

11 December 2025
EMA/CHMP/ICH/778800/2022
Committee for Medicinal Products for Human Use

ICH M11 Clinical electronic structured harmonised protocol (CeSHarP) - Technical specification

Step 5

| | |
|--|------------------|
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M11 Technical specification

Document history

| Code | History | Date |
|------|---|-------------------|
| M11 | Endorsement by the Members of the ICH Assembly under Step 2 and release for public consultation (document dated 6 September 2022) <i>Minor editorial changes made pre-publication (document dated 14 October 2022)</i> | 27 September 2022 |
| M11 | Updated <i>Step 2</i> Draft for second round of public consultation | 03 February 2025 |
| M11 | Adoption by the Regulatory Members of the ICH Assembly under <i>Step 4</i> . | 19 November 2025 |

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.

ICH and CDISC have signed an agreement for the maintenance and facilitation of the governance process for ICH controlled terminology. The goals of the agreement are to:

- Use a unified governance process and terminology services for the long-term support of ICH controlled terminologies.
- Curate and maintain ICH controlled terminologies.
- Follow a robust process for the public review and publication of ICH terminologies.
- Ensure the terminologies are freely available to the public following CDISC public review.
- Ensure there is a transparent process with the public.

Description of table elements

| | |
|---|---|
| Term (Variable) | Term (variable) is the verbatim term from the Template. |
| Data Type | Data type is a classification that specifies which type of value a variable has. |
| Data (D), Value (V) or Heading (H) | Specifies the type of data entry as Heading, Data or Value. Selections: Heading: section heading including table heading, non-numbered title. Data: Content such as text, image, equation, table VALUE: if there is a pick list for the data or when a universal text is required or conditionally required or when optional text is suggested |
| Definition | <p>CDISC publishes semantics for the ICH M11 protocol data elements and valid value sets. This terminology set is published and stored in the NCI Thesaurus <u>Subset C217023 - ICH M11 Terminology</u> (https://evsexplore.semantics.cancer.gov/evsexplore/subset/ncit/C217023) and each ICH M11 concept will be assigned an NCI C-code. See 'Definition' table element for more information about C-codes.</p> <p>This field contains the C-code corresponding to the meaning of the data element concept in the NCI Thesaurus.</p> <p>ICH Object Identifiers (OIDs) for M11 are available on the ICH Electronic Standards (ESTRI) webpage (https://www.ich.org/page/electronic-standards-estri).</p> <p>Note: The weblink (URL) may have changed following publication, please search using relevant keywords.</p> |
| User Guidance | User guidance is directly from the instructions of the template. |
| Conformance | Rules and actions in accordance with the Template conventions and general instructions which characterize how the Headers, data element or Text content will conform. |

| | |
|--|--|
| Term (Variable) | Term (variable) is the verbatim term from the Template. |
| Cardinality | Cardinality describes constraints on how many times a data element can be associated with instances in other data elements or entities. 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 its columns, or relationship to other data element. |
| Relationship content from ToC representing the protocol hierarchy | Relationship content from ToC representing the protocol hierarchy is relationship to the template Table of Contents. |
| Value | Indicates the value of a specific data element or heading. Specifies the actual value or value range of specific data (e.g. Value may be from the ICH M11 Valid Value List. For numbered heading, the number will NOT be included here). ICH M11 Controlled Terminology may appear with the appropriate Code List and Code Values. The values listed are accurate as of the publication date. For the most current information, please refer to the Code List or OID references. |
| Business rules | Value Allowed: Is a value allowed. If the header is required, the value will be No. If there is universal text, the Value will be No. Relationship: What is the relationship? Identify relationship for the element including the relationship to the ToC. For ToC, numbers are listed Lower to Higher. For Tables elements, there may be a row or a column heading as a relationship. Other Relationships are also defined, for example an Amendment number to a Protocol Identifier. Concept: Identify the Concept for headings expect to see Heading and for other elements expect reference to controlled terminology or detailed information. OIDs for the corresponding namespaces of C-codes are provided. |
| Repeating and/or Reuse Rules | Instructions on how components are repeated and/or reused within the protocol. Is this component repeated? Is this component reused? Is this component repeated/reused in other sections of the document? Repeating is defined as replication of the data element for new content. Reuse is defined as using verbatim content in more than one data element location in the protocol. |

Appendix 1: Detailed descriptions of information components

Title page

| | |
|---|------------------------------------|
| Term (Variable) | Sponsor Confidentiality Statement: |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | H |
| Definition | Heading |
| User Guidance | N/A |

| | |
|--|--|
| Term (Variable) | Sponsor Confidentiality Statement: |
| Conformance | Optional |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | Title Page |
| Value | Sponsor Confidentiality Statement: |
| Business rules | Value Allowed: No Relationship: Table row heading Concept: Heading |
| Repeating and/or Reuse Rules | No |

| | |
|--|---|
| Term (Variable) | <Sponsor Confidentiality Statement> |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C181236 |
| User Guidance | Insert the sponsor's confidentiality statement, if applicable; otherwise delete. |
| Conformance | Optional |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | Title Page |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: Heading Concept: C181236 ICH OID 2.16.840.1.113883.3.989.2.3.3.16 |
| Repeating and/or Reuse Rules | No |

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

| | |
|--|---|
| Term (Variable) | Full Title: |
| representing the protocol hierarchy | |
| Value | Full Title: |
| Business rules | Value Allowed: No Relationship: Table row heading Concept: Heading |
| Repeating and/or Reuse Rules | No |

| | |
|--|---|
| Term (Variable) | <Full Title> |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C132346 |
| User Guidance | The protocol should have a descriptive title that identifies the scientific aspects of the trial sufficiently to ensure it is immediately evident what the trial is investigating and on whom, and to allow retrieval from literature or internet searches. |
| Conformance | Required |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | Title page |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: Heading; Sponsor Protocol Identifier Concept: C132346 ICH OID 2.16.840.1.113883.3.989.2.3.3.16 |
| Repeating and/or Reuse Rules | No |

| | |
|--|----------------|
| Term (Variable) | Trial Acronym: |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | H |
| Definition | Heading |
| User Guidance | N/A |
| Conformance | Optional |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | Title Page |
| Value | Trial Acronym: |

| | |
|-------------------------------------|---|
| Term (Variable) | Trial Acronym: |
| Business rules | Value Allowed: No Relationship: Table row heading Concept: Heading |
| Repeating and/or Reuse Rules | No |

| | |
|--|---|
| Term (Variable) | <Trial Acronym> |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C94108 |
| User Guidance | Acronym or abbreviation used publicly to identify the clinical trial. Delete this line from the table if not applicable. |
| Conformance | Optional |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | Title Page |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: Heading; Protocol Identifier Concept: C94108 ICH OID 2.16.840.1.113883.3.989.2.3.3.16 |
| Repeating and/or Reuse Rules | No |

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

| | |
|--|--|
| Term (Variable) | <Sponsor Protocol Identifier> |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C132351 |
| User Guidance | A unique alphanumeric identifier for the trial, designated by the sponsor. |
| Conformance | Required |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | Title page |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: Heading Concept: C132351 ICH OID 2.16.840.1.113883.3.989.2.3.3.16 Note: Must have at least One Character, may not be space (null) |
| Repeating and/or Reuse Rules | No |

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

| | |
|---|-------------------------------|
| Term (Variable) | [Original Protocol Indicator] |
| Data Type | Valid Value |
| Data (D), Value (V) or Heading (H) | V |

| | |
|--|--|
| Term (Variable) | [Original Protocol Indicator] |
| Definition | C218672 |
| User Guidance | N/A |
| Conformance | Required |
| Cardinality | One to one; One to Sponsor Protocol Identifier |
| Relationship content from ToC representing the protocol hierarchy | Title page |
| Value | Code List C217046: ICH OID 2.16.840.1.113883.3.989.2.3.1.11 Yes (C49488), No (C49487) |
| Business rules | Value Allowed: Yes Relationship: Heading; Sponsor Protocol Identifier Concept: C218672 ICH OID 2.16.840.1.113883.3.989.2.3.3.16 |
| Repeating and/or Reuse Rules | No |

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

| | |
|---|---|
| Term (Variable) | <Version Number> |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C181232 |
| User Guidance | For use by the sponsor at their discretion. |
| Conformance | Optional |
| Cardinality | One to one, Protocol Identifier |

| | |
|--|--|
| Term (Variable) | <Version Number> |
| Relationship content from ToC representing the protocol hierarchy | Title Page |
| Value | Number |
| Business rules | Value Allowed: Yes Relationship: Heading; Sponsor Protocol Identifier Concept: C181232 ICH OID 2.16.840.1.113883.3.989.2.3.3.16 |
| Repeating and/or Reuse Rules | No |

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

| | |
|--|---|
| Term (Variable) | <Version Date> |
| Data Type | Date |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C93813 |
| User Guidance | For use by the sponsor at their discretion. |
| Conformance | Optional |
| Cardinality | One to one; one to Version Number |
| Relationship content from ToC representing the protocol hierarchy | Title page |
| Value | Date Format |
| Business rules | Value Allowed: Yes |

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|-------------------------------------|--|
| Term (Variable) | <Version Date> |
| | Relationship: Heading; Version Number; Sponsor Protocol Identifier Concept: C93813 ICH OID 2.16.840.1.113883.3.989.2.3.3.16 |
| Repeating and/or Reuse Rules | No |

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

| | |
|--|--|
| Term (Variable) | {Amendment Identifier} |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C218477 |
| User Guidance | Enter the amendment identifier (e.g., amendment number). If this is the original instance of the protocol, delete this row or enter "Not applicable" |
| Conformance | Conditional: when there is an amendment |
| Cardinality | One to one; One to Protocol Identifier if not original |
| Relationship content from ToC representing the protocol hierarchy | Title Page |
| Value | Text |
| Business rules | Value Allowed: Yes if Original Protocol = No; blank if Original Protocol = Yes Relationship: Heading, Sponsor Protocol Identifier Concept: C218477 ICH OID 2.16.840.1.113883.3.989.2.3.3.16 |
| Repeating and/or Reuse Rules | Yes, repeatable for Table for Document History |

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

| | |
|--|---|
| Term (Variable) | {[Amendment Scope]} |
| Data Type | Valid Value |
| Data (D), Value (V) or Heading (H) | V |
| Definition | C218673 |
| User Guidance | If this is the original instance of the protocol, delete this row or enter "Not applicable". For an amendment that applies to all sites in the trial, enter "Global" and delete the Country, Region and Site Identifier fields. If amending a single-country trial, enter "Global". |
| Conformance | Conditional: when there is an amendment |
| Cardinality | One to one, One to Amendment Identifier |
| Relationship content from ToC representing the protocol hierarchy | Title page |
| Value | Code List C217047: ICH OID 2.16.840.1.113883.3.989.2.3.1.3 Blank; Global (C68846), Not Global (C217026) |
| Business rules | Value Allowed: Yes; if Original Protocol = No; blank if Original Protocol = Yes Relationship: Heading, Amendment Identifier, Sponsor Protocol Identifier Concept: C218673 ICH OID 2.16.840.1.113883.3.989.2.3.3.16 |
| Repeating and/or Reuse Rules | No |

| | |
|--|--|
| Term (Variable) | {[Country Identifier] or [Region Identifier] or <Site Identifier>} |
| Data Type | Valid Value |
| Data (D), Value (V) or Heading (H) | V |
| Definition | C20108 C218674 C83081 |
| User Guidance | For an amendment that does not apply to all sites in the trial, select "Not Global" and utilise one of the identifiers based on amendment scope. |
| Conformance | Conditional: when Amendment scope is not global |
| Cardinality | One to one; Many to Amendment Scope; One to Amendment Identifier; One to Sponsor Protocol Identifier |
| Relationship content from ToC representing the protocol hierarchy | Title Page |
| Value | Country specific: [Country Identifier] (ISO 3166 Country Codes, Alpha 3; ISO 3166 Country Codes, Alpha 2; GENC) or Region Specific: [Region Identifier] (ISO 3166 Region Codes, Alpha 3; ISO 3166 Region Codes, Alpha 2; GENC) or Site specific: [Site Identifier] (Text) Site Identifier Text Conditional Blank for Original Protocol Indicator = yes |
| Business rules | Value Allowed: Yes Relationship: Heading, Amendment Scope, Amendment Identifier, Sponsor Protocol Identifier Concept: C20108 ICH OID 2.16.840.1.113883.3.989.2.3.3.16; C218674 ICH OID 2.16.840.1.113883.3.989.2.3.3.16; C83081 ICH OID 2.16.840.1.113883.3.989.2.3.3.16 |
| Repeating and/or Reuse Rules | Yes, repeatable in 12.2 Country/Region-Specific Differences |

| | |
|--|--|
| Term (Variable) | Sponsor's Investigational Product Code(s): |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | H |
| Definition | Heading |
| User Guidance | N/A |
| Conformance | Optional |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | Title Page |

| | |
|-------------------------------------|--|
| Term (Variable) | Sponsor's Investigational Product Code(s): |
| Value | Sponsor's Investigational Product Code(s): |
| Business rules | Value Allowed: No Relationship: Table row heading Concept: Heading |
| Repeating and/or Reuse Rules | Yes, repeatable for each Investigational compound |

| | |
|--|--|
| Term (Variable) | <Sponsor's Investigational Product Code(s)> |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C218675 |
| User Guidance | Enter the sponsor's unique identifier for investigational product(s) in the trial. Add fields as needed. |
| Conformance | Optional: if there is Sponsor Investigational Product Code |
| Cardinality | One to one, Many to Sponsor Protocol Identifier |
| Relationship content from ToC representing the protocol hierarchy | Title Page |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: Heading; Sponsor Protocol Identifier Concept: C218675 ICH OID 2.16.840.1.113883.3.989.2.3.3.16 |
| Repeating and/or Reuse Rules | Yes, repeatable for each Investigational compound Yes, repeatable in 1.1.2 under Intervention |

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

| | |
|-------------------------------------|----------------------------------|
| Term (Variable) | Investigational Product Name(s): |
| Repeating and/or Reuse Rules | No |

| | |
|--|---|
| Term (Variable) | <Nonproprietary Name(s)> |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C97054 |
| User Guidance | Omit nonproprietary name field if a nonproprietary name has not yet been assigned. |
| Conformance | Optional |
| Cardinality | One to many; Many to Sponsor Investigational Product Code(s); Many to Sponsor Protocol Identifier |
| Relationship content from ToC representing the protocol hierarchy | Title Page |
| Value | Text Use for example WHO INN, USAN, JAN, XEVMPD |
| Business rules | Value Allowed: Yes Relationship: Heading, Sponsor Protocol Identifier Concept: C97054 ICH OID 2.16.840.1.113883.3.989.2.3.3.16 |
| Repeating and/or Reuse Rules | Yes, repeatable for each nonproprietary name Yes, repeatable in 1.1.2 under intervention |

| | |
|--|--|
| Term (Variable) | <Proprietary Name(s)> |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C71898 |
| User Guidance | Omit proprietary name field if not yet established. |
| Conformance | Optional; Blank |
| Cardinality | One to many; Many to Sponsor Investigational Product Code(s); Many to Sponsor Protocol Identifier |
| Relationship content from ToC representing the protocol hierarchy | Title Page |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: Heading; Protocol Identifier; Compound Code Concept: C71898 ICH OID 2.16.840.1.113883.3.989.2.3.3.16 |
| Repeating and/or Reuse Rules | Yes, repeatable for each proprietary name |

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

| | |
|--|---|
| Term (Variable) | [Trial Phase] |
| Data Type | Valid Value |
| Data (D), Value (V) or Heading (H) | V |
| Definition | C48281 |
| 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; Sponsor Protocol Identifier |
| Relationship content from ToC representing the protocol hierarchy | Title Page |
| Value | Code List C217045: ICH OID 2.16.840.1.113883.3.989.2.3.1.18 Early Phase 1 (C54721); Phase 1 (C15600); Phase 1/Phase 2 (C15693); Phase 1/Phase 2/Phase 3 (C198366); Phase 1/Phase 3 (C198367); Phase 2 (C15601); Phase 2/Phase 3 (C15694); Phase 2/Phase 3/Phase 4 (C217024); Phase 3 (C15602); Phase 3/Phase 4 (C217025); Phase 4 (C15603) |
| Business rules | Value Allowed: Yes Relationship: Heading; Sponsor Protocol Identifier Concept: C48281 ICH OID 2.16.840.1.113883.3.989.2.3.3.16 |
| Repeating and/or Reuse Rules | No |

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

| | |
|--|--|
| Term (Variable) | <Trial Short Title> |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C94105 |
| User Guidance | Short title should convey <u>in plain language</u> what the trial is about and should be suitable for use as “Brief Title” or “Title in Plain Language” in global clinical trial registries. It can also be suitable for use with informed consent forms (ICF) and ethics committee submissions. |
| Conformance | Optional |
| Cardinality | One to one; One to Sponsor Protocol identifier |
| Relationship content from ToC representing the protocol hierarchy | Title Page |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: Heading; Sponsor Protocol Identifier Concept: C94105 ICH OID 2.16.840.1.113883.3.989.2.3.3.16 |
| Repeating and/or Reuse Rules | No |

| | |
|---|---------------------------|
| Term (Variable) | Sponsor Name and Address: |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | H |

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

| | |
|--|--|
| Term (Variable) | <Sponsor Name> |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C222495 |
| User Guidance | Provide the legal name and address 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 the Sponsor Name and Sponsor Legal Address fields. If co-sponsor is applicable, enter co-sponsor name and legal address. Add additional fields if more than one co-sponsor is applicable. |
| Conformance | Required |
| Cardinality | One to one; One to Sponsor Protocol Identifier |
| Relationship content from ToC representing the protocol hierarchy | Title Page |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: Heading; Sponsor Protocol Identifier Concept: C222495 ICH OID 2.16.840.1.113883.3.989.2.3.3.16 |
| Repeating and/or Reuse Rules | No |

| | |
|------------------------|-------------------------|
| Term (Variable) | <Sponsor Legal Address> |
| Data Type | Text |

| | |
|--|--|
| Term (Variable) | <Sponsor Legal Address> |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C222495 |
| User Guidance | Provide the legal name and address 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 the Sponsor Name and Sponsor Legal Address fields. If co-sponsor is applicable, enter co-sponsor name and legal address. Add additional fields if more than one co-sponsor is applicable. |
| Conformance | Required |
| Cardinality | One to one; One to Sponsor Name |
| Relationship content from ToC representing the protocol hierarchy | Title Page |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: Heading; Sponsor Name Concept: C222495 ICH OID 2.16.840.1.113883.3.989.2.3.3.16 |
| Repeating and/or Reuse Rules | No |

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

| | |
|--|--|
| Term (Variable) | <Co-Sponsor Name> |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C218678 |
| User Guidance | Provide the legal name and address 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 the Sponsor Name and Sponsor Legal Address fields. If co-sponsor is applicable, enter co-sponsor name and legal address. Add additional fields if more than one co-sponsor is applicable. |
| Conformance | Optional |
| Cardinality | One to one; One to Co-Sponsor Name; One to Sponsor Name; One to Sponsor Protocol Identifier |
| Relationship content from ToC representing the protocol hierarchy | Title Page |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: Heading; Co-Sponsor Name; Sponsor Name; Protocol Identifier Concept: C218678 ICH OID 2.16.840.1.113883.3.989.2.3.3.16 |
| Repeating and/or Reuse Rules | Yes. Repeat for each Co-Sponsor Name |

| | |
|---|--|
| Term (Variable) | <Co-Sponsor Legal Address> |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C218679 |
| User Guidance | Provide the legal name and address 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 the Sponsor Name and Sponsor Legal Address fields. If co-sponsor is applicable, enter co-sponsor name and legal address. Add additional fields if more than one co-sponsor is applicable. |
| Conformance | Optional |
| Cardinality | One to one; One to Heading; One to Co-Sponsor Name |
| Relationship content from ToC | Title Page |

| | |
|--|--|
| Term (Variable) | <Co-Sponsor Legal Address> |
| representing the protocol hierarchy | |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: Heading; Co-Sponsor Name Concept: C218679 ICH OID 2.16.840.1.113883.3.989.2.3.3.16 |
| Repeating and/or Reuse Rules | Yes Repeat for each associated Co-Sponsor Legal Address. There is only one Co-Sponsor Legal Address for each Co-Sponsor Name. |

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

| | |
|--|---|
| Term (Variable) | <Local Sponsor Name> |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C218680 |
| User Guidance | In some countries, the clinical trial Sponsor may be the local affiliate company (or designee). In such cases, indicate this in the Local Sponsor Name and Address Field. |
| Conformance | Optional |
| Cardinality | One to one; One to Sponsor Name and Address; Many to Sponsor Name |
| Relationship content from ToC representing the protocol hierarchy | Title Page |

| | |
|-------------------------------------|--|
| Term (Variable) | <Local Sponsor Name> |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: Heading; Sponsor Name and Address; Sponsor Name; Country Concept: C218680 ICH OID 2.16.840.1.113883.3.989.2.3.3.16 |
| Repeating and/or Reuse Rules | Yes, repeatable for each Local Sponsor Name |

| | |
|--|--|
| Term (Variable) | <Local Sponsor Legal Address> |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C218681 |
| User Guidance | In some countries, the clinical trial sponsor may be the local affiliate company (or designee). In such cases, indicate this in the Local Sponsor Name and Local Sponsor Legal Address Fields. |
| Conformance | Optional |
| Cardinality | One to one; One to Local Sponsor; One to Country |
| Relationship content from ToC representing the protocol hierarchy | Title page |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: Heading; Local Sponsor; Country Concept: C218681 ICH OID 2.16.840.1.113883.3.989.2.3.3.16 |
| Repeating and/or Reuse Rules | Yes Repeat for each associated Local Sponsor Name. There is only one Address for each Local Sponsor Name |

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

| | |
|-------------------------------------|---|
| Term (Variable) | Device Manufacturer Name and Address: |
| | Relationship: Table row heading Concept: Heading |
| Repeating and/or Reuse Rules | No |

| | |
|--|--|
| Term (Variable) | <Device Manufacturer Name> |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C218682 |
| User Guidance | Manufacturer name and address information is required only for drug/device combination protocols that include investigational device(s) and <u>should not</u> 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 or if there are multiple manufacturers for a single device. Delete this line if not applicable. |
| Conformance | Optional |
| Cardinality | One to one; One to Sponsor Protocol Identifier; One to Sponsor Name |
| Relationship content from ToC representing the protocol hierarchy | Title Page |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: Heading; Sponsor Protocol Identifier; Sponsor Name Concept: C218682 ICH OID 2.16.840.1.113883.3.989.2.3.3.16 |
| Repeating and/or Reuse Rules | Yes, repeatable for each Device Manufacturers |

| | |
|---|---|
| Term (Variable) | <Device Manufacturer Legal Address> |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C218683 |
| User Guidance | Manufacturer name and address information is required only for drug/device combination 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 or if there are multiple manufacturers for a single device. Delete this line if not applicable. |
| Conformance | Optional |
| Cardinality | One to one; One to Device Manufacturer Name |

| | |
|--|--|
| Term (Variable) | <Device Manufacturer Legal Address> |
| Relationship content from ToC representing the protocol hierarchy | Title Page |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: Heading; Device Manufacturing Name Concept: C218683 ICH OID 2.16.840.1.113883.3.989.2.3.3.16 |
| Repeating and/or Reuse Rules | Yes. Repeatable for each associated Device Manufacturer Name. There is only one Device Manufacturer Address for each associated Device Manufacturer Name |

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

| | |
|---|--|
| Term (Variable) | <EU CT Number> |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C218684 |
| User Guidance | Include all identifiers that are applicable for the trial and available at the time of protocol or amendment finalisation. Delete prompts for identifiers not available at the time of document finalisation. Delete unused fields. Add fields for "other" if more than one is needed. |
| Conformance | Optional |
| Cardinality | One to one; One to Sponsor Protocol Identifier |
| Relationship content from ToC | Title Page |

| | |
|--|---|
| Term (Variable) | <EU CT Number> |
| representing the protocol hierarchy | |
| Value | Text |
| Business rules | Value Allowed: Yes; EU CT number: yyyy-5xxxxx-xx with YYYY corresponding to a year i.e. 2024 and x being an integer Relationship: Heading; Sponsor Protocol Identifier Concept: C218684 ICH OID 2.16.840.1.113883.3.989.2.3.3.16 |
| Repeating and/or Reuse Rules | No |

| | |
|--|--|
| Term (Variable) | <FDA IND Number> |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C218685 |
| User Guidance | Include all identifiers that are applicable for the trial and available at the time of protocol or amendment finalisation. Delete prompts for identifiers not available at the time of document finalisation. Delete unused fields. Add fields for "other" if more than one is needed. |
| Conformance | Optional |
| Cardinality | One to one; One to Sponsor Protocol Identifier |
| Relationship content from ToC representing the protocol hierarchy | Title Page |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: Heading; Protocol Identifier Concept: C218685 ICH OID 2.16.840.1.113883.3.989.2.3.3.16 |
| Repeating and/or Reuse Rules | No |

| | |
|---|--|
| Term (Variable) | <IDE Number> |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C218686 |
| User Guidance | Include all identifiers that are applicable for the trial and available at the time of protocol or amendment finalisation. Delete prompts for identifiers not available at the time of document finalisation. Delete unused fields. Add fields for "other" if more than one is needed. |
| Conformance | Optional |
| Cardinality | One to one; One to Sponsor Protocol Identifier |

| | |
|--|--|
| Term (Variable) | <IDE Number> |
| Relationship content from ToC representing the protocol hierarchy | Title Page |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: Heading; Protocol Identifier Concept: C218686 ICH OID 2.16.840.1.113883.3.989.2.3.3.16 |
| Repeating and/or Reuse Rules | No |

| | |
|--|--|
| Term (Variable) | <jRCT Number> |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C218687 |
| User Guidance | Include all identifiers that are applicable for the trial and available at the time of protocol or amendment finalisation. Delete prompts for identifiers not available at the time of document finalisation. Delete unused fields. Add fields for "other" if more than one is needed. |
| Conformance | Optional |
| Cardinality | One to one; One to Sponsor Protocol Identifier |
| Relationship content from ToC representing the protocol hierarchy | Title Page |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: Heading; Protocol Identifier Concept: C218687 ICH OID 2.16.840.1.113883.3.989.2.3.3.16 |
| Repeating and/or Reuse Rules | No |

| | |
|---|--|
| Term (Variable) | <NCT Number> |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C172240 |
| User Guidance | Include all identifiers that are applicable for the trial and available at the time of protocol or amendment finalisation. Delete prompts for identifiers not available at the time of document finalisation. Delete unused fields. Add fields for "other" if more than one is needed. |
| Conformance | Optional |
| Cardinality | One to one; One to Sponsor Protocol Identifier |

| | |
|--|--|
| Term (Variable) | <NCT Number> |
| Relationship content from ToC representing the protocol hierarchy | Title Page |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: Heading; Sponsor Protocol Identifier Concept: C172240 ICH OID 2.16.840.1.113883.3.989.2.3.3.16 |
| Repeating and/or Reuse Rules | No |

| | |
|--|--|
| Term (Variable) | <NMPA IND Number> |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C218688 |
| User Guidance | Include all identifiers that are applicable for the trial and available at the time of protocol or amendment finalisation. Delete prompts for identifiers not available at the time of document finalisation. Delete unused fields. Add fields for "other" if more than one is needed. |
| Conformance | Optional |
| Cardinality | One to one; One to Sponsor Protocol Identifier |
| Relationship content from ToC representing the protocol hierarchy | Title Page |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: Heading; Sponsor Protocol Identifier Concept: C218688 ICH OID 2.16.840.1.113883.3.989.2.3.3.16 |
| Repeating and/or Reuse Rules | No |

| | |
|---|--|
| Term (Variable) | <WHO/UTN Number> |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C218689 |
| User Guidance | Include all identifiers that are applicable for the trial and available at the time of protocol or amendment finalisation. Delete prompts for identifiers not available at the time of document finalisation. Delete unused fields. Add fields for "other" if more than one is needed. |
| Conformance | Optional |
| Cardinality | One to one; One to Sponsor Protocol Identifier |

| | |
|--|--|
| Term (Variable) | <WHO/UTN Number> |
| Relationship content from ToC representing the protocol hierarchy | Title Page |
| Value | UTN/WHO: Uxxxx-xxxx-xxxx with X being an integer |
| Business rules | Value Allowed: Yes Relationship: Heading; Sponsor Protocol Identifier Concept: C218689 ICH OID 2.16.840.1.113883.3.989.2.3.3.16 |
| Repeating and/or Reuse Rules | No |

| | |
|--|--|
| Term (Variable) | <Other Regulatory or Clinical Trial Identifier> |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C218690 |
| User Guidance | Include all identifiers that are applicable for the trial and available at the time of protocol or amendment finalisation. Delete prompts for identifiers not available at the time of document finalisation. Delete unused fields. Add fields for "other" if more than one is needed. |
| Conformance | Optional |
| Cardinality | One to one; One to Sponsor Protocol Identifier |
| Relationship content from ToC representing the protocol hierarchy | Title Page |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: Heading; Sponsor Protocol Identifier Concept: C218690 ICH OID 2.16.840.1.113883.3.989.2.3.3.16 |
| Repeating and/or Reuse Rules | Yes, repeatable for each regulatory agency identifier |

| | |
|---|-------------------|
| Term (Variable) | Sponsor Approval: |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | H |
| Definition | Heading |
| User Guidance | N/A |
| Conformance | Required |
| Cardinality | One to one |
| Relationship content from ToC | Title page |

| | |
|--|---|
| Term (Variable) | Sponsor Approval: |
| representing the protocol hierarchy | |
| Value | Sponsor Approval: |
| Business rules | Value Allowed: No Relationship: Table row heading Concept: Heading |
| Repeating and/or Reuse Rules | No |

| | |
|--|--|
| Term (Variable) | {<Sponsor Approval Date> or <State location where sponsor approval information can be found>} |
| Data Type | Date or Text |
| Data (D), Value (V) or Heading (H) | V |
| Definition | C132352 C218484 |
| User Guidance | All versions should be uniquely identifiable. |
| Conformance | Required |
| Cardinality | One to one; One to Protocol Identifier; One to Original Protocol One to Amendment Identifier |
| Relationship content from ToC representing the protocol hierarchy | Title Page |
| Value | Sponsor Approval Date is a date Location where sponsor approval information can be found is text |
| Business rules | Value Allowed: Yes Relationship: Heading; Protocol Identifier; Protocol Amendment Concept: C132352 ICH OID 2.16.840.1.113883.3.989.2.3.3.16; C218484 ICH OID 2.16.840.1.113883.3.989.2.3.3.16 |
| Repeating and/or Reuse Rules | Yes, Not repeatable reuse to Sponsor Approval Date in Section 12.3 |

| | |
|---|--------------------|
| Term (Variable) | Sponsor Signatory: |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | H |
| Definition | Heading |
| User Guidance | N/A |
| Conformance | Optional |
| Cardinality | One to one |
| Relationship content from ToC | Title Page |

| | |
|--|---|
| Term (Variable) | Sponsor Signatory: |
| representing the protocol hierarchy | |
| Value | Sponsor Signatory: |
| Business rules | Value Allowed: No Relationship: Heading Concept: Heading |
| Repeating and/or Reuse Rules | No |

| | |
|--|---|
| Term (Variable) | {<sponsor signatory (e.g., name, title, signature and date)> or <state location where sponsor signatory information can be found (e.g., electronic signature>} |
| Data Type | Image and/or Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C222014 C222064 |
| User Guidance | N/A |
| Conformance | Optional |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | Title Page |
| Value | Sponsor Signatory Text and/or Image OR Location where Sponsor Signatory information can be found (Text) |
| Business rules | Value Allowed: Yes Relationship: Heading Concept: C222014 ICH OID 2.16.840.1.113883.3.989.2.3.3.16; C222064 ICH OID 2.16.840.1.113883.3.989.2.3.3.16 |
| Repeating and/or Reuse Rules | No |

| | |
|---|-------------------------|
| Term (Variable) | Medical Expert Contact: |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | H |
| Definition | Heading |
| User Guidance | N/A |
| Conformance | Optional |
| Cardinality | One to one |
| Relationship content from ToC | Title Page |

| | |
|--|---|
| Term (Variable) | Medical Expert Contact: |
| representing the protocol hierarchy | |
| Value | Medical Expert Contact: |
| Business rules | Value Allowed: No Relationship: Heading Concept: Heading |
| Repeating and/or Reuse Rules | No |

| | |
|--|---|
| Term (Variable) | {< Medical Expert contact information (as designated by sponsor)> or <state location where Medical Expert contact information can be found>} |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C218693 C222063 |
| User Guidance | N/A |
| Conformance | Optional |
| Cardinality | One to one; |
| Relationship content from ToC representing the protocol hierarchy | Title Page |
| Value | Medical Expert contact information (Text) OR Location where Medical Expert contact information can be found (Text) |
| Business rules | Value Allowed: Yes Relationship: Medical Expert Contact Response Concept: C218693 ICH OID 2.16.840.1.113883.3.989.2.3.3.16, C222063 ICH OID 2.16.840.1.113883.3.989.2.3.3.16 |
| Repeating and/or Reuse Rules | No |

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

| | |
|--|---|
| Term (Variable) | Amendment Details |
| representing the protocol hierarchy | |
| Value | Amendment Details |
| Business rules | Value Allowed: No Relationship: Heading Concept: Heading |
| Repeating and/or Reuse Rules | No |

| | |
|--|---|
| Term (Variable) | Amendment Details |
| Data Type | Valid Value |
| Data (D), Value (V) or Heading (H) | V |
| Definition | C218694 |
| User Guidance | Choose the applicable statement below. For an original protocol that has not been amended, retain the first statement below and delete the remainder of this entire section. {This protocol has not been amended.} Or {This is the first protocol amendment.} Or include the below {This protocol has been amended previously. Details of prior amendments are presented in Section 12.3 Prior Protocol Amendment(s).} |
| Conformance | Required |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | Amendment Details |
| Value | Code List C217274: ICH OID 2.16.840.1.113883.3.989.2.3.1.1 This protocol has not been amended. (C218485) OR This is the first protocol amendment. (C218486) OR This protocol has been amended previously. Details of prior amendments are presented in Section 12.3 Prior Protocol Amendment(s). (C218487) |
| Business rules | Value Allowed: Yes Relationship: Heading Concept: C218694 ICH OID 2.16.840.1.113883.3.989.2.3.3.15 |
| Repeating and/or Reuse Rules | No |

| | |
|------------------------|---------------------|
| Term (Variable) | {Current Amendment} |
| Data Type | Text |

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

| | |
|--|--|
| Term (Variable) | {The table below describes the current amendment.} |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | H |
| Definition | Universal text |
| User Guidance | N/A |
| Conformance | Optional |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | Amendment Details |
| Value | The table below describes the current amendment. |
| Business rules | Value Allowed: No Relationship: Current Amendment Concept: Universal text |
| Repeating and/or Reuse Rules | No |

| | |
|---|---|
| Term (Variable) | Approximate <#/%> Enrolled at Time of Sponsor Approval: |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | H |
| Definition | Heading |
| User Guidance | N/A |
| Conformance | Optional |
| Cardinality | One to one |

| | |
|--|--|
| Term (Variable) | Approximate <#/%> Enrolled at Time of Sponsor Approval: |
| Relationship content from ToC representing the protocol hierarchy | Amendment Details |
| Value | Approximate # enrolled at Time of Sponsor Approval: or Approximate % enrolled at Time of Sponsor Approval: |
| Business rules | Value Allowed: No Relationship: Table row heading Concept: Heading |
| Repeating and/or Reuse Rules | No |

| | |
|--|---|
| Term (Variable) | Approximately <#/%> enrolled |
| Data Type | Number |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C218478 |
| User Guidance | <p>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 percentage of enrollment. Estimates are adequate, as precise enrollment figures will likely be changing while an amendment is being prepared.</p> <ul style="list-style-type: none"> For a <u>global or single-country amendment</u>, provide the estimated total enrollment at the time the sponsor approved the amendment. For <u>global amendments providing (or consolidating) only country/region-specific requirements</u>, list approximate local enrollment (total or percentage) at the time of the amendment and select "locally". If consolidating a series of local amendments, list the status of all the relevant locations. <p><u>For a country/regional amendment</u>, provide the estimated local or regional enrollment at the time the sponsor approved the amendment.</p> |
| Conformance | Conditional if Original Protocol =No |
| Cardinality | One to Amendment Number |
| Relationship content from ToC representing the protocol hierarchy | Amendment Details |
| Value | Integer for Number or one decimal point for percent |
| Business rules | Value Allowed: Yes Relationship: Table Row Heading; Statement Concept: C218478 ICH OID 2.16.840.1.113883.3.989.2.3.3.15 |

| | |
|-------------------------------------|------------------------------|
| Term (Variable) | Approximately <#/%> enrolled |
| Repeating and/or Reuse Rules | Yes, reuse to section 12.3 |

| | |
|--|---|
| Term (Variable) | <Amendment Scope Enrollment Definition> |
| Data Type | Valid Value |
| Data (D), Value (V) or Heading (H) | V |
| Definition | C218695 |
| User Guidance | <p>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 percentage of enrollment. Estimates are adequate, as precise enrollment figures will likely be changing while an amendment is being prepared.</p> <ul style="list-style-type: none"> For a <u>global or single-country amendment</u>, provide the estimated total enrollment at the time the sponsor approved the amendment. For <u>global amendments providing (or consolidating) only country/region-specific requirements</u>, list approximate local enrollment (total or percentage) at the time of the amendment and select "locally". If consolidating a series of local amendments, list the status of all the relevant locations. <p>For a <u>country/regional amendment</u>, provide the estimated local or regional enrollment at the time the sponsor approved the amendment.</p> |
| Conformance | Conditional if Original Protocol =No |
| Cardinality | One to Amendment Number |
| Relationship content from ToC representing the protocol hierarchy | Amendment Details |
| Value | Code List C217275: ICH OID 2.16.840.1.113883.3.989.2.3.1.2 Globally (C68846); Locally (C41065); By Cohort (C218489) |
| Business rules | <p>Value Allowed: Yes</p> <p>Relationship: Statement</p> <p>Concept: C218695 ICH OID 2.16.840.1.113883.3.989.2.3.3.15</p> |
| Repeating and/or Reuse Rules | Yes, reuse to section 12.3 |

| | |
|---|----------------------------|
| Term (Variable) | {Reason(s) for Amendment:} |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | H |
| Definition | Heading |
| User Guidance | N/A |

| | |
|--|---|
| Term (Variable) | {Reason(s) for Amendment:} |
| Conformance | Conditional: If Original Protocol = No |
| Cardinality | One to one; Amendment Number |
| Relationship content from ToC representing the protocol hierarchy | Amendment Details |
| Value | Reason(s) for Amendment: |
| Business rules | Value Allowed: No Relationship: Table row heading Concept: Heading |
| Repeating and/or Reuse Rules | No |

