment Details |
| Relationship (reference to high level conceptual model) |  |
| Value | Integer |
| Business rules | Value Allowed: Yes  Relationship: Table Row Header, Statement  Concept: CNEW |
| Duplicate field in other sections | Table Header  Table Statement |

|  |  |
| --- | --- |
| Term (Variable) | Approximate <#/%> enrolled <Globally/Locally/Cohort> |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | D |
| Definition | Approximate <#/%> enrolled <Globally/Locally/Cohort> |
| 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 percent 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 (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 | Required if Original Protocol =No |
| Cardinality | One to Amendment Number |
| Relationship content from ToC representing the protocol hierarchy | Amendment Details |
| Relationship (reference to high level conceptual model) |  |
| Value | Approximate <#/%> enrolled <Globally/Locally/Cohort> |
| Business rules | Value Allowed: No  Relationship: Statement  Concept: Required Text |
| Duplicate field in other sections | No |

|  |  |
| --- | --- |
| Term (Variable) | Amendment Scope Enrollment |
| Data Type | Valid Value List |
| Data (D), Value (V) or Header (H) | D |
| Definition | See CNEW  For context CNEW 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 percent 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 (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 | Required if Original Protocol =No |
| Cardinality | One to Amendment Number |
| Relationship content from ToC representing the protocol hierarchy | Amendment Details |
| Relationship (reference to high level conceptual model) |  |
| Value | Globally, Locally, Cohort |
| Business rules | Value Allowed: Yes  Relationship: Statement  Concept: CNEW |
| Duplicate field in other sections | Table Header  Table Statement |

|  |  |
| --- | --- |
| Term (Variable) | Reason(s) for Amendment |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | H |
| Definition | Heading |
| User Guidance | Not applicable |
| Conformance | Required If Original Protocol= No |
| Cardinality | One to One; amendment Number |
| Relationship content from ToC representing the protocol hierarchy | Amendment Details |
| Relationship (reference to high level conceptual model) |  |
| Value | Reason(s) for Amendment: |
| Business rules | Value Allowed: No  Relationship: Table Row Header  Concept: Header |
| Duplicate field in other sections | No |

|  |  |
| --- | --- |
| Term (Variable) | Primary |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | H |
| Definition | Header |
| User Guidance | Note Applicable |
| Conformance | Required |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | Amendment Details |
| Relationship (reference to high level conceptual model) |  |
| Value | Primary: |
| Business rules | Value Allowed: No  Relationship: Table Column Header  Concept: Header |
| Duplicate field in other sections | No |

|  |  |
| --- | --- |
| Term (Variable) | Primary Reason for Amendment |
| Data Type | Valid Value List |
| Data (D), Value (V) or Header (H) | D |
| Definition | See CNEW  For context CNEW 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 | Required If Protocol Original = yes then the value is Original |
| Cardinality | Amendment Details |
| Relationship content from ToC representing the protocol hierarchy | Amendment Details |
| Relationship (reference to high level conceptual model) |  |
| Value | * Regulatory agency request to amend * New regulatory guidance * IRB/IEC feedback * New safety information available * Manufacturing change * IMP addition * Change in strategy * Change in standard of care * New data available (other than safety data) * Investigator/site feedback * Recruitment difficulty * Inconsistency and/or error in the protocol * Protocol design error * Other * Original * Not applicable |
| Business rules | Value Allowed: Yes  Relationship: Header, Protocol Identifier, Protocol Amendment  Concept: CNEW |
| Duplicate field in other sections | Multiple accepted except for Original |

|  |  |
| --- | --- |
| Term (Variable) | Other |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | H |
| Definition | Heading |
| User Guidance | Not applicable |
| Conformance | Required |
| Cardinality | One to One |
| Relationship content from ToC representing the protocol hierarchy | Amendment Details |
| Relationship (reference to high level conceptual model) |  |
| Value | Other: |
| Business rules | Value Allowed: No  Relationship: Selection of Other  Concept:Header |
| Duplicate field in other sections | No |

|  |  |
| --- | --- |
| Term (Variable) | Other description |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | D |
| Definition | See C17649  For Context C17649 Different than the one(s) previously specified or mentioned. (NCI) |
| 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 |
| Relationship (reference to high level conceptual model) |  |
| Value | Text |
| Business rules | Value Allowed:yes  Relationship: Header, reason, Protocol Identifier, Protocol Amendment  Concept:C17649 |
| Duplicate field in other sections |  |

|  |  |
| --- | --- |
| Term (Variable) | Secondary |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | H |
| Definition | Header |
| User Guidance | Note Applicable |
| Conformance | Required |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | Amendment Details |
| Relationship (reference to high level conceptual model) |  |
| Value | Secondary: |
| Business rules | Value Allowed: No  Relationship: Table Column Header  Concept: Header |
| Duplicate field in other sections | No |

|  |  |
| --- | --- |
| Term (Variable) | Secondary Reason for Amendment |
| Data Type | Valid Value List |
| Data (D), Value (V) or Header (H) | D |
| Definition | See CNEW  For context CNEW 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 | Required If Protocol Original = yes then the value is Original |
| Cardinality | Amendment Details |
| Relationship content from ToC representing the protocol hierarchy | Amendment Details |
| Relationship (reference to high level conceptual model) |  |
| Value | * Regulatory agency request to amend * New regulatory guidance * IRB/IEC feedback * New safety information available * Manufacturing change * IMP addition * Change in strategy * Change in standard of care * New data available (other than safety data) * Investigator/site feedback * Recruitment difficulty * Inconsistency and/or error in the protocol * Protocol design error * Other * Original * Not applicable |
| Business rules | Value Allowed: Yes  Relationship: Header, Protocol Identifier, Protocol Amendment  Concept: CNEW |
| Duplicate field in other sections | Multiple accepted except for Original |

|  |  |
| --- | --- |
| Term (Variable) | Other |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | H |
| Definition | Heading |
| User Guidance | Not applicable |
| Conformance | Required |
| Cardinality | One to One |
| Relationship content from ToC representing the protocol hierarchy | Amendment Details |
| Relationship (reference to high level conceptual model) |  |
| Value | Other: |
| Business rules | Value Allowed: No  Relationship: Selection of Other  Concept:Header |
| Duplicate field in other sections | No |

|  |  |
| --- | --- |
| Term (Variable) | Other description |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | D |
| Definition | See C17649  For Context C17649 Different than the one(s) previously specified or mentioned. (NCI) |
| 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 |
| Relationship (reference to high level conceptual model) |  |
| Value | Text |
| Business rules | Value Allowed:yes  Relationship: Header, reason, Protocol Identifier, Protocol Amendment  Concept:C17649 |
| Duplicate field in other sections |  |

|  |  |
| --- | --- |
| Term (Variable) | {Amendment Summary} |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | H |
| Definition | Heading |
| User Guidance | Not Applicable |
| Conformance | Conditional / Required; if Original Protocol=No |
| Cardinality |  |
| Relationship content from ToC representing the protocol hierarchy | Amendment Details |
| Relationship (reference to high level conceptual model) |  |
| Value | Summary of Amendment |
| Business rules | Value Allowed: No  Relationship: Amendment details; Amendment Identifier  Concept: Header |
| Duplicate field in other sections |  |

|  |  |
| --- | --- |
| Term (Variable) | {Amendment Summary} |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | D |
| Definition | See CNEW  For Context CNEW 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 / Required |
| Cardinality | One to Amendment identifier |
| Relationship content from ToC representing the protocol hierarchy | Amendment Details |
| Relationship (reference to high level conceptual model) |  |
| Value | Text |
| Business rules | Value Allowed: Yes  Relationship: Amendment Details; Amendment Identifier, Protocol Identifier  Concept: CNEW |
| Duplicate field in other sections | No |

|  |  |
| --- | --- |
| Term (Variable) | Question {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 Header (H) | H |
| Definition | Heading |
| User Guidance | Not applicable |
| Conformance | Conditional / Required |
| Cardinality | One to One amendment identifier |
| Relationship content from ToC representing the protocol hierarchy | Amendment Details |
| Relationship (reference to high level conceptual model) |  |
| Value | Is this amendment likely to have a substantial impact on   * safety or rights of the subjects, or * on the reliability and robustness of the data generated in the clinical trial? |
| Business rules | Value Allowed: No  Relationship: Amendment Details  Concept: Header |
| Duplicate field in other sections |  |

|  |  |
| --- | --- |
| Term (Variable) | Is this amendment likely to have a substantial impact on the safety or rights of the participants? Response |
| Data Type | Pick list |
| Data (D), Value (V) or Header (H) | V |
| Definition | See CNEW  For Context CNEW An indication as to whether the amendment likely to have a substantial impact on the safety or rights of the participants. |
| User Guidance | Is this amendment likely to have a substantial impact on the safety or rights of the participants? |
| Conformance | Conditional / Required |
| Cardinality | One to one, One to Amendment Identifier, One to Protocol Identifier |
| Relationship content from ToC representing the protocol hierarchy | Amendment Details |
| Relationship (reference to high level conceptual model) |  |
| Value | Yes  No |
| Business rules | Value Allowed: Yes  Relationship: Amendment Details, Amendment Identifier, Protocol Identifier  Concept: CNEW |
| Duplicate field in other sections | No |

|  |  |
| --- | --- |
| Term (Variable) | Briefly Explain Substantial Impact On Safety |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | D |
| Definition | See CNEW  For context CNEW 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 / Required |
| 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 |
| Relationship (reference to high level conceptual model) |  |
| Value | Text |
| Business rules | Value Allowed: Yes  Relationship: Amendment Details, Amendment Identifier, Protocol Identifier When the value is yes there is a text response for explanation  Concept:CNEW |
| Duplicate field in other sections | no |

|  |  |
| --- | --- |
| 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 Header (H) | H |
| Definition | Heading |
| User Guidance | Not applicable |
| Conformance | Conditional / Required |
| Cardinality | One to amendment details, One amendment identifier, Protocom Identifier |
| Relationship content from ToC representing the protocol hierarchy | Amendment Details |
| Relationship (reference to high level conceptual model) |  |
| 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,  Concept: Header |
| Duplicate field in other sections | No |

|  |  |
| --- | --- |
| 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 | Pick list |
| Data (D), Value (V) or Header (H) | V |
| Definition | See CNEW  For Context CNEW 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 | Is this amendment likely to have a substantial impact on the reliability and robustness of the data generated in the clinical trial? |
| Conformance | Conditional / Required |
| Cardinality | One to one, One to Amendment Identifier, One to Protocol Identifier |
| Relationship content from ToC representing the protocol hierarchy | Amendment Details |
| Relationship (reference to high level conceptual model) |  |
| Value | Yes  No |
| Business rules | Value Allowed: Yes  Relationship: Amendment Details, Amendment Identifier, Protocol Identifier  Concept: CNEW |
| Duplicate field in other sections | No |

|  |  |
| --- | --- |
| Term (Variable) | Briefly Explain Substantial Impact on Data |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | D |
| Definition | See CNEW  For context CNEW 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 / Required |
| Cardinality | One to One amendment identifier  Is this amendment likely to have a substantial impact on the reliability and robustness of the data generated in the clinical trial? |
| Relationship content from ToC representing the protocol hierarchy | Amendment Details |
| Relationship (reference to high level conceptual model) |  |
| Value | Text |
| Business rules | Value Allowed: Yes  Relationship: Amendment Details, Amendment Identifier, Protocol Identifier When the value is yes there is a text response for explanation  Concept:Header |
| Duplicate field in other sections | no |

|  |  |
| --- | --- |
| Term (Variable) | {Overview of Changes in the Current Amendment:} |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | H |
| Definition | Heading |
| User Guidance | Conditional if amendment |
| Conformance | Conditional / Required |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | Amendment Details |
| Relationship (reference to high level conceptual model) |  |
| Value | Overview of Changes in the Current Amendment: |
| Business rules | Value Allowed: No  Relationship:Amendment Details  Concept:Header |
| Duplicate field in other sections | No |

|  |  |
| --- | --- |
| Term (Variable) | {Description of Change} |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | H |
| Definition | Heading |
| User Guidance | Table |
| Conformance | Conditionally Required |
| Cardinality |  |
| Relationship content from ToC representing the protocol hierarchy | Amendment Details Table Column Heading |
| Relationship (reference to high level conceptual model) |  |
| Value | {Description of Change} |
| Business rules | Value Allowed: No  Relationship: Table Column Hading  Concept: Header |
| Duplicate field in other sections | No |

|  |  |
| --- | --- |
| Term (Variable) | <Enter Description of Amendment Change> |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | Data |
| Definition | See CNEW  FOr Context CNEW A narrative representation of the change introduced in the current version of the protocol. |
| User Guidance | <Enter Description of Amendment Change> |
| Conformance | Conditionally Required |
| Cardinality | Column Heading  Row Content |
| Relationship content from ToC representing the protocol hierarchy | Amendment Details Row Lead |
| Relationship (reference to high level conceptual model) |  |
| Value | Text |
| Business rules | Value Allowed: No  Relationship: Column Heading and Row  Concept: CNEW |
| Duplicate field in other sections | Yes for every Description of Change |

|  |  |
| --- | --- |
| Term (Variable) | {Brief Rationale for Change} |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | H |
| Definition | Heading |
| User Guidance |  |
| Conformance | Conditional Required if Amendments |
| Cardinality | Column Heading Table |
| Relationship content from ToC representing the protocol hierarchy | Amendment Details |
| Relationship (reference to high level conceptual model) |  |
| Value | {Brief Rationale for Change} |
| Business rules | Value Allowed: No  Relationship: Table Column  Concept: Header |
| Duplicate field in other sections | No |

|  |  |
| --- | --- |
| Term (Variable) | <Enter Rationale for Amendment Change> |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | D |
| Definition | See CNEW  For context CNew The brief reason for the change introduced in the current version of the protocol. |
| User Guidance | <Enter Rationale for Amendment Change> |
| Conformance | Conditionally Required |
| Cardinality | One to Column Heading Row description of change  Section# and Name |
| Relationship content from ToC representing the protocol hierarchy | Amendment Details |
| Relationship (reference to high level conceptual model) |  |
| Value | Text |
| Business rules | Value Allowed: yes  Relationship: Row Content, Column Content  Concept: n/a |
| Duplicate field in other sections | Yes as long as Description of Change Continues |

|  |  |
| --- | --- |
| Term (Variable) | {Section # and Name} |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | H |
| Definition | Heading |
| User Guidance |  |
| Conformance | Conditional Required if Amendment |
| Cardinality | Column Heading Table |
| Relationship content from ToC representing the protocol hierarchy | Amendment Details |
| Relationship (reference to high level conceptual model) |  |
| Value | {Section # and Name} |
| Business rules | Value Allowed: No  Relationship: Table Column  Concept: Header |
| Duplicate field in other sections | No |

|  |  |
| --- | --- |
| Term (Variable) | <Enter Section of Amendment Change> |
| Data Type | Pick List |
| Data (D), Value (V) or Header (H) | Value |
| Definition | See CNEW  For context CNew The protocol section number and name containing the change introduced in the current version of the protocol. |
| User Guidance | <Enter Section of Amendment Change> |
| Conformance | Conditionally Required |
| Cardinality | One to Column Heading Row description of change  Description of Change, Rational for Amendment Change |
| Relationship content from ToC representing the protocol hierarchy | Amendment Details  One to Column Heading Row description of change  Description of Change, Rational for Amendment Change |
| Relationship (reference to high level conceptual model) |  |
| Value | 1 PROTOCOL SUMMARY  1.1 Protocol Synopsis  1.1.1 Primary and Secondary Objectives and Estimands  1.1.2 Overall Design  1.2 Trial Schema  1.3 Schedule of Activities  2 INTRODUCTION  2.1 Purpose of Trial  2.2 Summary of Benefits and Risks  2.2.1 Benefit Summary  2.2.2 Risk Summary and Mitigation Strategy  2.2.3 Overall Benefit:Risk Conclusion  3 TRIAL OBJECTIVES AND ESTIMANDS  3.1 Primary Objective(s) and Associated Estimand(s)  3.1.1 Primary Estimand  3.2 Secondary Objective(s) and Associated Estimand(s)  3.3 Exploratory Objective(s)  4 TRIAL DESIGN  4.1 Description of Trial Design  4.1.1 Stakeholder Input into Design  4.2 Rationale for Trial Design  4.2.1 Rationale for Intervention Model  4.2.2 Rationale for Duration  4.2.3 Rationale for Estimands  4.2.4 Rationale for Interim Analysis  4.2.5 Rationale for Control Type  4.2.6 Rationale for Adaptive or Novel Trial Design  4.2.7 Rationale for Other Trial Design Aspects  4.3 Trial Stopping Rules  4.4 Start of Trial and End of Trial  4.5 Access to Trial Intervention After End of Trial  5 TRIAL POPULATION  5.1 Description of Trial Population and Rationale  5.2 Inclusion Criteria  5.3 Exclusion Criteria  5.4 Contraception  5.4.1 Definitions Related to Childbearing Potential  5.4.2 Contraception Requirements  5.5 Lifestyle Restrictions  5.5.1 Contraception Requirements  5.5.2 Caffeine, Alcohol, Tobacco, and Other Restrictions  5.5.3 Physical Activity Restrictions  5.5.4 Other Activity Restrictions  5.6 Screen Failure and Rescreening  6 TRIAL INTERVENTION AND CONCOMITANT THERAPY  6.1 Overview of Trial Interventions  6.2 Description of Investigational Trial Intervention  6.3 Rationale for Investigation Trial Intervention Dose and Regimen  6.4 Investigational Trial Intervention Administration  6.5 Investigational Trial Intervention Dose Modification  6.6 Management of Investigational Trial Intervention Overdose  6.7 Preparation, Storage, Handling and Accountability of Investigational Trial Intervention(s)  6.7.1 Preparation of Investigational Trial Intervention(s)  6.7.2 Storage and Handling of Investigational Trial Intervention  6.7.3 Accountability of Investigational Trial Intervention  6.8 Investigational Trial Intervention Assignment, Randomisation and Blinding  6.8.1 Participant Assignment to Investigational Trial Intervention  6.8.2 Randomisation  6.8.3 Blinding  6.8.4 Emergency Unblinding at the Site  6.9 Investigational Trial Intervention Compliance  6.10 Description of Non-Investigational Trial Intervention(s)  6.10.1 Background Intervention  6.10.2 Rescue Therapy  6.10.3 Other Non-investigational Intervention  6.11 Concomitant Therapy  6.11.1 Prohibited Concomitant Therapy  6.11.2 Permitted Concomitant Therapy  7 PARTICIPANT DISCONTINUATION OF TRIAL INTERVENTION AND DISCONTINUATION OR WITHDRAWAL FROM TRIAL  7.1 Discontinuation of Trial Intervention for Individual Participants  7.1.1 Permanent Discontinuation of Trial Intervention  7.1.2 Temporary Discontinuation of Trial Intervention  7.1.3 Rechallenge  7.2 Discontinuation or Withdrawal from the Trial  7.3 Lost to Follow-Up  8 TRIAL ASSESSMENTS AND PROCEDURES  8.1 Trial Assessments and Procedures Considerations  8.2 Screening/Baseline Assessments and Procedures  8.3 Efficacy Assessments and Procedures  8.4 Safety Assessments and Procedures  8.4.1 Physical Examination  8.4.2 Vital Signs  8.4.3 Electrocardiograms  8.4.4 Clinical Laboratory Assessments  8.4.5 Pregnancy Testing  8.4.6 Suicidal Ideation and Behaviour Risk Monitoring  8.5 Pharmacokinetics  8.6 Biomarkers  8.6.1 Genetics and Pharmacogenomics  8.6.2 Pharmacodynamic Biomarkers  8.6.3 Other Biomarkers  8.7 Immunogenicity Assessments  8.8 Medical Resource Utilisation and Health Economics  9 ADVERSE EVENTS, SERIOUS ADVERSE EVENTS, PRODUCT COMPLAINTS, PREGNANCY AND POSTPARTUM INFORMATION  9.1 Definitions  9.1.1 Definitions of Adverse Events  9.1.2 Definitions of Serious Adverse Events  9.1.3 Definition of Medical Device Product Complaints  9.2 Timing and Mechanism for Collection and Reporting  9.3 Identification, Recording and Follow-Up  9.3.1 Identification  9.3.2 Severity  9.3.3 Causality  9.3.4 Follow-up  9.4 Reporting  9.4.1 Regulatory Reporting Requirements  9.4.2 Adverse Events of Special Interest  9.4.3 Disease-related Events or Outcomes Not Qualifying as AEs or SAEs  9.5 Pregnancy and Postpartum Information  9.5.1 Participants Who Become Pregnant During the Trial  9.5.2 Participants Whose Partners Become Pregnant  10 Statistical Considerations  10.1 Geeral Considerations  10.2 Analysis Sets  10.3 Analyses of Demographics and Other Baseline Variables  10.4 Analyses Associated with the Primary Objective(s)  10.4.1 Statistical Method of Analysis  10.4.2 Handling of Data in Relation to Primary Estimand(s)  10.4.3 Handling of Missing Data  10.4.4 Sensitivity Analysis  10.4.5 Supplementary Analysis  10.5 Analysis Associated with the Secondary Objective(s)  10.5.1 Statistical Method of Analysis  10.5.2 Handling of Data in Relation to Secondary Estimand(s)  10.5.3 Handling of Missing Data  10.5.4 Sensitivity Analyses  10.5.5 Supplementary Analyses  10.6 Analysis Associated with the Exploratory Objective(s)  10.7 Safety Analyses  10.8 Other Analyses  10.9 Interim Analyses  10.10 Multiplicity Adjustments  10.11 Sample Size Determination  11 TRIAL OVERSIGHT AND OTHER GENERAL CONSIDERATIONS  11.1 Regulatory and Ethical Considerations  11.2 Trial Oversight  11.2.1 Investigator Responsibilities  11.2.2 Sponsor Responsibilities  11.3 Informed Consent Process  11.3.1 Informed Consent for Rescreening  11.3.2 Informed Consent for Use of Remaining Samples in Exploratory Research  11.4 Committees  11.5 Insurance and Indemnity  11.5 Risk Management  11.7 Data Governance  11.8 Source Data  11.9 Protocol Deviations  11.10 Early Site Closure  12 APPENDIX: SUPPORTING DETAILS  12.1 Clinical Laboratory Tests  12.2 Country/Region-Specific Differences  12.3 Prior Protocol Amendment(s)  13 APPENDIX: GLOSSARY OF TERMS AND ABBREVIATIONS  14 APPENDIX: REFERENCES |
| Business rules | Value Allowed: yes  Relationship: Column; Row description and rational amendment change Row  Concept: CNEW |
| Duplicate field in other sections | Yes for every Description of Change |

|  |  |
| --- | --- |
| Term (Variable) | Table of Contents |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | H |
| Definition | Heading |
| User Guidance |  |
| Conformance | Required |
| Cardinality |  |
| Relationship content from ToC representing the protocol hierarchy | Table of Contents |
| Relationship (reference to high level conceptual model) |  |
| Value | Table of Contents |
| Business rules | Value Allowed: Yes  Relationship: n/a  Concept: n/a |
| Duplicate field in other sections |  |

|  |  |
| --- | --- |
| Term (Variable) | Table of Contents |
| Data Type |  |
| Data (D), Value (V) or Header (H) |  |
| Definition |  |
| User Guidance |  |
| Conformance | Generated / Generated |
| Cardinality |  |
| Relationship content from ToC representing the protocol hierarchy |  |
| Relationship (reference to high level conceptual model) |  |
| Value |  |
| Business rules | Value Allowed: n/a  Relationship: n/a  Concept: n/a |
| Duplicate field in other sections |  |

# Protocol Summary

|  |  |
| --- | --- |
| Term (Variable) | Protocol Summary |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | H |
| Definition | Heading |
| User Guidance | No text is intended here (header only) |
| Conformance | Required |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 1 Protocol Summary |
| Relationship (reference to high level conceptual model) |  |
| Value | 1. Protocol Summary |
| Business rules | Value Allowed: No  Relationship: 1  Concept: Header |
| Duplicate field in other sections | No |

## Protocol Synopsis

|  |  |
| --- | --- |
| Term (Variable) | 1.1 Protocol Synopsis |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | H |
| Definition | Heading |
| User Guidance | The protocol synopsis is a short summary of the key points of the trial.  No text is intended here (header only). |
| Conformance | Required |
| Cardinality | One to One |
| Relationship content from ToC representing the protocol hierarchy | Protocol Summary |
| Relationship (reference to high level conceptual model) |  |
| Value | 1.1 Protocol Synopsis |
| Business rules | Value Allowed: No  Relationship:1.1  Concept: Header |
| Duplicate field in other sections | No |

|  |  |
| --- | --- |
| Term (Variable) | 1.1.1Primary and Secondary Objectives and Estimands |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | H |
| Definition | Heading |
| User Guidance | N/A |
| Conformance | Required |
| Cardinality | One to One |
| Relationship content from ToC representing the protocol hierarchy | Protocol Summary |
| Relationship (reference to high level conceptual model) |  |
| Value | 1.1.1Primary and Secondary Objectives and Estimands |
| Business rules | Value Allowed: No  Relationship: 1.1.1  Concept: Header |
| Duplicate field in other sections |  |

|  |  |
| --- | --- |
| Term (Variable) | <Enter Primary and Secondary Objectives and Estimands> |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | D |
| Definition |  |
| User Guidance | Summarize the primary and secondary objectives and any associated estimands. Consider including a copy of the table describing the estimands from Section 3 of the protocol and follow all the same instructions. |
| Conformance | Required |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 1.1.1Primary and Secondary Objectives and Estimands |
| Relationship (reference to high level conceptual model) |  |
| Value | text |
| Business rules | Value Allowed: yes  Relationship: 1.1.1  Concept: n/a |
| Duplicate field in other sections | Repeat as needed |

|  |  |
| --- | --- |
| Term (Variable) | 1.1.2 Overall Design |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | H |
| Definition | Heading |
| User Guidance |  |
| Conformance | Required |
| Cardinality | One to One |
| Relationship content from ToC representing the protocol hierarchy | Protocol Summary |
| Relationship (reference to high level conceptual model) |  |
| Value | 1.1.2 Overall Design |
| Business rules | Value Allowed: No  Relationship:  Concept: Header |
| Duplicate field in other sections | No |

|  |  |
| --- | --- |
| Term (Variable) | Key aspects of the trial design are summarised below. |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | H |
| Definition | Mandatory Sentence |
| User Guidance |  |
| Conformance | Required |
| Cardinality | One to 1.1.2 |
| Relationship content from ToC representing the protocol hierarchy | Protocol Summary |
| Relationship (reference to high level conceptual model) |  |
| Value | Key aspects of the trial design are summarised below. |
| Business rules | Value Allowed: No  Relationship: 1.1.2 Overall Design  Concept: Required sentence Header |
| Duplicate field in other sections |  |

|  |  |
| --- | --- |
| Term (Variable) | Intervention Model |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | H |
| Definition |  |
| User Guidance |  |
| Conformance | Required |
| Cardinality |  |
| Relationship content from ToC representing the protocol hierarchy | Protocol Summary |
| Relationship (reference to high level conceptual model) |  |
| Value | Intervention Model |
| Business rules | Value Allowed: Yes  Relationship: Table Cell title  Concept: n/a |
| Duplicate field in other sections |  |

|  |  |
| --- | --- |
| Term (Variable) | Intervention Model |
| Data Type | Pick List |
| Data (D), Value (V) or Header (H) | V |
| Definition |  |
| User Guidance | Intervention model (for example, single group, parallel group, cross-over, factorial, sequential, other) |
| Conformance | Required |
| Cardinality |  |
| Relationship content from ToC representing the protocol hierarchy | Protocol Summary |
| Relationship (reference to high level conceptual model) |  |
| Value | Single group, parallel group, cross-over, factorial, sequential, other |
| Business rules | Value Allowed: Yes  Relationship: n/a  Concept: n/a |
| Duplicate field in other sections |  |

|  |  |
| --- | --- |
| Term (Variable) | Population Type |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | H |
| Definition |  |
| User Guidance |  |
| Conformance | Required |
| Cardinality |  |
| Relationship content from ToC representing the protocol hierarchy | Protocol Summary |
| Relationship (reference to high level conceptual model) |  |
| Value | Population Type |
| Business rules | Value Allowed: Yes  Relationship: Table Cell title  Concept: n/a |
| Duplicate field in other sections |  |

|  |  |
| --- | --- |
| Term (Variable) | Population Type |
| Data Type | Pick List |
| Data (D), Value (V) or Header (H) | D |
| Definition |  |
| User Guidance |  |
| Conformance | Required |
| Cardinality |  |
| Relationship content from ToC representing the protocol hierarchy | Protocol Summary |
| Relationship (reference to high level conceptual model) |  |
| Value | healthy volunteers, adult patients, paediatric patients, other |
| Business rules | Value Allowed: Yes  Relationship: n/a  Concept: n/a |
| Duplicate field in other sections |  |

|  |  |
| --- | --- |
| Term (Variable) | Control Type |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | H |
| Definition |  |
| User Guidance |  |
| Conformance | Required |
| Cardinality |  |
| Relationship content from ToC representing the protocol hierarchy | Protocol Summary |
| Relationship (reference to high level conceptual model) |  |
| Value | Control |
| Business rules | Value Allowed: Yes  Relationship: Table cell title  Concept: n/a |
| Duplicate field in other sections |  |

|  |  |
| --- | --- |
| Term (Variable) | ControlType |
| Data Type | Pick List |
| Data (D), Value (V) or Header (H) | D |
| Definition |  |
| User Guidance | Control method (for example, placebo, active comparator, low dose, historical, standard of care, sham procedure, or none [uncontrolled]) |
| Conformance | Required |
| Cardinality |  |
| Relationship content from ToC representing the protocol hierarchy | Protocol Summary |
| Relationship (reference to high level conceptual model) |  |
| Value | placebo, active comparator, low dose, historical, standard of care, sham procedure, or none [uncontrolled] |
| Business rules | Value Allowed: Yes  Relationship: n/a  Concept: n/a |
| Duplicate field in other sections |  |

|  |  |
| --- | --- |
| Term (Variable) | Population Diagnosis or Condition |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | H |
| Definition |  |
| User Guidance |  |
| Conformance | Required |
| Cardinality |  |
| Relationship content from ToC representing the protocol hierarchy | Protocol Summary |
| Relationship (reference to high level conceptual model) |  |
| Value | Population Diagnosis or Condition |
| Business rules | Value Allowed: Yes  Relationship: Table cell title  Concept: n/a |
| Duplicate field in other sections |  |

|  |  |
| --- | --- |
| Term (Variable) | Population Diagnosis or Condition |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | D |
| Definition |  |
| User Guidance | Control method (for example, placebo, active comparator, low dose, historical, standard of care, sham procedure, or none [uncontrolled]) |
| Conformance | Required |
| Cardinality |  |
| Relationship content from ToC representing the protocol hierarchy | Protocol Summary |
| Relationship (reference to high level conceptual model) |  |
| Value | Use examples Medra PT or SNOMECT CT: “acute lung injury,” or a specific biomarker profile); indicate “N/A – Healthy” for studies in healthy volunteers |
| Business rules | Value Allowed: Yes  Relationship: n/a  Concept: n/a |
| Duplicate field in other sections |  |

|  |  |
| --- | --- |
| Term (Variable) | Control Description |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | H |
| Definition |  |
| User Guidance |  |
| Conformance | Required |
| Cardinality |  |
| Relationship content from ToC representing the protocol hierarchy | Protocol Summary |
| Relationship (reference to high level conceptual model) |  |
| Value | Active Comparator |
| Business rules | Value Allowed: Yes  Relationship: Table Cell title  Concept: n/a |
| Duplicate field in other sections |  |

|  |  |
| --- | --- |
| Term (Variable) | Control Description |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | D |
| Definition |  |
| User Guidance | Active comparator, if applicable; indicate N/A if not applicable. |
| Conformance | Conditional/ Required |
| Cardinality |  |
| Relationship content from ToC representing the protocol hierarchy | Protocol Summary |
| Relationship (reference to high level conceptual model) |  |
| Value | If applicable; indicate N/A if not applicable |
| Business rules | Value Allowed: Yes  Relationship: n/a  Concept: n/a |
| Duplicate field in other sections |  |

|  |  |
| --- | --- |
| Term (Variable) | Population Age |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | H |
| Definition |  |
| User Guidance | Population age range (for example 0-3 mos, 18-80 years old). List N/A if a maximum or minimum age limit does not apply. 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 |  |
| Relationship content from ToC representing the protocol hierarchy | Protocol Summary |
| Relationship (reference to high level conceptual model) |  |
| Value | Population Age |
| Business rules | Value Allowed: Yes  Relationship: Table cell title  Concept: n/a |
| Duplicate field in other sections |  |

|  |  |
| --- | --- |
| Term (Variable) | Minimum |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | H |
| Definition |  |
| User Guidance |  |
| Conformance | Required |
| Cardinality |  |
| Relationship content from ToC representing the protocol hierarchy | Protocol Summary |
| Relationship (reference to high level conceptual model) |  |
| Value | Minimum |
| Business rules | Value Allowed: Yes  Relationship: Table cell entry  Concept: n/a |
| Duplicate field in other sections |  |

|  |  |
| --- | --- |
| Term (Variable) | Minimum age |
| Data Type | Integer |
| Data (D), Value (V) or Header (H) | D |
| Definition |  |
| User Guidance |  |
| Conformance | Required |
| Cardinality |  |
| Relationship content from ToC representing the protocol hierarchy | Protocol Summary |
| Relationship (reference to high level conceptual model) |  |
| Value |  |
| Business rules | Value Allowed: n/a  Relationship: n/a  Concept: n/a |
| Duplicate field in other sections |  |

|  |  |
| --- | --- |
| Term (Variable) | Maximum |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | H |
| Definition |  |
| User Guidance |  |
| Conformance | Required |
| Cardinality |  |
| Relationship content from ToC representing the protocol hierarchy | Protocol Summary |
| Relationship (reference to high level conceptual model) |  |
| Value | Maximum |
| Business rules | Value Allowed: Yes  Relationship: Table Cell entry  Concept: n/a |
| Duplicate field in other sections |  |

|  |  |
| --- | --- |
| Term (Variable) | Maximum age |
| Data Type | Integer |
| Data (D), Value (V) or Header (H) | D |
| Definition |  |
| User Guidance |  |
| Conformance | Required |
| Cardinality |  |
| Relationship content from ToC representing the protocol hierarchy | Protocol Summary |
| Relationship (reference to high level conceptual model) |  |
| Value |  |
| Business rules | Value Allowed: n/a  Relationship: n/a  Concept: n/a |
| Duplicate field in other sections |  |

|  |  |
| --- | --- |
| Term (Variable) | Age units |
| Data Type | Pick List |
| Data (D), Value (V) or Header (H) | D |
| Definition |  |
| User Guidance |  |
| Conformance | Required |
| Cardinality |  |
| Relationship content from ToC representing the protocol hierarchy | Protocol Summary |
| Relationship (reference to high level conceptual model) |  |
| Value | Weeks, months, years |
| Business rules | Value Allowed: Yes  Relationship: n/a  Concept: n/a |
| Duplicate field in other sections |  |

|  |  |
| --- | --- |
| Term (Variable) | Trial Intervention Assignment Method |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | H |
| Definition |  |
| User Guidance |  |
| Conformance | Required |
| Cardinality |  |
| Relationship content from ToC representing the protocol hierarchy | Protocol Summary |
| Relationship (reference to high level conceptual model) |  |
| Value | Trial Intervention Assignment Method |
| Business rules | Value Allowed: Yes  Relationship: n/a  Concept: n/a |
| Duplicate field in other sections |  |

|  |  |
| --- | --- |
| Term (Variable) | Trial Intervention Assignment Method |
| Data Type | Pick List |
| Data (D), Value (V) or Header (H) | D |
| Definition |  |
| User Guidance | Trial intervention assignment method (for example, randomisation, stratification, or both). Do NOT state block size. If assignment to intervention is by randomisation, describe when randomisation occurs relative to screening. |
| Conformance | Required |
| Cardinality |  |
| Relationship content from ToC representing the protocol hierarchy | Protocol Summary |
| Relationship (reference to high level conceptual model) |  |
| Value | Randomisation, stratification, or both randomisation and stratification |
| Business rules | Value Allowed: Yes  Relationship: n/a  Concept: n/a |
| Duplicate field in other sections |  |

|  |  |
| --- | --- |
| Term (Variable) | Randomisation time |
| Data Type |  |
| Data (D), Value (V) or Header (H) | D |
| Definition |  |
| User Guidance |  |
| Conformance | Conditional |
| Cardinality |  |
| Relationship content from ToC representing the protocol hierarchy | Protocol Summary |
| Relationship (reference to high level conceptual model) |  |
| Value | Relative to screening |
| Business rules | Value Allowed: Yes  Relationship: Randomisation  Concept: n/a |
| Duplicate field in other sections |  |

