

医薬品規制調和国際会議

電子的に構造化・調和された臨床試験実施計画書
(CESHARP)

M11 技術仕様

ドラフト版

承認日：2025年3月14日

パブリック・コメントのため公開中

文書の変更履歴ページは省略する。

1 技術仕様

2 本文書の目的は、ICH M11 試験実施計画書テンプレートの技術的表現という役割を果たすことで
 3 ある。本技術仕様は、ICH M11 ガイドライン及び試験実施計画書テンプレートの最新版に沿って
 4 いるが、ICH 及び各地域の当局のデータ交換のニーズに対して柔軟に対応できるものである。

5

6 表の要素の定義

| | |
|--|---|
| Term (Variable) | 試験実施計画書テンプレートにおける変数名 |
| Data Type | 各変数のデータとしての分類 |
| Data (D), Value (V) or Heading (H) | 各データ要素が以下のいずれの種類に該当するかが示される。 Heading : 各項の見出し (表の見出し及び項番号が付されていない見出しを含む) Data : テキスト、画像、数式、表等のコンテンツ Value : 指定された用語から選択する値 |
| Definition | 各データ要素の説明 |
| User Guidance | 試験実施計画書テンプレートに記載される、各データ要素に対する指示内容 |
| Conformance | 試験実施計画書テンプレートで定義された、見出し、データ要素、又はテキストによるコンテンツの設定の必要性に関するルール |
| Cardinality | one to one、one to many、many to many といった多重度を示す。例えば、表に対する行の数値的な関係を示す。 |
| Relationship content from ToC representing the protocol hierarchy | 試験実施計画書テンプレートにおける目次との関係 |
| Value | データ要素又は見出しに記載する値 (記載する値の範囲を含む) を特定する。 (例: ICH M11 valid value から選択される場合がある。また、項番号が付された見出しの場合、項番号はここには含まれない)。 |
| Business rules | Value Allowed : 値を記載することが許容されるか否か。見出しの場合や、ユニバーサルテキストの場合は”No”となる。 Relationship : 目次との関係を含む、データ要素に関する関連性が特定される。目次との関連の場合、項番号は詳細なものから順に記載される。表に関するデータ要素の場合、 Relationship として行見出し又は列見出しが特定される場合がある。試験実施計画書の識別子に対する改訂番号等、その他の関係も定義される。 Concept : 見出しの場合は”Heading”、他の要素については、データ要素に対応する統制用語を特定する番号又は更なる詳細な情報が記載される。 |
| Repeating and/or Reuse Rules | 試験実施計画書内での各データ要素の繰り返しや再利用方法に関する指示。各データ要素の繰り返しが許容されるかや、他の項目で再利用されるかを示す。繰り返しとは、新しいコンテンツのためにデータ要素を複製することを意味し、再利用は、試験実施計画書内の複数のデータ要素の場所で同一のコンテンツとして使用することを意味する。 |

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10 **APPENDIX 1: DETAILED DESCRIPTIONS OF INFORMATION COMPONENTS**

11 **TITLE PAGE**

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

12

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

13

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

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

14

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

15

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

16

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

17

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

18

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

| | |
|-------------------------------------|---|
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: Heading Concept: C132351 Note: Must have at least One Character, May not be space (null) |
| Repeating and/or Reuse Rules | No |

19

| | |
|--|---|
| 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 |

20

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

21

| NCI C-code | M11 Preferred Term | Draft Definition |
|------------|--------------------|---|
| C49487 | No | The non-affirmative response to a question. |
| C49488 | Yes | The affirmative response to a question. |

22

| | |
|------------------------|-----------------|
| 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 |

23

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

24

| | |
|--|---|
| 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 |
|-------------------------------------|----|

25

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

26

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

27

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

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

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

29

| | |
|--|--|
| Term (Variable) | {[Amendment Scope]} |
| Data Type | Valid Value |
| Data (D), Value (V) or Heading (H) | V |
| Definition | CNEW For review purpose, see definition of the controlled terminology below A description as to whether the amendment scope applies globally across the trial. |
| User Guidance | Leave blank for original protocol. If this is the original instance of the protocol, delete the row or enter "Not applicable". If an amendment applies to all sites in the trial, enter "global" and delete the Country, Region and Site Identifier fields. If amending a single-country study, enter "global". |
| Conformance | Conditional: when there is an amendment |
| Cardinality | One to one, One to Amendment Identifier |
| Relationship content from ToC representing the protocol hierarchy | Title page |
| Value | Blank; Global (C68846), Not Global (CNEW) |
| Business rules | Value Allowed: Yes; es if Original Protocol = No; blank if Original Protocol = Yes Relationship: Heading, Amendment Identifier, Sponsor Protocol Identifier Concept: CNEW |
| Repeating and/or Reuse Rules | No |

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| NCI C-code | M11 Preferred Term | Draft Definition |
|------------|--------------------|--|
| C68846 | Global | Covering or affecting the whole of a system. |
| CNEW | Not Global | Covering or affecting a portion of the system. |

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| | |
|--|--|
| Term (Variable) | {[Country Identifier] or [Region Identifier] or <Site Identifier>} |
| Data Type | Valid Value |
| Data (D), Value (V) or Heading (H) | V |
| Definition | C20108 CNEW CNEW For review purpose, see definition of the controlled terminology below C20108 A sequence of characters used to identify and/or name the country. CNEW A sequence of characters used to identify and/or name the region CNEW A sequence of characters used to identify and/or name the study site. |
| User Guidance | Leave blank for original protocol. If the amendment does not apply to all sites in the trial, select “Not Global” and utilise one of the identifiers based on amendment scope. |
| Conformance | Conditional: when 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; CNEW; CNEW |
| Repeating and/or Reuse Rules | Yes, repeatable in 12.2 country/region-specific differences |

33

| | |
|---|--|
| Term (Variable) | Sponsor’s Investigational Product Code(s): |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | H |
| Definition | Heading |
| User Guidance | N/A |

| | |
|--|--|
| Conformance | Optional |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | Title Page |
| Value | Sponsor's Investigational Product Code(s): |
| Business rules | Value Allowed: No Relationship: Table row heading Concept: Heading |
| Repeating and/or Reuse Rules | Yes, repeatable for each Investigational compound |

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

35

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

36

| | |
|------------------------|--------------------------|
| Term (Variable) | <Nonproprietary Name(s)> |
|------------------------|--------------------------|

| | |
|--|---|
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C97054 For review purpose, see definition of the controlled terminology below Drug name that is not protected by a trademark, usually descriptive of its chemical structure, and sometimes a public name. (ICH E2B) |
| User Guidance | Omit nonproprietary name fields if a nonproprietary name has not yet been assigned. |
| Conformance | Optional; Blank |
| Cardinality | One to many; Many to Sponsor Investigational Product Code(s); Many to Sponsor Protocol Identifier |
| Relationship content from ToC representing the protocol hierarchy | Title Page |
| Value | Text Use for example WHO INN, USAN, JAN, XEVMPD |
| Business rules | Value Allowed: Yes Relationship: Heading, Sponsor Protocol Identifier Concept: C97054 |
| Repeating and/or Reuse Rules | Yes, repeatable for each nonproprietary name Yes, repeatable in 1.1.2 under intervention |

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

38

| | |
|---|--|
| 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 |

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| | |
|--|--|
| 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 For review purpose, see definition of the controlled terminology below A stage in the clinical research and development of a therapy from first-in-human to post-approval clinical trials. |
| 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 | Early Phase 1 (C54721); Phase 1(C15600); Phase 1/Phase 2 (C15693) Phase 1/Phase 2/Phase 3 (C198366); Phase 1/Phase 3(C198367); Phase 2(C15601); Phase 2/Phase 3(C15694); Phase2/Phase 3/Phase 4(CNEW); Phase 3(C15602); Phase 3/Phase 4 (CNEW); Phase 4 (C15603))) |
| Business rules | Value Allowed: Yes Relationship: Heading; Sponsor Protocol Identifier Concept: C48281 |
| Repeating and/or Reuse Rules | No |

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| <i>NCI C-code</i> | M11 Preferred Term | Draft Definition |
|-------------------|---------------------------|---|
| C54721 | Early Phase 1 | First-in-human trials, in a small number of participants, that are conducted before Phase 1 trials and are intended to assess new candidate therapeutic and imaging agents. The study agent is administered at a low dose for a limited time, and there is no therapeutic or diagnostic intent. |
| C15600 | Phase 1 | The initial administration of an investigational medicinal product (IMP) into humans in order to examine clinical tolerability and therapeutic intent. Phase 1 trials are typically closely monitored and may be conducted in patients or healthy volunteer participants. |
| C15693 | Phase 1/Phase 2 | A clinical trial that combines elements characteristic of traditional Phase 1 and Phase 2 trials. |
| C198366 | Phase 1/Phase 2/Phase 3 | A clinical trial that begins as a Phase 1 trial and transitions into Phases 2 and 3 based upon successful completion of a milestone that enables transition. |
| C198367 | Phase 1/Phase 3 | A clinical trial that begins as a Phase 1 trial and transitions into a Phase 3 trial based upon successful completion of a milestone that enables transition. |

| | | |
|--------|-------------------------|---|
| CNEW | Phase 2/Phase 3/Phase 4 | A study that begins as a Phase 2 study and transitions into Phases 3 and 4 based upon successful completion of each previous portion. A clinical trial that begins as a Phase 2 trial and transitions into Phases 3 and 4 based upon successful completion of a milestone that enables transition. |
| C15601 | Phase 2 | Exploratory trials conducted to evaluate the safety and efficacy of the investigational intervention in patients with the disease or condition. Objectives can be clinical pharmacology, dose-ranging (dose-response, frequency of dosing), type of patients, or numerous other characteristics of safety and efficacy. |
| C15694 | Phase 2/Phase 3 | A class of clinical study that combines elements characteristic of traditional Phase 2 and Phase 3 trials. A clinical trial that combines elements characteristic of traditional Phase 2 and Phase 3 trials. |
| CNEW | Phase 3/Phase 4 | A clinical trial that combines elements characteristic of traditional Phase 3 and Phase 4 trials. |
| C15602 | Phase 3 | Confirmatory trials conducted to demonstrate safety, efficacy and tolerability of the intervention in patients with the disease or condition. Their objectives are to evaluate the overall benefit-risk relationship and to provide substantial evidence for regulatory approval and labeling. |
| C15603 | Phase 4 | Post-approval trials conducted to further understand the safety and efficacy of the drug in its approved indication. They are not considered necessary for approval but are often important for optimising the drug's use. |
| C17649 | Other | Different than the one(s) previously specified or mentioned. |

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

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| | |
|---|---|
| Term (Variable) | <Trial Short Title> |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | CNEW For review purpose, see definition of the controlled terminology below The short descriptive name for the trial. |

| | |
|--|---|
| 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 consents and ethics committee submissions. |
| Conformance | Optional |
| Cardinality | One to one; One to Sponsor Protocol identifier |
| Relationship content from ToC representing the protocol hierarchy | Title Page |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: Heading; Sponsor Protocol Identifier Concept: CNEW |
| Repeating and/or Reuse Rules | No |

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

44

| | |
|--|---|
| Term (Variable) | <Sponsor Name> |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C70793 For review purpose, see definition of the controlled terminology below The literal identifier (i.e., distinctive designation) of the trial sponsor. |
| User Guidance | Provide the legal name of the individual or pharmaceutical or medical device company, governmental agency, academic institution, private organisation, or other organisation who takes primary responsibility for and initiates a clinical investigation. If more than one Sponsor, list the Primary Sponsor in this field. |
| Conformance | Required |
| Cardinality | One to one; One to Sponsor Protocol Identifier |
| Relationship content from ToC representing the protocol hierarchy | Title Page |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: Heading; Sponsor Protocol Identifier |

| | |
|-------------------------------------|------------------------|
| | Concept: C70793 |
| Repeating and/or Reuse Rules | No |

45

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

46

| | |
|--|--|
| 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 |

47

| | |
|---|---|
| Term (Variable) | <Co-Sponsor Name> |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | CNEW For review purpose, see definition of the controlled terminology below The literal identifier (i.e., distinctive designation) of the trial co-sponsor. |

| | |
|--|---|
| User Guidance | Provide the legal name of the individual or pharmaceutical or medical device company, governmental agency, academic institution, private organisation, or other organisation who takes primary responsibility for and initiates a clinical investigation. If more than one Sponsor, list the Primary Sponsor in this field. |
| Conformance | Optional |
| Cardinality | One to one; One to Co-Sponsor Name; One to Sponsor Name; One to Sponsor Protocol Identifier |
| Relationship content from ToC representing the protocol hierarchy | Title Page |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: Heading; Co-Sponsor Name; Sponsor Name; Protocol Identifier Concept: CNEW |
| Repeating and/or Reuse Rules | No |

48

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

49

| | |
|--|---|
| 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 |

50

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

51

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

52

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

53

| | |
|--|--|
| Term (Variable) | <Device Manufacturer Name> |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | CNEW For review purpose, see definition of the controlled terminology below The literal identifier (i.e., distinctive designation) of the organization defined as being responsible for creating the device as stated on the package in which the product is supplied. |
| User Guidance | Manufacturer name and address information is required only for protocols that include investigational device(s) and <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. Delete this line if not applicable. |
| Conformance | Optional |
| Cardinality | One to one; One to Sponsor Protocol Identifier; One to Sponsor Name |
| Relationship content from ToC representing the protocol hierarchy | Title Page |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: Heading; Sponsor Protocol Identifier; Sponsor Name Concept: CNEW |
| Repeating and/or Reuse Rules | Yes, repeatable for each device manufacturers |

54

| | |
|---|--|
| Term (Variable) | <Device Manufacturer Address> |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | CNEW For review purpose, see definition of the controlled terminology below The legally registered address of the device manufacturer. |

| | |
|--|---|
| User Guidance | Manufacturer name and address information is required only for protocols that include investigational device(s) and should not be included for other protocols. Include the manufacturer address only if the manufacturer is different than the Sponsor listed above. Add additional fields as needed if multiple investigational devices will be used in the trial. Delete this line if not applicable. |
| Conformance | Optional |
| Cardinality | One to One; One to Device Manufacturer Name |
| Relationship content from ToC representing the protocol hierarchy | Title Page |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: Heading; Device Manufacturing Name Concept: CNEW |
| Repeating and/or Reuse Rules | No |

55

| | |
|--|---|
| 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 |

56

| | |
|--|--|
| Term (Variable) | <EU CT Number> |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | CNEW For review purpose, see definition of the controlled terminology below A sequence of characters used to identify a clinical trial, as assigned by the Clinical Trials Information System (CTIS) of the European Medicines Agency. |
| User Guidance | Include all numbers that are applicable for the trial and available at the time of protocol or amendment finalisation. Delete prompts for numbers not available at the time of document finalisation. Delete unused fields. Add fields for "other" if more than one is needed. |
| Conformance | Optional |
| Cardinality | One to one; One to Sponsor Protocol Identifier |
| Relationship content from ToC representing the protocol hierarchy | Title Page |

| | |
|-------------------------------------|---|
| Value | Text |
| Business rules | Value Allowed: Yes; EU CT number: yyyy-5xxxxx-xx with YYYY corresponding to a year i.e. 2024 and x being an integer Relationship: Heading; Sponsor Protocol Identifier Concept: CNEW |
| Repeating and/or Reuse Rules | No |

57

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

58

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

| | |
|-------------------------------------|---|
| | Relationship: Heading; Protocol Identifier Concept: CNEW |
| Repeating and/or Reuse Rules | No |

59

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

60

| | |
|--|--|
| Term (Variable) | <NCT Number> |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | CNEW For review purpose, see definition of the controlled terminology below A sequence of characters used to identify a clinical trial, as assigned by the protocol registration and results (PRS) system of the US National Library of Medicine. |
| User Guidance | Include all numbers that are applicable for the trial and available at the time of protocol or amendment finalisation. Delete prompts for numbers not available at the time of document finalisation. Delete unused fields. Add fields for “other” if more than one is needed. |
| Conformance | Optional |
| Cardinality | One to one; One to Sponsor Protocol Identifier |
| Relationship content from ToC representing the protocol hierarchy | Title Page |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: Heading; Sponsor Protocol Identifier Concept: CNEW |

61

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

62

| | |
|--|--|
| Term (Variable) | <WHO/UTN Number> |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | CNEW For review purpose, see definition of the controlled terminology below A sequence of characters used to identify a clinical trial, as assigned by the World Health Organisation's International Clinical Trial's Registry Platform (ICTRP). |
| User Guidance | Include all numbers that are applicable for the trial and available at the time of protocol or amendment finalisation. Delete prompts for numbers not available at the time of document finalisation. Delete unused fields. Add fields for “other” if more than one is needed. |
| Conformance | Optional |
| Cardinality | One to one; One to Sponsor Protocol Identifier |
| Relationship content from ToC representing the protocol hierarchy | Title Page |
| Value | UTN/WHO: Uxxxx-xxxx-xxxx with X being an integer |
| Business rules | Value Allowed: Yes Relationship: Heading; Sponsor Protocol Identifier Concept: CNEW |
| Repeating and/or Reuse Rules | No |

63

| | |
|--|--|
| Term (Variable) | <Other Regulatory or Clinical Trial Identifier> |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | CNEW For review purpose, see definition of the controlled terminology below A sequence of characters assigned by a regulatory agency or other health authority that is used to identify a clinical trial, and that is different than the one(s) previously specified or mentioned. |
| 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: CNEW |
| Repeating and/or Reuse Rules | Yes, repeatable for each regulatory agency identifier |

64

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

65

| | |
|---|--|
| Term (Variable) | [<Approval Date> or <State location where Information can be found>] |
| Data Type | Valid Value |
| Data (D), Value (V) or Heading (H) | V |
| Definition | CNEW For review purpose, see definition of the controlled terminology below The date that the sponsor approved the current or prior version of the protocol, or the physical or virtual location of the date on which the sponsor approved the current or prior version of the protocol. |
| 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 (C132352) Location of Sponsor Approval Date (CNEW) |
| Business rules | Value Allowed: Yes Relationship: Heading; Protocol Identifier; Protocol Amendment Concept: CNEW |
| Repeating and/or Reuse Rules | Yes, reuse to approval date in Section 12.3 |

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| NCI C-code | M11 Preferred Term | Draft Definition |
|------------|-----------------------------------|---|
| C132352 | Sponsor Approval Date | The date that the sponsor approved the current version of the protocol. |
| CNEW | Location of Sponsor Approval Date | The physical or virtual location of the date on which the sponsor approved the current version of the protocol. |

67

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

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| | |
|---|--|
| Term (Variable) | [{<sponsor signature block (name and title of sponsor signatory and signature date)>} or {This protocol was approved via <describe method>}] |
| Data Type | Valid Value |
| Data (D), Value (V) or Heading (H) | V |
| Definition | CNEW For review purpose, see definition of the controlled terminology below A block of text containing the name and signature of the sponsor's signatory, along with a signature date, or a statement on behalf of the sponsor that describes the method of protocol approval. |
| User Guidance | Include either the Sponsor signature or the statement below. |
| Conformance | Optional |
| Cardinality | One to one |

| | |
|--|--|
| Relationship content from ToC representing the protocol hierarchy | Title Page |
| Value | Sponsor Signature Block (CNEW) OR Sponsor Protocol Approval Statement (CNEW) |
| Business rules | Value Allowed: Yes Relationship: Heading Concept: CNEW |
| Repeating and/or Reuse Rules | No |

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| NCI C-code | M11 Preferred Term | Draft Definition |
|------------|-------------------------------------|--|
| CNEW | Sponsor Signature Block | A block of text containing the name and signature of the sponsor's signatory, along with the signature date. |
| CNEW | Sponsor Protocol Approval Statement | A statement that the protocol was approved by a method as described. |

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| | |
|--|---|
| Term (Variable) | <Describe Method> |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | CNEW For review purpose, see definition of the controlled terminology below The narrative text describing the technique used to approve the protocol. |
| User Guidance | Include either the Sponsor signature or the statement below. |
| Conformance | Conditional if there is a Sponsor Protocol Approval Statement |
| Cardinality | One to Sponsor Protocol Approval Statement |
| Relationship content from ToC representing the protocol hierarchy | Title Page |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: Sponsor Protocol Approval Statement Concept: CNEW |
| Repeating and/or Reuse Rules | No |

71

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

| | |
|-------------------------------------|----|
| Repeating and/or Reuse Rules | No |
|-------------------------------------|----|