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

| | |
|---|---|
| Term (Variable) | [Primary Reason for Amendment]} |
| Data Type | Valid Value |
| Data (D), Value (V) or Heading (H) | V |
| Definition | C218696 |
| User Guidance | Choose from the available categories as the <u>primary</u> reason and <u>secondary</u> reason(s) for the amendment. Select the closest match among the choices. Changes to primary estimand, endpoints, or related measures should be listed as a change of strategy. If none of the choices apply, choose "other" and provide a description. If no secondary reason, indicate "not applicable" for the secondary reason. |
| Conformance | Conditional: if the protocol is = No |

| | |
|--|--|
| Term (Variable) | [Primary Reason for Amendment]} |
| Cardinality | One to Amendment Details |
| Relationship content from ToC representing the protocol hierarchy | Amendment Details |
| Value | Code List C217276: ICH OID 2.16.840.1.113883.3.989.2.3.1.14 <ul style="list-style-type: none"> Regulatory Agency Request To Amend (C218490) New Regulatory Guidance (C218491) IRB/IEC Feedback (C218492) New Safety Information Available (C218493) Manufacturing Change (C218494) IMP Addition (C218495) Change In Strategy (C218496) Change In Standard Of Care (C218497) New Data Available (Other Than Safety Data) (C218498) Investigator/Site Feedback (C218499) Recruitment Difficulty (C218500) Inconsistency And/Or Error In The Protocol (C218501) Protocol Design Error (C218502) Other (C17649) Not Applicable (C48660) |
| Business rules | Value Allowed: Yes Relationship: Heading; Sponsor Protocol Identifier; Protocol Amendment Concept: C218696 ICH OID 2.16.840.1.113883.3.989.2.3.3.15 |
| Repeating and/or Reuse Rules | Yes, Multiple values can be selected except when it is Original Protocol |

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

| | |
|--|--|
| Term (Variable) | <Other description> |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C17649 |
| User Guidance | * Choose from the available categories the <u>primary</u> reason and <u>secondary</u> reason(s) for the amendment. Select the closest match among the choices. Changes to primary estimand, endpoints, or related measures should be listed as a change of strategy. If none of the choices apply, choose "other" and provide a description. If no secondary reason, indicate "Not applicable" for the secondary reason. |
| Conformance | Conditional if Other is selected as a Valid Value |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | Amendment Details |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: Heading; Primary reason; Sponsor Protocol Identifier; Protocol Amendment Concept: C17649 ICH OID 2.16.840.1.113883.3.989.2.3.3.15 |
| Repeating and/or Reuse Rules | No |

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

| | |
|--|--|
| Term (Variable) | {[Secondary Reason for Amendment]} |
| Data Type | Valid Value |
| Data (D), Value (V) or Heading (H) | V |
| Definition | C218697 |
| User Guidance | Choose from the available categories as the <u>primary</u> reason and <u>secondary</u> reason(s) for the amendment. Select the closest match among the choices. Changes to primary estimand, endpoints, or related measures should be listed as a change of strategy. If none of the choices apply, choose "other" and provide a description. If no secondary reason, indicate "not applicable" for the secondary reason. |
| Conformance | Conditional If Protocol Original = No |
| Cardinality | One to one; One to Protocol Identifier; One to Amendment Identifier |
| Relationship content from ToC representing the protocol hierarchy | Amendment Details |
| Value | Code List C217276: ICH OID 2.16.840.1.113883.3.989.2.3.1.14 <ul style="list-style-type: none"> Regulatory Agency Request To Amend (C218490) New Regulatory Guidance (C218491) IRB/IEC Feedback (C218492) New Safety Information Available (C218493) Manufacturing Change (C218494) IMP Addition (C218495) Change In Strategy (C218496) Change In Standard Of Care (C218497) New Data Available (Other Than Safety Data) (C218498) Investigator/Site Feedback (C218499) Recruitment Difficulty (C218500) Inconsistency And/Or Error In The Protocol (C218501) Protocol Design Error (C218502) Other (C17649) Not applicable (C48660) |
| Business rules | Value Allowed: Yes Relationship: Heading, Sponsor Protocol Identifier, Protocol Amendment Concept: C218697 ICH OID 2.16.840.1.113883.3.989.2.3.3.15 |
| Repeating and/or Reuse Rules | Yes, Multiple accepted except for the Original |

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

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

| | |
|---|--|
| Term (Variable) | <Other description> |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C17649 |
| User Guidance | * Choose from the available categories the <u>primary</u> reason and <u>secondary</u> reason(s) for the amendment. Select the closest match among the choices. Changes to primary estimand, endpoints, or related measures should be listed as a change of strategy. If none of the choices apply, choose "other" and provide a description. If no secondary reason, indicate "Not applicable" for the secondary reason. |
| Conformance | Conditional if Other is selected as a Valid Value |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | Amendment Details |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: Heading; Secondary Reason; Sponsor Protocol Identifier; Protocol Amendment Concept: C17649 ICH OID 2.16.840.1.113883.3.989.2.3.3.15 |
| Repeating and/or Reuse Rules | No |

| | |
|---|--|
| Term (Variable) | {Amendment Summary:} |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | H |
| Definition | Heading |
| User Guidance | N/A |
| Conformance | Conditional: if original protocol = No |
| Cardinality | One to one |

| | |
|--|---|
| Term (Variable) | {Amendment Summary:} |
| Relationship content from ToC representing the protocol hierarchy | Amendment Details |
| Value | Amendment Summary: |
| Business rules | Value Allowed: No Relationship: Amendment details, Amendment Identifier Concept: Heading |
| Repeating and/or Reuse Rules | No |

| | |
|--|---|
| Term (Variable) | {<Amendment Summary>} |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C42581 |
| User Guidance | Briefly describe key changes. Changes that are included in the amendment but unrelated to the key changes do not need to be described here. |
| Conformance | Conditional: if there is an amendment |
| Cardinality | One to Amendment identifier |
| Relationship content from ToC representing the protocol hierarchy | Amendment Details |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: Amendment Details; Amendment Identifier; Sponsor Protocol Identifier Concept: C42581 ICH OID 2.16.840.1.113883.3.989.2.3.3.15 |
| Repeating and/or Reuse Rules | No |

| | |
|---|--|
| Term (Variable) | {Is this amendment likely to have a substantial impact on the safety or rights of the participants?} |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | H |
| Definition | Heading |
| User Guidance | N/A |
| Conformance | Conditional: if there is an amendment |
| Cardinality | One to one amendment identifier |
| Relationship content from ToC | Amendment Details |

| | |
|--|--|
| Term (Variable) | {Is this amendment likely to have a substantial impact on the safety or rights of the participants?} |
| representing the protocol hierarchy | |
| Value | Is this amendment likely to have a substantial impact on the safety or rights of the participants? |
| Business rules | Value Allowed: No Relationship: Amendment Details Concept: Heading |
| Repeating and/or Reuse Rules | No |

| | |
|--|--|
| Term (Variable) | {[Yes/No]} |
| Data Type | Valid Value |
| Data (D), Value (V) or Heading (H) | V |
| Definition | C218698 |
| User Guidance | N/A |
| Conformance | Conditional If there is an amendment |
| Cardinality | One to one; One to Amendment Identifier; One to Sponsor Protocol Identifier |
| Relationship content from ToC representing the protocol hierarchy | Amendment Details |
| Value | Code List C217046: ICH OID 2.16.840.1.113883.3.989.2.3.1.11 Yes (C49488); No (C49487) |
| Business rules | Value Allowed: Yes Relationship: Amendment Details; Amendment Identifier; Sponsor Protocol Identifier Concept: C218698 ICH OID 2.16.840.1.113883.3.989.2.3.3.15 |
| Repeating and/or Reuse Rules | No |

| | |
|---|---|
| Term (Variable) | {<If yes, briefly explain>} |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C218699 |
| User Guidance | N/A |
| Conformance | Conditional: if there is an amendment and if "Is this amendment likely to have a substantial impact on the safety or rights of the participants? " is Yes |
| Cardinality | One to one Amendment Identifier, |

| | |
|--|--|
| Term (Variable) | {<If yes, briefly explain>} |
| | Is this amendment likely to have a substantial impact on the safety or rights of the participants? Response when Yes |
| Relationship content from ToC representing the protocol hierarchy | Amendment Details |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: Amendment Details, Amendment Identifier, Sponsor Protocol Identifier When the value is yes there is a text response for explanation Concept: C218699 ICH OID 2.16.840.1.113883.3.989.2.3.3.15 |
| Repeating and/or Reuse Rules | 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 Heading (H) | H |
| Definition | Heading |
| User Guidance | N/A |
| Conformance | Conditional: If there is an amendment |
| Cardinality | One to amendment details, One amendment identifier, Sponsor Protocol Identifier |
| Relationship content from ToC representing the protocol hierarchy | Amendment Details |
| Value | Is this amendment likely to have a substantial impact on the reliability and robustness of the data generated in the clinical trial? |
| Business rules | Value Allowed: No Relationship: Amendment Details, Sponsor Protocol Identifier Concept: Heading |
| Repeating and/or Reuse Rules | No |

| | |
|---|-------------|
| Term (Variable) | {[Yes/No]} |
| Data Type | Valid Value |
| Data (D), Value (V) or Heading (H) | V |
| Definition | C218700 |
| User Guidance | N/A |

| | |
|---|--|
| Term (Variable) | {[Yes/No]} |
| Conformance | Conditional: if there is an amendment |
| Cardinality | One to one; One to Amendment Identifier; One to Sponsor Protocol Identifier |
| Relationship content from ToC representing the protocol hierarchy | Amendment Details |
| Value | Code List C217046: ICH OID 2.16.840.1.113883.3.989.2.3.1.11 Yes (C49488), No (C49487) |
| Business rules | Value Allowed: Yes Relationship: Amendment Details; Amendment Identifier; Sponsor Protocol Identifier Concept: C218700 ICH OID 2.16.840.1.113883.3.989.2.3.3.15 |
| Repeating and/or Reuse Rules | No |

| | |
|--|--|
| Term (Variable) | {<If yes, briefly explain>} |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C218701 |
| User Guidance | N/A |
| Conformance | Conditional: if there is an amendment and if the answer to "Is this amendment likely to have a substantial impact on the reliability and robustness of the data generated in the clinical trial?" is Yes |
| Cardinality | One to amendment identifier |
| Relationship content from ToC representing the protocol hierarchy | Amendment Details |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: Amendment Details; Amendment Identifier; Sponsor Protocol Identifier When the value is yes there is a text response for explanation Concept: C218701 ICH OID 2.16.840.1.113883.3.989.2.3.3.15 |
| Repeating and/or Reuse Rules | No |

| | |
|---|--|
| Term (Variable) | {Overview of Changes in the Current Amendment} |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | H |
| Definition | Heading |

| | |
|--|--|
| Term (Variable) | {Overview of Changes in the Current Amendment} |
| User Guidance | <p>Instructions for the Overview of Changes:</p> <ul style="list-style-type: none"> • If an Overview of Changes already exists from a prior amendment, move it to Section 12.3 Prior Protocol Amendment(s), and populate a new Overview of Changes table for the current amendment. • List the changes that apply to the current amendment. Provide a brief description of the change(s) and a <u>concise</u> scientific rationale for specific changes (e.g., change to inclusion/exclusion criteria). • If the same change affects multiple parts of the protocol, it is acceptable to list multiple locations in the right column. • Table can be sorted in any order preferred by the sponsor. • Minor edits such as clarifications and corrections to typographical errors do not need to be itemised in this table. • The changes listed in the table do not need to be detailed in revision marks, as these can be provided in a separate supporting document. • Tabular presentation is common but not required. The page can be changed to landscape orientation if necessary. <p>(Add rows as needed)</p> |
| Conformance | Conditional: if there is an amendment |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | Amendment Details |
| Value | Overview of Changes in the Current Amendment |
| Business rules | <p>Value Allowed: No</p> <p>Relationship: Amendment Details</p> <p>Concept: Heading</p> |
| Repeating and/or Reuse Rules | No |

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

| | |
|-------------------------------------|-------------------------|
| Term (Variable) | {Description of Change} |
| | Concept: Heading |
| Repeating and/or Reuse Rules | No |

| | |
|--|--|
| Term (Variable) | <Description of Change> |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C218483 |
| User Guidance | N/A |
| Conformance | Conditional: if there is an amendment |
| Cardinality | One to many |
| Relationship content from ToC representing the protocol hierarchy | Amendment Details |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: Table Column Heading and Row; Amendment Details; Column Heading; Row Heading Concept: C218483 ICH OID 2.16.840.1.113883.3.989.2.3.3.15 |
| Repeating and/or Reuse Rules | Yes, repeatable for each Description of Change in the amendment |

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

| | |
|--|--|
| Term (Variable) | <Brief Rationale for Change> |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C181233 |
| User Guidance | N/A |
| Conformance | Conditional: if there is an amendment |
| Cardinality | One to many |
| Relationship content from ToC representing the protocol hierarchy | Amendment Details |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: Amendment Details; Table Column Heading Row; Description of change; Section # and Name Concept: C181233 ICH OID 2.16.840.1.113883.3.989.2.3.3.15 |
| Repeating and/or Reuse Rules | Yes, repeatable for each Description of Change in the amendment |

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

| | |
|---|----------------------|
| Term (Variable) | <Section # and Name> |
| Data Type | Valid Value |
| Data (D), Value (V) or Heading (H) | V |

| | |
|---|---|
| Term (Variable) | <Section # and Name> |
| Definition | C218479 |
| User Guidance | N/A |
| Conformance | Conditional: if there is an amendment |
| Cardinality | One to many Row description of change Description of Change, Rationale for Amendment Change |
| Relationship content from ToC representing the protocol hierarchy | Amendment Details |
| Value | Code List C217272: ICH OID 2.16.840.1.113883.3.989.2.3.13 C217342 Section 1 C217343 Section 2 C217344 Section 3 C217345 Section 4 C217346 Section 5 C217347 Section 6 C217348 Section 7 C217349 Section 8 C217350 Section 9 C217351 Section 10 C217352 Section 11 C217353 Section 12 C217354 Section 13 C217355 Section 14 C217356 Section Title Page C217357 Section Amendment Details |
| Business rules | Value Allowed: Yes Relationship: Amendment Details, Brief Rational; Change description; Table Concept: C218479 ICH OID 2.16.840.1.113883.3.989.2.3.3.15 |
| Repeating and/or Reuse Rules | Yes, repeatable for each Description of Change in the amendment |

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

| | |
|-------------------------------------|---|
| Term (Variable) | Table of Contents |
| Value | Table of Contents |
| Business rules | Value Allowed: No Relationship: N/A Concept: N/A |
| Repeating and/or Reuse Rules | No |

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

1. Protocol summary

| | |
|--|---|
| Term (Variable) | 1 PROTOCOL SUMMARY |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | H |
| Definition | Heading |
| User Guidance | No text is intended here (heading only). |
| Conformance | Required |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 1 |
| Value | PROTOCOL SUMMARY |
| Business rules | Value Allowed: No Relationship: Table of Contents Concept: Heading |

| | |
|-------------------------------------|--------------------|
| Term (Variable) | 1 PROTOCOL SUMMARY |
| Repeating and/or Reuse Rules | No |

1.1. Protocol synopsis

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

1.1.1. Primary and secondary objectives and estimands

| | |
|--|--|
| Term (Variable) | 1.1.1 Primary and Secondary Objectives and Estimands |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | H |
| Definition | Heading |
| User Guidance | N/A |
| Conformance | Required |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 1.1.1 |
| Value | Primary and Secondary Objectives and Estimands |
| Business rules | Value Allowed: No Relationship: 1.1 Protocol Synopsis; 1 PROTOCOL SUMMARY; Table of Contents Concept: Heading |

| | |
|-------------------------------------|--|
| Term (Variable) | 1.1.1 Primary and Secondary Objectives and Estimands |
| Repeating and/or Reuse Rules | No |

| | |
|--|---|
| Term (Variable) | <Primary and Secondary Objectives and Estimands> |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C218839 |
| User Guidance | <p>Summarise the primary and secondary objectives and any associated estimands in natural, nontechnical (layperson) language.</p> <p>For trials intended to estimate a treatment effect or test a hypothesis related to a treatment effect, include the primary and secondary objectives and any associated estimands using a nontechnical summary describing the objective and treatment effect of interest (estimand).</p> <p>For other types of trials not intended to estimate a treatment effect or test a hypothesis related to a treatment effect, define trial objectives and describe additional information relevant to the clinical question(s) of interest (e.g., the endpoint(s) associated with each objective).</p> <p>For trials with numerous objectives in which the description of objectives will exceed half a page, consider including the most important objectives and estimands in the synopsis and refer to Section 3 Trial Objectives and Associated Estimands, which covers the objectives and estimands in technical detail. For considerations on estimands, refer to ICH E9(R1).</p> |
| Conformance | Required |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 1.1.1 |
| Value | Text |
| Business rules | <p>Value Allowed: Yes</p> <p>Relationship: 1.1.1 Primary and Secondary Objectives and Estimands</p> <p>Concept: C218839 ICH OID 2.16.840.1.113883.3.989.2.3.3.1</p> |
| Repeating and/or Reuse Rules | Yes, Reuse <Primary Objective> and <Endpoint> for each Primary Objective from section 3.1, reuse <Secondary Objective and <endpoint> for each Secondary Objective from section 3.2. |

1.1.2. Overall design

| | |
|------------------------|----------------------|
| Term (Variable) | 1.1.2 Overall Design |
| Data Type | Text |

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

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

| | |
|---|---------------|
| Term (Variable) | Intervention: |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | H |
| Definition | Heading |
| User Guidance | N/A |

| | |
|--|--|
| Term (Variable) | Intervention: |
| Conformance | Required |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 1.1.2 |
| Value | Intervention: |
| Business rules | Value Allowed: No Relationship: Table Cell title Concept: Heading |
| Repeating and/or Reuse Rules | No |

| | |
|--|---|
| Term (Variable) | [Sponsor's Investigational Product Code(s)] |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C218675 |
| User Guidance | N/A |
| Conformance | Required Either Sponsor Investigational Product Code or Nonproprietary Name |
| Cardinality | One to one; One to Heading; One to Protocol Identifier |
| Relationship content from ToC representing the protocol hierarchy | 1.1.2 |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: Row title; Sponsor's Protocol Identifier Concept: C218675 ICH OID 2.16.840.1.113883.3.989.2.3.3.1 |
| Repeating and/or Reuse Rules | Yes, repeatable from Title Page Sponsor Investigational Product Code(s) yes, reuse for each Investigational Product |

| | |
|---|---|
| Term (Variable) | [NonProprietary Name(s)] |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C97054 |
| User Guidance | N/A |
| Conformance | Required Either Sponsor Investigational Product Code or Nonproprietary Name |
| Cardinality | One to one; One to Heading; One to Protocol Identifier |
| Relationship content from ToC | 1.1.2 |

| | |
|--|--|
| Term (Variable) | [NonProprietary Name(s)] |
| representing the protocol hierarchy | |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: Row title; Sponsor's Protocol Identifier Concept: C97054 ICH OID 2.16.840.1.113883.3.989.2.3.3.1 |
| Repeating and/or Reuse Rules | Yes, repeatable from Title Page Nonproprietary Name(s) Yes, reuse for each Investigational Product |

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

| | |
|--|--|
| Term (Variable) | [Intervention Model] |
| Data Type | Valid Value |
| Data (D), Value (V) or Heading (H) | V |
| Definition | C98746 |
| User Guidance | N/A |
| Conformance | Required |
| Cardinality | One to one; One to Heading; One to Sponsor Protocol Identifier |
| Relationship content from ToC representing the protocol hierarchy | 1.1.2 |
| Value | Code List C217277: ICH OID 2.16.840.1.113883.3.989.2.3.1.6 Single Group (C82640); Parallel Group (C82639); Cross-over (C82637); Factorial (C82638); Sequential (C142568); Other (C17649) |
| Business rules | Value Allowed: Yes |

| | |
|-------------------------------------|---|
| Term (Variable) | [Intervention Model] |
| | Relationship: Row title; Sponsor Protocol Identifier Concept: C98746 ICH OID 2.16.840.1.113883.3.989.2.3.3.1 |
| Repeating and/or Reuse Rules | No |

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

| | |
|--|---|
| Term (Variable) | [Population Type] |
| Data Type | Valid Value |
| Data (D), Value (V) or Heading (H) | V |
| Definition | C218703 |
| User Guidance | N/A |
| Conformance | Required |
| Cardinality | One to one; One to Heading; One to Sponsor Protocol Identifier |
| Relationship content from ToC representing the protocol hierarchy | 1.1.2 |
| Value | Code List C217278: ICH OID 2.16.840.1.113883.3.989.2.3.1.12 With Disease (C218503); Without Disease (C218504) |
| Business rules | Value Allowed: Yes Relationship: Row Title; Sponsor Protocol Identifier Concept: C218703 ICH OID 2.16.840.1.113883.3.989.2.3.3.1 |
| Repeating and/or Reuse Rules | No |

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

| | |
|--|--|
| Term (Variable) | [Control Type] |
| Data Type | Valid Value |
| Data (D), Value (V) or Heading (H) | V |
| Definition | C49647 |
| User Guidance | N/A |
| Conformance | Required |
| Cardinality | One to one; One to Heading; One to Sponsor Protocol Identifier |
| Relationship content from ToC representing the protocol hierarchy | 1.1.2 |
| Value | Code List C217279: ICH OID 2.16.840.1.113883.3.989.2.3.1.4 Placebo (C49648); Active Comparator (C49649); Dose Response (C120841); Different Dose or Regimen (C218505); External (C218506); Sham Procedure (C184727); No Control (C28280) |
| Business rules | Value Allowed: Yes Relationship: Row Title; Sponsor Protocol Identifier Concept: C49647 ICH OID 2.16.840.1.113883.3.989.2.3.3.1 |
| Repeating and/or Reuse Rules | No |

| | |
|---|------------------------------------|
| Term (Variable) | Population Diagnosis or Condition: |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | H |

| | |
|--|--|
| Term (Variable) | Population Diagnosis or Condition: |
| Definition | Heading |
| User Guidance | N/A |
| Conformance | Required |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 1.1.2 |
| Value | Population Diagnosis or Condition: |
| Business rules | Value Allowed: No Relationship: Table cell title Concept: N/A |
| Repeating and/or Reuse Rules | No |

| | |
|--|---|
| Term (Variable) | [Population Diagnosis or Condition] |
| Data Type | Valid Value or Text |
| Data (D), Value (V) or Heading (H) | V or D |
| Definition | C112038 |
| User Guidance | Population Diagnosis or Condition: MedDRA Preferred Term(s) or indicate "other" and describe. |
| Conformance | Required |
| Cardinality | One to one; One to Heading; One to Sponsor Protocol Identifier |
| Relationship content from ToC representing the protocol hierarchy | 1.1.2 |
| Value | Use examples MedDRA PT or SNOMED CT: "acute lung injury," or a specific biomarker profile); indicate "N/A – Healthy" for studies in healthy volunteers |
| Business rules | Value Allowed: Yes Relationship: Row Title Heading; Sponsor Protocol Identifier Concept: C112038 ICH OID 2.16.840.1.113883.3.989.2.3.3.1 |
| Repeating and/or Reuse Rules | Yes, repeatable for each population diagnosis or condition |

| | |
|---|----------------------|
| Term (Variable) | Control Description: |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | H |
| Definition | Heading |
| User Guidance | N/A |
| Conformance | Required |

| | |
|--|---|
| Term (Variable) | Control Description: |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 1.1.2 |
| Value | Control Description: |
| Business rules | Value Allowed: No Relationship: Table Cell title; Sponsor Protocol Identifier Concept: Heading |
| Repeating and/or Reuse Rules | No |

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

| | |
|---|------------------------|
| Term (Variable) | [Nonproprietary Name] |
| Data Type | Valid Value |
| Data (D), Value (V) or Heading (H) | V |
| Definition | C97054 |
| User Guidance | Further clarification: |

| | |
|--|---|
| Term (Variable) | [Nonproprietary Name] |
| | Control Description: if active comparator or low dose, pick nonproprietary name or International Nonproprietary Name; indicate "Not applicable" if not applicable |
| Conformance | Conditional: if there is a Nonproprietary Name |
| Cardinality | One to many |
| Relationship content from ToC representing the protocol hierarchy | 1.1.2 |
| Value | Use for example WHO INN, USAN, JAN, XEVMPD |
| Business rules | Value Allowed: Yes Relationship: Row title; Control Description; Sponsor Protocol Identifier Concept: C97054 ICH OID 2.16.840.1.113883.3.989.2.3.3.1 |
| Repeating and/or Reuse Rules | Yes, repeatable for each Nonproprietary Name used as control |

| | |
|--|---|
| Term (Variable) | or [INN] or |
| Data Type | Valid Value |
| Data (D), Value (V) or Heading (H) | V |
| Definition | C142585 |
| User Guidance | Further clarification: Control Description: if active comparator or low dose, pick nonproprietary name or International Nonproprietary Name; indicate "Not applicable" if not applicable |
| Conformance | Conditional: if there is an INN |
| Cardinality | One to many |
| Relationship content from ToC representing the protocol hierarchy | 1.1.2 |
| Value | Use for example WHO INN, USAN, JAN, XEVMPD |
| Business rules | Value Allowed: Yes Relationship: Row title; Control Description; Protocol Identifier Concept: C142585 ICH OID 2.16.840.1.113883.3.989.2.3.3.1 |
| Repeating and/or Reuse Rules | Yes, repeatable for each INN used as control |

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|---|--------------------|
| Term (Variable) | <"Not applicable"> |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | V |
| Definition | Universal text |

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

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

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

| | |
|--|---|
| Term (Variable) | Minimum: |
| Cardinality | One to two; One to Sponsor Protocol Identifier |
| Relationship content from ToC representing the protocol hierarchy | 1.1.2 |
| Value | Minimum: |
| Business rules | Value Allowed: No Relationship: Population Age; Sponsor Protocol Identifier Concept: Heading |
| Repeating and/or Reuse Rules | No |

| | |
|--|--|
| Term (Variable) | <Minimum Age> |
| Data Type | Number |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C49693 |
| User Guidance | Population Age: for trials in which multiple age ranges may be eligible (e.g., a younger cohort and an older cohort), indicate the minimum and maximum ages for the trial overall, with an additional comment for any excluded age ranges. |
| Conformance | Required |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 1.1.2 |
| Value | Integer |
| Business rules | Value Allowed: Yes Relationship: Population Age; Minimum; Unit of Age Concept: C49693 ICH OID 2.16.840.1.113883.3.989.2.3.3.1 |
| Repeating and/or Reuse Rules | No |

| | |
|---|--|
| Term (Variable) | [Units of Age] |
| Data Type | Valid Value |
| Data (D), Value (V) or Heading (H) | V |
| Definition | C50400 |
| User Guidance | Population Age: For trials in which multiple age ranges may be eligible (e.g., 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 |

| | |
|--|--|
| Term (Variable) | [Units of Age] |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 1.1.2 |
| Value | Code List C217048: ICH OID 2.16.840.1.113883.3.989.2.3.1.23 Hours (C25529); Days (C25301); Weeks (C29844); Months (C29846); Years (C29848) |
| Business rules | Value Allowed: Yes Relationship: Population age; Minimum, Numeric Minimum Concept: C50400 ICH OID 2.16.840.1.113883.3.989.2.3.3.1 |
| Repeating and/or Reuse Rules | No |

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

| | |
|---|---|
| Term (Variable) | <Maximum Age> |
| Data Type | Number |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C49694 |
| User Guidance | Population Age: For trials in which multiple age ranges may be eligible (for example, a younger cohort and an older cohort), indicate the minimum and maximum ages for the trial overall, with an additional comment for any excluded age ranges. |
| Conformance | Required |
| Cardinality | One to one |

| | |
|--|--|
| Term (Variable) | <Maximum Age> |
| Relationship content from ToC representing the protocol hierarchy | 1.1.2 |
| Value | Integer |
| Business rules | Value Allowed: Yes Relationship: Population Age; Maximum Age; Unit of Age Concept: C49694 ICH OID 2.16.840.1.113883.3.989.2.3.3.1 |
| Repeating and/or Reuse Rules | No |

| | |
|--|---|
| Term (Variable) | [Units of Age] |
| Data Type | Valid Value |
| Data (D), Value (V) or Heading (H) | V |
| Definition | C50400 |
| User Guidance | Population Age: For trials in which multiple age ranges may be eligible (for example, a younger cohort and an older cohort), indicate the minimum and maximum ages for the trial overall, with an additional comment for any excluded age ranges. |
| Conformance | Required |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 1.1.2 |
| Value | Code List C217048: ICH OID 2.16.840.1.113883.3.989.2.3.1.23 Hours (C25529); Days (C25301); Weeks (C29844); Months (C29846); Years (C29848) |
| Business rules | Value Allowed: Yes Relationship: Population Age; Maximum, Numeric Maximum Concept: C50400 ICH OID 2.16.840.1.113883.3.989.2.3.3.1 |
| Repeating and/or Reuse Rules | No |

| | |
|---|---------------------------------|
| Term (Variable) | Intervention Assignment Method: |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | H |
| Definition | Heading |
| User Guidance | N/A |
| Conformance | Required |
| Cardinality | One to one |

| | |
|--|--|
| Term (Variable) | Intervention Assignment Method: |
| Relationship content from ToC representing the protocol hierarchy | 1.1.2 |
| Value | Intervention Assignment Method: |
| Business rules | Value Allowed: No Relationship: Row Table cell Title Concept: Heading |
| Repeating and/or Reuse Rules | No |

| | |
|--|--|
| Term (Variable) | [Intervention Assignment Method] |
| Data Type | Valid Value |
| Data (D), Value (V) or Heading (H) | V |
| Definition | C218475 |
| User Guidance | Intervention Assignment Method: If applicable, describe the type of randomisation to be used (e.g., simple randomisation, block randomisation). If applicable, describe the other intervention assignment method |
| Conformance | Required |
| Cardinality | One to one; One to Sponsor Protocol Identifier |
| Relationship content from ToC representing the protocol hierarchy | 1.1.2 |
| Value | Code List C217280: ICH OID 2.16.840.1.113883.3.989.2.3.1.18 Randomisation (C25196); No Intervention Assignment Method (C222801); Other (C17649) |
| Business rules | Value Allowed: Yes Relationship: Row title identifier; Sponsor Protocol Identifiers Concept: C218475 ICH OID 2.16.840.1.113883.3.989.2.3.3.1 |
| Repeating and/or Reuse Rules | No |

| | |
|---|--|
| Term (Variable) | {<Randomisation Type>} |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C223137 |
| User Guidance | Intervention Assignment Method: If applicable, describe the type of randomisation to be used (e.g., simple randomisation, block randomisation). If applicable, describe the other intervention assignment method |

| | |
|--|---|
| Term (Variable) | {<Randomisation Type>} |
| Conformance | Conditional if Randomisation is selected as Valid Value |
| Cardinality | One to one; One to Sponsor Protocol Identifier; One to Randomisation |
| Relationship content from ToC representing the protocol hierarchy | 1.1.2 |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: Intervention Assignment Row title identifier; Sponsor Protocol Identifiers Concept: C223137 ICH OID 2.16.840.1.113883.3.989.2.3.3.1 |
| Repeating and/or Reuse Rules | No |

| | |
|--|---|
| Term (Variable) | {<Other Intervention Assignment Method>} |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C223138 |
| User Guidance | Intervention Assignment Method: If applicable, describe the type of randomisation to be used (e.g., simple randomisation, block randomisation). If applicable, describe the other intervention assignment method. |
| Conformance | Conditional if Other is selected as a Valid Value |
| Cardinality | One to one; One to Sponsor Protocol Identifier; One to Other |
| Relationship content from ToC representing the protocol hierarchy | Amendment Details |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: Other, Row title identifier; Sponsor Protocol Identifiers Concept: C223138 ICH OID 2.16.840.1.113883.3.989.2.3.3.1 |
| Repeating and/or Reuse Rules | No |

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

| | |
|--|--|
| Term (Variable) | Stratification: |
| Relationship content from ToC representing the protocol hierarchy | 1.1.2 |
| Value | Stratification |
| Business rules | Value Allowed: No Relationship: Row Table cell Title Concept: Heading |
| Repeating and/or Reuse Rules | No |

| | |
|--|---|
| Term (Variable) | [Stratification Indicator] |
| Data Type | Valid Value |
| Data (D), Value (V) or Heading (H) | V |
| Definition | C223136 |
| User Guidance | N/A. |
| Conformance | Required |
| Cardinality | One to one; One to Sponsor Protocol Identifier |
| Relationship content from ToC representing the protocol hierarchy | 1.1.2 |
| Value | Code List C217046: ICH OID 2.16.840.1.113883.3.989.2.3.1.11 Yes (C49488), No (C49487) |
| Business rules | Value Allowed: Yes Relationship: Row title identifier; Sponsor Protocol Identifiers Concept: C223136 ICH OID 2.16.840.1.113883.3.989.2.3.3.1 |
| Repeating and/or Reuse Rules | No |

| | |
|--|---|
| Term (Variable) | Site Distribution and Geographic Scope: |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | H |
| Definition | Heading |
| User Guidance | N/A |
| Conformance | Required |
| Cardinality | One to two |
| Relationship content from ToC representing the protocol hierarchy | 1.1.2 |
| Value | Site Distribution and Geographic Scope: |

| | |
|-------------------------------------|---|
| Term (Variable) | Site Distribution and Geographic Scope: |
| Business rules | Value Allowed: No Relationship: Row title Heading; Site distribution; Site Geographic scope Concept: Heading |
| Repeating and/or Reuse Rules | No |

| | |
|--|---|
| Term (Variable) | [Site Distribution] |
| Data Type | Valid Value |
| Data (D), Value (V) or Heading (H) | V |
| Definition | C218704 |
| User Guidance | N/A |
| Conformance | Required |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 1.1.2 |
| Value | Code List C217049: ICH OID 2.16.840.1.113883.3.989.2.3.1.20 Single-Centre (C217004), Multicentre (C217005) |
| Business rules | Value Allowed: Yes Relationship: Row Title heading; Sponsor Protocol Identifier Concept: C218704 ICH OID 2.16.840.1.113883.3.989.2.3.3.1 |
| Repeating and/or Reuse Rules | No |

| | |
|--|---|
| Term (Variable) | [Site Geographic Scope] |
| Data Type | Valid Value |
| Data (D), Value (V) or Heading (H) | V |
| Definition | C218705 |
| User Guidance | N/A |
| Conformance | Required |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 1.1.2 |
| Value | Code List C217050: ICH OID 2.16.840.1.113883.3.989.2.3.1.21 Single Country (C217006); Multiple Countries (C217007) |
| Business rules | Value Allowed: Yes Relationship: Row Title Heading; Sponsor Protocol Identifier Concept: C218705 ICH OID 2.16.840.1.113883.3.989.2.3.3.1 |

| | |
|-------------------------------------|-------------------------|
| Term (Variable) | [Site Geographic Scope] |
| Repeating and/or Reuse Rules | No |

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

| | |
|--|---|
| Term (Variable) | [Master Protocol Indicator] |
| Data Type | Valid Value |
| Data (D), Value (V) or Heading (H) | V |
| Definition | C218707 |
| User Guidance | N/A |
| Conformance | Required |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 1.1.2 |
| Value | Code List C217046: ICH OID 2.16.840.1.113883.3.989.2.3.1.11 Yes (C49488), No (C49487) |
| Business rules | Value Allowed: Yes Relationship: Heading Master Protocol Indicator; Sponsor Protocol Identifier Concept: C218707 ICH OID 2.16.840.1.113883.3.989.2.3.3.1 |
| Repeating and/or Reuse Rules | No |

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

| | |
|--|---|
| Term (Variable) | [Drug/Device Combination Product Indicator] |
| Data Type | Valid Value |
| Data (D), Value (V) or Heading (H) | V |
| Definition | C218708 |
| User Guidance | N/A |
| Conformance | Required |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 1.1.2 |
| Value | Code List C217046: ICH OID 2.16.840.1.113883.3.989.2.3.1.11 Yes (C49488), No (C49487) |
| Business rules | Value Allowed: Yes Relationship: Heading Drug/Device Combination Product; Sponsor Protocol Identifier Concept: C218708 ICH OID 2.16.840.1.113883.3.989.2.3.3.1 |
| Repeating and/or Reuse Rules | No |

| | |
|---|------------------------|
| Term (Variable) | Adaptive Trial Design: |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | H |
| Definition | Heading |

| | |
|--|---|
| Term (Variable) | Adaptive Trial Design: |
| User Guidance | N/A |
| Conformance | Required |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 1.1.2 |
| Value | Adaptive Trial Design: |
| Business rules | Value Allowed: No Relationship: Table row heading Concept: Heading |
| Repeating and/or Reuse Rules | No |

| | |
|--|---|
| Term (Variable) | [Adaptive Trial Design Indicator] |
| Data Type | Valid Value |
| Data (D), Value (V) or Heading (H) | V |
| Definition | C218706 |
| User Guidance | N/A |
| Conformance | Required |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 1.1.2 |
| Value | Code List C217046: ICH OID 2.16.840.1.113883.3.989.2.3.1.11 Yes (C49488), No (C49487) |
| Business rules | Value Allowed: Yes Relationship: Heading; Sponsor Protocol Identifier Concept: C218706 ICH OID 2.16.840.1.113883.3.989.2.3.3.1 |
| Repeating and/or Reuse Rules | No |

| | |
|---|-----------------|
| Term (Variable) | Number of Arms: |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | H |
| Definition | Heading |
| User Guidance | N/A |
| Conformance | Required |
| Cardinality | One to one |
| Relationship content from ToC | 1.1.2 |

| | |
|--|--|
| Term (Variable) | Number of Arms: |
| representing the protocol hierarchy | |
| Value | Number of Arms: |
| Business rules | Value Allowed: No Relationship: 1.1.2 Overall Design; 1.1 Protocol Synopsis; 1 PROTOCOL SUMMARY; Table of Contents Concept: Heading |
| Repeating and/or Reuse Rules | No |

| | |
|--|---|
| Term (Variable) | [Number of Arms] |
| Data Type | Number |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C98771 |
| User Guidance | Select 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 total number of arms. |
| Conformance | Required |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 1.1.2 |
| Value | Integer |
| Business rules | Value Allowed: Yes Relationship: Number of Arms; Heading; Sponsor Protocol Identifier Concept: C98771 ICH OID 2.16.840.1.113883.3.989.2.3.3.1 |
| Repeating and/or Reuse Rules | No |

| | |
|--|---------------------|
| Term (Variable) | Trial Blind Schema: |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | H |
| Definition | Heading |
| User Guidance | N/A |
| Conformance | Required |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 1.1.2 |
| Value | Trial Blind Schema: |

| | |
|-------------------------------------|--|
| Term (Variable) | Trial Blind Schema: |
| Business rules | Value Allowed: No Relationship: 1.1.2 Overall Design; 1.1 Protocol Synopsis; 1 PROTOCOL SUMMARY; Table of Contents Concept: Heading |
| Repeating and/or Reuse Rules | No |

| | |
|--|--|
| Term (Variable) | [Trial Blind Schema] |
| Data Type | Valid Value |
| Data (D), Value (V) or Heading (H) | V |
| Definition | C49658 |
| User Guidance | For designs in which these details may differ in one or more trial periods, answer according to the portion of the trial in which the highest number of blinded roles occurs. Additional details can be provided in Section 6.7.3 Measures to Maintain Blinding. |
| Conformance | Required |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 1.1.2 |
| Value | Code List C217051: ICH OID 2.16.840.1.113883.3.989.2.3.1.17 Double Blind (C15228), Observer Blind (C187674), Open Label (C49659), Single Blind (C28233) |
| Business rules | Value Allowed: Yes Relationship: Trial Blind Schema; Heading; Protocol Sponsor Identifier Concept: C49658 ICH OID 2.16.840.1.113883.3.989.2.3.3.1 |
| Repeating and/or Reuse Rules | No |

| | |
|--|---|
| Term (Variable) | Blinded Roles: The following roles indicated will not be made aware of the treatment group assignment during the trial: |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | H |
| Definition | Heading |
| User Guidance | N/A |
| Conformance | Required |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 1.1.2 |

| | |
|-------------------------------------|--|
| Term (Variable) | Blinded Roles: The following roles indicated will not be made aware of the treatment group assignment during the trial: |
| Value | Blinded roles: The following roles indicated will not be made aware of the treatment group assignment during the trial: |
| Business rules | Value Allowed: No Relationship: 1.1.2 Overall Design; 1.1 Protocol Synopsis; 1 PROTOCOL SUMMARY; Table of Contents Concept: Heading |
| Repeating and/or Reuse Rules | No |

| | |
|--|--|
| Term (Variable) | [Blinded Roles] |
| Data Type | Valid Value |
| Data (D), Value (V) or Heading (H) | V |
| Definition | C218709 |
| User Guidance | "Not applicable (no blinding)" indicates an open-label trial. |
| Conformance | Required |
| Cardinality | One to many |
| Relationship content from ToC representing the protocol hierarchy | 1.1.2 |
| Value | Code List C217281: ICH OID 2.16.840.1.113883.3.989.2.3.1.16 Participant (C142710); Care Provider (C17445); Investigator (C25936); Outcomes Assessor (C207599); Sponsor (C70793); Not Applicable (C48660) |
| Business rules | Value Allowed: Yes, Multiple roles can be selected Relationship: Blinded Roles; Sponsor Protocol Identifier Concept: C218709 ICH OID 2.16.840.1.113883.3.989.2.3.3.1 |
| Repeating and/or Reuse Rules | No |

| | |
|--|-------------------------|
| Term (Variable) | Number of participants: |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | H |
| Definition | Heading |
| User Guidance | N/A |
| Conformance | Required |
| Cardinality | One to many |
| Relationship content from ToC representing the protocol hierarchy | 1.1.2 |

| | |
|-------------------------------------|--|
| Term (Variable) | Number of participants: |
| Value | Number of Participants: |
| Business rules | Value Allowed: No Relationship: 1.1.2 Overall Design; 1.1 Protocol Synopsis; 1 PROTOCOL SUMMARY; Table of Contents Concept: Heading |
| Repeating and/or Reuse Rules | No |

| | |
|--|--|
| Term (Variable) | [Target/Maximum] |
| Data Type | Valid Value |
| Data (D), Value (V) or Heading (H) | V |
| Definition | C218710 |
| User Guidance | State the expected number of participants to be assigned to trial intervention/enrolled. Indicate whether the number provided is the target or maximum number of individuals to be randomly assigned to trial intervention/enrolled. |
| Conformance | Required |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 1.1.2 |
| Value | A (choose Target/Maximum) of |
| Business rules | Value Allowed: Yes Relationship: Heading; Sponsor Protocol Identifier Concept: C218710 ICH OID 2.16.840.1.113883.3.989.2.3.3.1 |
| Repeating and/or Reuse Rules | No |

| | |
|---|--|
| Term (Variable) | <Number of Participants> |
| Data Type | Number |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C49692 |
| User Guidance | State the expected number of participants to be assigned to trial intervention/enrolled. Indicate whether the number provided is the target or maximum number of individuals to be randomly assigned to trial intervention/enrolled. |
| Conformance | Required |
| Cardinality | One to one |
| Relationship content from ToC | 1.1.2 |

| | |
|--|---|
| Term (Variable) | <Number of Participants> |
| representing the protocol hierarchy | |
| Value | Integer; <Number of Participants> participants will be |
| Business rules | Value Allowed: Yes Relationship: Heading; Sponsor Protocol Identifiers Concept: C49692 ICH OID 2.16.840.1.113883.3.989.2.3.3.1 |
| Repeating and/or Reuse Rules | No |

| | |
|--|---|
| Term (Variable) | [randomly assigned to trial intervention/enrolled] |
| Data Type | Valid Value |
| Data (D), Value (V) or Heading (H) | V |
| Definition | C218711 |
| User Guidance | State the expected number of participants to be assigned to trial intervention/enrolled. Indicate whether the number provided is the target or maximum number of individuals to be randomly assigned to trial intervention/enrolled |
| Conformance | Required |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 1.1.2 |
| Value | randomly assigned to trial intervention/enrolled |
| Business rules | Value Allowed: Yes Relationship: Heading; Sponsor Protocol Identifier Concept: C218711 ICH OID 2.16.840.1.113883.3.989.2.3.3.1 |
| Repeating and/or Reuse Rules | No |