|  |  |
| --- | --- |
| Term (Variable) | Site Distribution |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | H |
| Definition |  |
| User Guidance |  |
| Conformance | Required |
| Cardinality |  |
| Relationship content from ToC representing the protocol hierarchy | Protocol Summary |
| Relationship (reference to high level conceptual model) |  |
| Value | Site Distribution |
| Business rules | Value Allowed: Yes  Relationship: N/A  Concept: n/a |
| Duplicate field in other sections |  |

|  |  |
| --- | --- |
| Term (Variable) | Geographic scope |
| Data Type | Pick List |
| Data (D), Value (V) or Header (H) | D |
| Definition | Geographic scope of trial |
| User Guidance | Geographic scope of trial (select from: single-centre, multi-centre, or multi-centre and multi-national). If none of these applies, indicate other and describe. |
| Conformance | Required / Required |
| Cardinality |  |
| Relationship content from ToC representing the protocol hierarchy | Protocol Summary |
| Relationship (reference to high level conceptual model) |  |
| Value | Examples: single-center, multi-center, or multi-center, multi-national |
| Business rules | Value Allowed: Yes  Relationship: n/a  Concept: n/a |
| Duplicate field in other sections |  |

|  |  |
| --- | --- |
| Term (Variable) | Geographic scope other |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | D |
| Definition |  |
| User Guidance |  |
| Conformance | Conditional / Required |
| Cardinality |  |
| Relationship content from ToC representing the protocol hierarchy | Protocol Summary |
| Relationship (reference to high level conceptual model) |  |
| Value | ISO Country Code List |
| Business rules | Value Allowed: Yes  Relationship: n/a  Concept: n/a |
| Duplicate field in other sections |  |

|  |  |
| --- | --- |
| Term (Variable) | Adaptive Trial Design: |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | H |
| Definition | Heading |
| User Guidance | Not applicable |
| Conformance | Required |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 1.1.2 |
| Relationship (reference to high level conceptual model) |  |
| Value | Adaptive Trial Design: |
| Business rules | Value Allowed: No  Relationship: Table row heading  Concept: Header, Identifier |
| Duplicate field in other sections | No |

|  |  |
| --- | --- |
| Term (Variable) | Adaptive Trial Type Indicator |
| Data Type | Valid Value |
| Data (D), Value (V) or Header (H) | V |
| Definition | See CNEW  For review context CNEW 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 | Not applicable |
| Conformance | Required |
| Cardinality | One to One, Protocol Identifier |
| Relationship content from ToC representing the protocol hierarchy | Tit1.1.2; Protocol Identifier |
| Relationship (reference to high level conceptual model) |  |
| Value | Yes, No |
| Business rules | **Value** **Allowed**: Yes  **Relationship**: Heading Original Protocol; Protocol Identifier  **Concept**: CNEW |
| Duplicate field in other sections | No |

|  |  |
| --- | --- |
| Term (Variable) | Adaptive Trial Design Type |
| Data Type | Valid Value |
| Data (D), Value (V) or Header (H) | V |
| Definition | See CNEW  For review context CNEW A characterization or classification of the adaptive trial design used in the clinical trial. |
| User Guidance | If yes |
| Conformance | Conditional Required |
| Cardinality | One to One, Protocol Identifier |
| Relationship content from ToC representing the protocol hierarchy | 1.1.2 |
| Relationship (reference to high level conceptual model) |  |
| Value | Umbrella, Early Trial Stopping, Sample Size Adaption, Population Selection, Treatment Selection, Adapation to Patient Allocation, Other |
| Business rules | **Value** **Allowed**: Yes  **Relationship**: Adaptive or Novel Trial, Protocol Identifier  **Concept**: NEW |
| Duplicate field in other sections | No |

|  |  |
| --- | --- |
| Term (Variable) | Other |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | D |
| Definition | See C17649  For review context C17649 Different than the one(s) previously specified or mentioned. (NCI) |
| User Guidance | Not applicable |
| Conformance | Conditionally Required Adaptive or Novel Trial = yes; Other |
| Cardinality | One to One, Other Protocol Identifier |
| Relationship content from ToC representing the protocol hierarchy | 1.1.2  Adaptive or Novel Trial Yes |
| Relationship (reference to high level conceptual model) |  |
| Value | Text |
| Business rules | **Value** **Allowed**: Yes  **Relationship**: Heading Adaptive or Novel Trial; Protocol Identifier; Adaptive or Novel Trial=yes; Other  **Concept**: C |
| Duplicate field in other sections | No |

|  |  |
| --- | --- |
| Term (Variable) | Master Protocol Design: |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | H |
| Definition | Heading |
| User Guidance | Not applicable |
| Conformance | Required |
| Cardinality | One to one; Protocol Identifier |
| Relationship content from ToC representing the protocol hierarchy | 1.1.2 |
| Relationship (reference to high level conceptual model) |  |
| Value | Master Protocol Design |
| Business rules | Value Allowed: No  Relationship: Table row heading  Concept: Header, Identifier |
| Duplicate field in other sections | No |

|  |  |
| --- | --- |
| Term (Variable) | Master Protocol design Indicator |
| Data Type | Valid Value |
| Data (D), Value (V) or Header (H) | V |
| Definition | See CNEW  For review context CNEW An indication as to whether the study has a master protocol design. |
| User Guidance | Not applicable |
| Conformance | Required |
| Cardinality | One to One, Master Protocol Design Indicator; Protocol Identifier |
| Relationship content from ToC representing the protocol hierarchy | 1.1.2 |
| Relationship (reference to high level conceptual model) |  |
| Value | Yes, No |
| Business rules | **Value** **Allowed**: Yes  **Relationship**: Heading Master Protocol Design Indicator; Protocol Identifier  **Concept**: CNEW |
| Duplicate field in other sections | No |

|  |  |
| --- | --- |
| Term (Variable) | Is this a Master Protocol or Substudy? |
| Data Type | Valid Value |
| Data (D), Value (V) or Header (H) | V |
| Definition | See CNEW  For review context CNEW An indication as to whether the study with a master protocol design is the master protocol or a substudy. |
| User Guidance | If yes |
| Conformance | Conditional;ly Required |
| Cardinality | One to One, Master Protocol Design Indicator; Protocol Identifier |
| Relationship content from ToC representing the protocol hierarchy | 1.1.2 |
| Relationship (reference to high level conceptual model) |  |
| Value | Master Study, Substudy |
| Business rules | **Value** **Allowed**: Yes  **Relationship**: Heading Master Protocol Design Indicator; Protocol Identifier  **Concept**: CNEW |
| Duplicate field in other sections | No |

|  |  |
| --- | --- |
| Term (Variable) | Drug/Device Combination Product: |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | H |
| Definition | Heading |
| User Guidance | Not applicable |
| Conformance | Required |
| Cardinality | One to one; Protocol Identifier |
| Relationship content from ToC representing the protocol hierarchy | Title Page |
| Relationship (reference to high level conceptual model) |  |
| Value | Drug/device Combination Product: |
| Business rules | Value Allowed: No  Relationship: Table row heading  Concept: Header, Identifier |
| Duplicate field in other sections | No |

|  |  |
| --- | --- |
| Term (Variable) | NY |
| Data Type | Valid Value |
| Data (D), Value (V) or Header (H) | V |
| Definition | See C66742  For review context C66742 A term that is used to indicate a question with permissible values of yes/no/unknown/not applicable. |
| User Guidance | Not applicable |
| Conformance | Required |
| Cardinality | One to One, Drug Device Combination Product: Protocol Identifier |
| Relationship content from ToC representing the protocol hierarchy | Title page |
| Relationship (reference to high level conceptual model) |  |
| Value | Yes, No |
| Business rules | **Value** **Allowed**: Yes  **Relationship**: Heading Drug/Device Combination Product; Protocol Identifier  **Concept**: C66742 |
| Duplicate field in other sections | No |

|  |  |
| --- | --- |
| Term (Variable) | Number of Arms |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | H |
| Definition |  |
| User Guidance |  |
| Conformance | Required |
| Cardinality |  |
| Relationship content from ToC representing the protocol hierarchy | Protocol Summary |
| Relationship (reference to high level conceptual model) |  |
| Value | Number of Arms |
| Business rules | Value Allowed: Yes  Relationship: n/a  Concept: n/a |
| Duplicate field in other sections |  |

|  |  |
| --- | --- |
| Term (Variable) | Number of Arms |
| Data Type | integer |
| Data (D), Value (V) or Header (H) | D |
| Definition |  |
| 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 |  |
| Relationship content from ToC representing the protocol hierarchy | Protocol Summary |
| Relationship (reference to high level conceptual model) |  |
| Value | Greatest number of arms |
| Business rules | Value Allowed: Yes  Relationship: n/a  Concept: n/a |
| Duplicate field in other sections |  |

|  |  |
| --- | --- |
| Term (Variable) | Blinding |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | H |
| Definition |  |
| User Guidance |  |
| Conformance | Required |
| Cardinality |  |
| Relationship content from ToC representing the protocol hierarchy | Protocol Summary |
| Relationship (reference to high level conceptual model) |  |
| Value | Blinding |
| Business rules | Value Allowed: Yes  Relationship: n/a  Concept: n/a |
| Duplicate field in other sections |  |

|  |  |
| --- | --- |
| Term (Variable) | The following roles indicated below will not be made aware of the treatment group assignment during the trial |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | H |
| Definition |  |
| User Guidance |  |
| Conformance | Required |
| Cardinality |  |
| Relationship content from ToC representing the protocol hierarchy | Protocol Summary |
| Relationship (reference to high level conceptual model) |  |
| Value | The following roles indicated below will not be made aware of the treatment group assignment during the trial |
| Business rules | Value Allowed: Yes  Relationship: n/a  Concept: n/a |
| Duplicate field in other sections |  |

|  |  |
| --- | --- |
| Term (Variable) | Blinding roles |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | D |
| Definition |  |
| User Guidance | For trial designs in which these details may differ in one or more trial periods, answer according to the portion of the trial in which the greatest blinding occurs. More details can be provided in the main body of the protocol. Note that this list does not include Sponsor staff or their designees who are routinely unmasked to complete ongoing safety oversight and surveillance reporting. |
| Conformance | Required / Conditional |
| Cardinality |  |
| Relationship content from ToC representing the protocol hierarchy | Protocol Summary |
| Relationship (reference to high level conceptual model) |  |
| Value | Participant, Care Provider, Investigator, Outcomes Assessor, Not applicable, No Blinding |
| Business rules | Value Allowed: Yes  Relationship: n/a  Concept: n/a |
| Duplicate field in other sections |  |

|  |  |
| --- | --- |
| Term (Variable) | Number of participants |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | H |
| Definition |  |
| User Guidance |  |
| Conformance | Required |
| Cardinality |  |
| Relationship content from ToC representing the protocol hierarchy | Protocol Summary |
| Relationship (reference to high level conceptual model) |  |
| Value |  |
| Business rules | Value Allowed: n/a  Relationship: n/a  Concept: n/a |
| Duplicate field in other sections |  |

|  |  |
| --- | --- |
| Term (Variable) | Number |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | H |
| Definition |  |
| User Guidance | State the expected number of participants to be assigned to trial intervention. Indicate whether the number provided is the target or maximum number of individuals to be enrolled. |
| Conformance | Required |
| Cardinality |  |
| Relationship content from ToC representing the protocol hierarchy | Protocol Summary |
| Relationship (reference to high level conceptual model) |  |
| Value | Number |
| Business rules | Value Allowed: Yes  Relationship: n/a  Concept: n/a |
| Duplicate field in other sections |  |

|  |  |
| --- | --- |
| Term (Variable) | [randomly assigned to trial intervention/enrolled] |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | D |
| Definition |  |
| User Guidance |  |
| Conformance | Required |
| Cardinality |  |
| Relationship content from ToC representing the protocol hierarchy | Protocol Summary |
| Relationship (reference to high level conceptual model) |  |
| Value | Randomly assigned to Trial intervention/ enrolled |
| Business rules | Value Allowed: Yes  Relationship: n/a  Concept: n/a |
| Duplicate field in other sections |  |

|  |  |
| --- | --- |
| Term (Variable) | {x} |
| Data Type | Integer |
| Data (D), Value (V) or Header (H) | D |
| Definition |  |
| User Guidance |  |
| Conformance | Required |
| Cardinality |  |
| Relationship content from ToC representing the protocol hierarchy | Protocol Summary |
| Relationship (reference to high level conceptual model) |  |
| Value |  |
| Business rules | Value Allowed: Yes  Relationship: n/a  Concept: n/a |
| Duplicate field in other sections |  |

|  |  |
| --- | --- |
| Term (Variable) | [Target/Maximum] |
| Data Type | Integer |
| Data (D), Value (V) or Header (H) | D |
| Definition |  |
| User Guidance |  |
| Conformance | Required |
| Cardinality |  |
| Relationship content from ToC representing the protocol hierarchy | Protocol Summary |
| Relationship (reference to high level conceptual model) |  |
| Value | Target/Maximum |
| Business rules | Value Allowed: Yes  Relationship: n/a  Concept: n/a |
| Duplicate field in other sections |  |

|  |  |
| --- | --- |
| Term (Variable) | Arms and Duration |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | H |
| Definition |  |
| User Guidance | Select the text that applies to the trial. Note that total duration of participation should include any washout and any follow-up periods in which the participant is not receiving trial intervention. Where the total durations can be provided, indicate whether the duration is approximate, and delete terms that are not applicable (for example, for a trial of only a few days, delete the years and months terms). When duration cannot be approximated, provide a short explanation (for example, “event-driven” or “adaptive design”). |
| Conformance | Required |
| Cardinality |  |
| Relationship content from ToC representing the protocol hierarchy | Protocol Summary |
| Relationship (reference to high level conceptual model) |  |
| Value | Arms and Duration |
| Business rules | Value Allowed: Yes  Relationship: n/a  Concept: n/a |
| Duplicate field in other sections |  |

|  |  |
| --- | --- |
| Term (Variable) | Total duration of trial intervention for each participant: |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | H |
| Definition |  |
| User Guidance |  |
| Conformance | Required |
| Cardinality |  |
| Relationship content from ToC representing the protocol hierarchy | Protocol Summary |
| Relationship (reference to high level conceptual model) |  |
| Value | Total duration of trial intervention for each participant: |
| Business rules | Value Allowed: Yes  Relationship: n/a  Concept: n/a |
| Duplicate field in other sections |  |

|  |  |
| --- | --- |
| Term (Variable) | Approximately |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | D |
| Definition |  |
| User Guidance |  |
| Conformance | Choice 1 / Required |
| Cardinality |  |
| Relationship content from ToC representing the protocol hierarchy | Protocol Summary |
| Relationship (reference to high level conceptual model) |  |
| Value | Approximately |
| Business rules | Value Allowed: Yes  Relationship: n/a  Concept: n/a |
| Duplicate field in other sections |  |

|  |  |
| --- | --- |
| Term (Variable) | X |
| Data Type | Integer |
| Data (D), Value (V) or Header (H) | D |
| Definition |  |
| User Guidance |  |
| Conformance | Required |
| Cardinality |  |
| Relationship content from ToC representing the protocol hierarchy | Protocol Summary |
| Relationship (reference to high level conceptual model) |  |
| Value |  |
| Business rules | Value Allowed: n/a  Relationship: n/a  Concept: n/a |
| Duplicate field in other sections |  |

|  |  |
| --- | --- |
| Term (Variable) | Year(s)/[x] Month(s)/[x] Day(s) |
| Data Type | Pick List |
| Data (D), Value (V) or Header (H) | D |
| Definition |  |
| User Guidance |  |
| Conformance | Required |
| Cardinality |  |
| Relationship content from ToC representing the protocol hierarchy | Protocol Summary |
| Relationship (reference to high level conceptual model) |  |
| Value |  |
| Business rules | Value Allowed: n/a  Relationship: n/a  Concept: n/a |
| Duplicate field in other sections |  |

|  |  |
| --- | --- |
| Term (Variable) | Duration will vary |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | D |
| Definition |  |
| User Guidance |  |
| Conformance | Choice 2 |
| Cardinality |  |
| Relationship content from ToC representing the protocol hierarchy | Protocol Summary |
| Relationship (reference to high level conceptual model) |  |
| Value | Duration will vary |
| Business rules | Value Allowed: Yes  Relationship: n/a  Concept: n/a |
| Duplicate field in other sections |  |

|  |  |
| --- | --- |
| Term (Variable) | Reason duration of trial participation will vary |
| Data Type | Pick List |
| Data (D), Value (V) or Header (H) | D |
| Definition |  |
| User Guidance |  |
| Conformance | Required |
| Cardinality |  |
| Relationship content from ToC representing the protocol hierarchy | Protocol Summary |
| Relationship (reference to high level conceptual model) |  |
| Value | “Event-driven” or “adaptive design |
| Business rules | Value Allowed: Yes  Relationship: Complete  Concept: n/a |
| Duplicate field in other sections |  |

|  |  |
| --- | --- |
| Term (Variable) | Arms and Duration Description |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | H |
| Definition |  |
| User Guidance |  |
| Conformance | Optional |
| Cardinality |  |
| Relationship content from ToC representing the protocol hierarchy | Protocol Summary |
| Relationship (reference to high level conceptual model) |  |
| Value | Arms and Duration Description |
| Business rules | Value Allowed: Yes  Relationship: n/a  Concept: n/a |
| Duplicate field in other sections |  |

|  |  |
| --- | --- |
| Term (Variable) | Total duration of trial participation for each participant with sequence and duration of trial periods (for example, screening, run-in, fixed dose/titration, follow-up/washout periods |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | D |
| Definition |  |
| User Guidance |  |
| Conformance | Optional |
| Cardinality |  |
| Relationship content from ToC representing the protocol hierarchy | Protocol Summary |
| Relationship (reference to high level conceptual model) |  |
| Value |  |
| Business rules | Value Allowed: n/a  Relationship: n/a  Concept: n/a |
| Duplicate field in other sections |  |

|  |  |
| --- | --- |
| Term (Variable) | Dose regimens in each trial period and stage (if applicable) including frequency (for example, twice daily) and route of administration and criteria for individualised dosing (for example, participant weight or plasma concentrations), if applicable. |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | D |
| Definition |  |
| User Guidance |  |
| Conformance | Optional |
| Cardinality |  |
| Relationship content from ToC representing the protocol hierarchy | Protocol Summary |
| Relationship (reference to high level conceptual model) |  |
| Value |  |
| Business rules | Value Allowed: n/a  Relationship: n/a  Concept: n/a |
| Duplicate field in other sections |  |

|  |  |
| --- | --- |
| Term (Variable) | Rules/procedures for any dose changes/adjustments including flexible dosing; dose reductions, dose interruptions, or tapering; discontinuation; and any circumstances for resuming trial intervention, as applicable |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | D |
| Definition |  |
| User Guidance |  |
| Conformance | Optional |
| Cardinality |  |
| Relationship content from ToC representing the protocol hierarchy | Protocol Summary |
| Relationship (reference to high level conceptual model) |  |
| Value |  |
| Business rules | Value Allowed: n/a  Relationship: n/a  Concept: n/a |
| Duplicate field in other sections |  |

|  |  |
| --- | --- |
| Term (Variable) | Committee |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | H |
| Definition |  |
| 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 at the Sponsor’s discretion in the separate space provided. Committees listed here should be fully described in Section 10.3, Committees Structure. |
| Conformance | Required |
| Cardinality |  |
| Relationship content from ToC representing the protocol hierarchy | Protocol Summary |
| Relationship (reference to high level conceptual model) |  |
| Value | Committee |
| Business rules | Value Allowed: Yes  Relationship: n/a  Concept: n/a |
| Duplicate field in other sections |  |

|  |  |
| --- | --- |
| Term (Variable) | Committee Name |
| Data Type | Pick List |
| Data (D), Value (V) or Header (H) | D |
| Definition |  |
| User Guidance |  |
| Conformance | Required |
| Cardinality |  |
| Relationship content from ToC representing the protocol hierarchy | Protocol Summary |
| Relationship (reference to high level conceptual model) |  |
| Value | Data Monitoring Committee, Dose Escalation Committee, or Endpoint Adjudication Committee, other none |
| Business rules | Value Allowed: Yes  Relationship: n/a  Concept: n/a |
| Duplicate field in other sections |  |

|  |  |
| --- | --- |
| Term (Variable) | sponsor committee |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | D |
| Definition |  |
| User Guidance |  |
| Conformance | Optional |
| Cardinality |  |
| Relationship content from ToC representing the protocol hierarchy | Protocol Summary |
| Relationship (reference to high level conceptual model) |  |
| Value |  |
| Business rules | Value Allowed: n/a  Relationship: n/a  Concept: n/a |
| Duplicate field in other sections | Repeat as needed |

|  |  |
| --- | --- |
| Term (Variable) | Independent Committees: |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | H |
| Definition |  |
| User Guidance |  |
| Conformance | Required |
| Cardinality |  |
| Relationship content from ToC representing the protocol hierarchy | Protocol Summary |
| Relationship (reference to high level conceptual model) |  |
| Value | Independent Committees: |
| Business rules | Value Allowed: Yes  Relationship: n/a  Concept: n/a |
| Duplicate field in other sections |  |

|  |  |
| --- | --- |
| Term (Variable) | Independent Committee Name |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | D |
| Definition |  |
| User Guidance |  |
| Conformance | Required |
| Cardinality |  |
| Relationship content from ToC representing the protocol hierarchy | Protocol Summary |
| Relationship (reference to high level conceptual model) |  |
| Value | n/a or text value |
| Business rules | Value Allowed: Yes  Relationship: n/a  Concept: n/a |
| Duplicate field in other sections | Repeat as needed |

|  |  |
| --- | --- |
| Term (Variable) | Independent Other committee |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | D |
| Definition |  |
| User Guidance |  |
| Conformance | Optional |
| Cardinality |  |
| Relationship content from ToC representing the protocol hierarchy | Protocol Summary |
| Relationship (reference to high level conceptual model) |  |
| Value |  |
| Business rules | Value Allowed: n/a  Relationship: n/a  Concept: n/a |
| Duplicate field in other sections | Repeat as needed |

|  |  |
| --- | --- |
| Term (Variable) | other Committees: |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | H |
| Definition |  |
| User Guidance |  |
| Conformance | Optional |
| Cardinality |  |
| Relationship content from ToC representing the protocol hierarchy | Protocol Summary |
| Relationship (reference to high level conceptual model) |  |
| Value | other Committees: |
| Business rules | Value Allowed: Yes  Relationship: n/a  Concept: n/a |
| Duplicate field in other sections |  |

|  |  |
| --- | --- |
| Term (Variable) | Other Committee Name |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | D |
| Definition |  |
| User Guidance |  |
| Conformance | Optional |
| Cardinality |  |
| Relationship content from ToC representing the protocol hierarchy | Protocol Summary |
| Relationship (reference to high level conceptual model) |  |
| Value |  |
| Business rules | Value Allowed: n/a  Relationship: n/a  Concept: n/a |
| Duplicate field in other sections |  |

## Trial Schema

|  |  |
| --- | --- |
| Term (Variable) | Trial Schema |
| Data Type | Text |
| Data (D), Value (V) or Header (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 [for example, 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 |  |
| Relationship content from ToC representing the protocol hierarchy | Protocol Summary |
| Relationship (reference to high level conceptual model) |  |
| Value | Trial Schema |
| Business rules | Value Allowed: Yes  Relationship: n/a  Concept: n/a |
| Duplicate field in other sections |  |

|  |  |
| --- | --- |
| Term (Variable) | Trial Schema |
| Data Type | Image |
| Data (D), Value (V) or Header (H) | D |
| Definition | Visual depiction of the trial design, orienting users of the protocol to the key features of the trial design. The schema depicts the flow of individual participants through the progression of trialtrial period(s)/epochs (such as screening, washout/run-in, intervention, and key milestones (for example, randomisation, crossover, end of treatment). |
| User Guidance | Key visits may also be included to aid understanding and accurate execution of the trial and should correspond to the details presented in the Schedule of Activities. Reviewers will appreciate information regarding the number of subjects per treatment group, number of treatment groups, how participants are randomised to treatment groups, and duration of trial. Usually, trial schemas are presented with time progressing from left to right. The page can be changed to landscape orientation, if necessary.  The schema should fit onto a single page and reflect the entire duration of the trial. For complex trials, additional schemas may be added to describe activities or trial periods in greater detail. |
| Conformance | Required |
| Cardinality |  |
| Relationship content from ToC representing the protocol hierarchy | Protocol Summary |
| Relationship (reference to high level conceptual model) |  |
| Value |  |
| Business rules | Value Allowed: n/a  Relationship: n/a  Concept: n/a |
| Duplicate field in other sections |  |

|  |  |
| --- | --- |
| Term (Variable) | Trial Schema discussion |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | D |
| Definition |  |
| User Guidance |  |
| Conformance | Optional |
| Cardinality |  |
| Relationship content from ToC representing the protocol hierarchy | Protocol Summary |
| Relationship (reference to high level conceptual model) |  |
| Value |  |
| Business rules | Value Allowed: n/a  Relationship: n/a  Concept: n/a |
| Duplicate field in other sections |  |

## Schedule of Activities

|  |  |
| --- | --- |
| Term (Variable) | Schedule of Activities |
| Data Type | Text |
| Data (D), Value (V) or Header (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, for example, 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. |
| Conformance | Required |
| Cardinality |  |
| Relationship content from ToC representing the protocol hierarchy | Protocol Summary |
| Relationship (reference to high level conceptual model) |  |
| Value | Schedule of Activities |
| Business rules | Value Allowed: Yes  Relationship: n/a  Concept: n/a |
| Duplicate field in other sections |  |

|  |  |
| --- | --- |
| Term (Variable) | Schedule of Activities |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | D |
| Definition |  |
| User Guidance |  |
| Conformance | Required |
| Cardinality |  |
| Relationship content from ToC representing the protocol hierarchy | Protocol Summary |
| Relationship (reference to high level conceptual model) |  |
| Value |  |
| Business rules | Value Allowed: n/a  Relationship: n/a  Concept: n/a |
| Duplicate field in other sections |  |

# Introduction

|  |  |
| --- | --- |
| Term (Variable) | 2 Introduction |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | H |
| Definition | Heading |
| User Guidance | No text is intended here (header only). |
| Conformance | Required |
| Cardinality | One |
| Relationship content from ToC representing the protocol hierarchy | 2 Introduction |
| Relationship (reference to high level conceptual model) |  |
| Value | 2 Introduction |
| Business rules | Value Allowed: 2  Relationship: Table of content  Concept: Header, Identifier |
| Duplicate field in other sections | No |

## Purpose of Trial

|  |  |
| --- | --- |
| Term (Variable) | 2.1 Purpose of Trial |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | H |
| Definition | Heading |
| User Guidance | N/A |
| Conformance | Required |
| Cardinality | One |
| Relationship content from ToC representing the protocol hierarchy | 2 Introduction |
| Relationship (reference to high level conceptual model) |  |
| Value | 2.1 Purpose of Trial |
| Business rules | Value Allowed: 2.1  Relationship: Table of content  Concept: Header, Identifier |
| Duplicate field in other sections | No |

|  |  |
| --- | --- |
| Term (Variable) | <Description of Purpose of Trial> |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | D |
| Definition | C146997  The overall rationale, reason, or intention of the clinical trial. |
| User Guidance | Explain why the trial is needed, why the research questions being asked are important. Do not restate the objectives or estimands. Do not restate the IB, but may cross-reference to the IB as applicable to the description. |
| Conformance | Required |
| Cardinality | One |
| Relationship content from ToC representing the protocol hierarchy | Introduction |
| Relationship (reference to high level conceptual model) |  |
| Value | Text |
| Business rules | Value Allowed: Text  Relationship: 2.1 Purpose of Trial  Concept: C146997 |
| Duplicate field in other sections | No |

## Summary of Benefits and Risks

|  |  |
| --- | --- |
| Term (Variable) | 2.2 Summary of Benefits and Risks |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | H |
| Definition | Heading |
| User Guidance | Include an assessment of known and potential risks and benefits, if any, from the perspective of an individual participant, including the basis of the risk (for example, nonclinical studies or prior clinical trials). Optional level 3 subheadings are provided to assist with organization of the section; alternatively, the section may be summarized in a single section utilizing the overall benefit-risk entry point. |
| Conformance | Required |
| Cardinality | One |
| Relationship content from ToC representing the protocol hierarchy | Introduction |
| Relationship (reference to high level conceptual model) |  |
| Value | 2.2 Summary of Benefits and Risks |
| Business rules | Value Allowed: Yes  Relationship: Table of content  Concept: n/a |
| Duplicate field in other sections | No |

### Benefit Summary

|  |  |
| --- | --- |
| Term (Variable) | 2.2.1 Benefit Summary |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | H |
| Definition |  |
| User Guidance |  |
| Conformance | Optional |
| Cardinality |  |
| Relationship content from ToC representing the protocol hierarchy | Introduction |
| Relationship (reference to high level conceptual model) |  |
| Value | Benefit Summary |
| Business rules | Value Allowed: Yes  Relationship: n/a  Concept: n/a |
| Duplicate field in other sections | No |

|  |  |
| --- | --- |
| Term (Variable) | <Benefit Summary> |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | D |
| Definition | CNEW  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, 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 |  |
| Relationship content from ToC representing the protocol hierarchy | Introduction |
| Relationship (reference to high level conceptual model) |  |
| Value |  |
| Business rules | Value Allowed: n/a  Relationship: n/a  Concept: CNEW |
| Duplicate field in other sections | No |

### Risk Summary and Mitigation Strategy

|  |  |
| --- | --- |
| Term (Variable) | 2.2.2 Risk Summary and Mitigation Strategy |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | H |
| Definition | Heading |
| User Guidance | N/A |
| Conformance | Optional |
| Cardinality |  |
| Relationship content from ToC representing the protocol hierarchy | Introduction |
| Relationship (reference to high level conceptual model) |  |
| Value | Risk Summary and Mitigation Strategy |
| Business rules | Value Allowed: Yes  Relationship: n/a  Concept: n/a |
| Duplicate field in other sections | No |

|  |  |
| --- | --- |
| Term (Variable) | <Trial-specific Intervention Risks and Mitigations> |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | D |
| Definition | CNEW  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 |  |
| Relationship content from ToC representing the protocol hierarchy | Introduction |
| Relationship (reference to high level conceptual model) |  |
| Value |  |
| Business rules | Value Allowed: n/a  Relationship: n/a  Concept: n/a |
| Duplicate field in other sections | No |

|  |  |
| --- | --- |
| Term (Variable) | <Trial-specific Procedure Risks and Mitigations> |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | D |
| Definition | CNEW  A description of the potential risks associated with the trial procedures and mitigation strategies to be employed within the trial. |
| User Guidance | Trial Procedures – Consider risks associated with the design (for example, placebo arm) and procedures specific to THIS trial (for example, biopsies), and any measures to control or mitigate the risks. Provide a brief description of strategies to mitigate identified risks or provide a cross-reference to the relevant protocol section. This is not intended to be an exhaustive list of all possible risks associated with trial procedures but should focus on the unique risks inherent in the design or less common or high-risk procedures. As above, provide a brief description of strategies to mitigate identified risks or provide a cross-reference to the relevant protocol section. |
| Conformance | Optional |
| Cardinality |  |
| Relationship content from ToC representing the protocol hierarchy | Introduction |
| Relationship (reference to high level conceptual model) |  |
| Value |  |
| Business rules | Value Allowed: n/a  Relationship: n/a  Concept: n/a |
| Duplicate field in other sections | No |

|  |  |
| --- | --- |
| Term (Variable) | <Trial-specific Other Risks and Mitigations> |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | D |
| Definition | CNEW  A description of the potential risks associated with other trial-related agents and mitigation strategies to be employed within the trial. |
| User Guidance | Other – Consider risks associated with other items (for example, challenge agents, imaging agents, medical devices). This could include discussion of risk mitigation for special populations, if not described elsewhere. Insert a line for each, as needed. |
| Conformance | Optional |
| Cardinality |  |
| Relationship content from ToC representing the protocol hierarchy | Introduction |
| Relationship (reference to high level conceptual model) |  |
| Value |  |
| Business rules | Value Allowed: n/a  Relationship: n/a  Concept: n/a |
| Duplicate field in other sections | No |

### Overall Benefit:Risk:Conclusion

|  |  |
| --- | --- |
| Term (Variable) | 2.3.2 Overall Benefit:Risk Conclusion |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | H |
| Definition | Heading |
| User Guidance |  |
| Conformance | Optional |
| Cardinality |  |
| Relationship content from ToC representing the protocol hierarchy | Introduction |
| Relationship (reference to high level conceptual model) |  |
| Value | 2.3.2 Overall Benefit:Risk Conclusion |
| Business rules | Value Allowed: Yes  Relationship: n/a  Concept: CNEW |
| Duplicate field in other sections | No |

|  |  |
| --- | --- |
| Term (Variable) | <Overall Benefit:Risk Conclusion> |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | D |
| Definition | CNEW  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 |  |
| Relationship content from ToC representing the protocol hierarchy | Introduction |
| Relationship (reference to high level conceptual model) |  |
| Value |  |
| Business rules | Value Allowed: n/a  Relationship: n/a  Concept: CNEW |
| Duplicate field in other sections | No |

# Trial Objectives, Endpoints and Estimands

|  |  |
| --- | --- |
| Term (Variable) | Trial Objectives, Endpoints, and Estimands |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | H |
| Definition | Heading |
| User Guidance | In this section, precisely define each clinical question of interest by stating each trial objective and specifying the endpoint(s) and estimand(s) that correspond to each trial objective. Ensure alignment with every other section of the protocol.  Include additional level 2 headers under Section 3 Trial Objectives, Endpoints, and Estimands as needed. |
| Conformance | Required |
| Cardinality |  |
| Relationship content from ToC representing the protocol hierarchy | Trial Objectives, Endpoints, and Estimands |
| Relationship (reference to high level conceptual model) |  |
| Value | Trial Objectives, Endpoints, and Estimands |
| Business rules | Value Allowed:  Relationship: Master for Summary of Changes in Current Amendment  Concept: n/a |
| Duplicate field in other sections |  |

## {Primary/Secondary/Exploratory} Objective + Associated Endpoint {and Estimand}

|  |  |
| --- | --- |
| Term (Variable) | {Primary/Secondary/Exploratory} Objective + Associated Endpoint {and Estimand} |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | H |
| Definition |  |
| User Guidance |  |
| Conformance | Required / Repeated |
| Cardinality |  |
| Relationship content from ToC representing the protocol hierarchy | Trial Objectives, Endpoints, and Estimands |
| Relationship (reference to high level conceptual model) |  |
| Value | 3.X {Primary/Secondary/Exploratory} Objective + Associated Endpoint {and Estimand} |
| Business rules | Value Allowed: Yes  Relationship: Repeats for Primary, Secondary, Exploratory  Concept: n/a |
| Duplicate field in other sections | Repeated and numbered for each objective-endpoint(s) combination |

|  |  |
| --- | --- |
| Term (Variable) | {Primary/Secondary/Exploratory} Objective |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | H |
| Definition |  |
| User Guidance |  |
| Conformance | Required / Repeated |
| Cardinality |  |
| Relationship content from ToC representing the protocol hierarchy | Trial Objectives, Endpoints, and Estimands |
| Relationship (reference to high level conceptual model) |  |
| Value | {Primary/Secondary/Exploratory} Objective |
| Business rules | Value Allowed: Yes  Relationship: "Table Headers  Repeats for primary, Secondary, Exploratory"  Concept: n/a |
| Duplicate field in other sections | Repeated and numbered for each objective-endpoint(s) Combination |

|  |  |
| --- | --- |
| Term (Variable) | {Primary/Secondary/Exploratory} Endpoint |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | H |
| Definition |  |
| User Guidance |  |
| Conformance | Required / Repeated |
| Cardinality |  |
| Relationship content from ToC representing the protocol hierarchy | Trial Objectives, Endpoints, and Estimands |
| Relationship (reference to high level conceptual model) |  |
| Value | {Primary/Secondary/Exploratory} Endpoint |
| Business rules | Value Allowed: Yes  Relationship: Table Headers  Repeats for primary, Secondary, Exploratory  Concept: n/a |
| Duplicate field in other sections | Repeated and numbered for each objective-endpoint(s) Combination |

|  |  |
| --- | --- |
| Term (Variable) | [Objective] |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | D |
| Definition |  |
| User Guidance |  |
| Conformance | Required / one per number |
| Cardinality |  |
| Relationship content from ToC representing the protocol hierarchy | Trial Objectives, Endpoints, and Estimands |
| Relationship (reference to high level conceptual model) |  |
| Value |  |
| Business rules | Value Allowed: n/a  Relationship: "Table Entry one per number  Repeats for additional"  Concept: n/a |
| Duplicate field in other sections | Multiple relates to objective  Repeated and numbered for each objective-endpoint(s) combination |

|  |  |
| --- | --- |
| Term (Variable) | [Endpoint] |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | D |
| Definition |  |
| User Guidance |  |
| Conformance | Required / Repeated |
| Cardinality |  |
| Relationship content from ToC representing the protocol hierarchy | Trial Objectives, Endpoints, and Estimands |
| Relationship (reference to high level conceptual model) |  |
| Value |  |
| Business rules | Value Allowed: n/a  Relationship: Table entry relates to objective multiple for objective  Repeats as aligned with objective  Repeats  Concept: n/a |
| Duplicate field in other sections | One per number area  Repeated and numbered for each objective-endpoint(s) combination |

|  |  |
| --- | --- |
| Term (Variable) | {Primary/Secondary/Exploratory} Estimand |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | H |
| Definition | Heading |
| User Guidance |  |
| Conformance | Required / Repeated |
| Cardinality |  |
| Relationship content from ToC representing the protocol hierarchy | Trial Objectives, Endpoints, and Estimands |
| Relationship (reference to high level conceptual model) |  |
| Value | {Primary/Secondary/Exploratory} Estimand |
| Business rules | Value Allowed: Yes  Relationship: Repeat for  Concept: n/a |
| Duplicate field in other sections | Repeated and numbered for each objective-endpoint(s) combination |

|  |  |
| --- | --- |
| Term (Variable) | [Estimand Description] |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | D |
| Definition |  |
| User Guidance | Describe the attributes that construct the estimand: the treatment condition of interest, the population of patients targeted by the clinical question of interest, other intercurrent events (if applicable), a population level summary, and the endpoint (or variable) specified in the table above. |
| Conformance | Required / Repeat for |
| Cardinality |  |
| Relationship content from ToC representing the protocol hierarchy | Trial Objectives, Endpoints, and Estimands |
| Relationship (reference to high level conceptual model) |  |
| Value |  |
| Business rules | Value Allowed: n/a  Relationship: Repeat for  Concept: n/a |
| Duplicate field in other sections | Repeated and numbered for each objective-endpoint(s) Combination |