72

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

73

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

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| | |
|---|--|
| Term (Variable) | Amendment Details |
| Data Type | Valid Value |
| Data (D), Value (V) or Heading (H) | V |
| Definition | CNEW For review purpose, see definition of the controlled terminology below A written message within the study protocol that describes the amendment details, especially as to whether the protocol has been amended previously. |

| | |
|--|--|
| User Guidance | Choose the applicable statement below. For an original protocol that has not been amended, retain the first sentence below and delete the remainder of this entire section. {Not applicable. This protocol has not been amended.} Or include the below as applicable. {This protocol has been amended previously. Details of prior amendments are presented in Section 12.3 Prior Protocol Amendment(s).} |
| Conformance | Required |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | Amendment Details |
| Value | Not applicable. This protocol has not been amended. (CNEW) OR This is the first protocol amendment. (CNEW) OR This protocol has been amended previously. Details of prior amendments are presented in Prior Protocol Amendment(s). (CNEW) |
| Business rules | Value Allowed: Yes Relationship: Heading Concept: CNEW |
| Repeating and/or Reuse Rules | No |

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| NCI C-code | M11 Preferred Term | Draft Definition |
|-------------------|---|---|
| CNEW | Not applicable. This protocol has not been amended. | Not applicable. This protocol has not been amended. |
| CNEW | Not applicable. This is the first protocol amendment. | Not applicable. This is the first protocol amendment. |
| CNEW | This protocol has been amended previously. Details of prior amendments are presented in Section 12.3 Prior Protocol Amendments. | This protocol has been amended previously. Details of prior amendments are presented in Section 12.3 Prior Protocol Amendments. |
| CNEW | This protocol has been amended previously. The Protocol Amendment Summary of Changes for the current amendment is located directly before the Table of Contents. Prior amendment(s) to this protocol are listed in the table below, beginning with the most recent. | This protocol has been amended previously. The Protocol Amendment Summary of Changes for the current amendment is located directly before the Table of Contents. Prior amendment(s) to this protocol are listed in the table below, beginning with the most recent. |

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| | |
|---|---|
| Term (Variable) | {Current Amendment} |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | H |
| Definition | Heading |
| User Guidance | N/A |
| Conformance | Conditional: If Protocol is Original = No |
| Cardinality | One to one |

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

78

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

79

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

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| | |
|---|--|
| Term (Variable) | Approximately <#/%)> enrolled <Globally/Locally/by Cohort> |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | CNEW |

| | |
|--|---|
| | For review purpose, see definition of the controlled terminology below The value (expressed either numerically or as a percentage) for the estimated number of participants enrolled at the time of the protocol amendment. |
| User Guidance | Enter the approximate number or percentage of participants enrolled as a percentage of the expected total. If the number of expected participants is changing as a result of the current amendment, use the updated number of expected participants to estimate the current per cent of enrollment. Estimates are adequate, as precise enrollment figures will likely be changing while an amendment is being prepared. <ul style="list-style-type: none"> • <u>For a global or single-country amendment</u>, provide the estimated total enrollment at the time of 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, the status of all the relevant locations can be listed <u>For a country/regional amendment</u> , provide the estimated local or regional enrollment at the time the Sponsor approved the amendment. |
| Conformance | Optional |
| Cardinality | One to one; One to amendment number |
| Relationship content from ToC representing the protocol hierarchy | Amendment Details |
| Value | Approximate <#/%> enrolled <Globally/Locally/by Cohort> |
| Business rules | Value Allowed: Yes Relationship: Statement Concept: CNEW |
| Repeating and/or Reuse Rules | Yes, reuse to Section 12.3 |

81

| | |
|---|---|
| Term (Variable) | Number or % |
| Data Type | Number |
| Data (D), Value (V) or Heading (H) | D |
| Definition | CNEW For review purpose, see definition of the controlled terminology below The numeric value (expressed as an absolute value or percentage) for the estimated number of participants enrolled at the time of the protocol amendment. |
| User Guidance | Enter the approximate number or percentage of participants enrolled as a percentage of the expected total. If the number of expected participants is changing as a result of the current amendment, use the updated number of expected participants to estimate the current per cent of enrollment. Estimates are adequate, as precise enrollment figures will likely be changing while an amendment is being prepared. <ul style="list-style-type: none"> • <u>For a global or single-country amendment</u>, provide the estimated total enrollment at the time of 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, the status of all the relevant locations can be listed <u>For a country/regional amendment</u> , provide the estimated local or regional enrollment at the time the Sponsor approved the amendment. |

| | |
|--|--|
| Conformance | Conditional if Original Protocol =No |
| Cardinality | One to Amendment Number |
| Relationship content from ToC representing the protocol hierarchy | Amendment Details |
| Value | Integer for Number or one decimal point for percent |
| Business rules | Value Allowed: Yes Relationship: Table Row Heading; Statement Concept: CNEW |
| Repeating and/or Reuse Rules | Yes, reuse to section 12.3 |

82

| | |
|--|---|
| Term (Variable) | Amendment Scope Enrollment Description |
| Data Type | Valid Value |
| Data (D), Value (V) or Heading (H) | V or D |
| Definition | CNEW For review purpose, see definition of the controlled terminology below The enrollment description as to whether the amendment scope applies globally, locally, or per cohort across the trial. |
| User Guidance | Enter the approximate number or percentage of participants enrolled as a percentage of the expected total. If the number of expected participants is changing as a result of the current amendment, use the updated number of expected participants to estimate the current per cent of enrollment. Estimates are adequate, as precise enrollment figures will likely be changing while an amendment is being prepared. <ul style="list-style-type: none"> • For a <u>global or single-country amendment</u>, provide the estimated total enrollment at the time of 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, the status of all the relevant locations can be listed For a <u>country/regional amendment</u> , provide the estimated local or regional enrollment at the time the Sponsor approved the amendment. |
| Conformance | Conditional if Original Protocol =No |
| Cardinality | One to Amendment Number |
| Relationship content from ToC representing the protocol hierarchy | Amendment Details |
| Value | Globally (C68846); Locally (CNEW); Cohort (CNEW) |
| Business rules | Value Allowed: Yes Relationship: Statement Concept: CNEW |
| Repeating and/or Reuse Rules | Yes, reuse to section 12.3 |

83

| NCI C-code | M11 Preferred Term | Draft Definition |
|------------|--------------------|--|
| C68846 | Globally | Covering or affecting the whole of a system. |
| CNEW | Locally | Covering or affecting a portion of the system. |
| CNEW | Cohort | Covering or affecting a cohort of individuals. |

84

| | |
|------------------------|---------------------------|
| Term (Variable) | {Reason(s) for Amendment} |
|------------------------|---------------------------|

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

85

| | |
|--|--|
| 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 |

86

| | |
|--|---|
| Term (Variable) | [Primary Reason for Amendment]} |
| Data Type | Valid Value |
| Data (D), Value (V) or Heading (H) | V |
| Definition | CNEW For review purpose, see definition of the controlled terminology below The rationale for the change(s) to, or formal clarification of, a protocol. |
| 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 |
| Cardinality | One to Amendment Details |
| Relationship content from ToC representing the protocol hierarchy | Amendment Details |

| | |
|-------------------------------------|--|
| Value | <ul style="list-style-type: none"> • Regulatory agency request to amend (CNEW) • New regulatory guidance (CNEW) • IRB/IEC feedback (CNEW) • New safety information available (CNEW) • Manufacturing change (NEW) • IMP addition (CNEW) • Change in strategy (CNEW) • Change in standard of care (CNEW) • New data available (other than safety data) (CNEW) • Investigator/site feedback (CNEW) • Recruitment difficulty (CNEW) • Inconsistency and/or error in the protocol (CNEW) • Protocol design error (CNEW) • Other(C17649) • Not applicable(C48660) |
| Business rules | <p>Value Allowed: Yes</p> <p>Relationship: Heading; Sponsor Protocol Identifier; Protocol Amendment</p> <p>Concept: CNEW</p> |
| Repeating and/or Reuse Rules | Yes, Multiple values can be selected except when it is Original Protocol |

87

| NCI C-Code | M11 Preferred Term | Draft Definition |
|-------------------|---|--|
| CNEW | Regulatory Agency Request To Amend | A regulatory agency has expressed a need for a change(s) to, or formal clarification of, the protocol. |
| CNEW | New Regulatory Guidance | A regulatory agency has published a guidance document that necessitates a change(s) to, or formal clarification of, the protocol. |
| CNEW | IRB/IEC Feedback | Feedback from the institutional review board or independent ethics committee necessitates a change(s) to, or formal clarification of, the protocol. |
| CNEW | New Safety Information Available | Previously unavailable safety data becomes available, which necessitates a change(s) to, or formal clarification of, the protocol. |
| CNEW | Manufacturing Change | A change to manufacturing processes of the study agents necessitates a change(s) to, or formal clarification of, the protocol. |
| CNEW | IMP Addition | The addition of an investigational medicinal product to a clinical trial design necessitates a change(s) to, or formal clarification of, the protocol. |
| CNEW | Change In Strategy | A change in the study purpose or intent of the scientific plan necessitates a change(s) to, or formal clarification of, the protocol. |
| CNEW | Change In Standard Of Care | A change in the standard of care necessitates a change(s) to, or formal clarification of, the protocol. |
| CNEW | New Data Available (Other Than Safety Data) | Previously unavailable data (other than safety data) becomes available, which necessitates a change(s) to, or formal clarification of, the protocol. |
| CNEW | Investigator/Site Feedback | Feedback from the investigator or study site necessitates a change(s) to, or formal clarification of, the protocol. |
| CNEW | Recruitment Difficulty | Challenges with participant recruitment necessitates a change(s) to, or formal clarification of, the protocol. |
| CNEW | Inconsistency And/Or Error In The Protocol | An error or inconsistency in the protocol necessitates a change(s) to, or formal clarification of, the protocol. |

| | | |
|--------|-----------------------|--|
| CNEW | Protocol Design Error | A protocol design error necessitates a change(s) to, or formal clarification of, a document. |
| C17649 | Other | Different than the one(s) previously specified or mentioned. |
| C48660 | Not Applicable | Determination of a value is not relevant in the current context. |

88

| | |
|--|--|
| 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 |

89

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

90

| | |
|--|---|
| Term (Variable) | {[Secondary Reason for Amendment]} |
| Data Type | Valid Value |
| Data (D), Value (V) or Heading (H) | V |
| Definition | CNEW For review purpose, see definition of the controlled terminology below Additional rationale for the protocol amendment that is not considered the primary rationale. |
| User Guidance | Choose from the available categories as the <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 | <ul style="list-style-type: none"> • Regulatory agency request to amend (CNEW) • New regulatory guidance (CNEW) • IRB/IEC feedback (CNEW) • New safety information available (CNEW) • Manufacturing change (CNEW) • IMP addition (CNEW) • Change in strategy (CNEW) • Change in standard of care (CNEW) • New data available (other than safety data) (CNEW) • Investigator/site feedback (CNEW) • Recruitment difficulty (CNEW) • Inconsistency and/or error in the protocol (CNEW) • Protocol design error (CNEW) • Other(C17649) • Not applicable(C48660) |
| Business rules | Value Allowed: Yes Relationship: Heading, Sponsor Protocol Identifier, Protocol Amendment Concept: CNEW |
| Repeating and/or Reuse Rules | Yes, Multiple accepted except for the Original |

91

| | | |
|-------------------|---------------------------|-------------------------|
| NCI C-Code | M11 Preferred Term | Draft Definition |
|-------------------|---------------------------|-------------------------|

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

92

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

93

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

| | |
|--|---|
| Definition | CNEW For review purpose, see definition of the controlled terminology below A short description describing the changes introduced in the current version of the protocol. |
| User Guidance | Describe key changes briefly. Changes which are included in the amendment but unrelated to the key changes do not need to be described here. |
| Conformance | Conditional: if there is an amendment |
| Cardinality | One to Amendment identifier |
| Relationship content from ToC representing the protocol hierarchy | Amendment Details |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: Amendment Details; Amendment Identifier; Sponsor Protocol Identifier Concept: CNEW |
| Repeating and/or Reuse Rules | No |

94

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

95

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

| | |
|-------------------------------------|--|
| Value | Yes (C49488); No (C49487) |
| Business rules | Value Allowed: Yes Relationship: Amendment Details; Amendment Identifier; Sponsor Protocol Identifier Concept: CNEW |
| Repeating and/or Reuse Rules | No |

96

| NCI C-Code | M11 Preferred Term | Draft Definition |
|------------|--------------------|---|
| C49487 | No | The non-affirmative response to a question. |
| C49488 | Yes | The affirmative response to a question. |

97

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

98

| | |
|--|--|
| 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 |

99

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

100

| NCI C-Code | M11 Preferred Term | Draft Definition |
|------------|--------------------|---|
| C49487 | No | The non-affirmative response to a question. |
| C49488 | Yes | The affirmative response to a question. |

101

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

| | |
|-------------------------------------|---|
| | Relationship: Amendment Details; Amendment Identifier; Sponsor Protocol Identifier When the value is yes there is a text response for explanation Concept: CNEW |
| Repeating and/or Reuse Rules | No |

102

| | |
|--|---|
| Term (Variable) | {Overview of Changes in the Current Amendment:} |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | H |
| Definition | Heading |
| 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 clean overview table for the current amendment. • List the changes that apply to the current amendment. Provide a brief description of the change(s) and a concise scientific rationale for specific changes (e.g., change to inclusion/exclusion criteria). • If the same change affects multiple parts of the protocol, it is acceptable to list multiple locations in the right column. • Table can be sorted in any order preferred by the sponsor. • Minor edits such as clarifications and corrections to typographical errors do not need to be itemised in this table. • The changes in the table do not need to be detailed in revision marks, as these can be provided in a separate supporting document. <p>Tabular presentation is common but not required. The page can be changed to landscape orientation if necessary.</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 | Value Allowed: No Relationship: Amendment Details Concept: Heading |
| Repeating and/or Reuse Rules | No |

103

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

| | |
|-------------------------------------|---|
| | Relationship: Table Column Heading; Amendment Details Concept: Heading |
| Repeating and/or Reuse Rules | No |

104

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

105

| | |
|--|--|
| 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 |

106

| | |
|---|------------------------------|
| Term (Variable) | <Brief Rationale for Change> |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | CNEW |

| | |
|--|---|
| | For review purpose, see definition of the controlled terminology below The brief reason for the change introduced in the current or prior version of the protocol. |
| User Guidance | N/A |
| Conformance | Conditional: if there is an amendment |
| Cardinality | One to many |
| Relationship content from ToC representing the protocol hierarchy | Amendment Details |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: Amendment Details; Table Column Heading Row; Description of change; Section # and Name Concept: CNEW |
| Repeating and/or Reuse Rules | Yes, repeatable for each description of change in the amendment |

107

| | |
|--|---|
| 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 |

108

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

| | |
|-------------------------------------|--|
| Value | |
| Business rules | Value Allowed: Yes Relationship: Amendment Details, Brief Rational; Change description; Table Concept: CNEW |
| Repeating and/or Reuse Rules | Yes, repeatable for each description of change in the amendment |

| NCI C-code | M11 Preferred Term | Draft Definition |
|-------------------|---|--|
| CNEW | 1 PROTOCOL SUMMARY | Section 1 of the ICH M11 Protocol standard, PROTOCOL SUMMARY. |
| CNEW | 1.1 Protocol Synopsis | Section 1.1 of the ICH M11 Protocol standard, Protocol Synopsis. |
| CNEW | 1.1.1 Primary and Secondary Objectives and Estimands | Section 1.1.1 of the ICH M11 Protocol standard, Primary and Secondary Objectives and Estimands. |
| CNEW | 1.1.2 Overall Design | Section 1.1.2 of the ICH M11 Protocol standard, Overall Design. |
| CNEW | 1.2 Trial Schema | Section 1.2 of the ICH M11 Protocol standard, Trial Schema. |
| CNEW | 1.3 Schedule of Activities | Section 1.3 of the ICH M11 Protocol standard, Schedule of Activities. |
| CNEW | 2 INTRODUCTION | Section 2 of the ICH M11 Protocol standard, INTRODUCTION. |
| CNEW | 2.1 Purpose of Trial | Section 2.1 of the ICH M11 Protocol standard, Purpose of Trial. |
| CNEW | 2.2 Assessment of Risks and Benefits | Section 2.2 of the ICH M11 Protocol standard, Assessment of Risks and Benefits. |
| CNEW | 2.2.1 Risk Summary and Mitigation Strategy | Section 2.2.2 of the ICH M11 Protocol standard, Risk Summary and Mitigation Strategy. |
| CNEW | 2.2.2 Benefit Summary | Section 2.2.1 of the ICH M11 Protocol standard, Benefit Summary. |
| CNEW | 2.2.3 Overall Benefit-Risk Assessment | Section 2.2.3 of the ICH M11 Protocol standard, Overall Benefit:Risk Assessment. |
| CNEW | 3 TRIAL OBJECTIVES AND ASSOCIATED ESTIMANDS | Section 3 of the ICH M11 Protocol standard, TRIAL OBJECTIVES AND ASSOCIATED ESTIMANDS. |
| CNEW | 3.1 Primary Objective(s) and Associated Estimand(s) | Section 3.1 of the ICH M11 Protocol standard, Primary Objective(s) and Associated Estimand(s). |
| CNEW | 3.1.1 Primary Objective # | Section 3.1.1 of the ICH M11 Protocol standard, Primary Objective. |
| CNEW | 3.2 Secondary Objective(s) and Associated Estimand(s) | Section 3.2 of the ICH M11 Protocol standard, Secondary Objective(s) and Associated Estimand(s). |
| CNEW | 3.2.1 Secondary Objective # | Section 3.2.1 of the ICH M11 Protocol standard, Secondary Objective. |
| CNEW | 3.3 Exploratory Objective(s) | Section 3.3 of the ICH M11 Protocol standard, Exploratory Objective(s). |
| CNEW | 3.3.1 Exploratory Objective # | Section 3.3.1 of the ICH M11 Protocol standard, Exploratory Objective. |
| CNEW | 4 TRIAL DESIGN | Section 4 of the ICH M11 Protocol standard, TRIAL DESIGN. |
| CNEW | 4.1 Description of Trial Design | Section 4.1 of the ICH M11 Protocol standard, Description of Trial Design. |
| CNEW | 4.1.1 Stakeholder Input into Design | Section 4.1.1 of the ICH M11 Protocol standard, Stakeholder Input into Design. |