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

| | |
|-------------------------------------|--|
| Term (Variable) | Duration |
| Business rules | Value Allowed: No Relationship: 1.1.2 Overall Design, 1.1 Protocol Synopsis, 1 PROTOCOL SUMMARY; Table of Contents Concept: Heading |
| Repeating and/or Reuse Rules | No |

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

| | |
|---|---|
| Term (Variable) | {<total planned duration of trial intervention> [total planned duration of trial unit of time]} |
| Data Type | Integer, Valid value |
| Data (D), Value (V) or Heading (H) | D, V |
| Definition | C218712 C218713 |
| User Guidance | Select one of the two options for total planned duration of trial intervention and trial participation for each participant. Note that the total duration of trial participation should include any washout and any follow-up periods in which the participant is not receiving a trial intervention. When duration will vary, provide a short explanation (e.g., "event-driven" or "adaptive design"). |

| | |
|--|---|
| Term (Variable) | {<total planned duration of trial intervention> [total planned duration of trial unit of time]} |
| Conformance | Conditional: when Planned Duration of trial Intervention Number and unit of time |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 1.1.2 |
| Value | Total planned duration of trial intervention: Integer Total planned duration of trial intervention unit of time: Code List C217048: ICH OID 2.16.840.1.113883.3.989.2.3.1.23 Days (C25301); Hours (C25529); Months (C29846); Weeks (C29844); Years (C29848) |
| Business rules | Value Allowed: Yes Relationship: Total duration of trial intervention for each participant: Concept: C218712 ICH OID 2.16.840.1.113883.3.989.2.3.3.1; C218713 ICH OID 2.16.840.1.113883.3.989.2.3.3.1 |
| Repeating and/or Reuse Rules | No |

| | |
|--|--|
| Term (Variable) | {<alternate description of planned duration of trial intervention>} |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C218714 |
| User Guidance | Select one of the two options for total planned duration of trial intervention and trial participation for each participant. Note that the total duration of trial participation should include any washout and any follow-up periods in which the participant is not receiving a trial intervention. When duration will vary, provide a short explanation (e.g., "event-driven" or "adaptive design"). Or, if duration will vary |
| Conformance | Conditional: when an alternate description for planned duration of trial Intervention if the duration varies |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 1.1.2 |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: Total duration of trial intervention for each participant: Concept: C218714 ICH OID 2.16.840.1.113883.3.989.2.3.3.1 |

| | |
|-------------------------------------|---|
| Term (Variable) | {<alternate description of planned duration of trial intervention>} |
| Repeating and/or Reuse Rules | No |

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

| | |
|---|---|
| Term (Variable) | {<total planned duration of trial participation> [Total planned duration of trial participation unit of time]} |
| Data Type | Integer, Valid value |
| Data (D), Value (V) or Heading (H) | D, V |
| Definition | C218715 C218716 |
| User Guidance | Select one of the two options for total planned duration of trial intervention and trial participation for each participant. Note that the total duration of trial participation should include any washout and any follow-up periods in which the participant is not receiving a trial intervention. When duration will vary, provide a short explanation (e.g., "event-driven" or "adaptive design"). |
| Conformance | Conditional: when planned duration of trial participation number and unit of time |
| Cardinality | One to one |

| | |
|--|---|
| Term (Variable) | {<total planned duration of trial participation> [Total planned duration of trial participation unit of time]} |
| Relationship content from ToC representing the protocol hierarchy | 1.1.2 |
| Value | Total planned duration of trial participation: Integer Total planned duration of trial participation unit of time: Code List C217048: ICH OID 2.16.840.1.113883.3.989.2.3.1.23 Days (C25301); Hours (C25529); Months (C29846); Weeks (C29844); Years (C29848) |
| Business rules | Value Allowed: Yes Relationship: Total duration of trial participation for each participant: Concept: C218715 ICH OID 2.16.840.1.113883.3.989.2.3.3.1; C218716 ICH OID 2.16.840.1.113883.3.989.2.3.3.1 |
| Repeating and/or Reuse Rules | No |

| | |
|--|--|
| Term (Variable) | {<alternate description of planned duration of trial participation>} |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C218717 |
| User Guidance | Select one of the two options for total planned duration of trial intervention and trial participation for each participant. Note that the total duration of trial participation should include any washout and any follow-up periods in which the participant is not receiving a trial intervention. When duration will vary, provide a short explanation (e.g., "event-driven" or "adaptive design"). Or, if duration will vary |
| Conformance | Conditional: when an alternate description for planned duration of trial participation if duration will vary |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 1.1.2 |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: Total duration of planned duration of trial participation if duration will vary: Concept: C218717 ICH OID 2.16.840.1.113883.3.989.2.3.3.1 |
| Repeating and/or Reuse Rules | No |

| | |
|--|---|
| Term (Variable) | <Additional Description of Duration> |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C218838 |
| User Guidance | If necessary, include any clarifications or cross-references to details in the main body of the protocol in the optional field below. |
| Conformance | Optional |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 1.1.2 |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: Duration Concept: C218838 ICH OID 2.16.840.1.113883.3.989.2.3.3.1 |
| Repeating and/or Reuse Rules | No |

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

| | |
|---|-------------------------|
| Term (Variable) | Independent Committees: |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | H |
| Definition | Heading |

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

| | |
|--|---|
| Term (Variable) | <Independent Committees> |
| Data Type | Valid Value |
| Data (D), Value (V) or Heading (H) | V |
| Definition | C218718 |
| User Guidance | Indicate whether any committee(s) will be reviewing data while the trial is ongoing, and the type of committee. Common examples include Data Monitoring Committee, Dose Escalation Committee, or Endpoint Adjudication Committee; describe others, if applicable. List independent committees in the space indicated. Other committees may be included in the separate space provided. Committees listed here should be fully described in Section 11.4 Committees. |
| Conformance | Required |
| Cardinality | One to many |
| Relationship content from ToC representing the protocol hierarchy | 1.1.2 |
| Value | Code List C217282: ICH OID 2.16.840.1.113883.3.989.2.3.1.5 Independent Data Monitoring Committee (C142578); Dose Escalation Committee (C215671); Endpoint Adjudication Committee (C78726); Other (C17649); None (C41132) |
| Business rules | Value Allowed: Yes, more than one committee can be selected Relationship: Independent Committees Concept: C218718 ICH OID 2.16.840.1.113883.3.989.2.3.3.1 |
| Repeating and/or Reuse Rules | No |

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

| | |
|--|---|
| Term (Variable) | <Other Committees> |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C218719 |
| User Guidance | Indicate whether any committee(s) will be reviewing data while the trial is ongoing, and the type of committee. Common examples include Data Monitoring Committee, Dose Escalation Committee, or Endpoint Adjudication Committee; describe others, if applicable. List independent committees in the space indicated. Other committees may be included in the separate space provided. Committees listed here should be fully described in Section 11.4 Committees. Delete "Other Committees" if not applicable. |
| Conformance | Optional |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 1.1.2 |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: Other Committees Concept: C218719 ICH OID 2.16.840.1.113883.3.989.2.3.3.1 |
| Repeating and/or Reuse Rules | No |

1.2. Trial schema

| | |
|--|---|
| Term (Variable) | 1.2 Trial Schema |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | H |
| Definition | Heading |
| User Guidance | N/A |
| Conformance | Required |
| Cardinality | One to many |
| Relationship content from ToC representing the protocol hierarchy | 1.2 |
| Value | Trial Schema |
| Business rules | Value Allowed: No Relationship: 1 PROTOCOL SUMMARY; Table of Contents Concept: Heading |
| Repeating and/or Reuse Rules | No |

| | |
|--|--|
| Term (Variable) | <Trial Schema> |
| Data Type | Image; Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C93682 |
| User Guidance | The purpose of this section is to provide a visual depiction of the trial design, orienting users of the protocol to the key features of the design. The schema depicts the trial arms, the flow of individual participant through the progression of trial period(s)/epochs (such as screening, washout/run-in, intervention, and key milestones [e.g., randomisation, cross-over, end of treatment, end of study, post-treatment follow-up]). For complex trials, additional schemas may be added to describe activities or trial periods in greater detail. |
| Conformance | Required |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 1.2 |
| Value | Image; Text |
| Business rules | Value Allowed: Yes Relationship: 1.2 Trial Schema Concept: C93682 ICH OID 2.16.840.1.113883.3.989.2.3.3.1 |
| Repeating and/or Reuse Rules | Yes, repeatable within Section |

| | |
|--|--|
| Term (Variable) | <Schema Notes> |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C218720 |
| User Guidance | The purpose of this section is to provide a visual depiction of the trial design, orienting users of the protocol to the key features of the design. The schema depicts the trial arms, the flow of individual participant through the progression of trial period(s)/epochs (such as screening, washout/run-in, intervention, and key milestones [e.g., randomisation, cross-over, end of treatment, end of study, post-treatment follow-up]). For complex trials, additional schemas may be added to describe activities or trial periods in greater detail. |
| Conformance | Optional |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 1.2 |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: 1.2 Trial Schema Concept: C218720 ICH OID 2.16.840.1.113883.3.989.2.3.3.1 |
| Repeating and/or Reuse Rules | Yes, repeatable and aligned with appropriate schema |

1.3. Schedule of activities

| | |
|--|---|
| Term (Variable) | 1.3 Schedule of Activities |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | H |
| Definition | Heading |
| User Guidance | N/A |
| Conformance | Required |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 1.3 |
| Value | Schedule of Activities |
| Business rules | Value Allowed: No Relationship: 1 PROTOCOL SUMMARY; Table of Contents Concept: Heading |

| | |
|-------------------------------------|----------------------------|
| Term (Variable) | 1.3 Schedule of Activities |
| Repeating and/or Reuse Rules | No |

| | |
|--|--|
| Term (Variable) | <Schedule of Activities> |
| Data Type | Table; Text; Image |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C132349 |
| User Guidance | The schedule of activities must capture the procedures that will be accomplished at each trial visit, and all contact with participants (e.g., telephone contacts). This includes any tests that are used for eligibility, participant randomisation or stratification, or decisions on trial intervention discontinuation. Allowable windows should be stated for all visits and procedures. A tabular format is recommended. When applicable for studies with extensive sampling (e.g., serial PK sampling), a separate table may be added. |
| Conformance | Required |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 1.3 |
| Value | Table; text; Image |
| Business rules | Value Allowed: Yes Relationship: 1.3 Schedule of Activities Concept: C132349 ICH OID 2.16.840.1.113883.3.989.2.3.3.1 |
| Repeating and/or Reuse Rules | Yes, repeatable for each Schedule of Activity if needed |

2. Introduction

| | |
|--|----------------|
| Term (Variable) | 2 Introduction |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | H |
| Definition | Heading |
| User Guidance | |
| Conformance | Required |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 2 |
| Value | INTRODUCTION |

| | |
|-------------------------------------|---|
| Term (Variable) | 2 Introduction |
| Business rules | Value Allowed: No Relationship: Table of Contents Concept: Heading |
| Repeating and/or Reuse Rules | No |

2.1. Purpose of trial

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

| | |
|--|---|
| Term (Variable) | <Purpose of Trial> |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C146997 |
| User Guidance | |
| Conformance | Required |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 2.1 |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: 2.1 Purpose of Trial Concept: C146997 ICH OID 2.16.840.1.113883.3.989.2.3.3.2 |
| Repeating and/or Reuse Rules | No |

2.2. Assessment of risks and benefits

| | |
|--|---|
| Term (Variable) | 2.2 Assessment of Risks and Benefits |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | H |
| Definition | Heading |
| User Guidance | |
| Conformance | Required |
| Cardinality | One to many |
| Relationship content from ToC representing the protocol hierarchy | 2.2 |
| Value | Assessment of Risks and Benefits |
| Business rules | Value Allowed: No Relationship: 2 INTRODUCTION; Table of Contents Concept: Heading |
| Repeating and/or Reuse Rules | No |

2.2.1. Risk summary and mitigation strategy

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

| | |
|------------------------|---|
| Term (Variable) | <Trial-specific Intervention Risks and Mitigations> |
| Data Type | Text |

| | |
|--|---|
| Term (Variable) | <Trial-specific Intervention Risks and Mitigations> |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C218721 |
| User Guidance | |
| Conformance | Optional |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 2.2.1 |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: 2.2.1 Risk Summary and Mitigation Strategy Concept: C218721 ICH OID 2.16.840.1.113883.3.989.2.3.3.2 |
| Repeating and/or Reuse Rules | No |

| | |
|--|--|
| Term (Variable) | <Trial-specific Procedure Risks and Mitigations> |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C218722 |
| User Guidance | Trial Procedures – Describe risks associated with the design (e.g., placebo arm) and procedures specific to this trial (e.g., 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. |
| Conformance | Optional |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 2.2.1 |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: 2.2.1 Risk Summary and Mitigation Strategy Concept: C218722 ICH OID 2.16.840.1.113883.3.989.2.3.3.2 |
| Repeating and/or Reuse Rules | No |

| | |
|--|--|
| Term (Variable) | <Trial-specific Other Risks and Mitigations> |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C218723 |
| User Guidance | Other – Consider risks associated with other items (e.g., 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 | One to one |
| Relationship content from ToC representing the protocol hierarchy | 2.2.1 |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: 2.2.1 Risk Summary and Mitigation Strategy Concept: C218723 ICH OID 2.16.840.1.113883.3.989.2.3.3.2 |
| Repeating and/or Reuse Rules | No |

2.2.2. Benefit summary

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

| | |
|------------------------|-------------------|
| Term (Variable) | <Benefit Summary> |
| Data Type | Text |

| | |
|--|--|
| Term (Variable) | <Benefit Summary> |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C218724 |
| User Guidance | For early clinical trials such as Phase 1 or trials in healthy participants |
| Conformance | Optional |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 2.2.2 |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: 2.2.2 Benefit Summary Concept: C218724 ICH OID 2.16.840.1.113883.3.989.2.3.3.2 |
| Repeating and/or Reuse Rules | No |

2.2.3. Overall risk-benefit assessment

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

| | |
|---|-----------------------------------|
| Term (Variable) | <Overall Risk-Benefit Assessment> |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C218725 |
| User Guidance | |

| | |
|--|--|
| Term (Variable) | <Overall Risk-Benefit Assessment> |
| Conformance | Required |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 2.2.3 |
| Value | Text |
| Business rules | <p>Value Allowed: Yes</p> <p>Relationship: 2.2.3 Overall Risk-Benefit Assessment OR 2.2 Assessment of Risks and Benefits (when the Optional Level 3 subheading [2.2.3] is not used)</p> <p>If the Optional Level 3 subheadings [2.2.1, 2.2.2, 2.2.3] are not used, the user guidance below Section 2.2 applies.</p> <p>Concept: C218725 ICH OID 2.16.840.1.113883.3.989.2.3.3.2</p> |
| Repeating and/or Reuse Rules | No |

3. Trial objectives and associated estimands

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

3.1. Primary objective(s) and associated estimand(s)

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

3.1.1. Primary objective <#>

| | |
|---|--|
| Term (Variable) | 3.1.X Primary Objective <#> |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | H |
| Definition | Heading |
| User Guidance | <p>For all trials, precisely state each primary trial objective by providing a meaningful and concise description of the treatment effect of interest using natural, nontechnical language for clear understanding by sponsors, investigators, clinical site personnel, trial participants, ethics committees, and regulators.</p> <p>For trials intended to estimate a treatment effect or test a hypothesis related to a treatment effect, use the table to precisely describe the associated estimand(s). This includes specification of the population targeted by the clinical question, the treatment condition(s), the endpoint (or variable), and the population-level summary. Precise specifications of treatment, population, and variable are likely to address many of the intercurrent events. Other intercurrent events not already addressed in the clinical question of interest by the aforementioned attributes should be described with their associated strategies. For other types of trials not intended to estimate a treatment effect or test a hypothesis related to a treatment effect, describe additional information relevant to the clinical question(s) of interest (at a minimum, present the endpoint(s) associated with each objective).</p> <p>No text is intended here (heading only)</p> |

| | |
|--|---|
| Term (Variable) | 3.1.X Primary Objective <#> |
| Conformance | Required |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 3.1.X where X is a unique number for each Primary Objective |
| Value | Primary Objective <#>: # is a unique number for each Primary Objective; if there is only one Primary Objective, # is blank. If more than one Primary Objective, add sequential unique number for each objective |
| Business rules | Value Allowed: No Relationship: 3.1 Primary Objective and Associated Estimand(s); 3. TRIAL OBJECTIVES AND ASSOCIATED ESTIMAND; Table of Contents Concept: Heading |
| Repeating and/or Reuse Rules | Yes, repeatable for each numbered Primary Objective. Yes, reuse to the table in Section 1.1.1.for each Primary Objective |

| | |
|--|---|
| Term (Variable) | <Primary Objective> |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C85826 |
| User Guidance | N/A |
| Conformance | Required |
| Cardinality | One to one; One to Table of Contents Number 3.1.X; One to Estimand Characteristics Table, Primary Objective <#>, Protocol Identifier |
| Relationship content from ToC representing the protocol hierarchy | 3.1.X where X is a unique number for each Primary Objective |
| Value | Text and unique integer which is same as Level 3 number for the section. |
| Business rules | Value Allowed: Yes Relationship: 3.1.X Primary Objective <#> Concept: C85826 ICH OID 2.16.840.1.113883.3.989.2.3.3.3 |
| Repeating and/or Reuse Rules | Yes, repeatable for each numbered Primary Objective. Yes, reuse to the table in Section 1.1.1.for each Primary Objective |

| | |
|---|---|
| Term (Variable) | Estimand Characteristic |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | H |
| Definition | Table Column Heading |
| User Guidance | Enter information in table of estimand characteristics below including endpoint at a minimum. |
| Conformance | Required |

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

| | |
|--|---|
| Term (Variable) | Description |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | H |
| Definition | Table Column Heading |
| User Guidance | Enter information in table of estimand characteristics below including endpoint at a minimum. |
| Conformance | Required |
| Cardinality | One to many rows |
| Relationship content from ToC representing the protocol hierarchy | 3.1.X where X is a unique number for each Primary Objective |
| Value | Description |
| Business rules | Value Allowed: No Relationship: 3.1 Primary Objective(s) and associated Estimand(s); Table column Heading; Estimand Characteristic; Population; Treatment; Endpoint; Population-Level; Other Intercurrent Event; Strategy Concept: Heading |
| Repeating and/or Reuse Rules | Yes, repeatable for each numbered Primary Objective Yes, reuse to the table in Section 1.1.1.for each Primary Objective |

| | |
|---|--|
| Term (Variable) | {Population} |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | H |
| Definition | Heading |
| User Guidance | N/A |
| Conformance | Conditional: If there is a population as estimand characteristic |
| Cardinality | One to one |

| | |
|--|--|
| Term (Variable) | {Population} |
| Relationship content from ToC representing the protocol hierarchy | 3.1.X where X is a unique number for each Primary Objective |
| Value | Population |
| Business rules | Value Allowed: No Relationship: Row Heading; Estimand Characteristic Concept: Heading |
| Repeating and/or Reuse Rules | Yes, repeatable for each numbered Primary Objective |

| | |
|--|--|
| Term (Variable) | {<Population>} |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C70833 |
| User Guidance | List of key characteristics, such as demographic characteristics (e.g., age, sex) and clinical characteristics (e.g., prior therapies, symptoms, severity, biomarker status) |
| Conformance | Conditional: If there is a population as estimand characteristic |
| Cardinality | One to Row Heading; One to Primary Objective Table; Primary Objective <#>; Protocol Identifier |
| Relationship content from ToC representing the protocol hierarchy | 3.1.X where X is a unique number for each Primary Objective |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: Row Heading; Description Concept: C70833 ICH OID 2.16.840.1.113883.3.989.2.3.3.3 |
| Repeating and/or Reuse Rules | Yes, repeatable for each numbered Primary Objective |

| | |
|---|---|
| Term (Variable) | {Treatment} |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | H |
| Definition | Heading |
| User Guidance | N/A |
| Conformance | Conditional: If there is a treatment as estimand characteristic |
| Cardinality | One to one |
| Relationship content from ToC | 3.1.X where X is a unique number for each Primary Objective |

| | |
|--|--|
| Term (Variable) | {Treatment} |
| representing the protocol hierarchy | |
| Value | Treatment |
| Business rules | Value Allowed: No Relationship: Row Heading; Estimand Characteristic Concept: Heading |
| Repeating and/or Reuse Rules | Yes, repeatable for each numbered Primary Objective |

| | |
|--|--|
| Term (Variable) | {<Treatment>} |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C49236 |
| User Guidance | List of key aspects of treatment regimens in each treatment group, including at least investigational agents, dosage, and administration route |
| Conformance | Conditional: If there is a treatment as estimand characteristic |
| Cardinality | One to Row Heading; One to Primary Objective Table; Project Identifier |
| Relationship content from ToC representing the protocol hierarchy | 3.1.X where X is a unique number for each Primary Objective |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: Row Heading; Description Concept: C49236 ICH OID 2.16.840.1.113883.3.989.2.3.3.3 |
| Repeating and/or Reuse Rules | Yes, repeatable for each numbered Primary Objective |

| | |
|--|---|
| Term (Variable) | Endpoint |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | H |
| Definition | Heading |
| User Guidance | N/A |
| Conformance | Required |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 3.1.X where X is a unique number for each Primary Objective |
| Value | Endpoint |
| Business rules | Value Allowed: No Relationship: Row Heading; Estimand Characteristic |

| | |
|-------------------------------------|---|
| Term (Variable) | Endpoint |
| | Concept: Heading |
| Repeating and/or Reuse Rules | Yes, repeatable for each numbered Primary Objective |

| | |
|--|--|
| Term (Variable) | {< Endpoint >} |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C25212 |
| User Guidance | Definition of the endpoint |
| Conformance | Required |
| Cardinality | One to Row Heading; One to Primary Objective Table; Project Identifier |
| Relationship content from ToC representing the protocol hierarchy | 3.1.X where X is a unique number for each Primary Objective |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: Row Heading; Description Concept: C25212 ICH OID 2.16.840.1.113883.3.989.2.3.3.3 |
| Repeating and/or Reuse Rules | Yes, repeatable for each numbered Primary Objective |

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

| | |
|--|---|
| Term (Variable) | {<Population-level Summary>} |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C188853 |
| User Guidance | Description of the population-level summary (e.g., mean difference, relative risk) |
| Conformance | Conditional: If there is a population-level summary as estimand |
| Cardinality | One to Row Heading; One to Primary Objective Table; Project Identifier |
| Relationship content from ToC representing the protocol hierarchy | 3.1.X where X is a unique number for each Primary Objective |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: Row Heading; Description Concept: C188853 ICH OID 2.16.840.1.113883.3.989.2.3.3.3 |
| Repeating and/or Reuse Rules | Yes, repeatable for each numbered Primary Objective |

| | |
|--|---|
| Term (Variable) | {Other Intercurrent Event} |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | H |
| Definition | Table Column Heading |
| User Guidance | N/A |
| Conformance | Conditional: If there is one or more other intercurrent events as estimand characteristic. |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 3.1.X where X is a unique number for each Primary Objective |
| Value | Other Intercurrent Event |
| Business rules | Value Allowed: No Relationship: Row Heading; Estimand Characteristics Concept: Heading |
| Repeating and/or Reuse Rules | Yes, repeatable for each numbered Primary Objective |

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

| | |
|--|---|
| Term (Variable) | {Strategy} |
| User Guidance | N/A |
| Conformance | Conditional: If there is one or more other intercurrent events as estimand characteristic. |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 3.1.X where X is a unique number for each Primary Objective |
| Value | Strategy |
| Business rules | Value Allowed: No Relationship: Table column Heading; Other Intercurrent Event; Description Concept: Heading |
| Repeating and/or Reuse Rules | Yes, repeatable for each numbered Primary Objective |

| | |
|--|--|
| Term (Variable) | {<Description of Intercurrent Event>} |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C188856 |
| User Guidance | Description of the strategy to address the intercurrent event (e.g., a treatment policy strategy); cross reference the justification in Section 4 Trial Design. If there is >1 intercurrent event for an objective, add additional intercurrent event rows |
| Conformance | Conditional: If there is one or more other intercurrent events as estimand characteristic. |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 3.1.X where X is a unique number for each Primary Objective |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: Row Heading; Estimand Characteristics Concept: C188856 ICH OID 2.16.840.1.113883.3.989.2.3.3.3 |
| Repeating and/or Reuse Rules | Yes, repeatable for each intercurrent event |

| | |
|---|---------------------------------|
| Term (Variable) | {<Intercurrent Event Strategy>} |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C188857 |

| | |
|--|--|
| Term (Variable) | {<Intercurrent Event Strategy>} |
| User Guidance | Description of the strategy to address the intercurrent event (e.g., a treatment policy strategy); cross reference the justification in Section 4 Trial Design. If there is >1 intercurrent event for an objective, add additional intercurrent event rows |
| Conformance | Conditional: If there is one or more other intercurrent events as estimand characteristic. |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 3.1.X where X is a unique number for each Primary Objective |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: Row Heading; Strategy; Description Concept: C188857 ICH OID 2.16.840.1.113883.3.989.2.3.3.3 |
| Repeating and/or Reuse Rules | Yes, repeatable for each intercurrent event relationship |

3.2. Secondary objective(s) and associated estimand(s)

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

3.2.1. {Secondary objective <#>}

| | |
|---|---------------------------------|
| Term (Variable) | {3.2.X Secondary Objective <#>} |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | H |

| | |
|--|---|
| Term (Variable) | {3.2.X Secondary Objective <#>} |
| Definition | Heading |
| User Guidance | Describe the secondary objective(s) and associated estimand(s) as outlined in Section 3.1 Primary Objective(s) and Associated Estimand(s). Use the same approach as above and include table for a precise estimand description. No text is intended here (heading only) unless there is no secondary objective, in which case indicate "Not applicable". |
| Conformance | Conditional: when there are secondary objective heading for each secondary requirement |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 3.2.X where X is a unique number for each Secondary Objective |
| Value | Secondary Objective <#>: # is a unique number for each Secondary Objective; if there is only one Secondary Objective, # is blank. If more than one Secondary Objective, add sequential unique number for each objective |
| Business rules | Value Allowed: No Relationship: 3.2 Secondary Objective and Associated Endpoints; 3 TRIAL OBJECTIVES AND ASSOCIATED ESTIMAND(S); Table of Contents Concept: Heading |
| Repeating and/or Reuse Rules | Yes, repeatable for each numbered Secondary Objective. |

| | |
|--|---|
| Term (Variable) | {<Secondary Objective>} |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C85827 |
| User Guidance | N/A |
| Conformance | Required |
| Cardinality | One to one; Table of Contents Number 3.2.X; One to Estimand Characteristic Table, Secondary Objective <#>, Protocol Identifier |
| Relationship content from ToC representing the protocol hierarchy | 3.2.X where X is a unique number for each Secondary Objective |
| Value | Text and unique integer which is same as Level 3 number for the section. |
| Business rules | Value Allowed: Yes Relationship: 3.2.X Secondary Objective <#>; Estimand Characteristics table Concept: C85827 ICH OID 2.16.840.1.113883.3.989.2.3.3.3 |
| Repeating and/or Reuse Rules | Yes, repeatable for each numbered Secondary Objective. |

| | |
|--|--|
| Term (Variable) | {<Table of Estimand Characteristics including Endpoint at a minimum>} |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | N/A |
| User Guidance | If a Secondary Objective has been entered, enter information in table of estimand characteristics below including endpoint at a minimum} |
| Conformance | Conditional: either Enter Table of Estimand Characteristics or details of the characteristics relevant to objective |
| Cardinality | One to many rows |
| Relationship content from ToC representing the protocol hierarchy | 3.2.X where X is a unique number for each Secondary Objective |
| Value | Estimand Characteristics |
| Business rules | Value Allowed: No Relationship: 3.3.2 Secondary Objective(s) and associated Estimand(s) Concept: Heading |
| Repeating and/or Reuse Rules | Yes, repeatable for each numbered Secondary Objective. |

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

| | |
|--|--|
| Term (Variable) | {Description} |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | H |
| Definition | Table Column Heading |
| User Guidance | N/A |
| Conformance | Conditional |
| Cardinality | One to many rows |
| Relationship content from ToC representing the protocol hierarchy | 3.2.X where X is a unique number for each Secondary Objective |
| Value | Description |
| Business rules | Value Allowed: No Relationship: 3.3.2 Secondary Objective(s) and associated Estimand(s); Table column Heading; Estimand Characteristics; Population; Treatment; Endpoint, Population-Level Summary; Other Intercurrent Event; Strategy Concept: Heading |
| Repeating and/or Reuse Rules | Yes, repeatable for each numbered Secondary Objective. |

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

| | |
|---|----------------|
| Term (Variable) | {<Population>} |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C70833 |

| | |
|--|--|
| Term (Variable) | {<Population>} |
| User Guidance | List of key characteristics, such as demographic characteristics (e.g. age, sex) and clinical characteristics (e.g. prior therapies, symptoms, severity, biomarker status) |
| Conformance | Conditional: If there is a population for Secondary |
| Cardinality | One to Row Heading; One to Secondary Objective Table; Secondary Objective <#>; Protocol Identifier |
| Relationship content from ToC representing the protocol hierarchy | 3.2.X where X is a unique number for each Secondary Objective |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: Row Heading, Description; Estimand Characteristic Concept: C70833 ICH OID 2.16.840.1.113883.3.989.2.3.3.3 |
| Repeating and/or Reuse Rules | Yes, repeatable for each numbered Secondary Objective. |

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

| | |
|---|--|
| Term (Variable) | {<Treatment>} |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C49236 |
| User Guidance | List of key aspects of treatment regimens in each treatment group, including at least investigational agents, dosage, and administration route |
| Conformance | Conditional: If there is a population for Secondary |

| | |
|--|--|
| Term (Variable) | {<Treatment>} |
| Cardinality | One to Row Heading, One to Secondary Objective Table, Project Identifier |
| Relationship content from ToC representing the protocol hierarchy | 3.2.X where X is a unique number for each Secondary Objective |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: Row Heading, Description; Estimand Characteristics Concept: C49236 ICH OID 2.16.840.1.113883.3.989.2.3.3.3 |
| Repeating and/or Reuse Rules | Yes, repeatable for each numbered Secondary Objective. |

| | |
|--|---|
| Term (Variable) | {Endpoint} |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | H |
| Definition | Heading |
| User Guidance | N/A |
| Conformance | Conditional: if there is a Secondary Objective |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 3.2.X where X is a unique number for each Secondary Objective |
| Value | Endpoint |
| Business rules | Value Allowed: No Relationship: Row Heading; Description; Estimand Characteristic Concept: Heading |
| Repeating and/or Reuse Rules | Yes, repeatable for each numbered Secondary Objective. |

| | |
|--|--|
| Term (Variable) | {< Endpoint >} |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C25212 |
| User Guidance | Definition of the endpoint |
| Conformance | Conditional: if there is a Secondary Objective |
| Cardinality | One to Row Heading, One to Secondary Objective Table, Project Identifier |
| Relationship content from ToC representing the protocol hierarchy | 3.2.X where X is a unique number for each Secondary Objective |
| Value | Text |

| | |
|-------------------------------------|--|
| Term (Variable) | {< Endpoint >} |
| Business rules | Value Allowed: Yes Relationship: Row Heading; Description; Table Estimand Characteristics; Secondary (1...n) Estimand Concept: C25212 ICH OID 2.16.840.1.113883.3.989.2.3.3.3 |
| Repeating and/or Reuse Rules | Yes, repeatable for each numbered Secondary Objective. |

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

| | |
|--|--|
| Term (Variable) | {<Population-level Summary>} |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C188853 |
| User Guidance | Description of the population-level summary (e.g., mean difference, relative risk) |
| Conformance | Conditional: If there is a population for Secondary |
| Cardinality | One to Row Heading; One to Secondary Objective Table; Project Identifier |
| Relationship content from ToC representing the protocol hierarchy | 3.2.X where X is a unique number for each Secondary Objective |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: Row Heading; Description; Table estimand Characteristics; Secondary (1...n) Estimand; Protocol Identifier Concept: C188853 ICH OID 2.16.840.1.113883.3.989.2.3.3.3 |

| | |
|-------------------------------------|--|
| Term (Variable) | {<Population-level Summary>} |
| Repeating and/or Reuse Rules | Yes, repeatable for each numbered Secondary Objective. |

| | |
|--|--|
| Term (Variable) | {Other Intercurrent Event} |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | H |
| Definition | Table Column Heading |
| User Guidance | N/A |
| Conformance | Conditional: If there is one or more other intercurrent events |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 3.2.X where X is a unique number for each Secondary Objective |
| Value | Other Intercurrent Event |
| Business rules | Value Allowed: No Relationship: 3.3.2 Secondary Objective(s) and associated Estimand(s); Table Column Heading Concept: Heading |
| Repeating and/or Reuse Rules | Yes, repeatable for each numbered Secondary Objective. |

| | |
|--|--|
| Term (Variable) | {Strategy} |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | H |
| Definition | Table Column Heading |
| User Guidance | N/A |
| Conformance | Conditional: If there is one or more other intercurrent events |
| Cardinality | One to many rows |
| Relationship content from ToC representing the protocol hierarchy | 3.2.X where X is a unique number for each Secondary Objective |
| Value | Strategy |
| Business rules | Value Allowed: No Relationship: Table column Heading; Other Intercurrent Event (1...n) Concept: Heading |
| Repeating and/or Reuse Rules | Yes, repeatable for each numbered Secondary Objective. |

| | |
|--|--|
| Term (Variable) | {Description of Intercurrent Event} |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | H |
| Definition | C188856 |
| User Guidance | Enter Description of Intercurrent Event |
| Conformance | Conditional: If there is one or more other intercurrent events. |
| Cardinality | One to one or as many intercurrent event as available |
| Relationship content from ToC representing the protocol hierarchy | 3.2.X where X is a unique number for each Secondary Objective |
| Value | Text |
| Business rules | Value Allowed: No Relationship: Row Heading; Estimand Characteristics; Protocol Identifier Concept: C188856 ICH OID 2.16.840.1.113883.3.989.2.3.3.3 |
| Repeating and/or Reuse Rules | Yes, repeatable for each intercurrent event |

| | |
|--|--|
| Term (Variable) | {<Intercurrent Event Strategy>} |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C188857 |
| User Guidance | Description of the strategy to address the intercurrent event (e.g. a treatment policy strategy); cross-reference the justification in Section 4. If there is >1 intercurrent event for an objective, add additional intercurrent event rows |
| Conformance | Conditional: If there is one or more other intercurrent events. |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 3.2.X where X is a unique number for each Secondary Objective |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: Row Heading; Description of Intercurrent Event Concept: C188857 ICH OID 2.16.840.1.113883.3.989.2.3.3.3 |
| Repeating and/or Reuse Rules | Yes, repeatable for each intercurrent event relationship |

3.3. Exploratory objective(s)

| | |
|------------------------|------------------------------|
| Term (Variable) | 3.3 Exploratory Objective(s) |
| Data Type | Text |

| | |
|--|--|
| Term (Variable) | 3.3 Exploratory Objective(s) |
| Data (D), Value (V) or Heading (H) | H |
| Definition | Heading |
| User Guidance | State each exploratory objective. This should generally include documentation of associated exploratory endpoints. It may be helpful in some cases to describe precise estimands to provide clarity on what is being estimated. Use the same approach as above and include table for a precise estimand description. No text is intended here (heading only) unless there is no exploratory objective, in which case indicate "Not applicable". |
| Conformance | Required |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 3.3 |
| Value | Exploratory Objective(s) |
| Business rules | Value Allowed: No Relationship: TRIAL OBJECTIVES AND ENDPOINT; Table of Contents Concept: Heading |
| Repeating and/or Reuse Rules | No |