# Trial Design

|  |  |
| --- | --- |
| Term (Variable) | Trial Design |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | H |
| Definition | Heading |
| User Guidance | N/A |
| Conformance | Required |
| Cardinality | One |
| Relationship content from ToC representing the protocol hierarchy | Trial Design |
| Relationship (reference to high level conceptual model) | One to one |
| Value | Trial Design |
| Business rules | Value Allowed: 4. Trial Design  Relationship: Table of content  Concept: Header |
| Duplicate field in other sections | Yes, for |

## Description of Trial Design

|  |  |
| --- | --- |
| Term (Variable) | Description of Trial Design |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | H |
| Definition | Header |
| User Guidance | N/A |
| Conformance | Required |
| Cardinality | One to many |
| Relationship content from ToC representing the protocol hierarchy | Trial Design |
| Relationship (reference to high level conceptual model) |  |
| Value | Description of Trial Design |
| Business rules | Value Allowed: 4.1 Description of Trial Design  Relationship: Table of Contents  Concept: Header |
| Duplicate field in other sections | Repeatable  <Enter Description of Intervention Model>  <Enter Description of Trial Duration>  <Enter Method of Assignment to Trial Intervention>  <Enter Level of Blinding>  <Enter Method of Blinding> |

|  |  |
| --- | --- |
| Term (Variable) | <Description of Intervention Model> |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | D |
| Definition | See CNew  For review context CNEW  A narrative representation of the trial intervention model. |
| User Guidance | Describe the trial intervention model (for example, single group, parallel group, cross-over, factorial, sequential), the expected number of participants, and the control method (for example, placebo, active comparator, low dose, historical, standard of care, sham procedure, or none [uncontrolled]). If there are any key aspects of the investigational trial intervention that inform the selection of intervention model, this should be described.  If applicable, indicate other design characteristics (for example, superiority, non-inferiority, dose escalation, or equivalence).  If the trial will have an adaptive or novel design (for example, the trial will be conducted under a master protocol), provide a summary of these design aspects.  If applicable, describe within-trial transition rules, for example, transitions involving cohorts or trial parts. Dose escalation or dose-ranging details should also be described. |
| Conformance | Optional |
| Cardinality | One to many |
| Relationship content from ToC representing the protocol hierarchy | Trial Design |
| Relationship (reference to high level conceptual model) |  |
| Value | Text |
| Business rules | Value Allowed: Yes  Relationship: 4.1 Description of Trial Design  Concept: CNEW |
| Duplicate field in other sections | Repeatble for each unique study design |

|  |  |
| --- | --- |
| Term (Variable) | <Description of Trial Duration> |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | D |
| Definition | See CNew  For review context CNEW  A narrative representation of the trial duration. |
| 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 (for example, 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 | Trial Design |
| Relationship (reference to high level conceptual model) |  |
| Value | Text |
| Business rules | Value Allowed: Yes  Relationship: 4.1 Description of Trial Design  Concept: CNEW |
| Duplicate field in other sections | Repeatble for each unique study design |

|  |  |
| --- | --- |
| Term (Variable) | <Method of Assignment to Trial Intervention> |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | D |
| Definition | See CNew  For review context CNEW  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 6.8. |
| Conformance | Optional |
| Cardinality | One to many |
| Relationship content from ToC representing the protocol hierarchy | Trial Design |
| Relationship (reference to high level conceptual model) | Nick |
| Value | Text |
| Business rules | Value Allowed: Yes  Relationship: 4.1 Description of Trial Design  Concept: CNEW |
| Duplicate field in other sections | Repeatble for each unique study design |

|  |  |
| --- | --- |
| Term (Variable) | <Describe Level of Blinding> |
| Data Type |  |
| Data (D), Value (V) or Header (H) | Text |
| Definition | See CNew  For review context CNEW  We need definition |
| User Guidance | No text |
| Conformance | Optional |
| Cardinality | One to One |
| Relationship content from ToC representing the protocol hierarchy | Trial Design |
| Relationship (reference to high level conceptual model) |  |
| Value | Text |
| Business rules | Value Allowed: Yes  Relationship: 4.1 Description of Trial Design  Concept: CNEW |
| Duplicate field in other sections | Repeatble for each unique study design |

|  |  |
| --- | --- |
| Term (Variable) | <Describe Method of Blinding> |
| Data Type |  |
| Data (D), Value (V) or Header (H) | Text |
| Definition | See CNew  For review context CNEW  We need definition |
| User Guidance | No text |
| Conformance | Optional |
| Cardinality | One to One |
| Relationship content from ToC representing the protocol hierarchy | Trial Design |
| Relationship (reference to high level conceptual model) |  |
| Value | Text |
| Business rules | Value Allowed: Yes  Relationship: 4.1 Description of Trial Design  Concept: CNEW |
| Duplicate field in other sections | Repeatble for each unique study design |

|  |  |
| --- | --- |
| Term (Variable) | <Additional Description of Trial Design> |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | D |
| Definition | See CNew  For review context CNEW  An extra or further textual representation of the trial design. |
| User Guidance | Describe any other important aspects of the design, for example:   * Geographic scope of trial (for example, 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 10.4, Committees, for details, * Whether an interim analysis is planned and, if so, refer to details in Section 9.13, Interim Analysis, and/or * 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 | Trial Design |
| Relationship (reference to high level conceptual model) |  |
| Value | Text |
| Business rules | Value Allowed: Yes  Relationship: 4.1 Description of Trial Design  Concept: CNEW |
| Duplicate field in other sections | Repeatble for each unique study design |

### Stakeholder Input into Design

|  |  |
| --- | --- |
| Term (Variable) | Stakeholder Input into Design |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | H |
| Definition | Heading |
| User Guidance | N/A |
| Conformance | Optional |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | Trial Design |
| Relationship (reference to high level conceptual model) |  |
| Value | Description of Trial Design |
| Business rules | Value Allowed: 4.1. Description of Trial Design  Relationship: 4.1 Description of Trial Design and Table of Contents  Concept: Header |
| Duplicate field in other sections | No |

|  |  |
| --- | --- |
| Term (Variable) | <Stakeholder Input into Design> |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | D |
| Definition | See CNew  For review context CNEW  The textual representation of the way in which trial stakeholders were consulted when determining the trial design. |
| User Guidance | If applicable, describe any stakeholder (for example, patient, healthcare professional, regulatory agencies 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 | Trial Design |
| Relationship (reference to high level conceptual model) |  |
| Value | Text |
| Business rules | Value Allowed: Yes  Relationship: 4.1.1 Stakeholder Input into Design  Concept: CNEW |
| Duplicate field in other sections | Repeatble for each unique study design |

## Rationale for Trial Design

|  |  |
| --- | --- |
| Term (Variable) | Rationale for Trial Design |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | H |
| Definition | Heading |
| User Guidance | N/A |
| Conformance | Required |
| Cardinality | One to many |
| Relationship content from ToC representing the protocol hierarchy | Trial Design |
| Relationship (reference to high level conceptual model) |  |
| Value | Rationale for Trial Design |
| Business rules | Value Allowed: 4.2 Rationale for Trial Design  Relationship: Table of Contents  Concept: Header |
| Duplicate field in other sections | No |

### Rationale for Trial Intervention Model

|  |  |
| --- | --- |
| Term (Variable) | Rationale for Trial Intervention Model |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | H |
| Definition | Heading |
| User Guidance | N/A |
| Conformance | Optional |
| Cardinality | One |
| Relationship content from ToC representing the protocol hierarchy | Trial Design |
| Relationship (reference to high level conceptual model) |  |
| Value | Rationale for Trial Design |
| Business rules | Value Allowed: 4.2 Rational for Trial Design  Relationship: 4.2 Rational for Trial Design and Table of Contents  Concept: Header |
| Duplicate field in other sections | No |

|  |  |
| --- | --- |
| Term (Variable) | <Rationale for Trial Intervention Model> |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | D |
| Definition | See CNew  For review context CNEW  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 6.3, Rationale for Investigational Intervention(s). 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 | Optional |
| Cardinality | One to One |
| Relationship content from ToC representing the protocol hierarchy | Trial Design |
| Relationship (reference to high level conceptual model) |  |
| Value | Text |
| Business rules | Value Allowed: Yes  Relationship: 4.2.1 Rational for Intervention Model  Concept: CNEW |
| Duplicate field in other sections | No |

### Rationale for Trial Duration

|  |  |
| --- | --- |
| Term (Variable) | Rationale for Trial Duration |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | H |
| Definition | Heading |
| User Guidance | N/A |
| Conformance | Optional |
| Cardinality | One to One |
| Relationship content from ToC representing the protocol hierarchy | Trial Design |
| Relationship (reference to high level conceptual model) |  |
| Value | Rational for Trial Design |
| Business rules | Value Allowed: 4.2 Rational for Trial Design  Relationship: 4.2 Rational for Trial Design and Table of Contents  Concept: Header |
| Duplicate field in other sections | No |

|  |  |
| --- | --- |
| Term (Variable) | <Rationale for Trial Duration> |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | D |
| Definition | See CNew  For review context CNEW  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 | Optional |
| Cardinality | One to One |
| Relationship content from ToC representing the protocol hierarchy | Trial Design |
| Relationship (reference to high level conceptual model) |  |
| Value | Text |
| Business rules | Value Allowed: Yes  Relationship: 4.2.2 Rational for Trial Duration  Concept: CNEW |
| Duplicate field in other sections | No |

### Rationale for Estimands

|  |  |
| --- | --- |
| Term (Variable) | Rationale for Estimands |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | H |
| Definition | Heading |
| User Guidance | N/A |
| Conformance | Optional |
| Cardinality | One |
| Relationship content from ToC representing the protocol hierarchy | Trial Design |
| Relationship (reference to high level conceptual model) |  |
| Value | Rational for Trial Design |
| Business rules | Value Allowed: 4.2 Rationale for Trial Design  Relationship: 4.2 Rationale for Trial Design and Table of Contents  Concept: Header |
| Duplicate field in other sections | No |

|  |  |
| --- | --- |
| Term (Variable) | <Rationale for Estimands> |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | D |
| Definition | See CNew  For review context CNEW  An explanation as to the scientific reasons for the choice of the estimand(s), with a specific focus on the trial endpoints and strategies for handling intercurrent ivents. |
| User Guidance | Provide a rationale ~~that~~ for the trial ~~endpoint~~ estimand(s) described in Section 3, ~~Trial Objectives, Endpoints, and Estimands,~~. 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 | Optional |
| Cardinality | One to many |
| Relationship content from ToC representing the protocol hierarchy | Trial Design |
| Relationship (reference to high level conceptual model) |  |
| Value | Text |
| Business rules | Value Allowed: Yes  Relationship: 4.2.3 Rationale for Estimands  Concept: CNEW |
| Duplicate field in other sections | No |

### Rationale for Interim Analysis

|  |  |
| --- | --- |
| Term (Variable) | Rationale for Interim Analysis |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | H |
| Definition | Heading |
| User Guidance | N/A |
| Conformance | Optional |
| Cardinality | One |
| Relationship content from ToC representing the protocol hierarchy | Trial Design |
| Relationship (reference to high level conceptual model) |  |
| Value | Rational for Trial Design |
| Business rules | Value Allowed: 4.2 Rational for Trial Design  Relationship: 4.2 Rational for Trial Design and Table of Contents  Concept: Header |
| Duplicate field in other sections | No |

|  |  |
| --- | --- |
| Term (Variable) | <Rationale for Interim Analysis> |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | D |
| Definition | See CNew  For review context CNEW  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 (for example, stopping the trial early for efficacy or futility) and timing. |
| Conformance | Optional |
| Cardinality |  |
| Relationship content from ToC representing the protocol hierarchy | Trial Design |
| Relationship (reference to high level conceptual model) |  |
| Value | Text |
| Business rules | Value Allowed: Yes  Relationship: 4.2.4 Rational for Interim Analysis  Concept: CNEW |
| Duplicate field in other sections | No |

### Rationale for Control Type

|  |  |
| --- | --- |
| Term (Variable) | Rationale for Control Type |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | H |
| Definition | Header |
| User Guidance | N/A |
| Conformance | Optional |
| Cardinality | One |
| Relationship content from ToC representing the protocol hierarchy | Trial Design |
| Relationship (reference to high level conceptual model) |  |
| Value | Rational for Trial Design |
| Business rules | Value Allowed: 4.2 Rational for Trial Design  Relationship: 4.2 Rational for Trial Design and Table of Contents  Concept: Header |
| Duplicate field in other sections | No |

|  |  |
| --- | --- |
| Term (Variable) | <Rationale for Control Type> |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | D |
| Definition | See CNew  For review context CNEW  An explanation as to the scientific reasons for the choice of the comparator used in the trial. |
| User Guidance | If applicable, provide a rationale for the type and choice of control selected for the trial (for example, placebo, active drug, combination, historical). 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 6.3. |
| Conformance | Optional |
| Cardinality | One to One |
| Relationship content from ToC representing the protocol hierarchy | Trial Design |
| Relationship (reference to high level conceptual model) |  |
| Value | Text |
| Business rules | Value Allowed: Yes  Relationship: 4.2.5 Rational for Control Type  Concept: CNEW |
| Duplicate field in other sections | No |

### Rationale for Adaptive or Novel Trial Design

|  |  |
| --- | --- |
| Term (Variable) | Rationale for Adoptive or Novel Trial Design |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | H |
| Definition | Heading |
| User Guidance | N/A |
| Conformance | Optional |
| Cardinality | One |
| Relationship content from ToC representing the protocol hierarchy | Trial Design |
| Relationship (reference to high level conceptual model) |  |
| Value | Rational for Trial Design |
| Business rules | Value Allowed: 4.2 Rational for Trial Design  Relationship: 4.2 Rational for Trial Design and Table of Contents  Concept: Header |
| Duplicate field in other sections | No |

|  |  |
| --- | --- |
| Term (Variable) | <Rationale for Adoptive or Novel Trial Design> |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | D |
| Definition | See CNew  For review context CNEW  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 | Optional |
| Cardinality | One to One |
| Relationship content from ToC representing the protocol hierarchy | Trial Design |
| Relationship (reference to high level conceptual model) |  |
| Value | Text |
| Business rules | Value Allowed: 4.2 Rational for Trial Design  Relationship: 4.2.6 Rational for Adoptive or Novel Trial Design  Concept: CNEW |
| Duplicate field in other sections | No |

### Rationale for Other Trial Design Aspects

|  |  |
| --- | --- |
| Term (Variable) | Rationale for Other Trial Design Aspects |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | H |
| Definition | Heading |
| User Guidance | N/A |
| Conformance | Optional |
| Cardinality | One |
| Relationship content from ToC representing the protocol hierarchy | Trial Design |
| Relationship (reference to high level conceptual model) |  |
| Value | Rational for Trial Design |
| Business rules | Value Allowed: 4.2 Rational for Trial Design  Relationship: 4.2 Rational for Trial Design and Table of Contents  Concept: Header |
| Duplicate field in other sections |  |

|  |  |
| --- | --- |
| Term (Variable) | <Rationale for Other Trial Design Aspects> |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | D |
| Definition | See CNew  For review context CNEW  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 | Optional |
| Cardinality | One to One |
| Relationship content from ToC representing the protocol hierarchy | Trial Design |
| Relationship (reference to high level conceptual model) |  |
| Value | Text |
| Business rules | Value Allowed: 4.2 Rational for Trial Design  Relationship: 4.2.7 Rational for Other Trial Design Aspects  Concept: CNEW |
| Duplicate field in other sections | No |

## Trial Stopping Rules

|  |  |
| --- | --- |
| Term (Variable) | Trial Stopping Rules |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | H |
| Definition | Heading |
| User Guidance | N/A |
| Conformance | Required |
| Cardinality | One to many |
| Relationship content from ToC representing the protocol hierarchy | Trial Design |
| Relationship (reference to high level conceptual model) |  |
| Value | Trial Stopping Rules |
| Business rules | Value Allowed: 4.3 Trial Stopping Rules  Relationship: Table for Content  Concept: Header |
| Duplicate field in other sections | No |

|  |  |
| --- | --- |
| Term (Variable) | <Trial Stopping Rules> |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | D |
| Definition | See C142698  For review context C142698  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 trials 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 | Trial Design |
| Relationship (reference to high level conceptual model) |  |
| Value | Text |
| Business rules | Value Allowed: Yes  Relationship: 4.3 Trial Stopping Rules  Concept: C142698 |
| Duplicate field in other sections | No |

## Start of Trial and End of Trial

|  |  |
| --- | --- |
| Term (Variable) | Start of Trial and End of Trial |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | H |
| Definition | Heading |
| User Guidance | N/A |
| Conformance | Required |
| Cardinality | One to One |
| Relationship content from ToC representing the protocol hierarchy | Trial Design |
| Relationship (reference to high level conceptual model) |  |
| Value | Start of Trial and End of Trial |
| Business rules | Value Allowed: 4.4 Start of Trial and End of Trial  Relationship: Table of Contents  Concept: Header |
| Duplicate field in other sections | No |

|  |  |
| --- | --- |
| Term (Variable) | <Start of Trial> |
| Data Type | Number |
| Data (D), Value (V) or Header (H) | D |
| Definition | See CNEW  For review context CNEW  We need new def... |
| User Guidance | Define key timepoints in the trial, including trial start and end timepoint definitions. For example, 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 (for example, the first act of recruitment).  If appropriate, provide a cross-reference to Section 11.9 |
| Conformance | Required |
| Cardinality | One |
| Relationship content from ToC representing the protocol hierarchy | Trial Design |
| Relationship (reference to high level conceptual model) |  |
| Value | Number |
| Business rules | Value Allowed: Yes  Relationship: 4.4 Start of Trial and End of Trial  Concept: CNEW |
| Duplicate field in other sections | No |

|  |  |
| --- | --- |
| Term (Variable) | <End of Trial> |
| Data Type | Number |
| Data (D), Value (V) or Header (H) | D |
| Definition | See CNEW  For review context CNEW  We need new def.. |
| User Guidance | Define key timepoints in the trial, including trial start and end timepoint definitions. For example, 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 (for example, the first act of recruitment).  If appropriate, provide a cross-reference to Section 11.9 |
| Conformance | Required |
| Cardinality | One |
| Relationship content from ToC representing the protocol hierarchy | Trial Design |
| Relationship (reference to high level conceptual model) |  |
| Value | Number |
| Business rules | Value Allowed: Yes  Relationship: 4.4 Start of Trial and End of Trial  Concept: CNEW |
| Duplicate field in other sections | No |

## Access to Trial Intervention After End of Trial

|  |  |
| --- | --- |
| Term (Variable) | Access to Trial Intervention After End of Trial |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | H |
| Definition | Heading |
| User Guidance | No text is intended here (header only) |
| Conformance | Required |
| Cardinality | One to many |
| Relationship content from ToC representing the protocol hierarchy | Trial Design |
| Relationship (reference to high level conceptual model) |  |
| Value | Access to Trial Intervention After End of Trial |
| Business rules | Value Allowed: 4.5 Access to Trial Intervention After End of Trial  Relationship: Table of Contents  Concept: Header |
| Duplicate field in other sections | No |

|  |  |
| --- | --- |
| Term (Variable) | <Access to Trial Intervention after End of Trial> |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | D |
| Definition | See CNEW  For review context CNEW  A textual representation containing information about whether and how trial participants have access to the trial interventions after the trial ends. |
| User Guidance |  |
| Conformance | Required |
| Cardinality | One to One |
| Relationship content from ToC representing the protocol hierarchy | Trial Design |
| Relationship (reference to high level conceptual model) |  |
| Value | Text |
| Business rules | Value Allowed: Yes  Relationship: 4.5 Access to Trial Intervention After End of Trial  Concept: CNEW |
| Duplicate field in other sections | No |

# Trial Population

|  |  |
| --- | --- |
| Term (Variable) | 5 Trial Population |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | H |
| Definition | Heading |
| User Guidance | No text is intended here (header only).  In the sub-sections below, describe the trial population: inclusion and exclusion criteria, contraception requirements and lifestyle restrictions. The trial population should generally be aligned with the population attribute of the primary estimand that was defined in Section 3. Consider the following when developing participant eligibility criteria to be listed in Section 5.2, Inclusion Criteria, and Section 5.3, Exclusion Criteria.   * 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. * Identify specific laboratory tests or clinical characteristics that will be used as criteria for inclusion or exclusion. If permitting existing medical diagnosis, imaging, genetic tests, or laboratory results, state any required window or acceptable test type. * 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 Trial Population |
| Relationship (reference to high level conceptual model) |  |
| Value | 5 Trial Population |
| Business rules | Value Allowed: 5 Trial Population  Relationship: Table of content  Concept: Header, Identifier |
| Duplicate field in other sections | No |

## Description of Trial Population and Rationale

|  |  |
| --- | --- |
| Term (Variable) | 5.1 Description of Trial Population and Rationale |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | H |
| Definition | Heading |
| User Guidance | N/A |
| Conformance | Required |
| Cardinality | One-to-one |
| Relationship content from ToC representing the protocol hierarchy | Trial Population |
| Relationship (reference to high level conceptual model) |  |
| Value | Text |
| Business rules | Value Allowed: 5.1 Description of Trial Population and Rationale  Relationship: Table of content  Concept: Header, Identifier |
| Duplicate field in other sections | No |

|  |  |
| --- | --- |
| Term (Variable) | <Description of Trial Population and Rationale> |
| Data Type | Text |
| Data (D), Value (V) or Header (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 enrollment criteria reflect the targeted populations. |
| User Guidance | Describe the population selected (for example, 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 (for example, ≤3 months, ≥18 to ≤80 years old) including the time point at which qualification for age criteria is determined (for example, at time of screening vs randomization for paediatric trials). Specify any key diagnostic criteria for the population (for example, “acute lung injury”, or a specific biomarker profile). If applicable, describe similar conditions or diseases and their differential diagnosis. If the target population is based on a subset of the entire trial population defined by a particular characteristic measured at baseline (e.g., a specific biomarker), this subset should be defined and justified in this section.  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 targeted populations.  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 (for example, elderly, hepatic or renally impaired, or immunocompromised participants). |
| Conformance | Required |
| Cardinality | One-to-one |
| Relationship content from ToC representing the protocol hierarchy | Trial Population |
| Relationship (reference to high level conceptual model) |  |
| Value | 5.1 Description of Trial Population and Rationale |
| Business rules | Value Allowed: Text  Relationship: 5.1 Description of Trial Population and Rationale  Concept: Data Element CNEW |
| Duplicate field in other sections | 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 Header (H) | D |
| Definition | Universal text |
| User Guidance | N/A |
| Conformance | Required |
| Cardinality | One-to-one |
| Relationship content from ToC representing the protocol hierarchy | Trial Population |
| Relationship (reference to high level conceptual model) |  |
| 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: Text  Relationship: 5.1 Description of Trial Population and Rationale  Concept: Template universal text |
| Duplicate field in other sections | No |

## Inclusion Criteria

|  |  |
| --- | --- |
| Term (Variable) | 5.2 Inclusion Criteria |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | H |
| Definition | Header |
| User Guidance | Inclusion criteria are characteristics that define the trial population, for example, those criteria that every potential participant must satisfy, to qualify for trial entry. |
| Conformance | Required |
| Cardinality | One-to-one |
| Relationship content from ToC representing the protocol hierarchy | Trial Population |
| Relationship (reference to high level conceptual model) |  |
| Value | 5.2 Inclusion Criteria |
| Business rules | Value Allowed: 5.2 Inclusion Criteria  Relationship: Table of content  Concept: Heading, Identifier |
| Duplicate field in other sections | No |

|  |  |
| --- | --- |
| 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 Header (H) | D |
| Definition | Universal text |
| User Guidance | N/A |
| Conformance | Required |
| Cardinality | One-to-one |
| Relationship content from ToC representing the protocol hierarchy | 5 Trial Population |
| Relationship (reference to high level conceptual model) |  |
| Value | To be eligible to participate in this trial, an individual must meet all the following criteria: |
| Business rules | Value Allowed: Yes  Relationship: 5.2 Inclusion Criteria  Concept: Template universal text |
| Duplicate field in other sections | No |

|  |  |
| --- | --- |
| Term (Variable) | # Inclusion Criterion |
| Data Type | Number |
| Data (D), Value (V) or Header (H) | D |
| Definition | N/A |
| User Guidance | Add criteria as needed. Number sequentially |
| Conformance | Required  Repeatable new Number |
| Cardinality | One-to-many |
| Relationship content from ToC representing the protocol hierarchy | 5 Trial Population |
| Relationship (reference to high level conceptual model) |  |
| Value | # is an identifier <criterion identifier> unique number and not replaceable |
| Business rules | Value Allowed: Number  Relationship: 5.2 Inclusion Criteria  Concept: Sequential number |
| Duplicate field in other sections | Number consecutively, repeat for each inclusion criterion, if deleted do not replace, do not duplicate |

|  |  |
| --- | --- |
| Term (Variable) | Inclusion Criterion |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | D |
| Definition | See C25532  For review purposes C25532 The criteria in a protocol that prospective subjects must meet to be eligible for participation in a study. (CDISC glossary) |
| User Guidance | Add criteria as needed. Number sequentially |
| Conformance | Required Repeatable |
| Cardinality | One-to-many |
| Relationship content from ToC representing the protocol hierarchy | Trial Population |
| Relationship (reference to high level conceptual model) |  |
| Value | <Inclusion Criterion> |
| Business rules | Value Allowed: text and special characters  Relationship: to Number #  Concept: C25532 |
| Duplicate field in other sections | Repeat for each inclusion criterion, if deleted do not replace, do not duplicate |

## Exclusion Criteria

|  |  |
| --- | --- |
| Term (Variable) | Exclusion Criteria |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | H |
| Definition | Header |
| User Guidance | Exclusion criteria are characteristics that make an individual ineligible for participation. |
| Conformance | Required |
| Cardinality | One-to-one |
| Relationship content from ToC representing the protocol hierarchy | Trial Population |
| Relationship (reference to high level conceptual model) |  |
| Value | 5.3 Exclusion Criteria |
| Business rules | Value Allowed: 5.3 Exclusion Criteria  Relationship: Table of content  Concept: Heading, Identifier |
| Duplicate field in other sections | No |

|  |  |
| --- | --- |
| 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 Header (H) | D |
| Definition | Universal text |
| User Guidance | N/A |
| Conformance | Required |
| Cardinality | One-to-one |
| Relationship content from ToC representing the protocol hierarchy | 5 Trial Population |
| Relationship (reference to high level conceptual model) |  |
| Value | An individual who meets any of the following criteria will be excluded from participation in this trial: |
| Business rules | Value Allowed: Yes  Relationship: 5.3 Exclusion Criteria  Concept: Template universal text |
| Duplicate field in other sections | No |

|  |  |
| --- | --- |
| Term (Variable) | # Exclusion Criterion |
| Data Type | Number |
| Data (D), Value (V) or Header (H) | D |
| Definition | N/A |
| User Guidance | Add criteria as needed. Number the criteria sequentially |
| Conformance | Required  Repeatable new Number |
| Cardinality | One-to-many |
| Relationship content from ToC representing the protocol hierarchy | 5 Trial Population |
| Relationship (reference to high level conceptual model) |  |
| Value | # is an identifier <criterion identifier> unique number and not replaceable |
| Business rules | Value Allowed: Number  Relationship: 5.3 Exclusion Criteria  Concept: Sequential number |
| Duplicate field in other sections | Number consecutively, repeat for each exclusion criteria, if deleted do not replace, do not duplicate |

|  |  |
| --- | --- |
| Term (Variable) | Exclusion Criterion |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | D |
| Definition | See C25370 For review purposes C25370 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. Number the criteria sequentially |
| Conformance | Required Repeatable |
| Cardinality | One-to-many |
| Relationship content from ToC representing the protocol hierarchy | Trial Population |
| Relationship (reference to high level conceptual model) |  |
| Value | <Inclusion Criterion> |
| Business rules | Value Allowed: text and special characters  Relationship: to Number #  Concept: C25370 |
| Duplicate field in other sections | Repeat for each inclusion criterion, if deleted do not replace, do not duplicate |

## Contraception

|  |  |
| --- | --- |
| Term (Variable) | 5.4 Contraception |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | H |
| Definition | Header |
| User Guidance | No text is intended here (header only). |
| Conformance | Required |
| Cardinality | One-to-one |
| Relationship content from ToC representing the protocol hierarchy | 5 Trial Population |
| Relationship (reference to high level conceptual model) |  |
| Value | 5.4 Contraception |
| Business rules | Value Allowed: 5.4 Contraception  Relationship: Table of content  Concept: Header, Identifier |
| Duplicate field in other sections | No |

### Definitions Related to Childbearing Potential

|  |  |
| --- | --- |
| Term (Variable) | 5.4.1 Definitions Related to Childbearing Potential |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | H |
| Definition | Header |
| User Guidance | N/A |
| Conformance | Required |
| Cardinality | One-to-one |
| Relationship content from ToC representing the protocol hierarchy | Trial Population |
| Relationship (reference to high level conceptual model) |  |
| Value | 5.4.1 Definitions Related to Childbearing Potential |
| Business rules | Value Allowed: 5.4.1 Definitions Related to Childbearing Potential  Relationship: Table of content  Concept: Header, Identifier |
| Duplicate field in other sections | No |

|  |  |
| --- | --- |
| Term (Variable) | <Definitions Related to Childbearing Potential or state Not Applicable> |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | D |
| Definition | C106508  An indicator as to whether the female subject has the potential to become pregnant. (NCI) |
| User Guidance | Specify the definitions of:   * Participant of childbearing potential * Participant of non-childbearing potential |
| Conformance | Required |
| Cardinality | One-to-one |
| Relationship content from ToC representing the protocol hierarchy | Trial Population |
| Relationship (reference to high level conceptual model) |  |
| Value | Description of Trial Population and Rationale |
| Business rules | Value Allowed: Text  Relationship: 5.4 Contraception  Concept: C106508 |
| Duplicate field in other sections | No |

### Contraception Requirements

|  |  |
| --- | --- |
| Term (Variable) | 5.4.2 Contraception Requirements |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | H |
| Definition | Header |
| User Guidance | N/A |
| Conformance | Required |
| Cardinality | One-to-one |
| Relationship content from ToC representing the protocol hierarchy | Trial Population |
| Relationship (reference to high level conceptual model) |  |
| Value | 5.4.2 Contraception Requirements |
| Business rules | Value Allowed: 5.4.2  Relationship: Table of content  Concept: Header, Identifier |
| Duplicate field in other sections | No |

|  |  |
| --- | --- |
| Term (Variable) | <Contraception Requirements or state Not Applicable> |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | D |
| Definition | CNEW  A textual description of the requirements for the prevention of conception or impregnation by the use of devices or drugs or surgery (##TBC) |
| User Guidance | Specify the:   * Contraceptive methods required * Duration of use |
| Conformance | Required |
| Cardinality | One-to-one |
| Relationship content from ToC representing the protocol hierarchy | Trial Population |
| Relationship (reference to high level conceptual model) |  |
| Value | Description of Trial Population and Rationale |
| Business rules | Value Allowed: Text  Relationship: 5.4 Contraception  Concept: CNEW |
| Duplicate field in other sections | No |

## Lifestyle Restrictions

|  |  |
| --- | --- |
| Term (Variable) | 5.5 Lifestyle Restrictions |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | H |
| Definition | Header |
| User Guidance | N/A |
| Conformance | Required |
| Cardinality | One-to-one |
| Relationship content from ToC representing the protocol hierarchy | Trial Population |
| Relationship (reference to high level conceptual model) |  |
| Value | 5.5 Lifestyle Restrictions |
| Business rules | Value Allowed: 5.5  Relationship: Table of content  Concept: Header, Identifier |
| Duplicate field in other sections | No |

|  |  |
| --- | --- |
| Term (Variable) | <Lifestyle Restrictions> {N/A} or optional free text <Enter Lifestyle Restrictions> |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | D |
| Definition | CNEW  A textual 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 | Required (at least one item and repeat for each item) |
| Cardinality | One-to-one |
| Relationship content from ToC representing the protocol hierarchy | Trial Population |
| Relationship (reference to high level conceptual model) |  |
| Value | Lifestyle Restrictions |
| Business rules | Value Allowed: Text  Relationship: 5.5 Lifestyle Restrictions  Concept: CNEW |
| Duplicate field in other sections | No, repeat field as needed in 5.5 or use sub-headings optional structure |

### Meals and Dietary Restrictions

|  |  |
| --- | --- |
| Term (Variable) | 5.5.1 Meals and Dietary Restrictions |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | H |
| Definition | Header |
| User Guidance | N/A |
| Conformance | Optional, do not repeat |
| Cardinality | One-to-one |
| Relationship content from ToC representing the protocol hierarchy | Trial Population |
| Relationship (reference to high level conceptual model) |  |
| Value | 5.5.1 Meals and Dietary Restrictions |
| Business rules | Value Allowed: 5.5.1  Relationship: Table of content  Concept: Header, Identifier |
| Duplicate field in other sections | No |

|  |  |
| --- | --- |
| Term (Variable) | <Meals and Dietary Restrictions> |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | D |
| Definition | CNEW  A textual description of the restrictions related to participant diet during the trial. |
| User Guidance | If applicable, describe any restrictions on diet (for example, food and drink restrictions, timing of meals relative to dosing). |
| Conformance | Optional (repeat for each item) |
| Cardinality | One-to-one |
| Relationship content from ToC representing the protocol hierarchy | Trial Population |
| Relationship (reference to high level conceptual model) |  |
| Value | Text |
| Business rules | Value Allowed: Text  Relationship: 5.5.1 Meals and Dietary Restrictions  Concept: CNEW |
| Duplicate field in other sections | No, repeat field as needed in 5.5.1 |

### 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 Header (H) | H |
| Definition | Header |
| User Guidance | N/A |
| Conformance | Optional, do not repeat |
| Cardinality | One-to-one |
| Relationship content from ToC representing the protocol hierarchy | Trial Population |
| Relationship (reference to high level conceptual model) |  |
| Value | 5.5.2 Caffeine, Alcohol, Tobacco, and Other Restrictions |
| Business rules | Value Allowed: 5.5.2  Relationship: Table of content  Concept: Header, Identifier |
| Duplicate field in other sections | no |

|  |  |
| --- | --- |
| Term (Variable) | <Caffeine, Alcohol, Tobacco, and Other Restrictions> |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | D |
| Definition | CNEW  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 (repeat for each item) |
| Cardinality | One-to-one |
| Relationship content from ToC representing the protocol hierarchy | Trial Population |
| Relationship (reference to high level conceptual model) |  |
| Value | Text |
| Business rules | Value Allowed: Text  Relationship: 5.5.2 Caffeine, Alcohol, Tobacco, and Other Restrictions  Concept: CNEW |
| Duplicate field in other sections | No, repeat field as needed in 5.5.2 |