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| CNEW | 4.2 Rationale for Trial Design | Section 4.2 of the ICH M11 Protocol standard, Rationale for Trial Design. |
| CNEW | 4.2.1 Rationale for Estimand(s) | Section 4.2.1 of the ICH M11 Protocol standard, Rationale for Estimand(s). |
| CNEW | 4.2.2 Rationale for Intervention Model | Section 4.2.2 of the ICH M11 Protocol standard, Rationale for Intervention Model. |
| CNEW | 4.2.3 Rationale for Control Type | Section 4.2.3 of the ICH M11 Protocol standard, Rationale for Control Type. |
| CNEW | 4.2.4 Rationale for Trial Duration | Section 4.2.4 of the ICH M11 Protocol standard, Rationale for Trial Duration. |
| CNEW | 4.2.3 Rationale for Estimand Attributes | Section 4.2.3 of the ICH M11 Protocol standard, Rationale for Estimand Attributes. |
| CNEW | 4.2.5 Rationale for Adaptive or Novel Trial Design | Section 4.2.5 of the ICH M11 Protocol standard, Rationale for Adaptive or Novel Trial Design. |
| CNEW | 4.2.6 Rationale for Interim Analysis | Section 4.2.6 of the ICH M11 Protocol standard, Rationale for Interim Analysis. |
| CNEW | 4.2.7 Rationale for Other Trial Design Aspects | Section 4.2.7 of the ICH M11 Protocol standard, Rationale for Other Trial Design Aspects. |
| CNEW | 4.3 Trial Stopping Rules | Section 4.3 of the ICH M11 Protocol standard, Trial Stopping Rules. |
| CNEW | 4.4 Start of Trial and End of Trial | Section 4.4 of the ICH M11 Protocol standard, Start of Trial and End of Trial. |
| CNEW | 4.5 Access to Trial Intervention After End of Trial | Section 4.5 of the ICH M11 Protocol standard, Access to Trial Intervention After End of Trial. |
| CNEW | 5 TRIAL POPULATION | Section 5 of the ICH M11 Protocol standard, TRIAL POPULATION. |
| CNEW | 5.1 Description of Trial Population and Rationale | Section 5.1 of the ICH M11 Protocol standard, Description of Trial Population and Rationale. |
| CNEW | 5.2 Inclusion Criteria | Section 5.2 of the ICH M11 Protocol standard, Inclusion Criteria. |
| CNEW | 5.3 Exclusion Criteria | Section 5.3 of the ICH M11 Protocol standard, Exclusion Criteria. |
| CNEW | 5.4 Contraception | Section 5.4 of the ICH M11 Protocol standard, Contraception. |
| CNEW | 5.4.1 Definitions Related to Childbearing Potential | Section 5.4.1 of the ICH M11 Protocol standard, Definitions Related to Childbearing Potential. |
| CNEW | 5.4.2 Contraception Requirements | Section 5.4.2 of the ICH M11 Protocol standard, Contraception Requirements. |
| CNEW | 5.5 Lifestyle Restrictions | Section 5.5 of the ICH M11 Protocol standard, Lifestyle Restrictions. |
| CNEW | 5.5.1 Meals and Dietary Restrictions | Section 5.5.1 of the ICH M11 Protocol standard, Meals and Dietary Restrictions. |
| CNEW | 5.5.2 Caffeine, Alcohol, Tobacco, and Other Restrictions | Section 5.5.2 of the ICH M11 Protocol standard, Caffeine, Alcohol, Tobacco, and Other Restrictions. |
| CNEW | 5.5.3 Physical Activity Restrictions | Section 5.5.3 of the ICH M11 Protocol standard, Physical Activity Restrictions. |
| CNEW | 5.5.4 Other Activity Restrictions | Section 5.5.4 of the ICH M11 Protocol standard, Other Activity Restrictions. |
| CNEW | 5.6 Screen Failure and Rescreening | Section 5.6 of the ICH M11 Protocol standard, Screen Failure and Rescreening. |
| CNEW | 6 TRIAL INTERVENTION | Section 6 of the ICH M11 Protocol standard, TRIAL INTERVENTION AND CONCOMITANT THERAPY. |

| | AND CONCOMITANT THERAPY | |
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| CNEW | 6.1 Description of Investigational Trial Intervention | Section 6.1 of the ICH M11 Protocol standard, Description of Investigational Trial Intervention. |
| CNEW | 6.2 Rationale for Investigational Trial Intervention Dose and Regimen | Section 6.2 of the ICH M11 Protocol standard, Rationale for Investigational Trial Intervention Dose and Regimen. |
| CNEW | 6.3 Investigational Trial Intervention Administration | Section 6.3 of the ICH M11 Protocol standard, Investigational Trial Intervention Administration. |
| CNEW | 6.4 Investigational Trial Intervention Dose Modification | Section 6.4 of the ICH M11 Protocol standard, Investigational Trial Intervention Dose Modification. |
| CNEW | 6.5 Management of Investigational Trial Intervention Overdose | Section 6.5 of the ICH M11 Protocol standard, Management of Investigational Trial Intervention Overdose. |
| CNEW | 6.6 Preparation, Storage, Handling and Accountability of Investigational Trial Intervention | Section 6.6 of the ICH M11 Protocol standard, Preparation, Storage, Handling and Accountability of Investigational Trial Intervention. |
| CNEW | 6.6.1 Preparation of Investigational Trial Intervention | Section 6.6.1 of the ICH M11 Protocol standard, Preparation of Investigational Trial Intervention. |
| CNEW | 6.6.2 Storage and Handling of Investigational Trial Intervention | Section 6.6.2 of the ICH M11 Protocol standard, Storage and Handling of Investigational Trial Intervention. |
| CNEW | 6.6.3 Accountability of Investigational Trial Intervention | Section 6.6.3 of the ICH M11 Protocol standard, Accountability of Investigational Trial Intervention. |
| CNEW | 6.7 Investigational Trial Intervention Assignment, Randomisation and Blinding | Section 6.7 of the ICH M11 Protocol standard, Investigational Trial Intervention Assignment, Randomisation and Blinding. |
| CNEW | 6.7.1 Participant Assignment to Investigational Trial Intervention | Section 6.7.1 of the ICH M11 Protocol standard, Participant Assignment to Investigational Trial Intervention. |
| CNEW | 6.7.2 Randomisation | Section 6.7.2 of the ICH M11 Protocol standard, Randomisation. |
| CNEW | 6.7.3 Measures to Maintain Blinding | Section 6.7.3 of the ICH M11 Protocol standard, Measures to Maintain Blinding. |
| CNEW | 6.7.4 Emergency Unblinding at the Site | Section 6.7.4 of the ICH M11 Protocol standard, Emergency Unblinding at the Site. |
| CNEW | 6.8 Investigational Trial Intervention Adherence | Section 6.8 of the ICH M11 Protocol standard, Investigational Trial Intervention Adherence. |
| CNEW | 6.9 Description of Noninvestigational Trial Intervention | Section 6.9 of the ICH M11 Protocol standard, Description of Noninvestigational Trial Intervention. |

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| CNEW | 6.9.1 Background Trial Intervention | Section 6.9.1 of the ICH M11 Protocol standard, Background Trial Intervention. |
| CNEW | 6.9.2 Rescue Therapy | Section 6.9.2 of the ICH M11 Protocol standard, Rescue Therapy. |
| CNEW | 6.9.3 Other Noninvestigational Trial Intervention | Section 6.9.3 of the ICH M11 Protocol standard, Other Noninvestigational Trial Intervention. |
| CNEW | 6.10 Concomitant Therapy | Section 6.10 of the ICH M10 Protocol standard, Concomitant Therapy. |
| CNEW | 6.10.1 Prohibited Concomitant Therapy | Section 6.10.1 of the ICH M10 Protocol standard, Prohibited Concomitant Therapy. |
| CNEW | 6.10.2 Permitted Concomitant Therapy | Section 6.10.2 of the ICH M10 Protocol standard, Permitted Concomitant Therapy. |
| CNEW | 7 PARTICIPANT DISCONTINUATION OF TRIAL INTERVENTION AND DISCONTINUATION OR WITHDRAWAL FROM TRIAL | Section 7 of the ICH M11 Protocol standard, PARTICIPANT DISCONTINUATION OF TRIAL INTERVENTION AND DISCONTINUATION OR WITHDRAWAL FROM TRIAL. |
| CNEW | 7.1 Discontinuation of Trial Intervention for Individual Participants | Section 7.1 of the ICH M11 Protocol standard, Discontinuation of Trial Intervention for Individual Participants. |
| CNEW | 7.1.1 Permanent Discontinuation of Trial Intervention | Section 7.1.1 of the ICH M11 Protocol standard, Permanent Discontinuation of Trial Intervention. |
| CNEW | 7.1.2 Temporary Discontinuation of Trial Intervention | Section 7.1.2 of the ICH M11 Protocol standard, Temporary Discontinuation of Trial Intervention. |
| CNEW | 7.1.3 Rechallenge | Section 7.1.3 of the ICH M11 Protocol standard, Rechallenge. |
| CNEW | 7.2 Participant Discontinuation or Withdrawal from the Trial | Section 7.2 of the ICH M11 Protocol standard, Participant Discontinuation or Withdrawal from the Trial. |
| CNEW | 7.3 Lost to Follow-Up | Section 7.3 of the ICH M11 Protocol standard, Lost to Follow-Up. |
| CNEW | 8 TRIAL ASSESSMENTS AND PROCEDURES | Section 8 of the ICH M11 Protocol standard, TRIAL ASSESSMENTS AND PROCEDURES. |
| CNEW | 8.1 Trial Assessments and Procedures Considerations | Section 8.1 of the ICH M11 Protocol standard, Trial Assessments and Procedures Considerations. |
| CNEW | 8.2 Screening/Baseline Assessments and Procedures | Section 8.2 of the ICH M11 Protocol standard, Screening/Baseline Assessments and Procedures. |
| CNEW | 8.3 Efficacy Assessments and Procedures | Section 8.3 of the ICH M11 Protocol standard, Efficacy Assessments and Procedures. |
| CNEW | 8.4 Safety Assessments and Procedures | Section 8.4 of the ICH M11 Protocol standard, Safety Assessments and Procedures. |
| CNEW | 8.4.1 Physical Examination | Section 8.4.1 of the ICH M11 Protocol standard, Physical Examination. |
| CNEW | 8.4.2 Vital Signs | Section 8.4.2 of the ICH M11 Protocol standard, Vital Signs. |
| CNEW | 8.4.3 Electrocardiograms | Section 8.4.3 of the ICH M11 Protocol standard, Electrocardiograms. |

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| CNEW | 8.4.4 Clinical Laboratory Assessments | Section 8.4.4 of the ICH M11 Protocol standard, Clinical Laboratory Assessments. |
| CNEW | 8.4.5 Pregnancy Testing | Section 8.4.5 of the ICH M11 Protocol standard, Pregnancy Testing. |
| CNEW | 8.4.6 Suicidal Ideation and Behaviour Risk Monitoring | Section 8.4.6 of the ICH M11 Protocol standard, Suicidal Ideation and Behaviour Risk Monitoring. |
| CNEW | 8.5 Pharmacokinetics | Section 8.5 of the ICH M11 Protocol standard, Pharmacokinetics. |
| CNEW | 8.6 Biomarkers | Section 8.6 of the ICH M11 Protocol standard, Biomarkers. |
| CNEW | 8.6.1 Genetics and Pharmacogenomics | Section 8.6.1 of the ICH M11 Protocol standard, Genetics and Pharmacogenomics. |
| CNEW | 8.6.2 Pharmacodynamic Biomarkers | Section 8.6.2 of the ICH M11 Protocol standard, Pharmacodynamic Biomarkers. |
| CNEW | 8.6.3 Other Biomarkers | Section 8.6.3 of the ICH M11 Protocol standard, Other Biomarkers. |
| CNEW | 8.7 Immunogenicity Assessments | Section 8.7 of the ICH M11 Protocol standard, Immunogenicity Assessments. |
| CNEW | 8.8 Medical Resource Utilisation and Health Economics | Section 8.8 of the ICH M11 Protocol standard, Medical Resource Utilisation and Health Economics. |
| CNEW | 9 ADVERSE EVENTS, SERIOUS ADVERSE EVENTS, PRODUCT COMPLAINTS, PREGNANCY AND POSTPARTUM INFORMATION, AND SPECIAL SAFETY SITUATIONS | Section 9 of the ICH M11 Protocol standard, ADVERSE EVENTS, SERIOUS ADVERSE EVENTS, PRODUCT COMPLAINTS, PREGNANCY AND POSTPARTUM INFORMATION, AND SPECIAL SAFETY SITUATIONS. |
| CNEW | 9.1 Definitions | Section 9.1 of the ICH M11 Protocol standard, Definitions. |
| CNEW | 9.1.1 Definitions of Adverse Events | Section 9.1.1 of the ICH M11 Protocol standard, Definitions of Adverse Events. |
| CNEW | 9.1.2 Definitions of Serious Adverse Events | Section 9.1.2 of the ICH M11 Protocol standard, Definitions of Serious Adverse Events. |
| CNEW | 9.1.3 Definitions of Product Complaints | Section 9.1.3 of the ICH M11 Protocol standard, Definitions of Product Complaints. |
| CNEW | 9.1.3.1 Definitions of Medical Device Product Complaints | Section 9.1.3.1 of the ICH M11 Protocol standard, Definitions of Medical Device Product Complaints. |
| CNEW | 9.2 Timing and Procedures for Collection and Reporting | Section 9.2 of the ICH M11 Protocol standard, Timing and Procedures for Collection and Reporting. |
| CNEW | 9.2.1 Timing | Section 9.2.1 of the ICH M11 Protocol standard, Timing. |
| CNEW | 9.2.2 Collection Procedures | Section 9.2.2 of the ICH M11 Protocol standard, Collection Procedures. |
| CNEW | 9.2.3 Reporting | Section 9.2.3 of the ICH M11 Protocol standard, Reporting. |
| CNEW | 9.2.3.1 Regulatory Reporting Requirements | Section 9.2.3.1 of the ICH M11 Protocol standard, Regulatory Reporting Requirements. |

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| CNEW | 9.2.4 Adverse Events of Special Interest | Section 9.2.4 of the ICH M11 Protocol standard, Adverse Events of Special Interest. |
| CNEW | 9.2.5 Disease-related Events or Outcomes Not Qualifying as AEs or SAEs | Section 9.2.5 of the ICH M11 Protocol standard, Disease-related Events or Outcomes Not Qualifying as AEs or SAEs. |
| CNEW | 9.3 Pregnancy and Postpartum Information | Section 9.3 of the ICH M11 Protocol standard, Pregnancy and Postpartum Information. |
| CNEW | 9.3.1 Participants Who Become Pregnant During the Trial | Section 9.3.1 of the ICH M11 Protocol standard, Participants Who Become Pregnant During the Trial. |
| CNEW | 9.3.2 Participants Whose Partners Become Pregnant During the Trial | Section 9.3.2 of the ICH M11 Protocol standard, Participants Whose Partners Become Pregnant During the Trial. |
| CNEW | 9.4 Special Safety Situations | Section 9.4 of the ICH M11 Protocol standard, Special Safety Situations. |
| CNEW | 10 STATISTICAL CONSIDERATIONS | Section 10 of the ICH M11 Protocol standard, STATISTICAL CONSIDERATIONS. |
| CNEW | 10.1 General Considerations | Section 10.1 of the ICH M11 Protocol standard, General Considerations. |
| CNEW | 10.2 Analysis Sets | Section 10.2 of the ICH M11 Protocol standard, Analysis Sets. |
| CNEW | 10.3 Analyses of Demographics and Other Baseline Variables | Section 10.3 of the ICH M11 Protocol standard, Analyses of Demographics and Other Baseline Variables. |
| CNEW | 10.4 Analyses Associated with the Primary Objective(s) | Section 10.4 of the ICH M11 Protocol standard, Analyses Associated with the Primary Objective(s). |
| CNEW | 10.4.1 Primary Objective # | Section 10.4.1 of the ICH M11 Protocol standard, Primary Objective. |
| CNEW | 10.4.1.1 Statistical Analysis Method | Section 10.4.1.1 of the ICH M11 Protocol standard, Statistical Analysis Method. |
| CNEW | 10.4.1.2 Handling of Data in Relation to Primary Estimand(s) | Section 10.4.1.2 of the ICH M11 Protocol standard, Handling of Data in Relation to Primary Estimand(s). |
| CNEW | 10.4.1.3 Handling of Missing Data in Relation to Primary Estimand(s) | Section 10.4.1.3 of the ICH M11 Protocol standard, Handling of Missing Data in Relation to Primary Estimand(s) |
| CNEW | 10.4.1.4 Sensitivity Analysis | Section 10.4.1.4 of the ICH M11 Protocol standard, Sensitivity Analysis. |
| CNEW | 10.4.1.5 Supplementary Analysis | Section 10.4.1.5 of the ICH M11 Protocol standard, Supplementary Analysis. |
| CNEW | 10.5 Analyses Associated with the Secondary Objective(s) | Section 10.5 of the ICH M11 Protocol standard, Analyses Associated with the Secondary Objective(s). |
| CNEW | 10.5.1 Secondary Objective # | Section 10.5.1 of the ICH M11 Protocol standard, Secondary Objective. |
| CNEW | 10.5.1.1 Statistical Analysis Method | Section 10.5.1.1 of the ICH M11 Protocol standard, Statistical Analysis Method. |

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| CNEW | 10.5.1.2 Handling of Data in Relation to Secondary Estimand(s) | Section 10.5.1.2 of the ICH M11 Protocol standard, Handling of Data in Relation to Secondary Estimand(s). |
| CNEW | 10.5.1.3 Handling of Missing Data in Relation to Secondary Estimand(s) | Section 10.5.1.3 of the ICH M11 Protocol standard, Handling of Missing Data in Relation to Secondary Estimand(s). |
| CNEW | 10.5.1.4 Sensitivity Analysis | Section 10.5.1.4 of the ICH M11 Protocol standard, Sensitivity Analysis. |
| CNEW | 10.5.1.5 Supplementary Analysis | Section 10.5.1.5 of the ICH M11 Protocol standard, Supplementary Analysis. |
| CNEW | 10.6 Analysis Associated with the Exploratory Objective(s) | Section 10.6 of the ICH M11 Protocol standard, Analysis Associated with the Exploratory Objective(s). |
| CNEW | 10.7 Safety Analyses | Section 10.7 of the ICH M11 Protocol standard, Safety Analyses. |
| CNEW | 10.8 Other Analyses | Section 10.8 of the ICH M11 Protocol standard, Other Analyses. |
| CNEW | 10.9 Interim Analyses | Section 10.9 of the ICH M11 Protocol standard, Interim Analyses. |
| CNEW | 10.10 Multiplicity Adjustments | Section 10.10 of the ICH M11 Protocol standard, Multiplicity Adjustments. |
| CNEW | 10.11 Sample Size Determination | Section 10.11 of the ICH M11 Protocol standard, Sample Size Determination. |
| CNEW | 11 TRIAL OVERSIGHT AND OTHER GENERAL CONSIDERATIONS | Section 11 of the ICH M11 Protocol standard, TRIAL OVERSIGHT AND OTHER GENERAL CONSIDERATIONS. |
| CNEW | 11.1 Regulatory and Ethical Considerations | Section 11.1 of the ICH M11 Protocol standard, Regulatory and Ethical Considerations. |
| CNEW | 11.2 Trial Oversight | Section 11.2 of the ICH M11 Protocol standard, Trial Oversight. |
| CNEW | 11.2.1 Investigator Responsibilities | Section 11.2.1 of the ICH M11 Protocol standard, Investigator Responsibilities. |
| CNEW | 11.2.2 Sponsor Responsibilities | Section 11.2.2 of the ICH M11 Protocol standard, Sponsor Responsibilities. |
| CNEW | 11.3 Informed Consent Process | Section 11.3 of the ICH M11 Protocol standard, Informed Consent Process. |
| CNEW | 11.3.1 Informed Consent for Rescreening | Section 11.3.1 of the ICH M11 Protocol standard, Informed Consent for Rescreening. |
| CNEW | 11.3.2 Informed Consent for Use of Remaining Samples in Exploratory Research | Section 11.3.2 of the ICH M11 Protocol standard, Informed Consent for Use of Remaining Samples in Exploratory Research. |
| CNEW | 11.4 Committees | Section 11.4 of the ICH M11 Protocol standard, Committees. |
| CNEW | 11.5 Insurance and Indemnity | Section 11.5 of the ICH M11 Protocol standard, Insurance and Indemnity. |
| CNEW | 11.6 Risk-Based Quality Management | Section 11.6 of the ICH M11 Protocol standard, Risk-Based Quality Management. |
| CNEW | 11.7 Data Governance | Section 11.7 of the ICH M11 Protocol standard, Data Governance. |
| CNEW | 11.8 Data Protection | Section 11.8 of the ICH M11 Protocol standard, Data Protection. |
| CNEW | 11.9 Source Data | Section 11.9 of the ICH M11 Protocol standard, Source Data. |
| CNEW | 11.10 Protocol Deviations | Section 11.10 of the ICH M11 Protocol standard, Protocol Deviations. |

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| CNEW | 11.11 Early Site Closure | Section 11.11 of the ICH M11 Protocol standard, Early Site Closure. |
| CNEW | 11.12 Data Dissemination | Section 11.12 of the ICH M11 Protocol standard, Data Dissemination. |
| CNEW | 12 APPENDIX: SUPPORTING DETAILS | Section 12 of the ICH M11 Protocol standard, APPENDIX: SUPPORTING DETAILS. |
| CNEW | 12.1 Clinical Laboratory Tests | Section 12.1 of the ICH M11 Protocol standard, Clinical Laboratory Tests. |
| CNEW | 12.2 Country/Region-Specific Differences | Section 12.2 of the ICH M11 Protocol standard, Country/Region-Specific Differences. |
| CNEW | 12.3 Prior Protocol Amendment(s) | Section 12.3 of the ICH M11 Protocol standard, Prior Protocol Amendment(s). |
| CNEW | 13 APPENDIX: GLOSSARY OF TERMS AND ABBREVIATIONS | Section 13 of the ICH M11 Protocol standard, APPENDIX: GLOSSARY OF TERMS AND ABBREVIATIONS. |
| CNEW | 14 APPENDIX: REFERENCES | Section 14 of the ICH M11 Protocol standard, APPENDIX: REFERENCES. |

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

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|--|--|
| Term (Variable) | Table of Contents |
| Data Type | Word Generated Table of Contents |
| Data (D), Value (V) or Heading (H) | D |
| Definition | N/A |
| User Guidance | N/A |
| Conformance | Generated |
| Cardinality | N/A |
| Relationship content from ToC representing the protocol hierarchy | Table of Contents |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: N/A Concept: N/A |

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| Repeating and/or Reuse Rules | No |
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112 **1 PROTOCOL SUMMARY**

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

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114 **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 |

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116 **1.1.1 Primary and Secondary Objectives and Estimands**