3.3.1. {Exploratory objective <#>}

| | |
|--|--|
| Term (Variable) | {3.3.X Exploratory Objective <#>} |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | H |
| Definition | Heading |
| User Guidance | State each exploratory objective. This should generally include documentation of associated exploratory endpoints. It may be helpful in some cases to describe precise estimands to provide clarity on what is being estimated. Use the same approach as above and include table for a precise estimand description. No text is intended here (heading only) unless there is no exploratory objective, in which case indicate "Not applicable". |
| Conformance | Conditional: when there are exploratory objective heading for each exploratory requirement |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 3.3.X where X is a unique number for each Exploratory Objective |
| Value | Exploratory Objective <#>: # is a unique number for each Exploratory Objective; if there is only one Exploratory Objective, # is blank If more |

| | |
|-------------------------------------|--|
| Term (Variable) | {3.3.X Exploratory Objective <#>} |
| | than one Exploratory Objective, add sequential unique number for each objective |
| Business rules | Value Allowed: No Relationship: 3.3 Exploratory Objective(s); 3 TRIAL OBJECTIVES AND ASSOCIATED ESTIMANDS; Table of Contents Concept: Heading |
| Repeating and/or Reuse Rules | Yes, repeatable for each numbered Exploratory Objective. |

| | |
|--|--|
| Term (Variable) | {<Exploratory Objective>} |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C163559 |
| User Guidance | N/A |
| Conformance | Conditional: if an Exploratory Objective is part of the trial |
| Cardinality | One to Table of Contents Number 3.3.X; One to Estimand Characteristic Table, Exploratory Objective <#>, Protocol Identifier |
| Relationship content from ToC representing the protocol hierarchy | 3.3.X where X is a unique number for each Exploratory Objective |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: 3.3.X Exploratory Objective <#> Concept: C163559 ICH OID 2.16.840.1.113883.3.989.2.3.3.3 |
| Repeating and/or Reuse Rules | Yes, repeatable for each numbered Exploratory Objective. |

| | |
|--|---|
| Term (Variable) | {<Table of Estimand Characteristics> including Endpoint at a minimum} |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | N/A |
| User Guidance | If an Exploratory Objective has been entered, enter information in table of estimand characteristics below including endpoint at a minimum: |
| Conformance | Conditional: either Enter Table of Estimand Characteristics or details of the characteristics relevant to objective |
| Cardinality | One to many |
| Relationship content from ToC representing the protocol hierarchy | 3.3.X where X is a unique number for each Exploratory Objective |
| Value | Text |

| | |
|-------------------------------------|--|
| Term (Variable) | {<Table of Estimand Characteristics> including Endpoint at a minimum} |
| Business rules | Value Allowed: Yes Relationship: 3.3.3 Exploratory Objective(s) and associated Estimand(s); Table column Heading; Description; Population; Treatment; Endpoint; Population-Level; Intercurrent Event (1...n) Concept: Heading |
| Repeating and/or Reuse Rules | Yes, repeatable for each numbered Exploratory Objective. |

| | |
|--|---|
| Term (Variable) | {Estimand Characteristic} |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | H |
| Definition | Table Column Heading |
| User Guidance | N/A |
| Conformance | Conditional: if there is exploratory endpoint(s). |
| Cardinality | One to many rows |
| Relationship content from ToC representing the protocol hierarchy | 3.3.X where X is a unique number for each Exploratory Objective |
| Value | Estimand Characteristics |
| Business rules | Value Allowed: No Relationship: 3.3.X Exploratory Objective; Table Column Heading; Description; Population; Treatment; Endpoint; Population-Level; Intercurrent Event Concept: Heading |
| Repeating and/or Reuse Rules | Yes, repeatable for each numbered Exploratory Objective. |

| | |
|--|--|
| Term (Variable) | {Description} |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | H |
| Definition | Table Column Heading |
| User Guidance | N/A |
| Conformance | Conditional: if there is exploratory endpoint(s) |
| Cardinality | One to many rows |
| Relationship content from ToC representing the protocol hierarchy | 3.3.X where X is a unique number for each Exploratory Objective |
| Value | Description |
| Business rules | Value Allowed: No |

| | |
|-------------------------------------|--|
| Term (Variable) | {Description} |
| | Relationship: 3.3.X Exploratory Objective Table Column Heading; Estimand Characteristic; Population; Treatment; Endpoint; Population-Level; Intercurrent Event (1...n); Strategy Concept: Heading |
| Repeating and/or Reuse Rules | Yes, repeatable for each numbered Exploratory Objective. |

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

| | |
|--|--|
| Term (Variable) | {<Population>} |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C70833 |
| User Guidance | List of key characteristics, such as demographic characteristics (e.g. age, sex) and clinical characteristics (e.g. prior therapies, symptoms, severity, biomarker status) |
| Conformance | Conditional: If there is a population as estimand characteristic |
| Cardinality | One to Row Heading; One to Exploratory Objective Table, Exploratory Objective <#>, Protocol Identifier |
| Relationship content from ToC representing the protocol hierarchy | 3.3.X where X is a unique number for each Exploratory Objective |
| Value | Text |
| Business rules | Value Allowed: Yes |

| | |
|------------------------------|---|
| Term (Variable) | {<Population>} |
| | Relationship: Row Heading, Description; Table Estimand Characteristics; Exploratory (1...n) Estimand Concept: C70833 ICH OID 2.16.840.1.113883.3.989.2.3.3.3 |
| Repeating and/or Reuse Rules | Yes, repeatable for each numbered Exploratory Objective. |

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

| | |
|--|---|
| Term (Variable) | {<Treatment>} |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C49236 |
| User Guidance | List of key aspects of treatment regimens in each treatment group, including at least investigational agents, dosage, and administration route |
| Conformance | Conditional: If there is a treatment as estimand |
| Cardinality | One to Row Heading; One to Exploratory Objective Table; Project Identifier |
| Relationship content from ToC representing the protocol hierarchy | 3.3.X where X is a unique number for each Exploratory Objective |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: Row Heading, Description; Table Estimand Characteristics; Exploratory (1...n) Estimand; Protocol Identifier Concept: C49236 ICH OID 2.16.840.1.113883.3.989.2.3.3.3 |

| | |
|-------------------------------------|--|
| Term (Variable) | {<Treatment>} |
| Repeating and/or Reuse Rules | Yes, repeatable for each numbered Exploratory Objective. |

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

| | |
|--|--|
| Term (Variable) | {<Endpoint>} |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C25212 |
| User Guidance | Definition of the endpoint |
| Conformance | Conditional: if there is exploratory endpoint(s). |
| Cardinality | One to Row Heading; One to Exploratory Objective Table, Project Identifier |
| Relationship content from ToC representing the protocol hierarchy | 3.3.X where X is a unique number for each Exploratory Objective |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: Row Heading; Description; Table Estimand Characteristics; Exploratory (1...n) Estimand Concept: C25212 ICH OID 2.16.840.1.113883.3.989.2.3.3.3 |
| Repeating and/or Reuse Rules | Yes, repeatable for each numbered Exploratory Objective. |

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

| | |
|--|---|
| Term (Variable) | {<Population-level Summary>} |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C188853 |
| User Guidance | List of key characteristics, such as demographic characteristics (e.g. age, sex) and clinical characteristics (e.g. prior therapies, symptoms, severity, biomarker status) |
| Conformance | Conditional: If there is a population-level summary |
| Cardinality | One to Row Heading; One to Exploratory Objective Table, Project Identifier |
| Relationship content from ToC representing the protocol hierarchy | 3.3.X where X is a unique number for each Exploratory Objective |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: Row Heading; Description; Table Estimand Characteristics; Exploratory (1...n) Estimand Concept: C188853 ICH OID 2.16.840.1.113883.3.989.2.3.3.3 |
| Repeating and/or Reuse Rules | Yes, repeatable for each numbered Exploratory Objective. |

| | |
|---|----------------------------|
| Term (Variable) | {Other Intercurrent Event} |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | H |

| | |
|--|--|
| Term (Variable) | {Other Intercurrent Event} |
| Definition | Table Column Heading |
| User Guidance | N/A |
| Conformance | Conditional: If there is one or more other intercurrent event as estimand characteristic. |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 3.3.X where X is a unique number for each Exploratory Objective |
| Value | Other Intercurrent Event |
| Business rules | Value Allowed: No Relationship: 3.3.3 Exploratory Objective(s) and associated Estimand(s); Table column Heading; Estimand Characteristic Concept: Heading |
| Repeating and/or Reuse Rules | Yes, repeatable for each numbered Exploratory Objective. |

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

| | |
|---|---|
| Term (Variable) | {Description of Intercurrent Event} |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C188856 |
| User Guidance | Enter Description of Intercurrent Event |

| | |
|--|--|
| Term (Variable) | {Description of Intercurrent Event} |
| Conformance | Conditional: If there is one or more other intercurrent events as estimand characteristic. |
| Cardinality | One to one or as many intercurrent event as available |
| Relationship content from ToC representing the protocol hierarchy | 3.3.X where X is a unique number for each Exploratory Objective |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: Row Heading, Estimand Characteristics Concept: C188856 ICH OID 2.16.840.1.113883.3.989.2.3.3.3 |
| Repeating and/or Reuse Rules | Yes, repeatable for each intercurrent event |

| | |
|--|--|
| Term (Variable) | {<Intercurrent Event Strategy>} |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C188857 |
| User Guidance | Description of the strategy to address the intercurrent event (e.g., a treatment policy strategy); cross reference the justification in Section 4 Trial Design. If there is >1 intercurrent event for an objective, add additional intercurrent event rows |
| Conformance | Conditional: If there is one or more other intercurrent events as estimand characteristic. |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 3.3.X where X is a unique number for each Exploratory Objective |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: Row Heading; Strategy; Description Concept: C188857 ICH OID 2.16.840.1.113883.3.989.2.3.3.3 |
| Repeating and/or Reuse Rules | Yes, repeatable for each intercurrent event relationship |

4. Trial design

| | |
|---|----------------|
| Term (Variable) | 4 TRIAL DESIGN |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | H |
| Definition | Heading |

| | |
|--|---|
| Term (Variable) | 4 TRIAL DESIGN |
| User Guidance | <p>In the subsections below, describe the trial design with specific mention, as applicable, of the components of an adequate and well-controlled trial and reflect the principles of Quality by Design. The description of the design should be concise and consistent with Section 1.1 Protocol Synopsis and Section 1.2 Trial Schema. The trial design should align with objectives/estimand(s) described in Section 3 Trial Objectives and Associated Estimands.</p> <p>This section is intended to provide a description for the important aspects of the trial design and rationale for its key attributes. Operational details needed to implement the trial design should be covered in more detail in subsequent sections.</p> <p>No text is intended here (heading only).</p> |
| Conformance | Required |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 4 |
| Value | TRIAL DESIGN |
| Business rules | Value Allowed: No Relationship: Table of Contents Concept: Heading |
| Repeating and/or Reuse Rules | No |

4.1. Description of trial design

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

| | |
|--|---|
| Term (Variable) | <Overall Description of Trial Design and Description of Intervention Model> |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C147139 |
| User Guidance | <p>Describe the overall trial design and intervention model (e.g., single group, parallel group, cross-over, factorial, sequential), the expected number of participants, and the control method (e.g., placebo, active comparator, low dose, external, standard of care, sham procedure, or none [uncontrolled]). If there are any key aspects of the investigational trial intervention that inform the selection of the intervention model, this should be described.</p> <p>If applicable, indicate other design characteristics (e.g., superiority, noninferiority, dose escalation, or equivalence).</p> <p>If the trial will have an adaptive or novel design (e.g., the trial will be conducted under a master protocol), provide a summary of these design aspects.</p> <p>If applicable, describe within-trial transition rules (e.g., transitions involving cohorts or trial parts). Dose escalation or dose-ranging details should also be described.</p> |
| Conformance | Optional |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 4.1 |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: 4.1 Description of Trial Design Concept: C147139 ICH OID 2.16.840.1.113883.3.989.2.3.3.4 |
| Repeating and/or Reuse Rules | No |

| | |
|---|---|
| Term (Variable) | <Description of Trial Duration> |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C218726 |
| User Guidance | <p>Describe the trial duration with reference to Section 1.2 Trial Schema. Explain what the overall duration for an individual participant is anticipated to be and why, including the sequence and duration of trial periods (e.g., screening, run-in, randomisation, treatment [fixed dose/titration], follow-up/washout periods). Where applicable, include discussion of sentinel dosing (or lack thereof), dose escalation, and cohort</p> |

| | |
|--|---|
| Term (Variable) | <Description of Trial Duration> |
| | expansion. If dose modification decisions are dependent upon review by a committee, include details in Section 11.4 Committees. |
| Conformance | Optional |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 4.1 |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: 4.1 Description of Trial Design Concept: C218726 ICH OID 2.16.840.1.113883.3.989.2.3.3.4 |
| Repeating and/or Reuse Rules | No |

| | |
|--|---|
| Term (Variable) | <Description of Method of Assignment to Trial Intervention> |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C219658 |
| User Guidance | State the method of assignment to trial intervention and the level and method of blinding that will be used, with cross reference to Section 6.7 Investigational Trial Intervention Assignment, Randomisation and Blinding. |
| Conformance | Optional |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 4.1 |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: 4.1 Description of Trial Design Concept: C219658 ICH OID 2.16.840.1.113883.3.989.2.3.3.4 |
| Repeating and/or Reuse Rules | No |

| | |
|---|---|
| Term (Variable) | <Description of Level and Method of Blinding> |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C218727 |
| User Guidance | State the method of assignment to trial intervention and the level and method of blinding that will be used, with cross reference to Section 6.7 Investigational Trial Intervention Assignment, Randomisation and Blinding. |

| | |
|--|--|
| Term (Variable) | <Description of Level and Method of Blinding> |
| Conformance | Optional |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 4.1 |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: 4.1 Description of Trial Design Concept: C218727 ICH OID 2.16.840.1.113883.3.989.2.3.3.4 |
| Repeating and/or Reuse Rules | No |

| | |
|--|--|
| Term (Variable) | <Additional Description of Trial Design> |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C218728 |
| User Guidance | Describe any other important aspects of the design, e.g.: <ul style="list-style-type: none"> • geographic scope of trial (e.g., single-centre, multicentre, or multicentre and multinational) • use of decentralised elements in the trial • planned use of a Data Monitoring Committee, or similar review group and cross reference Section 11.4 Committees, for details • whether an interim analysis is planned; if so, refer to details in Section 10.9 Interim Analyses • any planned extension trial, long-term follow-up/registry, future use of samples or data, or post-trial sample analysis or other data-related activities |
| Conformance | Optional |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 4.1 |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: 4.1 Description of Trial Design Concept: C218728 ICH OID 2.16.840.1.113883.3.989.2.3.3.4 |
| Repeating and/or Reuse Rules | No |

4.1.1. Stakeholder input into design

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

| | |
|--|--|
| Term (Variable) | <Stakeholder Input into Design> |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C218729 |
| User Guidance | If applicable, describe any stakeholder (e.g., patient, healthcare professional and patient advocacy groups) involvement in the design of the trial and any suggestions implemented. |
| Conformance | Optional |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 4.1.1 |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: 4.1.1 Stakeholder Input into Design Concept: C218729 ICH OID 2.16.840.1.113883.3.989.2.3.3.4 |
| Repeating and/or Reuse Rules | No |

4.2. Rationale for trial design

| | |
|--|---|
| Term (Variable) | 4.2 Rationale for Trial Design |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | H |
| Definition | Heading |
| User Guidance | N/A |
| Conformance | Required |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 4.2 |
| Value | Rationale for Trial Design |
| Business rules | Value Allowed: No Relationship: 4 TRIAL DESIGN; Table of Contents Concept: Heading |
| Repeating and/or Reuse Rules | No |

| | |
|--|---|
| Term (Variable) | {<Overall Rationale for Trial Design>} |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C142705 |
| User Guidance | if not using below optional subheadings. |
| Conformance | Conditional: If Level 3 subheadings are not used |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 4.2 |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: 4.2 Rationale for Trial Design Concept: C142705 ICH OID 2.16.840.1.113883.3.989.2.3.3.4 |
| Repeating and/or Reuse Rules | No |

4.2.1. Rationale for estimand(s)

| | |
|---|---------------------------------|
| Term (Variable) | 4.2.1 Rationale for Estimand(s) |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | H |

| | |
|--|---|
| Term (Variable) | 4.2.1 Rationale for Estimand(s) |
| Definition | Heading |
| User Guidance | N/A |
| Conformance | Conditional: when <Overall Rationale for Trial Design> is not used |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 4.2.1 |
| Value | Rationale for Estimand(s) |
| Business rules | Value Allowed: No Relationship: 4.2 Rationale for Trial Design; 4 TRIAL DESIGN; Table of Contents Concept: Heading |
| Repeating and/or Reuse Rules | No |

| | |
|--|--|
| Term (Variable) | <Rationale for Estimand(s)> |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C218730 |
| User Guidance | When estimands are associated with the Primary and Secondary Objectives described in Section 3 Trial Objectives and Associated Estimands, provide a rationale for the estimand(s) not described elsewhere in the document. This should include a rationale that the selected endpoint(s) are clinically relevant and provide a reliable and valid measurement of the intended intervention effect(s). It should also include a rationale for the selected strategies for handling intercurrent events. |
| Conformance | Conditional: when <Overall Rationale for Trial Design> is not used |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 4.2.1 |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: 4.2.1 Rationale for Estimand(s) Concept: C218730 ICH OID 2.16.840.1.113883.3.989.2.3.3.4 |
| Repeating and/or Reuse Rules | No |

4.2.2. Rationale for intervention model

| | |
|------------------------|--|
| Term (Variable) | 4.2.2 Rationale for Intervention Model |
| Data Type | Text |

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

| | |
|--|---|
| Term (Variable) | <Rationale for Intervention Model> |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C215629 |
| User Guidance | Provide a rationale for the trial intervention model described in Section 4.1 Description of Trial Design with a cross reference to Section 6.2 Rationale for Investigational Trial Intervention Dose and Regimen. Rationale for choice of comparator, if applicable, should be described separately in Section 4.2.3 Rationale for Control Type. A rationale for the choice of trial population should be described separately in Section 5.1 Description of Trial Population and Rationale. |
| Conformance | Conditional: when <Overall Rationale for Trial Design> is not used |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 4.2.2 |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: 4.2.2 Rationale for Intervention Model Concept: C215629 ICH OID 2.16.840.1.113883.3.989.2.3.3.4 |
| Repeating and/or Reuse Rules | No |

4.2.3. Rationale for control type

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

| | |
|--|---|
| Term (Variable) | <Rationale for Control Type> |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C218731 |
| User Guidance | If applicable, provide a rationale for the type and choice of control selected for the trial (e.g., placebo, active drug, combination, external). Describe any known or potential problems associated with the control group selected in light of the specific disease and intervention(s) being studied. If comparators will differ by region, describe. The rationale for dose and/or dose regimen is explained in Section 6.2 Rationale for Investigational Trial Intervention Dose and Regimen. |
| Conformance | Conditional: when <Overall Rationale for Trial Design> is not used |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 4.2.3 |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: 4.2.3 Rationale for Control Type Concept: C218731 ICH OID 2.16.840.1.113883.3.989.2.3.3.4 |
| Repeating and/or Reuse Rules | No |

4.2.4. Rationale for trial duration

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

| | |
|--|---|
| Term (Variable) | <Rationale for Trial Duration> |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C218732 |
| User Guidance | Provide a rationale that the trial duration is appropriate for a reliable and relevant evaluation of the trial intervention per the trial objective(s). |
| Conformance | Conditional: when <Overall Rationale for Trial Design> is not used |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 4.2.4 |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: 4.2.4 Rationale for Trial Duration Concept: C218732 ICH OID 2.16.840.1.113883.3.989.2.3.3.4 |
| Repeating and/or Reuse Rules | No |

4.2.5. Rationale for adaptive or novel trial design

| | |
|------------------------|--|
| Term (Variable) | 4.2.5 Rationale for Adaptive or Novel Trial Design |
| Data Type | Text |

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

| | |
|--|---|
| Term (Variable) | <Rationale for Adaptive or Novel Trial Design> |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C218733 |
| User Guidance | If applicable, provide a rationale for the use of an adaptive or novel design. |
| Conformance | Conditional: when <Overall Rationale for Trial Design> is not used |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 4.2.5 |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: 4.2.5 Rationale for Adoptive or Novel Trial Design Concept: C218733 ICH OID 2.16.840.1.113883.3.989.2.3.3.4 |
| Repeating and/or Reuse Rules | No |

4.2.6. Rationale for interim analysis

| | |
|---|--------------------------------------|
| Term (Variable) | 4.2.6 Rationale for Interim Analysis |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | H |
| Definition | Heading |
| User Guidance | N/A |

| | |
|--|---|
| Term (Variable) | 4.2.6 Rationale for Interim Analysis |
| Conformance | Conditional: when <Overall Rationale for Trial Design> is not used |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 4.2.6 |
| Value | Rationale for Interim Analysis |
| Business rules | Value Allowed: No Relationship: 4.2 Rationale for Trial Design; 4 TRIAL DESIGN; Table of Contents Concept: Heading |
| Repeating and/or Reuse Rules | No |

| | |
|--|---|
| Term (Variable) | <Rationale for Interim Analysis> |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C218734 |
| User Guidance | If applicable, provide a rationale for any interim analysis planned with respect to its purpose (e.g., stopping the trial early for efficacy or futility) and timing. |
| Conformance | Conditional: when <Overall Rationale for Trial Design> is not used |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 4.2.6 |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: 4.2.6 Rationale for Interim Analysis Concept: C218734 ICH OID 2.16.840.1.113883.3.989.2.3.3.4 |
| Repeating and/or Reuse Rules | No |

4.2.7. Rationale for other trial design aspects

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

| | |
|--|---|
| Term (Variable) | 4.2.7 Rationale for Other Trial Design Aspects |
| Relationship content from ToC representing the protocol hierarchy | 4.2.7 |
| Value | Rationale for Other Trial Design Aspects |
| Business rules | Value Allowed: No Relationship: 4.2 Rationale for Trial Design, 4 TRIAL DESIGN; Table of Contents Concept: Heading |
| Repeating and/or Reuse Rules | No |

| | |
|--|---|
| Term (Variable) | <Rationale for Other Trial Design Aspects> |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C218735 |
| User Guidance | Discuss rationale for any additional aspects of the design not addressed above. |
| Conformance | Conditional: when <Overall Rationale for Trial Design> is not used |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 4.2.7 |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: 4.2.7 Rationale for Other Trial Design Aspects Concept: C218735 ICH OID 2.16.840.1.113883.3.989.2.3.3.4 |
| Repeating and/or Reuse Rules | No |

4.3. Trial stopping rules

| | |
|---|--------------------------|
| Term (Variable) | 4.3 Trial Stopping Rules |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | H |
| Definition | Heading |
| User Guidance | N/A |
| Conformance | Required |
| Cardinality | One to one |
| Relationship content from ToC | 4.3 |

| | |
|--|---|
| Term (Variable) | 4.3 Trial Stopping Rules |
| representing the protocol hierarchy | |
| Value | Trial Stopping Rules |
| Business rules | Value Allowed: No Relationship: 4 TRIAL DESIGN; Table of Contents Concept: Heading |
| Repeating and/or Reuse Rules | No |

| | |
|--|---|
| Term (Variable) | <Trial Stopping Rules> |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C142698 |
| User Guidance | If applicable, describe any trial-specific stopping rules, including guidance on when the trial should be stopped for efficacy or safety reasons, when a cohort or dose escalation should be terminated, and/or when a given treatment arm should be terminated. If applicable, describe any rules that may result in a temporary pause of dosing and/or enrollment into the trial and criteria for restarting enrollment. Ensure that the trial-specific stopping rules are aligned with the specifications that are described in Section 10.9 Interim Analyses. |
| Conformance | Required |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 4.3 |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: 4.3 Trial Stopping Rules Concept: C142698 ICH OID 2.16.840.1.113883.3.989.2.3.3.4 |
| Repeating and/or Reuse Rules | No |

4.4. Start of trial and end of trial

| | |
|---|-------------------------------------|
| Term (Variable) | 4.4 Start of Trial and End of Trial |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | H |
| Definition | Heading |
| User Guidance | N/A |
| Conformance | Required |
| Cardinality | One to many |

| | |
|--|---|
| Term (Variable) | 4.4 Start of Trial and End of Trial |
| Relationship content from ToC representing the protocol hierarchy | 4.4 |
| Value | Start of Trial and End of Trial |
| Business rules | Value Allowed: No Relationship: 4 TRIAL DESIGN; Table of Contents Concept: Heading |
| Repeating and/or Reuse Rules | No |

| | |
|--|--|
| Term (Variable) | <Start of Trial> |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C218736 |
| User Guidance | Define key timepoints in the trial, including trial start and end definitions (e.g., a key timepoint definition for start of trial might be when the ICF is signed by the first participant, and a key timepoint definition for end of trial might be when participants are no longer being examined or the last participant's last trial assessment has occurred). Consider local regulatory requirements for these and other definitions (e.g., the first act of recruitment). If appropriate, provide a cross reference to Section 11.11 Early Site Closure. |
| Conformance | Required |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 4.4 |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: 4.4 Start of Trial and End of Trial Concept: C218736 ICH OID 2.16.840.1.113883.3.989.2.3.3.4 |
| Repeating and/or Reuse Rules | No |

| | |
|---|----------------|
| Term (Variable) | <End of Trial> |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C218737 |

| | |
|--|--|
| Term (Variable) | <End of Trial> |
| User Guidance | Define key timepoints in the trial, including trial start and end definitions (e.g., a key timepoint definition for start of trial might be when the informed consent is signed by the first participant, and a key timepoint definition for end of trial might be when participants are no longer being examined or the last participant's last trial assessment has occurred). If applicable, consider local regulatory requirements for these and other definitions (e.g., the first act of recruitment). If appropriate, provide a cross reference to Section 11.11 Early Site Closure. |
| Conformance | Required |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 4.4 |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: 4.4 Start of Trial Concept: C218737 ICH OID 2.16.840.1.113883.3.989.2.3.3.4 |
| Repeating and/or Reuse Rules | No |

4.5. Access to trial intervention after end of trial

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

| | |
|--|--|
| Term (Variable) | <Access to Trial Intervention After End of Trial> |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C218738 |
| User Guidance | If applicable, describe any possibilities for access to trial intervention, if any, beyond completion of the trial. Planned extension trials, if described in Section 4.1 Description of Trial Design, do not need to be repeated in this section. |
| Conformance | Required |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 4.5 |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: 4.5 Access to Trial Intervention After End of Trial Concept: C218738 ICH OID 2.16.840.1.113883.3.989.2.3.3.4 |
| Repeating and/or Reuse Rules | No |

5. Trial population

| | |
|--|---|
| Term (Variable) | 5 TRIAL POPULATION |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | H |
| Definition | Heading |
| User Guidance | <ul style="list-style-type: none"> • • • • • |
| Conformance | Required |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 5 |
| Value | TRIAL POPULATION |
| Business rules | Value Allowed: No Relationship: Table of contents Concept: Heading |

| | |
|-------------------------------------|--------------------|
| Term (Variable) | 5 TRIAL POPULATION |
| Repeating and/or Reuse Rules | No |

5.1. Description of trial population and rationale

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

| | |
|---|--|
| Term (Variable) | <Description of Trial Population and Rationale> |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C218739 |
| User Guidance | <p>Describe the population selected (e.g., healthy participants, adult participants, paediatric participants, pregnant participants, or breastfeeding participants) and how the enrollment criteria reflect the populations that are likely to use the drug if approved. Specify the population age range (e.g., ≤ 3 months, ≥ 18 to ≤ 80 years old) including the timepoint at which qualification for age criteria is determined (e.g., at time of screening vs randomisation for paediatric trials). Specify any key diagnostic criteria for the population (e.g., "acute lung injury", or a specific biomarker profile). If applicable, describe similar conditions or diseases and their differential diagnosis.</p> <p>Provide a rationale for the trial population ensuring that the population selected is well defined and clinically recognisable. Describe how the selected population can meet the trial objectives and how the enrollment criteria reflect the population of interest.</p> <p>If a clinical question targets a subset of the entire trial population, such as one defined by a particular baseline characteristic (e.g., a specific</p> |

| | |
|--|--|
| Term (Variable) | <Description of Trial Population and Rationale> |
| | <p>biomarker), the rationale for selecting this subset should be provided in this section.</p> <p>Justify whether the trial intervention is to be evaluated in paediatric participants, in adults unable to consent for themselves, other vulnerable participant populations, or those that may respond to the trial intervention differently (e.g., elderly, hepatic or renally impaired, or immunocompromised participants).</p> |
| Conformance | Required |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 5.1 |
| Value | Text |
| Business rules | <p>Value Allowed: Yes</p> <p>Relationship: 5.1 Description of Trial Population and Rationale</p> <p>Concept: C218739 ICH OID 2.16.840.1.113883.3.989.2.3.3.5</p> |
| Repeating and/or Reuse Rules | No |

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

5.2. Inclusion criteria

| | |
|------------------------|------------------------|
| Term (Variable) | 5.2 Inclusion Criteria |
| Data Type | Text |

| | |
|--|---|
| Term (Variable) | 5.2 Inclusion Criteria |
| Data (D), Value (V) or Heading (H) | H |
| Definition | Heading |
| User Guidance | |
| Conformance | Required |
| Cardinality | One to many |
| Relationship content from ToC representing the protocol hierarchy | 5.2 |
| Value | 5.2 Inclusion Criteria |
| Business rules | Value Allowed: No Relationship: 5 TRIAL POPULATION; Table of Contents Concept: Heading |
| Repeating and/or Reuse Rules | 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 Heading (H) | H |
| Definition | Universal text |
| User Guidance | N/A |
| Conformance | Required |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 5.2 |
| Value | To be eligible to participate in this trial, an individual must meet all the following criteria: |
| Business rules | Value Allowed: No Relationship: 5.2 Inclusion Criteria Concept: Universal text |
| Repeating and/or Reuse Rules | No |

| | |
|---|--------|
| Term (Variable) | <#> |
| Data Type | Number |
| Data (D), Value (V) or Heading (H) | D |
| Definition | N/A |
| User Guidance | |

| | |
|--|---|
| Term (Variable) | <#> |
| Conformance | Optional |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 5.2 |
| Value | # is an integer <criteria identifier> unique number and not replaceable |
| Business rules | Value Allowed: Yes Relationship: 5.2 Inclusion Criteria Concept: Sequential number |
| Repeating and/or Reuse Rules | Yes, repeatable for each Inclusion Criterion |

| | |
|--|--|
| Term (Variable) | <Inclusion Criterion> |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C25532 |
| User Guidance | Add criteria as needed. Consider numbering the criteria sequentially. |
| Conformance | Required |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 5.2 |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: to Number #, 5.2 Inclusion Criteria Concept: C25532 ICH OID 2.16.840.1.113883.3.989.2.3.3.5 |
| Repeating and/or Reuse Rules | Yes, number consecutively, repeatable for each Inclusion Criterion. If deleted for an amendment, do not replace and do not duplicate |

5.3. Exclusion criteria

| | |
|---|--|
| Term (Variable) | 5.3 Exclusion Criteria |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | H |
| Definition | Heading |
| User Guidance | Exclusion criteria are characteristics that make an individual ineligible for participation. |
| Conformance | Required |
| Cardinality | One to many |

| | |
|--|---|
| Term (Variable) | 5.3 Exclusion Criteria |
| Relationship content from ToC representing the protocol hierarchy | 5.3 |
| Value | Exclusion Criteria |
| Business rules | Value Allowed: No Relationship: 5 TRIAL POPULATION; Table of Contents Concept: Heading |
| Repeating and/or Reuse Rules | 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 Heading (H) | H |
| Definition | Universal text |
| User Guidance | N/A |
| Conformance | Required |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 5.3 |
| Value | An individual who meets any of the following criteria will be excluded from participation in this trial: |
| Business rules | Value Allowed: No Relationship: 5.3 Exclusion Criteria; 5 TRIAL POPULATION; Table of Contents Concept: Universal text |
| Repeating and/or Reuse Rules | No |

| | |
|---|------------|
| Term (Variable) | <#> |
| Data Type | Number |
| Data (D), Value (V) or Heading (H) | D |
| Definition | N/A |
| User Guidance | |
| Conformance | Optional |
| Cardinality | One to one |
| Relationship content from ToC | 5.3 |

| | |
|--|--|
| Term (Variable) | <#> |
| representing the protocol hierarchy | |
| Value | # is an identifier <criteria identifier> unique number and not replaceable |
| Business rules | Value Allowed: Yes Relationship: 5.3 Exclusion Criteria Concept: Sequential number |
| Repeating and/or Reuse Rules | Yes. number consecutively, repeatable for each Exclusion Criterion. If deleted for an amendment, do not replace and do not duplicate |

| | |
|--|---|
| Term (Variable) | <Exclusion Criterion> |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C25370 |
| User Guidance | Add criteria as needed. Consider numbering the criteria sequentially. |
| Conformance | Required |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 5.3 |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: to Number #; 5.3 Exclusion Criteria Concept: C25370 ICH OID 2.16.840.1.113883.3.989.2.3.3.5 |
| Repeating and/or Reuse Rules | Yes, repeatable for each Exclusion Criterion, if deleted do not replace, do not duplicate |

5.4. Contraception

| | |
|--|--------------------------|
| Term (Variable) | 5.4 Contraception |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | H |
| Definition | Heading |
| User Guidance | |
| Conformance | Required |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 5.4 |
| Value | Contraception |
| Business rules | Value Allowed: No |

| | |
|-------------------------------------|---|
| Term (Variable) | 5.4 Contraception |
| | Relationship: 5 TRIAL POPULATION; Table of Contents Concept: Heading |
| Repeating and/or Reuse Rules | No |

5.4.1. Definitions related to childbearing potential

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

| | |
|--|--|
| Term (Variable) | <Definitions Related to Childbearing Potential> |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C218740 |
| User Guidance | |
| Conformance | Required |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 5.4.1 |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: 5.4.1 Definitions Related to Childbearing Potential Concept: C218740 ICH OID 2.16.840.1.113883.3.989.2.3.3.5 |

| | |
|-------------------------------------|---|
| Term (Variable) | <Definitions Related to Childbearing Potential> |
| Repeating and/or Reuse Rules | No |

5.4.2. Contraception requirements

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

| | |
|--|---|
| Term (Variable) | <Contraception Requirements> |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C218741 |
| User Guidance | |
| Conformance | Required |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 5.4 |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: 5.4.2 Contraception Requirements Concept: C218741 ICH OID 2.16.840.1.113883.3.989.2.3.3.5 |
| Repeating and/or Reuse Rules | No |

5.5. Lifestyle restrictions

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

| | |
|--|---|
| Term (Variable) | {<Lifestyle Restrictions>} |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C218742 |
| User Guidance | |
| Conformance | Conditional: If Level 3 subheadings are not used |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 5.5 |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: 5.5 Lifestyle Restrictions Concept: C218742 ICH OID 2.16.840.1.113883.3.989.2.3.3.5 |
| Repeating and/or Reuse Rules | No |

5.5.1. Meals and dietary restrictions

| | |
|---|--------------------------------------|
| Term (Variable) | 5.5.1 Meals and Dietary Restrictions |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | H |

| | |
|---|---|
| Term (Variable) | 5.5.1 Meals and Dietary Restrictions |
| Definition | Heading |
| User Guidance | N/A |
| Conformance | Optional |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 5.5.1 |
| Value | Meals and Dietary Restrictions |
| Business rules | Value Allowed: No Relationship: 5.5 Lifestyle Restrictions; 5 TRIAL POPULATION; Table of Contents Concept: Heading |
| Repeating and/or Reuse Rules | No |

| | |
|--|---|
| Term (Variable) | <Meals and Dietary Restrictions> |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C218743 |
| User Guidance | |
| Conformance | Optional |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 5.5.1 |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: 5.5.1 Meals and Dietary Restrictions Concept: C218743 ICH OID 2.16.840.1.113883.3.989.2.3.3.5 |
| Repeating and/or Reuse Rules | No |

5.5.2. Caffeine, alcohol, tobacco, and other restrictions

| | |
|---|--|
| Term (Variable) | 5.5.2 Caffeine, Alcohol, Tobacco, and Other Restrictions |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | H |
| Definition | Heading |
| User Guidance | N/A |
| Conformance | Optional |
| Cardinality | One to one |

| | |
|--|---|
| Term (Variable) | 5.5.2 Caffeine, Alcohol, Tobacco, and Other Restrictions |
| Relationship content from ToC representing the protocol hierarchy | 5.5.2 |
| Value | Caffeine, Alcohol, Tobacco, and Other Restrictions |
| Business rules | Value Allowed: No Relationship: 5.5 Lifestyle Restrictions; 5 TRIAL POPULATION; Table of Contents Concept: Heading |
| Repeating and/or Reuse Rules | No |

| | |
|--|---|
| Term (Variable) | <Caffeine, Alcohol, Tobacco, and Other Restrictions> |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C218744 |
| User Guidance | |
| Conformance | Optional |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 5.5.2 |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: 5.5.2 Caffeine, Alcohol, Tobacco, and Other Restrictions Concept: C218744 ICH OID 2.16.840.1.113883.3.989.2.3.3.5 |
| Repeating and/or Reuse Rules | No |

5.5.3. Physical activity restrictions

| | |
|--|--------------------------------------|
| Term (Variable) | 5.5.3 Physical Activity Restrictions |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | H |
| Definition | Heading |
| User Guidance | N/A |
| Conformance | Optional |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 5.5.3 |

| | |
|-------------------------------------|---|
| Term (Variable) | 5.5.3 Physical Activity Restrictions |
| Value | Physical Activity Restrictions |
| Business rules | Value Allowed: No Relationship: 5.5 Lifestyle Restrictions; 5 TRIAL POPULATION; Table of Contents Concept: Heading |
| Repeating and/or Reuse Rules | No |

| | |
|--|---|
| Term (Variable) | <Physical Activity Restrictions> |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C218745 |
| User Guidance | |
| Conformance | Optional |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 5.5.3 |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: 5.5.3 Physical Activity Restrictions Concept: C218745 ICH OID 2.16.840.1.113883.3.989.2.3.3.5 |
| Repeating and/or Reuse Rules | No |

5.5.4. Other activity restrictions

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

| | |
|-------------------------------------|-----------------------------------|
| Term (Variable) | 5.5.4 Other Activity Restrictions |
| | Concept: Heading |
| Repeating and/or Reuse Rules | No |

| | |
|--|--|
| Term (Variable) | <Other Activity Restrictions> |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C218746 |
| User Guidance | e.g. |
| Conformance | Optional |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 5.5.4 |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: 5.5.4 Other Activity Restrictions Concept: C218746 ICH OID 2.16.840.1.113883.3.989.2.3.3.5 |
| Repeating and/or Reuse Rules | No |

5.6. Screen failure and rescreening

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

| | |
|--|--|
| Term (Variable) | <Screen Failure> |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C49628 |
| User Guidance | |
| Conformance | Required |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 5.6 |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: 5.6 Screen Failure and Rescreening Concept: C49628 ICH OID 2.16.840.1.113883.3.989.2.3.3.5 |
| Repeating and/or Reuse Rules | No |

| | |
|--|---|
| Term (Variable) | <Rescreening> |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C179373 |
| User Guidance | |
| Conformance | Required |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 5.6 |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: 5.6 Screen Failure and Rescreening Concept: C179373 ICH OID 2.16.840.1.113883.3.989.2.3.3.5 |
| Repeating and/or Reuse Rules | No |

6. Trial intervention and concomitant therapy

| | |
|---|--|
| Term (Variable) | 6 TRIAL INTERVENTION AND CONCOMITANT THERAPY |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | H |
| Definition | Heading |