### Physical Activity Restrictions

|  |  |
| --- | --- |
| Term (Variable) | 5.5.3 Physical Activity Restrictions |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | H |
| Definition | Header |
| User Guidance | N/A |
| Conformance | Optional, do not repeat |
| Cardinality | One-to-one |
| Relationship content from ToC representing the protocol hierarchy | Trial Population |
| Relationship (reference to high level conceptual model) |  |
| Value | 5.5.3 Physical Activity Restrictions |
| Business rules | Value Allowed: 5.5.3  Relationship: Table of content  Concept: Header, Identifier |
| Duplicate field in other sections | no |

|  |  |
| --- | --- |
| Term (Variable) | <Physical Activity Restrictions> |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | D |
| Definition | C17708  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 (for example, in first-in-human trials, activity may be restricted by ensuring participants remain in bed for 4 to 6 hours after dosing). |
| Conformance | Optional (repeat for each item) |
| Cardinality | One-to-one |
| Relationship content from ToC representing the protocol hierarchy | Trial Population |
| Relationship (reference to high level conceptual model) |  |
| Value | Text |
| Business rules | Value Allowed: Text  Relationship: 5.5.3 Physical Activity Restrictions  Concept: C17708 |
| Duplicate field in other sections | no |

### Other Activity Restrictions

|  |  |
| --- | --- |
| Term (Variable) | 5.5.4 Other Activity Restrictions |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | H |
| Definition | Header |
| User Guidance | N/A |
| Conformance | Optional, do not repeat |
| Cardinality | One-to-one |
| Relationship content from ToC representing the protocol hierarchy | Trial Population |
| Relationship (reference to high level conceptual model) |  |
| Value | 5.5.4 Other Activity Restrictions |
| Business rules | Value Allowed: 5.5.4  Relationship: Table of content  Concept: Header, Identifier |
| Duplicate field in other sections | No |

|  |  |
| --- | --- |
| Term (Variable) | <Other Activity Restrictions> |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | D |
| Definition | CNEW  An activity that is different than the one(s) previously specified or mentioned. |
| User Guidance | If applicable, describe restrictions on any other activity (for example, blood or tissue donation, driving, heavy machinery use, or sun exposure). |
| Conformance | Optional (repeat for each item) |
| Cardinality | One-to-one |
| Relationship content from ToC representing the protocol hierarchy | Trial Population |
| Relationship (reference to high level conceptual model) |  |
| Value | Text |
| Business rules | Value Allowed: Text  Relationship: 5.5.4 Other Activity Restrictions  Concept: n/a |
| Duplicate field in other sections | No |

## Screen Failures and Rescreening

|  |  |
| --- | --- |
| Term (Variable) | 5.6 Screen Failure and Rescreening |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | H |
| Definition | Header |
| User Guidance | N/A |
| Conformance | Required |
| Cardinality | One-to-one |
| Relationship content from ToC representing the protocol hierarchy | Trial Population |
| Relationship (reference to high level conceptual model) |  |
| Value | 5.6 Screen Failure and Rescreening |
| Business rules | Value Allowed: 5.6  Relationship: Table of content  Concept: Header, Identifier |
| Duplicate field in other sections | No |

|  |  |
| --- | --- |
| Term (Variable) | <Screen Failure> |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | D |
| Definition | C49628  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 | Trial Population |
| Relationship (reference to high level conceptual model) |  |
| Value | Text |
| Business rules | Value Allowed: Text  Relationship: 5.6 Screen Failure and Rescreening  Concept: C49628 |
| Duplicate field in other sections | No |

|  |  |
| --- | --- |
| Term (Variable) | <Rescreening> |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | D |
| Definition | CNEW  The process of active consideration of subjects for enrollment 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 | Trial Population |
| Relationship (reference to high level conceptual model) |  |
| Value | Text |
| Business rules | Value Allowed: Text  Relationship: 5.6 Screen Failure and Rescreening  Concept: Data Element CNEW |
| Duplicate field in other sections | No |

# Trial Intervention and Concomitant Therapy

|  |  |
| --- | --- |
| Term (Variable) | 6. Trial Intervention and Concomitant Therapy |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | H |
| Definition | Heading |
| User Guidance | N/A |
| Conformance | Required |
| Cardinality | One |
| Relationship content from ToC representing the protocol hierarchy | Trial Intervention and Concomitant Therapy |
| Relationship (reference to high level conceptual model) |  |
| Value | 6. Trial Intervention and Concomitant Therapy |
| Business rules | Value Allowed:6. Trial Intervention and Concomitant Therapy  Relationship: Table of content  Concept: Header, Identifier |
| Duplicate field in other sections | No |

## Overview of Trial Interventions

|  |  |
| --- | --- |
| Term (Variable) | 6.1 Overview of Trial Interventions |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | H |
| Definition | Heading |
| User Guidance | N/A |
| Conformance | Required |
| Cardinality | One |
| Relationship content from ToC representing the protocol hierarchy | Overview of Trial Interventions |
| Relationship (reference to high level conceptual model) |  |
| Value | Description of Trial Intervention |
| Business rules | Value Allowed: Description of Trial Intervention  Relationship: Table row headers  Concept: n/a |
| Duplicate field in other sections | No |

|  |  |
| --- | --- |
| Term (Variable) | Arm Name |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | H |
| Definition | C93729  The literal identifier (i.e., distinctive designation) for the arm. |
| User Guidance |  |
| Conformance | Required |
| Cardinality | One |
| Relationship content from ToC representing the protocol hierarchy | Trial Intervention and Concomitant Therapy |
| Relationship (reference to high level conceptual model) |  |
| Value | Arm Name |
| Business rules | Value Allowed: Yes  Relationship: Table header  Concept: n/a |
| Duplicate field in other sections | No |

|  |  |
| --- | --- |
| Term (Variable) | Arm Type |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | H |
| Definition |  |
| User Guidance |  |
| Conformance | Required |
| Cardinality |  |
| Relationship content from ToC representing the protocol hierarchy | Trial Intervention and Concomitant Therapy |
| Relationship (reference to high level conceptual model) |  |
| Value | Arm Type |
| Business rules | Value Allowed: Yes  Relationship: Table header  Concept: n/a |
| Duplicate field in other sections |  |

|  |  |
| --- | --- |
| Term (Variable) | Intervention Name |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | H |
| Definition |  |
| User Guidance |  |
| Conformance | Required |
| Cardinality |  |
| Relationship content from ToC representing the protocol hierarchy | Trial Intervention and Concomitant Therapy |
| Relationship (reference to high level conceptual model) |  |
| Value | Intervention Name |
| Business rules | Value Allowed: Yes  Relationship: Table Header  Concept: n/a |
| Duplicate field in other sections |  |

|  |  |
| --- | --- |
| Term (Variable) | Intervention Type |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | H |
| Definition |  |
| User Guidance |  |
| Conformance | Required |
| Cardinality |  |
| Relationship content from ToC representing the protocol hierarchy | Trial Intervention and Concomitant Therapy |
| Relationship (reference to high level conceptual model) |  |
| Value | Intervention Type |
| Business rules | Value Allowed: Yes  Relationship: Table header  Concept: n/a |
| Duplicate field in other sections |  |

|  |  |
| --- | --- |
| Term (Variable) | Use |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | H |
| Definition |  |
| User Guidance |  |
| Conformance | Required |
| Cardinality |  |
| Relationship content from ToC representing the protocol hierarchy | Trial Intervention and Concomitant Therapy |
| Relationship (reference to high level conceptual model) |  |
| Value | Use |
| Business rules | Value Allowed: Yes  Relationship: Table header  Concept: n/a |
| Duplicate field in other sections |  |

|  |  |
| --- | --- |
| Term (Variable) | Formulation |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | H |
| Definition |  |
| User Guidance |  |
| Conformance | Required |
| Cardinality |  |
| Relationship content from ToC representing the protocol hierarchy | Trial Intervention and Concomitant Therapy |
| Relationship (reference to high level conceptual model) |  |
| Value | Formulation |
| Business rules | Value Allowed: Yes  Relationship: Table header  Concept: n/a |
| Duplicate field in other sections |  |

|  |  |
| --- | --- |
| Term (Variable) | Unit Dose Strength |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | H |
| Definition |  |
| User Guidance |  |
| Conformance | Required |
| Cardinality |  |
| Relationship content from ToC representing the protocol hierarchy | Trial Intervention and Concomitant Therapy |
| Relationship (reference to high level conceptual model) |  |
| Value | Unit Dose Strength |
| Business rules | Value Allowed: Yes  Relationship: Table header  Concept: n/a |
| Duplicate field in other sections |  |

|  |  |
| --- | --- |
| Term (Variable) | Dose Level |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | H |
| Definition |  |
| User Guidance |  |
| Conformance | Required |
| Cardinality |  |
| Relationship content from ToC representing the protocol hierarchy | Trial Intervention and Concomitant Therapy |
| Relationship (reference to high level conceptual model) |  |
| Value | Dose Level |
| Business rules | Value Allowed: Yes  Relationship: Table header  Concept: n/a |
| Duplicate field in other sections |  |

|  |  |
| --- | --- |
| Term (Variable) | Route of Administration |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | H |
| Definition |  |
| User Guidance |  |
| Conformance | Required |
| Cardinality |  |
| Relationship content from ToC representing the protocol hierarchy | Trial Intervention and Concomitant Therapy |
| Relationship (reference to high level conceptual model) |  |
| Value | Route of Administration |
| Business rules | Value Allowed: Yes  Relationship: Table Header  Concept: n/a |
| Duplicate field in other sections |  |

|  |  |
| --- | --- |
| Term (Variable) | Regimen/Treatment Period |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | H |
| Definition |  |
| User Guidance |  |
| Conformance | Required |
| Cardinality |  |
| Relationship content from ToC representing the protocol hierarchy | Trial Intervention and Concomitant Therapy |
| Relationship (reference to high level conceptual model) |  |
| Value | Regimen/Treatment Period |
| Business rules | Value Allowed: Yes  Relationship: Table Heading  Concept: n/a |
| Duplicate field in other sections |  |

|  |  |
| --- | --- |
| Term (Variable) | Arm Name |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | D |
| Definition |  |
| User Guidance |  |
| Conformance | Required |
| Cardinality |  |
| Relationship content from ToC representing the protocol hierarchy | Trial Intervention and Concomitant Therapy |
| Relationship (reference to high level conceptual model) |  |
| Value | Text |
| Business rules | Value Allowed: Yes  Relationship: n/a  Concept: n/a |
| Duplicate field in other sections |  |

|  |  |
| --- | --- |
| Term (Variable) | Arm Type |
| Data Type | Pick List |
| Data (D), Value (V) or Header (H) | D |
| Definition |  |
| User Guidance |  |
| Conformance | Required |
| Cardinality |  |
| Relationship content from ToC representing the protocol hierarchy | Trial Intervention and Concomitant Therapy |
| Relationship (reference to high level conceptual model) |  |
| Value | Experimental, Active Comparator, Placebo Comparator, Sham Comparator, No Intervention |
| Business rules | Value Allowed: Yes  Relationship: Relates to Arm and intervention formulation dosage  Concept: n/a |
| Duplicate field in other sections | Once for each arm  Replicate for number of arms |

|  |  |
| --- | --- |
| Term (Variable) | Intervention Name |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | D |
| Definition |  |
| User Guidance |  |
| Conformance | Required |
| Cardinality |  |
| Relationship content from ToC representing the protocol hierarchy | Trial Intervention and Concomitant Therapy |
| Relationship (reference to high level conceptual model) |  |
| Value |  |
| Business rules | Value Allowed: n/a  Relationship: Relates to arm  Concept: n/a |
| Duplicate field in other sections | Relates to Arm |

|  |  |
| --- | --- |
| Term (Variable) | Intervention Type |
| Data Type | Pick List |
| Data (D), Value (V) or Header (H) | D |
| Definition |  |
| User Guidance |  |
| Conformance | Required |
| Cardinality |  |
| Relationship content from ToC representing the protocol hierarchy | Trial Intervention and Concomitant Therapy |
| Relationship (reference to high level conceptual model) |  |
| Value | Drug, device, biologic/vaccine, procedure/surgery, radiation, behavioral, genetic, dietary supplement, combination product, dietary |
| Business rules | Value Allowed: Yes  Relationship: Relates to arm and intervention formulation dosage  Concept: n/a |
| Duplicate field in other sections | Replicate for all interventions in the arm |

|  |  |
| --- | --- |
| Term (Variable) | IMP/NIMP |
| Data Type | Pick List |
| Data (D), Value (V) or Header (H) | D |
| Definition |  |
| User Guidance |  |
| Conformance | Required |
| Cardinality |  |
| Relationship content from ToC representing the protocol hierarchy | Trial Intervention and Concomitant Therapy |
| Relationship (reference to high level conceptual model) |  |
| Value | IMP, NIMP |
| Business rules | Value Allowed: Yes  Relationship: Relates to arm and intervention formulation dosage  Concept: n/a |
| Duplicate field in other sections | Replicate for all interventions in the arm |

|  |  |
| --- | --- |
| Term (Variable) | Formulation |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | D |
| Definition |  |
| User Guidance |  |
| Conformance | Required |
| Cardinality |  |
| Relationship content from ToC representing the protocol hierarchy | Trial Intervention and Concomitant Therapy |
| Relationship (reference to high level conceptual model) |  |
| Value | Reference IDMP Codes |
| Business rules | Value Allowed: Yes  Relationship: Relates to arm and intervention formulation dosage  Concept: n/a |
| Duplicate field in other sections | Replicate for all interventions in the arm |

|  |  |
| --- | --- |
| Term (Variable) | Unit Dose Strength |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | D |
| Definition |  |
| User Guidance |  |
| Conformance | Required |
| Cardinality |  |
| Relationship content from ToC representing the protocol hierarchy | Trial Intervention and Concomitant Therapy |
| Relationship (reference to high level conceptual model) |  |
| Value | Reference IDMP Codes |
| Business rules | Value Allowed: n/a  Relationship: Relates to Arm and intervention formulation dosage  Concept: n/a |
| Duplicate field in other sections | Replicate for all interventions in the arm |

|  |  |
| --- | --- |
| Term (Variable) | Dose Level |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | D |
| Definition |  |
| User Guidance |  |
| Conformance | Required |
| Cardinality |  |
| Relationship content from ToC representing the protocol hierarchy | Trial Intervention and Concomitant Therapy |
| Relationship (reference to high level conceptual model) |  |
| Value | Reference IDMP Codes |
| Business rules | Value Allowed: n/a  Relationship: Relates to arm and intervention formulation dosage  Concept: n/a |
| Duplicate field in other sections | Replicate for all interventions in the arm |

|  |  |
| --- | --- |
| Term (Variable) | Route of Administration |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | D |
| Definition |  |
| User Guidance |  |
| Conformance | Required |
| Cardinality |  |
| Relationship content from ToC representing the protocol hierarchy | Trial Intervention and Concomitant Therapy |
| Relationship (reference to high level conceptual model) |  |
| Value | Reference IDMP Codes |
| Business rules | Value Allowed: Yes  Relationship: Relates to arm and intervention formulation dosage  Concept: n/a |
| Duplicate field in other sections | Replicate for all interventions in the arm |

|  |  |
| --- | --- |
| Term (Variable) | Regimen/Treatment Period |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | D |
| Definition |  |
| User Guidance |  |
| Conformance | Required |
| Cardinality |  |
| Relationship content from ToC representing the protocol hierarchy | Trial Intervention and Concomitant Therapy |
| Relationship (reference to high level conceptual model) |  |
| Value | Regimen/Treatment Period |
| Business rules | Value Allowed: Yes  Relationship: Relates to arm and intervention formulation dosage  Concept: n/a |
| Duplicate field in other sections | Replicate for all interventions in the arm |

|  |  |
| --- | --- |
| Term (Variable) | [Additional Text, if Needed] |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | D |
| Definition |  |
| User Guidance |  |
| Conformance | Optional |
| Cardinality |  |
| Relationship content from ToC representing the protocol hierarchy | Trial Intervention and Concomitant Therapy |
| Relationship (reference to high level conceptual model) |  |
| Value |  |
| Business rules | Value Allowed: n/a  Relationship: n/a  Concept: n/a |
| Duplicate field in other sections |  |

## Description of Investigational Trial Intervention

|  |  |
| --- | --- |
| Term (Variable) | 6.2 Description of Investigational Trial Intervention |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | H |
| Definition | Heading |
| User Guidance | N/A |
| Conformance | Required |
| Cardinality | One |
| Relationship content from ToC representing the protocol hierarchy | 6.2 Description of Investigational Trial Intervention |
| Relationship (reference to high level conceptual model) |  |
| Value | 6.2 Description of Investigational Trial Intervention |
| Business rules | Value Allowed: 6.2 Description of Investigational Trial Intervention  Relationship: Table of content  Concept: Header, Identifier |
| Duplicate field in other sections | No |

|  |  |
| --- | --- |
| Term (Variable) | <Description of Investigational Trial Intervention> |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | D |
| Definition | CNEW  A narrative representation of the investigational trial intervention. |
| User Guidance | The investigational trial intervention is the product used in the trial as part of trial objectives. Other trial interventions that are not part of trial objectives (not an investigational role in this trial) are described in Section 6.10 Description of Non-investigational trial interventions. For IMP, NIMP, AxMP designations based on local legislation, please refer to Table of Trial Interventions above.  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 |
| Relationship content from ToC representing the protocol hierarchy | 6.2 Description of Investigational Trial Intervention |
| Relationship (reference to high level conceptual model) |  |
| Value | Text |
| Business rules | Value Allowed: Text  Relationship: n/a  Concept: CNEW |
| Duplicate field in other sections |  |

|  |  |
| --- | --- |
| Term (Variable) | < Additional Text, if Needed> |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | D |
| Definition | CNEW  Extra or further descriptive text that is optionally added as needed. |
| User Guidance | The investigational trial intervention is the product used in the trial as part of trial objectives. Other trial interventions that are not part of trial objectives (not an investigational role in this trial) are described in Section 6.10 Description of Non-investigational trial interventions. For IMP, NIMP, AxMP designations based on local legislation, please refer to Table of Trial Interventions above.  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 | Optional |
| Cardinality | One |
| Relationship content from ToC representing the protocol hierarchy | 6.2 Description of Investigational Trial Intervention |
| Relationship (reference to high level conceptual model) |  |
| Value | Text |
| Business rules | Value Allowed: Text  Relationship: n/a  Concept: CNEW |
| Duplicate field in other sections | No |

## Rationale for Investigational Trial Intervention Dose and Regimen

|  |  |
| --- | --- |
| Term (Variable) | 6.3 Rationale for Investigational Trial Intervention Dose and Regimen |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | H |
| Definition | Heading |
| User Guidance | N/A |
| Conformance | Required |
| Cardinality | One |
| Relationship content from ToC representing the protocol hierarchy | 6.3 Rationale for Investigational Trial Intervention Dose and Regimen |
| Relationship (reference to high level conceptual model) |  |
| Value | 6.3 Rationale for Investigational Trial Intervention Dose and Regimen |
| Business rules | Value Allowed: 6.3 Rationale for Investigational Trial Intervention Dose and Regimen  Relationship: Table of content  Concept: Header, Identifier |
| Duplicate field in other sections | No |

|  |  |
| --- | --- |
| Term (Variable) | <Rationale for Investigational Trial Intervention Dose and Regimen> |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | D |
| Definition | CNEW  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 |
| Relationship content from ToC representing the protocol hierarchy | 6.3 Rationale for Investigational Trial Intervention Dose and Regimen |
| Relationship (reference to high level conceptual model) |  |
| Value | Text |
| Business rules | Value Allowed: Text  Relationship: n/a  Concept: CNEW |
| Duplicate field in other sections |  |

## Investigational Trial Intervention Administration

|  |  |
| --- | --- |
| Term (Variable) | 6.4 Investigational Trial Intervention Administration |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | H |
| Definition | Heading |
| User Guidance | N/A |
| Conformance | Required |
| Cardinality | One |
| Relationship content from ToC representing the protocol hierarchy | 6.4 Investigational Trial Intervention Administration |
| Relationship (reference to high level conceptual model) |  |
| Value | 6.4 Investigational Trial Intervention Administration |
| Business rules | Value Allowed: 6.4 Investigational Trial Intervention Administration  Relationship: Table of content  Concept: Header, Identifier |
| Duplicate field in other sections | No |

|  |  |
| --- | --- |
| Term (Variable) | <Investigational Trial Intervention Administration > |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | D |
| Definition | CNEW  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 |
| Relationship content from ToC representing the protocol hierarchy | 6.4 Investigational Trial Intervention Administration |
| Relationship (reference to high level conceptual model) |  |
| Value | Text |
| Business rules | Value Allowed: Text  Relationship: n/a  Concept: CNEW |
| Duplicate field in other sections |  |

## Investigational Trial Intervention Dose Modification

|  |  |
| --- | --- |
| Term (Variable) | 6.5 Investigational Trial Intervention Dose Modification |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | H |
| Definition | Heading |
| User Guidance | N/A |
| Conformance | Required |
| Cardinality | One |
| Relationship content from ToC representing the protocol hierarchy | 6.5 Investigational Trial Intervention Dose Modification |
| Relationship (reference to high level conceptual model) |  |
| Value | 6.5 Investigational Trial Intervention Dose Modification |
| Business rules | Value Allowed: 6.5 Investigational Trial Intervention Dose Modification  Relationship: Table of content  Concept: Header, Identifier |
| Duplicate field in other sections | No |

|  |  |
| --- | --- |
| Term (Variable) | <Investigational Trial Intervention Dose Modification> |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | D |
| Definition | CNEW  A change, alteration, or adjustment to the dose of a investigational trial intervention. |
| 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 |
| Relationship content from ToC representing the protocol hierarchy | 6.5 Investigational Trial Intervention Dose Modification |
| Relationship (reference to high level conceptual model) |  |
| Value | Text |
| Business rules | Value Allowed: Text  Relationship: n/a  Concept: CNEW |
| Duplicate field in other sections | No |

## Management of Investigational Trial Intervention Overdose

|  |  |
| --- | --- |
| Term (Variable) | 6.6 Management of Investigational Trial Intervention Overdose |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | H |
| Definition | Heading |
| User Guidance | N/A |
| Conformance | Required |
| Cardinality | One |
| Relationship content from ToC representing the protocol hierarchy | 6.6 Management of Investigational Trial Intervention Overdose |
| Relationship (reference to high level conceptual model) |  |
| Value | 6.6 Management of Investigational Trial Intervention Overdose |
| Business rules | Value Allowed: 6.6 Management of Investigational Trial Intervention Overdose Relationship: Table of content  Concept: Header, Identifier |
| Duplicate field in other sections | No |

|  |  |
| --- | --- |
| Term (Variable) | <Management of Investigational Trial Intervention Overdose> |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | D |
| Definition | CNEW  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 |
| Relationship content from ToC representing the protocol hierarchy | 6.6 Management of Investigational Trial Intervention Overdose |
| Relationship (reference to high level conceptual model) |  |
| Value | Text |
| Business rules | Value Allowed: Text  Relationship: n/a  Concept: CNEW |
| Duplicate field in other sections | No |

## Preparation, Storage, Handling and Accountability of Investigational Trial Intervention(s)

|  |  |
| --- | --- |
| Term (Variable) | 6.7 Preparation, Storage, Handling and Accountability of Investigational Trial Intervention(s) |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | H |
| Definition | Heading |
| User Guidance | N/A |
| Conformance | Required |
| Cardinality | One |
| Relationship content from ToC representing the protocol hierarchy | 6.7 Preparation, Storage, Handling and Accountability of Investigational Trial Intervention(s) |
| Relationship (reference to high level conceptual model) |  |
| Value | 6.7 Preparation, Storage, Handling and Accountability of Investigational Trial Intervention(s) |
| Business rules | Value Allowed: 6.7 Preparation, Storage, Handling and Accountability of Investigational Trial Intervention(s)  Relationship: Table of content  Concept: Header, Identifier |
| Duplicate field in other sections | No |

### Preparation of Investigational Trial Intervention(s)

|  |  |
| --- | --- |
| Term (Variable) | 6.7.1 Preparation of Investigational Trial Intervention(s) |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | H |
| Definition | Heading |
| User Guidance | N/A |
| Conformance | Required |
| Cardinality | One |
| Relationship content from ToC representing the protocol hierarchy | 6.7.1 Preparation of Investigational Trial Intervention(s) |
| Relationship (reference to high level conceptual model) |  |
| Value | 6.7.1 Preparation of Investigational Trial Intervention(s) |
| Business rules | Value Allowed: 6.7.1 Preparation of Investigational Trial Intervention(s)  Relationship: Table of content  Concept: Header, Identifier |
| Duplicate field in other sections | No |

|  |  |
| --- | --- |
| Term (Variable) | <Preparation of Investigational Trial Intervention> |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | D |
| Definition | C176274  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 |
| Relationship content from ToC representing the protocol hierarchy | 6.7.1 Preparation of Investigational Trial Intervention(s) |
| Relationship (reference to high level conceptual model) |  |
| Value | Text |
| Business rules | Value Allowed: Text  Relationship: n/a  Concept: C176274 |
| Duplicate field in other sections | No |

### Storage and Handling of Investigational Trial Intervention

|  |  |
| --- | --- |
| Term (Variable) | 6.7.2 Storage and Handling of Investigational Trial Intervention |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | H |
| Definition | Heading |
| User Guidance | N/A |
| Conformance | Required |
| Cardinality | One |
| Relationship content from ToC representing the protocol hierarchy | 6.7.2 Storage and Handling of Investigational Trial Intervention |
| Relationship (reference to high level conceptual model) |  |
| Value | 6.7.2 Storage and Handling of Investigational Trial Intervention |
| Business rules | Value Allowed: 6.7.2 Storage and Handling of Investigational Trial Intervention  Relationship: Table of content  Concept: Header, Identifier |
| Duplicate field in other sections | No |

|  |  |
| --- | --- |
| Term (Variable) | <Storage and Handling of Investigational Trial Intervention> |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | D |
| Definition | C115525  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 |
| Relationship content from ToC representing the protocol hierarchy | Trial Intervention and Concomitant Therapy |
| Relationship (reference to high level conceptual model) |  |
| Value | Text |
| Business rules | Value Allowed: Text  Relationship: n/a  Concept: C115525 |
| Duplicate field in other sections | No |

### Accountability of Trial Intervention

|  |  |
| --- | --- |
| Term (Variable) | 6.7.3 Accountability of Trial Intervention |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | H |
| Definition | Heading |
| User Guidance | N/A |
| Conformance | Required |
| Cardinality | One |
| Relationship content from ToC representing the protocol hierarchy | 6.7.3 Accountability of Trial Intervention |
| Relationship (reference to high level conceptual model) |  |
| Value | 6.7.3 Accountability of Trial Intervention |
| Business rules | Value Allowed: 6.7.3 Accountability of Trial Intervention  Relationship: Table of content  Concept: Header, Identifier |
| Duplicate field in other sections | No |

|  |  |
| --- | --- |
| Term (Variable) | <Accountability of Investigational Trial Intervention> |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | D |
| Definition | C176267 |
| 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, and * expectations for reconciliation. |
| Conformance | Required |
| Cardinality | One |
| Relationship content from ToC representing the protocol hierarchy | 6.7.3 Accountability of Trial Intervention |
| Relationship (reference to high level conceptual model) |  |
| Value | Text |
| Business rules | Value Allowed: Text  Relationship: n/a  Concept: C176267 |
| Duplicate field in other sections | No |

## Investigational Trial Intervention Assignment, Randomisation and Blinding

|  |  |
| --- | --- |
| Term (Variable) | 6.8 Investigational Trial Intervention Assignment, Randomisation and Blinding |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | H |
| Definition | Heading |
| User Guidance | N/A |
| Conformance | Required |
| Cardinality | One |
| Relationship content from ToC representing the protocol hierarchy | 6.8 Investigational Trial Intervention Assignment, Randomisation and Blinding |
| Relationship (reference to high level conceptual model) |  |
| Value | 6.8 Investigational Trial Intervention Assignment, Randomisation and Blinding |
| Business rules | Value Allowed: Yes  Relationship: Table of content  Concept: Header, Identifier |
| Duplicate field in other sections | No |

### Participant Assignment to Investigational Trial Intervention

|  |  |
| --- | --- |
| Term (Variable) | 6.8..11 Participant Assignment to Investigational Trial Intervention |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | H |
| Definition | Heading |
| User Guidance | N/A |
| Conformance | Required |
| Cardinality | One |
| Relationship content from ToC representing the protocol hierarchy | 6.8 Participant Assignment to Investigational Trial Intervention |
| Relationship (reference to high level conceptual model) |  |
| Value | 6.8.1 Participant Assignment to Investigational Trial Intervention |
| Business rules | Value Allowed: 6.8.1 Participant Assignment to Investigational Trial Intervention  Relationship: Table of content  Concept: Header, Identifier |
| Duplicate field in other sections | No |

|  |  |
| --- | --- |
| Term (Variable) | <Participant Assignment to Investigational Trial Intervention> |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | D |
| Definition | CNEW  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 |
| Relationship content from ToC representing the protocol hierarchy | Trial Intervention and Concomitant Therapy |
| Relationship (reference to high level conceptual model) |  |
| Value | Text |
| Business rules | Value Allowed: Text  Relationship: n/a  Concept: CNEW |
| Duplicate field in other sections | No |

### Randomisation

|  |  |
| --- | --- |
| Term (Variable) | 6.8.2 Randomisation |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | H |
| Definition | Heading |
| User Guidance | N/A |
| Conformance | Required |
| Cardinality | One |
| Relationship content from ToC representing the protocol hierarchy | 6.8.2 Randomisation |
| Relationship (reference to high level conceptual model) |  |
| Value | 6.8.2 Randomisation |
| Business rules | Value Allowed: 6.8.2 Randomisation  Relationship: Table of content  Concept: Header, Identifier |
| Duplicate field in other sections | No |

|  |  |
| --- | --- |
| Term (Variable) | <Randomisation> |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | D |
| Definition | C25196  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. Note the use of any computer systems and programmes – and their validation status – in randomization, stratification, and unblinding. |
| Conformance | Required |
| Cardinality | One |
| Relationship content from ToC representing the protocol hierarchy | 6.8.2 Randomisation |
| Relationship (reference to high level conceptual model) |  |
| Value | Text |
| Business rules | Value Allowed: Text  Relationship: n/a  Concept: C25196 |
| Duplicate field in other sections | No |

### Blinding

|  |  |
| --- | --- |
| Term (Variable) | 6.8.3 Blinding |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | H |
| Definition | Heading |
| User Guidance | N/A |
| Conformance | Conditionally required, in the case of blind trial |
| Cardinality | One |
| Relationship content from ToC representing the protocol hierarchy | 6.8.3 Blinding |
| Relationship (reference to high level conceptual model) |  |
| Value | 6.8.3 Blinding |
| Business rules | Value Allowed: 6.8.3 Blinding  Relationship: Table of content  Concept: Header, Identifier |
| Duplicate field in other sections | No |

|  |  |
| --- | --- |
| Term (Variable) | <Blinding> |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | D |
| Definition | C189349  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), see Section 6.8.4.nIf 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. For transparency and trial integrity reasons, consider including a table where different roles (e.g. statistician, sponsor, investigator, site staff, DMC, CRO, etc.) and level of blinding are described. It needs to be clear how access to unblinded results will be controlled and what type of information will be disseminated from whom, and to whom. Distinction should be made between knowledge of individual treatment assignments and access to patient-level data or results by treatment group.n  .. |
| Conformance | Conditionally Required, in the case of blind trial |
| Cardinality | One |
| Relationship content from ToC representing the protocol hierarchy | 6.8.3 Blinding |
| Relationship (reference to high level conceptual model) |  |
| Value | Text |
| Business rules | Value Allowed: Text  Relationship: n/a  Concept: C189349 |
| Duplicate field in other sections | No |

### Emergency Unblinding at the Site

|  |  |
| --- | --- |
| Term (Variable) | 6.8.4 Emergency Unblinding at the Site |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | H |
| Definition | Heading |
| User Guidance | N/A |
| Conformance | Conditionally Required, in the case of blind trial |
| Cardinality | One |
| Relationship content from ToC representing the protocol hierarchy | 6.8.4 Emergency Unblinding at the Site |
| Relationship (reference to high level conceptual model) |  |
| Value | 6.8.4 Emergency Unblinding at the Site |
| Business rules | Value Allowed: 6.8.4 Emergency Unblinding at the Site  Relationship: Table of content  Concept: Header, Identifier |
| Duplicate field in other sections | No |

|  |  |
| --- | --- |
| Term (Variable) | {<Emergency Unblinding at the Site>} |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | D |
| Definition | CNEW  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 | Conditionally Required, in the case of blind trial |
| Cardinality | One |
| Relationship content from ToC representing the protocol hierarchy | 6.8.4 Emergency Unblinding at the Site |
| Relationship (reference to high level conceptual model) |  |
| Value | Text |
| Business rules | Value Allowed: Text  Relationship: n/a  Concept: CNEW |
| Duplicate field in other sections | No |

## Investigational Trial Intervention Compliance

|  |  |
| --- | --- |
| Term (Variable) | 6.9 Investigational Trial Intervention Compliance |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | H |
| Definition | Heading |
| User Guidance | N/A |
| Conformance | Required |
| Cardinality | One |
| Relationship content from ToC representing the protocol hierarchy | 6.9 Investigational Trial Intervention Compliance |
| Relationship (reference to high level conceptual model) |  |
| Value | 6.9 Investigational Trial Intervention Compliance |
| Business rules | Value Allowed: 6.9 Investigational Trial Intervention Compliance  Relationship: Table of content  Concept: Header, Identifier |
| Duplicate field in other sections | No |

|  |  |
| --- | --- |
| Term (Variable) | <Investigational Trial Intervention Compliance> |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | D |
| Definition | CNEW  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 |
| Relationship content from ToC representing the protocol hierarchy | 6.9 Investigational Trial Intervention Compliance |
| Relationship (reference to high level conceptual model) |  |
| Value | Text |
| Business rules | Value Allowed: Text  Relationship: n/a  Concept: CNEW |
| Duplicate field in other sections | No |

## Description of Non-Investigational Trial Intervention

|  |  |
| --- | --- |
| Term (Variable) | 6.10 Description of Non-Investigational Trial Intervention |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | H |
| Definition | Heading |
| User Guidance | N/A |
| Conformance | Required |
| Cardinality | One |
| Relationship content from ToC representing the protocol hierarchy | 6.10 Description of Non-Investigational Trial Intervention |
| Relationship (reference to high level conceptual model) |  |
| Value | 6.10 Description of Non-Investigational Trial Intervention |
| Business rules | Value Allowed: 6.10 Description of Non-Investigational Trial Intervention  Relationship: Table of content  Concept: Header, Identifier |
| Duplicate field in other sections | No |

|  |  |
| --- | --- |
| Term (Variable) | <Description of Non-Investigational Trial Intervention> |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | D |
| Definition | CNEW  Description of 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 |
| Relationship content from ToC representing the protocol hierarchy | 6.10 Description of Non-Investigational Trial Intervention |
| Relationship (reference to high level conceptual model) |  |
| Value | Text |
| Business rules | Value Allowed: Text  Relationship: n/a  Concept: CNEW |
| Duplicate field in other sections | No |

### Background Intervention

|  |  |
| --- | --- |
| Term (Variable) | 6.10.1 Background Intervention |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | H |
| Definition | Heading |
| User Guidance | N/A |
| Conformance | Conditionally Required, when any background interventions are defined |
| Cardinality | One |
| Relationship content from ToC representing the protocol hierarchy | 6.10.1 Background Intervention |
| Relationship (reference to high level conceptual model) |  |
| Value | 6.10.1 Background Intervention |
| Business rules | Value Allowed: 6.10.1 Background Intervention  Relationship: Table of content  Concept: Header, Identifier |
| Duplicate field in other sections | No |

|  |  |
| --- | --- |
| Term (Variable) | {<Background Intervention>} |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | D |
| Definition | C165822  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. (CDISC Glossary) |
| User Guidance | Describe permitted background intervention(s), including administration and any conditions for use. |
| Conformance | Conditionally Required, when any background interventions are defined |
| Cardinality | One |
| Relationship content from ToC representing the protocol hierarchy | 6.10.1 Background Intervention |
| Relationship (reference to high level conceptual model) |  |
| Value | Text |
| Business rules | Value Allowed: Text  Relationship: n/a  Concept: C165822 |
| Duplicate field in other sections | No |