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|---|--|
| Term (Variable) | 1.1.1 Primary and Secondary Objectives and Estimands |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | H |
| Definition | Heading |

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|--|---|
| 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 | Primary and Secondary Objectives and Estimands |
| Business rules | <p>Value Allowed: No</p> <p>Relationship: 1.1 Protocol Synopsis; 1 PROTOCOL SUMMARY; Table of Contents</p> <p>Concept: Heading</p> |
| 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 | <p>CNEW</p> <p>For review purpose, see definition of the controlled terminology below</p> <p>A descriptive summary of the primary and secondary objectives and their associated estimands related to the trial.</p> |
| 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 |

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|--|---|
| Relationship content from ToC representing the protocol hierarchy | 1.1.1 |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: 1.1.1 Primary and Secondary Objectives and Estimands Concept: CNEW |
| Repeating and/or Reuse Rules | Yes, Reuse <Primary Objective> and <Endpoint> for each Primary Objective from section 3.1, reuse <Secondary Objective and <endpoint> for each Secondary Objective from section 3.2. |

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1.1.2 Overall Design

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

120

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

121

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

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

122

| | |
|--|--|
| Term (Variable) | [Sponsor's Investigational Product Code(s)] |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | CNEW For review purpose, see definition of the controlled terminology below A symbol or combination of symbols that are assigned by the sponsor to uniquely identify an experimental intervention. |
| User Guidance | N/A |
| Conformance | Optional Required Either Sponsor Investigational Product Code or Nonproprietary Name |
| Cardinality | One to one; One to Heading; One to Protocol Identifier |
| Relationship content from ToC representing the protocol hierarchy | 1.1.2 |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: Row title; Sponsor's Protocol Identifier Concept: |
| Repeating and/or Reuse Rules | Yes, repeatable from Title Page Sponsor Investigational Product Code(s) yes, reuse for each Investigational Product |

123

| | |
|--|--|
| Term (Variable) | [NonProprietary Name(s)] |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | CNEW For review purpose, see definition of the controlled terminology below Drug name that is not protected by a trademark, usually descriptive of its chemical structure, and sometimes a public name |
| User Guidance | N/A |
| Conformance | Optional Required Either Sponsor Investigational Product Code or Nonproprietary Name |
| Cardinality | One to one; One to Heading; One to Protocol Identifier |
| Relationship content from ToC representing the protocol hierarchy | 1.1.2 |

| | |
|-------------------------------------|---|
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: Row title; Sponsor's Protocol Identifier Concept: |
| Repeating and/or Reuse Rules | Yes, repeatable from Title Page Nonproprietary Name(s) Yes, reuse for each Investigational Product |

124

| | |
|--|--|
| 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 |

125

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

126

| NCI C-code | M11 Preferred Term | Draft Definition |
|------------|--------------------|--|
| C82637 | Cross-over | Participants receive one of two or more alternative intervention(s) during the initial epoch of the study and receive other intervention(s) during the subsequent epoch(s) of the trial. |
| C82638 | Factorial | Two or more interventions, each alone or in combination, are evaluated in parallel against a control group. This study design allows for the comparison of active drug to placebo, presence of |

| | | |
|---------|----------------|--|
| | | drug-drug interactions, and comparison of active drugs against each other. |
| C82639 | Parallel Group | Participants are assigned to one of two or more treatment groups in parallel for the duration of the study. |
| C142568 | Sequential | Groups of participants are assigned to receive interventions based on prior milestones being reached in the study. |
| C82640 | Single Group | All trial participants are assigned to a single treatment group for the duration of the study. |
| C17649 | Other | Different than the one(s) previously specified or mentioned. |

127

| | |
|--|--|
| 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 |

128

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

129

| NCI C-Code | M11 Preferred Term | Draft Definition |
|------------|--------------------|---|
| CNEW | With Disease | An indication that the individual or group of individuals has been diagnosed with the disease of interest or under study. |
| CNEW | Without Disease | An indication that the individual or group of individuals has not been diagnosed with the disease of interest or under study. |

130

| | |
|--|--|
| 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 |

131

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

132

| NCI C-code | M11 Preferred Term | Draft Definition |
|-------------------|---------------------------|---|
| C49649 | Active Comparator | A type of control, which has a demonstrated effect, administered as a comparator to participants in a clinical trial. |
| C120841 | Dose Response | A type of control using different doses or regimens of the same treatment across the treatment arms. |
| C28280 | No Control | A clinical study that lacks a comparison (i.e., a control) group. |
| C49648 | Placebo | An inactive, identical-appearing drug or treatment that does not contain the test product. |

| | | |
|---------|---------------------------|---|
| CNEW | Different Dose or Regimen | A type of control that comprises a different dose or dosage regimen in comparison to the investigational intervention dose or dosage regimen. |
| CNEW | External | The use of external control data as a control arm for those studies where ethical concerns and/or underserved disease indications may make it difficult to enroll participants. |
| C184727 | Sham Procedure | A type of negative control in which a procedure is performed that mimics the procedure under study but does not include investigational processes or components. |

133

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

134

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

135

| | |
|------------------------|---------------------|
| Term (Variable) | Control Description |
| Data Type | Text |

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

136

| | |
|--|--|
| Term (Variable) | {[Nonproprietary name] or [INN] or <Enter “Not applicable”>} |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | CNEW For review purpose, see definition of the controlled terminology below A narrative representation of the comparator against which the study intervention is evaluated. |
| User Guidance | Further clarification: <ul style="list-style-type: none"> Control description - if active comparator or low dose, pick nonproprietary name or International Nonproprietary Name, indicate N/A if not applicable |
| Conformance | Conditional: if there is a nonproprietary name or INN or Not applicable |
| Cardinality | One to many |
| Relationship content from ToC representing the protocol hierarchy | 1.1.2 |
| Value | [Nonproprietary name] or [INN] or <Enter “N/A”> |
| Business rules | Value Allowed: Yes Relationship: Row title; Sponsor Protocol Identifier Concept: CNEW |
| Repeating and/or Reuse Rules | No |

137

| | |
|---|--|
| Term (Variable) | [Nonproprietary name] |
| Data Type | Valid Value |
| Data (D), Value (V) or Heading (H) | V |
| Definition | C97054 For review purpose, see definition of the controlled terminology below Drug name that is not protected by a trademark, usually descriptive of its chemical structure. |
| User Guidance | Further clarification: <ul style="list-style-type: none"> 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 |

138

| | |
|--|---|
| Cardinality | One to many |
| Relationship content from ToC representing the protocol hierarchy | 1.1.2 |
| Value | Use for example WHO INN, USAN, JAN, XEVMPD |
| Business rules | Value Allowed: Yes Relationship: Row title; Control Description; Sponsor Protocol Identifier Concept: C97054 |
| Repeating and/or Reuse Rules | Yes, repeatable for each nonproprietary name used as control |

| | |
|--|--|
| Term (Variable) | or [INN] or |
| Data Type | Valid Value |
| Data (D), Value (V) or Heading (H) | V |
| Definition | C142585 For review purpose, see definition of the controlled terminology below A unique name that is globally recognized and public property, which identifies pharmaceutical substances or active pharmaceutical ingredients. |
| User Guidance | Further clarification: <ul style="list-style-type: none"> Control description - if active comparator or low dose, pick nonproprietary name or International Nonproprietary Name, indicate N/A if not applicable |
| Conformance | Conditional: if there is an INN |
| Cardinality | One to many |
| Relationship content from ToC representing the protocol hierarchy | 1.1.2 |
| Value | or use for example WHO INN, USAN, JAN, XEVMPD |
| Business rules | Value Allowed: Yes Relationship: Row title; Control Description; Protocol Identifier Concept: C142585 |
| Repeating and/or Reuse Rules | Yes, repeatable for each INN used as control |

139

| | |
|--|--|
| Term (Variable) | <<“Not applicable”>> |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | Verbatim Text |
| User Guidance | Further clarification: <ul style="list-style-type: none"> Control description - if active comparator or low dose, pick nonproprietary name or International Nonproprietary Name, indicate N/A if not applicable |
| Conformance | Conditional: if there is no nonproprietary name and INN |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 1.1.2 |
| Value | N/A |
| Business rules | Value Allowed: Yes, cannot have not applicable if Nonproprietary or INN are completed Relationship: Row title; Control Description; Protocol Identifier |

| | |
|-------------------------------------|-------------------------------|
| | Concept: Verbatim Text |
| Repeating and/or Reuse Rules | No |

140

| | |
|--|--|
| Term (Variable) | Population Age |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | H |
| Definition | Heading The ages, or range of ages, for a trial population |
| 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 |

141

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

142

| | |
|---|--|
| Term (Variable) | <Minimum age> |
| Data Type | Number |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C49693 For review purpose, see definition of the controlled terminology below The anticipated minimum age of the participants to be entered in a clinical trial. |
| User Guidance | Population age range - For trials in which multiple age ranges may be eligible (for example, a younger cohort and an older cohort), indicate the minimum and maximum ages for the trial overall, with an additional comment for any excluded age ranges. |
| Conformance | Required |

| | |
|--|--|
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 1.1.2 |
| Value | Integer |
| Business rules | Value Allowed: Yes Relationship: Population Age; Minimum; unit of minimum age Concept: C49693 |
| Repeating and/or Reuse Rules | No |

143

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

144

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

145

| | |
|---|----------|
| 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 |

146

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

147

| | |
|--|--|
| Term (Variable) | [units of maximum age] |
| Data Type | Valid Value |
| Data (D), Value (V) or Heading (H) | V |
| Definition | C50400 For review purpose, see definition of the controlled terminology below Those units of time that are routinely used to express the age of a person. |
| User Guidance | Population age range - For trials in which multiple age ranges may be eligible (for example, a younger cohort and an older cohort), indicate the minimum and maximum ages for the trial overall, with an additional comment for any excluded age ranges. |
| Conformance | Required |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 1.1.2 |
| Value | Hours (C25529); Days (C25301); Weeks (C29844); Months (C29846); Years (C29848) |
| Business rules | Value Allowed: Yes |

| | |
|-------------------------------------|---|
| | Relationship: Population Age; Maximum, Numeric Maximum Concept: C50400 |
| Repeating and/or Reuse Rules | No |

148

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

149

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

150

| | |
|--|---|
| Term (Variable) | [Intervention Assignment Method] |
| Data Type | Valid Value |
| Data (D), Value (V) or Heading (H) | V |
| Definition | CNEW For review purpose, see definition of the controlled terminology below The process used to assign trial participants to a trial intervention or trial arm. |
| User Guidance | Intervention assignment method - Do NOT state block size. |
| Conformance | Required |
| Cardinality | One to one; One to Sponsor Protocol Identifier |
| Relationship content from ToC representing the protocol hierarchy | 1.1.2 |
| Value | Randomisation (C25196); Stratification (C25689); Stratified Randomisation (CNEW); Other (C17649); or Not Applicable (C48660) |
| Business rules | Value Allowed: Yes Relationship: Row title identifier; Sponsor Protocol Identifiers Concept: CNEW |

| | |
|-------------------------------------|----|
| Repeating and/or Reuse Rules | No |
|-------------------------------------|----|

151

| NCI C-Code | M11 Preferred Term | Draft Definition |
|-------------------|---------------------------|---|
| C25196 | Randomisation | The process of assigning trial participants to treatment or control groups using an element of chance to determine the assignments in order to reduce bias. |
| C25689 | Stratification | Grouping defined by important prognostic factors measured at baseline. |
| C147145 | Stratified Randomisation | The process of grouping trial participants into strata according to important prognostic factors and then assigning participants within each stratum to different treatment or control groups using an element of chance and in order to reduce bias. |

152

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

153

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

154

| NCI C-Code | M11 Preferred Term | Draft Definition |
|------------|--------------------|--|
| CNEW | Single-Centre | A clinical study that is conducted at a single study site. |
| CNEW | Multicentre | A clinical trial conducted according to a single protocol but at more than one site, and therefore, carried out by more than one investigator. |

155

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

156

| NCI C-Code | M11 Preferred Term | Draft Definition |
|------------|--------------------|---|
| CNEW | Single Country | Of, or pertaining to, an occurrence in one country. |
| CNEW | Multiple Countries | Of, or pertaining to, an occurrence in more than one country. |

157

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

158

| | |
|---|-------------------------------------|
| Term (Variable) | [Adaptative Trial Design Indicator] |
| Data Type | Valid Value |
| Data (D), Value (V) or Heading (H) | V |

| | |
|--|---|
| Definition | CNEW For review purpose, see definition of the controlled terminology below An indication as to whether the clinical trial uses an adaptive trial design. |
| User Guidance | N/A |
| Conformance | Required |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 1.1.2 |
| Value | Yes (C49488), No (C49487) |
| Business rules | Value Allowed: Yes Relationship: Heading; Sponsor Protocol Identifier Concept: CNEW |
| Repeating and/or Reuse Rules | No |

159

| | |
|--|---|
| 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 |

160

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

161

| NCI C-Code | M11 Preferred Term | Draft Definition |
|------------|--------------------|---|
| C49487 | No | The non-affirmative response to a question. |
| C49488 | Yes | The affirmative response to a question. |

162

| | |
|--|---|
| 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 |

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

164

| NCI C-Code | M11 Preferred Term | Draft Definition |
|------------|--------------------|---|
| C49487 | No | The non-affirmative response to a question. |
| C49488 | Yes | The affirmative response to a question. |

165

| | |
|---|----------------|
| Term (Variable) | Number of Arms |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | H |

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

166

| | |
|--|---|
| Term (Variable) | [Number of Arms] |
| Data Type | Number |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C98771 For review purpose, see definition of the controlled terminology below The planned number of intervention groups. |
| User Guidance | 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 |
| Repeating and/or Reuse Rules | No |

167

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

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| | |
|--|--|
| 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 For review purpose, see definition of the controlled terminology below The type of experimental design used to describe the level of awareness of the trial participants and/ or personnel as it relates to the respective intervention(s) or assessments being observed, received or administered. |
| User Guidance | For designs in which these details may differ in one or more trial periods, answer according to the portion of the trial in which the highest number of blinded roles occurs. Additional details can be provided in Section 6.7.3 Blinding. |
| Conformance | Required |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 1.1.2 |
| Value | Double Blind (C15228), Observer Blind (C187674), Open Label (C49659), Single Blind (C28233) |
| Business rules | Value Allowed: Yes Relationship: Trial Blind Schema; Heading; Protocol Sponsor Identifier Concept: C49658 |
| Repeating and/or Reuse Rules | No |

169

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

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

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

171

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

172

| NCI C-Code | M11 Preferred Term | Draft Definition |
|-------------------|---------------------------|--|
| CNEW | Trial Blinding Role | A terminology value set relevant to the trial blinding roles within the ICH M11 Protocol model. |
| C142710 | Participant | A member of the clinical study population from whom data are being collected. |
| C17445 | Care Provider | The primary person in charge of the care of a patient, usually a family member or a designated health care professional. |
| C25936 | Investigator | A person responsible for the conduct of the clinical trial at a trial site. If a trial is conducted by a team of individuals at the trial site, the investigator is the responsible leader of the team and may be called the principal investigator. |
| C207599 | Outcomes Assessor | The individual who evaluates the outcome(s) of interest. |
| C70793 | Sponsor | An individual, company, institution, or organization that takes responsibility for the initiation, management, and/or financing of a clinical study. |
| C48660 | Not Applicable | Determination of a value is not relevant in the current context. |

173

| | |
|---|-------------------------|
| Term (Variable) | Number of participants: |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | H |
| Definition | Heading |

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

174

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

175

| | |
|---|---|
| Term (Variable) | <Number of Participants> |
| Data Type | Number |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C49692 For review purpose, see definition of the controlled terminology below The planned number of participant be entered in a clinical trial. |
| User Guidance | State the expected number of participants to be assigned to trial intervention/enrolled. Indicate whether the number provided is the target or maximum number of individuals to be randomly assigned to trial intervention/enrolled |
| Conformance | Required |
| Cardinality | One to one |

| | |
|--|--|
| Relationship content from ToC representing the protocol hierarchy | 1.1.2 |
| Value | Integer; <Number of Participants> participants will be |
| Business rules | Value Allowed: Universal Text and Yes Relationship: Heading; Sponsor Protocol Identifiers Concept: C49692 |
| Repeating and/or Reuse Rules | No |

176

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

177

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

178

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

| | |
|--|--|
| Term (Variable) | {<total planned duration of trial intervention> [total planned duration of trial unit of time]} |
| Data Type | Integer, Valid value |
| Data (D), Value (V) or Heading (H) | D, V |
| Definition | Total planned duration of trial intervention CNEW Total planned duration of trial intervention unit of time: CNEW For review purpose, see definition of the controlled terminology below <ul style="list-style-type: none"> • Number: The numeric value for the planned duration of trial intervention. • Unit of time: The unit of time associated with the numeric value for the planned duration of trial intervention. |
| User Guidance | Select one of the two options for total planned duration of trial intervention and trial participation for each participant. Note that the total duration of trial participation should include any washout and any follow-up periods in which the participant is not receiving trial intervention. When duration will vary, provide a short explanation (e.g., “event-driven” or “adaptive design”) |
| Conformance | Conditional: when Planned Duration of trial Intervention Number and unit of time |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 1.1.2 |
| Value | Total planned duration of trial intervention: Integer Total planned duration of trial intervention unit of time: Days (C25301); Hours (25529); Months (C29846); Weeks (C29844); Years (C29848) |
| Business rules | Value Allowed: Yes Relationship: Total duration of trial intervention for each participant: Concept: CNEW; CNEW |
| Repeating and/or Reuse Rules | No |

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

181

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

182

| | |
|--|---|
| Term (Variable) | Total planned duration of trial participation for each participant: |
| Data Type | Universal Text |
| Data (D), Value (V) or Heading (H) | H |
| Definition | Heading |
| User Guidance | Select one of the two options for total planned duration of trial intervention and trial participation for each participant. Note that the total duration of trial participation should include any washout and any follow-up periods in which the participant is not receiving trial intervention. When duration will vary, provide a short explanation (e.g., “event-driven” or “adaptive design” |
| Conformance | Required |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 1.1.2 |

183

| | |
|-------------------------------------|--|
| Value | Total planned duration of trial participation for each participant: |
| Business rules | Value Allowed: No Relationship: Duration Concept: Heading |
| Repeating and/or Reuse Rules | No |

| | |
|--|---|
| Term (Variable) | {<total planned duration of trial participation> [Total planned duration of trial participation unit of time]} |
| Data Type | Integer, Valid value |
| Data (D), Value (V) or Heading (H) | D, V |
| Definition | Total planned duration of trial participation: CNEW Total planned duration of trial participation Unit of time: CNEW For review purpose, see definition of the controlled terminology below <ul style="list-style-type: none"> • Number: The numeric value for the planned duration of trial participation. • Unit of time: The unit of time associated with the numeric value for the planned duration of trial participation. |
| User Guidance | Select one of the two options for total planned duration of trial intervention and trial participation for each participant. Note that the total duration of trial participation should include any washout and any follow-up periods in which the participant is not receiving trial intervention. When duration will vary, provide a short explanation (e.g., “event-driven” or “adaptive design” |
| Conformance | Conditional: when planned duration of trial participation number and unit of time |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 1.1.2 |
| Value | Total planned duration of trial participation: Integer Total planned duration of trial participation unit of time: Days (C25301); Hours (25529); Months (C29846); Weeks (C29844); Years (C29848) |
| Business rules | Value Allowed: Yes Relationship: Total duration of trial participation for each participant: Concept: CNEW; CNEW |
| Repeating and/or Reuse Rules | No |

184

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

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| | |
|------------------------|--|
| Term (Variable) | {<alternate description of planned duration of trial participation if duration will vary>} |
| Data Type | Text |

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

186

| | |
|--|---|
| Term (Variable) | <Additional Description of Duration> |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | CNEW For review purpose, see definition of the controlled terminology below A narrative providing additional details about the duration of an participant's use of a trial intervention or their planned participation time in the trial. |
| User Guidance | If necessary, include any clarifications or cross-references to details in the main body of the protocol in the optional field below. |
| Conformance | Optional |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 1.1.2 |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: Duration Concept: CNEW |
| Repeating and/or Reuse Rules | No |

187

| | |
|---|-------------|
| 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 |