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

| | |
|--|--|
| Term (Variable) | <description of the overview of trial interventions or a heading for the optional table> |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C218747 |
| User Guidance | <p>Trial interventions are all pre-specified investigational and noninvestigational medicinal products, medical devices or other interventions intended for the participants during the trial. The investigational trial intervention is the product(s) used in the trial as part of trial objectives, including control(s) (e.g., active comparator, placebo). Description of the investigational trial intervention is provided in Section 6.1 Description of Investigational Trial Intervention. Other trial interventions that are not part of trial objectives or do not have an investigational role in this trial are described in Section 6.9 Description of Noninvestigational Trial Intervention.</p> <p>Any regional requirements should be noted in the appropriate subsections. Provide an overview of investigational and noninvestigational trial interventions. Designate the trial intervention as IMP or NIMP/AxMP based on trial design and regional requirements. Consider the optional table below.</p> |
| Conformance | Required |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 6 |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: 6 TRIAL INTERVENTION AND CONCOMITANT THERAPY Concept: C218747 ICH OID 2.16.840.1.113883.3.989.2.3.3.6 |

| | |
|-------------------------------------|--|
| Term (Variable) | <description of the overview of trial interventions or a heading for the optional table> |
| Repeating and/or Reuse Rules | No |

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

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

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

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

| | |
|---|-----------------------------|
| Term (Variable) | Pharmaceutical Dose Form |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | H |
| Definition | Table Column Heading |
| User Guidance | N/A |
| Conformance | Optional: if the table used |

| | |
|--|--|
| Term (Variable) | Pharmaceutical Dose Form |
| Cardinality | One to many |
| Relationship content from ToC representing the protocol hierarchy | 6 |
| Value | Pharmaceutical Dose Form |
| Business rules | Value Allowed: No Relationship: Optional Table Heading Concept: Heading |
| Repeating and/or Reuse Rules | No |

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

| | |
|--|-----------------------------|
| Term (Variable) | Dosage Level(s) |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | H |
| Definition | Table Column Heading |
| User Guidance | N/A |
| Conformance | Optional: if the table used |
| Cardinality | One to many |
| Relationship content from ToC representing the protocol hierarchy | 6 |
| Value | Dosage Level(s) |

| | |
|-------------------------------------|--|
| Term (Variable) | Dosage Level(s) |
| Business rules | Value Allowed: No Relationship: Optional Table Heading Concept: Heading |
| Repeating and/or Reuse Rules | No |

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

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

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

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

| | |
|---|-----------------------------|
| Term (Variable) | Sourcing |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | H |
| Definition | Table Column Heading |
| User Guidance | N/A |
| Conformance | Optional: if the table used |

| | |
|--|--|
| Term (Variable) | Sourcing |
| Cardinality | One to many |
| Relationship content from ToC representing the protocol hierarchy | 6 |
| Value | Sourcing |
| Business rules | Value Allowed: No Relationship: Optional Table Heading Concept: Heading |
| Repeating and/or Reuse Rules | No |

| | |
|--|--|
| Term (Variable) | <Arm Name> |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C93729 |
| User Guidance | N/A |
| Conformance | Optional: if the table used |
| Cardinality | One to many; one to interventions for Arm Name |
| Relationship content from ToC representing the protocol hierarchy | 6 |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: Arm Name Concept: C93729 ICH OID 2.16.840.1.113883.3.989.2.3.3.6 |
| Repeating and/or Reuse Rules | Yes, repeatable for each Arm Name and Intervention Name and Use combination |

| | |
|--|---|
| Term (Variable) | <Arm Type> |
| Data Type | Valid Value |
| Data (D), Value (V) or Heading (H) | V |
| Definition | C172457 |
| User Guidance | N/A |
| Conformance | Optional: if the table used |
| Cardinality | One to each Arm Name |
| Relationship content from ToC representing the protocol hierarchy | 6 |
| Value | Code List C217283: ICH OID 2.16.840.1.113883.3.989.2.3.1.15 |

| | |
|-------------------------------------|---|
| Term (Variable) | <Arm Type> |
| | Active Comparator Arm (C174267), Control Arm (C174226), Experimental Arm (C174266), No Intervention Arm (C174270), Placebo Comparator Arm (C174268), Sham Comparator Arm (C174269). |
| Business rules | Value Allowed: Yes Relationship: Arm Name and Arm Type Concept: C172457 ICH OID 2.16.840.1.113883.3.989.2.3.3.6 |
| Repeating and/or Reuse Rules | Yes, repeatable for each Arm Name |

| | |
|--|---|
| Term (Variable) | <Intervention Name> |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C177930 |
| User Guidance | N/A |
| Conformance | Optional: if the table used |
| Cardinality | One to Arm Name and Arm Type |
| Relationship content from ToC representing the protocol hierarchy | 6 |
| Value | Select Nonproprietary Name or Sponsor Investigational Product Code |
| Business rules | Value Allowed: Yes Relationship: Arm Name and Intervention Name Concept: C177930 ICH OID 2.16.840.1.113883.3.989.2.3.3.6 |
| Repeating and/or Reuse Rules | Yes, repeatable for each Arm Name and Arm Type |

| | |
|--|--|
| Term (Variable) | <Intervention Type> |
| Data Type | Valid Value |
| Data (D), Value (V) or Heading (H) | V |
| Definition | C98747 |
| User Guidance | N/A |
| Conformance | Optional: if the table used |
| Cardinality | One to each Intervention Name |
| Relationship content from ToC representing the protocol hierarchy | 6 |
| Value | Code List C217284: ICH OID 2.16.840.1.113883.3.989.2.3.1.7 Drug (C1909), Medical Device (C16830), Biologic (C307), Vaccine (C923), Non-Surgical Procedure (C218507), Surgery (C15329), Radiation |

| | |
|-------------------------------------|--|
| Term (Variable) | <Intervention Type> |
| | (C15313), Behavioral (C15184), Genetic (C15238), Dietary Supplement (C1505), Combination Product (C54696), Diagnostic (C18020) |
| Business rules | Value Allowed: Yes Relationship: Arm Name, Arm Type and Intervention Name Concept: C98747 ICH OID 2.16.840.1.113883.3.989.2.3.3.6 |
| Repeating and/or Reuse Rules | Yes, repeatable for each Arm Name and Arm Type combination |

| | |
|--|---|
| Term (Variable) | <Pharmaceutical Dose Form> |
| Data Type | Valid Value |
| Data (D), Value (V) or Heading (H) | V |
| Definition | C42636 |
| User Guidance | N/A |
| Conformance | Optional: if the table used |
| Cardinality | One to each Arm Name, Arm Type and Intervention Name combination |
| Relationship content from ToC representing the protocol hierarchy | 6 |
| Value | Use IDMP (ISO 11239) or CDISC SDTM Terminology |
| Business rules | Value Allowed: Yes Relationship: Arm Name and Pharmaceutical Dose Form Concept: C42636 ICH OID 2.16.840.1.113883.3.989.2.3.3.6 |
| Repeating and/or Reuse Rules | Yes, repeatable for each Intervention Name and Pharmaceutical Dose Form |

| | |
|--|---|
| Term (Variable) | <Dosage Strength(s)> |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C142517 |
| User Guidance | N/A |
| Conformance | Optional: if the table used |
| Cardinality | One to each Pharmaceutical Dose Form |
| Relationship content from ToC representing the protocol hierarchy | 6 |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: Arm Name and Dosage Strength Concept: C142517 ICH OID 2.16.840.1.113883.3.989.2.3.3.6 |

| | |
|-------------------------------------|---|
| Term (Variable) | <Dosage Strength(s)> |
| Repeating and/or Reuse Rules | Yes, repeatable for each Intervention Name and Pharmaceutical Dose Form per Arm Name and Arm Type |

| | |
|--|---|
| Term (Variable) | <Dosage Level(s)> |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C94394 |
| User Guidance | N/A |
| Conformance | Optional: if the table used |
| Cardinality | One to each Intervention Name and Pharmaceutical Dose Form |
| Relationship content from ToC representing the protocol hierarchy | 6 |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: Arm Name and Dose Level Concept: C94394 ICH OID 2.16.840.1.113883.3.989.2.3.3.6 |
| Repeating and/or Reuse Rules | Yes, repeatable for each Intervention Name, Pharmaceutical Dose Form, Dosage Strength and Dosage Level per Arm Name |

| | |
|--|--|
| Term (Variable) | <Route of Administration> |
| Data Type | Valid Value |
| Data (D), Value (V) or Heading (H) | V |
| Definition | C38114 |
| User Guidance | N/A |
| Conformance | Optional: if the table used |
| Cardinality | One to each Intervention Name and Pharmaceutical Dose Form |
| Relationship content from ToC representing the protocol hierarchy | 6 |
| Value | Use IDMP (ISO 11239) or CDISC SDTM Terminology |
| Business rules | Value Allowed: Yes Relationship: Arm Name and Route of Administration Concept: C38114 ICH OID 2.16.840.1.113883.3.989.2.3.3.6 |
| Repeating and/or Reuse Rules | Yes, repeatable for each Intervention Name, Pharmaceutical Dose Form, per Arm Name |

| | |
|------------------------|--|
| Term (Variable) | <Regimen/Treatment Period/Vaccination Regimen> |
| Data Type | Text |

| | |
|--|---|
| Term (Variable) | <Regimen/Treatment Period/Vaccination Regimen> |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C15697 |
| User Guidance | N/A |
| Conformance | Optional: if the table used |
| Cardinality | One to each Intervention Name, Pharmaceutical Dose Form, Dosage Strength per Arm Name |
| Relationship content from ToC representing the protocol hierarchy | 6 |
| Value | Describe Regimen/Treatment Period/Vaccination Regimen |
| Business rules | Value Allowed: Yes Relationship: Arm Name and Regimen/Treatment Period/Vaccination Regimen Concept: C15697 ICH OID 2.16.840.1.113883.3.989.2.3.3.6 |
| Repeating and/or Reuse Rules | Yes, repeatable for each arm name |

| | |
|--|---|
| Term (Variable) | <Use> |
| Data Type | Valid Value |
| Data (D), Value (V) or Heading (H) | V |
| Definition | C218748 |
| User Guidance | N/A |
| Conformance | Optional: if the table used |
| Cardinality | One to each Intervention Name |
| Relationship content from ToC representing the protocol hierarchy | 6 |
| Value | Code List C217285: ICH OID 2.16.840.1.113883.3.989.2.3.1.8 Experimental Intervention (C41161), Placebo (C753), Rescue Medicine (C165835), Background Treatment (C165822), Challenge Agent (C158128), Diagnostic (C18020), Additional Required Treatment (C207614) |
| Business rules | Value Allowed: Yes Relationship: Arm Name and Use Concept: C218748 ICH OID 2.16.840.1.113883.3.989.2.3.3.6 |
| Repeating and/or Reuse Rules | Yes, repeatable for each Intervention Name per Arm Name |

| | |
|------------------------|---------------|
| Term (Variable) | <IMP or NIMP> |
| Data Type | Valid value |

| | |
|--|---|
| Term (Variable) | <IMP or NIMP> |
| Data (D), Value (V) or Heading (H) | V |
| Definition | C218749 |
| User Guidance | N/A |
| Conformance | Optional: if the table used |
| Cardinality | One to each Intervention Name |
| Relationship content from ToC representing the protocol hierarchy | 6 |
| Value | Code List C217286: ICH OID 2.16.840.1.113883.3.989.2.3.1.10 IMP (C202579), NIMP (C156473) |
| Business rules | Value Allowed: Yes Relationship: One per each Intervention Name Concept: C218749 ICH OID 2.16.840.1.113883.3.989.2.3.3.6 |
| Repeating and/or Reuse Rules | Yes, repeatable for each Intervention Name per Arm Name |

| | |
|--|---|
| Term (Variable) | <Sourcing> |
| Data Type | Valid Value |
| Data (D), Value (V) or Heading (H) | V |
| Definition | C218750 |
| User Guidance | N/A |
| Conformance | Optional: if the table used |
| Cardinality | One to many |
| Relationship content from ToC representing the protocol hierarchy | 6 |
| Value | Code List C217052: ICH OID 2.16.840.1.113883.3.989.2.3.1.9 Centrally Sourced (C215659), Locally Sourced (C215660) |
| Business rules | Value Allowed: Yes Relationship: One per each Intervention Name Concept: C218750 ICH OID 2.16.840.1.113883.3.989.2.3.3.6 |
| Repeating and/or Reuse Rules | Yes, repeatable for each Intervention Name per Arm Name |

6.1. Description of investigational trial intervention

| | |
|---|---|
| Term (Variable) | 6.1 Description of Investigational Trial Intervention |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | H |
| Definition | Heading |

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

| | |
|--|--|
| Term (Variable) | <Description of Investigational Trial Intervention> |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C218751 |
| User Guidance | Describe the investigational trial intervention to be administered in each arm of the trial and for each period of the trial including route and mode of administration, dose, dosage regimen, duration of intervention, use, packaging and labelling. Refer to approved regional labelling, as appropriate. For investigational drug/device combination products, include details on the configuration and use of the device and device manufacturer. A device user manual may be referenced in this section. |
| Conformance | Required |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 6.1 |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: 6.1 Description of Investigational Trial Intervention Concept: C218751 ICH OID 2.16.840.1.113883.3.989.2.3.3.6 |
| Repeating and/or Reuse Rules | No |

6.2. Rationale for investigational trial intervention dose and regimen

| | |
|------------------------|---|
| Term (Variable) | 6.2 Rationale for Investigational Trial Intervention Dose and Regimen |
| Data Type | Text |

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

| | |
|--|---|
| Term (Variable) | <Rationale for Investigational Trial Intervention Dose and Regimen> |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C218752 |
| User Guidance | Provide a rationale for the selection of the dose(s) or dose range, pharmaceutical dose form, route of administration, and dosing regimen of the investigational trial interventions, as applicable. This rationale should include relevant results from nonclinical studies and clinical trials that support selection of the dose and regimen. Discuss impact of differences in trial population characteristics (e.g., age, sex, race) that could lead to differences in pharmacokinetics and pharmacodynamics in this trial as compared to previous trials. 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 trial intervention. Include a rationale for prospective dose adjustments incorporated in the trial, if any. |
| Conformance | Required |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 6.2 |
| Value | Text |
| Business rules | Value Allowed: Yes |

| | |
|-------------------------------------|---|
| Term (Variable) | <Rationale for Investigational Trial Intervention Dose and Regimen> |
| | Relationship: 6.2 Rationale for Investigational Trial Intervention Dose and Regimen Concept: C218752 ICH OID 2.16.840.1.113883.3.989.2.3.3.6 |
| Repeating and/or Reuse Rules | No |

6.3. Investigational trial intervention administration

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

| | |
|---|--|
| Term (Variable) | <Investigational Trial Intervention Administration> |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C218753 |
| 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 (e.g., time of day, interval), the duration (e.g., the length of time participants will be administered the investigational trial intervention), and the timing of dosing relative to meals. Include any specific instructions on who, when or how to prepare and take the dose(s) and how to handle any delayed or missed doses. Dose escalation or cohort expansion as part of the overall design should be covered in Section 4.1 Description of Trial Design. |
| Conformance | Required |
| Cardinality | One to one |

| | |
|--|--|
| Term (Variable) | <Investigational Trial Intervention Administration> |
| Relationship content from ToC representing the protocol hierarchy | 6.3 |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: 6.3 Investigational Trial Intervention Administration Concept: C218753 ICH OID 2.16.840.1.113883.3.989.2.3.3.6 |
| Repeating and/or Reuse Rules | No |

6.4. Investigational trial intervention dose modification

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

| | |
|---|---|
| Term (Variable) | <Investigational Trial Intervention Dose Modification> |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C218754 |
| User Guidance | For each participant, describe any dose modifications allowed, including conditions for such dose modifications, particularly regarding failure to respond or safety concerns. State any minimum period required before a participant's dose might be raised to the next higher dose or dose range. Include whether it is permissible to start and stop treatment and how dose reductions (if permitted) are to be managed. |

| | |
|--|--|
| Term (Variable) | <Investigational Trial Intervention Dose Modification> |
| | Information on stopping investigational trial intervention for participants due to safety/other reasons should be described in Section 7 Participant Discontinuation of Trial Intervention and Discontinuation or Withdrawal from Trial. |
| Conformance | Required |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 6.4 |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: 6.4 Investigational Trial Intervention Dose Modification Concept: C218754 ICH OID 2.16.840.1.113883.3.989.2.3.3.6 |
| Repeating and/or Reuse Rules | No |

6.5. Management of investigational trial intervention overdose

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

| | |
|---|---|
| Term (Variable) | <Management of Investigational Trial Intervention Overdose> |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C218755 |

| | |
|--|---|
| Term (Variable) | <Management of Investigational Trial Intervention Overdose> |
| User Guidance | Describe what is meant by investigational trial intervention overdose. Provide any available information on managing overdose and ensure it is consistent with the Investigator's Brochure or product labelling. Cross reference these documents as applicable. |
| Conformance | Required |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 6.5 |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: 6.5 Management of Investigational Trial Intervention Overdose Concept: C218755 ICH OID 2.16.840.1.113883.3.989.2.3.3.6 |
| Repeating and/or Reuse Rules | No |

6.6. Preparation, storage, handling and accountability of investigational trial intervention

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

6.6.1. Preparation of investigational trial intervention

| | |
|------------------------|---|
| Term (Variable) | 6.6.1 Preparation of Investigational Trial Intervention |
| Data Type | Text |

| | |
|--|--|
| Term (Variable) | 6.6.1 Preparation of Investigational Trial Intervention |
| Data (D), Value (V) or Heading (H) | H |
| Definition | Heading |
| User Guidance | N/A |
| Conformance | Required |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 6.6.1 |
| Value | Preparation of Investigational Trial Intervention |
| Business rules | Value Allowed: No Relationship: 6.6 Preparation, Storage, Handling and Accountability of Investigational Trial Intervention; 6 TRIAL INTERVENTION AND CONCOMITANT THERAPY; Table of Contents Concept: Heading |
| Repeating and/or Reuse Rules | No |

| | |
|--|---|
| Term (Variable) | <Preparation of Investigational Trial Intervention> |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C176274 |
| User Guidance | Describe any preparation of the investigational trial intervention, and when necessary, who should prepare it. 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 separate documents provided to the site (e.g., a pharmacy manual) and reference the separate documents. |
| Conformance | Required |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 6.6.1 |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: 6.6.1 Preparation of Investigational Trial Intervention Concept: C176274 ICH OID 2.16.840.1.113883.3.989.2.3.3.6 |

| | |
|-------------------------------------|---|
| Term (Variable) | <Preparation of Investigational Trial Intervention> |
| Repeating and/or Reuse Rules | No |

6.6.2. Storage and handling of investigational trial intervention

| | |
|--|--|
| Term (Variable) | 6.6.2 Storage and Handling of Investigational Trial Intervention |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | H |
| Definition | Heading |
| User Guidance | N/A |
| Conformance | Required |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 6.6.2 |
| Value | Storage and Handling of Investigational Trial Intervention |
| Business rules | Value Allowed: No Relationship: 6.6 Preparation, Storage, Handling and Accountability of Investigational Trial Intervention; 6 TRIAL INTERVENTION AND CONCOMITANT THERAPY; Table of Contents Concept: Heading |
| Repeating and/or Reuse Rules | No |

| | |
|---|---|
| Term (Variable) | <Storage and Handling of Investigational Trial Intervention> |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C115525 |
| User Guidance | <p>Describe storage and handling requirements (e.g., protection from light, temperature, humidity) for the investigational trial intervention(s). For trials in which multidose vials are utilised, provide additional information regarding stability and expiration time after initial use (e.g., if the seal is broken).</p> <p>Explain how the investigational trial intervention will be provided to the investigator. If applicable, include details about kits, packaging, or other material of the investigational trial intervention for blinding purposes.</p> <p>If the instructions are lengthy or complicated, it is acceptable to reference the package insert (if applicable) or include instructions in separate documents provided to the site (e.g., a pharmacy manual) and reference the separate documents.</p> |
| Conformance | Required |
| Cardinality | One to one |

| | |
|--|---|
| Term (Variable) | <Storage and Handling of Investigational Trial Intervention> |
| Relationship content from ToC representing the protocol hierarchy | 6.6.2 |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: 6.6.2 Storage and Handling of Investigational Trial Intervention Concept: C115525 ICH OID 2.16.840.1.113883.3.989.2.3.3.6 |
| Repeating and/or Reuse Rules | No |

6.6.3. Accountability of investigational trial intervention

| | |
|--|--|
| Term (Variable) | 6.6.3 Accountability of Investigational Trial Intervention |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | H |
| Definition | Heading |
| User Guidance | N/A |
| Conformance | Required |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 6.6.3 |
| Value | Accountability of Investigational Trial Intervention |
| Business rules | Value Allowed: No Relationship: 6.6 Preparation, Storage, Handling and Accountability of Investigational Trial Intervention; 6 TRIAL INTERVENTION AND CONCOMITANT THERAPY; Table of Contents Concept: Heading |
| Repeating and/or Reuse Rules | No |

| | |
|---|--|
| Term (Variable) | <Accountability of Investigational Trial Intervention> |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C176267 |
| User Guidance | Describe the accountability method, including: <ul style="list-style-type: none"> • how the investigational trial intervention will be distributed • who will distribute the investigational trial intervention • participation of a drug storage repository or pharmacy, if applicable • plans for disposal or return of unused product |

| | |
|--|---|
| Term (Variable) | <Accountability of Investigational Trial Intervention> |
| | <ul style="list-style-type: none"> plans for reconciliation of investigational trial intervention, if applicable |
| Conformance | Required |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 6.6.3 |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: 6.6.3 Accountability of Investigational Trial Intervention Concept: C176267 ICH OID 2.16.840.1.113883.3.989.2.3.3.6 |
| Repeating and/or Reuse Rules | No |

6.7. Investigational trial intervention assignment, randomisation and blinding

| | |
|--|---|
| Term (Variable) | 6.7 Investigational Trial Intervention Assignment, Randomisation and Blinding |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | H |
| Definition | Heading |
| User Guidance | No text is intended here (heading only). |
| Conformance | Required |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 6.7 |
| Value | Investigational Trial Intervention Assignment, Randomisation and Blinding |
| Business rules | Value Allowed: No Relationship: 6 TRIAL INTERVENTION AND CONCOMITANT THERAPY; Table of Contents Concept: Heading |
| Repeating and/or Reuse Rules | No |

6.7.1. Participant assignment to investigational trial intervention

| | |
|---|--|
| Term (Variable) | 6.7.1 Participant Assignment to Investigational Trial Intervention |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | H |
| Definition | Heading |
| User Guidance | N/A |

| | |
|--|--|
| Term (Variable) | 6.7.1 Participant Assignment to Investigational Trial Intervention |
| Conformance | Required |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 6.7.1 |
| Value | Participant Assignment to Investigational Trial Intervention |
| Business rules | Value Allowed: No Relationship: 6.7 Investigational Trial Intervention Assignment, Randomisation and Blinding; 6 TRIAL INTERVENTION AND CONCOMITANT THERAPY; Table of Contents Concept: Heading |
| Repeating and/or Reuse Rules | No |

| | |
|--|--|
| Term (Variable) | <Participant Assignment to Investigational Trial Intervention> |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C218756 |
| User Guidance | <p>State that at enrollment, participant identification codes should be assigned. 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 will occur relative to screening.</p> <p>If permuted block randomisation is employed, do not state the block size in the protocol. 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.</p> |
| Conformance | Required |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 6.7.1 |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: 6.7.1 Participant Assignment to Investigational Trial Intervention Concept: C218756 ICH OID 2.16.840.1.113883.3.989.2.3.3.6 |
| Repeating and/or Reuse Rules | No |

6.7.2. {Randomisation}

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

| | |
|--|---|
| Term (Variable) | {<Randomisation>} |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C25196 |
| User Guidance | Describe the randomisation procedures (e.g., central randomisation procedures), the method used to generate the randomisation schedule (e.g., computer generated), the source of the randomisation schedule (e.g., sponsor, investigator, or other), and whether IRT(s) will be used. To maintain the integrity of the blinding, do not include the block size. |
| Conformance | Conditional: when randomised trial |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 6.7.2 |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: 6.7.2 Randomisation Concept: C25196 ICH OID 2.16.840.1.113883.3.989.2.3.3.6 |
| Repeating and/or Reuse Rules | No |

6.7.3. {Measures to maintain blinding}

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

| | |
|---|---|
| Term (Variable) | {<Measures to Maintain Blinding>} |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C189349 |
| User Guidance | <p>Describe measures that will be used to maintain blinding:</p> <ul style="list-style-type: none"> • The investigational trial interventions are as indistinguishable as possible • Plans for the maintenance of randomisation codes and appropriate blinding for the trial • Procedures for planned (e.g., interim analysis) and unintentional (e.g., breach of procedure) breaking of randomisation codes <p>For unplanned but intentional actions (e.g., safety events), refer to Section 6.7.4 Emergency Unblinding at the Site.</p> <p>If the trial allows for some investigators or other designated staff to remain unblinded (e.g., 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.</p> |
| Conformance | Conditional: when blind trial |
| Cardinality | One to one |
| Relationship content from ToC | 6.7.3 |

| | |
|--|--|
| Term (Variable) | {<Measures to Maintain Blinding>} |
| representing the protocol hierarchy | |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: 6.7.3 Measures to Maintain Blinding Concept: C189349 ICH OID 2.16.840.1.113883.3.989.2.3.3.6 |
| Repeating and/or Reuse Rules | No |

6.7.4. {Emergency unblinding at the site}

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

| | |
|---|---|
| Term (Variable) | {<Emergency Unblinding at the Site>} |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C218757 |
| User Guidance | Describe the criteria for breaking the trial blind or participant code. Describe the circumstances that would require breaking the blind, either for an individual participant or for all participants, and specify who will be responsible for this decision. Include the procedure for emergency unblinding as well as documentation of unblinding. Indicate to whom the intentional and unplanned unblinding should be reported. |
| Conformance | Conditional: when blind trial |
| Cardinality | One to one |

| | |
|--|---|
| Term (Variable) | {<Emergency Unblinding at the Site>} |
| Relationship content from ToC representing the protocol hierarchy | 6.7.4 |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: 6.7.4 Emergency Unblinding at the Site Concept: C218757 ICH OID 2.16.840.1.113883.3.989.2.3.3.6 |
| Repeating and/or Reuse Rules | No |

6.8. Investigational trial intervention adherence

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

| | |
|---|---|
| Term (Variable) | <Investigational Trial Intervention Adherence> |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C218758 |
| User Guidance | Describe the measures to monitor and document participants' adherence to investigational trial intervention (e.g., trial intervention accountability records, paper or electronic diaries, or investigational trial intervention concentration measurements). List what documents are mandatory to complete (e.g., participant drug log) and identify which records will be used as the source records for documenting investigational trial intervention adherence. |

| | |
|--|---|
| Term (Variable) | <Investigational Trial Intervention Adherence> |
| Conformance | Required |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 6.8 |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: 6.8 Investigational Trial Intervention Adherence Concept: C218758 ICH OID 2.16.840.1.113883.3.989.2.3.3.6 |
| Repeating and/or Reuse Rules | No |

6.9. Description of noninvestigational trial intervention

| | |
|--|--|
| Term (Variable) | 6.9 Description of Noninvestigational Trial Intervention |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | H |
| Definition | Heading |
| User Guidance | N/A |
| Conformance | Required |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 6.9 |
| Value | Description of Noninvestigational Trial Intervention |
| Business rules | Value Allowed: No Relationship: 6 TRIAL INTERVENTION AND CONCOMITANT THERAPY; Table of Contents Concept: Heading |
| Repeating and/or Reuse Rules | No |

| | |
|---|---|
| Term (Variable) | <Description of Noninvestigational Trial Intervention> |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C218759 |
| User Guidance | As stated in Section 6 Trial Intervention and Concomitant Therapy, noninvestigational interventions are pre-specified products used in the trial but are not part of trial objectives and hence, are not investigational trial interventions. |
| Conformance | Required |

| | |
|--|---|
| Term (Variable) | <Description of Noninvestigational Trial Intervention> |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 6.9 |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: 6.9 Description of Noninvestigational Trial Intervention Concept: C218759 ICH OID 2.16.840.1.113883.3.989.2.3.3.6 |
| Repeating and/or Reuse Rules | No |

6.9.1. {Background trial intervention}

| | |
|--|--|
| Term (Variable) | 6.9.1 {Background Trial Intervention} |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | H |
| Definition | Heading |
| User Guidance | N/A |
| Conformance | Conditional: when any background interventions are defined |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 6.9.1 |
| Value | Background Trial Intervention |
| Business rules | Value Allowed: No Relationship: 6.9 Description of Noninvestigational Trial Intervention; 6 TRIAL INTERVENTION AND CONCOMITANT THERAPY; Table of Contents Concept: Heading |
| Repeating and/or Reuse Rules | No |

| | |
|---|---|
| Term (Variable) | {<Background Trial Intervention>} |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C222329 |
| User Guidance | Describe any background intervention(s), including administration and any conditions for use. |
| Conformance | Conditional: when any background interventions are defined |
| Cardinality | One to one |
| Relationship content from ToC | 6.9.1 |

| | |
|--|--|
| Term (Variable) | {<Background Trial Intervention>} |
| representing the protocol hierarchy | |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: 6.9.1 Background Trial Intervention Concept: C222329 |
| Repeating and/or Reuse Rules | No |

6.9.2. {Rescue therapy}

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

| | |
|---|---|
| Term (Variable) | {<Rescue Therapy>} |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C222330 |
| User Guidance | List all permitted rescue medications, treatments, and/or procedures, including any relevant instructions on administration and any conditions of use. If administration of rescue therapy leads to the temporary or permanent discontinuation of trial intervention, refer to Section 7 Participant Discontinuation of Trial Intervention and Discontinuation or Withdrawal from Trial. |
| Conformance | Conditional: when any rescue therapies are defined |
| Cardinality | One to one |

| | |
|--|---|
| Term (Variable) | {<Rescue Therapy>} |
| Relationship content from ToC representing the protocol hierarchy | 6.9.2 |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: 6.9.2 Rescue Therapy Concept: C222330 ICH OID 2.16.840.1.113883.3.989.2.3.3.6 |
| Repeating and/or Reuse Rules | No |

6.9.3. {Other noninvestigational trial intervention}

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

| | |
|---|---|
| Term (Variable) | {<Other Noninvestigational Trial Intervention>} |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C218761 |
| User Guidance | If applicable, describe the use of any other noninvestigational trial intervention (e.g., challenge agents or diagnostics). |
| Conformance | Conditional: when any other noninvestigational trial interventions are defined |
| Cardinality | One to one |

| | |
|--|--|
| Term (Variable) | {<Other Noninvestigational Trial Intervention>} |
| Relationship content from ToC representing the protocol hierarchy | 6.9.3 |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: 6.9.3 Other Noninvestigational Trial Intervention Concept: C218761 ICH OID 2.16.840.1.113883.3.989.2.3.3.6 |
| Repeating and/or Reuse Rules | No |

6.10. Concomitant therapy

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

| | |
|---|--|
| Term (Variable) | <Concomitant Therapy> |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C53630 |
| User Guidance | Specify the concomitant medications, supplements, complementary and alternative therapies, treatments, and/or procedures that are prohibited or permitted during the trial and include details about when the information will be collected (e.g., during screening, at each visit). When appropriate to separate the content, the below subheadings may be used. |
| Conformance | Required |

| | |
|--|--|
| Term (Variable) | <Concomitant Therapy> |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 6.10 |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: 6.10 Concomitant Therapy Concept: C53630 ICH OID 2.16.840.1.113883.3.989.2.3.3.6 |
| Repeating and/or Reuse Rules | No |

6.10.1. {Prohibited concomitant therapy}

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

| | |
|---|--|
| Term (Variable) | {<Prohibited Concomitant Therapy>} |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C218762 |
| User Guidance | If applicable, describe any prohibited concomitant therapy. |
| Conformance | Conditional: when any prohibited concomitant therapies are defined |
| Cardinality | One to one |
| Relationship content from ToC | 6.10.1 |

| | |
|--|--|
| Term (Variable) | {<Prohibited Concomitant Therapy>} |
| representing the protocol hierarchy | |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: 6.10.1 Prohibited Concomitant Therapy Concept: C218762 ICH OID 2.16.840.1.113883.3.989.2.3.3.6 |
| Repeating and/or Reuse Rules | No |

6.10.2. {Permitted concomitant therapy}

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

| | |
|--|---|
| Term (Variable) | {<Permitted Concomitant Therapy>} |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C218763 |
| User Guidance | If applicable, describe any permitted concomitant therapy. |
| Conformance | Conditional: when any permitted concomitant therapies are defined |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 6.10.2 |
| Value | Text |
| Business rules | Value Allowed: Yes |

| | |
|-------------------------------------|--|
| Term (Variable) | {<Permitted Concomitant Therapy>} |
| | Relationship: 6.10.2 Permitted Concomitant Therapy Concept: C218763 ICH OID 2.16.840.1.113883.3.989.2.3.3.6 |
| Repeating and/or Reuse Rules | No |

7. Participant discontinuation of trial intervention and discontinuation or withdrawal from trial

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

7.1. Discontinuation of trial intervention for individual participants

| | |
|---|---|
| Term (Variable) | 7.1 Discontinuation of Trial Intervention for Individual Participants |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | H |
| Definition | Heading |
| User Guidance | No text is intended here (heading only). |
| Conformance | Required |
| Cardinality | One to one |

| | |
|--|---|
| Term (Variable) | 7.1 Discontinuation of Trial Intervention for Individual Participants |
| Relationship content from ToC representing the protocol hierarchy | 7.1 |
| Value | Discontinuation of Trial Intervention for Individual Participants |
| Business rules | Value Allowed: No Relationship: 7 PARTICIPANT DISCONTINUATION OF TRIAL INTERVENTION AND DISCONTINUATION OR WITHDRAWAL FROM TRIAL; Table of Contents Concept: Heading |
| Repeating and/or Reuse Rules | No |

7.1.1. Permanent discontinuation of trial intervention

| | |
|--|--|
| Term (Variable) | 7.1.1 Permanent Discontinuation of Trial Intervention |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | H |
| Definition | Heading |
| User Guidance | N/A |
| Conformance | Required |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 7.1.1 |
| Value | Permanent Discontinuation of Trial Intervention |
| Business rules | Value Allowed: No Relationship: 7.1 Discontinuation of Trial Intervention for Individual Participants, 7 PARTICIPANT DISCONTINUATION OF TRIAL INTERVENTION AND DISCONTINUATION OR WITHDRAWAL FROM TRIAL; Table of Contents Concept: Heading |
| Repeating and/or Reuse Rules | No |

| | |
|---|---|
| Term (Variable) | <Permanent Discontinuation of Trial Intervention> |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C218764 |
| User Guidance | Describe: |

| | |
|--|--|
| Term (Variable) | <Permanent Discontinuation of Trial Intervention> |
| | <ul style="list-style-type: none"> the criteria for discontinuation of a participant from any trial intervention, carefully evaluating which are appropriate for the trial population and therapy being studied how participants who discontinue trial intervention will be followed after discontinuation. Depending on the chosen intercurrent event handling strategy, it will be important to continue to follow and ascertain outcomes in participants who discontinue trial intervention through the end of the trial to prevent missing data in important analyses. Refer to Section 1.3 Schedule of Activities for assessments to be performed at the time of and following discontinuation of trial intervention the process for collecting and recording the detailed reasons for discontinuing trial intervention if not described elsewhere |
| Conformance | Required |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 7.1.1 |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: 7.1.1 Permanent Discontinuation of Trial Intervention Concept: C218764 ICH OID 2.16.840.1.113883.3.989.2.3.3.7 |
| Repeating and/or Reuse Rules | No |

7.1.2. Temporary discontinuation of trial intervention

| | |
|--|---|
| Term (Variable) | 7.1.2 Temporary Discontinuation of Trial Intervention |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | H |
| Definition | Heading |
| User Guidance | N/A |
| Conformance | Required |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 7.1.2 |
| Value | Temporary Discontinuation of Trial Intervention |
| Business rules | Value Allowed: No Relationship: 7.1 Discontinuation of Trial Intervention for Individual Participants; 7 PARTICIPANT DISCONTINUATION OF TRIAL INTERVENTION AND DISCONTINUATION OR WITHDRAWAL FROM TRIAL; Table of Contents. Concept: Heading |

| | |
|-------------------------------------|---|
| Term (Variable) | 7.1.2 Temporary Discontinuation of Trial Intervention |
| Repeating and/or Reuse Rules | No |

| | |
|--|--|
| Term (Variable) | <Temporary Discontinuation of Trial Intervention> |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C218765 |
| User Guidance | Describe: <ul style="list-style-type: none"> the criteria for temporary discontinuation or interruption of trial intervention for an individual participant what to do and which restrictions still apply if the participant has to temporarily discontinue or interrupt trial intervention which assessments will be performed for the stated duration of the trial Details of any rechallenge or restart after temporary discontinuation of trial intervention due to a safety-related event should be included in Section 7.1.3 Rechallenge. |
| Conformance | Required |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 7.1.2 |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: 7.1.2 Temporary Discontinuation of Trial Intervention Concept: C218765 ICH OID 2.16.840.1.113883.3.989.2.3.3.7 |
| Repeating and/or Reuse Rules | No |

7.1.3. Rechallenge

| | |
|--|-------------------|
| Term (Variable) | 7.1.3 Rechallenge |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | H |
| Definition | Heading |
| User Guidance | N/A |
| Conformance | Required |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 7.1.3 |
| Value | Rechallenge |

| | |
|-------------------------------------|---|
| Term (Variable) | 7.1.3 Rechallenge |
| Business rules | Value Allowed: No Relationship: 7.1 Discontinuation of Trial Intervention for Individual Participants; 7 PARTICIPANT DISCONTINUATION OF TRIAL INTERVENTION AND DISCONTINUATION OR WITHDRAWAL FROM TRIAL; Table of Contents. Concept: Heading |
| Repeating and/or Reuse Rules | No |

| | |
|--|---|
| Term (Variable) | <Rechallenge> |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C218766 |
| User Guidance | Describe the criteria for rechallenge/restarting trial intervention, how and when to perform rechallenge, the number of rechallenges allowed during the trial, and whether all, or specify which, assessments will be performed for the stated duration of the trial. If rechallenge is not allowed, state this. |
| Conformance | Required |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 7.1.3 |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: 7.1.3 Rechallenge Concept: C218766 ICH OID 2.16.840.1.113883.3.989.2.3.3.7 |
| Repeating and/or Reuse Rules | No |

7.2. Participant discontinuation or withdrawal from the trial

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

| | |
|--|--|
| Term (Variable) | 7.2 Participant Discontinuation or Withdrawal from the Trial |
| representing the protocol hierarchy | |
| Value | Participant Discontinuation or Withdrawal from the Trial |
| Business rules | Value Allowed: No Relationship: 7 PARTICIPANT DISCONTINUATION OF TRIAL INTERVENTION AND DISCONTINUATION OR WITHDRAWAL FROM TRIAL; Table of Contents. Concept: Heading |
| Repeating and/or Reuse Rules | No |

| | |
|--|--|
| Term (Variable) | <Participant Discontinuation or Withdrawal from Trial> |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C218767 |
| User Guidance | <p>Describe the criteria for participant discontinuation or withdrawal from the trial.</p> <p>Describe the reason for withdrawal and the type of data to be collected for the final assessments with reference to the schedule of activities for the participant's end of study visit unless provided in another section.</p> <p>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 trial intervention, should remain in the trial and continue to be followed to prevent missing data in important analyses. Refer to Section 10 Statistical Considerations for the data that must be collected for the trial estimands.</p> |
| Conformance | Required |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 7.2 |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: 7.2 Participants Discontinuation or Withdrawal from the Trial Concept: C218767 ICH OID 2.16.840.1.113883.3.989.2.3.3.7 |
| Repeating and/or Reuse Rules | No |