### Rescue Therapy

|  |  |
| --- | --- |
| Term (Variable) | 6.10.2 Rescue Therapy |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | H |
| Definition | Heading |
| User Guidance | N/A |
| Conformance | Conditionally Required, when any rescue therapies are defined |
| Cardinality | One |
| Relationship content from ToC representing the protocol hierarchy | 6.10.2 Rescue Therapy |
| Relationship (reference to high level conceptual model) |  |
| Value | 6.10.2 Rescue Therapy |
| Business rules | Value Allowed: 6.10.2 Rescue Therapy  Relationship: Table of content  Concept: Header, Identifier |
| Duplicate field in other sections |  |

|  |  |
| --- | --- |
| Term (Variable) | {<Rescue Therapy>} |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | D |
| Definition | C165835  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. (CDISC Glossary) |
| 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 | Conditionally Required, when any rescue therapies are defined |
| Cardinality | One |
| Relationship content from ToC representing the protocol hierarchy | 6.10.2 Rescue Therapy |
| Relationship (reference to high level conceptual model) |  |
| Value | Text |
| Business rules | Value Allowed: Text  Relationship: n/a  Concept: C165835 |
| Duplicate field in other sections | No |

### Other Non-investigational Intervention

|  |  |
| --- | --- |
| Term (Variable) | 6.10.3 Other Non-investigational Intervention |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | H |
| Definition | Heading |
| User Guidance | N/A |
| Conformance | Conditionally Required, when any other non-investigational interventions are defined |
| Cardinality |  |
| Relationship content from ToC representing the protocol hierarchy | 6.10.3 Other Non-investigational Intervention |
| Relationship (reference to high level conceptual model) |  |
| Value | 6.10.3 Other Non-investigational Intervention |
| Business rules | Value Allowed: 6.10.3 Other Non-investigational Intervention  Relationship: Table of content  Concept: Header, Identifier |
| Duplicate field in other sections | No |

|  |  |
| --- | --- |
| Term (Variable) | {<Other Therapy>} |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | D |
| Definition | CNEW  A non-investigational trial therapy that is different than the one(s) previously specified or mentioned.  If applicable, describe the use of any other non-investigational intervention, for example, challenge agents or diagnostics. |
| User Guidance | If applicable, describe the use of any other non-investigational intervention, for example, challenge agents or diagnostics. |
| Conformance | Conditionally Required , when any other non-investigational interventions are defined |
| Cardinality | One |
| Relationship content from ToC representing the protocol hierarchy | 6.10.3 Other Non-investigational Intervention |
| Relationship (reference to high level conceptual model) |  |
| Value | Text |
| Business rules | Value Allowed: Text  Relationship: n/a  Concept: CNEW |
| Duplicate field in other sections | No |

## Concomitant Therapy

|  |  |
| --- | --- |
| Term (Variable) | 6.11 Concomitant Therapy |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | H |
| Definition | Heading |
| User Guidance | N/A |
| Conformance | Required |
| Cardinality | One |
| Relationship content from ToC representing the protocol hierarchy | 6.11 Concomitant Therapy |
| Relationship (reference to high level conceptual model) |  |
| Value | 6.11 Concomitant Therapy |
| Business rules | Value Allowed: 6.11 Concomitant Therapy  Relationship: Table of content  Concept: Header, Identifier |
| Duplicate field in other sections | No |

|  |  |
| --- | --- |
| Term (Variable) | <Concomitant Therapy> |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | D |
| Definition | C53630  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 |
| Relationship content from ToC representing the protocol hierarchy | 6.11 Concomitant Therapy |
| Relationship (reference to high level conceptual model) |  |
| Value | Text |
| Business rules | Value Allowed: Text  Relationship: n/a  Concept: C53630 |
| Duplicate field in other sections | No |

### Prohibited Concomitant Therapy

|  |  |
| --- | --- |
| Term (Variable) | 6.11.1 Prohibited Concomitant Therapy |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | H |
| Definition | Heading |
| User Guidance | N/A |
| Conformance | Conditionally Required, when any prohibited concomitant therapies are defined |
| Cardinality | One |
| Relationship content from ToC representing the protocol hierarchy | 6.11.1 Prohibited Concomitant Therapy |
| Relationship (reference to high level conceptual model) |  |
| Value | 6.11.1 Prohibited Concomitant Therapy |
| Business rules | Value Allowed: 6.11.1 Prohibited Concomitant Therapy  Relationship: Table of content  Concept: Header, Identifier |
| Duplicate field in other sections | No |

|  |  |
| --- | --- |
| Term (Variable) | {<Prohibited Concomitant Therapy>} |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | D |
| Definition | CNEW  Concomitant therapy that is banned from use in the trial. |
| User Guidance | If applicable, describe any prohibited concomitant therapy. |
| Conformance | Conditionally Required, when any prohibited concomitant therapies are defined |
| Cardinality | One |
| Relationship content from ToC representing the protocol hierarchy | 6.11.1 Prohibited Concomitant Therapy |
| Relationship (reference to high level conceptual model) |  |
| Value | Text |
| Business rules | Value Allowed: Text  Relationship: n/a  Concept: CNEW |
| Duplicate field in other sections | No |

### Permitted Concomitant Therapy

|  |  |
| --- | --- |
| Term (Variable) | 6.11.2 Permitted Concomitant Therapy |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | H |
| Definition | Heading |
| User Guidance | N/A |
| Conformance | Conditionally Required, when any permitted concomitant therapies are defined |
| Cardinality | One |
| Relationship content from ToC representing the protocol hierarchy | 6.11.2 Permitted Concomitant Therapy |
| Relationship (reference to high level conceptual model) |  |
| Value | 6.11.2 Permitted Concomitant Therapy |
| Business rules | Value Allowed: 6.11.2 Permitted Concomitant Therapy  Relationship: Table of content  Concept: Header, Identifier |
| Duplicate field in other sections | No |

|  |  |
| --- | --- |
| Term (Variable) | {<Permitted Concomitant Therapy>} |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | D |
| Definition | CNEW  Concomitant therapy that is approved for use in the trial. |
| User Guidance |  |
| Conformance | Conditionally Required, when any permitted concomitant therapies are defined |
| Cardinality | One |
| Relationship content from ToC representing the protocol hierarchy | 6.11.2 Permitted Concomitant Therapy |
| Relationship (reference to high level conceptual model) |  |
| Value | Text |
| Business rules | Value Allowed: Text  Relationship: n/a  Concept: CNEW |
| Duplicate field in other sections | No |

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

|  |  |
| --- | --- |
| Term (Variable) | Participants Discontinuation of Trial Intervention and Discontinuation or Withdrawal from Trial |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | H |
| Definition | Heading |
| User Guidance | N/A |
| Conformance | Required |
| Cardinality | One to One |
| Relationship content from ToC representing the protocol hierarchy | PARTICIPANT DISCONTINUATION OF TRIAL INTERVENTION AND DISCONTINUATION OR WITHDRAWAL FROM TRIAL |
| Relationship (reference to high level conceptual model) |  |
| Value | Participants Discontinuation of Trial Intervention and Discontinuation or Withdrawal from Trial |
| Business rules | Value Allowed: 7. PARTICIPANT DISCONTINUATION OF TRIAL INTERVENTION AND DISCONTINUATION OR WITHDRAWAL FROM TRIAL  Relationship: Table of Contents  Concept: Header |
| Duplicate field in other sections | Yes, section 4.4 Trial stopping Rules |

## Discontinuation of Trial Intervention for Individual Participants

|  |  |
| --- | --- |
| Term (Variable) | Discontinuation of Trial Intervention for Individual Participants |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | H |
| Definition | Heading |
| User Guidance | N/A |
| Conformance | Required |
| Cardinality | One to One |
| Relationship content from ToC representing the protocol hierarchy | PARTICIPANT DISCONTINUATION OF TRIAL INTERVENTION AND DISCONTINUATION OR WITHDRAWAL FROM TRIAL |
| Relationship (reference to high level conceptual model) |  |
| Value | Discontinuation of Trial Intervention for Individual Participants |
| Business rules | Value Allowed: 7.1 Discontinuation of Trial Intervention for Individual Participants  Relationship: Table of Contents  Concept: Header |
| Duplicate field in other sections | No |

### Permanent Discontinuation of Trial Intervention

|  |  |
| --- | --- |
| Term (Variable) | Permanent Discontinuation of Trial Intervention |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | H |
| Definition | Headeing |
| User Guidance | N/A |
| Conformance | Required |
| Cardinality | One to One |
| Relationship content from ToC representing the protocol hierarchy | PARTICIPANT DISCONTINUATION OF TRIAL INTERVENTION AND DISCONTINUATION OR WITHDRAWAL FROM TRIAL |
| Relationship (reference to high level conceptual model) |  |
| Value | Discontinuation of Trial Intervention for Individual Participants |
| Business rules | Value Allowed: 7.1 Discontinuation of Trial Intervention for Individual Participants  Relationship: 7.1 Discontinuation of Trial Intervention for Individual Participants and Table of Contents  Concept: Header |
| Duplicate field in other sections | No |

|  |  |
| --- | --- |
| Term (Variable) | <Criteria for Permanent Discontinuation of Trial Intervention> |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | D |
| Definition | See CNEW  For review context CNEW  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.  Specify whether participants who discontinue trial intervention can or cannot continue the trial (continue trial visits). In many cases, 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.  Explain the process for collecting and recording the detailed reasons for discontinuing trial intervention(s) if not described elsewhere. |
| Conformance | Required |
| Cardinality | One to Many |
| Relationship content from ToC representing the protocol hierarchy | PARTICIPANT DISCONTINUATION OF TRIAL INTERVENTION AND DISCONTINUATION OR WITHDRAWAL FROM TRIAL |
| Relationship (reference to high level conceptual model) |  |
| Value | Text |
| Business rules | Value Allowed: Yes  Relationship: 7.1.1 Permanent Discontinuation of Trial Intervention  Concept: CNEW |
| Duplicate field in other sections | No |

### Temporary Discontinuation of Trial Intervention

|  |  |
| --- | --- |
| Term (Variable) | Temporary Discontinuation of Trial Intervention |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | H |
| Definition | Heading |
| User Guidance | N/A |
| Conformance | Required |
| Cardinality | One to One |
| Relationship content from ToC representing the protocol hierarchy | PARTICIPANT DISCONTINUATION OF TRIAL INTERVENTION AND DISCONTINUATION OR WITHDRAWAL FROM TRIAL |
| Relationship (reference to high level conceptual model) |  |
| Value | Discontinuation of Trial Intervention for Individual Participants |
| Business rules | Value Allowed: 7.1 Discontinuation of Trial Intervention for Individual Participants  Relationship: Discontinuation of Trial Intervention for Individual Participants and Table of Contents  Concept: Header |
| Duplicate field in other sections | No |

|  |  |
| --- | --- |
| Term (Variable) | Criteria for Temporary Discontinuation of Trial Intervention> |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | D |
| Definition | See CNEW  For review context CNEW  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 needs to temporarily discontinue or interrupt trial intervention * whether they will continue in the trial, and * whether all, or specify 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 | PARTICIPANT DISCONTINUATION OF TRIAL INTERVENTION AND DISCONTINUATION OR WITHDRAWAL FROM TRIAL |
| Relationship (reference to high level conceptual model) |  |
| Value | Text |
| Business rules | Value Allowed: Yes  Relationship: 7.1.2 Temporary Discontinuation of Trial Intervention  Concept: CNEW |
| Duplicate field in other sections | No |

### Rechallenge

|  |  |
| --- | --- |
| Term (Variable) | Rechallenge |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | H |
| Definition | Heading |
| User Guidance | N/A |
| Conformance | Required |
| Cardinality | One to One |
| Relationship content from ToC representing the protocol hierarchy | PARTICIPANT DISCONTINUATION OF TRIAL INTERVENTION AND DISCONTINUATION OR WITHDRAWAL FROM TRIAL |
| Relationship (reference to high level conceptual model) |  |
| Value | Discontinuation of Trial Intervention for Individual Participants |
| Business rules | Value Allowed: 7.1 Discontinuation of Trial Intervention for Individual Participants  Relationship: Discontinuation of Trial Intervention for Individual Participants and Table of Contents  Concept: Header |
| Duplicate field in other sections | No |

|  |  |
| --- | --- |
| Term (Variable) | <Rechallenge> |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | D |
| Definition | See CNEW  For review context CNEW  The requirements that must be met in order to reintroduce previously withdrawn medical intervention in the same patient. |
| User Guidance | Describe the criteria for rechallenge/restarting trial intervention, how 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 re-challenge is not allowed, state this. |
| Conformance | Required |
| Cardinality | One to One |
| Relationship content from ToC representing the protocol hierarchy | PARTICIPANT DISCONTINUATION OF TRIAL INTERVENTION AND DISCONTINUATION OR WITHDRAWAL FROM TRIAL |
| Relationship (reference to high level conceptual model) |  |
| Value | Text |
| Business rules | Value Allowed: Yes  Relationship: 7.1.3 Rechallenge  Concept: CNEW |
| Duplicate field in other sections | No |

## Discontinuation or Withdrawal from the Trial

|  |  |
| --- | --- |
| Term (Variable) | Discontinuation or Withdrawal from Trial |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | H |
| Definition | Heading |
| User Guidance | N/A |
| Conformance | Required |
| Cardinality | One to One |
| Relationship content from ToC representing the protocol hierarchy | PARTICIPANT DISCONTINUATION OF TRIAL INTERVENTION AND DISCONTINUATION OR WITHDRAWAL FROM TRIAL |
| Relationship (reference to high level conceptual model) |  |
| Value | Discontinuation or Withdrawal from Trial |
| Business rules | Value Allowed: 7.2 Discontinuation or Withdrawal from Trial  Relationship: Table of Contents  Concept: Header |
| Duplicate field in other sections | No |

|  |  |
| --- | --- |
| Term (Variable) | <Participant Discontinuation or Withdrawal from Trial> |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | D |
| Definition | See CNEW  For review context CNEW  The reason for participant 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 and data to be collected for the final assessments with reference to the schedule of activities for the participant end of study visit unless provided in another section.  ~~If applicable, describe any trial-specific discontinuation criteria that would apply to individual participants such as treatment or study non-compliance or due to safety reasons. Address the procedure ensuring alignment with the intercurrent events and their handling strategies introduced in Section 3 Trial Objectives, Endpoints and Estimands.~~ 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 continued to be followed to prevent missing data in important analyses. Please refer to Section 10 about the data that need to be collected for the trial estimands. |
| Conformance | Required |
| Cardinality | One to One |
| Relationship content from ToC representing the protocol hierarchy | PARTICIPANT DISCONTINUATION OF TRIAL INTERVENTION AND DISCONTINUATION OR WITHDRAWAL FROM TRIAL |
| Relationship (reference to high level conceptual model) |  |
| Value | Text |
| Business rules | Value Allowed: Yes  Relationship: 7.2 Discontinuation of Trial Intervention  Concept: CNEW |
| Duplicate field in other sections | Yes Section 11.3 Informed Consent Process |

## Lost to Follow-Up

|  |  |
| --- | --- |
| Term (Variable) | Lost to Follow-Up |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | H |
| Definition | Heading |
| User Guidance | N/A |
| Conformance | Required |
| Cardinality | One to Many |
| Relationship content from ToC representing the protocol hierarchy | PARTICIPANT DISCONTINUATION OF TRIAL INTERVENTION AND DISCONTINUATION OR WITHDRAWAL FROM TRIAL |
| Relationship (reference to high level conceptual model) |  |
| Value | Lost to Follow-Up |
| Business rules | Value Allowed: 7.3 Lost to Follow-up  Relationship: Table to Contents  Concept: Header |
| Duplicate field in other sections | Yes, Section 10 |

|  |  |
| --- | --- |
| Term (Variable) | <Lost to Follow-Up> |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | D |
| Definition | See CNEW  For review context CNEW  The mitigation strategies to be employed for the loss or lack of continuation of a subject to follow-up, including the frequency by which follow-up occurs. |
| User Guidance | ~~Describe the measures to be taken to reduce the frequency of participants lost to follow up. Describe how the trial will define and address participants who are lost to follow-up to help limit the amount and impact of missing data. Describe the nature and duration of follow-up, as appropriate.~~Describe how the trial will define loss to follow-up. In general, participants should be considered lost to follow-up only if they cannot be reached despite multiple attempts at contact. Describe how reasons for loss to follow-up (when available) will be documented. Also describe approaches that will be used to minimize 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). |
| Conformance | Required |
| Cardinality | One to Many |
| Relationship content from ToC representing the protocol hierarchy | PARTICIPANT DISCONTINUATION OF TRIAL INTERVENTION AND DISCONTINUATION OR WITHDRAWAL FROM TRIAL |
| Relationship (reference to high level conceptual model) |  |
| Value | Text |
| Business rules | Value Allowed: Yes  Relationship: 7.3 Lost to Follow-up  Concept: CNEW |
| Duplicate field in other sections | Yes, Section 10 |

# TRIAL ASSESSMENTS AND PROCEDURES

|  |  |
| --- | --- |
| Term (Variable) | TRIAL ASSESSMENTS AND PROCEDURES |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | H |
| Definition | Heading |
| User Guidance | N/A |
| Conformance | Required |
| Cardinality | One to One |
| Relationship content from ToC representing the protocol hierarchy | TRIAL ASSESSMENTS AND PROCEDURES |
| Relationship (reference to high level conceptual model) |  |
| Value | TRIAL ASSESSMENTS AND PROCEDURES |
| Business rules | Value Allowed: 8. TRIAL ASSESSMENTS AND PROCEDURES  Relationship: Table of Contents  Concept: Header |
| Duplicate field in other sections | Yes, Section1.3 Schedule of Activities |

## Trial Assessments and Procedures Considerations

|  |  |
| --- | --- |
| Term (Variable) | Trial Assessment and Procedures Considerations |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | H |
| Definition | Heading |
| User Guidance | N/A |
| Conformance | Required |
| Cardinality | One to One |
| Relationship content from ToC representing the protocol hierarchy | TRIAL ASSESSMENTS AND PROCEDURES |
| Relationship (reference to high level conceptual model) |  |
| Value | Trial assessments and procedures Considerations |
| Business rules | Value Allowed: 8.1 Trial assessments and procedures Considerations  Relationship: Table of Contents  Concept: Header |
| Duplicate field in other sections | Yes, Section1.3 Schedule of Activities |

|  |  |
| --- | --- |
| Term (Variable) | <General Trial Assessment and Procedures Considerations> |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | D |
| Definition | See CNEW  For review context CNEW  General trial assessments and procedures required for each part of the trial. |
| User Guidance | No text |
| Conformance | Optional |
| Cardinality | One to One |
| Relationship content from ToC representing the protocol hierarchy | TRIAL ASSESSMENTS AND PROCEDURES |
| Relationship (reference to high level conceptual model) |  |
| Value | Text |
| Business rules | Value Allowed: Yes  Relationship: 8.1 Trial assessments and procedures Considerations  Concept: CNEW |
| Duplicate field in other sections | Yes, Section1.3 Schedule of Activities |

## Screening/Baseline Assessments and procedures

|  |  |
| --- | --- |
| Term (Variable) | Screening/Baseline assessments and procedures |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | H |
| Definition | Heading |
| User Guidance | N/A |
| Conformance | Required |
| Cardinality | One to One |
| Relationship content from ToC representing the protocol hierarchy | TRIAL ASSESSMENTS AND PROCEDURES |
| Relationship (reference to high level conceptual model) |  |
| Value | Screening/Baseline assessments and procedures |
| Business rules | Value Allowed: 8.2 Screening/Baseline assessments and procedures  Relationship: Table of Contents  Concept: Header |
| Duplicate field in other sections | Yes, Section1.3 Schedule of Activities |

|  |  |
| --- | --- |
| Term (Variable) | < Screening Assessments and Procedures> |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | D |
| Definition | See CNEW  For review context CNEW  Trial assessments and procedures related to the screening epoch of the trial. |
| User Guidance | Describe any assessments and procedures that are unique to screening (for example, 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 if screening and baseline are performed at different visits. |
| Conformance | Required |
| Cardinality | One to One |
| Relationship content from ToC representing the protocol hierarchy | TRIAL ASSESSMENTS AND PROCEDURES |
| Relationship (reference to high level conceptual model) |  |
| Value | Text |
| Business rules | Value Allowed: Yes  Relationship: 8.2 Screening/Baseline assessments and procedures  Concept: CNEW |
| Duplicate field in other sections | Yes, Section1.3 Schedule of Activities |

|  |  |
| --- | --- |
| Term (Variable) | {< Baseline Assessments and Procedures>} |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | D |
| Definition | See CNEW  For review context CNEW  Trial assessments and procedures related to the baseline epoch of the trial. |
| User Guidance | Describe any assessments and procedures that are unique to baseline (for example, 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 if screening and baseline are performed at different visits. |
| Conformance | Conditionally required |
| Cardinality | One to One |
| Relationship content from ToC representing the protocol hierarchy | TRIAL ASSESSMENTS AND PROCEDURES |
| Relationship (reference to high level conceptual model) |  |
| Value | Text |
| Business rules | Value Allowed: Conditionally yes  Relationship: 8.2 Screening/Baseline assessments and procedures  Concept: CNEW |
| Duplicate field in other sections | Yes, Section1.3 Schedule of Activities |

## Efficacy Assessments and Procedures

|  |  |
| --- | --- |
| Term (Variable) | Efficacy Assessments and Procedures |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | H |
| Definition | Heading |
| User Guidance | N/A |
| Conformance | Required |
| Cardinality | One to One |
| Relationship content from ToC representing the protocol hierarchy | TRIAL ASSESSMENTS AND PROCEDURES |
| Relationship (reference to high level conceptual model) |  |
| Value | Efficacy Assessments and Procedures |
| Business rules | Value Allowed: 8.3 Efficacy Assessments and Procedures  Relationship: Table of Contents  Concept: Header |
| Duplicate field in other sections | No |

|  |  |
| --- | --- |
| Term (Variable) | <Efficacy Assessments and Procedures> |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | D |
| Definition | CNEW  For review context CNEW  Trial assessments and procedures related to trial intervention efficacy. |
| User Guidance | Describe efficacy assessments and procedures in this section. Cross-refer to Section 8.7 if immunogenicity assessments are used in efficacy determination. |
| Conformance | Required |
| Cardinality | One to Many |
| Relationship content from ToC representing the protocol hierarchy | TRIAL ASSESSMENTS AND PROCEDURES |
| Relationship (reference to high level conceptual model) |  |
| Value | Text |
| Business rules | Value Allowed: Yes  Relationship: 8.3 Efficacy Assessments and Procedures  Concept: CNEW |
| Duplicate field in other sections | No |

## Safety Assessments and Procedures

|  |  |
| --- | --- |
| Term (Variable) | Safety Assessments and Procedures |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | H |
| Definition | Heading |
| User Guidance | N/A |
| Conformance | Required |
| Cardinality | One to One |
| Relationship content from ToC representing the protocol hierarchy | TRIAL ASSESSMENTS AND PROCEDURES |
| Relationship (reference to high level conceptual model) |  |
| Value | Safety Assessments and Procedures |
| Business rules | Value Allowed: 8.4 Safety Assessments and Procedures  Relationship: Table of Contents  Concept: Header |
| Duplicate field in other sections | No |

|  |  |
| --- | --- |
| Term (Variable) | <Safety Assessments and Procedures> |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | D |
| Definition | CNEW  WE NEED A DEFINITION |
| User Guidance | Describe safety assessments and procedures utilizing the following subsections as applicable. Add Level 3 headings as needed.  Identify any non-investigator party responsible for evaluation of laboratory or other safety assessments (for example, Sponsor or external Independent Data Monitoring Committee; cross refer to Section 11.4 for details as applicable).  Include guidelines for the medical management of relevant laboratory or other safety assessment abnormalities. |
| Conformance | Required |
| Cardinality | One to Many |
| Relationship content from ToC representing the protocol hierarchy | TRIAL ASSESSMENTS AND PROCEDURES |
| Relationship (reference to high level conceptual model) | Safety Assessments and Procedures |
| Value | Text |
| Business rules | Value Allowed: Yes  Relationship: 8.4 Safety Assessments and Procedures  Concept: CNEW |
| Duplicate field in other sections | No |

### {Physical Examination}

|  |  |
| --- | --- |
| Term (Variable) | {Physical Examination} |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | H |
| Definition | Heading |
| User Guidance | N/A |
| Conformance | Conditional |
| Cardinality | One to Many |
| Relationship content from ToC representing the protocol hierarchy | TRIAL ASSESSMENTS AND PROCEDURES |
| Relationship (reference to high level conceptual model) |  |
| Value | Safety Assessment and Procedures |
| Business rules | Value Allowed: 8.4 Safety Assessment and Procedures  Relationship: 8.4 Safety Assessment and Procedures and Table of Contents  Concept: Header |
| Duplicate field in other sections | No |

|  |  |
| --- | --- |
| Term (Variable) | {<Physical Examination>} |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | D |
| Definition | See C20989  For review context C20989  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 |
| Cardinality | One to Many |
| Relationship content from ToC representing the protocol hierarchy | TRIAL ASSESSMENTS AND PROCEDURES |
| Relationship (reference to high level conceptual model) |  |
| Value | Text |
| Business rules | Value Allowed: Yes  Relationship: 8.4.1 {Physical Examination}  Concept: C20989 |
| Duplicate field in other sections | Repeatable for each procedure |

### {Vital Signs}

|  |  |
| --- | --- |
| Term (Variable) | {Vital Signs} |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | H |
| Definition | Heading |
| User Guidance | N/A |
| Conformance | Conditional |
| Cardinality | One to One |
| Relationship content from ToC representing the protocol hierarchy | TRIAL ASSESSMENTS AND PROCEDURES |
| Relationship (reference to high level conceptual model) |  |
| Value | Safety Assessment and Procedures |
| Business rules | Value Allowed: 8.4 Safety Assessment and Procedures  Relationship: 8.4 Safety Assessments and Procedures and Table of Contents  Concept: Header |
| Duplicate field in other sections | Repeatable for each vital sign |

|  |  |
| --- | --- |
| Term (Variable) | {<Vital Signs>} |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | D |
| Definition | See C154628  For review context C154628  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 |
| Cardinality | One to One |
| Relationship content from ToC representing the protocol hierarchy | TRIAL ASSESSMENTS AND PROCEDURES |
| Relationship (reference to high level conceptual model) |  |
| Value | Text |
| Business rules | Value Allowed: Yes  Relationship: 8.4.2 {Vital Signs}  Concept: C154628 |
| Duplicate field in other sections | Repeat for each Vital Signs |

### {Electrocardiograms}

|  |  |
| --- | --- |
| Term (Variable) | {Electrocardiograms} |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | H |
| Definition | Heading |
| User Guidance | N/A |
| Conformance | Conditionally Required |
| Cardinality | One to One |
| Relationship content from ToC representing the protocol hierarchy | TRIAL ASSESSMENTS AND PROCEDURES |
| Relationship (reference to high level conceptual model) |  |
| Value | Safety Assessment and Procedures |
| Business rules | Value Allowed: 8.4 Safety Assessment and Procedures  Relationship: 8.4 Safety Assessments and Procedures and Table of Contents  Concept: Header |
| Duplicate field in other sections | No |

|  |  |
| --- | --- |
| Term (Variable) | {<Electrocardiograms>} |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | D |
| Definition | See C168186  For review context  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. (ACC/AHA) |
| User Guidance | Include any specific instructions for the collection, interpretation, and archiving of ECGs. |
| Conformance | Conditionally Required |
| Cardinality | One to One |
| Relationship content from ToC representing the protocol hierarchy | TRIAL ASSESSMENTS AND PROCEDURES |
| Relationship (reference to high level conceptual model) |  |
| Value | Text |
| Business rules | Value Allowed: Yes  Relationship: 8.4.3 {Electrocardiograms}  Concept: C168186 |
| Duplicate field in other sections | Repeat for each procedure |

### {Clinical Laboratory Assessments}

|  |  |
| --- | --- |
| Term (Variable) | {Clinical Laboratory Assessments} |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | H |
| Definition | Heading |
| User Guidance | N/A |
| Conformance | Conditionally Required |
| Cardinality | One to One |
| Relationship content from ToC representing the protocol hierarchy | TRIAL ASSESSMENTS AND PROCEDURES |
| Relationship (reference to high level conceptual model) |  |
| Value | Safety Assessment and Procedures |
| Business rules | Value Allowed: 8.4 Safety Assessment and Procedures  Relationship: 8.4 Safety Assessments and Procedures and Table of Contents  Concept: Header |
| Duplicate field in other sections | No |

|  |  |
| --- | --- |
| Term (Variable) | {<Clinical Safety Laboratory Assessments>} |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | D |
| Definition | See CNEW  For review context CNEW  Trial assessments and Procedures related to participant safety. |
| User Guidance | Include any specific instructions for the collection and interpretation of clinical laboratory assessments.  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 (for example, a pandemic or natural disaster) * treatment algorithms for results out of normal range * Cross-refer to Section 12.1 Clinical Laboratory Tests for lab assessment panels |
| Conformance | Conditionally Required |
| Cardinality | One to One |
| Relationship content from ToC representing the protocol hierarchy | TRIAL ASSESSMENTS AND PROCEDURES |
| Relationship (reference to high level conceptual model) |  |
| Value | Text |
| Business rules | Value Allowed: Yes  Relationship: 8.4.4 {Clinical Laboratory Assessments}  Concept: CNEW |
| Duplicate field in other sections | Repeat for each procedure |

### {Pregnancy Testing}

|  |  |
| --- | --- |
| Term (Variable) | {Pregnancy Testing} |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | H |
| Definition | Heading |
| User Guidance | N/A |
| Conformance | Conditionally Required |
| Cardinality | One to One |
| Relationship content from ToC representing the protocol hierarchy | TRIAL ASSESSMENTS AND PROCEDURES |
| Relationship (reference to high level conceptual model) |  |
| Value | Safety Assessment and Procedures |
| Business rules | Value Allowed: 8.4 Safety Assessment and Procedures  Relationship: 8.4 Safety Assessments and Procedures and Table of Contents  Concept: Header |
| Duplicate field in other sections | No |

|  |  |
| --- | --- |
| Term (Variable) | {< Pregnancy Testing >} |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | D |
| Definition | See C92949  For review context C92949  Any examination performed to assess if a female is gravid. |
| User Guidance | Include any specific instructions for the collection and interpretation of clinical laboratory assessments.  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 (for example, a pandemic or natural disaster) * treatment algorithms for results out of normal range * Cross-refer to Section 12.1 Clinical Laboratory Tests for lab assessment panels |
| Conformance | Conditionally Required |
| Cardinality | One to One |
| Relationship content from ToC representing the protocol hierarchy | TRIAL ASSESSMENTS AND PROCEDURES |
| Relationship (reference to high level conceptual model) |  |
| Value | Text |
| Business rules | Value Allowed: Yes  Relationship: 8.4.5 {< Pregnancy Testing >}  Concept: C92949 |
| Duplicate field in other sections | Repeat for each procedure |

### {Suicidal Ideation and Behaviour Risk Monitoring}

|  |  |
| --- | --- |
| Term (Variable) | {Suicidal Ideation and Behaviour Risk Monitoring} |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | H |
| Definition | Heading |
| User Guidance | N/A |
| Conformance | Conditionally Required |
| Cardinality | One to One |
| Relationship content from ToC representing the protocol hierarchy | TRIAL ASSESSMENTS AND PROCEDURES |
| Relationship (reference to high level conceptual model) |  |
| Value | Safety Assessment and Procedures |
| Business rules | Value Allowed: 8.4 Safety Assessment and Procedures  Relationship: 8.4 Safety Assessments and Procedures and Table of Contents  Concept: Header |
| Duplicate field in other sections | No |

|  |  |
| --- | --- |
| Term (Variable) | {<Suicidal Ideation and Behaviour Risk Monitoring>} |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | D |
| Definition | See CNEW  For review context CNEW  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 will also need to be provided in the appropriate subsection of Section 9.4. |
| Conformance | Conditionally Required |
| Cardinality | One to One |
| Relationship content from ToC representing the protocol hierarchy | TRIAL ASSESSMENTS AND PROCEDURES |
| Relationship (reference to high level conceptual model) |  |
| Value | Text |
| Business rules | Value Allowed: Yes  Relationship: 8.4.6 {Suicidal Ideation and Behaviour Risk Monitoring}  Concept: CNEW |
| Duplicate field in other sections | No |

## Pharmacokinetics

|  |  |
| --- | --- |
| Term (Variable) | Pharmacokinetics |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | H |
| Definition | Heading |
| User Guidance | N/A |
| Conformance | Required |
| Cardinality | One to One |
| Relationship content from ToC representing the protocol hierarchy | TRIAL ASSESSMENTS AND PROCEDURES |
| Relationship (reference to high level conceptual model) |  |
| Value | Pharmacokinetics |
| Business rules | Value Allowed: 8.5 Pharmacokinetics  Relationship: Table of Contents  Concept: |
| Duplicate field in other sections | Header |

|  |  |
| --- | --- |
| Term (Variable) | <Pharmacokinetics> |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | D |
| Definition | See CNEW  For review context CNEW  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. If pharmacokinetic testing is not included in the study, state “Not Applicable.”  Describe the biological sample(s) collected, the handling of samples, and the assay method.  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.  Define the PK parameters to be calculated and the calculation methods. |
| Conformance | Required |
|  | One to One |
| Relationship content from ToC representing the protocol hierarchy | TRIAL ASSESSMENTS AND PROCEDURES |
| Relationship (reference to high level conceptual model) |  |
| Value | Text |
| Business rules | Value Allowed: Yes  Relationship: 8.5 Pharmacokinetics  Concept: CNEW |
| Duplicate field in other sections | No |

## Biomarkers

|  |  |
| --- | --- |
| Term (Variable) | Biomarkers |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | H |
| Definition | Heading |
| User Guidance | N/A |
| Conformance | Required |
| Cardinality | One to One |
| Relationship content from ToC representing the protocol hierarchy | TRIAL ASSESSMENTS AND PROCEDURES |
| Relationship (reference to high level conceptual model) |  |
| Value | Biomarkers |
| Business rules | Value Allowed: 8.6 Biomarkers  Relationship: Table of Contents  Concept: Header |
| Duplicate field in other sections | No |

### Genetics and Pharmacogenomics

|  |  |
| --- | --- |
| Term (Variable) | Genetics and Pharmacogenomics |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | H |
| Definition | Heading |
| User Guidance | N/A |
| Conformance | Required |
| Cardinality | One to One |
| Relationship content from ToC representing the protocol hierarchy | TRIAL ASSESSMENTS AND PROCEDURES |
| Relationship (reference to high level conceptual model) |  |
| Value | Biomarkers |
| Business rules | Value Allowed: 8.6 Biomarkers  Relationship: 8.6 Biomarkers and Table of Contents  Concept: Header |
| Duplicate field in other sections | No |

|  |  |
| --- | --- |
| Term (Variable) | < Genetics and Pharmacogenomics> |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | D |
| Definition | See CNEW  For review context CNEW  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. If genetic testing is not included in the study, state “Not Applicable.”  Describe the biological samples that will be collected (for example, tissue, serum, plasma, etc.), handling of samples, and the assay method.  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 | TRIAL ASSESSMENTS AND PROCEDURES |
| Relationship (reference to high level conceptual model) |  |
| Value | Text |
| Business rules | Value Allowed: Yes  Relationship: 8.6.1 Genetics and Pharmacogenomics  Concept: CNEW |
| Duplicate field in other sections | No |

### Pharmacodynamic Biomarkers

|  |  |
| --- | --- |
| Term (Variable) | Pharmacodynamic Biomarkers |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | H |
| Definition | Heading |
| User Guidance | N/A |
| Conformance | Required |
| Cardinality | One to One |
| Relationship content from ToC representing the protocol hierarchy | TRIAL ASSESSMENTS AND PROCEDURES |
| Relationship (reference to high level conceptual model) |  |
| Value | Biomarkers |
| Business rules | Value Allowed: 8.6 Biomarkers  Relationship: 8.6 Biomarkers and Table of Contents  Concept: Header |
| Duplicate field in other sections |  |

|  |  |
| --- | --- |
| Term (Variable) | < Pharmacodynamic Biomarkers> |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | D |
| Definition | See CNEW  For review context CNEW  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. If pharmacodynamic biomarker testing is not included in the study, state “Not Applicable.”  Describe the biological samples that will be collected (for example, tissue, serum, plasma, etc.).  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 | TRIAL ASSESSMENTS AND PROCEDURES |
| Relationship (reference to high level conceptual model) |  |
| Value | Text |
| Business rules | Value Allowed: Yes  Relationship: 8.6.2 Pharmacodynamic Biomarkers  Concept: CNEW |
| Duplicate field in other sections | No |