188

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

189

| | |
|--|---|
| Term (Variable) | Independent Committees |
| Data Type | Valid Value |
| Data (D), Value (V) or Heading (H) | V |
| Definition | CNEW For review purpose, see definition of the controlled terminology below An independent group of experts that has oversight over, and conducts periodic review of, specific trial activities. |
| User Guidance | Indicate whether any committee(s) will be reviewing data while the trial is ongoing, and the type of committee. Common examples include Data Monitoring Committee, Dose Escalation Committee, or Endpoint Adjudication Committee; describe others, if applicable. List independent committees in the space indicated. Other committees may be included in the separate space provided. Committees listed here should be fully described in Section 11.4 Committees. |
| Conformance | Required |
| Cardinality | One to many |
| Relationship content from ToC representing the protocol hierarchy | 1.1.2 |
| Value | Independent Data Monitoring Committee (C142578); Dose Escalation Committee (C78726); Endpoint Adjudication Committee (C78726); Other (C17649); None (C41132) |

| | |
|-------------------------------------|---|
| Business rules | Value Allowed: Yes, more than one committee can be selected Relationship: Independent Committees Concept: CNEW |
| Repeating and/or Reuse Rules | No |

190

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

191

| | |
|--|--|
| 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 |

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| | |
|--|--|
| Term (Variable) | Other Committees |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | CNEW For review purpose, see definition of the controlled terminology below A committee that is different than the one(s) previously specified or mentioned. |
| User Guidance | Delete "Other Committees" if not applicable. |
| Conformance | Optional |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 1.1.2 |
| Value | Text |
| Business rules | Value Allowed: Yes |

| | |
|-------------------------------------|---|
| | Relationship: Other Committees Concept: CNEW |
| Repeating and/or Reuse Rules | No |

193

194

1.2 Trial Schema

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

195

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

196

| | |
|-------------------------------------|--|
| Business rules | Value Allowed: Yes Relationship: 1.2 Trial Schema Concept: C93682 |
| 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 | CNEW For review purpose, see definition of the controlled terminology below A brief written record describing the trial schematic. |
| User Guidance | The purpose of this section is to provide a visual depiction of the trial design, orienting users of the protocol to the key features of the design. The schema depicts the trial arms, the flow of individual participants through the progression of trial period(s)/epochs (such as screening, washout/run-in, intervention, and key milestones [e.g., randomisation, cross-over, end of treatment, end of study, post-treatment follow-up]). For complex trials, additional schemas may be added to describe activities or trial periods in greater detail. |
| Conformance | Optional |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 1.2 |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: 1.2 Trial Schema Concept: CNEW |
| Repeating and/or Reuse Rules | Yes, repeatable and aligned with appropriate schema |

197

198

1.3 Schedule of Activities

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

199

| | |
|-------------------------------------|---|
| Business rules | Value Allowed: No Relationship: 1 PROTOCOL SUMMARY; Table of Contents Concept: Heading |
| 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 | CNEW For review purpose, see definition of the controlled terminology below A standardised representation of planned clinical trial activities including interventions (e.g. administering drug, surgery) and study administrative activities (e.g. obtaining informed consent, distributing clinical trial material and diaries, randomisation) as well as assessments. |
| User Guidance | The schedule of activities must capture the procedures that will be accomplished at each trial visit, and all contact with participants, e.g., telephone contacts. This includes any tests that are used for eligibility, participant randomisation or stratification, or decisions on trial intervention discontinuation. Allowable windows should be stated for all visits and procedures. A tabular format is recommended. When applicable for studies with extensive sampling, e.g., serial PK sampling, a separate table may be added. |
| Conformance | Required |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 1.3 |
| Value | Table; text; Image |
| Business rules | Value Allowed: Yes Relationship: 1.3 Schedule of Activities Concept: CNEW |
| Repeating and/or Reuse Rules | Yes, repeatable for each Schedule of Activity if needed |

200

201

2 INTRODUCTION

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

| | |
|-------------------------------------|----|
| Repeating and/or Reuse Rules | No |
|-------------------------------------|----|

202

203

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 |

204

| | |
|--|---|
| Term (Variable) | <Purpose of Trial> |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C146997 For review purpose, see definition of the controlled terminology below The overall rationale, reason, or intention of the clinical trial. |
| User Guidance | Explain why the trial is needed, and why the research questions being asked are important. Do not restate the objectives or estimands. Do not restate the IB; rather, cross reference to the IB as applicable to the description. |
| Conformance | Required |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 2.1 |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: 2.1 Purpose of Trial Concept: C146997 |
| Repeating and/or Reuse Rules | No |

205

206

2.2 Assessment of Risks and Benefits

| | |
|---|--------------------------------------|
| Term (Variable) | 2.2 Assessment of Risks and Benefits |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | H |
| Definition | Heading |

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

207

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 |

208

| | |
|---|---|
| Term (Variable) | <Trial-specific Intervention Risks and Mitigations> |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | CNEW For review purpose, see definition of the controlled terminology below A description of the potential risks associated with the trial interventions and mitigation strategies to be employed within the trial. |
| User Guidance | Trial Intervention – Describe risks related to trial-specific treatments and interventions. For the protocol, focus on the relevant key risks for THIS trial. Provide a brief description of strategies to mitigate identified risks or provide a cross-reference to the relevant protocol section. |
| Conformance | Optional |
| Cardinality | One to one |

209

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

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

210

| | |
|---|---|
| Term (Variable) | <Trial-specific Other Risks and Mitigations> |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | CNEW For review purpose, see definition of the controlled terminology below A description of the potential risks associated with the trial procedures and mitigation strategies to be employed within the trial that are different than the one(s) previously specified or mentioned. |
| 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: CNEW |
| Repeating and/or Reuse Rules | No |

211

212

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 |

213

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

| | |
|--|---|
| Relationship content from ToC representing the protocol hierarchy | 2.2.2 |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: 2.2.2 Benefit Summary Concept: CNEW |
| Repeating and/or Reuse Rules | No |

214

215 **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 |

216

| | |
|--|--|
| Term (Variable) | <Overall Risk-Benefit Assessment> |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | CNEW For review purpose, see definition of the controlled terminology below A short textual description containing the risks and benefits associated with participation in the trial. |
| User Guidance | Provide a succinct, concluding statement on the perceived balance between risks that have been identified from cumulative safety data, protocol procedures, and anticipated efficacy/benefits within the context of the proposed trial. |
| Conformance | Required |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 2.2.3 |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: 2.2.3 Overall Risk-Benefit Assessment OR 2.2 Assessment of Risks and Benefits (when the Optional Level 3 subheading (2.2.3) is not used) If the Optional Level 3 subheadings (2.2.1, 2.2.2, 2.2.3) are not used, the user guidance below Section 2.2 applies. |

| | |
|-------------------------------------|----------------------|
| | Concept: CNEW |
| Repeating and/or Reuse Rules | No |

217

218

3 TRIAL OBJECTIVES AND ASSOCIATED ESTIMANDS

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

219

220

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 |

222 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, non-technical language for clear understanding of 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 target population, the treatment condition(s), the endpoint (or variable) and the population-level summary. Precise specifications of treatment, population, and variable are likely to address many of the key intercurrent events. Other key intercurrent events not already addressed in the clinical question of interest by the aforementioned attributes should be described with their associated strategies. For other types of trials not intended to estimate a treatment effect or test a hypothesis related to a treatment effect, describe additional information relevant to the clinical question(s) of interest (at a minimum, present the endpoint(s) associated with each objective). For these trials, including the table is not required.</p> |
| 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 | <p>Value Allowed: No</p> <p>Relationship: 3.1 Primary Objective and Associated Estimand(s); 3. TRIAL OBJECTIVES AND ASSOCIATED ESTIMAND; Table of Contents</p> <p>Concept: Heading</p> |
| Repeating and/or Reuse Rules | <p>Yes, repeatable for each numbered primary objective.</p> <p>Yes, reuse to the table in Section 1.1.1 for each primary objective</p> |

| | |
|---|--|
| Term (Variable) | <Primary Objective> |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | <p>C85826</p> <p>For review purpose, see definition of the controlled terminology below</p> <p>The principle reason for performing a study in terms of the scientific questions to be answered by the analysis of data collected during the study.</p> |
| 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: X is a unique number for each primary objective. |
| Value | Text and unique integer which is same as Level 3 number for the section. |
| Business rules | Value Allowed: Yes Relationship: 3.1.X Primary Objective <#> Concept: C85826 |
| Repeating and/or Reuse Rules | Yes, repeatable for each numbered primary objective. Yes, reuse to the table in Section 1.1.1.for each primary objective |

224

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

225

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

226

| | |
|---|-------------|
| Term (Variable) | Description |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | H |

| | |
|--|---|
| Definition | Table Column Heading |
| User Guidance | N/A |
| Conformance | Required |
| Cardinality | One to many rows |
| Relationship content from ToC representing the protocol hierarchy | 3.1.X |
| Value | Description |
| Business rules | Value Allowed: No Relationship: 3.1 Primary Objective(s) and associated Estimand(s); Table column Heading; Estimand 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 |

227

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

228

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

229

| | |
|--|--|
| Relationship content from ToC representing the protocol hierarchy | 3.1.X |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: Row Heading; Description Concept: C70833 |
| Repeating and/or Reuse Rules | Yes, repeatable for each numbered primary objective |

230

| | |
|--|--|
| Term (Variable) | {Treatment} |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | H |
| Definition | Heading |
| User Guidance | N/A |
| Conformance | Conditional: If there is a treatment as estimand characteristic |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 3.1.X |
| Value | {Treatment} |
| Business rules | Value Allowed: No Relationship: Row Heading; Estimand 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 For review purpose, see definition of the controlled terminology below The treatment condition of interest and, as appropriate, the alternative treatment condition to which comparison will be made (referred to as “treatment” through the remainder of this document). These might be individual interventions, combinations of interventions administered concurrently, e.g. as add-on to standard of care, or might consist of an overall regimen involving a complex sequence of interventions. |
| User Guidance | List of key aspects of treatment regimens in each study group, including at least investigational agents, dosage, and administration route |
| Conformance | Conditional: If there is a treatment as estimand characteristic |
| Cardinality | One to Row Heading; One to Primary Objective Table; Project Identifier |
| Relationship content from ToC representing the protocol hierarchy | 3.1.X |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: Row Heading; Description Concept: C49236 |
| Repeating and/or Reuse Rules | Yes, repeatable for each numbered primary objective |

231

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

232

| | |
|--|--|
| Term (Variable) | {< Endpoint >} |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C25212 For review purpose, see definition of the controlled terminology below The variable to be obtained for each patient that is required to address the clinical question. The specification of the variable might include whether the patient experiences an intercurrent event. |
| User Guidance | 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 |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: Row Heading; Description Concept: C25212 |
| Repeating and/or Reuse Rules | Yes, repeatable for each numbered primary objective |

233

| | |
|--|---|
| Term (Variable) | {Population-level Summary} |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | H |
| Definition | Heading |
| User Guidance | N/A |
| Conformance | Conditional: If there is a population -level summary as estimand characteristic |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 3.1.X |
| Value | {Population-level Summary} |

| | |
|-------------------------------------|---|
| Business rules | Value Allowed: No Relationship: Row Heading; Estimand Characteristics Concept: Heading |
| Repeating and/or Reuse Rules | Yes, repeatable for each numbered primary objective |

234

| | |
|--|--|
| Term (Variable) | {<Population-level Summary>} |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C188853 For review purpose, see definition of the controlled terminology below Population level summary for the clinical endpoint of interest, which provides a basis for comparison between treatment conditions. |
| User Guidance | Description of the population-level summary (e.g., mean difference, relative risk) |
| Conformance | Conditional: If there is a population-level summary as estimand |
| Cardinality | One to Row Heading; One to Primary Objective Table; Project Identifier |
| Relationship content from ToC representing the protocol hierarchy | 3.1.X |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: Row Heading; Description Concept: C188853 |
| Repeating and/or Reuse Rules | Yes, repeatable for each numbered primary objective |

235

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

236

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

237

| | |
|--|---|
| Conformance | Conditional: If there is one or more other intercurrent events as estimand characteristic. |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 3.1.X |
| Value | Strategy |
| Business rules | Value Allowed: No Relationship: Table column Heading; Other Intercurrent Event; Description Concept: Heading |
| Repeating and/or Reuse Rules | Yes, repeatable for each numbered primary objective |

238

| | |
|--|--|
| Term (Variable) | {Description of Intercurrent Event} |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C188856 For review purpose, see definition of the controlled terminology below A description of the intercurrent event. |
| 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 |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: Row Heading; Estimand Characteristics Concept: C188856 |
| Repeating and/or Reuse Rules | Yes, repeatable for each intercurrent event |

| | |
|---|--|
| Term (Variable) | {Intercurrent Event 1 Strategy} |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C188857 For review purpose, see definition of the controlled terminology below A description of the planned strategy to address intercurrent events. |
| User Guidance | Description of the strategy to address the intercurrent event (e.g., a treatment policy strategy); cross reference the justification in Section 4 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 |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: Row Heading; Strategy; Description Concept: C188857 |
| Repeating and/or Reuse Rules | Yes, repeatable for each intercurrent event |

239

240 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 |

241

242 3.2.1 Secondary Objective <#>

| | |
|--|--|
| Term (Variable) | {3.2.X Secondary Objective <#> |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | H |
| Definition | Heading |
| User Guidance | Describe the secondary objective(s) and associated estimand(s) as outlined in Section 3.1 Primary Objective(s) and Associated Estimand(s). Use the same approach as above and consider including a 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 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. |

243

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

244

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

245

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

246

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

247

| | |
|--|---------------------------------------|
| Term (Variable) | {Population} |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | H |
| Definition | Heading |
| User Guidance | N/A |
| Conformance | Conditional: If there is a population |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 3.2.X |
| Value | {Population} |
| Business rules | Value Allowed: No |

248

| | |
|--|---|
| | 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 For review purpose, see definition of the controlled terminology below The population of patients targeted by the clinical question. This will be represented by the entire trial population, a subgroup defined by a particular characteristic measured at baseline, or a principal stratum defined by the occurrence (or non-occurrence, depending on context) of a specific intercurrent event. |
| User Guidance | List of key characteristics, such as demographic characteristics (e.g. age, sex) and clinical characteristics (e.g. prior therapies, symptoms, severity, biomarker status) |
| Conformance | Conditional: If there is a population for Secondary |
| Cardinality | One to Row Heading; One to Secondary Objective Table; Secondary Objective <#>; Protocol Identifier |
| Relationship content from ToC representing the protocol hierarchy | 3.2.X |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: Row Heading, Description; Estimand Characteristic Concept: C70833 |
| Repeating and/or Reuse Rules | Yes, repeatable for each numbered secondary objective. |

249

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

250

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

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

251

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

252

| | |
|---|---|
| Term (Variable) | {< Endpoint >} |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C25212 For review purpose, see definition of the controlled terminology below The variable to be obtained for each patient that is required to address the clinical question. The specification of the variable might include whether the patient experiences an intercurrent event |
| User Guidance | Definition of the endpoint |
| Conformance | Required |

| | |
|--|--|
| Cardinality | One to Row Heading, One to Secondary Objective Table, Project Identifier |
| Relationship content from ToC representing the protocol hierarchy | 3.2.X |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: Row Heading; Description; Table Estimand Characteristics; Secondary (1...n) Estimand Concept: C25212 |
| Repeating and/or Reuse Rules | Yes, repeatable for each numbered secondary objective. |

253

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

254

| | |
|--|--|
| Term (Variable) | {<Population-level Summary>} |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C188853 For review purpose, see definition of the controlled terminology below Population level summary for the clinical endpoint of interest, which provides a basis for comparison between treatment conditions. |
| 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 |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: Row Heading; Description; Table estimand Characteristics; Secondary (1...n) Estimand; Protocol Identifier Concept: C188853 |
| Repeating and/or Reuse Rules | Yes, repeatable for each numbered secondary objective. |

255

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

256

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

257

| | |
|--|---|
| Term (Variable) | {Description of Intercurrent Event} |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | H |
| Definition | C188856 For review purpose, see definition of the controlled terminology below A description of the intercurrent event. |
| User Guidance | Enter Description of Intercurrent Event |
| Conformance | Conditional: If there is one or more other intercurrent events. |
| Cardinality | One to one or as many intercurrent event as available |
| Relationship content from ToC representing the protocol hierarchy | 3.2.X |
| Value | Text |
| Business rules | Value Allowed: No Relationship: Row Heading; Estimand Characteristics; Protocol Identifier |

258

| | |
|--|--|
| | Concept: C188856 |
| Repeating and/or Reuse Rules | Yes, repeatable for each intercurrent event |
| Term (Variable) | {Intercurrent Event 1 Strategy} |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C188857 For review purpose, see definition of the controlled terminology below A description of the planned strategy to address intercurrent events. |
| User Guidance | Description of the strategy to address the intercurrent event (e.g. a treatment policy strategy); cross-reference the justification in Section 4. If there is >1 intercurrent event for an objective, add additional intercurrent event rows |
| Conformance | Conditional: If there is one or more other intercurrent events. |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 3.2.X |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: Row Heading; Description of Intercurrent Event Concept: C188857 |
| Repeating and/or Reuse Rules | Yes, repeatable for each intercurrent event |

259

260

3.3 Exploratory Objective(s)

| | |
|--|---|
| Term (Variable) | 3.3 Exploratory Objective(s) |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | H |
| Definition | Heading |
| User Guidance | 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. 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 |

261

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 | N/A |
| Conformance | Conditional: when there are exploratory objective heading for each exploratory requirement |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 3.3.X where X is a unique 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 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. |

262

| | |
|--|---|
| Term (Variable) | <Exploratory Objective> |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C163559 For review purpose, see definition of the controlled terminology below The exploratory reason for performing a study in terms of the scientific questions to be answered by the analysis of data collected during the study. |
| User Guidance | State each exploratory objective. This should generally include documentation of associated exploratory endpoints. It may be helpful in some cases to describe precise estimands to provide clarity on what is being estimated. No text is intended here (heading only) unless there is no exploratory objective, in which case indicate "Not applicable". |
| 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 |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: 3.3.X Exploratory Objective <#> Concept: C163559 |
| Repeating and/or Reuse Rules | Yes, repeatable for each numbered exploratory objective. |

263

| | |
|---|--|
| Term (Variable) | {If an Exploratory Objective has been entered: <Enter Table of Estimand Characteristics> including Endpoint at a minimum } |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | N/A |

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

264

| | |
|--|---|
| 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 |
| 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. |

265

| | |
|--|--------------------------|
| Term (Variable) | Description |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | H |
| Definition | Table Column Heading |
| User Guidance | N/A |
| Conformance | Required |
| Cardinality | One to many rows |
| Relationship content from ToC representing the protocol hierarchy | 3.3.X |
| Value | Description |
| Business rules | Value Allowed: No |

| | |
|-------------------------------------|--|
| | Relationship: 3 3.X Exploratory Objective Table Column Heading; Estimand Characteristic; Population; Treatment; Endpoint; Population-Level; Intercurrent Event (1...n); Strategy Concept: Heading |
| Repeating and/or Reuse Rules | Yes, repeatable for each numbered exploratory objective. |

266

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

267

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

268

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

269

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

270

| | |
|---|---|
| Term (Variable) | Endpoint |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | H |
| Definition | Heading |
| User Guidance | N/A |
| Conformance | Conditional: if there is exploratory endpoint(s). |
| Cardinality | One to one |

| | |
|--|--|
| Relationship content from ToC representing the protocol hierarchy | 3.3.X |
| Value | Endpoint |
| Business rules | Value Allowed: No Relationship: Row Heading; Estimand Characteristic Concept: Heading |
| Repeating and/or Reuse Rules | Yes, repeatable for each numbered exploratory objective. |

271

| | |
|--|---|
| Term (Variable) | Endpoint |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C25212 For review purpose, see definition of the controlled terminology below The variable to be obtained for each patient that is required to address the clinical question. The specification of the variable might include whether the patient experiences an intercurrent event |
| User Guidance | 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 |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: Row Heading; Description; Table Estimand Characteristics; Exploratory (1...n) Estimand Concept: C25212 |
| Repeating and/or Reuse Rules | Yes, repeatable for each numbered exploratory objective. |

272

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

273

| | |
|------------------------|------------------------------|
| Term (Variable) | {<Population-level Summary>} |
| Data Type | Text |

| | |
|--|--|
| Data (D), Value (V) or Heading (H) | D |
| Definition | C188853 For review purpose, see definition of the controlled terminology below Population level summary for the clinical endpoint of interest, which provides a basis for comparison between treatment conditions. |
| User Guidance | List of key characteristics, such as demographic characteristics (e.g. age, sex) and clinical characteristics (e.g. prior therapies, symptoms, severity, biomarker status) |
| Conformance | Conditional: If there is a population-level summary |
| Cardinality | One to Row Heading; One to Exploratory Objective Table, Project Identifier |
| Relationship content from ToC representing the protocol hierarchy | 3.3.X |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: Row Heading; Description; Table Estimand Characteristics; Exploratory (1...n) Estimand Concept: C188853 |
| Repeating and/or Reuse Rules | Yes, repeatable for each numbered exploratory objective. |