7.3. Management of loss to follow-up

| | |
|--|--|
| Term (Variable) | 7.3 Management of Loss to Follow-Up |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | H |
| Definition | Heading |
| User Guidance | N/A |
| Conformance | Required |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 7.3 |
| Value | Management of Loss to Follow-Up |
| Business rules | Value Allowed: No Relationship: 7 PARTICIPANT DISCONTINUATION OF TRIAL INTERVENTION AND DISCONTINUATION OR WITHDRAWAL FROM TRIAL; Table of Contents. Concept: Heading |
| Repeating and/or Reuse Rules | No |

| | |
|--|--|
| Term (Variable) | <Management of Loss to Follow-Up> |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C218768 |
| User Guidance | Describe how the trial will define how participants are lost to follow-up. In general, participants should be considered lost to follow-up only if they cannot be reached despite multiple attempts to contact them. Also describe approaches that will be used to minimise loss to follow-up, such as multiple, diverse methods to remain in contact with participants (e.g., telephone calls, texts, and emails to the participant) and how contacts will be recorded. |
| Conformance | Required |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 7.3 |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: 7.3 Management of Loss to Follow-up Concept: C218768 ICH OID 2.16.840.1.113883.3.989.2.3.3.7 |

| | |
|-------------------------------------|-----------------------------------|
| Term (Variable) | <Management of Loss to Follow-Up> |
| Repeating and/or Reuse Rules | No |

8. Trial assessments and procedures

| | |
|--|--|
| Term (Variable) | 8 TRIAL ASSESSMENTS AND PROCEDURES |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | H |
| Definition | Heading |
| User Guidance | <p>In this section:</p> <ul style="list-style-type: none"> Describe the assessments and procedures required during each phase of the trial that are relevant to the stated endpoints and related intercurrent events (e.g., surgery or use of rescue therapy). Provide details that are not already presented in the SoA, taking care not to duplicate information. Ensure alignment with every other section of the protocol. In particular, this section must align with: <ul style="list-style-type: none"> the intercurrent events and associated strategies for handling them described in Section 3 Trial Objectives and Associated Estimands trial intervention and therapies outlined in Section 6 Trial Intervention and Concomitant Therapy discontinuation and withdrawal procedures in Section 7 Participant Discontinuation of Trial Intervention and Discontinuation or Withdrawal From Trial the statistical analysis that is defined in Section 10 Statistical Considerations Reference the literature for the validation of scales/instruments/questionnaires/assays. Instructions or protocols for specialised tests and scales/instruments/questionnaires/assays may be presented in an appendix or a separate document and cross referenced. If the trial includes qualitative interviews, describe these evaluations. Include minimums and limits for procedures (e.g., number of imaging procedures/biopsies, radiation exposure, etc.) if appropriate to the trial. <p>No text is intended here (heading only).</p> |
| Conformance | Required |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 8 |
| Value | TRIAL ASSESSMENTS AND PROCEDURES |
| Business rules | Value Allowed: No |

| | |
|-------------------------------------|---|
| Term (Variable) | 8 TRIAL ASSESSMENTS AND PROCEDURES |
| | Relationship: Table of Contents Concept: Heading |
| Repeating and/or Reuse Rules | No |

8.1. Trial assessments and procedures considerations

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

| | |
|--|--|
| Term (Variable) | <Trial Assessments and Procedures Considerations> |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C218769 |
| User Guidance | Describe general considerations applicable across trial assessments and procedures. |
| Conformance | Required |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 8.1 |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: 8.1 Trial Assessments and Procedures Considerations Concept: C218769 ICH OID 2.16.840.1.113883.3.989.2.3.3.8 |

| | |
|-------------------------------------|---|
| Term (Variable) | <Trial Assessments and Procedures Considerations> |
| Repeating and/or Reuse Rules | No |

8.2. Screening/baseline assessments and procedures

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

| | |
|--|---|
| Term (Variable) | <Screening Assessments and Procedures> |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C218770 |
| User Guidance | Describe any assessments and procedures that are unique to screening/baseline (e.g., collection of data on participant characteristics, assessments/procedures performed for the purpose of determining eligibility or for stratification) in this section. Describe screening and baseline assessments and procedures separately when screening and baseline are different or performed at different visits. |
| Conformance | Required |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 8.2 |
| Value | Text |
| Business rules | Value Allowed: Yes |

| | |
|-------------------------------------|---|
| Term (Variable) | <Screening Assessments and Procedures> |
| | Relationship: 8.2 Screening/Baseline Assessments and Procedures Concept: C218770 ICH OID 2.16.840.1.113883.3.989.2.3.3.8 |
| Repeating and/or Reuse Rules | No |

| | |
|--|---|
| Term (Variable) | { <Baseline Assessments and Procedures> } |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C218771 |
| User Guidance | Describe any assessments and procedures that are unique to screening/baseline (e.g., collection of data on participant characteristics, assessments/procedures performed for the purpose of determining eligibility or for stratification) in this section. Describe screening and baseline assessments and procedures separately when screening and baseline are different or performed at different visits. |
| Conformance | Conditional: when the Baseline Assessments and Procedures are different from Screening |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 8.2 |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: 8.2 Screening/Baseline Assessments and Procedures Concept: C218771 ICH OID 2.16.840.1.113883.3.989.2.3.3.8 |
| Repeating and/or Reuse Rules | No |

8.3. Efficacy assessments and procedures

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

| | |
|-------------------------------------|---|
| Term (Variable) | 8.3 Efficacy Assessments and Procedures |
| Value | Efficacy Assessments and Procedures |
| Business rules | Value Allowed: No Relationship: 8 TRIAL ASSESSMENTS AND PROCEDURES; Table of Contents Concept: Heading |
| Repeating and/or Reuse Rules | No |

| | |
|--|--|
| Term (Variable) | <Efficacy Assessments and Procedures> |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C218772 |
| User Guidance | Describe efficacy assessments and procedures in this section. Cross reference Section 8.7 Immunogenicity Assessments if immunogenicity assessments are used in efficacy determination. |
| Conformance | Required |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 8.3 |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: 8.3 Efficacy Assessments and Procedures Concept: C218772 ICH OID 2.16.840.1.113883.3.989.2.3.3.8 |
| Repeating and/or Reuse Rules | No |

8.4. Safety assessments and procedures

| | |
|--|---------------------------------------|
| Term (Variable) | 8.4 Safety Assessments and Procedures |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | H |
| Definition | Heading |
| User Guidance | N/A |
| Conformance | Required |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 8.4 |
| Value | Safety Assessments and Procedures |
| Business rules | Value Allowed: No |

| | |
|-------------------------------------|--|
| Term (Variable) | 8.4 Safety Assessments and Procedures |
| | Relationship: 8 TRIAL ASSESSMENTS AND PROCEDURES; Table of Contents. Concept: Heading |
| Repeating and/or Reuse Rules | No |

| | |
|--|---|
| Term (Variable) | <Safety Assessments and Procedures> |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C218773 |
| User Guidance | Describe safety assessments and procedures utilising the following subsections as applicable. Add level 3 headings as needed. <ul style="list-style-type: none"> Identify any noninvestigator party involved in the evaluation of laboratory or other safety assessments (e.g., sponsor or external Independent Data Monitoring Committee; cross reference Section 11.4 Committees for details as applicable). Include guidelines for the medical management of relevant laboratory or other safety assessment abnormalities. |
| Conformance | Required |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 8.4 |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: 8.4 Safety Assessments and Procedures Concept: C218773 ICH OID 2.16.840.1.113883.3.989.2.3.3.8 |
| Repeating and/or Reuse Rules | No |

8.4.1. {Physical examination}

| | |
|---|--|
| Term (Variable) | 8.4.1 {Physical Examination} |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | H |
| Definition | Heading |
| User Guidance | N/A |
| Conformance | Conditional: when Physical Examination is required |
| Cardinality | One to one |
| Relationship content from ToC | 8.4.1 |

| | |
|--|---|
| Term (Variable) | 8.4.1 {Physical Examination} |
| representing the protocol hierarchy | |
| Value | Physical Examination |
| Business rules | Value Allowed: No Relationship: 8.4 Safety Assessment and Procedures; 8 TRIAL ASSESSMENTS AND PROCEDURES; Table of Contents Concept: Heading |
| Repeating and/or Reuse Rules | No |

| | |
|--|--|
| Term (Variable) | {<Physical Examination>} |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C20989 |
| User Guidance | Include any specific instructions for the collection and interpretation of physical examinations. |
| Conformance | Conditional: when Physical Examination is required |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 8.4.1 |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: 8.4.1 Physical Examination Concept: C20989 ICH OID 2.16.840.1.113883.3.989.2.3.3.8 |
| Repeating and/or Reuse Rules | No |

8.4.2. {Vital signs}

| | |
|--|--|
| Term (Variable) | 8.4.2{Vital Signs} |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | H |
| Definition | Heading |
| User Guidance | N/A |
| Conformance | Conditional: when Vital Signs are required |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 8.4.2 |
| Value | Vital Signs |

| | |
|-------------------------------------|--|
| Term (Variable) | 8.4.2{Vital Signs} |
| Business rules | Value Allowed: No Relationship: 8.4 Safety Assessments and Procedures; 8 TRIAL ASSESSMENTS AND PROCEDURES; Table of Contents Concept: Heading |
| Repeating and/or Reuse Rules | No |

| | |
|--|--|
| Term (Variable) | {<Vital Signs>} |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C154628 |
| User Guidance | Include any specific instructions for the collection and interpretation of vital signs. |
| Conformance | Conditional: when Vital Signs are required |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 8.4.2 |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: 8.4.2 Vital Signs Concept: C154628 ICH OID 2.16.840.1.113883.3.989.2.3.3.8 |
| Repeating and/or Reuse Rules | No |

8.4.3. {Electrocardiograms}

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

| | |
|-------------------------------------|---------------------------|
| Term (Variable) | 8.4.3{Electrocardiograms} |
| | Concept: Heading |
| Repeating and/or Reuse Rules | No |

| | |
|--|---|
| Term (Variable) | {<Electrocardiograms>} |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C168186 |
| User Guidance | Include any specific instructions for the collection, interpretation, and archiving of ECGs. |
| Conformance | Conditional: when Electrocardiograms are required |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 8.4.3 |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: 8.4.3 Electrocardiograms Concept: C168186 ICH OID 2.16.840.1.113883.3.989.2.3.3.8 |
| Repeating and/or Reuse Rules | No |

8.4.4. {Clinical laboratory assessments}

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

| | |
|--|---|
| Term (Variable) | {<Clinical Laboratory Assessments>} |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C218774 |
| User Guidance | Describe any specific instructions for the collection and interpretation of clinical laboratory assessments, including: <ul style="list-style-type: none"> • type of laboratory (central/local/hybrid) • acceptability of additional tests deemed necessary by the investigator or local regulations • instructions for situations in which central laboratory results are not available in time for trial intervention and/or response evaluation, or in the event of a severe disruption (e.g., a pandemic or natural disaster) • treatment algorithms for results out of normal range • cross reference Section 12.1 Clinical Laboratory Tests for laboratory assessment panels |
| Conformance | Conditional: when Clinical Laboratory Assessments are required |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 8.4.4 |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: 8.4.4 Clinical Laboratory Assessments Concept: C218774 ICH OID 2.16.840.1.113883.3.989.2.3.3.8 |
| Repeating and/or Reuse Rules | No |

8.4.5. {Pregnancy testing}

| | |
|--|---|
| Term (Variable) | 8.4.5 {Pregnancy Testing} |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | H |
| Definition | Heading |
| User Guidance | N/A |
| Conformance | Conditional: when Pregnancy Testing is required |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 8.4.5 |
| Value | Pregnancy Testing |
| Business rules | Value Allowed: No |

| | |
|-------------------------------------|--|
| Term (Variable) | 8.4.5 {Pregnancy Testing} |
| | Relationship: 8.4 Safety Assessments and Procedures; 8 TRIAL ASSESSMENTS AND PROCEDURES; Table of Contents Concept: Heading |
| Repeating and/or Reuse Rules | No |

| | |
|--|---|
| Term (Variable) | {<Pregnancy Testing>} |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C92949 |
| User Guidance | Include any specific instructions for the collection and interpretation of pregnancy testing. |
| Conformance | Conditional: when Pregnancy Testing is required |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 8.4.5 |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: 8.4.5 Pregnancy Testing Concept: C92949 ICH OID 2.16.840.1.113883.3.989.2.3.3.8 |
| Repeating and/or Reuse Rules | No |

8.4.6. {Suicidal ideation and behaviour risk monitoring}

| | |
|--|---|
| Term (Variable) | 8.4.6 {Suicidal Ideation and Behaviour Risk Monitoring} |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | H |
| Definition | Heading |
| User Guidance | N/A |
| Conformance | Conditional: when Suicidal Ideation and Behaviour Risk Monitoring are required |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 8.4.6 |
| Value | Suicidal Ideation and Behaviour Risk Monitoring |
| Business rules | Value Allowed: No Relationship: 8.4 Safety Assessments and Procedures; 8 TRIAL ASSESSMENTS AND PROCEDURES; Table of Contents |

| | |
|-------------------------------------|---|
| Term (Variable) | 8.4.6 {Suicidal Ideation and Behaviour Risk Monitoring} |
| | Concept: Heading |
| Repeating and/or Reuse Rules | No |

| | |
|--|--|
| Term (Variable) | {<Suicidal Ideation and Behaviour Risk Monitoring>} |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C218775 |
| User Guidance | If the trial meets any of the criteria requiring suicidal ideation and behaviour risk monitoring by the guidance/guideline in each region, include justification for the need for suicidal ideation and behaviour risk monitoring in the study and add any specific instructions for the collection and interpretation of the assessment. In case this is an AESI in the study, justification should also be provided in Section 9.2.4 Adverse Events of Special Interest. |
| Conformance | Conditional: when Suicidal Ideation and Behaviour Risk Monitoring are required |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 8.4.6 |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: 8.4.6 Suicidal Ideation and Behaviour Risk Monitoring Concept: C218775 ICH OID 2.16.840.1.113883.3.989.2.3.3.8 |
| Repeating and/or Reuse Rules | No |

8.5. Pharmacokinetics

| | |
|--|----------------------|
| Term (Variable) | 8.5 Pharmacokinetics |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | H |
| Definition | Heading |
| User Guidance | N/A |
| Conformance | Required |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 8.5 |
| Value | Pharmacokinetics |

| | |
|-------------------------------------|---|
| Term (Variable) | 8.5 Pharmacokinetics |
| Business rules | Value Allowed: No Relationship: 8 TRIAL ASSESSMENTS AND PROCEDURES; Table of Contents Concept: Heading |
| Repeating and/or Reuse Rules | No |

| | |
|--|--|
| Term (Variable) | <Pharmacokinetics> |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C218776 |
| User Guidance | <p>Include any specific instructions for the collection and assay of samples and interpretation of PK assessments.</p> <ul style="list-style-type: none"> Describe the biological samples collected, the handling of samples, and the assay method. <ul style="list-style-type: none"> Specific sample collection and processing instructions can be described in an appendix or a separate document and cross referenced. Describe the retention time for the samples (ensuring alignment with the ICF). Indicate the types of analyses for each sample. Define the PK parameters to be calculated and the calculation methods. |
| Conformance | Required |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 8.5 |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: 8.5 Pharmacokinetics Concept: C218776 ICH OID 2.16.840.1.113883.3.989.2.3.3.8 |
| Repeating and/or Reuse Rules | No |

8.6. Biomarkers

| | |
|---|---|
| Term (Variable) | 8.6 Biomarkers |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | H |
| Definition | Heading |
| User Guidance | Include any specific instructions for the collection of samples and interpretation of biomarkers in the subsections below as applicable. Safety |

| | |
|--|---|
| Term (Variable) | 8.6 Biomarkers |
| | biomarkers should be included in Section 8.4 Safety Assessments and Procedures, and immunogenicity biomarkers should be included in Section 8.7 Immunogenicity Assessments. No text is intended here (heading only). |
| Conformance | Required |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 8.6 |
| Value | Biomarkers |
| Business rules | Value Allowed: No Relationship: 8 TRIAL ASSESSMENTS AND PROCEDURES; Table of Contents Concept: Heading |
| Repeating and/or Reuse Rules | No |

8.6.1. Genetics, genomics, pharmacogenetics, and pharmacogenomics

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

| | |
|---|---|
| Term (Variable) | <Genetics, Genomics, Pharmacogenetics and Pharmacogenomics> |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C218777 |

| | |
|--|--|
| Term (Variable) | <Genetics, Genomics, Pharmacogenetics and Pharmacogenomics> |
| User Guidance | <p>Include any specific instructions for the collection and assay of samples for genetic, genomics, pharmacogenetics and/or pharmacogenomic analysis.</p> <ul style="list-style-type: none"> Describe the biological samples that will be collected (e.g., tissue, serum, plasma), handling of samples, and the assay method. <ul style="list-style-type: none"> Specific sample collection and processing instructions can be described in an appendix or a separate document and cross referenced. Describe the retention time for the samples (ensuring alignment with the ICF). Indicate the types of analyses that may be studied for each sample. |
| Conformance | Required |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 8.6.1 |
| Value | Text |
| Business rules | <p>Value Allowed: Yes</p> <p>Relationship: 8.6.1 Genetics, Genomics, Pharmacogenetics, and Pharmacogenomics</p> <p>Concept: C218777 ICH OID 2.16.840.1.113883.3.989.2.3.3.8</p> |
| Repeating and/or Reuse Rules | No |

8.6.2. Pharmacodynamic biomarkers

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

| | |
|--|---|
| Term (Variable) | <Pharmacodynamic Biomarkers> |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C218778 |
| User Guidance | <p>Include any specific instructions for the collection of samples and assessment of pharmacodynamic biomarkers.</p> <ul style="list-style-type: none"> Describe the biological samples that will be collected (e.g., tissue, serum, plasma). <ul style="list-style-type: none"> Specific sample collection and processing instructions can be described in an appendix or a separate document and cross referenced. Describe the retention time for the samples (ensuring alignment with the ICF). Indicate the types of biomarkers that will be studied for each sample. Specify whether each sample is optional or required. Required samples must be based on a protocol objective. |
| Conformance | Required |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 8.6.2 |
| Value | Text |
| Business rules | <p>Value Allowed: Yes</p> <p>Relationship: 8.6.2 Pharmacodynamic Biomarkers</p> <p>Concept: C218778 ICH OID 2.16.840.1.113883.3.989.2.3.3.8</p> |
| Repeating and/or Reuse Rules | No |

8.6.3. {Other biomarkers}

| | |
|--|---|
| Term (Variable) | 8.6.3 {Other Biomarkers} |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | H |
| Definition | Heading |
| User Guidance | N/A |
| Conformance | Conditional: when Other Biomarkers are required |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 8.6.3 |
| Value | Other Biomarkers |
| Business rules | Value Allowed: No |

| | |
|-------------------------------------|---|
| Term (Variable) | 8.6.3 {Other Biomarkers} |
| | Relationship: 8.6 Biomarkers; 8 TRIAL ASSESSMENTS AND PROCEDURES; Table of Contents Concept: Heading |
| Repeating and/or Reuse Rules | No |

| | |
|--|---|
| Term (Variable) | {<Other Biomarkers>} |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C218779 |
| User Guidance | <p>Include any specific instructions for the collection of samples and assessment of other biomarkers.</p> <ul style="list-style-type: none"> Describe the biological samples that will be collected (e.g., tissue, serum, plasma). <ul style="list-style-type: none"> Specific sample collection and processing instructions can be described in an appendix or a separate document and cross referenced. Describe the retention time for the samples (ensuring alignment with the ICF). Indicate the types of biomarkers that will be studied for each sample. Specify whether each sample is optional or required. Required samples must be based on a protocol objective. |
| Conformance | Conditional: when Other Biomarkers are required |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 8.6.3 |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: 8.6.3 Other Biomarkers Concept: C218779 ICH OID 2.16.840.1.113883.3.989.2.3.3.8 |
| Repeating and/or Reuse Rules | No |

8.7. Immunogenicity assessments

| | |
|---|--------------------------------|
| Term (Variable) | 8.7 Immunogenicity Assessments |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | H |
| Definition | Heading |
| User Guidance | N/A |
| Conformance | Required |

| | |
|--|---|
| Term (Variable) | 8.7 Immunogenicity Assessments |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 8.7 |
| Value | Immunogenicity Assessments |
| Business rules | Value Allowed: No Relationship: 8 TRIAL ASSESSMENTS AND PROCEDURES; Table of Contents Concept: Heading |
| Repeating and/or Reuse Rules | No |

| | |
|--|---|
| Term (Variable) | <Immunogenicity Assessments> |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C218780 |
| User Guidance | <p>Include any specific instructions for the collection of samples and interpretation of immunogenicity. If immunogenicity assessments are included within Section 8.3 Efficacy Assessments and Procedures or Section 8.4 Safety Assessments and Procedures, cross reference that section.</p> <ul style="list-style-type: none"> Describe the biological samples that will be collected (e.g., tissue, serum, plasma). <ul style="list-style-type: none"> Specific sample collection and processing instructions can be described in an appendix or a separate document and cross referenced. Describe the retention time for the samples (ensuring alignment with the ICF). Indicate the types of biomarkers that will be studied for each sample. Specify whether each sample is optional or required. Required samples must be based on a protocol objective. |
| Conformance | Required |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 8.7 |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: 8.7 Immunogenicity Assessments Concept: C218780 ICH OID 2.16.840.1.113883.3.989.2.3.3.8 |
| Repeating and/or Reuse Rules | No |

8.8. Medical resource utilisation and health economics

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

| | |
|--|---|
| Term (Variable) | <Medical Resource Utilisation and Health Economics> |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C176849 |
| User Guidance | This section does not apply to COAs. Include this section only for any value evidence and outcomes assessments not included in either the efficacy or safety sections. Describe the health outcome measures, collection method (e.g., diary, physician interview), and participant burden. |
| Conformance | Required |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 8.8 |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: 8.8 Medical Resource Utilisation and Health Economics Concept: C176849 ICH OID 2.16.840.1.113883.3.989.2.3.3.8 |
| Repeating and/or Reuse Rules | No |

9. Adverse events, serious adverse events, product complaints, pregnancy and postpartum information, and special safety situations

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

9.1. Definitions

| | |
|--|--|
| Term (Variable) | 9.1 Definitions |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | H |
| Definition | Heading |
| User Guidance | No text is intended here (heading only). |
| Conformance | Required |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 9.1 |
| Value | Definitions |
| Business rules | Value Allowed: No Relationship: 9 ADVERSE EVENTS, SERIOUS ADVERSE EVENTS, PRODUCT COMPLAINTS, PREGNANCY AND POSTPARTUM INFORMATION, AND SPECIAL SAFETY SITUATIONS; Table of Contents Concept: Heading |

| | |
|------------------------------|-----------------|
| Term (Variable) | 9.1 Definitions |
| Repeating and/or Reuse Rules | No |

9.1.1. Definitions of adverse events

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

| | |
|--|--|
| Term (Variable) | <Definitions of Adverse Events> |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C218476 |
| User Guidance | Specify the AE definitions, including: <ul style="list-style-type: none"> any relevant regional AE requirements any events that meet and do not meet the AE definition any trial-specific AE clarifications if applicable, any clarifications on the AE and SAE definitions for efficacy trials (e.g., lack of efficacy or failure of pharmacological actions) |
| Conformance | Required |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 9.1.1 |
| Value | Text |

| | |
|-------------------------------------|--|
| Term (Variable) | <Definitions of Adverse Events> |
| Business rules | Value Allowed: Yes Relationship: 9.1.1 Definitions of Adverse Events Concept: C218476 ICH OID 2.16.840.1.113883.3.989.2.3.3.9 |
| Repeating and/or Reuse Rules | No |

9.1.2. Definitions of serious adverse events

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

| | |
|--|--|
| Term (Variable) | <Definitions of Serious Adverse Events> |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C218781 |
| User Guidance | Specify the SAE definitions, including: <ul style="list-style-type: none"> any relevant regional SAE requirements any events that meet and do not meet the SAE definition any trial-specific SAE clarifications |
| Conformance | Required |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 9.1.2 |
| Value | Text |

| | |
|-------------------------------------|--|
| Term (Variable) | <Definitions of Serious Adverse Events> |
| Business rules | Value Allowed: Yes Relationship: 9.1.2 Definitions of Serious Adverse Events Concept: C218781 ICH OID 2.16.840.1.113883.3.989.2.3.3.9 |
| Repeating and/or Reuse Rules | No |

9.1.3. Definitions of product complaints

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

| | |
|--|--|
| Term (Variable) | <Definitions of Product Complaints> |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C218782 |
| User Guidance | Specify the definitions of product complaints in the context of the trial. |
| Conformance | Required |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 9.1.3 |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: 9.1.3 Definitions of Product Complaints Concept: C218782 ICH OID 2.16.840.1.113883.3.989.2.3.3.9 |

| | |
|-------------------------------------|-------------------------------------|
| Term (Variable) | <Definitions of Product Complaints> |
| Repeating and/or Reuse Rules | No |

9.1.3.1. {Definitions of medical device product complaints}

| | |
|--|--|
| Term (Variable) | 9.1.3.1 {Definitions of Medical Device Product Complaints} |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | H |
| Definition | Heading |
| User Guidance | N/A |
| Conformance | Conditional: when there is Medical Device Product Complaints |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 9.1.3.1 |
| Value | Definitions of Medical Device Product Complaints |
| Business rules | Value Allowed: No Relationship: 9.3.1 Definition of Product Complaints; 9.1 Definitions; 9 ADVERSE EVENTS, SERIOUS ADVERSE EVENTS, PRODUCT COMPLAINTS, PREGNANCY AND POSTPARTUM INFORMATION, AND SPECIAL SAFETY SITUATIONS; Table of Contents. Concept: Heading |
| Repeating and/or Reuse Rules | No |

| | |
|--|---|
| Term (Variable) | {<Definitions of Medical Device Product Complaints>} |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C218783 |
| User Guidance | N/A |
| Conformance | Conditional: when there is Medical Device Product Complaints |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 9.1.3.1 |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: 9.1.3.1 Definitions of Medical Device Product Complaints Concept: C218783 ICH OID 2.16.840.1.113883.3.989.2.3.3.9 |
| Repeating and/or Reuse Rules | No |

9.2. Timing and procedures for collection and reporting

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

| | |
|--|---|
| Term (Variable) | This table describes the timing and procedures for collecting and reporting events. |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | H |
| Definition | Optional text |
| User Guidance | Specify timing and procedures for collection and reporting of AEs, SAEs, product complaints (including medical device product complaints if applicable) and pregnancy and postpartum information in the sections below. This information may be summarised in a tabular format as shown in the example table below. |
| Conformance | Optional |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 9.2 |
| Value | This table describes the timing and procedures for collecting and reporting events. |
| Business rules | Value Allowed: No Relationship: Timing and Procedures for Collection and Reporting Concept: Optional text |

| | |
|-------------------------------------|---|
| Term (Variable) | This table describes the timing and procedures for collecting and reporting events. |
| Repeating and/or Reuse Rules | No |

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

| | |
|--|---|
| Term (Variable) | <Event Type> |
| Data Type | Valid Value |
| Data (D), Value (V) or Heading (H) | V |
| Definition | C218784 |
| User Guidance | N/A |
| Conformance | Optional if the table is used |
| Cardinality | One to many |
| Relationship content from ToC representing the protocol hierarchy | 9.2 |
| Value | Code List C217287: ICH OID 2.16.840.1.113883.3.989.2.3.1.22 Adverse Event (C41331), Serious Adverse Event (C41335), Trial Intervention Complaint (C218508), Drug/Device Combination Product Complaint (C222331), Pregnancy Event (C25742), Lactation Event (C218510), Post-Partum Event (C218511), Reportable Adverse Event of Special Interest (C218512), Not Reportable Adverse Event of Special Interest (C218513), Other (C17649) |
| Business rules | Value Allowed: Yes Relationship: Event Type |

| | |
|-------------------------------------|---|
| Term (Variable) | <Event Type> |
| | Concept: C218784 ICH OID 2.16.840.1.113883.3.989.2.3.3.9 |
| Repeating and/or Reuse Rules | Yes, repeatable for each Event Type |

| | |
|--|--|
| Term (Variable) | <Other Event Type> |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C222263 |
| User Guidance | N/A |
| Conformance | Optional if table used |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 9.2 |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: Other Concept: C222263 ICH OID 2.16.840.1.113883.3.989.2.3.3.9 |
| Repeating and/or Reuse Rules | No |

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

| | |
|--|--|
| Term (Variable) | <Situational Scope> |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C218785 |
| User Guidance | N/A |
| Conformance | Optional if table used |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 9.2 |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: Event Type, Situational Scope Concept: C218785 ICH OID 2.16.840.1.113883.3.989.2.3.3.9 |
| Repeating and/or Reuse Rules | Yes, repeatable for each Event Type |

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

| | |
|---|---------------------------|
| Term (Variable) | <Reportable Period Start> |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C218786 |
| User Guidance | N/A |
| Conformance | Optional if table used |

| | |
|--|--|
| Term (Variable) | <Reportable Period Start> |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 9.2 |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: Event Type; Situational Scope Concept: C218786 ICH OID 2.16.840.1.113883.3.989.2.3.3.9 |
| Repeating and/or Reuse Rules | Yes, repeatable for each Event Type and Situational Scope |

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

| | |
|--|--------------------------------------|
| Term (Variable) | <Reportable Period End> |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C218787 |
| User Guidance | N/A |
| Conformance | Optional if table used |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 9.2 |
| Value | Text |

| | |
|-------------------------------------|---|
| Term (Variable) | <Reportable Period End> |
| Business rules | Value Allowed: Yes Relationship: Event Type; Situational Scope; Reportable Period Start Concept: C218787 ICH OID 2.16.840.1.113883.3.989.2.3.3.9 |
| Repeating and/or Reuse Rules | Yes, repeatable for each Reportable Period Start |

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

| | |
|--|--|
| Term (Variable) | <Timing for Reporting to Sponsor or Designee> |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C218788 |
| User Guidance | N/A |
| Conformance | Optional if table used |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 9.2 |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: Event Type, Situational Scope Concept: C218788 ICH OID 2.16.840.1.113883.3.989.2.3.3.9 |
| Repeating and/or Reuse Rules | Yes, repeatable for each Event Type, Situational Scope, and Reportable Period Start |

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

| | |
|--|--|
| Term (Variable) | <Method for Reporting> |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C218789 |
| User Guidance | N/A |
| Conformance | Optional if used |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 9.2 |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: Event Type, Situational Scope Concept: C218789 ICH OID 2.16.840.1.113883.3.989.2.3.3.9 |
| Repeating and/or Reuse Rules | Yes, repeatable for each Event Type, Situational Scope and Reportable Period Start |

| | |
|---|------------------------------|
| Term (Variable) | Back-up Method for Reporting |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | H |
| Definition | Table Column Heading |
| User Guidance | N/A |

| | |
|--|--|
| Term (Variable) | Back-up Method for Reporting |
| Conformance | Optional if table is used |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 9.2 |
| Value | Back-up Method for Reporting |
| Business rules | Value Allowed: No Relationship: Table Column Heading Concept: Heading |
| Repeating and/or Reuse Rules | No |

| | |
|--|--|
| Term (Variable) | <Back-up Method for Reporting> |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C218790 |
| User Guidance | N/A |
| Conformance | Optional if table is used |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 9.2 |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: Event Type; Situational Scope Concept: C218790 ICH OID 2.16.840.1.113883.3.989.2.3.3.9 |
| Repeating and/or Reuse Rules | Yes, repeatable for each Event Type, Situational Scope, and Reportable Period Start. |

9.2.1. Timing

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

| | |
|--|--|
| Term (Variable) | 9.2.1 Timing |
| representing the protocol hierarchy | |
| Value | Timing |
| Business rules | Value Allowed: No Relationship: 9.2 Timing and Procedures for Collection and Reporting, 9 ADVERSE EVENTS, SERIOUS ADVERSE EVENTS, PRODUCT COMPLAINTS, PREGNANCY AND POSTPARTUM INFORMATION, AND SPECIAL SAFETY SITUATIONS; Table of Contents Concept: Heading |
| Repeating and/or Reuse Rules | No |

| | |
|--|---|
| Term (Variable) | <Event Collection and Reporting Timing> |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C218791 |
| User Guidance | Specify timing for collection and reporting, including: start and end dates for collection and reporting frequency of collection and reporting cross reference to the Schedule of Assessments as appropriate |
| Conformance | Required |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 9.2.1 |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: 9.2.1 Timing Concept: C218791 ICH OID 2.16.840.1.113883.3.989.2.3.3.9 |
| Repeating and/or Reuse Rules | No |

9.2.2. Collection procedures

| | |
|---|--|
| Term (Variable) | 9.2.2 Collection Procedures |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | H |
| Definition | Heading |
| User Guidance | Specify procedures for collection and recording of AEs, SAEs, product complaints (including medical device product complaints if applicable) and pregnancy and postpartum information in the sections below. |
| Conformance | Required |

| | |
|--|---|
| Term (Variable) | 9.2.2 Collection Procedures |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 9.2.2 |
| Value | Collection Procedures |
| Business rules | Value Allowed: No Relationship: 9.2 Timing and Procedures for Collection and Reporting; 9 ADVERSE EVENTS, SERIOUS ADVERSE EVENTS, PRODUCT COMPLAINTS, PREGNANCY AND POSTPARTUM INFORMATION, AND SPECIAL SAFETY SITUATIONS; Table of Contents. Concept: Heading |
| Repeating and/or Reuse Rules | No |

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

| | |
|---|--|
| Term (Variable) | <Identification> |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C218792 |
| User Guidance | Specify how information will be identified (e.g., self-reported, solicited questions). |

| | |
|--|---|
| Term (Variable) | <Identification> |
| Conformance | Required |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 9.2.2 |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: Identification and 9.2.2 Collection Procedures Concept: C218792 ICH OID 2.16.840.1.113883.3.989.2.3.3.9 |
| Repeating and/or Reuse Rules | No |

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

| | |
|---|--|
| Term (Variable) | <Severity> |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C25676 |
| User Guidance | Specify the intensity rating categories/scale. |
| Conformance | Required |
| Cardinality | One to one |

| | |
|--|---|
| Term (Variable) | <Severity> |
| Relationship content from ToC representing the protocol hierarchy | 9.2.2 |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: Severity; 9.2.2 Collection Procedures Concept: C25676 ICH OID 2.16.840.1.113883.3.989.2.3.3.9 |
| Repeating and/or Reuse Rules | No |

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

| | |
|---|---|
| Term (Variable) | <Causality> |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C82552 |
| User Guidance | Specify: <ul style="list-style-type: none"> the causality categories/scale procedures for assessing causality |
| Conformance | Required |
| Cardinality | One to one |

| | |
|--|--|
| Term (Variable) | <Causality> |
| Relationship content from ToC representing the protocol hierarchy | 9.2.2 |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: Causality; 9.2.2 Collection Procedures Concept: C82552 ICH OID 2.16.840.1.113883.3.989.2.3.3.9 |
| Repeating and/or Reuse Rules | No |

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

| | |
|---|-----------------------------------|
| Term (Variable) | <Recording> |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C218793 |
| User Guidance | Specify procedures for recording. |
| Conformance | Required |
| Cardinality | One to one |
| Relationship content from ToC | 9.2.2 |

| | |
|--|---|
| Term (Variable) | <Recording> |
| representing the protocol hierarchy | |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: Recording; 9.2.2 Collection Procedures Concept: C218793 ICH OID 2.16.840.1.113883.3.989.2.3.3.9 |
| Repeating and/or Reuse Rules | No |

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

| | |
|---|--|
| Term (Variable) | <Follow-up> |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C218794 |
| User Guidance | Specify the procedures for follow-up. Include the assessment tools that will be used to monitor the events and the duration of follow-up after appearance of the events. |
| Conformance | Required |
| Cardinality | One to one |
| Relationship content from ToC | 9.2.2 |

| | |
|--|--|
| Term (Variable) | <Follow-up> |
| representing the protocol hierarchy | |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: Follow-up and 9.2.2 Collection Procedures Concept: C218794 ICH OID 2.16.840.1.113883.3.989.2.3.3.9 |
| Repeating and/or Reuse Rules | No |

9.2.3. Reporting

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

| | |
|---|--|
| Term (Variable) | <Reporting> |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C218795 |
| User Guidance | Specify the reporting method (e.g., an electronic data collection tool or a paper CRF), backup reporting method, if applicable, and reporting timeline to the sponsor. |
| Conformance | Required |
| Cardinality | One to one |
| Relationship content from ToC | 9.2.3 |

| | |
|--|--|
| Term (Variable) | <Reporting> |
| representing the protocol hierarchy | |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: 9.2.3 Reporting Concept: C218795 ICH OID 2.16.840.1.113883.3.989.2.3.3.9 |
| Repeating and/or Reuse Rules | No |

9.2.3.1. Regulatory Reporting Requirements

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

| | |
|---|--|
| Term (Variable) | <Regulatory Reporting Requirements> |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C218796 |
| User Guidance | Specify: <ul style="list-style-type: none"> the investigator's responsibilities for reporting to the sponsor (and to ethics committees, where required), specifying timing of reporting to allow the sponsor to meet their responsibilities the sponsor's legal/regulatory responsibilities for reporting to regulatory authorities, ethics committees, and investigators suspected unexpected serious adverse reaction reporting |

| | |
|--|--|
| Term (Variable) | <Regulatory Reporting Requirements> |
| Conformance | Required |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 9.2.3.1 |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: 9.2.3.1 Regulatory Reporting Requirements Concept: C218796 ICH OID 2.16.840.1.113883.3.989.2.3.3.9 |
| Repeating and/or Reuse Rules | No |

9.2.4. Adverse events of special interest

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

| | |
|---|---|
| Term (Variable) | {<Adverse Events of Special Interest>} Or {<Not applicable>} |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C217358 |

| | |
|--|--|
| Term (Variable) | {<Adverse Events of Special Interest>} Or {<Not applicable>} |
| User Guidance | Specify any AESI, including: <ul style="list-style-type: none"> any event (serious or nonserious) of scientific and medical concern relative to the trial intervention, for which ongoing monitoring and rapid communication by the investigator to the sponsor can be appropriate other events that merit reporting to the sponsor, trial leadership, IRB, and regulatory agencies Include the following for each AESI: <ul style="list-style-type: none"> the definition the approach for ascertaining information if applicable, any approach to confirm or adjudicate the event |
| Conformance | Required |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 9.2.4 |
| Value | Text or state "Not applicable" |
| Business rules | Value Allowed: Yes Relationship: 9.2.4 Adverse Events of Special Interest Concept: C217358 ICH OID 2.16.840.1.113883.3.989.2.3.3.9 |
| Repeating and/or Reuse Rules | No |

9.2.5. Disease-related events or outcomes not qualifying as AEs or SAEs

| | |
|--|--|
| Term (Variable) | 9.2.5 Disease-related Events or Outcomes Not Qualifying as AEs or SAEs |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | H |
| Definition | Heading |
| User Guidance | N/A |
| Conformance | Required |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 9.2.5 |
| Value | Disease-related Events or Outcomes Not Qualifying as AEs or SAEs |
| Business rules | Value Allowed: No Relationship: 9.2 Timing and Procedures for Collection and Reporting; 9 ADVERSE EVENTS, SERIOUS ADVERSE EVENTS, PRODUCT COMPLAINTS, |

| | |
|-------------------------------------|---|
| Term (Variable) | 9.2.5 Disease-related Events or Outcomes Not Qualifying as AEs or SAEs |
| | PREGNANCY AND POSTPARTUM INFORMATION, AND SPECIAL SAFETY SITUATIONS; Table of Contents Concept: Heading |
| Repeating and/or Reuse Rules | No |

| | |
|--|---|
| Term (Variable) | <Disease-related Events or Outcomes Not Qualifying as AEs or SAEs> |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C218797 |
| User Guidance | Specify any DREs, DROs, or both that will not be reported as AEs or SAEs (e.g., seizures in anticonvulsant trials) or state "Not applicable." |
| Conformance | Required |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 9.2.5 |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: 9.2.5 Disease-related Events or Outcomes Not Qualifying as AEs or SAEs Concept: C218797 ICH OID 2.16.840.1.113883.3.989.2.3.3.9 |
| Repeating and/or Reuse Rules | No |