### {Other Biomarkers}

|  |  |
| --- | --- |
| Term (Variable) | Other Biomarkers |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | H |
| Definition | Heading |
| User Guidance | N/A |
| Conformance | Conditional |
| Cardinality | One to One |
| Relationship content from ToC representing the protocol hierarchy | TRIAL ASSESSMENTS AND PROCEDURES |
| Relationship (reference to high level conceptual model) |  |
| Value | Biomarkers |
| Business rules | Value Allowed: 8.6 Biomarkers  Relationship: 8.6 Biomarkers and Table of Contents  Concept: Header |
| Duplicate field in other sections |  |

|  |  |
| --- | --- |
| Term (Variable) | {< Other Biomarkers>} |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | D |
| Definition | See CNEW  For review context CNEW  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 (for example, tissue, serum, plasma, etc.).  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 | TRIAL ASSESSMENTS AND PROCEDURES |
| Relationship (reference to high level conceptual model) |  |
| Value | Text |
| Business rules | Value Allowed: Yes  Relationship: 8.6.3 Other Biomarkers  Concept: CNEW |
| Duplicate field in other sections | No |

## Immunogenicity Assessments

|  |  |
| --- | --- |
| Term (Variable) | Immunogenicity Assessment |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | H |
| Definition | Heading |
| User Guidance | N/A |
| Conformance | Required |
| Cardinality | One to One |
| Relationship content from ToC representing the protocol hierarchy | TRIAL ASSESSMENTS AND PROCEDURES |
| Relationship (reference to high level conceptual model) |  |
| Value | Immunogenicity Assessment |
| Business rules | Value Allowed: 8.7 Immunogenicity Assessment  Relationship: Table of Contents  Concept: Header |
| Duplicate field in other sections |  |

|  |  |
| --- | --- |
| Term (Variable) | < Immunogenicity Assessment> |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | D |
| Definition | See CNEW  For review context CNEW  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. If immunogenicity testing is not included in the study, state “Not Applicable.”  Describe the biological samples that will be collected (for example, tissue, serum, plasma, etc.).  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 | TRIAL ASSESSMENTS AND PROCEDURES |
| Relationship (reference to high level conceptual model) |  |
| Value | Text |
| Business rules | Value Allowed: Yes  Relationship: 8.7 Immunogenicity Assessment  Concept: CNEW |
| Duplicate field in other sections | No |

## Medical Resource Utilisation and Health Economics

|  |  |
| --- | --- |
| Term (Variable) | Medical Resource Utilisation and Health Economics |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | H |
| Definition | Heading |
| User Guidance | N/A |
| Conformance | Required |
| Cardinality | One to One |
| Relationship content from ToC representing the protocol hierarchy | TRIAL ASSESSMENTS AND PROCEDURES |
| Relationship (reference to high level conceptual model) |  |
| Value | Medical Resource Utilisation and Health Economics |
| Business rules | Value Allowed: 8.8 Medical Resource Utilisation and Health Economics  Relationship: Table of Contents  Concept: Header |
| Duplicate field in other sections |  |

|  |  |
| --- | --- |
| Term (Variable) | < Medical Resource Utilisation and Health Economics> |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | D |
| Definition | See CNEW  For review context CNEW  The supply and demand of health care resources and the impact of health care resources on the trial population including usage of the medical resources and associated costs. |
| 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. If medical resource utilization and health economics assessment is not included in the study, state “Not Applicable.”  Describe the health outcome measures, collection method (for example, diary, physician interview), and participant burden. |
| Conformance | Required |
| Cardinality | One to One |
| Relationship content from ToC representing the protocol hierarchy | TRIAL ASSESSMENTS AND PROCEDURES |
| Relationship (reference to high level conceptual model) |  |
| Value | Text |
| Business rules | Value Allowed: Yes  Relationship: 8.8 Medical Resource Utilisation and Health Economics  Concept: CNEW |
| Duplicate field in other sections | No |

# ADVERSE EVENTS, SERIOUS ADVERSE EVENTS, PRODUCT COMPLAINTS, PREGNANCY AND POSTPARTUM INFORMATION

|  |  |
| --- | --- |
| Term (Variable) | ADVERSE EVENTS, SERIOUS ADVERSE EVENTS, PRODUCT COMPLAINTS, PREGNANCY AND POSTPARTUM INFORMATION |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | H |
| Definition | Heading |
| User Guidance | N/A |
| Conformance | Required |
| Cardinality | One to Many |
| Relationship content from ToC representing the protocol hierarchy | ADVERSE EVENTS, SERIOUS ADVERSE EVENTS, PRODUCT COMPLAINTS, PREGNANCY AND POSTPARTUM INFORMATION |
| Relationship (reference to high level conceptual model) |  |
| Value | ADVERSE EVENTS, SERIOUS ADVERSE EVENTS, PRODUCT COMPLAINTS, PREGNANCY AND POSTPARTUM INFORMATION |
| Business rules | Value Allowed: 9. ADVERSE EVENTS, SERIOUS ADVERSE EVENTS, PRODUCT COMPLAINTS, PREGNANCY AND POSTPARTUM INFORMATION  Relationship: Table of contents  Concept: Header |
| Duplicate field in other sections | No |

## Definitions

|  |  |
| --- | --- |
| Term (Variable) | Definitions |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | H |
| Definition | Heading |
| User Guidance | N/A |
| Conformance | Required |
| Cardinality | One to |
| Relationship content from ToC representing the protocol hierarchy | ADVERSE EVENTS, SERIOUS ADVERSE EVENTS, PRODUCT COMPLAINTS, PREGNANCY AND POSTPARTUM INFORMATION |
| Relationship (reference to high level conceptual model) |  |
| Value | Definitions |
| Business rules | **Value Allowed:** 9.1 Definitions  **Relationship:** Table of Contents  **Concept:** Header |
| Duplicate field in other sections | No |

### Definitions of Adverse Events

|  |  |
| --- | --- |
| Term (Variable) | Definitions of Adverse Events |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | H |
| Definition | Heading |
| User Guidance | N/A |
| Conformance | Required |
| Cardinality | One to One |
| Relationship content from ToC representing the protocol hierarchy | ADVERSE EVENTS, SERIOUS ADVERSE EVENTS, PRODUCT COMPLAINTS, PREGNANCY AND POSTPARTUM INFORMATION |
| Relationship (reference to high level conceptual model) |  |
| Value | Definitions |
| Business rules | Value Allowed: 9.1 Definitions  Relationship: 9.1 Definitions and Table of Contents  Concept: Header |
| Duplicate field in other sections | No |

|  |  |
| --- | --- |
| Term (Variable) | <AE definition> |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | D |
| Definition | See C41331  For review context C41331  Any untoward medical occurrence in a patient or clinical investigation subject administered a pharmaceutical product and which does not necessarily have a causal relationship with this treatment. an adverse event (AE) can therefore be any unintended sign (including an abnormal laboratory finding), symptom, or disease temporally associated with the use of a medicinal (investigational) product, whether or not related to the medicinal (investigational) product. [ICH E2A] |
| 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 (for example, lack of efficacy or failure of pharmacological actions reporting). |
| Conformance | Required |
| Cardinality | One to One |
| Relationship content from ToC representing the protocol hierarchy | ADVERSE EVENTS, SERIOUS ADVERSE EVENTS, PRODUCT COMPLAINTS, PREGNANCY AND POSTPARTUM INFORMATION |
| Relationship (reference to high level conceptual model) |  |
| Value | Text |
| Business rules | Value Allowed: Yes  Relationship: 9.1.1 Definition of Adverse Events  Concept: C41331 |
| Duplicate field in other sections | No |

### Definitions of Serious Adverse Events

|  |  |
| --- | --- |
| Term (Variable) | Definitions of Serious Adverse Events |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | H |
| Definition | Heading |
| User Guidance | N/A |
| Conformance | Required |
| Cardinality | One to One |
| Relationship content from ToC representing the protocol hierarchy | ADVERSE EVENTS, SERIOUS ADVERSE EVENTS, PRODUCT COMPLAINTS, PREGNANCY AND POSTPARTUM INFORMATION |
| Relationship (reference to high level conceptual model) |  |
| Value | Definitions |
| Business rules | Value Allowed: 9.1 Definitions  Relationship: 9.1 Definitions and Table of Contents  Concept: Header |
| Duplicate field in other sections | No |

|  |  |
| --- | --- |
| Term (Variable) | <SAE definition> |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | D |
| Definition | See C41335  For review context C41335  Adverse event that: 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. (ICH E2A, ICH E2B). |
| 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 | ADVERSE EVENTS, SERIOUS ADVERSE EVENTS, PRODUCT COMPLAINTS, PREGNANCY AND POSTPARTUM INFORMATION |
| Relationship (reference to high level conceptual model) |  |
| Value | Text |
| Business rules | Value Allowed: Yes  Relationship: 9.1.2 Definitions of Serious Adverse Events  Concept: C41335 |
| Duplicate field in other sections | No |

### {Definition of Medical Device Product Complaints}

|  |  |
| --- | --- |
| Term (Variable) | {Definition of Medical Device Product Complaints} |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | H |
| Definition | Heading |
| User Guidance | N/A |
| Conformance | Conditionally Required |
| Cardinality | One to One |
| Relationship content from ToC representing the protocol hierarchy | ADVERSE EVENTS, SERIOUS ADVERSE EVENTS, PRODUCT COMPLAINTS, PREGNANCY AND POSTPARTUM INFORMATION |
| Relationship (reference to high level conceptual model) |  |
| Value | 9.1 Definitions |
| Business rules | Value Allowed: 9.1 Definitions  Relationship: 9.1 Definitions and Table of Contents. Conditional if drug-device combination product is yes  Concept: Header |
| Duplicate field in other sections | No |

|  |  |
| --- | --- |
| Term (Variable) | {<Definition of Medical Device Product Complaints>} |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | D |
| Definition | CNEW  For review context CNEW  A concise explanation of the meaning of medical device product complaints within the context of the trial. |
| User Guidance | No Text |
| Conformance | Conditionally Required |
| Cardinality | One to One |
| Relationship content from ToC representing the protocol hierarchy | ADVERSE EVENTS, SERIOUS ADVERSE EVENTS, PRODUCT COMPLAINTS, PREGNANCY AND POSTPARTUM INFORMATION |
| Relationship (reference to high level conceptual model) |  |
| Value | Text |
| Business rules | Value Allowed: Yes  Relationship: 9.1.3 {Definition of Medical Device Product Complaints}. Conditional if drug-device combination product is yes  Concept: CNEW |
| Duplicate field in other sections | Conditionally required for drug-device combination products |

## Timing and Mechanism for Collection and Reporting

|  |  |
| --- | --- |
| Term (Variable) | Timing and Mechanism for Collection and Reporting |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | H |
| Definition | Heading |
| User Guidance | N/A |
| Conformance | Required |
| Cardinality | One to One |
| Relationship content from ToC representing the protocol hierarchy | ADVERSE EVENTS, SERIOUS ADVERSE EVENTS, PRODUCT COMPLAINTS, PREGNANCY AND POSTPARTUM INFORMATION |
| Relationship (reference to high level conceptual model) |  |
| Value | Timing and Mechanism for Collection and Reporting |
| Business rules | Value Allowed: 9.2 Timing and Mechanism for Collection and Reporting  Relationship: Table of Contents  Concept: Header |
| Duplicate field in other sections | No |

|  |  |
| --- | --- |
| Term (Variable) | Event Type |
| Data Type | Pick List |
| Data (D), Value (V) or Header (H) | Value |
| Definition |  |
| User Guidance |  |
| Conformance | Required |
| Cardinality | One to Many |
| Relationship content from ToC representing the protocol hierarchy | ADVERSE EVENTS, SERIOUS ADVERSE EVENTS, PRODUCT COMPLAINTS, PREGNANCY AND POSTPARTUM INFORMATION |
| Relationship (reference to high level conceptual model) |  |
| Value | AE, SAE, Pregnancy, Other (specify value) |
| Business rules | Value Allowed: Yes  Relationship: Table  Concept: CNEW |
| Duplicate field in other sections | Yes |

|  |  |
| --- | --- |
| Term (Variable) | Situational scope |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | D |
| Definition | See CNEW |
| User Guidance | N/A |
| Conformance | Required |
| Cardinality | One to Many |
| Relationship content from ToC representing the protocol hierarchy | ADVERSE EVENTS, SERIOUS ADVERSE EVENTS, PRODUCT COMPLAINTS, PREGNANCY AND POSTPARTUM INFORMATION |
| Relationship (reference to high level conceptual model) |  |
| Value | Text |
| Business rules | Value Allowed: Yes  Relationship: Table of AE  Concept: CNEW |
| Duplicate field in other sections | Yes |

|  |  |
| --- | --- |
| Term (Variable) | Reportable Period Start |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | D |
| Definition | See CNEW  For review context CNEW |
| User Guidance | N/A |
| Conformance | Required |
| Cardinality | One to Many |
| Relationship content from ToC representing the protocol hierarchy | ADVERSE EVENTS, SERIOUS ADVERSE EVENTS, PRODUCT COMPLAINTS, PREGNANCY AND POSTPARTUM INFORMATION |
| Relationship (reference to high level conceptual model) |  |
| Value | Text |
| Business rules | Value Allowed: Yes  Relationship: Table of AE  Concept: CNEW |
| Duplicate field in other sections | Yes |

|  |  |
| --- | --- |
| Term (Variable) | Reportable Period End |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | D |
| Definition | See CNEW  For review context CNEW |
| User Guidance | N/A |
| Conformance | Required |
| Cardinality | One to Many |
| Relationship content from ToC representing the protocol hierarchy | ADVERSE EVENTS, SERIOUS ADVERSE EVENTS, PRODUCT COMPLAINTS, PREGNANCY AND POSTPARTUM INFORMATION |
| Relationship (reference to high level conceptual model) |  |
| Value | Text |
| Business rules | Value Allowed: Yes  Relationship: Table of AE  Concept: CNEW |
| Duplicate field in other sections | Yes |

|  |  |
| --- | --- |
| Term (Variable) | Timing for Reporting to Sponsor or Designee |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | D |
| Definition | See CNEW  For review context CNEW |
| User Guidance | N/A |
| Conformance | Required |
| Cardinality | One to Many |
| Relationship content from ToC representing the protocol hierarchy | ADVERSE EVENTS, SERIOUS ADVERSE EVENTS, PRODUCT COMPLAINTS, PREGNANCY AND POSTPARTUM INFORMATION |
| Relationship (reference to high level conceptual model) |  |
| Value | Text |
| Business rules | Value Allowed: Yes  Relationship: Table of AE  Concept: CNEW |
| Duplicate field in other sections | Yes |

|  |  |
| --- | --- |
| Term (Variable) | Method for Reporting |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | D |
| Definition | See CNEW  For review context CNEW |
| User Guidance | N/A |
| Conformance | Required |
| Cardinality | One to Many |
| Relationship content from ToC representing the protocol hierarchy | ADVERSE EVENTS, SERIOUS ADVERSE EVENTS, PRODUCT COMPLAINTS, PREGNANCY AND POSTPARTUM INFORMATION |
| Relationship (reference to high level conceptual model) |  |
| Value | Text |
| Business rules | Value Allowed: Yes  Relationship: Table of AE  Concept: CNEW |
| Duplicate field in other sections | Yes |

|  |  |
| --- | --- |
| Term (Variable) | Back-up Method for Reporting |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | D |
| Definition | See CNEW  For review context CNEW |
| User Guidance | N/A |
| Conformance | Required |
| Cardinality | One to Many |
| Relationship content from ToC representing the protocol hierarchy | ADVERSE EVENTS, SERIOUS ADVERSE EVENTS, PRODUCT COMPLAINTS, PREGNANCY AND POSTPARTUM INFORMATION |
| Relationship (reference to high level conceptual model) |  |
| Value | Text |
| Business rules | Value Allowed: Yes  Relationship: Table of AE  Concept: CNEW |
| Duplicate field in other sections | Yes |

**TABLE**

9.2.1 Timing

|  |  |
| --- | --- |
| Term (Variable) | <Time period and/or frequency for collection and reporting product complaints> |
| Data Type | Pick list (hourly, daily, weekly, monthly, annually) |
| Data (D), Value (V) or Header (H) | D |
| Definition | CNEW  For review context CNEW  A set of Collection Timing, mechanism, reporting Aes, SAEs, Pregnancy, and Product Complaints events arranged in rows and columns. |
| User Guidance | Specify the starting and ending time periods for and frequency of collecting AEs, SAEs, product complaints and pregnancy and postpartum information. Cross refer to the Schedule of Assessments as appropriate. |
| Conformance | Required |
| Cardinality | One to One |
| Relationship content from ToC representing the protocol hierarchy | ADVERSE EVENTS, SERIOUS ADVERSE EVENTS, PRODUCT COMPLAINTS, PREGNANCY AND POSTPARTUM INFORMATION |
| Relationship (reference to high level conceptual model) |  |
| Value | Text |
| Business rules | Value Allowed: Yes  Relationship: 9.2 Timing and Mechanism for Collection and Reporting  Concept: CNEW |
| Duplicate field in other sections | No |

9.2.2 Identification and Assessment

## Identification, Recording and Follow-Up

|  |  |
| --- | --- |
| Term (Variable) | Identification, Recording and Follow-Up |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | H |
| Definition | Heading |
| User Guidance | N/A |
| Conformance | Required |
| Cardinality | One to Many |
| Relationship content from ToC representing the protocol hierarchy | ADVERSE EVENTS, SERIOUS ADVERSE EVENTS, PRODUCT COMPLAINTS, PREGNANCY AND POSTPARTUM INFORMATION |
| Relationship (reference to high level conceptual model) |  |
| Value | Identification, Recording and Follow-Up |
| Business rules | Value Allowed: 9.3 Identification, Recording and Follow-Up  Relationship: Table of Contents  Concept: Header |
| Duplicate field in other sections | No |

|  |  |
| --- | --- |
| Term (Variable) | <Identification, Recording and Follow-Up of AEs, SAEs, product complaints and pregnancy and postpartum information> |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | D |
| Definition |  |
| User Guidance | Specify the Investigator’s actions for recording AEs and SAEs, including severity, causality, and the final outcome. |
| Conformance | One to One |
| Cardinality |  |
| Relationship content from ToC representing the protocol hierarchy | ADVERSE EVENTS, SERIOUS ADVERSE EVENTS, PRODUCT COMPLAINTS, PREGNANCY AND POSTPARTUM INFORMATION |
| Relationship (reference to high level conceptual model) |  |
| Value | Text |
| Business rules | Value Allowed: Yes  Relationship: 9.3 Identification, Recording and Follow-Up  Concept: xx |
| Duplicate field in other sections | Yes |

|  |  |
| --- | --- |
| Term (Variable) | <Identification of AEs> |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | D |
| Definition |  |
| User Guidance | Specify the Investigator’s actions for recording AEs and SAEs, including severity, causality, and the final outcome. |
| Conformance | One to One |
| Cardinality |  |
| Relationship content from ToC representing the protocol hierarchy | ADVERSE EVENTS, SERIOUS ADVERSE EVENTS, PRODUCT COMPLAINTS, PREGNANCY AND POSTPARTUM INFORMATION |
| Relationship (reference to high level conceptual model) |  |
| Value | Text |
| Business rules | Value Allowed: Yes  Relationship: 9.3 Identification, Recording and Follow-Up  Concept: xx |
| Duplicate field in other sections | Yes |

|  |  |
| --- | --- |
| Term (Variable) | <Recording of AEs> |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | D |
| Definition |  |
| User Guidance | Specify the Investigator’s actions for recording AEs and SAEs, including severity, causality, and the final outcome. |
| Conformance | One to One |
| Cardinality |  |
| Relationship content from ToC representing the protocol hierarchy | ADVERSE EVENTS, SERIOUS ADVERSE EVENTS, PRODUCT COMPLAINTS, PREGNANCY AND POSTPARTUM INFORMATION |
| Relationship (reference to high level conceptual model) |  |
| Value | Text |
| Business rules | Value Allowed: Yes  Relationship: 9.3 Identification, Recording and Follow-Up  Concept: xx |
| Duplicate field in other sections | Yes |

|  |  |
| --- | --- |
| Term (Variable) | <Follow-Up of AEs, SAEs, product complaints and pregnancy and postpartum information> |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | D |
| Definition |  |
| User Guidance | Specify the Investigator’s actions for recording AEs and SAEs, including severity, causality, and the final outcome. |
| Conformance | One to One |
| Cardinality |  |
| Relationship content from ToC representing the protocol hierarchy | ADVERSE EVENTS, SERIOUS ADVERSE EVENTS, PRODUCT COMPLAINTS, PREGNANCY AND POSTPARTUM INFORMATION |
| Relationship (reference to high level conceptual model) |  |
| Value | Text |
| Business rules | Value Allowed: Yes  Relationship: 9.3 Identification, Recording and Follow-Up  Concept: xx |
| Duplicate field in other sections | Yes |

### Identification

|  |  |
| --- | --- |
| Term (Variable) | Identification |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | H |
| Definition | Heading |
| User Guidance | N/A |
| Conformance | Required |
| Cardinality | One to One |
| Relationship content from ToC representing the protocol hierarchy | ADVERSE EVENTS, SERIOUS ADVERSE EVENTS, PRODUCT COMPLAINTS, PREGNANCY AND POSTPARTUM INFORMATION |
| Relationship (reference to high level conceptual model) |  |
| Value | Identification, Recording and Follow-Up |
| Business rules | Value Allowed: 9.3 Identification, Recording and Follow-Up  Relationship: Table of Contents  Concept: Header |
| Duplicate field in other sections | No |

|  |  |
| --- | --- |
| Term (Variable) | <Identification> |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | D |
| Definition | See CNEW  For review context CNEW  A description of the processes and procedures used to establish identity of adverse events and serious adverse events. |
| User Guidance | Specify how AEs, SAEs, product complaints and pregnancy and postpartum information will be identified (for example, spontaneous reporting, solicited questions). |
| Conformance | Required |
| Cardinality | One to One |
| Relationship content from ToC representing the protocol hierarchy | ADVERSE EVENTS, SERIOUS ADVERSE EVENTS, PRODUCT COMPLAINTS, PREGNANCY AND POSTPARTUM INFORMATION |
| Relationship (reference to high level conceptual model) |  |
| Value | Text |
| Business rules | Value Allowed: Yes  Relationship: 9.3.1 Identification  Concept: CNEW |
| Duplicate field in other sections | No |

### Severity

|  |  |
| --- | --- |
| Term (Variable) | Severity |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | H |
| Definition | Header |
| User Guidance | N/A |
| Conformance | Required |
| Cardinality |  |
| Relationship content from ToC representing the protocol hierarchy | ADVERSE EVENTS, SERIOUS ADVERSE EVENTS, PRODUCT COMPLAINTS, PREGNANCY AND POSTPARTUM INFORMATION |
| Relationship (reference to high level conceptual model) |  |
| Value | Identification, Recording and Follow-Up |
| Business rules | Value Allowed: 9.3 Identification, Recording and Follow-Up  Relationship: Table of Contents  Concept: Header |
| Duplicate field in other sections | No |

|  |  |
| --- | --- |
| Term (Variable) | <Severity> |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | D |
| Definition | See C25676  For review context C25676  The degree of something undesirable. |
| User Guidance | Specify the intensity rating categories/scale. |
| Conformance | Required |
| Cardinality | One to One |
| Relationship content from ToC representing the protocol hierarchy | ADVERSE EVENTS, SERIOUS ADVERSE EVENTS, PRODUCT COMPLAINTS, PREGNANCY AND POSTPARTUM INFORMATION |
| Relationship (reference to high level conceptual model) |  |
| Value | Text |
| Business rules | Value Allowed: Yes  Relationship: 9.3.2 Severity  Concept: C25676 |
| Duplicate field in other sections | No |

### Causality

|  |  |
| --- | --- |
| Term (Variable) | Causality |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | H |
| Definition | Heading |
| User Guidance | N/A |
| Conformance | Required |
| Cardinality | One to One |
| Relationship content from ToC representing the protocol hierarchy | ADVERSE EVENTS, SERIOUS ADVERSE EVENTS, PRODUCT COMPLAINTS, PREGNANCY AND POSTPARTUM INFORMATION |
| Relationship (reference to high level conceptual model) |  |
| Value | Identification, Recording and Follow-Up |
| Business rules | Value Allowed: 9.3 Identification, Recording and Follow-Up  Relationship: Table of Contents  Concept: Header |
| Duplicate field in other sections | No |

|  |  |
| --- | --- |
| Term (Variable) | <Causality> |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | D |
| Definition | See C82552  For review context C82552  The principle that a relationship exists between a primary entity A, or cause, and the occurrence of a secondary entity B, or effect. |
| 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 | ADVERSE EVENTS, SERIOUS ADVERSE EVENTS, PRODUCT COMPLAINTS, PREGNANCY AND POSTPARTUM INFORMATION |
| Relationship (reference to high level conceptual model) |  |
| Value | Text |
| Business rules | Value Allowed: Yes  Relationship: 9.3.3 Causality  Concept: C82552 |
| Duplicate field in other sections | No |

### Follow-Up

|  |  |
| --- | --- |
| Term (Variable) | Follow-Up |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | H |
| Definition | Header |
| User Guidance | No text is intended here (header only). |
| Conformance | Required |
| Cardinality |  |
| Relationship content from ToC representing the protocol hierarchy | ADVERSE EVENTS, SERIOUS ADVERSE EVENTS, PRODUCT COMPLAINTS, PREGNANCY AND POSTPARTUM INFORMATION |
| Relationship (reference to high level conceptual model) |  |
| Value | Identification, Recording and Follow-Up |
| Business rules | Value Allowed: 9.3 Identification, Recording and Follow-Up  Relationship: Table of Contents  Concept: Header |
| Duplicate field in other sections | No |

|  |  |
| --- | --- |
| Term (Variable) | <Follow-Up of AE and SAEs> |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | D |
| Definition | See CNEW  For context review CNEW  A description of the processes and procedures used to stabilize and/or resolve adverse events and serious adverse events. |
| User Guidance | Specify the procedures for follow-up of AEs, SAEs, pregnancy and product complaints. 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 | ADVERSE EVENTS, SERIOUS ADVERSE EVENTS, PRODUCT COMPLAINTS, PREGNANCY AND POSTPARTUM INFORMATION |
| Relationship (reference to high level conceptual model) |  |
| Value | Text |
| Business rules | Value Allowed: Yes  Relationship: 9.3.4 Follow-Up  Concept: CNEW |
| Duplicate field in other sections |  |

## REPORTING

|  |  |
| --- | --- |
| Term (Variable) | Reporting |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | H |
| Definition | Heading |
| User Guidance | N/A |
| Conformance | Required |
| Cardinality | One to One |
| Relationship content from ToC representing the protocol hierarchy | ADVERSE EVENTS, SERIOUS ADVERSE EVENTS, PRODUCT COMPLAINTS, PREGNANCY AND POSTPARTUM INFORMATION |
| Relationship (reference to high level conceptual model) |  |
| Value | Reporting |
| Business rules | Value Allowed: 9.4 Reporting  Relationship: Table of Contents  Concept: Header |
| Duplicate field in other sections | No |

|  |  |
| --- | --- |
| Term (Variable) | <Reporting of SAEs> |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | D |
| Definition |  |
| User Guidance |  |
| Conformance | Required |
| Cardinality | One to One |
| Relationship content from ToC representing the protocol hierarchy | ADVERSE EVENTS, SERIOUS ADVERSE EVENTS, PRODUCT COMPLAINTS, PREGNANCY AND POSTPARTUM INFORMATION |
| Relationship (reference to high level conceptual model) |  |
| Value | Text |
| Business rules | Value Allowed: Yes  Relationship: 9.4 Reporting  Concept: |
| Duplicate field in other sections | Duplicated for each SAE |

### Regulatory Reporting Requirements

|  |  |
| --- | --- |
| Term (Variable) | Regulatory Reporting Requirements |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | H |
| Definition | Heading |
| User Guidance | N/A |
| Conformance | Required |
| Cardinality | One to Many |
| Relationship content from ToC representing the protocol hierarchy | ADVERSE EVENTS, SERIOUS ADVERSE EVENTS, PRODUCT COMPLAINTS, PREGNANCY AND POSTPARTUM INFORMATION |
| Relationship (reference to high level conceptual model) |  |
| Value | Reporting |
| Business rules | Value Allowed: 9.4 Reporting  Relationship: Table of Contents  Concept: Header |
| Duplicate field in other sections | No |

|  |  |
| --- | --- |
| Term (Variable) | < Regulatory Reporting Requirements> |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | D |
| Definition | See CNEW  For review context CNEW  Pending |
| User Guidance | Specify:   * The investigators’ responsibilities for reporting SAEs and Medical Device Product Complaints 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 SAEs to regulatory authorities, ethics committees, and investigators * Serious and unexpected adverse reaction reporting |
| Conformance | Required |
| Cardinality | One to Many |
| Relationship content from ToC representing the protocol hierarchy | ADVERSE EVENTS, SERIOUS ADVERSE EVENTS, PRODUCT COMPLAINTS, PREGNANCY AND POSTPARTUM INFORMATION |
| Relationship (reference to high level conceptual model) |  |
| Value | Text |
| Business rules | Value Allowed: Yes  Relationship: 9.4.1 Regulatory Reporting Requirements  Concept: CNEW |
| Duplicate field in other sections | No |

### Adverse events of Special Interest

|  |  |
| --- | --- |
| Term (Variable) | Adverse Events of Special Interest |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | H |
| Definition | Heading |
| User Guidance | N/A |
| Conformance | Required |
| Cardinality | One to Many |
| Relationship content from ToC representing the protocol hierarchy | ADVERSE EVENTS, SERIOUS ADVERSE EVENTS, PRODUCT COMPLAINTS, PREGNANCY AND POSTPARTUM INFORMATION |
| Relationship (reference to high level conceptual model) |  |
| Value | Reporting |
| Business rules | Value Allowed: 9.4 Reporting  Relationship: 9.4 Reporting and Table of Contents  Concept: Header |
| Duplicate field in other sections | No |

|  |  |
| --- | --- |
| Term (Variable) | <Adverse Events of Special interest or state Not Applicable> |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | D |
| Definition | See CNEW  For review context CNEW  Pending |
| User Guidance | Specify any Adverse Events of Special Interest (AESI):   * Other events that merit reporting to the Sponsor, trial leadership, IRB, and regulatory agencies (for example, secondary malignancies in oncology trials). * Other reportable events not already included in the previous sections, such as cardiovascular events, medical device incidents (including malfunctions), laboratory test abnormalities, and trial intervention overdose.   Include the following for each AESI:   * The definition of the event. * If it is a measurable quantity, specify how will the measurement be done. * If it is a clinical event, specify how will it be confirmed. |
| Conformance | Required |
| Cardinality | One to Many |
| Relationship content from ToC representing the protocol hierarchy | ADVERSE EVENTS, SERIOUS ADVERSE EVENTS, PRODUCT COMPLAINTS, PREGNANCY AND POSTPARTUM INFORMATION |
| Relationship (reference to high level conceptual model) |  |
| Value | Text |
| Business rules | Value Allowed: Yes  Relationship: 9.4.2 Adverse Events of Special Interest  Concept: CNEW |
| Duplicate field in other sections | Duplicated for each Adverse Events of Special interest |

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

|  |  |
| --- | --- |
| Term (Variable) | Disease-related Events or Outcomes Not Qualifying as AEs and SAEs |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | H |
| Definition | Heading |
| User Guidance | N/A |
| Conformance | Required |
| Cardinality | One to Many |
| Relationship content from ToC representing the protocol hierarchy | ADVERSE EVENTS, SERIOUS ADVERSE EVENTS, PRODUCT COMPLAINTS, PREGNANCY AND POSTPARTUM INFORMATION |
| Relationship (reference to high level conceptual model) |  |
| Value | Pharmacokinetics |
| Business rules | Value Allowed: Yes  Relationship: n/a  Concept: n/a |
| Duplicate field in other sections |  |

|  |  |
| --- | --- |
| Term (Variable) |  |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | D |
| Definition |  |
| User Guidance |  |
| Conformance | One to Many |
| Cardinality |  |
| Relationship content from ToC representing the protocol hierarchy | ADVERSE EVENTS, SERIOUS ADVERSE EVENTS, PRODUCT COMPLAINTS, PREGNANCY AND POSTPARTUM INFORMATION |
| Relationship (reference to high level conceptual model) |  |
| Value | Text |
| Business rules | Value Allowed: Yes  Relationship: 9.4 Reporting  Concept: |
| Duplicate field in other sections | Duplicate for each Disease-related Events or Outcomes Not Qualifying as AEs and SAEs |

## Pregnancy and Postpartum Information

|  |  |
| --- | --- |
| Term (Variable) |  |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | H |
| Definition | Heading |
| User Guidance |  |
| Conformance | Required |
| Cardinality |  |
| Relationship content from ToC representing the protocol hierarchy |  |
| Relationship (reference to high level conceptual model) |  |
| Value | Genetics |
| Business rules | Value Allowed: Yes  Relationship: n/a  Concept: n/a |
| Duplicate field in other sections |  |

|  |  |
| --- | --- |
| Term (Variable) |  |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | D |
| Definition |  |
| User Guidance |  |
| Conformance | Optional/Repeated |
| Cardinality |  |
| Relationship content from ToC representing the protocol hierarchy |  |
| Relationship (reference to high level conceptual model) |  |
| Value |  |
| Business rules | Value Allowed: potential controlled terminology  Relationship: n/a  Concept: n/a |
| Duplicate field in other sections | Repeat for each analysis |

### {Participants Who Become Pregnant During the Trial}

|  |  |
| --- | --- |
| Term (Variable) |  |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | H |
| Definition | Heading |
| User Guidance |  |
| Conformance | Required |
| Cardinality |  |
| Relationship content from ToC representing the protocol hierarchy |  |
| Relationship (reference to high level conceptual model) |  |
| Value |  |
| Business rules | Value Allowed: Yes  Relationship: n/a  Concept: n/a |
| Duplicate field in other sections |  |

|  |  |
| --- | --- |
| Term (Variable) |  |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | D |
| Definition |  |
| User Guidance |  |
| Conformance | Optional/Repeated |
| Cardinality |  |
| Relationship content from ToC representing the protocol hierarchy |  |
| Relationship (reference to high level conceptual model) |  |
| Value |  |
| Business rules | Value Allowed: y  Relationship: n/a  Concept: n/a |
| Duplicate field in other sections | Repeat for each biomarker |

### {Participants Whose Partners Become Pregnant}

|  |  |
| --- | --- |
| Term (Variable) |  |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | H |
| Definition | Section Heading |
| User Guidance | . |
| Conformance | Required |
| Cardinality |  |
| Relationship content from ToC representing the protocol hierarchy |  |
| Relationship (reference to high level conceptual model) |  |
| Value |  |
| Business rules | Value Allowed: Yes  Relationship: n/a  Concept: n/a |
| Duplicate field in other sections |  |

|  |  |
| --- | --- |
| Term (Variable) |  |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | D |
| Definition |  |
| User Guidance |  |
| Conformance | Optional/Repeated |
| Cardinality |  |
| Relationship content from ToC representing the protocol hierarchy |  |
| Relationship (reference to high level conceptual model) |  |
| Value |  |
| Business rules | Value Allowed: n/a  Relationship: n/a  Concept: n/a |
| Duplicate field in other sections | Repeat for each procedure |

# Statistical Considerations

|  |  |
| --- | --- |
| Term (Variable) | Medical Resource Utilization and Health Economics |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | H |
| Definition | Section Heading |
| User Guidance |  |
| Conformance | Required/Required |
| Cardinality |  |
| Relationship content from ToC representing the protocol hierarchy | Trial Assessments and Procedures |
| Relationship (reference to high level conceptual model) |  |
| Value | Medical Resource Utilization and Health Economics |
| Business rules | Value Allowed: Yes  Relationship: n/a  Concept: n/a |
| Duplicate field in other sections |  |

|  |  |
| --- | --- |
| Term (Variable) | Medical Resource Utilization and Health Economics |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | D |
| Definition | Describes the health outcome measures, collection method (for example, diary, physician interview), and participant burden. |
| User Guidance | If this section is not applicable, include a statement to this effect.  “Health Economics/Medical Resource Utilization and Health Economics parameters are not evaluated in this trial.”  This section does not apply to Patient Reported Outcomes [PROs] (for PROs cross reference the instructions in the efficacy and safety sections).  Include this section only for any value evidence and outcomes assessment not included in either the efficacy or safety sections. |
| Conformance | Optional/ Repeated |
| Cardinality |  |
| Relationship content from ToC representing the protocol hierarchy | Trial Assessments and Procedures |
| Relationship (reference to high level conceptual model) | Medical Resource Utilisation and Health Economics Assessments and Procedures  Link to objective endpoint or estimand |
| Value |  |
| Business rules | Value Allowed: n/a  Relationship: n/a  Concept: n/a |
| Duplicate field in other sections | Repeat for each evidence and outcome |