274

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

275

| | |
|--|--|
| Term (Variable) | {Strategy} |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | H |
| Definition | Table Column Heading |
| User Guidance | N/A |
| Conformance | Conditional: If there is one or more other intercurrent event as estimand. |
| Cardinality | One to many rows |
| Relationship content from ToC representing the protocol hierarchy | 3.3.X |

| | |
|-------------------------------------|--|
| Value | Strategy |
| Business rules | Value Allowed: No Relationship: Table Column Heading; Estimand Characteristics; Other Intercurrent Event Concept: Heading |
| Repeating and/or Reuse Rules | Yes, repeatable for each numbered exploratory objective. |

276

| | |
|--|---|
| Term (Variable) | {Description of Intercurrent Event} |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C188856 For review purpose, see definition of the controlled terminology below A description of the intercurrent event. |
| User Guidance | Enter Description of Intercurrent Event |
| Conformance | Conditional: If there is one or more other intercurrent events as estimand characteristic. |
| Cardinality | One to one or as many intercurrent event as available |
| Relationship content from ToC representing the protocol hierarchy | 3.3.X |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: Row Heading, Estimand Characteristics Concept: C188856 |
| Repeating and/or Reuse Rules | Yes, repeatable for each intercurrent event |

277

| | |
|--|--|
| Term (Variable) | {<Intercurrent Event # Strategy>} |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C188857 For review purpose, see definition of the controlled terminology below A description of the planned strategy to address intercurrent events. |
| User Guidance | Description of the strategy to address the intercurrent event (e.g., a treatment policy strategy); cross reference the justification in Section 4 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 |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: Row Heading; Strategy; Description Concept: C188857 |
| Repeating and/or Reuse Rules | Yes, repeatable for each intercurrent event |

278

| | |
|--|--|
| Term (Variable) | 4 TRIAL DESIGN |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | H |
| Definition | Heading |
| User Guidance | In the subsections below, describe the trial design with specific mention, as applicable, of the components of an adequate and well-controlled trial and reflect the principles of Quality by Design. The description of the design should be concise and consistent with Section 1.1 Protocol Synopsis and Section 1.2 Trial Schema. The trial design should align with objectives/estimand(s) described in Section 3 Trial Objectives and Associated Estimands. This section is intended to provide a description for the important aspects of the trial design and rationale for its key attributes. Operational details needed to implement the trial design should be covered in more detail in subsequent sections. No text is intended here (heading only). |
| 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 |

280

281 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 |

282

283

284

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

285

| | |
|--|--|
| Term (Variable) | <Description of Trial Duration> |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | CNEW For review purpose, see definition of the controlled terminology below A description of the trial duration. |
| User Guidance | Describe the trial duration with reference to Section 1.2, Trial Schema. Explain what the overall duration for an individual participant is anticipated to be and why, including the sequence and duration of trial periods (for example, screening, run-in, randomisation, treatment [fixed dose/titration], follow-up/washout periods). Where applicable, include discussion of sentinel dosing (or lack thereof), dose escalation, and cohort expansion. If dose modification decisions are dependent upon review by a committee, include details in Section 11.4 Committees. |
| Conformance | Optional |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 4.1 |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: 4.1 Description of Trial Design Concept: CNEW |

| | |
|-------------------------------------|----|
| Repeating and/or Reuse Rules | No |
|-------------------------------------|----|

286
287

| | |
|--|--|
| Term (Variable) | <Method of Assignment to Trial Intervention> |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | CNEW For review purpose, see definition of the controlled terminology below The technique used to assign trial participants to a trial intervention or trial arm. |
| User Guidance | State the method of assignment to trial intervention the level and method of blinding that will be used with reference to Section 6.7 Investigational Trial Intervention Assignment, Randomisation and Blinding. |
| Conformance | Optional |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 4.1 |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: 4.1 Description of Trial Design Concept: CNEW |
| Repeating and/or Reuse Rules | No |

288

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

289
290

| | |
|---|--|
| Term (Variable) | <Additional Description of Trial Design> |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |

| | |
|--|--|
| Definition | CNEW For review purpose, see definition of the controlled terminology below An extra or further textual representation of the trial design. |
| User Guidance | Describe any other important aspects of the design, e.g.: <ul style="list-style-type: none"> • Geographic scope of trial (e.g., single-centre, multi-centre, or multi-centre and multi-national); • Use of decentralised processes, tools, or features in the trial; • Planned use of a Data Monitoring Committee, or similar review group and cross-reference Section 11.4, Committees, for details; • Whether an interim analysis is planned and, if so, refer to details in Section 10.9, Interim Analyses • Any planned extension trial, long-term follow-up/registry, planned future use of samples or data, or post-trial sample analysis or other data-related activities. |
| Conformance | Optional |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 4.1 |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: 4.1 Description of Trial Design Concept: CNEW |
| Repeating and/or Reuse Rules | No |

291

292

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 |

293

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

| | |
|--|---|
| | A description of the way in which trial stakeholders were consulted when determining the trial design. |
| User Guidance | If applicable, describe any stakeholder (e.g., patient, healthcare professional and patient advocacy groups) involvement in the design of the trial and any suggestions implemented |
| Conformance | Optional |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 4.1.1 |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: 4.1.1 Stakeholder Input into Design Concept: CNEW |
| Repeating and/or Reuse Rules | No |

294

295

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 |

296

| | |
|--|---|
| Term (Variable) | <Overall Rationale for Trial Design> |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | CNEW For review purpose, see definition of the controlled terminology below An explanation as to the scientific reasons for the choice of the trial design. |
| User Guidance | N/A |
| Conformance | Conditional: If Level 3 subheadings are not used |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 4.2 |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: 4.2 Rationale for Trial Design Concept: CNEW |

| | |
|-------------------------------------|----|
| Repeating and/or Reuse Rules | No |
|-------------------------------------|----|

297

298

4.2.1 Rationale for Estimand(s)

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

299

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

300

301 **4.2.2 Rationale for Intervention Model**

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

302

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

303

304 **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 |

305

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

306

307

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 |

308

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

309

310

4.2.5 Rationale for Adaptive or Novel Trial Design

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

311

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

312 **4.2.6 Rationale for Interim Analysis**

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

313

| | |
|---|--|
| Term (Variable) | <Rationale for Interim Analysis> |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | CNEW For review purpose, see definition of the controlled terminology below An explanation for the analysis comparing intervention groups at any time before the formal completion of the trial, usually before recruitment is complete. |
| User Guidance | If applicable, provide a rationale for any interim analysis planned with respect to its purpose (e.g., stopping the trial early for efficacy or futility) and timing. |
| Conformance | Conditional: when <Overall Rationale for Trial Design> is not used |
| Cardinality | One to one |

| | |
|--|--|
| Relationship content from ToC representing the protocol hierarchy | 4.2.6 |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: 4.2.6 Rationale for Interim Analysis Concept: CNEW |
| Repeating and/or Reuse Rules | No |

314

315 **4.2.7 Rationale for Other Trial Design Aspects**

| | |
|--|---|
| Term (Variable) | 4.2.7 Rationale for Other Trial Design Aspects |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | H |
| Definition | Heading |
| User Guidance | N/A |
| Conformance | Conditional: when<Overall Rationale for Trial Design> is not used |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 4.2.7 |
| Value | Rationale for Other Trial Design Aspects |
| Business rules | Value Allowed: No Relationship: 4.2 Rationale for Trial Design, 4 TRIAL DESIGN; Table of Contents Concept: Heading |
| Repeating and/or Reuse Rules | No |

316

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

317

318 **4.3 Trial Stopping Rules**

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

319

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

320

321 **4.4 Start of Trial and End of Trial**

| | |
|------------------------|-------------------------------------|
| Term (Variable) | 4.4 Start of Trial and End of Trial |
| Data Type | Text |

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

322

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

323

| | |
|---|--|
| Term (Variable) | <End of Trial> |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | CNEW For review purpose, see definition of the controlled terminology below A description containing a concise explanation, any local regulatory requirements and considerations, extensions, follow-up, and analysis for the trial end. |
| User Guidance | Define key timepoints in the trial, including trial start and end timepoint 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: CNEW |
| Repeating and/or Reuse Rules | No |

324

325

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 |

326

| | |
|--|--|
| Term (Variable) | <Access to Trial Intervention after End of Trial> |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | CNEW For review purpose, see definition of the controlled terminology below A narrative description containing information about whether and how trial participants have access to the trial interventions after the trial ends. |
| User Guidance | If applicable, describe any possibilities for access to trial intervention, if any, beyond completion of the trial. Planned extension trials, if described in Section 4.1 Description of Trial Design, do not need to be repeated in this section. |
| Conformance | Required |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 4.5 |

| | |
|-------------------------------------|---|
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: 4.5 Access to Trial Intervention After End of Trial Concept: CNEW |
| Repeating and/or Reuse Rules | No |

327

328

5 TRIAL POPULATION

| | |
|--|---|
| Term (Variable) | 5 TRIAL POPULATION |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | H |
| Definition | Heading |
| User Guidance | In the subsections below, describe the trial population: inclusion and exclusion criteria, contraception requirements and lifestyle restrictions. The trial population should generally be aligned with the population attribute of the primary estimand that was defined in Section 3 Trial Objectives and Associated Estimands. Consider the following when developing participant eligibility criteria to be listed in Section 5.2 Inclusion Criteria, and Section 5.3 Exclusion Criteria: <ul style="list-style-type: none"> List the criteria necessary for participation in the trial. Ensure that each criterion can be easily assessed definitively and answered with yes/no responses. Criteria should be written to avoid protocol waivers or exemptions. If participants require screening, distinguish between screening vs enrolling participants. Identify specific laboratory tests or clinical characteristics that will be used as criteria for inclusion or exclusion and any documentation needed to demonstrate the criterion is met (e.g., laboratory tests or imaging). If permitting existing medical diagnosis, imaging, genetic tests, or laboratory results, state any required window or acceptable test type. If measures to enrich the trial population for pre-specified subgroups of interest are used, these should be described. No text is intended here (heading only). |
| Conformance | Required |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 5 |
| Value | TRIAL POPULATION |
| Business rules | Value Allowed: No Relationship: Table of contents Concept: Heading |
| Repeating and/or Reuse Rules | No |

329

330

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 |

331

| | |
|--|---|
| Term (Variable) | <Description of Trial Population and Rationale> |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | CNEW A description of the rationale for selection of trial population describing how the selected population can meet the trial objectives and how the enrollment criteria reflect the targeted populations. |
| User Guidance | Describe the population selected (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 time point at which qualification for age criteria is determined (e.g., at time of screening vs randomisation for paediatric trials). Specify any key diagnostic criteria for the population (e.g., “acute lung injury”, or a specific biomarker profile). If applicable, describe similar conditions or diseases and their differential diagnosis. Provide a rationale for the trial population ensuring that the population selected is well defined and clinically recognisable. Describe how the selected population can meet the trial objectives and how the enrollment criteria reflect the population of interest. If the population targeted by a clinical question is based on a subset of the entire trial population, e.g., defined by a particular characteristic measured at baseline (e.g., a specific biomarker), this subset should be justified in this section. Justify whether the trial intervention is to be evaluated in paediatric participants, in adults unable to consent for themselves, other vulnerable participant populations, or those that may respond to the trial intervention differently (e.g., elderly, hepatic or renally impaired, or immunocompromised participants). |
| Conformance | Required |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 5.1 |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: 5.1 Description of Trial Population and Rationale Concept: CNEW |
| Repeating and/or Reuse Rules | No |

332

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

333

334

5.2 Inclusion Criteria

| | |
|--|--|
| Term (Variable) | 5.2 Inclusion Criteria |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | H |
| Definition | Heading |
| User Guidance | Inclusion criteria are characteristics that define the trial population, i.e., those criteria that every potential participant must satisfy to qualify for trial enrollment. |
| 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 |

335

| | |
|--|--|
| Term (Variable) | To be eligible to participate in this trial, an individual must meet all the following criteria: |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | V |
| Definition | Universal text |
| User Guidance | N/A |
| Conformance | Required |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 5.2 |

| | |
|-------------------------------------|---|
| Value | To be eligible to participate in this trial, an individual must meet all the following criteria: |
| Business rules | Value Allowed: No Relationship: 5.2 Inclusion Criteria Concept: Universal text |
| Repeating and/or Reuse Rules | No |

336

| | |
|--|---|
| Term (Variable) | <#> |
| Data Type | Number |
| Data (D), Value (V) or Heading (H) | D |
| Definition | N/A |
| User Guidance | Add criteria as needed. Consider numbering the criteria sequentially. |
| Conformance | Optional |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 5.2 |
| Value | # is an integer <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 |

337

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

338

339

5.3 Exclusion Criteria

| | |
|------------------------|------------------------|
| Term (Variable) | 5.3 Exclusion Criteria |
| Data Type | Text |

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

340

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

341

| | |
|--|---|
| Term (Variable) | <#> |
| Data Type | Number |
| Data (D), Value (V) or Heading (H) | D |
| Definition | N/A |
| User Guidance | Add criteria as needed. Number the criteria sequentially |
| Conformance | Required |
| Cardinality | One to many |
| Relationship content from ToC representing the protocol hierarchy | 5.3 |
| Value | # is an identifier <criteria identifier> unique number and not replaceable |
| Business rules | Value Allowed: Yes Relationship: 5.3 Exclusion Criteria Concept: Sequential number |

342

| | |
|-------------------------------------|--|
| Repeating and/or Reuse Rules | Yes, number consecutively, repeatable for each exclusion criteria, if deleted do not replace, do not duplicate |
|-------------------------------------|--|

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

343

344

5.4 Contraception

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

345

346

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 |

347

| | |
|--|---|
| Term (Variable) | <Definitions Related to Childbearing Potential> |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | CNEW For review purpose, see definition of the controlled terminology below A concise explanation of the meaning of participants of childbearing potential and non-childbearing potential within the context of a trial, or state not applicable. |
| User Guidance | Specify the definitions of: <ul style="list-style-type: none"> • participant of childbearing potential • participant of non-childbearing potential |
| Conformance | Required |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 5.4.1 |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: 5.4.1 Definitions Related to Childbearing Potential Concept: CNEW |
| Repeating and/or Reuse Rules | No |

348

349

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 |

350

| | |
|--|--|
| Repeating and/or Reuse Rules | No |
| Term (Variable) | <Contraception Requirements> |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | CNEW For review purpose, see definition of the controlled terminology below A description of the requirements for the prevention of conception or impregnation by the use of devices or drugs or surgery within a context of a trial, or state not applicable. |
| User Guidance | Specify the: <ul style="list-style-type: none"> • contraceptive methods required • duration of use |
| Conformance | Required |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 5.4 |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: 5.4.2 Contraception requirements Concept: CNEW |
| Repeating and/or Reuse Rules | No |

351

352

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 |

353

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

| | |
|--|--|
| | A description of the restrictions related to trial participant lifestyle such as diet, substance intake, and physical or other daily activities. |
| User Guidance | In the following subsections, describe any restrictions during the trial pertaining to lifestyle and/or diet, intake of caffeine, alcohol, or tobacco, or physical and other activities. If not applicable, include a statement that no restrictions are required. |
| Conformance | Conditional: If Level 3 subheadings are not used |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 5.5 |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: 5.5 Lifestyle Restrictions Concept: CNEW |
| Repeating and/or Reuse Rules | No |

354

355 **5.5.1 Meals and Dietary Restrictions**

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

356

| | |
|--|---|
| Term (Variable) | <Meals and Dietary Restrictions> |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | CNEW For review purpose, see definition of the controlled terminology below A description of the restrictions related to participant diet during the trial. |
| User Guidance | If applicable, describe any restrictions on diet (e.g., food and drink restrictions, timing of meals relative to dosing). |
| Conformance | Optional |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 5.5.1 |

| | |
|-------------------------------------|--|
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: 5.5.1 Meals and Dietary Restrictions Concept: CNEW |
| Repeating and/or Reuse Rules | No |

357

358 **5.5.2 Caffeine, Alcohol, Tobacco, and Other Restrictions**

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

359

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

360

361 **5.5.3 Physical Activity Restrictions**

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

362

| | |
|--|---|
| Term (Variable) | <Physical Activity Restrictions> |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | CNEW For review purpose, see definition of the controlled terminology below A description of the restrictions related to participant physical activity during the trial. |
| User Guidance | If applicable, describe any restrictions on activity (e.g., in first-in-human trials, activity may be restricted by ensuring participants remain in bed for 4 to 6 hours after dosing). |
| Conformance | Optional |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 5.5.3 |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: 5.5.3 Physical Activity Restrictions Concept: CNEW |
| Repeating and/or Reuse Rules | No |

363

364 **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 Concept: Heading |
| Repeating and/or Reuse Rules | No |

365

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

366

367

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 |

368

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

369

| | |
|--|---|
| Term (Variable) | <Rescreening> |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | CNEW For review purpose, see definition of the controlled terminology below The process of active consideration of subjects for enrollment in a trial, for those potential subjects who have failed a prior screening attempt. |
| User Guidance | Describe screen failure and indicate how screen failure will be handled in the trial, including conditions and criteria upon which rescreening is acceptable. If applicable, indicate the circumstances and time window under which a repeat procedure is allowed for screen failure relating to specific inclusion/exclusion criteria for the trial. |
| Conformance | Required |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 5.6 |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: 5.6 Screen Failure and Rescreening Concept: CNEW |
| Repeating and/or Reuse Rules | No |

370

371 **6 TRIAL INTERVENTION AND CONCOMITANT THERAPY**

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

372

| | |
|--|---|
| Term (Variable) | <Description of the overview of trial interventions or a heading for the optional table below> |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | CNEW For review purpose, see definition of the controlled terminology below A free text description of the trial intervention; alternatively can be used as a heading for a table containing information about the trial intervention. |
| User Guidance | Trial interventions are all pre-specified, investigational and non-investigational medicinal products, medical devices or other interventions intended for the participants during the trial. The investigational trial intervention is the product used in the trial as part of trial objectives. Description of investigational trial intervention is provided in Section 6.1. Other trial interventions that are not part of trial objectives (not an investigational role in this trial) are described in Section 6.9 Description of Non-investigational trial interventions. Any regional requirements should be noted in the appropriate subsections. Provide an overview of investigational and non-investigational trial interventions. Classify the trial intervention as IMP, NIMP/AxMP designations based on study design and local legislation. Consider the optional table below |
| Conformance | Required |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 6 |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: 6 TRIAL INTERVENTION AND CONCOMITANT THERAPY Concept: CNEW |
| Repeating and/or Reuse Rules | No |

373

| | |
|------------------------|----------|
| 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 |

374

| | |
|--|--|
| 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 |

375

| | |
|--|--|
| 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 |

376

| | |
|--|--|
| 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 |

377

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

378

| | |
|--|--|
| 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 |

379

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

380

| | |
|--|--|
| 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 |

381

| | |
|--|--|
| 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 |

382

| | |
|--|--|
| 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 |

383

| | |
|--|--|
| 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 |

384

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

385

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

386

| | |
|--|--|
| Term (Variable) | <Arm Type> |
| Data Type | Valid Value |
| Data (D), Value (V) or Heading (H) | V |
| Definition | C172457 For review purpose, see definition of the controlled terminology below A characterization or classification of the study arm. |
| User Guidance | N/A |
| Conformance | Optional: if the table used |
| Cardinality | One to each arm name |
| Relationship content from ToC representing the protocol hierarchy | 6 |
| Value | Experimental Arm(C174266), Active Comparator Arm(C174267), Placebo Comparator Arm (C174268, Sham Comparator Arm (C174269), No Intervention Arm (C174270), Control Arm(C174226) |
| Business rules | Value Allowed: Yes Relationship: Arm name and arm type Concept: C172457 |
| Repeating and/or Reuse Rules | Yes, repeatable for each arm name |

387

| NCI C-Code | M11 Preferred Term | Draft Definition |
|------------|-----------------------|--|
| C174267 | Active Comparator Arm | An arm describing the active comparator. |
| C174226 | Control Arm | An arm describing the intervention or treatment plan for a group of participants in the study receiving a control. The control may comprise a non-investigational product (active control) or regimen, placebo, or no treatment. |

| | | |
|---------|------------------------|--|
| C174266 | Experimental Arm | An arm describing the intervention or treatment plan for a group of participants in the study receiving test product(s). |
| C174270 | No Intervention Arm | A study arm without an intervention or treatment. |
| C174268 | Placebo Comparator Arm | An arm describing the placebo comparator. |
| C174269 | Sham Comparator Arm | An arm describing the sham comparator. |