9.3. Pregnancy and postpartum information

| | |
|---|---|
| Term (Variable) | 9.3 Pregnancy and Postpartum Information |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | H |
| Definition | Heading |
| User Guidance | Whenever possible, pregnancy (direct or via partner) should be documented and followed up to collect relevant pregnancy outcomes. Any negative or consequential outcome(s) in the pregnant participant/partner or foetus, neonate or infant should be reported as an AE or SAE. Refer to Section 9.2 Timing and Procedures for Collection and Reporting for AE and SAE related procedures as applicable. If the negative event meets the seriousness criteria, then this is considered an SAE (e.g., spontaneous abortion, foetal death, stillbirth, congenital anomalies, ectopic pregnancy, or pre-eclampsia) and reported per Section 9.2.3 Reporting. |

| | |
|--|--|
| Term (Variable) | 9.3 Pregnancy and Postpartum Information |
| | No text is intended here (heading only). |
| Conformance | Required |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 9.3 |
| Value | Pregnancy and Postpartum Information |
| Business rules | Value Allowed: No Relationship: 9 ADVERSE EVENTS, SERIOUS ADVERSE EVENTS, PRODUCT COMPLAINTS, PREGNANCY AND POSTPARTUM INFORMATION, AND SPECIAL SAFETY SITUATIONS; Table of Contents Concept: Heading |
| Repeating and/or Reuse Rules | No |

9.3.1. {Participants who become pregnant during the trial}

| | |
|--|--|
| Term (Variable) | 9.3.1 {Participants Who Become Pregnant During the Trial} |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | H |
| Definition | Heading |
| User Guidance | N/A |
| Conformance | Conditional: when collecting pregnancy data for a trial participant who becomes pregnant during the trial. |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 9.3.1 |
| Value | Participants Who Become Pregnant During the Trial |
| Business rules | Value Allowed: No Relationship: 9.3 Pregnancy and Postpartum Information; 9 ADVERSE EVENTS, SERIOUS ADVERSE EVENTS, PRODUCT COMPLAINTS, PREGNANCY AND POSTPARTUM INFORMATION, AND SPECIAL SAFETY SITUATIONS; Table of Contents Concept: Heading |
| Repeating and/or Reuse Rules | No |

| | |
|------------------------|---|
| Term (Variable) | {<Participants Who Become Pregnant During the Trial>} |
| Data Type | Text |

| | |
|--|---|
| Term (Variable) | {<Participants Who Become Pregnant During the Trial>} |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C218798 |
| User Guidance | <p>Specify:</p> <ul style="list-style-type: none"> the assessments to be performed type and duration of monitoring whether participants who become pregnant during the trial may continue with trial intervention or must be discontinued from trial intervention (refer to Section 7 Participant Discontinuation of Trial Intervention and Discontinuation or Withdrawal from Trial as applicable) any trial modifications that need to be made for participants who become pregnant what information will be collected about a participant who becomes pregnant during the trial (e.g., recording and reporting to the sponsor, postpartum follow-up, trial intervention discontinuation or continuation, or trial withdrawal) <p>For postpartum follow-up, include the time period (e.g., initial child development) with justification.</p> <p>If exposure to trial intervention during breastfeeding is applicable, specify:</p> <ul style="list-style-type: none"> the assessments to be performed type and duration of monitoring information to be collected for both the participant and child |
| Conformance | Conditional: when collecting pregnancy data for a trial participant who becomes pregnant during the trial. |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 9.3.1 |
| Value | Text |
| Business rules | <p>Value Allowed: Yes</p> <p>Relationship: 9.3.1 Participants Who Become Pregnant During the Trial</p> <p>Concept: C218798 ICH OID 2.16.840.1.113883.3.989.2.3.3.9</p> |
| Repeating and/or Reuse Rules | No |

9.3.2. {Participants whose partners become pregnant}

| | |
|---|--|
| Term (Variable) | 9.3.2 {Participants Whose Partners Become Pregnant During the Trial} |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | H |
| Definition | Heading |
| User Guidance | N/A |

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

| | |
|--|--|
| Term (Variable) | {<Participants Whose Partners Become Pregnant During the Trial>} |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C218799 |
| User Guidance | Specify: whether the investigator will attempt to collect pregnancy information about a participant's partner who becomes pregnant during the specified period in the trial whether the participant whose partner becomes pregnant should be discontinued from trial intervention (refer to Section 7 Participant Discontinuation of Trial Intervention and Discontinuation or Withdrawal from Trial as applicable) the assessments to be performed, type and duration of monitoring, and the information to be collected |
| Conformance | Conditional: when collecting pregnancy data for the partner of a trial participant who becomes pregnant during the trial. |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 9.3.2 |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: 9.3.2 Participants Whose Partners Become Pregnant During the Trial Concept: C218799 ICH OID 2.16.840.1.113883.3.989.2.3.3.9 |

| | |
|-------------------------------------|--|
| Term (Variable) | {<Participants Whose Partners Become Pregnant During the Trial>} |
| Repeating and/or Reuse Rules | No |

9.4. Special safety situations

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

| | |
|---|--|
| Term (Variable) | <Special Safety Situations> |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C218800 |
| User Guidance | Specify special safety situations associated with the trial intervention(s) that do not qualify as an AE or SAE but require regulatory reporting. Examples include: <ul style="list-style-type: none"> • misuse or abuse • off-label use (if applicable) • medication error (prescription or dispensing error) • occupational exposure • use outside of what is foreseen in the protocol • unintended exposure of embryo, foetus, or child via maternal exposure (pregnancy or breastfeeding) or via paternal exposure (semen) • lack of therapeutic efficacy; this is not applicable for studies that measure efficacy as a study endpoint • suspected transmission of an infectious agent; this is only applicable for injected or biologic medicinal products |

| | |
|--|--|
| Term (Variable) | <Special Safety Situations> |
| | <ul style="list-style-type: none"> product complaint, including falsified or counterfeit products suspected drug-food or drug-drug interaction |
| Conformance | Required |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 9.4 |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: 9.4 Special Safety Situations Concept: C218800 ICH OID 2.16.840.1.113883.3.989.2.3.3.9 |
| Repeating and/or Reuse Rules | No |

10. Statistical considerations

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

10.1. General considerations

| | |
|------------------------|-----------------------------|
| Term (Variable) | 10.1 General Considerations |
| Data Type | Text |

| | |
|--|--|
| Term (Variable) | 10.1 General Considerations |
| Data (D), Value (V) or Heading (H) | H |
| Definition | Heading |
| User Guidance | N/A |
| Conformance | Required |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 10.1 |
| Value | General Considerations |
| Business rules | Value Allowed: No Relationship: 10 STATISTICAL CONSIDERATIONS; Table of Contents Concept: Heading |
| Repeating and/or Reuse Rules | No |

| | |
|--|--|
| Term (Variable) | <General Considerations> |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C164387 |
| User Guidance | Provide general statements related to statistical considerations, such as whether a separate statistical analysis plan exists, which summary statistics will be provided, and the timing of analyses (e.g., "The analysis will include all participant data at trial completion"). |
| Conformance | Required |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 10.1 |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: 10.1 General Considerations; 10 STATISTICAL CONSIDERATIONS; Table of Contents Concept: C164387 ICH OID 2.16.840.1.113883.3.989.2.3.3.10 |
| Repeating and/or Reuse Rules | No |

10.2. Analysis sets

| | |
|------------------------|--------------------|
| Term (Variable) | 10.2 Analysis Sets |
| Data Type | Text |

| | |
|--|--|
| Term (Variable) | 10.2 Analysis Sets |
| Data (D), Value (V) or Heading (H) | H |
| Definition | Heading |
| User Guidance | N/A |
| Conformance | Required |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 10.2 |
| Value | Analysis Sets |
| Business rules | Value Allowed: No Relationship: 10 STATISTICAL CONSIDERATIONS; Table of Contents Concept: Heading |
| Repeating and/or Reuse Rules | No |

| | |
|--|--|
| Term (Variable) | <Analysis Sets> |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C218801 |
| User Guidance | Describe analysis sets to be considered at the trial level, i.e., the set of participants whose data are to be included in the analyses, aligned with estimands. Clearly specify the analysis set to be used for each analysis described in Section 10 Statistical Considerations. |
| Conformance | Required |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 10.2 |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: 10.2 Analysis Sets; 10 STATISTICAL CONSIDERATIONS; Table of Contents Concept: C218801 ICH OID 2.16.840.1.113883.3.989.2.3.3.10 |
| Repeating and/or Reuse Rules | No |

10.3. Analyses of demographics and other baseline variables

| | |
|------------------------|---|
| Term (Variable) | 10.3 Analyses of Demographics and Other Baseline Variables |
| Data Type | Text |

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

| | |
|--|---|
| Term (Variable) | <Analyses of Demographics and Other Baseline Variables> |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C218802 |
| User Guidance | Describe the summary statistics that will be used to characterise the distribution of demographic and other relevant variables at baseline. Specify when the variables will be measured (e.g., at trial inclusion, prior to randomisation, or at the time of randomisation). Relevant variables include but are not limited to: stratification variables specified in Section 6.7 Investigational Trial Intervention Assignment, Randomisation and Blinding, covariates for the statistical models specified in Section 10.4 Analyses Associated with the Primary Objective(s), other suspected predictive or prognostic variables, and variables used for planned subgroup analyses. |
| Conformance | Required |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 10.3 |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: 10.3 Analyses of Demographics and Other Baseline Variables; 10 STATISTICAL CONSIDERATIONS; Table of Contents Concept: C218802 ICH OID 2.16.840.1.113883.3.989.2.3.3.10 |
| Repeating and/or Reuse Rules | No |

10.4. Analyses associated with the primary objective(s)

| | |
|--|---|
| Term (Variable) | 10.4 Analyses Associated with the Primary Objective(s) |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | H |
| Definition | Heading |
| User Guidance | Include additional level 3 headings for each primary objective as needed. If there is more than one primary objective, number each objective consecutively as the level 3 heading (e.g., Primary Objective 1, Primary Objective 2, etc.). No text is intended here (heading only). |
| Conformance | Required |
| Cardinality | One to many |
| Relationship content from ToC representing the protocol hierarchy | 10.4 |
| Value | Analyses Associated with the Primary Objective(s) |
| Business rules | Value Allowed: No Relationship: 10 STATISTICAL CONSIDERATIONS; Table of Contents Concept: Heading |
| Repeating and/or Reuse Rules | No |

10.4.1. Primary objective <#>

| | |
|--|---|
| Term (Variable) | 10.4.X Primary Objective <#> |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | H |
| Definition | Heading |
| User Guidance | No text is intended here (heading only). |
| Conformance | Required: Collection for each Primary Objective (e.g., 10.4.1, 10.4.2, 10.4.3, 10.4.4, 10.4.5). For more than one Primary Objective repeat the collection as level 4 headings where X is = to the number of Primary Objectives |
| Cardinality | One to many |
| Relationship content from ToC representing the protocol hierarchy | 10.4.X |
| Value | Primary Objective <#>: # is a unique number for each Primary Objective; if there is only one Primary Objective, # is blank. If more than one Primary Objective, add sequential unique number for each objective. |
| Business rules | Value Allowed: No |

| | |
|-------------------------------------|---|
| Term (Variable) | 10.4.X Primary Objective <#> |
| | Relationship: 3.1.X Primary Objective <#>; 10.4 Analyses Associated with the Primary Objective(s); 10 STATISTICAL CONSIDERATIONS; Table of Contents Concept: Heading |
| Repeating and/or Reuse Rules | Yes, repeatable for each objective. |

10.4.1.1. Statistical analysis method

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

| | |
|---|--|
| Term (Variable) | <Statistical Analysis Method > |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C218482 |
| User Guidance | Describe the statistical analysis methods that will be used to evaluate the primary objective(s) and associated estimand(s) in Section 3.1 Primary Objective(s) and Associated Estimand(s). Ensure that the statistical hypothesis/model/analysis (and corresponding assumptions) is aligned with the primary estimand(s). For each objective, when applicable, state the null and alternative hypotheses, including the pre-planned type 1 error rate, or alternative criteria for evaluating whether the objective has been met, and relevant operating characteristics if appropriate. Describe the statistical model used |

| | |
|--|---|
| Term (Variable) | <Statistical Analysis Method > |
| | and the factors that will be included (e.g., covariates and interactions) and any rules for handling these factors (e.g., pooling of centres). If modelling and simulation methods are to be used, describe the model (inputs and outputs), the underlying assumptions, and the method of model fitting. |
| Conformance | Required |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 10.4.X.1 |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: 10.4.X.1 Statistical Analysis Method Concept: C218482 ICH OID 2.16.840.1.113883.3.989.2.3.3.10 |
| Repeating and/or Reuse Rules | Yes, repeatable for each objective as a series of level 4 sections (10.4.X.1, 10.4.X.2, 10.4.X.3, 10.4.X.4, 10.4.X.5). |

10.4.1.2. Handling of data in relation to primary estimand(s)

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

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

| | |
|--|---|
| Term (Variable) | <Handling of Data in Relation to Primary Estimand(s)> |
| Definition | C218803 |
| User Guidance | For each intercurrent event of the primary estimand(s) defined in Section 3.1 Primary Objective(s) and Associated Estimand(s), explain how data will be handled for the statistical analysis in line with the primary estimand. The handling of intercurrent events in the statistical analysis should be aligned with the specific estimand strategies being used. This section should describe in more detail the rationale and handling of the data rather than repeating information from the preceding sections. |
| Conformance | Required |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 10.4.X.2 |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: 10.4.X.2 Handling of Data in Relation to Primary Estimand(s) Concept: C218803 ICH OID 2.16.840.1.113883.3.989.2.3.3.10 |
| Repeating and/or Reuse Rules | Yes, repeatable for each objective as a series of level 4 sections (10.4.X.1, 10.4.X.2, 10.4.X.3, 10.4.X.4, 10.4.X.5). |

10.4.1.3. Handling of missing data in relation to primary estimand(s)

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

| | |
|--|--|
| Term (Variable) | <Handling of Missing Data in Relation to Primary Estimand(s)> |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C218804 |
| User Guidance | Describe how missing data will be addressed (e.g., imputation method and model), state the underlying assumptions, and provide a rationale for the approach. |
| Conformance | Required |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 10.4.X.3 |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: 10.4.X.3 Handling of Missing Data Concept: C218804 ICH OID 2.16.840.1.113883.3.989.2.3.3.10 |
| Repeating and/or Reuse Rules | Yes, repeatable for each objective as a series of level 4 sections (10.4.X.1, 10.4.X.2, 10.4.X.3, 10.4.X.4, 10.4.X.5). |

10.4.1.4. {Sensitivity analysis}

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

| | |
|------------------------|--------------------------|
| Term (Variable) | {<Sensitivity Analysis>} |
| Data Type | Text |

| | |
|--|---|
| Term (Variable) | {<Sensitivity Analysis>} |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C218480 |
| User Guidance | Describe any sensitivity analyses and how their assumptions changed from the assumptions of the main statistical analysis. Sensitivity analyses are a series of analyses conducted with the intent to explore the robustness of inferences from the main estimator to deviations from its underlying modelling assumptions and limitations in the data. |
| Conformance | Conditional: when there is Sensitivity Analysis for a Primary Objective |
| Cardinality | One to many |
| Relationship content from ToC representing the protocol hierarchy | 10.4.X.4 |
| Value | Text |
| Business rules | Value Allowed Yes Relationship: 10.4.X.4 Sensitivity Analysis Concept: C218480 ICH OID 2.16.840.1.113883.3.989.2.3.3.10 |
| Repeating and/or Reuse Rules | Yes, repeatable for each objective as a series of level 4 sections (10.4.X.1, 10.4.X.2, 10.4.X.3, 10.4.X.4, 10.4.X.5). |

10.4.1.5. {Supplementary analysis}

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

| | |
|--|--|
| Term (Variable) | {<Supplementary Analysis>} |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C218481 |
| User Guidance | Describe any supplementary analysis, if applicable. Supplementary analyses are conducted in addition to the main and sensitivity analyses with the intent to provide additional insights into the understanding of the treatment effect. |
| Conformance | Conditional: when there is Supplementary Analysis for a Primary Objective |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 10.4.X.5 |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: 10.4.X.5 Supplementary Analysis Concept: C218481 ICH OID 2.16.840.1.113883.3.989.2.3.3.10 |
| Repeating and/or Reuse Rules | Yes, repeatable for each objective as a series of level 4 sections (10.4.X.1, 10.4.X.2, 10.4.X.3, 10.4.X.4, 10.4.X.5). |

10.5. Analysis associated with the secondary objective(s)

| | |
|--|---|
| Term (Variable) | 10.5 Analyses Associated with the Secondary Objective(s) |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | H |
| Definition | Heading |
| User Guidance | Describe the statistical analysis methods that will be used to evaluate the secondary objective(s) and associated estimand(s) in Section 3.2 Secondary Objective(s) and Associated Estimand(s). Use the same section structure as Section 10.4 Analyses Associated with the Primary Objective(s). Include additional level 3 headings for each secondary objective as needed. If there is more than one secondary objective, number each objective consecutively as the level 3 heading (e.g., Secondary Objective 1, Secondary Objective 2, etc.). No text is intended here (heading only) unless there is no secondary objective, in which case indicate "Not applicable." |
| Conformance | Required |
| Cardinality | One to many |
| Relationship content from ToC representing the protocol hierarchy | 10.5 |
| Value | Analyses Associated with the Secondary Objective(s) |
| Business rules | Value Allowed: No |

| | |
|-------------------------------------|--|
| Term (Variable) | 10.5 Analyses Associated with the Secondary Objective(s) |
| | Relationship: 10 STATISTICAL CONSIDERATIONS; Table of Contents Concept: Heading |
| Repeating and/or Reuse Rules | No |

10.5.1. {Secondary objective <#>}

| | |
|--|--|
| Term (Variable) | 10.5.X {Secondary Objective <#>} |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | H |
| Definition | Heading |
| User Guidance | No text is intended here (heading only). |
| Conformance | Conditional: Collection for each Secondary Objective (e.g., 10.5.1, 10.5.2, 10.5.3, 10.5.4, 10.5.5). For more than one Secondary Objective repeat the collection as level 4 headings where X is = to the number of Secondary Objectives |
| Cardinality | One to many |
| Relationship content from ToC representing the protocol hierarchy | 10.5.X |
| Value | Secondary Objective <#>. # is a unique number for each Secondary Objective; if there is only one Secondary Objective, # is blank. If more than one Secondary Objective, add sequential unique number for each objective. |
| Business rules | Value Allowed: No Relationship: 3.2.X Secondary Objective <#>; 10.5 Analyses Associated with the Secondary Objective(s); 10 STATISTICAL CONSIDERATIONS; Table of Contents Concept: Heading |
| Repeating and/or Reuse Rules | Yes, repeatable for each objective. |

10.5.1.1. {Statistical analysis method}

| | |
|---|--|
| Term (Variable) | 10.5.X.1 {Statistical Analysis Method} |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | H |
| Definition | Heading |
| User Guidance | N/A |
| Conformance | Conditional: when there is Secondary Objective |
| Cardinality | One to one |

| | |
|--|--|
| Term (Variable) | 10.5.X.1 {Statistical Analysis Method} |
| Relationship content from ToC representing the protocol hierarchy | 10.5.X.1 |
| Value | Statistical Analysis Method |
| Business rules | Value Allowed: No Relationship: 10.5.X Secondary Objective <#>; 10.5 Analyses Associated with the Secondary Objective(s); 10 STATISTICAL CONSIDERATIONS; Table of Contents Concept: Heading |
| Repeating and/or Reuse Rules | Yes, repeatable for each objective as a series of Level 4 sections (10.5.X.1, 10.5.X.2, 10.5.X.3, 10.5.X.4, 10.5.X.5). |

| | |
|--|--|
| Term (Variable) | {<Statistical Analysis Method>} |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C218482 |
| User Guidance | Describe the statistical analysis methods that will be used to evaluate the secondary objective(s) and associated estimand(s) in Section 3.2 Secondary Objective(s) and Associated Estimand(s). Use the same section structure as Section 10.4 Analyses Associated with the Primary Objective(s). Include additional level 3 headings for each secondary objective as needed. If there is more than one secondary objective, number each objective consecutively as the level 3 heading (e.g., Secondary Objective 1, Secondary Objective 2, etc.). No text is intended here (heading only) unless there is no secondary objective, in which case indicate "Not applicable." Clearly specify any secondary hypotheses that will be tested for confirmatory purposes. |
| Conformance | Conditional: when there is Secondary Objective |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 10.5.X.1 |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: 10.5.X.1 Statistical Analysis Method Concept: C218482 ICH OID 2.16.840.1.113883.3.989.2.3.3.10 |
| Repeating and/or Reuse Rules | Yes, repeatable for each objective as a series of level 4 sections (10.5.X.1, 10.5.X.2, 10.5.X.3, 10.5.X.4, 10.5.X.5). |

10.5.1.2. {Handling of data in relation to secondary estimand(s)}

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

| | |
|--|--|
| Term (Variable) | {<Handling of Data in Relation to Secondary Estimand(s)>} |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C218805 |
| User Guidance | <p>Describe the statistical analysis methods that will be used to evaluate the secondary objective(s) and associated estimand(s) in Section 3.2 Secondary Objective(s) and Associated Estimand(s). Use the same section structure as Section 10.4 Analyses Associated with the Primary Objective(s). Include additional level 3 headings for each secondary objective as needed. If there is more than one secondary objective, number each objective consecutively as the level 3 heading (e.g., Secondary Objective 1, Secondary Objective 2, etc.).</p> <p>No text is intended here (heading only) unless there is no secondary objective, in which case indicate "Not applicable."</p> |
| Conformance | Conditional: when there is Secondary Estimand |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 10.5.X.2 |
| Value | Text |
| Business rules | Value Allowed: Yes |

| | |
|-------------------------------------|---|
| Term (Variable) | {<Handling of Data in Relation to Secondary Estimand(s)>} |
| | Relationship: 10.5.X.2 Handling of Data in Relation to Secondary Estimand(s) Concept: C218805 ICH OID 2.16.840.1.113883.3.989.2.3.3.10 |
| Repeating and/or Reuse Rules | Yes, repeatable for each objective as a series of level 4 sections (10.5.X.1, 10.5.X.2, 10.5.X.3, 10.5.X.4, 10.5.X.5). |

10.5.1.3. {Handling of missing data in relation to secondary estimand(s)}

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

| | |
|---|---|
| Term (Variable) | {<Handling of Missing Data in Relation to Secondary Estimand(s)>} |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C218806 |
| User Guidance | Describe the statistical analysis methods that will be used to evaluate the secondary objective(s) and associated estimand(s) in Section 3.2 Secondary Objective(s) and Associated Estimand(s). Use the same section structure as Section 10.4 Analyses Associated with the Primary Objective(s). Include additional level 3 headings for each secondary objective as needed. If there is more than one secondary objective, number each objective consecutively as the level 3 heading (e.g., Secondary Objective 1, Secondary Objective 2, etc.). No text is intended here (heading only) unless there is no secondary objective, in which case indicate "Not applicable." |
| Conformance | Conditional: when there is Secondary Estimand |

| | |
|--|--|
| Term (Variable) | {<Handling of Missing Data in Relation to Secondary Estimand(s)>} |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 10.5.X.3 |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: 10.5.X.3 Handling of Missing Data in Relation to Secondary Estimand(s) Concept: C218806 ICH OID 2.16.840.1.113883.3.989.2.3.3.10 |
| Repeating and/or Reuse Rules | Yes, repeatable for each objective as a series of level 4 sections (10.5.X.1, 10.5.X.2, 10.5.X.3, 10.5.X.4, 10.5.X.5). |

10.5.1.4. {Sensitivity analysis}

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

| | |
|---|--|
| Term (Variable) | {<Sensitivity Analysis>} |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C218480 |
| User Guidance | Describe the statistical analysis methods will be used to evaluate the secondary objective(s) and associated estimand(s) in Section 3.2 Secondary Objective(s) and Associated Estimand(s). Use the same section structure as Section 10.4 Analyses Associated with the Primary |

| | |
|--|---|
| Term (Variable) | {<Sensitivity Analysis>} |
| | Objective(s). Include additional level 3 headings for each secondary objective as needed. If there is more than one secondary objective, number each objective consecutively as the level 3 heading (e.g., Secondary Objective 1, Secondary Objective 2, etc.). No text is intended here (heading only) unless there is no secondary objective, in which case indicate "Not applicable." |
| Conformance | Conditional: when there is Secondary Objective and Sensitivity Analysis for a Secondary Objective |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 10.5.X.4 |
| Value | Text |
| Business rules | Value Allowed Yes Relationship: 10.5.X.4 Sensitivity Analysis Concept: C218480 ICH OID 2.16.840.1.113883.3.989.2.3.3.10 |
| Repeating and/or Reuse Rules | Yes, repeatable for each objective as a series of level 4 sections (10.5.X.1, 10.5.X.2, 10.5.X.3, 10.5.X.4, 10.5.X.5). |

10.5.1.5. {Supplementary analysis}

| | |
|--|--|
| Term (Variable) | 10.5.X.5 {Supplementary Analysis} |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | H |
| Definition | Heading |
| User Guidance | N/A |
| Conformance | Conditional: when there is a Supplementary Analysis for a Secondary Objective |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 10.5.X.5 |
| Value | Supplementary Analysis |
| Business rules | Value Allowed: No Relationship: 10.5.X Secondary Objective <#>; 10.5 Analysis Associated with the Secondary Objective(s); 10 STATISTICAL CONSIDERATIONS; Table of Contents Concept: Heading |
| Repeating and/or Reuse Rules | Yes, repeatable for each objective. |

| | |
|--|---|
| Term (Variable) | {<Supplementary Analysis>} |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C218481 |
| User Guidance | Describe the statistical analysis methods that will be used to evaluate the secondary objective(s) and associated estimand(s) in Section 3.2 Secondary Objective(s) and Associated Estimand(s). Use the same section structure as Section 10.4 Analyses Associated with the Primary Objective(s). Include additional level 3 headings for each secondary objective as needed. If there is more than one secondary objective, number each objective consecutively as the level 3 heading (e.g., Secondary Objective 1, Secondary Objective 2, etc.). No text is intended here (heading only) unless there is no secondary objective, in which case indicate "Not applicable." |
| Conformance | Conditional: when there is Supplementary Analysis for a Secondary Objective |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 10.5.X.5 |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: 10.5.X.5 Supplementary Analysis Concept: C218481 ICH OID 2.16.840.1.113883.3.989.2.3.3.10 |
| Repeating and/or Reuse Rules | Yes, repeatable for each objective as a series of level 4 sections (10.5.X.1, 10.5.X.2, 10.5.X.3, 10.5.X.4, 10.5.X.5). |

10.6. Analyses associated with the exploratory objective(s)

| | |
|--|--|
| Term (Variable) | 10.6 Analyses Associated with the Exploratory Objective(s) |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | H |
| Definition | Heading |
| User Guidance | N/A |
| Conformance | Required |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 10.6 |
| Value | Analyses Associated with the Exploratory Objective(s) |
| Business rules | Value Allowed: No Relationship: 3.3.X Exploratory Objective <#>; 10 STATISTICAL CONSIDERATIONS; Table of Contents |

| | |
|-------------------------------------|--|
| Term (Variable) | 10.6 Analyses Associated with the Exploratory Objective(s) |
| | Concept: Heading |
| Repeating and/or Reuse Rules | No |

| | |
|--|--|
| Term (Variable) | <Analyses Associated with the Exploratory Objective(s)> |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C218807 |
| User Guidance | Describe any exploratory analyses, if applicable. Additional subsections may be created to describe the analyses for each exploratory objective, as needed. If there is no exploratory objective, indicate "Not applicable". |
| Conformance | Required |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 10.6 |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: 10.6 Analysis Associated with the Exploratory Objective(s), Concept: C218807 ICH OID 2.16.840.1.113883.3.989.2.3.3.10 |
| Repeating and/or Reuse Rules | No |

10.7. Safety analyses

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

| | |
|--|--|
| Term (Variable) | <Safety Analyses> |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C218808 |
| User Guidance | If safety is a primary and/or secondary objective, describe the corresponding safety analyses in the appropriate section above (Section 10.4 Analyses Associated with the Primary Objective[s] or Section 10.5 Analyses Associated with the Secondary Objective[s]). In this section, describe statistical methods that will be used to analyse relevant safety outcomes, including any AESI. This should typically include specification of a measure to estimate risk within treatment arms, a measure to compare risks across treatment arms, and a measure of statistical uncertainty around the comparison (e.g., a confidence interval). |
| Conformance | Required |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 10.7 |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: 10.7 Safety Analyses Concept: C218808 ICH OID 2.16.840.1.113883.3.989.2.3.3.10 |
| Repeating and/or Reuse Rules | No |

10.8. Other analyses

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

| | |
|--|---|
| Term (Variable) | <Other Analyses> |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C218809 |
| User Guidance | Describe other analyses not included in Sections 10.3-10.7, such as subgroup analyses. |
| Conformance | Required |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 10.8 |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: 10.8 Other Analyses Concept: C218809 ICH OID 2.16.840.1.113883.3.989.2.3.3.10 |
| Repeating and/or Reuse Rules | No |

10.9. Interim analyses

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

| | |
|------------------------|--------------------|
| Term (Variable) | <Interim Analyses> |
| Data Type | Text |

| | |
|--|--|
| Term (Variable) | <Interim Analyses> |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C142582 |
| User Guidance | <p>Describe any interim analyses and criteria for stopping or adapting the trial. Ensure alignment with Section 4.3 Trial Stopping Rules. The description should include, but is not limited to, the following. Under circumstances where interim analysis details could impede the integrity of the trial, some of the information can be added in other documents outside of the protocol.</p> <ul style="list-style-type: none"> • any planned interim analysis, even if it is only to be performed at the request of an oversight body (for example, DMC) • the purpose of the interim analysis, including whether the interim analysis may be used for stopping and/or other trial adaptations (e.g., sample size re-estimation, alteration to the proportion of participants allocated to each trial group, or changes to eligibility criteria) • the applied statistical method (e.g., group sequential test) and spending function (e.g., O'Brien-Fleming), as applicable • the parties responsible for performing and reviewing the results of the analyses (e.g., DMC, independent statistician) • when the analyses will be conducted (timing and/or triggers) • the decision criteria—statistical or other—that will be adopted to judge the interim results as part of a guideline for early stopping or other adaptations • who will see the outcome data while the trial is ongoing • whether these individuals will remain blinded to trial groups • how the integrity of the trial will be protected (e.g., maintaining blinding) when decisions are made after interim analyses (e.g., a decision to continue the trial or implement a specific adaptation) |
| Conformance | Required |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 10.9 |
| Value | Text |
| Business rules | <p>Value Allowed: Yes</p> <p>Relationship: 10.9 Interim Analyses</p> <p>Concept: C142582 ICH OID 2.16.840.1.113883.3.989.2.3.3.10</p> |
| Repeating and/or Reuse Rules | Yes, repeatable for each interim analysis |

10.10. Multiplicity adjustments

| | |
|------------------------|--------------------------------|
| Term (Variable) | 10.10 Multiplicity Adjustments |
| Data Type | Text |

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

| | |
|---|--|
| Term (Variable) | <Multiplicity Adjustments> |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C218810 |
| User Guidance | <p>Multiple testing procedures may be needed to limit the probability of false positive findings in a trial. Reasons for carrying out multiple statistical tests include, but are not restricted to, multiple endpoints, multiple treatment groups, multiple hypotheses, subgroups, and multiple timepoints. Describe any approaches to multiplicity control for the trial. This description might go beyond the analysis of primary objectives.</p> <p>Specify the statistical approach to control the overall type I error rate as well as the (adjusted) significance levels to test specific hypotheses, as applicable. Clarify whether the tests/confidence intervals are one- or two-sided.</p> <p>State the circumstances under which a trial will be considered to have met its primary objective(s). For example, in a study with two primary efficacy endpoints, this section should state whether the study would be expected to provide statistical evidence on at least one or on both of the endpoints in order to confirm the efficacy of the treatment.</p> <p>For some statistical approaches it might be helpful to include a graphical depiction, as visualisation will be helpful for understanding, coupled with the clinical translation of the mathematical choices.</p> <p>Details regarding interim analyses should be provided in Section 10.9 Interim Analyses.</p> |
| Conformance | Required |
| Cardinality | One to one |

| | |
|--|--|
| Term (Variable) | <Multiplicity Adjustments> |
| Relationship content from ToC representing the protocol hierarchy | 10.10 |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: 10.10 Multiplicity Adjustments Concept: C218810 ICH OID 2.16.840.1.113883.3.989.2.3.3.10 |
| Repeating and/or Reuse Rules | No |

10.11. Sample size determination

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

| | |
|---|--|
| Term (Variable) | <Sample Size Determination> |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C115467 |
| User Guidance | <p>This section should detail the methods used for the determination of the sample size.</p> <p>The sample size calculation should be aligned with the primary estimand(s) and the primary analysis; otherwise, a justification is needed. Details of sample size calculation should include all relevant information to enable reproduction of the sample size, e.g.:</p> <ul style="list-style-type: none"> • references to any prior studies on which assumptions were based |

| | |
|--|---|
| Term (Variable) | <Sample Size Determination> |
| | <ul style="list-style-type: none"> significance level (including information on the choice of one- or two-sided level) power assumed treatment effect and variability how dropout rate and intercurrent events have been incorporated into sample size calculation precision of estimator/length of confidence interval <p>Any assumptions made should be stated and justified. Further analysis of how deviations from the assumptions will affect the sample size should be included.</p> <p>If complex simulations were used to calculate the sample size, consider including details in a separate simulation report as an appendix to the protocol.</p> <p>If the planned sample size is not derived statistically, then this should be explicitly stated along with a rationale for the intended sample size (e.g., exploratory nature of pilot trials; pragmatic considerations for trials in rare diseases).</p> |
| Conformance | Required |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 10.11 |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: 10.11 Sample Size Determination Concept: C115467 ICH OID 2.16.840.1.113883.3.989.2.3.3.10 |
| Repeating and/or Reuse Rules | No |

11. Trial oversight and other general considerations

| | |
|--|---|
| Term (Variable) | 11 TRIAL OVERSIGHT AND OTHER GENERAL CONSIDERATIONS |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | H |
| Definition | Heading |
| User Guidance | No text is intended here (heading only). |
| Conformance | Required |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 11 |
| Value | TRIAL OVERSIGHT AND OTHER GENERAL CONSIDERATIONS |
| Business rules | Value Allowed: No |

| | |
|-------------------------------------|---|
| Term (Variable) | 11 TRIAL OVERSIGHT AND OTHER GENERAL CONSIDERATIONS |
| | Relationship: Table of Contents Concept: Heading |
| Repeating and/or Reuse Rules | No |

11.1. Regulatory and ethical considerations

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

| | |
|---|---|
| Term (Variable) | <Regulatory and Ethical Considerations> |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C218811 |
| User Guidance | <p>Provide a high-level statement on the prevailing ethical, legal, and regulatory guidelines that will be applied throughout the trial. This trial will be conducted in accordance with the protocol and with the following:</p> <ul style="list-style-type: none"> • Ethical principles that have their origin in the Declaration of Helsinki for medical research involving human subjects • Consensus ethical principles derived from international guidelines including the Declaration of Helsinki and the Council for International Organisations of Medical Sciences (CIOMS) International Ethical Guidelines • ICH Good Clinical Practice (GCP) Guidelines • Applicable laws and regulations |
| Conformance | Required |

| | |
|--|---|
| Term (Variable) | <Regulatory and Ethical Considerations> |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 11.1 |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: 11.1 Regulatory and Ethical Considerations Concept: C218811 ICH OID 2.16.840.1.113883.3.989.2.3.3.11 |
| Repeating and/or Reuse Rules | No |

11.2. Trial oversight

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

| | |
|---|--|
| Term (Variable) | {<Trial Oversight>} |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C218812 |
| User Guidance | Concisely summarise the trial oversight, listing the investigator and sponsor responsibilities not covered in other sections of the protocol that are essential for trial conduct, specifying the ones related to quality assurance. if not using below optional subheadings. |

| | |
|--|--|
| Term (Variable) | {<Trial Oversight>} |
| Conformance | Conditional: if not using the optional subheadings Level 3 (11.2.1 and 11.2.2) |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 11.2 |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: 11.2 Trial Oversight Concept: C218812 ICH OID 2.16.840.1.113883.3.989.2.3.3.11 |
| Repeating and/or Reuse Rules | No |

11.2.1. Investigator responsibilities

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

| | |
|---|--|
| Term (Variable) | <Investigator Responsibilities> |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C218813 |
| User Guidance | Describe the investigator responsibilities, including the oversight of trial-related activities delegated to a third party that may impact the trial conduct at sites, if applicable and if not addressed elsewhere. |
| Conformance | Optional |

| | |
|--|--|
| Term (Variable) | <Investigator Responsibilities> |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 11.2.1 |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: 11.2.1 Investigator Responsibilities Concept: C218813 ICH OID 2.16.840.1.113883.3.989.2.3.3.11 |
| Repeating and/or Reuse Rules | No |

11.2.2. Sponsor responsibilities

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

| | |
|---|---|
| Term (Variable) | <Sponsor Responsibilities> |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C218814 |
| User Guidance | Describe the sponsor responsibilities, including activities to be transferred to a third party that may impact the investigator sites, if applicable. |
| Conformance | Optional |
| Cardinality | One to one |

| | |
|--|---|
| Term (Variable) | <Sponsor Responsibilities> |
| Relationship content from ToC representing the protocol hierarchy | 11.2.2 |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: 11.2.2 Sponsor Responsibilities Concept: C218814 ICH OID 2.16.840.1.113883.3.989.2.3.3.11 |
| Repeating and/or Reuse Rules | No |

11.3. Informed consent process

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

| | |
|---|---|
| Term (Variable) | <Description of Informed Consent Process> |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C184390 |
| User Guidance | Specify the key elements of the informed consent process, including any special needs and how these are addressed (e.g., assent, capacity, legally acceptable representative, adolescents who may reach age of majority during the trial, pregnant participants and pregnant partners of participants). |
| Conformance | Required |
| Cardinality | One to one |

| | |
|--|---|
| Term (Variable) | <Description of Informed Consent Process> |
| Relationship content from ToC representing the protocol hierarchy | 11.3 |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: 11.3 Informed Consent Process Concept: C184390 ICH OID 2.16.840.1.113883.3.989.2.3.3.11 |
| Repeating and/or Reuse Rules | No |

| | |
|--|---|
| Term (Variable) | <Description of Assent Process> |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C218815 |
| User Guidance | Specify the key elements of the informed consent process, including any special needs and how these are addressed (e.g., assent, capacity, legally acceptable representative, adolescents who may reach age of majority during the trial, pregnant participants and pregnant partners of participants). |
| Conformance | Optional |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 11.3 |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: 11.3 Informed Consent Process Concept: C218815 ICH OID 2.16.840.1.113883.3.989.2.3.3.11 |
| Repeating and/or Reuse Rules | No |

| | |
|---|--|
| Term (Variable) | <Description of Emergency Consent Process> |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C218816 |
| User Guidance | If enrollment in the trial may occur during an emergency in which the participant or their legally acceptable representative is not able or available to give consent, describe the consent process. |
| Conformance | Optional |
| Cardinality | One to one |

| | |
|--|---|
| Term (Variable) | <Description of Emergency Consent Process> |
| Relationship content from ToC representing the protocol hierarchy | 11.3 |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: 11.3 Informed Consent Process Concept: C218816 ICH OID 2.16.840.1.113883.3.989.2.3.3.11 |
| Repeating and/or Reuse Rules | No |