## Statistical Considerations

|  |  |
| --- | --- |
| Term (Variable) | Statistical Considerations |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | H |
| Definition | Section Heading |
| User Guidance | Ensure that the data analysis complies with ICH E9 and ICH E9(R1). |
| Conformance | Required |
| Cardinality |  |
| Relationship content from ToC representing the protocol hierarchy | Statistical Considerations |
| Relationship (reference to high level conceptual model) |  |
| Value | Statistical Considerations |
| Business rules | Value Allowed: Y  Relationship: n/a  Concept: n/a |
| Duplicate field in other sections |  |

|  |  |
| --- | --- |
| Term (Variable) | Statistical Considerations |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | D |
| Definition | Section Heading |
| User Guidance | Ensure that the data analysis complies with ICH E9 and ICH E9(R1).  In general, all relevant data collected in the trial should be considered in this statistical considerations section.  Provide a statement with regard to when the primary analyses will be conducted. For example: The analysis will be conducted on all subject data at the time the trial ends. |
| Conformance | Required |
| Cardinality |  |
| Relationship content from ToC representing the protocol hierarchy | Statistical Considerations |
| Relationship (reference to high level conceptual model) |  |
| Value | Statistical Considerations |
| Business rules | Value Allowed: n/a  Relationship: n/a  Concept: n/a |
| Duplicate field in other sections |  |

## Analysis Sets

|  |  |
| --- | --- |
| Term (Variable) | Analysis Sets |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | H |
| Definition | Section Heading |
| User Guidance | Analysis sets to support each analysis will be specified here and described in the Statistical Analysis Plan. |
| Conformance | Required |
| Cardinality |  |
| Relationship content from ToC representing the protocol hierarchy | Analysis Sets |
| Relationship (reference to high level conceptual model) |  |
| Value | Analysis Sets |
| Business rules | Value Allowed: Yes  Relationship: n/a  Concept: n/a |
| Duplicate field in other sections |  |

|  |  |
| --- | --- |
| Term (Variable) | Analysis Datasets |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | D |
| Definition | Detailed description of all efficacy assessments presented in the SoA |
| User Guidance | Analysis sets to support each analysis will be specified here and described in the Statistical Analysis Plan. |
| Conformance | Required |
| Cardinality |  |
| Relationship content from ToC representing the protocol hierarchy | Analysis Sets |
| Relationship (reference to high level conceptual model) |  |
| Value |  |
| Business rules | Value Allowed: n/a  Relationship: n/a  Concept: n/a |
| Duplicate field in other sections |  |

## Analyses Supporting Primary Objective(s)

|  |  |
| --- | --- |
| Term (Variable) | Analysis Supporting Primary Objective(s) |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | H |
| Definition | Section Heading |
| User Guidance | This section introduces the Statistical Analysis Plan, with the detail to be provided in the subsequent subsections. This includes describing the methods for defining the estimate in alignment with how the estimands are defined. Sensitivity analyses should be aligned with how the estimands and estimators are defined. |
| Conformance | Required |
| Cardinality |  |
| Relationship content from ToC representing the protocol hierarchy | Analysis Supporting Primary Objective(s) |
| Relationship (reference to high level conceptual model) |  |
| Value | Analysis Supporting Primary Objective(s) |
| Business rules | Value Allowed: Yes  Relationship: n/a  Concept: n/a |
| Duplicate field in other sections |  |

|  |  |
| --- | --- |
| Term (Variable) | Analysis Supporting Primary Objective(s) |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | D |
| Definition | This section introduces the Statistical Analysis Plan, with the detail to be provided in the subsequent subsections. This includes describing the methods for defining the estimate in alignment with how the estimands are defined. Sensitivity analyses should be aligned with how the estimands and estimators are defined. |
| User Guidance | Analysis sets to support each analysis will be specified here and described in the Statistical Analysis Plan. |
| Conformance | Required/Repeated |
| Cardinality |  |
| Relationship content from ToC representing the protocol hierarchy | Analysis Supporting Primary Objective(s) |
| Relationship (reference to high level conceptual model) |  |
| Value |  |
| Business rules | Value Allowed: n/a  Relationship: n/a  Concept: n/a |
| Duplicate field in other sections |  |

### Statistical Model, Hypothesis, and Method of Analysis

|  |  |
| --- | --- |
| Term (Variable) | Statistical Model, Hypothesis, and Method of Analysis |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | H |
| Definition |  |
| User Guidance | Ensure that the statistical hypothesis/model (and corresponding assumptions)/analysis is aligned with the primary estimand(s).  For all applicable objectives (e.g. primary, secondary), under the appropriate header, state the null and alternative hypotheses, including the pre-planned type 1 error, or alternative criteria to define trial success 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 applicable, state and discuss any adjustments to account for multiplicity.  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 |  |
| Relationship content from ToC representing the protocol hierarchy | Statistical Considerations/Analyses Supporting Primary Objective(s)/Statistical Model, Hypothesis, and Method of Analysis |
| Relationship (reference to high level conceptual model) |  |
| Value |  |
| Business rules | Value Allowed: yes  Relationship: n/a  Concept: n/a |
| Duplicate field in other sections |  |

|  |  |
| --- | --- |
| Term (Variable) | Statistical Model, Hypothesis, and Method of Analysis |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | D |
| Definition |  |
| User Guidance | Ensure that the statistical hypothesis/model (and corresponding assumptions)/analysis is aligned with the primary estimand(s).  For all applicable objectives (e.g. primary, secondary), under the appropriate header, state the null and alternative hypotheses, including the pre-planned type 1 error, or alternative criteria to define trial success 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 applicable, state and discuss any adjustments to account for multiplicity.  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/Repeated |
| Cardinality |  |
| Relationship content from ToC representing the protocol hierarchy | Statistical Considerations/Analyses Supporting Primary Objective(s)/Statistical Model, Hypothesis, and Method of Analysis |
| Relationship (reference to high level conceptual model) | For each primary estimand as related to secondary endpoint combination |
| Value | Statistical Model, Hypothesis, and Method of Analysis |
| Business rules | Value Allowed: n/a  Relationship: n/a  Concept: n/a |
| Duplicate field in other sections |  |

|  |  |
| --- | --- |
| Term (Variable) | Statistical Model, Hypothesis, and Method of Analysis |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | D |
| Definition |  |
| User Guidance | Ensure that the statistical hypothesis/model (and corresponding assumptions)/analysis is aligned with the primary estimand(s).  For all applicable objectives (e.g. primary, secondary), under the appropriate header, state the null and alternative hypotheses, including the pre-planned type 1 error, or alternative criteria to define trial success 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 applicable, state and discuss any adjustments to account for multiplicity.  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/Repeated |
| Cardinality |  |
| Relationship content from ToC representing the protocol hierarchy | Statistical Considerations/Analyses Supporting Primary Objective(s)/Statistical Model, Hypothesis, and Method of Analysis |
| Relationship (reference to high level conceptual model) | For all applicable primary objectives sate the null state the null and alternative hypotheses, including the pre-planned type 1 error, or alternative criteria to define Trial success 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 applicable, state and discuss any adjustments to account for multiplicity. |
| Value | Statistical Model, Hypothesis, and Method of Analysis |
| Business rules | Value Allowed: n/a  Relationship: n/a  Concept: n/a |
| Duplicate field in other sections |  |

|  |  |
| --- | --- |
| Term (Variable) | Statistical Model, Hypothesis, and Method of Analysis |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | D |
| Definition |  |
| User Guidance | Ensure that the statistical hypothesis/model (and corresponding assumptions)/analysis is aligned with the primary estimand(s).  For all applicable objectives (e.g. primary, secondary), under the appropriate header, state the null and alternative hypotheses, including the pre-planned type 1 error, or alternative criteria to define trial success 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 applicable, state and discuss any adjustments to account for multiplicity.  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 | Optional/Repeated |
| Cardinality |  |
| Relationship content from ToC representing the protocol hierarchy | Statistical Considerations/Analyses Supporting Primary Objective(s)/Statistical Model, Hypothesis, and Method of Analysis |
| Relationship (reference to high level conceptual model) | Modelling and simulation methods are to be used, please describe the model (inputs and outputs), the underlying assumptions, and the method of model fitting |
| Value | Statistical Model, Hypothesis, and Method of Analysis |
| Business rules | Value Allowed: n/a  Relationship: n/a  Concept: n/a |
| Duplicate field in other sections |  |

### Handling of Intercurrent Events of Primary Estimand(s)

|  |  |
| --- | --- |
| Term (Variable) | Handling of Intercurrent Events of Primary Estimand(s) |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | H |
| Definition |  |
| 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 avoid repetition with prior sections with more detail here on rationale and handling the data rather than repeating the guidance from the preceding sections. |
| Conformance | Required |
| Cardinality |  |
| Relationship content from ToC representing the protocol hierarchy | Statistical Considerations/Analyses Supporting Primary Objective(s / Handling of Intercurrent Events of Primary Estimand(s) |
| Relationship (reference to high level conceptual model) |  |
| Value |  |
| Business rules | Value Allowed: Yes  Relationship: n/a  Concept: n/a |
| Duplicate field in other sections |  |

|  |  |
| --- | --- |
| Term (Variable) | Handling of Intercurrent Events of Primary Estimand(s) |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | D |
| Definition |  |
| 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 avoid repetition with prior sections with more detail here on rationale and handling the data rather than repeating the guidance from the preceding sections. |
| Conformance | Required/Repeated |
| Cardinality |  |
| Relationship content from ToC representing the protocol hierarchy | Statistical Considerations/Analyses Supporting Primary Objective(s / Handling of Intercurrent Events of Primary Estimand(s) |
| Relationship (reference to high level conceptual model) |  |
| Value |  |
| Business rules | Value Allowed: n/a  Relationship: n/a  Concept: n/a |
| Duplicate field in other sections |  |

### Handling of Missing Data

|  |  |
| --- | --- |
| Term (Variable) | Handling of Missing Data |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | H |
| Definition |  |
| User Guidance | This section should describe how missing data will be dealt with. Refer to the E9(R1) addendum when estimand framework is used.  The protocol should describe how missing data will be handled (for example, type of imputation technique, if any, and provide justification)  In cases where the Primary Objective is related to safety, this section should also be completed. It may also be helpful to include additional statements regarding handling of missing data in general for other important efficacy or safety endpoints or this information can be included in the analysis of secondary endpoint section below. |
| Conformance | Required |
| Cardinality |  |
| Relationship content from ToC representing the protocol hierarchy | Statistical Considerations/Analyses Supporting Primary Objective(s / Handling of Missing Data |
| Relationship (reference to high level conceptual model) |  |
| Value |  |
| Business rules | Value Allowed: yes  Relationship: n/a  Concept: n/a |
| Duplicate field in other sections | For each estimand |

|  |  |
| --- | --- |
| Term (Variable) | Handling of Missing Data |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | D |
| Definition |  |
| User Guidance | This section should describe how missing data will be dealt with. Refer to the E9(R1) addendum when estimand framework is used.  The protocol should describe how missing data will be handled (for example, type of imputation technique, if any, and provide justification)  In cases where the Primary Objective is related to safety, this section should also be completed. It may also be helpful to include additional statements regarding handling of missing data in general for other important efficacy or safety endpoints or this information can be included in the analysis of secondary endpoint section below. |
| Conformance | Required/Repeated |
| Cardinality |  |
| Relationship content from ToC representing the protocol hierarchy | Statistical Considerations/Analyses Supporting Primary Objective(s / Handling of Missing Data |
| Relationship (reference to high level conceptual model) |  |
| Value |  |
| Business rules | Value Allowed: n/a  Relationship: n/a  Concept: n/a |
| Duplicate field in other sections |  |

### Sensitivity Analysis

|  |  |
| --- | --- |
| Term (Variable) | Sensitivity Analysis |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | H |
| Definition |  |
| User Guidance | 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 | Required |
| Cardinality |  |
| Relationship content from ToC representing the protocol hierarchy | Statistical Considerations/Analyses Supporting Primary Objective(s)/Sensitivity Analysis |
| Relationship (reference to high level conceptual model) |  |
| Value |  |
| Business rules | Value Allowed: yes  Relationship: n/a  Concept: n/a |
| Duplicate field in other sections |  |

|  |  |
| --- | --- |
| Term (Variable) | Sensitivity Analysis |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | D |
| Definition |  |
| User Guidance | 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 | Required |
| Cardinality |  |
| Relationship content from ToC representing the protocol hierarchy | Statistical Considerations/Analyses Supporting Primary Objective(s)/Sensitivity Analysis |
| Relationship (reference to high level conceptual model) |  |
| Value |  |
| Business rules | Value Allowed: n/a  Relationship: n/a  Concept: n/a |
| Duplicate field in other sections |  |

### Supplementary Analysis

|  |  |
| --- | --- |
| Term (Variable) | Supplementary Analysis |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | H |
| Definition |  |
| User Guidance | Describe any supplementary analysis if applicable. |
| Conformance | Required |
| Cardinality |  |
| Relationship content from ToC representing the protocol hierarchy | Statistical Considerations/Analyses Supporting Primary Objective(s)/Supplementary Analysis |
| Relationship (reference to high level conceptual model) |  |
| Value | Supplementary Analysis |
| Business rules | Value Allowed: yes  Relationship: n/a  Concept: n/a |
| Duplicate field in other sections |  |

|  |  |
| --- | --- |
| Term (Variable) | Supplementary Analysis |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | D |
| Definition |  |
| User Guidance | Describe any supplementary analysis if applicable. |
| Conformance | Required |
| Cardinality |  |
| Relationship content from ToC representing the protocol hierarchy | Statistical Considerations/Analyses Supporting Primary Objective(s)/Supplementary Analysis |
| Relationship (reference to high level conceptual model) |  |
| Value |  |
| Business rules | Value Allowed: n/a  Relationship: n/a  Concept: n/a |
| Duplicate field in other sections |  |

## Analysis Supporting Secondary Objective(s)

|  |  |
| --- | --- |
| Term (Variable) | Analysis Supporting Secondary Objective(s) |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | H |
| Definition | Section Heading |
| User Guidance | This section should focus on estimands for Secondary Objectives.  In this section describe the statistical analysis, handling of intercurrent events, handling of missing data, and if applicable, sensitivity analysis corresponding to each secondary estimand. |
| Conformance | Required |
| Cardinality |  |
| Relationship content from ToC representing the protocol hierarchy | Statistical Considerations/Analysis Supporting Secondary Objective(s) |
| Relationship (reference to high level conceptual model) |  |
| Value | Analysis Supporting Secondary Objective(s) |
| Business rules | Value Allowed: Yes  Relationship: n/a  Concept: n/a |
| Duplicate field in other sections |  |

|  |  |
| --- | --- |
| Term (Variable) | Statistical Models, Hypothesis and method Analysis |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | D |
| Definition |  |
| User Guidance | This section should focus on estimands for Secondary Objectives.  In this section describe the statistical analysis, handling of intercurrent events, handling of missing data, and if applicable, sensitivity analysis corresponding to each secondary estimand. |
| Conformance | Required/Repeated |
| Cardinality |  |
| Relationship content from ToC representing the protocol hierarchy | Analysis Supporting Secondary Objective(s) |
| Relationship (reference to high level conceptual model) | For each secondary estimand each statistical hypothese/model (and corresponding assumptions)/analysis |
| Value |  |
| Business rules | Value Allowed: n/a  Relationship: n/a  Concept: n/a |
| Duplicate field in other sections |  |

|  |  |
| --- | --- |
| Term (Variable) | Statistical Models, Hypothesis and method Analysis |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | D |
| Definition |  |
| User Guidance | This section should focus on estimands for Secondary Objectives.  In this section describe the statistical analysis, handling of intercurrent events, handling of missing data, and if applicable, sensitivity analysis corresponding to each secondary estimand. |
| Conformance | Required/Repeated |
| Cardinality |  |
| Relationship content from ToC representing the protocol hierarchy | Analysis Supporting Secondary Objective(s) |
| Relationship (reference to high level conceptual model) | For all applicable Secondary objectives sate the null state the null and alternative hypotheses, including the pre-planned type 1 error, or alternative criteria to define Trial success 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 applicable, state and discuss any adjustments to account for multiplicity. |
| Value |  |
| Business rules | Value Allowed: n/a  Relationship: n/a  Concept: n/a |
| Duplicate field in other sections |  |

|  |  |
| --- | --- |
| Term (Variable) | Handling of Intercurrent events and Method Analysis |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | D |
| Definition |  |
| User Guidance | This section should focus on estimands for Secondary Objectives.  In this section describe the statistical analysis, handling of intercurrent events, handling of missing data, and if applicable, sensitivity analysis corresponding to each secondary estimand. |
| Conformance | Required/Repeatable  Optional/Repeatable |
| Cardinality |  |
| Relationship content from ToC representing the protocol hierarchy | Analysis Supporting Secondary Objective(s) |
| Relationship (reference to high level conceptual model) |  |
| Value |  |
| Business rules | Value Allowed: n/a  Relationship: n/a  Concept: n/a |
| Duplicate field in other sections |  |

|  |  |
| --- | --- |
| Term (Variable) | Statistical Models, Hypothesis and method Analysis |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | D |
| Definition |  |
| User Guidance | This section should focus on estimands for Secondary Objectives.  In this section describe the statistical analysis, handling of intercurrent events, handling of missing data, and if applicable, sensitivity analysis corresponding to each secondary estimand. |
| Conformance | Optional/Repeated |
| Cardinality |  |
| Relationship content from ToC representing the protocol hierarchy | Analysis Supporting Secondary Objective(s) |
| Relationship (reference to high level conceptual model) | Secondary modelling and simulation methods are to be used, please describe the model (inputs and outputs), the underlying assumptions, and the method of model fitting |
| Value |  |
| Business rules | Value Allowed: n/a  Relationship: n/a  Concept: n/a |
| Duplicate field in other sections |  |

|  |  |
| --- | --- |
| Term (Variable) | Handling of Intercurrent events and Method Analysis |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | D |
| Definition |  |
| User Guidance | This section should focus on estimands for Secondary Objectives.  In this section describe the statistical analysis, handling of intercurrent events, handling of missing data, and if applicable, sensitivity analysis corresponding to each secondary estimand. |
| Conformance | Required/Repeated |
| Cardinality |  |
| Relationship content from ToC representing the protocol hierarchy | Analysis Supporting Secondary Objective(s) |
| Relationship (reference to high level conceptual model) |  |
| Value |  |
| Business rules | Value Allowed: n/a  Relationship: n/a  Concept: n/a |
| Duplicate field in other sections |  |

|  |  |
| --- | --- |
| Term (Variable) | Handling of Missing Data |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | D |
| Definition |  |
| User Guidance | This section should focus on estimands for Secondary Objectives.  In this section describe the statistical analysis, handling of intercurrent events, handling of missing data, and if applicable, sensitivity analysis corresponding to each secondary estimand. |
| Conformance | Required/Repeated |
| Cardinality |  |
| Relationship content from ToC representing the protocol hierarchy | Analysis Supporting Secondary Objective(s) |
| Relationship (reference to high level conceptual model) |  |
| Value |  |
| Business rules | Value Allowed: n/a  Relationship: n/a  Concept: n/a |
| Duplicate field in other sections |  |

## Analysis of Exploratory Objective(s)

|  |  |
| --- | --- |
| Term (Variable) | Analysis of Exploratory Objectives |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | H |
| Definition | Section Heading |
| User Guidance | Analyses Supporting Tertiary/Exploratory Endpoint(s) |
| Conformance | Required |
| Cardinality |  |
| Relationship content from ToC representing the protocol hierarchy | Statistical Considerations/ Analysis of Exploratory Endpoint(s) |
| Relationship (reference to high level conceptual model) |  |
| Value | Analysis of Exploratory Endpoint(s) |
| Business rules | Value Allowed: Yes  Relationship: n/a  Concept: n/a |
| Duplicate field in other sections |  |

|  |  |
| --- | --- |
| Term (Variable) | Analysis Supporting Tertiary/Exploratory Objectives(s) |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | D |
| Definition |  |
| User Guidance | This section should focus on estimands for Secondary Objectives.  In this section describe the statistical analysis, handling of intercurrent events, handling of missing data, and if applicable, sensitivity analysis corresponding to each secondary estimand. |
| Conformance | Required/Repeated |
| Cardinality |  |
| Relationship content from ToC representing the protocol hierarchy | Analysis Supporting Tertiary/Exploratory Objective(s) |
| Relationship (reference to high level conceptual model) | Exploratory endpoint combination |
| Value |  |
| Business rules | Value Allowed: n/a  Relationship: n/a  Concept: n/a |
| Duplicate field in other sections | Repeat as related to tertiary/exploratory endpoint combination |

## Safety Analyses

|  |  |
| --- | --- |
| Term (Variable) | Safety Analyses |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | H |
| Definition |  |
| User Guidance |  |
| Conformance | Required |
| Cardinality |  |
| Relationship content from ToC representing the protocol hierarchy | Statistical Considerations / Safety Analyses |
| Relationship (reference to high level conceptual model) |  |
| Value |  |
| Business rules | Value Allowed: Yes  Relationship: n/a  Concept: n/a |
| Duplicate field in other sections |  |

|  |  |
| --- | --- |
| Term (Variable) | Safety Analyses |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | D |
| Definition |  |
| User Guidance |  |
| Conformance | Required |
| Cardinality |  |
| Relationship content from ToC representing the protocol hierarchy | Statistical Considerations / Safety Analyses |
| Relationship (reference to high level conceptual model) |  |
| Value |  |
| Business rules | Value Allowed: n/a  Relationship: n/a  Concept: n/a |
| Duplicate field in other sections |  |

## Other Analyses

|  |  |
| --- | --- |
| Term (Variable) | Other Analyses |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | H |
| Definition |  |
| User Guidance |  |
| Conformance | Required |
| Cardinality |  |
| Relationship content from ToC representing the protocol hierarchy | Statistical Considerations / Other Analyses |
| Relationship (reference to high level conceptual model) |  |
| Value | Other Analyses |
| Business rules | Value Allowed: yes  Relationship: n/a  Concept: n/a |
| Duplicate field in other sections |  |

|  |  |
| --- | --- |
| Term (Variable) | Other Analyses |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | D |
| Definition |  |
| User Guidance |  |
| Conformance | Required |
| Cardinality |  |
| Relationship content from ToC representing the protocol hierarchy | Statistical Considerations / Other Analyses |
| Relationship (reference to high level conceptual model) |  |
| Value |  |
| Business rules | Value Allowed: n/a  Relationship: n/a  Concept: n/a |
| Duplicate field in other sections |  |

## Interim Analyses

|  |  |
| --- | --- |
| Term (Variable) | Interim Analyses |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | H |
| Definition |  |
| User Guidance |  |
| Conformance | Required |
| Cardinality |  |
| Relationship content from ToC representing the protocol hierarchy | Statistical Considerations / Interim Analyses |
| Relationship (reference to high level conceptual model) |  |
| Value | Interim Analyses |
| Business rules | Value Allowed: yes  Relationship: n/a  Concept: n/a |
| Duplicate field in other sections |  |

|  |  |
| --- | --- |
| Term (Variable) | Interim Analyses |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | D |
| Definition |  |
| User Guidance |  |
| Conformance | Required/Repeated |
| Cardinality |  |
| Relationship content from ToC representing the protocol hierarchy | Statistical Considerations / Interim Analyses |
| Relationship (reference to high level conceptual model) |  |
| Value |  |
| Business rules | Value Allowed: n/a  Relationship: n/a  Concept: n/a |
| Duplicate field in other sections | For each interim |

## Sample Size Determination

|  |  |
| --- | --- |
| Term (Variable) | Sample Size Determination |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | H |
| Definition |  |
| User Guidance | This section should detail the methods used for the determination of the sample size and a reference to tables or statistical software used to carry out the calculation. Sufficient information should be provided so that the sample size calculation can be reproduced or described.  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 studies; pragmatic considerations for trials in rare diseases). |
| Conformance | Required |
| Cardinality |  |
| Relationship content from ToC representing the protocol hierarchy | Statistical Considerations / Sample Size Determination |
| Relationship (reference to high level conceptual model) |  |
| Value | Sample Size Determination |
| Business rules | Value Allowed: yes  Relationship: n/a  Concept: n/a |
| Duplicate field in other sections |  |

## Protocol Deviations

|  |  |
| --- | --- |
| Term (Variable) | Protocol Deviations |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | H |
| Definition |  |
| User Guidance |  |
| Conformance | Required |
| Cardinality |  |
| Relationship content from ToC representing the protocol hierarchy | Statistical Considerations / Sample Size Determination |
| Relationship (reference to high level conceptual model) |  |
| Value | Protocol Deviations |
| Business rules | Value Allowed: yes  Relationship: n/a  Concept: n/a |
| Duplicate field in other sections |  |

|  |  |
| --- | --- |
| Term (Variable) | Protocol Deviations Plans |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | D |
| Definition |  |
| User Guidance |  |
| Conformance | Required |
| Cardinality |  |
| Relationship content from ToC representing the protocol hierarchy | Statistical Considerations / Sample Size Determination |
| Relationship (reference to high level conceptual model) |  |
| Value |  |
| Business rules | Value Allowed: yes  Relationship: n/a  Concept: n/a |
| Duplicate field in other sections |  |

# Trial Oversight and Other General Considerations

|  |  |
| --- | --- |
| Term (Variable) | TRIAL OVERSIGHT AND OTHER GENERAL CONSIDERATION |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | H |
| Definition | Heading |
| User Guidance | N/A |
| Conformance | Required |
| Cardinality |  |
| Relationship content from ToC representing the protocol hierarchy | TRIAL OVERSIGHT AND OTHER GENERAL CONSIDERATION |
| Relationship (reference to high level conceptual model) |  |
| Value | TRIAL OVERSIGHT AND OTHER GENERAL CONSIDERATION |
| Business rules | Value Allowed: 11. TRIAL OVERSIGHT AND OTHER GENERAL CONSIDERATION  Relationship: Table of Contents  Concept: Header |
| Duplicate field in other sections | No |

## Regulatory and Ethical Considerations

|  |  |
| --- | --- |
| Term (Variable) | Regulatory and Ethical Considerations |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | H |
| Definition | Heading |
| User Guidance | N/A |
| Conformance | Required |
| Cardinality |  |
| Relationship content from ToC representing the protocol hierarchy | TRIAL OVERSIGHT AND OTHER GENERAL CONSIDERATION |
| Relationship (reference to high level conceptual model) |  |
| Value | Regulatory and Ethical Considerations |
| Business rules | Value Allowed: 11.1 Regulatory and Ethical Considerations  Relationship: Table of Contents  Concept: Heading |
| Duplicate field in other sections | No |

|  |  |
| --- | --- |
| Term (Variable) | <Regulatory and Ethical Considerations> |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | D |
| Definition | See CNEW  For review context CNEW  A textual description of the regulatory and ethical considerations regarding the trial. |
| User Guidance | Concisely summarize 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:   * 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 | TRIAL OVERSIGHT AND OTHER GENERAL CONSIDERATION |
| Relationship (reference to high level conceptual model) |  |
| Value | Text |
| Business rules | Value Allowed: Yes  Relationship: 11.1 Regulatory and Ethical Considerations  Concept: CNEW |
| Duplicate field in other sections | No |

## Trial oversight

|  |  |
| --- | --- |
| Term (Variable) | Trial Oversight |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | H |
| Definition | Heading |
| User Guidance | N/A |
| Conformance | Required |
| Cardinality |  |
| Relationship content from ToC representing the protocol hierarchy | TRIAL OVERSIGHT AND OTHER GENERAL CONSIDERATION |
| Relationship (reference to high level conceptual model) |  |
| Value | 11.2 Trial Oversight |
| Business rules | Value Allowed: 11.2 Trial Oversight  Relationship: Table of Contents  Concept: Heading |
| Duplicate field in other sections | No |

11.2.1 Investigator Responsibilities

|  |  |
| --- | --- |
| Term (Variable) | Investigator Responsibilities |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | H |
| Definition | Heading |
| User Guidance | N/A |
| Conformance | Required |
| Cardinality | One to One |
| Relationship content from ToC representing the protocol hierarchy | TRIAL OVERSIGHT AND OTHER GENERAL CONSIDERATION |
| Relationship (reference to high level conceptual model) |  |
| Value | 11.2 Trial Oversight |
| Business rules | Value Allowed: 11.2 Trial Oversight  Relationship: 11.2 Trial Oversight and the Table of Contents  Concept: Heading |
| Duplicate field in other sections | No |

|  |  |
| --- | --- |
| Term (Variable) | <Investigator Responsibilities> |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | D |
| Definition | See CNEW  For review context CNEW  A textual description of the obligations of the investigator with respect to the trial. |
| User Guidance | N/A |
| Conformance | Required |
| Cardinality | One to One |
| Relationship content from ToC representing the protocol hierarchy | TRIAL OVERSIGHT AND OTHER GENERAL CONSIDERATION |
| Relationship (reference to high level conceptual model) |  |
| Value | Text |
| Business rules | Value Allowed: Yes  Relationship: 11.2.1 Investigator Responsibilities  Concept: CNEW |
| Duplicate field in other sections | No |

11.2.2 Sponsor Responsibilities

|  |  |
| --- | --- |
| Term (Variable) | Sponsor Responsibilities |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | H |
| Definition | Heading |
| User Guidance | N/A |
| Conformance | Required |
| Cardinality | One to One |
| Relationship content from ToC representing the protocol hierarchy | TRIAL OVERSIGHT AND OTHER GENERAL CONSIDERATION |
| Relationship (reference to high level conceptual model) |  |
| Value | Text |
| Business rules | Value Allowed: Yes  Relationship: 11.2.2 Sponsor Responsibilities  Concept: Heading |
| Duplicate field in other sections | No |

|  |  |
| --- | --- |
| Term (Variable) | <Sponsor Responsibilities> |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | D |
| Definition | See CNEW  For review context CNEW  A textual description of the obligations of the sponsor with respect to the trial. |
| User Guidance | Describe the sponsor duties to be delegated to a third party that may impact the investigators sites, if applicable. |
| Conformance | Required |
| Cardinality | One to One |
| Relationship content from ToC representing the protocol hierarchy | TRIAL OVERSIGHT AND OTHER GENERAL CONSIDERATION |
| Relationship (reference to high level conceptual model) |  |
| Value | Text |
| Business rules | Value Allowed: Yes  Relationship: 11.2.2 Sponsor Responsibilities  Concept: CNEW |
| Duplicate field in other sections | No |

## Informed Consent Process

|  |  |
| --- | --- |
| Term (Variable) | Informed Consent Process |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | H |
| Definition | Heading |
| User Guidance | N/A |
| Conformance | Required |
| Cardinality | One to One |
| Relationship content from ToC representing the protocol hierarchy | TRIAL OVERSIGHT AND OTHER GENERAL CONSIDERATION |
| Relationship (reference to high level conceptual model) |  |
| Value | 11.3 Informed Consent Process |
| Business rules | Value Allowed: 11.3 Informed Consent Process  Relationship: Table of Contents  Concept: Heading |
| Duplicate field in other sections | No |

|  |  |
| --- | --- |
| Term (Variable) | < Description of Informed Consent Process> |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | D |
| Definition | See C184390  For review context C184390  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 subjects with legally authorized representatives. (ICH GCP) |
| User Guidance | Specify the key elements of the informed consent process, including any special needs and how these are addressed (for example, 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 | TRIAL OVERSIGHT AND OTHER GENERAL CONSIDERATION |
| Relationship (reference to high level conceptual model) |  |
| Value | Text |
| Business rules | Value Allowed: Yes  Relationship: 11.3 Informed Consent Process  Concept: C184390 |
| Duplicate field in other sections | No |

|  |  |
| --- | --- |
| Term (Variable) | < Description of Assent Process> |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | D |
| Definition | See CNEW  For review context CNEW  A narrative representation 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 | Conditional Required |
| Cardinality |  |
| Relationship content from ToC representing the protocol hierarchy | TRIAL OVERSIGHT AND OTHER GENERAL CONSIDERATION |
| Relationship (reference to high level conceptual model) |  |
| Value | Test |
| Business rules | Value Allowed: Yes  Relationship: 11.3 Informed Consent Process  Concept: CNEW |
| Duplicate field in other sections | No |

|  |  |
| --- | --- |
| Term (Variable) | < Description of Emergency Consent Process> |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | D |
| Definition | See CNEW  For review context CNEW  A type of informed consent process that may occur during an emergency situation in which the participant or their legally authorized 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 | Conditional Required |
| Cardinality | One to One |
| Relationship content from ToC representing the protocol hierarchy | TRIAL OVERSIGHT AND OTHER GENERAL CONSIDERATION |
| Relationship (reference to high level conceptual model) |  |
| Value | Text |
| Business rules | Value Allowed: Yes  Relationship: 11.3 Informed Consent Process  Concept: CNEW |
| Duplicate field in other sections | No |

11.3.1 Informed Consent for Rescreening

|  |  |
| --- | --- |
| Term (Variable) | Informed Consent for Rescreening |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | H |
| Definition | Heading |
| User Guidance | N/A |
| Conformance | Required |
| Cardinality |  |
| Relationship content from ToC representing the protocol hierarchy | TRIAL OVERSIGHT AND OTHER GENERAL CONSIDERATION |
| Relationship (reference to high level conceptual model) |  |
| Value | Informed Consent Process |
| Business rules | Value Allowed:  Relationship:  Concept: |
| Duplicate field in other sections |  |

|  |  |
| --- | --- |
| Term (Variable) | <Consent requirements for Rescreening> |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | D |
| Definition | See CNEW  For review context CNEW  A description of the consent requirements for participants in the event of screen failure and rescreening. |
| User Guidance | If participants can be rescreened, add the text to 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 | Optional Required |
| Cardinality | One to One |
| Relationship content from ToC representing the protocol hierarchy | TRIAL OVERSIGHT AND OTHER GENERAL CONSIDERATION |
| Relationship (reference to high level conceptual model) |  |
| Value | Text |
| Business rules | Value Allowed: Yes  Relationship: 11.3.1 Informed Consent for Rescreening  Concept: CNEW |
| Duplicate field in other sections | No |

11.3.2 Informed Consent for Use of Remaining Samples in Exploratory Research

|  |  |
| --- | --- |
| Term (Variable) | Informed Consent for Use of Remaining Samples in Exploratory Research |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | H |
| Definition | Heading |
| User Guidance | N/A |
| Conformance | Required |
| Cardinality | One to One |
| Relationship content from ToC representing the protocol hierarchy | TRIAL OVERSIGHT AND OTHER GENERAL CONSIDERATION |
| Relationship (reference to high level conceptual model) |  |
| Value | Informed Consent Process |
| Business rules | Value Allowed: 11.3 Informed Consent Process  Relationship: Table of Contents  Concept: Heading |
| Duplicate field in other sections | No |

|  |  |
| --- | --- |
| Term (Variable) | <Additional ICF text for Use of Remaining Samples in Exploratory Research> |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | D |
| Definition | See CNEW  For review context CNEW  A description of the consent requirements for optional 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 an additional text. |
| User Guidance | If participants will be asked to consent to optional exploratory research using the remainder of mandatory samples, include text that addresses 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 Required |
| Cardinality | One to One |
| Relationship content from ToC representing the protocol hierarchy | TRIAL OVERSIGHT AND OTHER GENERAL CONSIDERATION |
| Relationship (reference to high level conceptual model) |  |
| Value | Text |
| Business rules | Value Allowed: Yes  Relationship: 11.3.1 Informed Consent for Rescreening  Concept: CNEW |
| Duplicate field in other sections | No |

## Committees

|  |  |
| --- | --- |
| Term (Variable) | Committees |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | H |
| Definition | Heading |
| User Guidance | N/A |
| Conformance | Required |
| Cardinality |  |
| Relationship content from ToC representing the protocol hierarchy | TRIAL OVERSIGHT AND OTHER GENERAL CONSIDERATION |
| Relationship (reference to high level conceptual model) |  |
| Value |  |
| Business rules | Value Allowed:  Relationship:  Concept: |
| Duplicate field in other sections |  |

|  |  |
| --- | --- |
| Term (Variable) | <Committees> |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | D |
| Definition | See CNEW  For review context CNEW  A textual 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 (for example, 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 | TRIAL OVERSIGHT AND OTHER GENERAL CONSIDERATION |
| Relationship (reference to high level conceptual model) |  |
| Value | Text |
| Business rules | Value Allowed: Yes  Relationship: 11.4 Committees  Concept: CNEW |
| Duplicate field in other sections | No |

## Insurance and indemnity

|  |  |
| --- | --- |
| Term (Variable) | Insurance and Indemnity |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | H |
| Definition | Heading |
| User Guidance | N/A |
| Conformance | Required |
| Cardinality |  |
| Relationship content from ToC representing the protocol hierarchy | TRIAL OVERSIGHT AND OTHER GENERAL CONSIDERATION |
| Relationship (reference to high level conceptual model) |  |
| Value | Insurance and Indemnity |
| Business rules | Value Allowed: 11.5 Insurance and Indemnity  Relationship: Table of Contents  Concept: Heading |
| Duplicate field in other sections |  |

|  |  |
| --- | --- |
| Term (Variable) | <Insurance and Indemnity> |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | D |
| Definition | See CNEW  For review Context CNEW  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 Ome |
| Relationship content from ToC representing the protocol hierarchy | TRIAL OVERSIGHT AND OTHER GENERAL CONSIDERATION |
| Relationship (reference to high level conceptual model) |  |
| Value | Text |
| Business rules | Value Allowed: Yes  Relationship: 11.5 Insurance and Indemnity  Concept: CNEW |
| Duplicate field in other sections | No |