388

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

389

| | |
|--|--|
| Term (Variable) | <Intervention Type> |
| Data Type | Valid Value |
| Data (D), Value (V) or Heading (H) | V |
| Definition | C98747 For review purpose, see definition of the controlled terminology below The kind of product or procedure studied in a trial. |
| User Guidance | N/A |
| Conformance | Optional: if the table used |
| Cardinality | One to each intervention name |
| Relationship content from ToC representing the protocol hierarchy | 6 |
| Value | Drug (C1909), Device (C16830), Biologic (C307), Vaccine (C923), Non-Surgical Procedure (CNEW), Surgery (C15329), Radiation (C15313), Behavioral (C15184), Genetic (C15238), Dietary Supplement (C1505), Combination Product (C54696), Diagnostic Test (C18020) |
| Business rules | Value Allowed: Yes Relationship: Arm name, arm type and intervention name Concept: C98747 |
| Repeating and/or Reuse Rules | Yes, repeatable for each arm name and arm type combination |

390

| NCI C-Code | M11 Preferred Term | Draft Definition |
|------------|--------------------|--|
| C15184 | Behavioral | A technique used to change the behavior of a participant (e.g., psychotherapy, lifestyle counseling, or hypnosis). |

| | | |
|--------|------------------------|---|
| C307 | Biologic | A product of biological origin applicable to the prevention, treatment, or cure of a disease or condition, for example: virus, therapeutic serum, toxin, antitoxin, vaccine, blood, blood component or derivative, allergenic product, or analogous product. |
| C923 | Vaccine | A medicinal product inducing immunity against disease, most often to prevent occurrence of a disease, (e.g., a preventative vaccine against infectious disease), but also to treat a disease, (e.g., a therapeutic vaccine against cancer). |
| C54696 | Combination Product | A product composed of two or more different types of medical products (i.e., a combination of a drug, device, and/or biological product with one another and are referred to as "constituent parts" of the combination product). |
| C16830 | Device | Any instrument, apparatus, implement, machine, appliance, implant, reagent for in vitro use, software, material or other similar or related article, intended by the manufacturer to be used, alone or in combination for, one or more specific medical purpose(s). |
| C1505 | Dietary Supplement | Preparations containing ingredient(s) intended to supplement the diet. |
| C1909 | Drug | An active natural, synthetic or semi-synthetic ingredient including endogenous body substance that is intended to furnish pharmacological activity or other direct effect in the diagnosis, cure, mitigation, treatment, or prevention of disease or to affect the structure or any function of the human body, but does not include intermediates used in the synthesis of such ingredient |
| C15238 | Genetic | Introduction of genetic material into cells in order to correct or treat an inherited or acquired disease. |
| C15329 | Surgery | A diagnostic or treatment procedure performed by manual and/or instrumental means, often involving an incision and the removal or replacement of a diseased organ or tissue; of or relating to or involving or used in surgery or requiring or amenable to treatment by surgery. |
| CNEW | Non-Surgical Procedure | A medical procedure that produces an effect, or that is intended to alter the course of a disease in a patient or population, which is not considered a surgical procedure. |
| C15313 | Radiation | Use of targeted or whole body radiation to treat a disease. |
| C18020 | Diagnostic Test | Any procedure or test to diagnose a disease or disorder. |

391

| | |
|--|---|
| Term (Variable) | <Pharmaceutical Dose Formulation> |
| Data Type | Valid Value |
| Data (D), Value (V) or Heading (H) | V |
| Definition | C42636 For review purpose, see definition of the controlled terminology below Physical characteristics of a drug product, (e.g., tablet, capsule, or solution) that contains a drug substance, generally-but not necessarily-in association with one or more other ingredients. |
| User Guidance | N/A |
| Conformance | Optional: if the table used |
| Cardinality | One to each arm name, arm type and intervention combination |
| Relationship content from ToC representing the protocol hierarchy | 6 |
| Value | Use IDMP (ISO 11239) or CDISC SDTM Terminology |
| Business rules | Value Allowed: Yes |

| | |
|-------------------------------------|--|
| | Relationship: Arm name and dosage formulation Concept: C42636 |
| Repeating and/or Reuse Rules | Yes, repeatable for each intervention name and Pharmaceutical Dose Formulation |

392

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

393

| | |
|--|---|
| Term (Variable) | <Dosage Level(s)> |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C94394 For review purpose, see definition of the controlled terminology below Specified quantity of a medicine, to be taken at one time or at stated intervals. |
| User Guidance | N/A |
| Conformance | Optional: if the table used |
| Cardinality | One to each intervention name and pharmaceutical dose formulation |
| Relationship content from ToC representing the protocol hierarchy | 6 |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: Arm name and dose level Concept: C94394 |
| Repeating and/or Reuse Rules | Yes, repeatable for each intervention name, pharmaceutical dose formulation, dosage strength and dosage level per arm |

394

| | |
|---|---------------------------|
| Term (Variable) | <Route of Administration> |
| Data Type | Valid Value |
| Data (D), Value (V) or Heading (H) | V |
| Definition | C38114 |

| | |
|--|--|
| | For review purpose, see definition of the controlled terminology below Path by which the pharmaceutical product is taken into or makes contact with the body. |
| User Guidance | N/A |
| Conformance | Optional: if the table used |
| Cardinality | One to each intervention name and pharmaceutical dose formulation |
| 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 |
| Repeating and/or Reuse Rules | Yes, repeatable for each intervention name, pharmaceutical dose formulation, per arm name |

395

| | |
|--|--|
| Term (Variable) | {<Regimen/Treatment Period/Vaccination Regimen>} |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | CNEW For review purpose, see definition of the controlled terminology below A description of the schedule and periodicity of a treatment or vaccination regimen. |
| User Guidance | N/A |
| Conformance | Optional: if the table used |
| Cardinality | One to each intervention name, pharmaceutical dose formulation, 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/vaccine regimen Concept: CNEW |
| Repeating and/or Reuse Rules | Yes, repeatable for each arm name |

396

| | |
|--|---|
| Term (Variable) | <Use> |
| Data Type | Valid Value |
| Data (D), Value (V) or Heading (H) | V |
| Definition | CNEW For review purpose, see definition of the controlled terminology below The reason or intention for the use of the trial intervention within the trial arm. |
| User Guidance | N/A |
| Conformance | Optional: if the table used |
| Cardinality | One to each intervention |
| Relationship content from ToC representing the protocol hierarchy | 6 |

397

| | |
|-------------------------------------|---|
| Value | Experimental Intervention (C41161), Placebo (C753), Rescue Medicine (C165835), Background treatment (C165822), Challenge Agent (C158128), Diagnostic (C18020), Additional Required treatment (CNEW) |
| Business rules | Value Allowed: Yes Relationship: Arm name and use Concept: CNEW |
| Repeating and/or Reuse Rules | Yes, repeatable for each intervention name per arm |

398

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

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

| | |
|-------------------------------------|---|
| | Relationship: One per each intervention name Concept: CNEW |
| Repeating and/or Reuse Rules | Yes, repeatable for each intervention name per arm |

399

| NCI C-Code | M11 Preferred Term | Draft Definition |
|------------|--------------------|--|
| CNEW | IMP | A medicinal product which is being tested or used as a reference, including as a placebo, in a clinical trial. |
| C156473 | NIMP | A medicinal product that is related to the specific needs of the clinical trial as described in the protocol, but not as an investigational medicinal product. |

400

| | |
|--|---|
| Term (Variable) | <Sourcing> |
| Data Type | Valid Value |
| Data (D), Value (V) or Heading (H) | V |
| Definition | CNEW For review purpose, see definition of the controlled terminology below An indication as to whether the investigational intervention is centrally or locally sourced. |
| User Guidance | N/A |
| Conformance | Optional: if the table used |
| Cardinality | One to many |
| Relationship content from ToC representing the protocol hierarchy | 6 |
| Value | Centrally Sourced (CNEW); Locally Sourced (CNEW) |
| Business rules | Value Allowed: Yes Relationship: One per each Intervention name Concept: CNEW |
| Repeating and/or Reuse Rules | Yes, repeatable for each intervention name per arm name |

401

| NCI C-Code | M11 Preferred Term | Draft Definition |
|------------|--------------------|--|
| CNEW | Centrally Sourced | An indication that the entity is obtained from a central source. |
| CNEW | Locally Sourced | An indication that the entity is obtained from a local source. |

402

403

6.1 Description of Investigational Trial Intervention

| | |
|--|---|
| Term (Variable) | 6.1 Description of Investigational Trial Intervention |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | H |
| Definition | Heading |
| User Guidance | N/A |
| Conformance | Required |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 6.1 |
| Value | Description of Investigational Trial Intervention |
| Business rules | Value Allowed: No |

404

| | |
|-------------------------------------|--|
| | 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 | CNEW For review purpose, see definition of the controlled terminology below A description of the investigational trial intervention. |
| User Guidance | Describe the investigational trial intervention to be administered in each arm of the trial and for each period of the trial including route and mode of administration, dose, dosage regimen, duration of intervention, use, packaging and labelling. Refer to approved regional labelling, as appropriate. For drug/device combination products, include details on the configuration and use of the device and device manufacturer. A device user manual may be referenced in this section. |
| Conformance | Required |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 6.1 |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: 6.1 Description of Investigational Trial Intervention Concept: CNEW |
| Repeating and/or Reuse Rules | No |

405

406

6.2 Rationale for Investigational Trial Intervention Dose and Regimen

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

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

6.3 Investigational Trial Intervention Administration

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

410

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

411

412

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 |

413

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

414

415

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 |

416

| | |
|--|---|
| Term (Variable) | <Management of Investigational Trial Intervention Overdose> |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | CNEW For review purpose, see definition of the controlled terminology below A description of how a potential investigational trial intervention overdose will be handled. |
| User Guidance | Describe what is meant by investigational trial intervention overdose. Provide any available information on managing the overdose and ensure it is consistent with the Investigator's Brochure or product labelling. Cross 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: CNEW |
| Repeating and/or Reuse Rules | No |

417

418

419

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 |

420

421

6.6.1 Preparation of Investigational Trial Intervention

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

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

422

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

423

424

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 |

425

| | |
|--|---|
| Term (Variable) | <Storage and Handling of Investigational Trial Intervention> |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C115525 For review purpose, see definition of the controlled terminology below A narrative description containing information about the handling, storage, and distribution of investigational trial intervention. |
| User Guidance | Describe storage and handling requirements (e.g., protection from light, temperature, humidity) for the investigational trial intervention(s). For trials in which multi-dose vials are utilised, provide additional information regarding stability and expiration time after initial use (e.g., if the seal is broken). 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. 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 | 6.6.2 |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: 6.6.2 Storage and Handling of Investigational Trial Intervention Concept: C115525 |
| Repeating and/or Reuse Rules | No |

426

427 **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 |

428

| | |
|--|---|
| Term (Variable) | <Accountability of Investigational Trial Intervention> |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C176267 For review purpose, see definition of the controlled terminology below The act or process for documenting the storage, inventory tracking, and disposition of the investigational trial intervention. |
| User Guidance | Describe the 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 • if applicable, plans for reconciliation of investigational trial intervention |
| Conformance | Required |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 6.6.3 |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: 6.6.3 Accountability of Investigational Trial Intervention Concept: C176267 |
| Repeating and/or Reuse Rules | No |

429

430 **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 many |
| Relationship content from ToC representing the protocol hierarchy | 6.7 |
| Value | Investigational Trial Intervention Assignment, Randomisation and Blinding |
| Business rules | Value Allowed: No Relationship: 6 TRIAL INTERVENTION AND CONCOMITANT THERAPY; Table of Contents Concept: Heading |
| Repeating and/or Reuse Rules | No |

431

432 **6.7.1 Participant Assignment to Investigational Trial Intervention**

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

433

| | |
|---|---|
| Term (Variable) | <Participant Assignment to Investigational Trial Intervention> |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | CNEW For review purpose, see definition of the controlled terminology below The technique used to assign trial participants to a trial arm. |
| User Guidance | 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 occurs relative to screening. |

| | |
|--|---|
| | If adaptive randomisation or other methods of covariate balancing/minimisation are employed, include a cross reference to the methods of analysis in Section 10 Statistical Considerations. As applicable, details regarding the implementation of procedures to minimise bias should be described. |
| Conformance | Required |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 6.7.1 |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: 6.7.1 Participant Assignment to Investigational Trial Intervention Concept: CNEW |
| Repeating and/or Reuse Rules | No |

434

435

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 |

436

| | |
|---|---|
| Term (Variable) | {<Randomisation>} |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C25196 For review purpose, see definition of the controlled terminology below The process of assigning trial subjects to treatment or control groups using an element of chance to determine the assignments in order to reduce bias. |
| 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 IxRS will be used. To maintain the integrity of the blinding, do not include the block size. |
| Conformance | Conditional: when randomised trial |
| Cardinality | One to one |

| | |
|--|---|
| Relationship content from ToC representing the protocol hierarchy | 6.7.2 |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: 6.7.2 Randomisation Concept: C25196 |
| Repeating and/or Reuse Rules | No |

437

438 **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 |

439

| | |
|---|---|
| Term (Variable) | {<Measures to Maintain Blinding>} |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C189349 For review purpose, see definition of the controlled terminology below A description of the measures taken to ensure the blinding is maintained. |
| User Guidance | Describe efforts to maintain blinding: <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 For unplanned but intentional actions (e.g., safety events), refer to Section 6.7.4 Emergency Unblinding at the Site. If the trial allows for some investigators or other designated staff to remain unblinded (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. |
| Conformance | Conditional: when blind trial |

| | |
|--|---|
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 6.7.3 |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: 6.7.3 Blinding Concept: C189349 |
| Repeating and/or Reuse Rules | No |

440

441 **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 |

442

| | |
|--|---|
| Term (Variable) | {<Emergency Unblinding at the Site>} |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | CNEW For review purpose, see definition of the controlled terminology below A description of the methodology used for unblinding of the trial treatment in the case of a sudden unforeseen crisis that requires immediate medical care of the participant. |
| User Guidance | Describe the criteria for breaking the trial blind or participant code. Describe the circumstances that would require breaking the blind, either for an individual participant or 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 |
| Relationship content from ToC representing the protocol hierarchy | 6.7.4 |

| | |
|-------------------------------------|--|
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: 6.7.4 Emergency Unblinding at the Site Concept: CNEW |
| Repeating and/or Reuse Rules | No |

443

444

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 |

445

| | |
|--|---|
| Term (Variable) | <Investigational Trial Intervention Adherence> |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | CNEW For review purpose, see definition of the controlled terminology below A description of the measures taken to ensure trial intervention adherence, including mandatory documentation to be filled out and the source data that will be used to document investigational trial intervention compliance. |
| User Guidance | Describe the measures to monitor and document participants' compliance with investigational intervention (e.g. study intervention accountability records, diary cards, or investigational intervention concentration measurements). List what documents are mandatory to complete (for example, participant drug log) and what source data/records will be used to document investigational intervention compliance. |
| Conformance | Required |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 6.8 |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: 6.8 Investigational Trial Intervention Adherence Concept: CNEW |

| | |
|-------------------------------------|----|
| Repeating and/or Reuse Rules | No |
|-------------------------------------|----|

446

447

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 |

448

| | |
|--|---|
| Term (Variable) | <Description of Noninvestigational Trial Intervention> |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | CNEW For review purpose, see definition of the controlled terminology below A description of the noninvestigational trial intervention. |
| 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. The non-investigational trial intervention(s) may be described concisely in a table or in the following sections as applicable. |
| Conformance | Required |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 6.9 |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: 6.9 Description of Noninvestigational Trial Intervention Concept: CNEW |
| Repeating and/or Reuse Rules | No |

449

450

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 |

451

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

452

453

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 |

454

| | |
|--|---|
| Term (Variable) | {<Rescue Therapy>} |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C165835 For review purpose, see definition of the controlled terminology below Any rescue medications, treatments, and/or procedures identified in the protocol as those that may be administered to participants when the efficacy of the investigational intervention is not satisfactory, its effect is too great and is likely to cause a hazard to the patient, or to manage an emergency situation. |
| 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 discontinuation of trial intervention or a participant's withdrawal from the trial, 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 |
| Relationship content from ToC representing the protocol hierarchy | 6.9.2 |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: 6.9.2 Rescue Therapy Concept: C165835 |
| Repeating and/or Reuse Rules | No |

455

456

6.9.3 Other Noninvestigational Intervention

| | |
|--|--|
| Term (Variable) | 6.9.3 {Other Noninvestigational Intervention} |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | H |
| Definition | Heading |
| User Guidance | N/A |
| Conformance | Conditional: when any other noninvestigational interventions are defined |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 6.9.3 |
| Value | Other 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 |

457

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

458

459

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 |

460

| | |
|------------------------|-----------------------|
| Term (Variable) | <Concomitant Therapy> |
| Data Type | Text |

| | |
|--|---|
| Data (D), Value (V) or Heading (H) | D |
| Definition | C53630 For review purpose, see definition of the controlled terminology below Any pharmaceutical agent, other than the trial interventions, that is administered to or used by the subject prior to or during a specified time period. |
| User Guidance | Specify the concomitant medications, supplements, complementary and alternative therapies, treatments, and/or procedures which are prohibited or permitted during the trial and include details about when the information will be collected (e.g., during screening, at each visit). When appropriate to separate the content, subheadings may be used. |
| Conformance | Required |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 6.10 |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: 6.10 Concomitant Therapy Concept: C53630 |
| Repeating and/or Reuse Rules | No |

461

462

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 |

463

| | |
|---|---|
| Term (Variable) | {<Prohibited Concomitant Therapy>} |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | CNEW For review purpose, see definition of the controlled terminology below Concomitant therapy that is banned from use in the trial. |
| User Guidance | If applicable, describe any prohibited concomitant therapy. |
| Conformance | Conditional: when any prohibited concomitant therapies are defined |

| | |
|--|---|
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 6.10.1 |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: 6.10.1 Prohibited Concomitant Therapy Concept: CNEW |
| Repeating and/or Reuse Rules | No |

464

465

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 |

466

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

467

468 7 PARTICIPANT DISCONTINUATION OF TRIAL INTERVENTION AND
 469 DISCONTINUATION OR WITHDRAWAL FROM TRIAL

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

470

471 7.1 Discontinuation of Trial Intervention for Individual Participants

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

472

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 | CNEW For review purpose, see definition of the controlled terminology below The requirements that must be met in order to permanently discontinue the administration of trial intervention. |
| User Guidance | Describe: <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 treatment through the end of the trial to prevent missing data in important analyses. Refer to the Section 1.3 Schedule of Activities for assessments to be performed at the time of and following discontinuation of trial intervention. the process for collecting and recording the detailed reasons for discontinuing trial intervention if not described elsewhere. |
| Conformance | Required |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 7.1.1 |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: 7.1.1 Permanent Discontinuation of Trial Intervention Concept: CNEW |

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|-------------------------------------|----|
| Repeating and/or Reuse Rules | No |
|-------------------------------------|----|

475

476

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 |
| Repeating and/or Reuse Rules | No |

477

| | |
|--|---|
| Term (Variable) | <Temporary Discontinuation of Trial Intervention> |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | CNEW For review purpose, see definition of the controlled terminology below The requirements that must be met in order to temporarily discontinue the administration of trial intervention. |
| User Guidance | Describe: <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 whether the participant will continue in the trial which assessments will be performed for the stated duration of the trial Details of any rechallenge or restart after a safety-related event should be included in Section 7.1.3 Rechallenge. |
| Conformance | Required |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 7.1.2 |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: 7.1.2 Temporary Discontinuation of Trial Intervention Concept: CNEW |

| | |
|-------------------------------------|----|
| Repeating and/or Reuse Rules | No |
|-------------------------------------|----|

478

479

7.1.3 Rechallenge

| | |
|--|---|
| Term (Variable) | 7.1.3 Rechallenge |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | H |
| Definition | Heading |
| User Guidance | N/A |
| Conformance | Required |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 7.1.3 |
| Value | Rechallenge |
| Business rules | Value Allowed: No Relationship: 7.1 Discontinuation of Trial Intervention for Individual Participants; 7 PARTICIPANT DISCONTINUATION OF TRIAL INTERVENTION AND DISCONTINUATION OR WITHDRAWAL FROM TRIAL; Table of Contents. Concept: Heading |
| Repeating and/or Reuse Rules | No |