11.3.1. {Informed consent for rescreening}

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

| | |
|---|---|
| Term (Variable) | {<Informed Consent for Rescreening>} |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C218817 |
| User Guidance | If participants can be rescreened as described in Section 5.6 Screen Failure and Rescreening, state whether the participant needs to complete a new ICF. Screen failure and rescreening should be clearly defined in the protocol, with a cross reference to those definitions. |
| Conformance | Conditional |
| Cardinality | One to one |

| | |
|--|---|
| Term (Variable) | {<Informed Consent for Rescreening>} |
| Relationship content from ToC representing the protocol hierarchy | 11.3.1 |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: 11.3.1 Informed Consent for Rescreening Concept: C218817 ICH OID 2.16.840.1.113883.3.989.2.3.3.11 |
| Repeating and/or Reuse Rules | No |

11.3.2. {Informed consent for use of remaining samples in exploratory research}

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

| | |
|---|--|
| Term (Variable) | {<Informed Consent for Use of Remaining Samples in Exploratory Research>} |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C218818 |
| User Guidance | If participants will be asked to consent to optional exploratory research using the remainder of mandatory samples, describe the use of remaining samples for optional exploratory research. |

| | |
|--|--|
| Term (Variable) | {<Informed Consent for Use of Remaining Samples in Exploratory Research>} |
| | If any exploratory research is planned and additional written consent regarding the use of remaining samples for exploratory research will be obtained, describe the consent process. |
| Conformance | Conditional |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 11.3.2 |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: 11.3.2 Informed Consent for Use of Remaining Samples in Exploratory Research Concept: C218818 ICH OID 2.16.840.1.113883.3.989.2.3.3.11 |
| Repeating and/or Reuse Rules | No |

11.4. Committees

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

| | |
|---|--------------|
| Term (Variable) | <Committees> |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C218819 |

| | |
|--|--|
| Term (Variable) | <Committees> |
| User Guidance | Briefly describe the administrative structure of committees that will be reviewing data while the trial is ongoing, and the type of committee (e.g., Dose Escalation Committee, Data Monitoring Committee or Data Safety Monitoring Board). Note that specific details may be required depending on local law or regulation. If applicable, committee charters may be cross referenced. If no committees are involved, state "Not applicable." |
| Conformance | Required |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 11.4 |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: 11.4 Committees Concept: C218819 ICH OID 2.16.840.1.113883.3.989.2.3.3.11 |
| Repeating and/or Reuse Rules | No |

11.5. Insurance and indemnity

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

| | |
|---|---------------------------|
| Term (Variable) | <Insurance and Indemnity> |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C218820 |

| | |
|--|---|
| Term (Variable) | <Insurance and Indemnity> |
| User Guidance | Concisely summarise the arrangements for participant insurance and indemnity if not addressed in a separate agreement, if required by the applicable regulatory requirements. |
| Conformance | Required |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 11.5 |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: 11.5 Insurance and Indemnity Concept: C218820 ICH OID 2.16.840.1.113883.3.989.2.3.3.11 |
| Repeating and/or Reuse Rules | No |

11.6. Risk-based quality management

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

| | |
|---|--|
| Term (Variable) | <Risk-Based Quality Management> |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C218821 |
| User Guidance | Describe the identified critical to quality factors, associated risks and risk mitigation strategies for the trial or refer to the location where this is described and updated during the trial based on emerging data. |

| | |
|--|--|
| Term (Variable) | <Risk-Based Quality Management> |
| Conformance | Required |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 11.6 |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: 11.6 Risk-Based Quality Management Concept: C218821 ICH OID 2.16.840.1.113883.3.989.2.3.3.11 |
| Repeating and/or Reuse Rules | No |

11.7. Data governance

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

| | |
|---|---|
| Term (Variable) | <Data Governance> |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C218822 |
| User Guidance | Describe the key systems and processes for critical trial integrity, traceability and security including a summary of the approaches enabling accurate data collection, reporting, monitoring, transfer, retention, and access if not addressed in separate agreement(s). |
| Conformance | Required |

| | |
|--|--|
| Term (Variable) | <Data Governance> |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 11.7 |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: 11.7 Data Governance Concept: C218822 ICH OID 2.16.840.1.113883.3.989.2.3.3.11 |
| Repeating and/or Reuse Rules | No |

11.8. Data protection

| | |
|--|--|
| Term (Variable) | 11.8 Data Protection |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | H |
| Definition | Heading |
| User Guidance | N/A |
| Conformance | Required |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 11.8 |
| Value | Data Protection |
| Business rules | Value Allowed: No Relationship: 11 TRIAL OVERSIGHT AND OTHER GENERAL CONSIDERATIONS; Table of Contents Concept: Heading |
| Repeating and/or Reuse Rules | No |

| | |
|---|---|
| Term (Variable) | <Data Protection> |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C218823 |
| User Guidance | Describe the measures to protect the privacy and confidentiality of personal information of trial participants in accordance with applicable regulatory requirements on personal data protection and any measures that should be taken in case of a data security breach. |
| Conformance | Required |

| | |
|--|--|
| Term (Variable) | <Data Protection> |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 11.8 |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: 11.8 Data Protection Concept: C218823 ICH OID 2.16.840.1.113883.3.989.2.3.3.11 |
| Repeating and/or Reuse Rules | No |

11.9. Source records

| | |
|--|--|
| Term (Variable) | 11.9 Source Records |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | H |
| Definition | Heading |
| User Guidance | N/A |
| Conformance | Required |
| Cardinality | One to many |
| Relationship content from ToC representing the protocol hierarchy | 11.9 |
| Value | Source Records |
| Business rules | Value Allowed: No Relationship: 11 TRIAL OVERSIGHT AND OTHER GENERAL CONSIDERATIONS; Table of Contents Concept: Heading |
| Repeating and/or Reuse Rules | No |

| | |
|---|--|
| Term (Variable) | <Source Records Introduction> |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C218824 |
| User Guidance | State the importance of source records and expectation for traceability. Delineate expectations for investigators (e.g., maintain and ensure availability of essential records) and trial monitors (e.g., ensure participant protections, ensure that the trial is conducted according to GCP). Identify what constitutes source records and its origin or provide a reference to the location of this information, if contained in a separate document. |

| | |
|--|---|
| Term (Variable) | <Source Records Introduction> |
| | Describe the provision for direct access to source records enabling clinical trial-related monitoring, audits and regulatory inspections, if not included in separate agreement(s). |
| Conformance | Required |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 11.9 |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: 11.9 Source Records Concept: C218824 ICH OID 2.16.840.1.113883.3.989.2.3.3.11 |
| Repeating and/or Reuse Rules | No |

| | |
|--|--|
| Term (Variable) | <Investigator Expectations for Source Records> |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C218825 |
| User Guidance | State the importance of source records and expectation for traceability. Delineate expectations for investigators (e.g., maintain and ensure availability of essential records) and trial monitors (e.g., ensure participant protections, ensure that the trial is conducted according to GCP). Identify what constitutes source records and its origin or provide a reference to the location of this information, if contained in a separate document. Describe the provision for direct access to source records enabling clinical trial-related monitoring, audits and regulatory inspections, if not included in separate agreement(s). |
| Conformance | Required |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 11.9 |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: 11.9 Source Records Concept: C218825 ICH OID 2.16.840.1.113883.3.989.2.3.3.11 |
| Repeating and/or Reuse Rules | No |

| | |
|--|--|
| Term (Variable) | <Trial Monitor Expectations for Source Records> |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C218826 |
| User Guidance | State the importance of source records and expectation for traceability. Delineate expectations for investigators (e.g., maintain and ensure availability of essential records) and trial monitors (e.g., ensure participant protections, ensure that the trial is conducted according to GCP). Identify what constitutes source records and its origin or provide a reference to the location of this information, if contained in a separate document. Describe the provision for direct access to source records enabling clinical trial-related monitoring, audits and regulatory inspections, if not included in separate agreement(s). |
| <Conformance | Required |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 11.9 |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: 11.9 Source Records Concept: C218826 ICH OID 2.16.840.1.113883.3.989.2.3.3.11 |
| Repeating and/or Reuse Rules | No |

| | |
|---|--|
| Term (Variable) | <Identification of Source Records> |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C222675 |
| User Guidance | State the importance of source records and expectation for traceability. Delineate expectations for investigators (e.g., maintain and ensure availability of essential records) and trial monitors (e.g., ensure participant protections, ensure that the trial is conducted according to GCP). Identify what constitutes source records and its origin or provide a reference to the location of this information, if contained in a separate document. Describe the provision for direct access to source records 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 | 11.9 |

| | |
|--|---|
| Term (Variable) | <Identification of Source Records> |
| representing the protocol hierarchy | |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: 11.9 Source Records Concept: C222675 ICH OID 2.16.840.1.113883.3.989.2.3.3.11 |
| Repeating and/or Reuse Rules | No |

11.10. Protocol deviations

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

| | |
|--|--|
| Term (Variable) | <Protocol Deviations> |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C218827 |
| User Guidance | Describe plans for detecting, reviewing, and reporting any deviations from the protocol or include reference to a separate document. |
| Conformance | Required |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 11.10 |
| Value | Text |

| | |
|-------------------------------------|---|
| Term (Variable) | <Protocol Deviations> |
| Business rules | Value Allowed: Yes Relationship: 11.10 Protocol Deviations Concept: C218827 ICH OID 2.16.840.1.113883.3.989.2.3.3.11 |
| Repeating and/or Reuse Rules | No |

11.11. Early site closure

| | |
|--|--|
| Term (Variable) | 11.11 Early Site Closure |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | H |
| Definition | Heading |
| User Guidance | N/A |
| Conformance | Required |
| Cardinality | One to many |
| Relationship content from ToC representing the protocol hierarchy | 11.11 |
| Value | Early Site Closure |
| Business rules | Value Allowed: No Relationship: 11 TRIAL OVERSIGHT AND OTHER GENERAL CONSIDERATIONS; Table of Contents Concept: Heading |
| Repeating and/or Reuse Rules | No |

| | |
|--|--|
| Term (Variable) | <Decision Rights for Site Closure> |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C218828 |
| User Guidance | List the sponsor's rights to close a site early. Likewise, list the investigator's rights to initiate early site closure. |
| Conformance | Required |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 11.11 |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: 11.11 Early Site Closure Concept: C218828 ICH OID 2.16.840.1.113883.3.989.2.3.3.11 |

| | |
|-------------------------------------|------------------------------------|
| Term (Variable) | <Decision Rights for Site Closure> |
| Repeating and/or Reuse Rules | No |

| | |
|--|--|
| Term (Variable) | <Criteria for Early Closure> |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C218829 |
| User Guidance | List the criteria for early closure of a site by the sponsor or investigator. |
| Conformance | Required |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 11.11 |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: 11.11 Early Site Closure Concept: C218829 ICH OID 2.16.840.1.113883.3.989.2.3.3.11 |
| Repeating and/or Reuse Rules | No |

| | |
|--|--|
| Term (Variable) | <Responsibilities Following Early Site Closure> |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C218830 |
| User Guidance | List the responsibilities of the sponsor and investigator following early site closure (e.g., informing the ethics committee[s], and prompt notification of the participant and their transition to appropriate therapy and/or follow-up). |
| Conformance | Required |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 11.11 |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: 11.11 Early Site Closure Concept: C218830 ICH OID 2.16.840.1.113883.3.989.2.3.3.11 |
| Repeating and/or Reuse Rules | No |

11.12. Data dissemination

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

| | |
|--|--|
| Term (Variable) | <Data Dissemination> |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C218831 |
| User Guidance | Describe whether the clinical trial will be registered in public databases, including reporting of results, if applicable. |
| Conformance | Required |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 11.12 |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: 11.12 Data Dissemination Concept: C218831 ICH OID 2.16.840.1.113883.3.989.2.3.3.11 |
| Repeating and/or Reuse Rules | No |

12. Appendix: supporting details

| | |
|------------------------|---------------------------------|
| Term (Variable) | 12 APPENDIX: SUPPORTING DETAILS |
| Data Type | Text |

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

12.1. Clinical laboratory tests

| | |
|--|--|
| Term (Variable) | 12.1 Clinical Laboratory Tests |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | H |
| Definition | Heading |
| User Guidance | N/A |
| Conformance | Required |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 12.1 |
| Value | Clinical Laboratory Tests |
| Business rules | Value Allowed: No Relationship: 12 APPENDIX: SUPPORTING DETAILS; Table of Contents Concept: Heading |
| Repeating and/or Reuse Rules | No |

| | |
|---|-----------------------------|
| Term (Variable) | <Clinical Laboratory Tests> |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C25294 |

| | |
|--|---|
| Term (Variable) | <Clinical Laboratory Tests> |
| User Guidance | Specify which laboratory parameters should be included in each clinical laboratory assessment panel (e.g., haematology, chemistry, urinalysis). A tabular presentation for such information is common. If applicable, include equations and references for locally calculated laboratory results. If not applicable, retain heading and enter "Not applicable." |
| Conformance | Required |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 12.1 |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: 12.1 Clinical Laboratory Tests Concept: C25294 ICH OID 2.16.840.1.113883.3.989.2.3.3.12 |
| Repeating and/or Reuse Rules | No |

12.2. Country/region-specific differences

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

| | |
|---|------------------|
| Term (Variable) | <Not applicable> |
| Data Type | Optional Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | N/A |

| | |
|--|---|
| Term (Variable) | <Not applicable> |
| User Guidance | <p>Although global clinical trial practices are increasingly harmonised, some country/ region-specific differences in requirements do exist (e.g., document retention periods, contraception requirements). Where differences in requirements cannot be reconciled, the sponsor should explain how country/region-specific differences will be documented and communicated (e.g., by country/region-specific amendments or addenda). An alternative to country/region-specific amendments is to list the specific differences by country or countries in this section, including a reference to the relevant section of the protocol where each differing requirement applies.</p> <p>If not applicable, retain the heading and enter "Not applicable."</p> |
| Conformance | Optional: if there are no Country/Region-Specific Differences |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 12.2 |
| Value | Not Applicable |
| Business rules | <p>Value Allowed: No</p> <p>Relationship: 12.2 Country/Region-Specific Differences</p> <p>Concept: Optional Text</p> |
| Repeating and/or Reuse Rules | No |

| | |
|---|---|
| Term (Variable) | [Country/Region Identifier] |
| Data Type | Valid Value |
| Data (D), Value (V) or Heading (H) | H |
| Definition | C218832 |
| User Guidance | <p>Although global clinical trial practices are increasingly harmonised, some country/ region-specific differences in requirements do exist (e.g., document retention periods, contraception requirements). Where differences in requirements cannot be reconciled, the sponsor should explain how they will document and communicate country/region-specific differences (e.g., by country/region-specific amendments or addenda). An alternative to country/region-specific amendments is to list the specific differences by country or countries in this section, including a reference to the relevant section of the protocol where the differing requirement applies.</p> <p>If not applicable, retain the heading and enter "Not applicable."</p> |
| Conformance | Optional: if there is Country/Region-Specific Differences |
| Cardinality | One to many |
| Relationship content from ToC | 12.2 |

| | |
|--|--|
| Term (Variable) | [Country/Region Identifier] |
| representing the protocol hierarchy | |
| Value | Country Identifier (ISO 3166 Country Codes, Alpha 3; ISO 3166 Country Codes, Alpha 2; GENC) or Region Identifier (ISO 3166 Region Codes, Alpha 3; ISO 3166 Region Codes, Alpha 2; GENC) |
| Business rules | Value Allowed: Yes Relationship: 12.2 Country/Region-Specific Differences Concept: C218832 ICH OID 2.16.840.1.113883.3.989.2.3.3.12, Heading, Identifier, ISO 3166 Country Codes, Alpha 2; ISO 3166 Region Codes, Alpha 2 |
| Repeating and/or Reuse Rules | Yes, repeatable for each Country/Region |

| | |
|--|---|
| Term (Variable) | <Country/Region-Specific Requirements> |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C218833 |
| User Guidance | Although global clinical trial practices are increasingly harmonised, some country/ region-specific differences in requirements do exist (e.g., document retention periods, contraception requirements). Where differences in requirements cannot be reconciled, the sponsor should explain how they will document and communicate country/region-specific differences (e.g., by country/region-specific amendments or addenda). An alternative to country/region-specific amendments is to list the specific differences by country or countries in this section, including a reference to the relevant section of the protocol where the differing requirement applies. |
| Conformance | Optional if there is Country/Region-Specific Differences |
| Cardinality | One to many |
| Relationship content from ToC representing the protocol hierarchy | 12.2 |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: 12.2 Country /Region Identifier; Country/Region-Specific Differences Concept: C218833 ICH OID 2.16.840.1.113883.3.989.2.3.3.12 |
| Repeating and/or Reuse Rules | Yes, repeatable for each Country/Region |

| | |
|--|--|
| Term (Variable) | <Country/Region-Specific Protocol Clarifications> |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C218834 |
| User Guidance | <p>Although global clinical trial practices are increasingly harmonised, some country/region-specific differences in requirements do exist (e.g., document retention periods, contraception requirements). Where differences in requirements cannot be reconciled, the sponsor should explain how they will document and communicate country/region-specific differences (e.g., by country/region-specific amendments or addenda). An alternative to country/region-specific amendments is to list the specific differences by country or countries in this section, including a reference to the relevant section of the protocol where the differing requirement applies.</p> <p>If not applicable, retain the heading and enter "Not applicable."</p> |
| Conformance | Optional if there is Country/Region-Specific Differences |
| Cardinality | One to many |
| Relationship content from ToC representing the protocol hierarchy | 12.2 |
| Value | Text |
| Business rules | <p>Value Allowed: Yes</p> <p>Relationship: Country /Region Identifier; 12.2 Country/Region-Specific Differences</p> <p>Concept: C218834 ICH OID 2.16.840.1.113883.3.989.2.3.3.12</p> |
| Repeating and/or Reuse Rules | Yes, repeatable for each country/region |

12.3. Prior protocol amendment(s)

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

| | |
|-------------------------------------|----------------------------------|
| Term (Variable) | 12.3 Prior Protocol Amendment(s) |
| | Concept: Heading |
| Repeating and/or Reuse Rules | No |

| | |
|--|---|
| Term (Variable) | Prior Protocol Amendment(s) |
| Data Type | Valid Value |
| Data (D), Value (V) or Heading (H) | V |
| Definition | C218835 |
| User Guidance | <p>Choose the applicable statement below. For an original protocol that has not been amended, retain the first statement below and delete the remainder of this entire section.</p> <p>{This protocol has not been amended.}</p> <p>Or</p> <p>{This is the first protocol amendment.}</p> <p>Or include the below as applicable.</p> <p>{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.}</p> |
| Conformance | Required |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 12.3 |
| Value | <p>Code List C217274: ICH OID 2.16.840.1.113883.3.989.2.3.1.1</p> <p>This protocol has not been amended. (C218485)</p> <p>Or</p> <p>This is the first protocol amendment. (C218486)</p> <p>Or include the below as applicable.</p> <p>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. (C218488)</p> |
| Business rules | <p>Value Allowed: Yes</p> <p>Relationship: 12.3 Prior Protocol Amendment(s)</p> <p>Concept: C218835 ICH OID 2.16.840.1.113883.3.989.2.3.3.12</p> |
| Repeating and/or Reuse Rules | No |

| | |
|------------------------|----------|
| Term (Variable) | Document |
| Data Type | Text |

| | |
|--|--|
| Term (Variable) | Document |
| Data (D), Value (V) or Heading (H) | H |
| Definition | Table Column Heading |
| User Guidance | <p>Previous amendments should appear in reverse chronological order with the most recent at the top (e.g., Amendment 3, 2, 1). Delete or add lines as needed. Inclusion of region-, country-, and site-specific amendments in the table is optional. If included, ensure that the scope is clearly distinguishable from global amendments.</p> <p>If including the column with enrollment numbers, follow the instructions below.</p> <ul style="list-style-type: none"> For global amendments to international clinical trials or amendments to a single-country trial, list the 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, list the status of all the relevant locations. For country/region-specific amendments to international clinical trials, list the approximate local enrollment total or percentage at the time of the amendment and select "locally". For trials in which enrollment status by cohort is more meaningful, such as for single-site or early-phase studies, listing the approximate enrollment by cohort is an option. If multiple cohorts are ongoing at the time of the amendment, list the status of all the ongoing cohorts. Enter the approximate number or percentage of participants enrolled as a percentage of the expected total. |
| Conformance | Required |
| Cardinality | One to many |
| Relationship content from ToC representing the protocol hierarchy | 12.3 |
| Value | Document |
| Business rules | <p>Value Allowed: No</p> <p>Relationship: Table Column Heading; 12.3 Prior Protocol Amendment(s)</p> <p>Concept: Table Column Heading</p> |
| Repeating and/or Reuse Rules | No |

| | |
|---|-----------------------|
| Term (Variable) | Sponsor Approval Date |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | H |
| Definition | Table Column Heading |

| | |
|--|--|
| Term (Variable) | Sponsor Approval Date |
| User Guidance | <p>Previous amendments should appear in reverse chronological order with the most recent at the top (e.g., Amendment 3, 2, 1). Delete or add lines as needed. Inclusion of region-, country-, and site-specific amendments in the table is optional. If included, ensure that the scope is clearly distinguishable from global amendments.</p> <p>If including the column with enrollment numbers, follow the instructions below.</p> <ul style="list-style-type: none"> For global amendments to international clinical trials or amendments to a single-country trial, list the 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, list the status of all the relevant locations. For country/region-specific amendments to international clinical trials, list the approximate local enrollment total or percentage at the time of the amendment and select "locally". For trials in which enrollment status by cohort is more meaningful, such as for single-site or early-phase studies, listing the approximate enrollment by cohort is an option. If multiple cohorts are ongoing at the time of the amendment, list the status of all the ongoing cohorts. Enter the approximate number or percentage of participants enrolled as a percentage of the expected total. |
| Conformance | Required |
| Cardinality | One to many |
| Relationship content from ToC representing the protocol hierarchy | 12.3 |
| Value | Sponsor Approval Date |
| Business rules | <p>Value Allowed: No</p> <p>Relationship: Table Column Heading; 12.3 Prior Protocol Amendment(s)</p> <p>Concept: Table Column Heading</p> |
| Repeating and/or Reuse Rules | No |

| | |
|---|---|
| Term (Variable) | Approximate Enrollment when Sponsor Approved Amendment |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | H |
| Definition | Table Column Heading |
| User Guidance | <p>Previous amendments should appear in reverse chronological order with the most recent at the top (e.g., Amendment 3, 2, 1). Delete or add lines as needed. Inclusion of region-, country-, and site-specific amendments in</p> |

| | |
|--|---|
| Term (Variable) | Approximate Enrollment when Sponsor Approved Amendment |
| | <p>the table is optional. If included, ensure that the scope is clearly distinguishable from global amendments.</p> <p>If including the column with enrollment numbers, follow the instructions below.</p> <ul style="list-style-type: none"> For global amendments to international clinical trials or amendments to a single-country trial, list the 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, list the status of all the relevant locations. For country/region-specific amendments to international clinical trials, list the approximate local enrollment total or percentage at the time of the amendment and select "locally". For trials in which enrollment status by cohort is more meaningful, such as for single-site or early-phase studies, listing the approximate enrollment by cohort is an option. If multiple cohorts are ongoing at the time of the amendment, list the status of all the ongoing cohorts. Enter the approximate number or percentage of participants enrolled as a percentage of the expected total. |
| Conformance | Optional if there is an amendment and sponsor chooses to use |
| Cardinality | One to many |
| Relationship content from ToC representing the protocol hierarchy | 12.3 |
| Value | Approximate Enrollment when Sponsor Approved Amendment |
| Business rules | <p>Value Allowed: No</p> <p>Relationship: Table Column Heading; 12.3 Prior Protocol Amendment(s)</p> <p>Concept: Table Column Heading</p> |
| Repeating and/or Reuse Rules | No |

| | |
|---|---|
| Term (Variable) | <Amendment Identifier> |
| Data Type | Text or Universal Text "Original Protocol" |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C218477 |
| User Guidance | <p>Previous amendments should appear in reverse chronological order with the most recent at the top (e.g., Amendment 3, 2, 1). Delete or add lines as needed. Inclusion of region-, country-, and site-specific amendments in the table is optional. If included, ensure that the scope is clearly distinguishable from global amendments.</p> <p>If including the column with enrollment numbers, follow the instructions below.</p> |

| | |
|--|--|
| Term (Variable) | <Amendment Identifier> |
| | <ul style="list-style-type: none"> For global amendments to international clinical trials or amendments to a single-country trial, list the 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, list the status of all the relevant locations. For country/region-specific amendments to international clinical trials, list the approximate local enrollment total or percentage at the time of the amendment and select "locally". For trials in which enrollment status by cohort is more meaningful, such as for single-site or early-phase studies, listing the approximate enrollment by cohort is an option. If multiple cohorts are ongoing at the time of the amendment, list the status of all the ongoing cohorts. Enter the approximate number or percentage of participants enrolled as a percentage of the expected total. |
| Conformance | Required |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 12.3 |
| Value | Text or Universal Text "Original Protocol" |
| Business rules | Value Allowed: Yes Relationship: Table Column Heading "Document" Concept: C218477 ICH OID 2.16.840.1.113883.3.989.2.3.3.12 |
| Repeating and/or Reuse Rules | Yes, reuse from the title page or other previous amendment |

| | |
|---|--|
| Term (Variable) | <Sponsor Approval Date> |
| Data Type | Date |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C132352 |
| User Guidance | <p>Previous amendments should appear in reverse chronological order with the most recent at the top (e.g., Amendment 3, 2, 1). Delete or add lines as needed. Inclusion of region-, country-, and site-specific amendments in the table is optional. If included, ensure that the scope is clearly distinguishable from global amendments.</p> <p>If including the column with enrollment numbers, follow the instructions below.</p> <ul style="list-style-type: none"> For global amendments to international clinical trials or amendments to a single-country trial, list the approximate global enrollment total or percentage at the time of the amendment and select "globally". |

| | |
|--|--|
| Term (Variable) | <Sponsor Approval Date> |
| | <ul style="list-style-type: none"> 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, list the status of all the relevant locations. For country/region-specific amendments to international clinical trials, list the approximate local enrollment total or percentage at the time of the amendment and select "locally". For trials in which enrollment status by cohort is more meaningful, such as for single-site or early-phase studies, listing the approximate enrollment by cohort is an option. If multiple cohorts are ongoing at the time of the amendment, list the status of all the ongoing cohorts. Enter the approximate number or percentage of participants enrolled as a percentage of the expected total. |
| Conformance | Required |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 12.3 |
| Value | Date |
| Business rules | Value Allowed: Yes Relationship: Table Column Heading "Amendment Identifier "Sponsor Approval Date" Concept: C132352 ICH OID 2.16.840.1.113883.3.989.2.3.3.12 |
| Repeating and/or Reuse Rules | Yes, reuse from the title page or other previous amendment |

| | |
|--|---|
| Term (Variable) | Approximately <#/%> enrolled |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C218478 |
| User Guidance | N/A |
| Conformance | Optional: if Original Protocol =No |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | Amendment Details |
| Value | Integer for Number or one decimal point for percent |
| Business rules | Value Allowed: Yes Relationship: Amendment Identifier; Sponsor Approval Date Concept: C218478 ICH OID 2.16.840.1.113883.3.989.2.3.3.12 |
| Repeating and/or Reuse Rules | Yes, reuse from the title page or other previous amendment |

| | |
|--|---|
| Term (Variable) | <Amendment Scope Enrollment Description> |
| Data Type | Valid Value |
| Data (D), Value (V) or Heading (H) | V |
| Definition | C218695 |
| User Guidance | <p>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 percentage of enrollment. Estimates are adequate, as precise enrollment figures will likely be changing while an amendment is being prepared.</p> <ul style="list-style-type: none"> For a <u>global or single-country amendment</u>, provide the estimated total enrollment at the time the sponsor approved the amendment. For <u>global amendments providing (or consolidating) only country/region-specific requirements</u>, list approximate local enrollment (total or percentage) at the time of the amendment and select "locally". If consolidating a series of local amendments, list the status of all the relevant locations. <p>For a <u>country/regional amendment</u>, provide the estimated local or regional enrollment at the time the sponsor approved the amendment.</p> |
| Conformance | Conditional if Original Protocol =No |
| Cardinality | One to Amendment Number |
| Relationship content from ToC representing the protocol hierarchy | Amendment Details |
| Value | Code List C217275: ICH OID 2.16.840.1.113883.3.989.2.3.1.2 Globally (C68846); Locally (C41065); By Cohort (C218489) |
| Business rules | <p>Value Allowed: Yes</p> <p>Relationship: Amendment Identifier; Sponsor Approval Date</p> <p>Concept: C218695 ICH OID 2.16.840.1.113883.3.989.2.3.3.12</p> |
| Repeating and/or Reuse Rules | Yes, reuse from the title page or other previous amendment |

| | |
|---|---|
| Term (Variable) | {The Overview of Changes from each prior protocol amendment is {provided below} or <specify alternative location>.} |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | Universal text and V, D |
| Definition | N/A |
| User Guidance | Move the Overview of Changes table from the previous amendments to this section in reverse chronological order (most recent first). |
| Conformance | Conditional: if not original protocol or first amendment |
| Cardinality | One to one |

| | |
|--|---|
| Term (Variable) | {The Overview of Changes from each prior protocol amendment is {provided below} or <specify alternative location>. |
| Relationship content from ToC representing the protocol hierarchy | 12.3 |
| Value | The Overview of Changes from each prior protocol amendment is Choose provided below or <specify alternative location>. |
| Business rules | Value Allowed: Yes Relationship: 12.3 Prior Protocol Amendment(s); {The Overview of Changes from each prior protocol amendment is {provided below} or <specify alternative location>}. Concept: Universal text |
| Repeating and/or Reuse Rules | No |

| | |
|--|--|
| Term (Variable) | <specify alternative location> |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C218836 |
| User Guidance | N/A |
| Conformance | Conditional: when a specify alternative location is selected |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 12.3 |
| Value | Text Location where information can be found |
| Business rules | Value Allowed: Yes Relationship: Location for previous amendments Concept: C218836 ICH OID 2.16.840.1.113883.3.989.2.3.3.12 |
| Repeating and/or Reuse Rules | Yes, reuse from the title page |

| | |
|---|---|
| Term (Variable) | {Overview of Changes in Amendment <Amendment Identifier> (<Sponsor Approval Date>)} |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | H |
| Definition | Heading |

| | |
|--|---|
| Term (Variable) | {Overview of Changes in Amendment <Amendment Identifier> (<Sponsor Approval Date>)} |
| User Guidance | Move the Overview of Changes table from the previous amendments to this section in reverse chronological order (most recent first). (Add rows as needed) Add additional Overview of Changes tables as protocol amendments accrue. |
| Conformance | Conditional: when there is an amendment |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 12.3 |
| Value | Overview of Changes in Amendment: |
| Business rules | Value Allowed: No Relationship: {The Overview of Changes from each prior protocol amendment is {provided below} or <specify alternative location>}. Concept: Heading |
| Repeating and/or Reuse Rules | Yes, repeatable one table per amendment |

| | |
|--|---|
| Term (Variable) | <Amendment Identifier> |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C218477 |
| User Guidance | Move the Overview of Changes table from the previous amendments to this section in reverse chronological order (most recent first). |
| Conformance | Conditional: if amendment |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 12.3 |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: {The Overview of Changes from each prior protocol amendment is {provided below} or <specify alternative location>}. Concept: C218477 ICH OID 2.16.840.1.113883.3.989.2.3.3.12 |
| Repeating and/or Reuse Rules | Yes, repeatable one table per amendment identifier |

| | |
|------------------------|-------------------------|
| Term (Variable) | <Sponsor Approval Date> |
| Data Type | Date |

| | |
|--|--|
| Term (Variable) | <Sponsor Approval Date> |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C132352 |
| User Guidance | Move the Overview of Changes table from the previous amendments to this section in reverse chronological order (most recent first). |
| Conformance | Conditional: if amendment |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 12.3 |
| Value | Date |
| Business rules | Value Allowed: Yes Relationship: {The Overview of Changes from each prior protocol amendment is {provided below} or <specify alternative location>. Concept: C132352 ICH OID 2.16.840.1.113883.3.989.2.3.3.12 |
| Repeating and/or Reuse Rules | Yes, repeatable one table per amendment |

| | |
|--|--|
| Term (Variable) | {Description of Change} |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | H |
| Definition | Table Column Heading |
| User Guidance | N/A |
| Conformance | Conditional: if there is a previous amendment |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 12.3 |
| Value | Description of Change |
| Business rules | Value Allowed: No Relationship: Table; 12.3 Prior Protocol Amendment(s) Concept: Table Column Heading |
| Repeating and/or Reuse Rules | No |

| | |
|---|-------------------------|
| Term (Variable) | <Description of Change> |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C218483 |

| | |
|--|--|
| Term (Variable) | <Description of Change> |
| User Guidance | N/A |
| Conformance | Conditional: if there is a previous amendment. Table optional |
| Cardinality | Column Heading Row Content |
| Relationship content from ToC representing the protocol hierarchy | 12.3 |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: Table Column Heading "Description of Change"; 12.3 Prior Protocol Amendment(s) Concept: C218483 ICH OID 2.16.840.1.113883.3.989.2.3.3.12 |
| Repeating and/or Reuse Rules | Yes, repeatable for each Description of Change in the amendment |

| | |
|--|--|
| Term (Variable) | {Brief Rationale for Change} |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | H |
| Definition | Table Column Heading |
| User Guidance | N/A |
| Conformance | Conditional: if there is a previous amendment |
| Cardinality | Column Heading Table |
| Relationship content from ToC representing the protocol hierarchy | 12.3 |
| Value | Brief Rationale for Change |
| Business rules | Value Allowed: No Relationship: Table; 12.3 Prior Protocol Amendment(s) Concept: Table Column Heading |
| Repeating and/or Reuse Rules | No |

| | |
|---|---|
| Term (Variable) | <Brief Rationale for Change> |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C181233 |
| User Guidance | N/A |
| Conformance | Conditional: if there is a previous amendment. Table optional |

| | |
|--|---|
| Term (Variable) | <Brief Rationale for Change> |
| Cardinality | One to Column Heading Row description of change Section # and Name |
| Relationship content from ToC representing the protocol hierarchy | 12.3 |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: Table Column Heading {Brief Rationale for Change} and <Description of Change> Concept: C181233 ICH OID 2.16.840.1.113883.3.989.2.3.3.12 |
| Repeating and/or Reuse Rules | Yes, repeatable for each Description of Change in the amendment |

| | |
|--|--|
| Term (Variable) | {Section # and Name} |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | H |
| Definition | Table Column Heading |
| User Guidance | N/A |
| Conformance | Conditional: if there is a previous amendment |
| Cardinality | Column Heading Table |
| Relationship content from ToC representing the protocol hierarchy | 12.3 |
| Value | Section # and Name |
| Business rules | Value Allowed: No Relationship: Table; 12.3 Prior Protocol Amendment(s) Concept: Table Column Heading |
| Repeating and/or Reuse Rules | No |

| | |
|---|---|
| Term (Variable) | <Section # and Name> |
| Data Type | Valid Value |
| Data (D), Value (V) or Heading (H) | V |
| Definition | C218479 |
| User Guidance | N/A |
| Conformance | Conditional: if there is a previous amendment. Table optional |
| Cardinality | One to one |

| | |
|--|---|
| Term (Variable) | <Section # and Name> |
| Relationship content from ToC representing the protocol hierarchy | 12.3 |
| Value | Code List C217272: ICH OID 2.16.840.1.113883.3.989.2.3.13 C217342 Section 1 C217343 Section 2 C217344 Section 3 C217345 Section 4 C217346 Section 5 C217347 Section 6 C217348 Section 7 C217349 Section 8 C217350 Section 9 C217351 Section 10 C217352 Section 11 C217353 Section 12 C217354 Section 13 C217355 Section 14 C217356 Section Title Page C217357 Section Amendment Details |
| Business rules | Value Allowed: Yes Relationship: Table Column Heading {Section # and Name} and <Description of Change> Concept: C218479 ICH OID 2.16.840.1.113883.3.989.2.3.3.12 |
| Repeating and/or Reuse Rules | Yes, repeatable for each Description of Change in the amendment |

12.4. {Additional appendices}

| | |
|--|---|
| Term (Variable) | 12.X {Additional Appendices} |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | H |
| Definition | Heading |
| User Guidance | N/A |
| Conformance | Conditional |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 12 X where X is a unique number for each Additional Appendix |
| Value | Title of Appendix |
| Business rules | Value Allowed: Yes Relationship: 12 APPENDIX: SUPPORTING DETAILS; Table of Contents Concept: Heading |

| | |
|-------------------------------------|--|
| Term (Variable) | 12.X {Additional Appendices} |
| Repeating and/or Reuse Rules | Yes, repeatable for each Additional Appendix |

| | |
|--|--|
| Term (Variable) | {<Additional Appendices>} |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C220640 |
| User Guidance | N/A |
| Conformance | Conditional |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 12.X where X is a unique number for each Additional Appendix |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: 12.X Additional Appendices Concept: C220640 ICH OID 2.16.840.1.113883.3.989.2.3.3.12 |
| Repeating and/or Reuse Rules | Yes, repeatable for each additional Appendix |

13. Appendix: Glossary of terms and abbreviations

| | |
|--|---|
| Term (Variable) | 13 APPENDIX: GLOSSARY OF TERMS AND ABBREVIATIONS |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | H |
| Definition | Heading |
| User Guidance | N/A |
| Conformance | Required |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 13 |
| Value | APPENDIX: GLOSSARY OF TERMS AND ABBREVIATIONS |
| Business rules | Value Allowed: No Relationship: Table of Contents Concept: Heading |
| Repeating and/or Reuse Rules | No |

| | |
|--|--|
| Term (Variable) | <Glossary of Terms and Abbreviations> |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C218837 |
| User Guidance | Define abbreviations and other terms used in the protocol. A tabular presentation is common and may serve as the definition at first use. |
| Conformance | Required |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 13 |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: 13 APPENDIX: GLOSSARY OF TERMS AND ABBREVIATIONS Concept: C218837 ICH OID 2.16.840.1.113883.3.989.2.3.3.13 |
| Repeating and/or Reuse Rules | No |

14. Appendix: References

| | |
|--|---|
| Term (Variable) | 14 APPENDIX: REFERENCES |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | H |
| Definition | Heading |
| User Guidance | N/A |
| Conformance | Required |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 14 |
| Value | APPENDIX: REFERENCES |
| Business rules | Value Allowed: No Relationship: Table of Contents Concept: Heading |
| Repeating and/or Reuse Rules | No |

| | |
|--|---|
| Term (Variable) | <References> |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C184397 |
| User Guidance | References should be listed in a common format that includes all relevant information to identify the source and date published. If a reference is not published, this should be clearly indicated. |
| Conformance | Required |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 14 |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: 14 APPENDIX: REFERENCES Concept: C184397 ICH OID 2.16.840.1.113883.3.989.2.3.3.14 |
| Repeating and/or Reuse Rules | No |