11.6 Risk Management

|  |  |
| --- | --- |
| Term (Variable) | Risk Management |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | H |
| Definition | Heading |
| User Guidance | N/A |
| Conformance | Required |
| Cardinality |  |
| Relationship content from ToC representing the protocol hierarchy | TRIAL OVERSIGHT AND OTHER GENERAL CONSIDERATION |
| Relationship (reference to high level conceptual model) |  |
| Value | Risk Management |
| Business rules | Value Allowed: 11.6 Risk Management  Relationship: Table of Contents  Concept: Heading |
| Duplicate field in other sections | No |

|  |  |
| --- | --- |
| Term (Variable) | <Risk Management> |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | D |
| Definition | See CNEW  For review context CNEW  A description of how potential risks associated with the trial will be handled. |
| User Guidance | Describe how the critical to quality factors will be mitigated or refer to separate document where this is described. It is important to determine the risks that threaten their integrity and decide whether they can be accepted or should be mitigated, based on their probability, detectability and impact. Where it is decided that risks should be mitigated, the necessary control processes should be put in place and communicated, and the necessary actions taken to mitigate the risks. |
| Conformance | Required |
| Cardinality | One to One |
| Relationship content from ToC representing the protocol hierarchy | TRIAL OVERSIGHT AND OTHER GENERAL CONSIDERATION |
| Relationship (reference to high level conceptual model) |  |
| Value | Text |
| Business rules | Value Allowed: Yes  Relationship: 11.6 Risk Management  Concept: CNEW |
| Duplicate field in other sections | No |

11.7 Data Governance

|  |  |
| --- | --- |
| Term (Variable) | Data Governance |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | H |
| Definition | Heading |
| User Guidance | N/A |
| Conformance | Required |
| Cardinality | One to One |
| Relationship content from ToC representing the protocol hierarchy | TRIAL OVERSIGHT AND OTHER GENERAL CONSIDERATION |
| Relationship (reference to high level conceptual model) |  |
| Value | Data Governance |
| Business rules | Value Allowed: 11.7 Data Governance  Relationship: Table of Contents  Concept: Heading |
| Duplicate field in other sections | No |

|  |  |
| --- | --- |
| Term (Variable) | <Data Governance> |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | D |
| Definition | See CNEW  For review context CNEW  A describe the key processes for data integrity, traceability and security, to enable accurate collection, reporting, monitoring, transfer, retention, access and publication. |
| User Guidance | Describe the key processes for critical trial integrity, traceability and security enabling accurate collection, reporting, monitoring, transfer, retention, access and publication if not addressed in separate agreement(s).  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 | TRIAL OVERSIGHT AND OTHER GENERAL CONSIDERATION |
| Relationship (reference to high level conceptual model) |  |
| Value | Text |
| Business rules | Value Allowed: Yes  Relationship: 11.7 Data Governance  Concept: CNEW |
| Duplicate field in other sections | No |

11.8 Source Data

|  |  |
| --- | --- |
| Term (Variable) | Source Data |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | H |
| Definition | Heading |
| User Guidance | N/A |
| Conformance | Required |
| Cardinality | One to One |
| Relationship content from ToC representing the protocol hierarchy | TRIAL OVERSIGHT AND OTHER GENERAL CONSIDERATION |
| Relationship (reference to high level conceptual model) |  |
| Value | Source Data |
| Business rules | Value Allowed: 11.8 Source Data  Relationship: Table of Contents  Concept: Heading |
| Duplicate field in other sections | No |

|  |  |
| --- | --- |
| Term (Variable) | <Source Data Introduction> |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | D |
| Definition | See CNEW  For review context CNEW  A textual 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 (for example, maintain source data at the site, ensure availability of current records) and trial monitors (for example, verify CRF data relative to source, safety of participants is being protected, conduct is in accordance with GCP). Define what constitutes source data and its origin or provide a reference to the location of these definitions, 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 | TRIAL OVERSIGHT AND OTHER GENERAL CONSIDERATION |
| Relationship (reference to high level conceptual model) |  |
| Value | Text |
| Business rules | Value Allowed: Yes  Relationship: 11.8 Source Data  Concept: CNEW |
| Duplicate field in other sections | No |

|  |  |
| --- | --- |
| Term (Variable) | <Investigator Expectations for Source Data> |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | D |
| Definition | See CNEW  For review context CNEW  A textual description of the obligations of the investigator with respect to maintaining and ensuring availability of the source data. |
| User Guidance | No text |
| Conformance | Required |
| Cardinality | One to One |
| Relationship content from ToC representing the protocol hierarchy | TRIAL OVERSIGHT AND OTHER GENERAL CONSIDERATION |
| Relationship (reference to high level conceptual model) |  |
| Value | Text |
| Business rules | Value Allowed: Yes  Relationship: 11.8 Source Data  Concept: CNEW |
| Duplicate field in other sections | No |

|  |  |
| --- | --- |
| Term (Variable) | <Trial Monitor Expectations for Source Data> |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | D |
| Definition | See CNEW  For review context CNEW  A textual description of the obligations of the trial monitor with respect to maintaining and ensuring availability of the source data. |
| User Guidance | No text |
| Conformance | Required |
| Cardinality | One to One |
| Relationship content from ToC representing the protocol hierarchy | TRIAL OVERSIGHT AND OTHER GENERAL CONSIDERATION |
| Relationship (reference to high level conceptual model) |  |
| Value | Text |
| Business rules | Value Allowed: Yes  Relationship: 11.8 Source Data  Concept: CNEW |
| Duplicate field in other sections | No |

|  |  |
| --- | --- |
| Term (Variable) | <Definitions of Source Data> |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | D |
| Definition | See C125442  For review context C125442  All information in original records and certified copies of original records of clinical findings, observations, or other activities in a clinical trial necessary for the reconstruction and evaluation of the trial. Source data are contained in source documents (original records or certified copies). [ICH E6; CSUCT] |
| User Guidance | No text |
| Conformance | Required |
| Cardinality | One to One |
| Relationship content from ToC representing the protocol hierarchy | TRIAL OVERSIGHT AND OTHER GENERAL CONSIDERATION |
| Relationship (reference to high level conceptual model) |  |
| Value | Text |
| Business rules | Value Allowed: Yes  Relationship: 11.8 Source Data  Concept: C125442 |
| Duplicate field in other sections | No |

11.9 Protocol Deviations

|  |  |
| --- | --- |
| Term (Variable) | Protocol Deviations |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | H |
| Definition | Heading |
| User Guidance | N/A |
| Conformance | Required |
| Cardinality |  |
| Relationship content from ToC representing the protocol hierarchy | TRIAL OVERSIGHT AND OTHER GENERAL CONSIDERATION |
| Relationship (reference to high level conceptual model) |  |
| Value | Protocol Deviations |
| Business rules | Value Allowed: 11.9 Protocol Deviations  Relationship: Table of Contents  Concept: Heading |
| Duplicate field in other sections | No |

|  |  |
| --- | --- |
| Term (Variable) | <Protocol Deviations Plans> |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | D |
| Definition | See CNEW  For review context CNEW  A document that describes the planned strategy, methods, responsibilities, and requirements for detecting, reviewing, and reporting protocol deviations. |
| User Guidance | N/A |
| Conformance | Required |
| Cardinality | Plans for detecting, reviewing, and reporting any deviations from the protocol should be described or a reference to separate document included. |
| Relationship content from ToC representing the protocol hierarchy | TRIAL OVERSIGHT AND OTHER GENERAL CONSIDERATION |
| Relationship (reference to high level conceptual model) |  |
| Value | Text |
| Business rules | Value Allowed: Yes  Relationship: 11.9 Protocol Deviations  Concept: CNEW |
| Duplicate field in other sections | No |

11.10 Early Site Closure

|  |  |
| --- | --- |
| Term (Variable) | Early Site Closure |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | H |
| Definition | Heading |
| User Guidance | N/A |
| Conformance | Required |
| Cardinality | One to One |
| Relationship content from ToC representing the protocol hierarchy | TRIAL OVERSIGHT AND OTHER GENERAL CONSIDERATION |
| Relationship (reference to high level conceptual model) |  |
| Value | Early Site Closure |
| Business rules | Value Allowed: 11.10 Early Site Closure  Relationship: Table of Contents  Concept: Heading |
| Duplicate field in other sections | No |

|  |  |
| --- | --- |
| Term (Variable) | <Decision Rights for Site Closure> |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | D |
| Definition | See CNEW  For review context CNEW  A textual 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. 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 | TRIAL OVERSIGHT AND OTHER GENERAL CONSIDERATION |
| Relationship (reference to high level conceptual model) |  |
| Value | Text |
| Business rules | Value Allowed: Yes  Relationship: 11.10 Early Site Closure  Concept: CNEW |
| Duplicate field in other sections | No |

|  |  |
| --- | --- |
| Term (Variable) | <Criteria for Early Closure> |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | D |
| Definition | See CNEW  For review context CNEW  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 | TRIAL OVERSIGHT AND OTHER GENERAL CONSIDERATION |
| Relationship (reference to high level conceptual model) |  |
| Value | Text |
| Business rules | Value Allowed: Yes  Relationship: 11.10 Early Site Closure  Concept: CNEW |
| Duplicate field in other sections | No |

|  |  |
| --- | --- |
| Term (Variable) | <Responsibilities Following Early Site Closure> |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | D |
| Definition | See CNEW  For review context CNEW  The responsibilities of the sponsor and/or investigator following termination or suspension of the trial at an individual site or for the whole trial. |
| 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 transition to appropriate therapy and/or follow-up. |
| Conformance | Required |
| Cardinality | One to One |
| Relationship content from ToC representing the protocol hierarchy | TRIAL OVERSIGHT AND OTHER GENERAL CONSIDERATION |
| Relationship (reference to high level conceptual model) |  |
| Value | Text |
| Business rules | Value Allowed: Yes  Relationship: 11.10 Early Site Closure  Concept: CNEW |
| Duplicate field in other sections | No |

# Appendix: Supporting Details

|  |  |
| --- | --- |
| Term (Variable) | 12 Appendix: Supporting Details |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | H |
| Definition | Heading |
| User Guidance | No text is intended here (header only). |
| Conformance | Required |
| Cardinality | One |
| Relationship content from ToC representing the protocol hierarchy | 12 Appendix: Supporting Details |
| Relationship (reference to high level conceptual model) |  |
| Value | 12 Appendix: Supporting Details |
| Business rules | Value Allowed: 12 Appendix: Supporting Details  Relationship: Table of content  Concept: Header, Identifier |
| Duplicate field in other sections | No |

## Clinical Laboratory Tests

|  |  |
| --- | --- |
| Term (Variable) | 12.1 Clinical Laboratory Tests |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | H |
| Definition | Heading |
| User Guidance | N/A |
| Conformance | Required |
| Cardinality | One |
| Relationship content from ToC representing the protocol hierarchy | 12.1 Clinical Laboratory Tests |
| Relationship (reference to high level conceptual model) |  |
| Value | 12.1 Clinical Laboratory Tests |
| Business rules | Value Allowed: 12.1 Clinical Laboratory Tests  Relationship: Table of content  Concept: Header, Identifier |
| Duplicate field in other sections | No |

|  |  |
| --- | --- |
| Term (Variable) | <Clinical Laboratory Tests> |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | D |
| Definition | C25294  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 (for example, 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 header and enter “Not Applicable.” |
| Conformance | Required |
| Cardinality | One |
| Relationship content from ToC representing the protocol hierarchy | 12.1 Clinical Laboratory Tests its |
| Relationship (reference to high level conceptual model) |  |
| Value | Text |
| Business rules | Value Allowed: Text  Relationship: n/a  Concept: C25294 |
| Duplicate field in other sections | No |

## Country/Region-Specific Differences

|  |  |
| --- | --- |
| Term (Variable) | 12.2 Country/Region-Specific Differences |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | H |
| Definition | Heading |
| User Guidance | N/A |
| Conformance | Required |
| Cardinality | One |
| Relationship content from ToC representing the protocol hierarchy | 12.2 Country/Region-Specific Differences |
| Relationship (reference to high level conceptual model) |  |
| Value | 12.2 Country/Region-Specific Differences |
| Business rules | Value Allowed: 12.2 Country/Region-Specific Differences  Relationship: Table of content  Concept: Header, Identifier |
| Duplicate field in other sections | No |

### <Country/Region Identifier>

|  |  |
| --- | --- |
| Term (Variable) | <Country/Region Identifier> |
| Data Type | Valid Value List |
| Data (D), Value (V) or Header (H) | H |

|  |  |
| --- | --- |
| Definition | Heading with a value See C20108 For Context C20108 A sequence of characters used to identify and/or name the country. See CNEW For Context CNEW 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 (for example, 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 (for example, 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 header and enter “Not Applicable.” |
| Conformance | Conditionally Required |
| Cardinality | One for each Country Region Difference; Protocol Identifier |
| Relationship content from ToC representing the protocol hierarchy | 12.2 Country/Region-Specific Differences |
| Relationship (reference to high level conceptual model) |  |
| Value | Country Data element ISO 3166 Alpha 2 or Not Applicable |
| Business rules | Value Allowed: Country/Region from ISO 3166 Alpha 2  Relationship 12.2  Concept: CNEW, Header, Identifier; SO 3166 Country Codes, Alpha 2; ISO 3166 Region Codes, Alpha 2 |
| Duplicate field in other sections | Yes for each Country/Region |

|  |  |
| --- | --- |
| Term (Variable) | <Country/Region-Specific Requirements> |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | D |
| Definition | CNEW  For Context CNEW  . |
| User Guidance | Although global clinical trial practices are increasingly harmonised, some country/ region-specific differences in requirements do exist (for example, 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 (for example, 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 | Required If Country/Region |
| Cardinality | One to Country/Region |
| Relationship content from ToC representing the protocol hierarchy | Country/Region |
| Relationship (reference to high level conceptual model) |  |
| Value | Text |
| Business rules | Value Allowed: Yes  Relationship: Country/Region  Concept: CNEW |
| Duplicate field in other sections | One for each Country/Region |

|  |  |
| --- | --- |
| Term (Variable) | <Country/Region-specific Protocol Clarification> |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | D |
| Definition | See CNEW  For Context CNEW  . |
| User Guidance | Although global clinical trial practices are increasingly harmonised, some country/ region-specific differences in requirements do exist (for example, 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 (for example, 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 | Conditional Required if Country Region d |
| Cardinality | One to Country/Region |
| Relationship content from ToC representing the protocol hierarchy | <Country/Region> |
| Relationship (reference to high level conceptual model) |  |
| Value | Text |
| Business rules | Value Allowed:Yes  Relationship: Country/Region  Concept: CNEW |
| Duplicate field in other sections | One for each Country/Region |

## Prior Protocol Amendment(s)

|  |  |
| --- | --- |
| Term (Variable) | 12.3 Prior Protocol Amendment(s) |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | H |
| Definition | Heading |
| User Guidance | N/A |
| Conformance | Required |
| Cardinality | One-to-one |
| Relationship content from ToC representing the protocol hierarchy | 12.3 Prior Protocol Amendment(s) |
| Relationship (reference to high level conceptual model) |  |
| Value | 12.3 Prior Protocol Amendment(s) |
| Business rules | Value Allowed: 12.3 Prior Protocol Amendment(s)  Relationship: Table of content  Concept: Header, Identifier |
| Duplicate field in other sections | No |

|  |  |
| --- | --- |
| Term (Variable) | Prior Protocol Amendment(s) |
| Data Type | Valid Value List |
| Data (D), Value (V) or Header (H) | V |
| Definition | CNEW  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 Prior Protocol Amendment(s) |
| Relationship (reference to high level conceptual model) |  |
| Value | {Not applicable. This protocol has not been amended.}  Or  {Not applicable. This is the first protocol amendment.}  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.} |
| Business rules | Value Allowed: Yes  Relationship: 12.3 Prior Protocol Amendment(s)  Concept: CNEW |
| Duplicate field in other sections |  |

|  |  |
| --- | --- |
| Term (Variable) | [Protocol Amendment Summary] |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | D |
| Definition |  |
| User Guidance |  |
| Conformance | Required/Repeated |
| Cardinality |  |
| Relationship content from ToC representing the protocol hierarchy | Appendix: Definitions and Supporting Operational Details/Prior Protocol Amendments/Protocol Amendment Summary |
| Relationship (reference to high level conceptual model) |  |
| Value |  |
| Business rules | Value Allowed: n/a  Relationship: 104 to 144 from preceding amendment list all in most recent order  Concept: n/a |
| Duplicate field in other sections |  |

|  |  |
| --- | --- |
| Term (Variable) | History of Amendment |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | H |
| Definition | Table Heading |
| User Guidance | Do not include the current amendment in the table below, as the table is focused on previous amendments. Previous amendments should appear in reverse chronological order with the most recent at the top (for example, 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. |
| Conformance | Required |
| Cardinality | One-to-one |
| Relationship content from ToC representing the protocol hierarchy | 12.3 Prior Protocol Amendment(s) |
| Relationship (reference to high level conceptual model) |  |
| Value | History of Amendment |
| Business rules | Value Allowed: Yes  Relationship: 12.3 Prior Protocol Amendment(s)  Concept: |
| Duplicate field in other sections |  |

|  |  |
| --- | --- |
| Term (Variable) | {#/A total of #} prior {global} amendments have occurred, as shown in the table below: |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | H |
| Definition |  |
| User Guidance | Do not include the current amendment in the table below, as final approval dates are often difficult to predict during document preparation. Previous amendments should appear in reverse chronological order with the most recent at the top (for example, 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, list approximate global enrollment total or percentage at the time of the amendment and select “globally”. * For local amendments, list the approximate local enrollment total or percentage at the time of the amendment and select “locally”. |
| Conformance | Required |
| Cardinality |  |
| Relationship content from ToC representing the protocol hierarchy | Amendment Details |
| Relationship (reference to high level conceptual model) |  |
| Value | {#/A total of #} prior {global} amendments have occurred, as shown in the table below: |
| Business rules | Value Allowed: Yes  Relationship: n/a  Concept: n/a |
| Duplicate field in other sections |  |

|  |  |
| --- | --- |
| Term (Variable) | prior amendments have occurred as shown in table below: |
| Data Type | Number |
| Data (D), Value (V) or Header (H) | D |
| Definition |  |
| User Guidance |  |
| Conformance | Required / Required |
| Cardinality |  |
| Relationship content from ToC representing the protocol hierarchy | Amendment Details |
| Relationship (reference to high level conceptual model) |  |
| Value |  |
| Business rules | Value Allowed: n/a  Relationship: n/a  Concept: n/a |
| Duplicate field in other sections |  |

|  |  |
| --- | --- |
| Term (Variable) | Document |
| Data Type | Table col head |
| Data (D), Value (V) or Header (H) | H |
| Definition |  |
| User Guidance |  |
| Conformance | Required / Required |
| Cardinality |  |
| Relationship content from ToC representing the protocol hierarchy | Amendment Details |
| Relationship (reference to high level conceptual model) |  |
| Value | Document |
| Business rules | Value Allowed: Yes  Relationship: row title  Concept: Amendment Date |
| Duplicate field in other sections |  |

|  |  |
| --- | --- |
| Term (Variable) | Sponsor Approval Date (dd/mm/yyyy) |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | H |
| Definition |  |
| User Guidance |  |
| Conformance | Required |
| Cardinality |  |
| Relationship content from ToC representing the protocol hierarchy | Amendment Details |
| Relationship (reference to high level conceptual model) |  |
| Value | Sponsor Approval Date (dd/mm/yyyy) |
| Business rules | Value Allowed: Yes  Relationship: Row title  Concept: n/a |
| Duplicate field in other sections |  |

|  |  |
| --- | --- |
| Term (Variable) | Approximate {(#/%)} enrolled |
| Data Type | Table col head |
| Data (D), Value (V) or Header (H) | H |
| Definition |  |
| User Guidance |  |
| Conformance | Required |
| Cardinality |  |
| Relationship content from ToC representing the protocol hierarchy | Amendment Details |
| Relationship (reference to high level conceptual model) |  |
| Value | Approximate {(#/%)} enrolled |
| Business rules | Value Allowed: Yes  Relationship: Row title  Concept: n/a |
| Duplicate field in other sections |  |

|  |  |
| --- | --- |
| Term (Variable) | Original or Amendment X |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | H |
| Definition | Heading |
| User Guidance |  |
| Conformance | Required / Repeatable |
| Cardinality |  |
| Relationship content from ToC representing the protocol hierarchy | Amendment Details |
| Relationship (reference to high level conceptual model) |  |
| Value | Original or Amendment |
| Business rules | Value Allowed: Yes  Relationship: Row title  Concept: n/a |
| Duplicate field in other sections | Repeat for each amendment |

|  |  |
| --- | --- |
| Term (Variable) | X |
| Data Type | integer |
| Data (D), Value (V) or Header (H) | D |
| Definition |  |
| User Guidance |  |
| Conformance | Conditional / Required |
| Cardinality |  |
| Relationship content from ToC representing the protocol hierarchy | Amendment Details |
| Relationship (reference to high level conceptual model) |  |
| Value |  |
| Business rules | Value Allowed: n/a  Relationship: Rows content  Concept: n/a |
| Duplicate field in other sections | Repeat for each amendment |

|  |  |
| --- | --- |
| Term (Variable) | Amendment X Date |
| Data Type | date dd/mmm/yyyy |
| Data (D), Value (V) or Header (H) | D |
| Definition |  |
| User Guidance |  |
| Conformance | Conditional / Required |
| Cardinality |  |
| Relationship content from ToC representing the protocol hierarchy | Amendment Details |
| Relationship (reference to high level conceptual model) |  |
| Value |  |
| Business rules | Value Allowed: n/a  Relationship: Rows content  Concept: n/a |
| Duplicate field in other sections | Repeat for each amendment |

|  |  |
| --- | --- |
| Term (Variable) | {(#/%)} {globally/locally}} |
| Data Type | integer |
| Data (D), Value (V) or Header (H) | D |
| Definition | Estimated # of participants enrolled as a percentage of the expected total. |
| User Guidance | Good estimates are adequate, as precise enrolment figures will likely be changing while an amendment is being prepared. |
| Conformance | Conditional / Required |
| Cardinality |  |
| Relationship content from ToC representing the protocol hierarchy | Amendment Details |
| Relationship (reference to high level conceptual model) |  |
| Value | " " % |
| Business rules | Value Allowed: Yes  Relationship: Rows content  Concept: n/a |
| Duplicate field in other sections | Repeat for each amendment |

|  |  |
| --- | --- |
| Term (Variable) | {(#/%)} {globally/locally}} |
| Data Type | Pick list |
| Data (D), Value (V) or Header (H) | D |
| Definition |  |
| User Guidance |  |
| Conformance | Conditional / Required |
| Cardinality |  |
| Relationship content from ToC representing the protocol hierarchy | Amendment Details |
| Relationship (reference to high level conceptual model) |  |
| Value | Global  Local |
| Business rules | Value Allowed: Yes  Relationship: Rows content  Concept: n/a |
| Duplicate field in other sections | Repeat for each amendment |

|  |  |
| --- | --- |
| Term (Variable) | {Overview of Changes in the Current Amendment:} |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | H |
| Definition | Heading |
| User Guidance | Conditional if amendment |
| Conformance | Conditional / Required |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | Amendment Details |
| Relationship (reference to high level conceptual model) |  |
| Value | Overview of Changes in the Current Amendment: |
| Business rules | Value Allowed: No  Relationship:Amendment Details  Concept:Header |
| Duplicate field in other sections | No |

|  |  |
| --- | --- |
| Term (Variable) | {Description of Change} |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | H |
| Definition | Heading |
| User Guidance | Table |
| Conformance | Conditionally Required |
| Cardinality |  |
| Relationship content from ToC representing the protocol hierarchy | Amendment Details Table Column Heading |
| Relationship (reference to high level conceptual model) |  |
| Value | {Description of Change} |
| Business rules | Value Allowed: No  Relationship: Table Column Hading  Concept: Header |
| Duplicate field in other sections | No |

|  |  |
| --- | --- |
| Term (Variable) | <Enter Description of Amendment Change> |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | Data |
| Definition | See CNEW  FOr Context CNEW A narrative representation of the change introduced in the current version of the protocol. |
| User Guidance | <Enter Description of Amendment Change> |
| Conformance | Conditionally Required |
| Cardinality | Column Heading  Row Content |
| Relationship content from ToC representing the protocol hierarchy | Amendment Details Row Lead |
| Relationship (reference to high level conceptual model) |  |
| Value | Text |
| Business rules | Value Allowed: No  Relationship: Column Heading and Row  Concept: CNEW |
| Duplicate field in other sections | Yes for every Description of Change |

|  |  |
| --- | --- |
| Term (Variable) | {Brief Rationale for Change} |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | H |
| Definition | Heading |
| User Guidance |  |
| Conformance | Conditional Required if Amendments |
| Cardinality | Column Heading Table |
| Relationship content from ToC representing the protocol hierarchy | Amendment Details |
| Relationship (reference to high level conceptual model) |  |
| Value | {Brief Rationale for Change} |
| Business rules | Value Allowed: No  Relationship: Table Column  Concept: Header |
| Duplicate field in other sections | No |

|  |  |
| --- | --- |
| Term (Variable) | <Enter Rationale for Amendment Change> |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | D |
| Definition | See CNEW  For context CNew The brief reason for the change introduced in the current version of the protocol. |
| User Guidance | <Enter Rationale for Amendment Change> |
| Conformance | Conditionally Required |
| Cardinality | One to Column Heading Row description of change  Section# and Name |
| Relationship content from ToC representing the protocol hierarchy | Amendment Details |
| Relationship (reference to high level conceptual model) |  |
| Value | Text |
| Business rules | Value Allowed: yes  Relationship: Row Content, Column Content  Concept: n/a |
| Duplicate field in other sections | Yes as long as Description of Change Continues |

|  |  |
| --- | --- |
| Term (Variable) | {Section # and Name} |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | H |
| Definition | Heading |
| User Guidance |  |
| Conformance | Conditional Required if Amendment |
| Cardinality | Column Heading Table |
| Relationship content from ToC representing the protocol hierarchy | Amendment Details |
| Relationship (reference to high level conceptual model) |  |
| Value | {Section # and Name} |
| Business rules | Value Allowed: No  Relationship: Table Column  Concept: Header |
| Duplicate field in other sections | No |

|  |  |
| --- | --- |
| Term (Variable) | <Enter Section of Amendment Change> |
| Data Type | Pick List |
| Data (D), Value (V) or Header (H) | Value |
| Definition | See CNEW  For context CNew The protocol section number and name containing the change introduced in the current version of the protocol. |
| User Guidance | <Enter Section of Amendment Change> |
| Conformance | Conditionally Required |
| Cardinality | One to Column Heading Row description of change  Description of Change, Rational for Amendment Change |
| Relationship content from ToC representing the protocol hierarchy | Amendment Details  One to Column Heading Row description of change  Description of Change, Rational for Amendment Change |
| Relationship (reference to high level conceptual model) |  |
| Value | 1 PROTOCOL SUMMARY  1.1 Protocol Synopsis  1.1.1 Primary and Secondary Objectives and Estimands  1.1.2 Overall Design  1.2 Trial Schema  1.3 Schedule of Activities  2 INTRODUCTION  2.1 Purpose of Trial  2.2 Summary of Benefits and Risks  2.2.1 Benefit Summary  2.2.2 Risk Summary and Mitigation Strategy  2.2.3 Overall Benefit:Risk Conclusion  3 TRIAL OBJECTIVES AND ESTIMANDS  3.1 Primary Objective(s) and Associated Estimand(s)  3.1.1 Primary Estimand  3.2 Secondary Objective(s) and Associated Estimand(s)  3.3 Exploratory Objective(s)  4 TRIAL DESIGN  4.1 Description of Trial Design  4.1.1 Stakeholder Input into Design  4.2 Rationale for Trial Design  4.2.1 Rationale for Intervention Model  4.2.2 Rationale for Duration  4.2.3 Rationale for Estimands  4.2.4 Rationale for Interim Analysis  4.2.5 Rationale for Control Type  4.2.6 Rationale for Adaptive or Novel Trial Design  4.2.7 Rationale for Other Trial Design Aspects  4.3 Trial Stopping Rules  4.4 Start of Trial and End of Trial  4.5 Access to Trial Intervention After End of Trial  5 TRIAL POPULATION  5.1 Description of Trial Population and Rationale  5.2 Inclusion Criteria  5.3 Exclusion Criteria  5.4 Contraception  5.4.1 Definitions Related to Childbearing Potential  5.4.2 Contraception Requirements  5.5 Lifestyle Restrictions  5.5.1 Contraception Requirements  5.5.2 Caffeine, Alcohol, Tobacco, and Other Restrictions  5.5.3 Physical Activity Restrictions  5.5.4 Other Activity Restrictions  5.6 Screen Failure and Rescreening  6 TRIAL INTERVENTION AND CONCOMITANT THERAPY  6.1 Overview of Trial Interventions  6.2 Description of Investigational Trial Intervention  6.3 Rationale for Investigation Trial Intervention Dose and Regimen  6.4 Investigational Trial Intervention Administration  6.5 Investigational Trial Intervention Dose Modification  6.6 Management of Investigational Trial Intervention Overdose  6.7 Preparation, Storage, Handling and Accountability of Investigational Trial Intervention(s)  6.7.1 Preparation of Investigational Trial Intervention(s)  6.7.2 Storage and Handling of Investigational Trial Intervention  6.7.3 Accountability of Investigational Trial Intervention  6.8 Investigational Trial Intervention Assignment, Randomisation and Blinding  6.8.1 Participant Assignment to Investigational Trial Intervention  6.8.2 Randomisation  6.8.3 Blinding  6.8.4 Emergency Unblinding at the Site  6.9 Investigational Trial Intervention Compliance  6.10 Description of Non-Investigational Trial Intervention(s)  6.10.1 Background Intervention  6.10.2 Rescue Therapy  6.10.3 Other Non-investigational Intervention  6.11 Concomitant Therapy  6.11.1 Prohibited Concomitant Therapy  6.11.2 Permitted Concomitant Therapy  7 PARTICIPANT DISCONTINUATION OF TRIAL INTERVENTION AND DISCONTINUATION OR WITHDRAWAL FROM TRIAL  7.1 Discontinuation of Trial Intervention for Individual Participants  7.1.1 Permanent Discontinuation of Trial Intervention  7.1.2 Temporary Discontinuation of Trial Intervention  7.1.3 Rechallenge  7.2 Discontinuation or Withdrawal from the Trial  7.3 Lost to Follow-Up  8 TRIAL ASSESSMENTS AND PROCEDURES  8.1 Trial Assessments and Procedures Considerations  8.2 Screening/Baseline Assessments and Procedures  8.3 Efficacy Assessments and Procedures  8.4 Safety Assessments and Procedures  8.4.1 Physical Examination  8.4.2 Vital Signs  8.4.3 Electrocardiograms  8.4.4 Clinical Laboratory Assessments  8.4.5 Pregnancy Testing  8.4.6 Suicidal Ideation and Behaviour Risk Monitoring  8.5 Pharmacokinetics  8.6 Biomarkers  8.6.1 Genetics and Pharmacogenomics  8.6.2 Pharmacodynamic Biomarkers  8.6.3 Other Biomarkers  8.7 Immunogenicity Assessments  8.8 Medical Resource Utilisation and Health Economics  9 ADVERSE EVENTS, SERIOUS ADVERSE EVENTS, PRODUCT COMPLAINTS, PREGNANCY AND POSTPARTUM INFORMATION  9.1 Definitions  9.1.1 Definitions of Adverse Events  9.1.2 Definitions of Serious Adverse Events  9.1.3 Definition of Medical Device Product Complaints  9.2 Timing and Mechanism for Collection and Reporting  9.3 Identification, Recording and Follow-Up  9.3.1 Identification  9.3.2 Severity  9.3.3 Causality  9.3.4 Follow-up  9.4 Reporting  9.4.1 Regulatory Reporting Requirements  9.4.2 Adverse Events of Special Interest  9.4.3 Disease-related Events or Outcomes Not Qualifying as AEs or SAEs  9.5 Pregnancy and Postpartum Information  9.5.1 Participants Who Become Pregnant During the Trial  9.5.2 Participants Whose Partners Become Pregnant  10 Statistical Considerations  10.1 Geeral Considerations  10.2 Analysis Sets  10.3 Analyses of Demographics and Other Baseline Variables  10.4 Analyses Associated with the Primary Objective(s)  10.4.1 Statistical Method of Analysis  10.4.2 Handling of Data in Relation to Primary Estimand(s)  10.4.3 Handling of Missing Data  10.4.4 Sensitivity Analysis  10.4.5 Supplementary Analysis  10.5 Analysis Associated with the Secondary Objective(s)  10.5.1 Statistical Method of Analysis  10.5.2 Handling of Data in Relation to Secondary Estimand(s)  10.5.3 Handling of Missing Data  10.5.4 Sensitivity Analyses  10.5.5 Supplementary Analyses  10.6 Analysis Associated with the Exploratory Objective(s)  10.7 Safety Analyses  10.8 Other Analyses  10.9 Interim Analyses  10.10 Multiplicity Adjustments  10.11 Sample Size Determination  11 TRIAL OVERSIGHT AND OTHER GENERAL CONSIDERATIONS  11.1 Regulatory and Ethical Considerations  11.2 Trial Oversight  11.2.1 Investigator Responsibilities  11.2.2 Sponsor Responsibilities  11.3 Informed Consent Process  11.3.1 Informed Consent for Rescreening  11.3.2 Informed Consent for Use of Remaining Samples in Exploratory Research  11.4 Committees  11.5 Insurance and Indemnity  11.5 Risk Management  11.7 Data Governance  11.8 Source Data  11.9 Protocol Deviations  11.10 Early Site Closure  12 APPENDIX: SUPPORTING DETAILS  12.1 Clinical Laboratory Tests  12.2 Country/Region-Specific Differences  12.3 Prior Protocol Amendment(s)  13 APPENDIX: GLOSSARY OF TERMS AND ABBREVIATIONS  14 APPENDIX: REFERENCES |
| Business rules | Value Allowed: yes  Relationship: Column; Row description and rational amendment change Row  Concept: CNEW |
| Duplicate field in other sections | Yes for every Description of Change |

# Appendix: Glossary of Terms and Abbreviations

|  |  |
| --- | --- |
| Term (Variable) | 13 Appendix: Glossary of Terms and Abbreviations |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | H |
| Definition | Heading |
| User Guidance | N/A |
| Conformance | Required |
| Cardinality | One-to-one |
| Relationship content from ToC representing the protocol hierarchy | 13 Appendix: Glossary of Terms and Abbreviations |
| Relationship (reference to high level conceptual model) |  |
| Value | 13 Appendix: Glossary of Terms and Abbreviations |
| Business rules | Value Allowed: 13 Appendix: Glossary of Terms and Abbreviations  Relationship: Table of content  Concept: Header, Identifier |
| Duplicate field in other sections | No |

|  |  |
| --- | --- |
| Term (Variable) | <Glossary of Terms and Abbreviations> |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | D |
| Definition | CNEW  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 | Appendix 13: Glossary of Terms and Abbreviations |
| Relationship (reference to high level conceptual model) |  |
| Value | Text |
| Business rules | Value Allowed: Text  Relationship: Appendix 13: Glossary of Terms and Abbreviations  Concept: CNEW |
| Duplicate field in other sections | No |

# Appendix: References

|  |  |
| --- | --- |
| Term (Variable) | 14 Appendix: References |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | H |
| Definition | Heading |
| User Guidance | N/A |
| Conformance | Required |
| Cardinality | One-to-one |
| Relationship content from ToC representing the protocol hierarchy | 14 Appendix: References |
| Relationship (reference to high level conceptual model) |  |
| Value | 14 Appendix: References |
| Business rules | Value Allowed: 14 Appendix: References  Relationship: Table of content  Concept: Header, Identifier |
| Duplicate field in other sections | No |

|  |  |
| --- | --- |
| Term (Variable) | < References> |
| Data Type | Text |
| Data (D), Value (V) or Header (H) | D |
| Definition | C184397  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 Appendix: References |
| Relationship (reference to high level conceptual model) |  |
| Value | Text |
| Business rules | Value Allowed: Text  Relationship: 14 Appendix: References  Concept: C184397 |
| Duplicate field in other sections | No |