480

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

481

482 7.2 Participant Discontinuation or Withdrawal from the Trial

| | |
|--|--|
| Term (Variable) | 7.2 Participant Discontinuation or Withdrawal from the Trial |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | H |
| Definition | Heading |
| User Guidance | N/A |
| Conformance | Required |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 7.2 |
| Value | Participant Discontinuation or Withdrawal from the Trial |
| Business rules | Value Allowed: No Relationship: 7 PARTICIPANT DISCONTINUATION OF TRIAL INTERVENTION AND DISCONTINUATION OR WITHDRAWAL FROM TRIAL; Table of Contents. Concept: Heading |
| Repeating and/or Reuse Rules | No |

483

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

484

485 **7.3 Management of Loss to Follow-Up**

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

486

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

487

488 **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 | <p>Value Allowed: No</p> <p>Relationship: Table of Contents</p> <p>Concept: Heading</p> |
| Repeating and/or Reuse Rules | No |

489

490

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 |

491

| | |
|--|---|
| Term (Variable) | <Trial Assessments and Procedures Considerations> |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | CNEW For review purpose, see definition of the controlled terminology below A description of general considerations applicable across trial assessments and procedures. |
| User Guidance | Describe general considerations applicable across trial assessments and procedures. |
| Conformance | Required |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 8.1 |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: 8.1 Trial Assessments and Procedures Considerations Concept: CNEW |
| Repeating and/or Reuse Rules | No |

492

493

8.2 Screening/Baseline Assessments and Procedures

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

494

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

495

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

496

497 **8.3 Efficacy Assessments and Procedures**

| | |
|--|---|
| Term (Variable) | 8.3 Efficacy Assessments and Procedures |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | H |
| Definition | Heading |
| User Guidance | N/A |
| Conformance | Required |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 8.3 |
| Value | Efficacy Assessments and Procedures |
| Business rules | Value Allowed: No Relationship: 8 TRIAL ASSESSMENTS AND PROCEDURES; Table of Contents Concept: Heading |
| Repeating and/or Reuse Rules | No |

498

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

499

500 **8.4 Safety Assessments and Procedures**

| | |
|---|---------------------------------------|
| Term (Variable) | 8.4 Safety Assessments and Procedures |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | H |
| Definition | Heading |
| User Guidance | N/A |

| | |
|--|--|
| Conformance | Required |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 8.4 |
| Value | Safety Assessments and Procedures |
| Business rules | Value Allowed: No Relationship: 8 TRIAL ASSESSMENTS AND PROCEDURES; Table of Contents. Concept: Heading |
| Repeating and/or Reuse Rules | No |

501

| | |
|--|--|
| Term (Variable) | <Safety Assessments and Procedures> |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | CNEW For review purpose, see definition of the controlled terminology below A description of the assessments and procedures related to participant safety within the trial. |
| User Guidance | Describe safety assessments and procedures utilizing the following subsections as applicable. Add level 3 headings as needed. <ul style="list-style-type: none"> Identify any noninvestigator party responsible for evaluation of laboratory or other safety assessments (e.g., Sponsor or external Independent Data Monitoring Committee; cross refer to Section 11.4 Committees for details as applicable). Include guidelines for the medical management of relevant laboratory or other safety assessment abnormalities. |
| Conformance | Required |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 8.4 |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: 8.4 Safety Assessments and Procedures Concept: CNEW |
| Repeating and/or Reuse Rules | No |

502

503 **8.4.1 {Physical Examination}**

| | |
|---|---|
| Term (Variable) | 8.4.1 {Physical Examination} |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | H |
| Definition | Heading |
| User Guidance | N/A |
| Conformance | Conditional: when Physical Exams are required |

| | |
|--|---|
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 8.4.1 |
| Value | Physical Examination |
| Business rules | Value Allowed: No Relationship: 8.4 Safety Assessment and Procedures; 8 TRIAL ASSESSMENTS AND PROCEDURES; Table of Contents Concept: Heading |
| Repeating and/or Reuse Rules | No |

504

| | |
|--|--|
| Term (Variable) | {<Physical Examination>} |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | CNEW For review purpose, see definition of the controlled terminology below The procedures for a physical examination of the body and its functions to be conducted for the trial. |
| User Guidance | Include any specific instructions for the collection and interpretation of physical examinations. |
| Conformance | Conditional: when Physical Exams are required |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 8.4.1 |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: 8.4.1 Physical Examination Concept: CNEW |
| Repeating and/or Reuse Rules | No |

505

506

8.4.2 {Vital Signs}

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

507

| | |
|--|---|
| Repeating and/or Reuse Rules | No |
| Term (Variable) | {<Vital Signs>} |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C154628 For review purpose, see definition of the controlled terminology below The procedures for measurements of the body's basic functions that provide insight into the health status of the person. |
| User Guidance | Include any specific instructions for the collection and interpretation of vital signs. |
| Conformance | Conditional: when Vital Signs are required |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 8.4.2 |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: 8.4.2 Vital Signs Concept: C154628 |
| Repeating and/or Reuse Rules | No |

508

509

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 Concept: Heading |
| Repeating and/or Reuse Rules | No |

510

| | |
|---|---|
| Term (Variable) | {<Electrocardiograms>} |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C168186 For review purpose, see definition of the controlled terminology below |

| | |
|--|---|
| | The procedures for the recordings produced by the variations in electrical potential caused by electrical activity of the heart muscle and detected at the body surface, as a method for studying the action of the heart muscle. |
| User Guidance | Include any specific instructions for the collection, interpretation, and archiving of ECGs. |
| Conformance | Conditional: when Electrocardiograms are required |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 8.4.3 |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: 8.4.3 Electrocardiograms Concept: C168186 |
| Repeating and/or Reuse Rules | No |

511 **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 |

512

| | |
|---|--|
| Term (Variable) | {<Clinical Safety Laboratory Assessments>} |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | CNEW For review purpose, see definition of the controlled terminology below Trial-related laboratory assessments and procedures. |
| 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 |

| | |
|--|---|
| | <ul style="list-style-type: none"> instructions for situations in which central laboratory results are not available in time for trial intervention and/or response evaluation, or in the event of a severe disruption (e.g., a pandemic or natural disaster) treatment algorithms for results out of normal range cross reference Section 12.1 Clinical Laboratory Tests for laboratory assessment panels |
| Conformance | Conditional: when Clinical Laboratory Assessments are required |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 8.4.4 |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: 8.4.4 Clinical Laboratory Assessments Concept: CNEW |
| Repeating and/or Reuse Rules | No |

513

514

8.4.5 {Pregnancy Testing}

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

515

| | |
|---|--|
| Term (Variable) | {<Pregnancy Testing>} |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C92949 For review purpose, see definition of the controlled terminology below Any examination performed to assess if a female is gravid. |
| User Guidance | Include any specific instructions for the collection and interpretation of pregnancy testing. |
| Conformance | Conditional: when Pregnancy Testing is required |
| Cardinality | One to one |

| | |
|--|---|
| Relationship content from ToC representing the protocol hierarchy | 8.4.5 |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: 8.4.5 Pregnancy Testing Concept: C92949 |
| Repeating and/or Reuse Rules | No |

516

517 **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 Concept: Heading |
| Repeating and/or Reuse Rules | No |

518

| | |
|--|--|
| Term (Variable) | {<Suicidal Ideation and Behaviour Risk Monitoring>} |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | CNEW For review purpose, see definition of the controlled terminology below A description of data collection procedures and analysis related to suicidal ideation and behaviour risk monitoring. |
| User Guidance | If the trial meets any of the criteria requiring suicidal ideation and behaviour risk monitoring by the guidance/guideline in each region, include justification for the need for suicidal ideation and behaviour risk monitoring in the study and add any specific instructions for the collection and interpretation of the assessment. In case this is an AESI in the study, justification should also be provided in Section 9.2.4 Adverse Events of Special Interest. |
| Conformance | Conditional: when Suicidal Ideation and Behaviour Risk Monitoring are required |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 8.4.6 |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: 8.4.6 Suicidal Ideation and Behaviour Risk Monitoring |

| | |
|-------------------------------------|----------------------|
| | Concept: CNEW |
| Repeating and/or Reuse Rules | No |

519

520

8.5 Pharmacokinetics

| | |
|--|---|
| Term (Variable) | 8.5 Pharmacokinetics |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | H |
| Definition | Heading |
| User Guidance | N/A |
| Conformance | Required |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 8.5 |
| Value | Pharmacokinetics |
| Business rules | Value Allowed: No Relationship: 8 TRIAL ASSESSMENTS AND PROCEDURES; Table of Contents Concept: Heading |
| Repeating and/or Reuse Rules | No |

521

| | |
|--|---|
| Term (Variable) | <Pharmacokinetics> |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | CNEW For review purpose, see definition of the controlled terminology below A narrative description containing information about the collection, use, and retention of biospecimens, and their use in pharmacokinetic assessments within the trial. |
| User Guidance | Include any specific instructions for the collection and assay of samples and interpretation of PK assessments. <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: CNEW |
| Repeating and/or Reuse Rules | No |

522

523

8.6 Biomarkers

| | |
|--|--|
| Term (Variable) | 8.6 Biomarkers |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | H |
| Definition | Heading |
| User Guidance | Include any specific instructions for the collection of samples and interpretation of biomarkers in the subsections below as applicable. Safety biomarkers should be included in Section 8.4 Safety Assessments and Procedures and immunogenicity markers in Section 8.7 Immunogenicity Assessments. No text is intended here (heading only). |
| Conformance | Required |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 8.6 |
| Value | Biomarkers |
| Business rules | Value Allowed: No Relationship: 8 TRIAL ASSESSMENTS AND PROCEDURES; Table of Contents Concept: Heading |
| Repeating and/or Reuse Rules | No |

524

525

8.6.1 Genetics and Pharmacogenomics

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

| | |
|--|---|
| Term (Variable) | <Genetics and Pharmacogenomics> |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | CNEW For review purpose, see definition of the controlled terminology below A narrative description containing information about the collection, use, and retention of biospecimens, and their use in genetic and pharmacogenomic biomarker assessments within the trial. |
| User Guidance | Include any specific instructions for the collection and assay of samples for genetic and/or pharmacogenomic analysis. <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 | Value Allowed: Yes Relationship: 8.6.1 Genetics and Pharmacogenomics Concept: CNEW |
| 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 | 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) | <Pharmacodynamic Biomarkers> |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | CNEW For review purpose, see definition of the controlled terminology below A narrative description containing information about the collection, use, and retention of biospecimens, and their use in pharmacodynamic biomarker assessments within the trial. |
| User Guidance | Include any specific instructions for the collection of samples and assessment of pharmacodynamic biomarkers. <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 | Value Allowed: Yes Relationship: 8.6.2 Pharmacodynamic Biomarkers Concept: CNEW |
| 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 Relationship: 8.6 Biomarkers; 8 TRIAL ASSESSMENTS AND PROCEDURES; Table of Contents |

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| | |
|--|--|
| | Concept: Heading |
| Repeating and/or Reuse Rules | No |
| Term (Variable) | {<Other Biomarkers>} |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | CNEW For review purpose, see definition of the controlled terminology below A narrative description containing information about the collection, use, and retention of biospecimens, and their use in other biomarker assessments within the trial. |
| User Guidance | Include any specific instructions for the collection of samples and assessment of other biomarkers. <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: CNEW |
| Repeating and/or Reuse Rules | No |

533

534

8.7 Immunogenicity Assessments

| | |
|--|--------------------------------|
| Term (Variable) | 8.7 Immunogenicity Assessments |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | H |
| Definition | Heading |
| User Guidance | N/A |
| Conformance | Required |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 8.7 |
| Value | Immunogenicity Assessments |

535

| | |
|-------------------------------------|---|
| 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 | CNEW For review purpose, see definition of the controlled terminology below A narrative description containing information about the collection, use, and retention of biospecimens, and their use in immunogenicity assessments within the trial. |
| User Guidance | Include any specific instructions for the collection of samples and interpretation of immunogenicity. If immunogenicity assessments are included within Efficacy Assessments or Safety Assessments, cross reference to that section. <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: CNEW |
| Repeating and/or Reuse Rules | No |

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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 |

538

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

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540

541

542

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 |

543

544

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 |
| Repeating and/or Reuse Rules | No |

545

546

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 |

547

| | |
|--|--|
| Term (Variable) | <Definitions of Adverse Events> |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | CNEW For review purpose, see definition of the controlled terminology below A concise explanation of the meaning of adverse events within the context of the trial. |
| User Guidance | Specify the AE definitions, including: <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 reporting) |
| Conformance | Required |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 9.1.1 |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: 9.1.1 Definitions of Adverse Events Concept: CNEW |
| Repeating and/or Reuse Rules | No |

548

549

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 |

550

| | |
|------------------------|---|
| Term (Variable) | <Definitions of Serious Adverse Events> |
| Data Type | Text |

| | |
|--|--|
| Data (D), Value (V) or Heading (H) | D |
| Definition | CNEW For review purpose, see definition of the controlled terminology below A concise explanation of the meaning of serious adverse events within the context of the trial. |
| User Guidance | Specify the SAE definitions, including: <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 |
| Business rules | Value Allowed: Yes Relationship: 9.1.2 Definitions of Serious Adverse Events Concept: CNEW |
| Repeating and/or Reuse Rules | No |

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9.1.3 Definitions of Product Complaints

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

553

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

| | |
|--|--|
| | A concise explanation of the meaning of product complaints within the context of the trial. |
| User Guidance | Specify the definition of product complaints in the context of the trial. |
| Conformance | Required |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 9.1.3 |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: 9.1.3 Definition of Product Complaints Concept: CNEW |
| Repeating and/or Reuse Rules | No |

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555 **9.1.3.1 {Definition of Medical Device Product Complaints}**

| | |
|--|--|
| Term (Variable) | 9.1.3.1 {Definition of Medical Device Product Complaints} |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | H |
| Definition | Heading |
| User Guidance | N/A |
| Conformance | Conditional: when there is Medical Device Product Complaints |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 9.1.3.1 |
| Value | {Definition of Medical Device Product Complaints} |
| Business rules | Value Allowed: No Relationship: 9.3.1 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 |

556

| | |
|---|--|
| Term (Variable) | {<Definition of Medical Device Product Complaints>} |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | CNEW For review purpose, see definition of the controlled terminology below A concise explanation of the meaning of medical device product complaints within the context of the trial. |
| User Guidance | N/A |
| Conformance | Conditional: when there is Medical Device Product Complaints |
| Cardinality | One to one |

| | |
|--|---|
| Relationship content from ToC representing the protocol hierarchy | 9.1.3.1 |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: 9.1.3.1 Definition of Medical Device Product Complaints Concept: CNEW |
| Repeating and/or Reuse Rules | No |

557

558

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 |

559

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

| | |
|-------------------------------------|--------------------------------|
| | Concept: Universal Text |
| Repeating and/or Reuse Rules | No |

560
561

| | |
|--|--|
| 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 |

562

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

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| NCI C-Code | M11 Preferred Term | Draft Definition |
|------------|--------------------|---|
| C41331 | Adverse Event | Any untoward medical occurrence in a patient or clinical investigation participant administered a pharmaceutical product and which does not necessarily have to have a causal relationship with this treatment. |

| | | |
|--------|--|--|
| C41335 | Serious Adverse Event | Any untoward medical occurrence that at any dose: results in death, is life-threatening, requires inpatient hospitalization or prolongation of existing hospitalization, results in persistent or significant disability/ incapacity, or is a congenital anomaly/ birth defect. |
| CNEW | Trial Intervention Complaint | Any concern about the safety and/or quality of any trial-related interventions. |
| C54026 | Medical Device Product Complaint | Any concern about the safety, quality, and/or performance of a trial-related drug-device combination. |
| C25742 | Pregnancy Event | Any event that occurs when the participant is pregnant. |
| CNEW | Lactation Event | Any event that occurs when the participant is lactating. |
| CNEW | Post-Partum Event | Any event that occurs when the participant is in the stages of recovery post pregnancy and birth event. |
| CNEW | Reportable Adverse Event of Special Interest | An adverse event of special interest (serious or non-serious) is one of scientific and medical concern specific to the sponsor's product or program, for which ongoing monitoring and rapid communication by the investigator to the sponsor could be appropriate, and which is deemed to be reportable to the appropriate regulatory authority. |
| CNEW | Not Reportable Adverse Event of Special Interest | An adverse event of special interest (serious or non-serious) is one of scientific and medical concern specific to the sponsor's product or program, for which ongoing monitoring and rapid communication by the investigator to the sponsor could be appropriate, and which is deemed to be not reportable to the appropriate regulatory authority. |

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| | |
|--|--|
| 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 |

565

| | |
|---|---|
| Term (Variable) | <Situational Scope> |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | CNEW For review purpose, see definition of the controlled terminology below A description of the specific circumstances and context in which safety events are collected and monitored. |
| User Guidance | N/A |
| Conformance | Optional if table used |
| Cardinality | One to one |

| | |
|--|---|
| Relationship content from ToC representing the protocol hierarchy | 9.2 |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: Event Type, Situational scope Concept: CNEW |
| Repeating and/or Reuse Rules | Yes, repeatable for each event type |

566

| | |
|--|--|
| 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 |

567

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

568

| | |
|------------------------|-----------------------|
| 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 |

569

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

570

| | |
|--|--|
| 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 |
|-------------------------------------|----|

571

| | |
|--|---|
| Term (Variable) | <Timing for Reporting to Sponsor or Designee> |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | CNEW For review purpose, see definition of the controlled terminology below A description of the timing window between trial related events and their reporting to the sponsor or designee. |
| User Guidance | N/A |
| Conformance | Optional if table used |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 9.2 |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: Event Type, situational scope Concept: CNEW |
| Repeating and/or Reuse Rules | Yes, repeatable for each event type and situational scope |

572

| | |
|--|--|
| 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 |

573

| | |
|---|--|
| Term (Variable) | <Method for Reporting> |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | CNEW For review purpose, see definition of the controlled terminology below A description of the technique by which trial related events, such as adverse events, serious adverse events, product complaints, medical device product complaints, and pregnancy and postpartum events, are reported to the sponsor and/or regulatory authority. |

| | |
|--|---|
| User Guidance | N/A |
| Conformance | Optional if used |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 9.2 |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: Event Type, situational scope Concept: CNEW |
| Repeating and/or Reuse Rules | Yes, repeatable for each event type and situational scope |

574

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

575

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

| | |
|-------------------------------------|---|
| Repeating and/or Reuse Rules | Yes, repeatable for each event type and situational scope |
|-------------------------------------|---|

576

577 **9.2.1 Timing**

| | |
|--|--|
| Term (Variable) | 9.2.1 Timing |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | H |
| Definition | Heading |
| User Guidance | N/A |
| Conformance | Required |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 9.2.1 |
| Value | Timing |
| Business rules | Value Allowed: No Relationship: 9.2 Timing and Procedures for Collection and Reporting, 9 ADVERSE EVENTS, SERIOUS ADVERSE EVENTS, PRODUCT COMPLAINTS, PREGNANCY AND POSTPARTUM INFORMATION, AND SPECIAL SAFETY SITUATIONS; Table of Contents Concept: Heading |
| Repeating and/or Reuse Rules | No |

578

| | |
|--|--|
| Term (Variable) | <Event Collection and Reporting Timing> |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | CNEW For review purpose, see definition of the controlled terminology below A description of the timing as it relates to the collection and reporting of trial related events, and the frequency of collection of those events to the sponsor or designee. |
| User Guidance | Specify timing for collection and reporting, including: <ul style="list-style-type: none"> • start and end dates for collection and reporting • frequency of collection and reporting • cross reference to the Schedule of Assessments as appropriate |
| Conformance | Required |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 9.2.1 |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: 9.2.1 Timing Concept: CNEW |
| Repeating and/or Reuse Rules | No |

579

580 9.2.2 Collection Procedures

| | |
|--|---|
| Term (Variable) | 9.2.2 Collection Procedures |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | H |
| Definition | Heading |
| User Guidance | Specify procedures for collection and recording of AEs, SAEs, product complaints (including medical device product complaints if applicable) and pregnancy and postpartum information in the sections below. |
| Conformance | Required |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 9.2.2 |
| Value | Collection Procedures |
| Business rules | Value Allowed: No Relationship: 9.2 Timing and Procedures for Collection and Reporting; 9 ADVERSE EVENTS, SERIOUS ADVERSE EVENTS, PRODUCT COMPLAINTS, PREGNANCY AND POSTPARTUM INFORMATION, AND SPECIAL SAFETY SITUATIONS; Table of Contents. Concept: Heading |
| Repeating and/or Reuse Rules | No |

581

| | |
|--|--|
| 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 |

582

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

| | |
|--|--|
| | A description of how trial-related events, such as adverse events, serious adverse events, product complaints, medical device product complaints, and pregnancy and postpartum events, will be identified. |
| User Guidance | Specify how information will be identified (e.g., spontaneous reporting, solicited questions). |
| Conformance | Required |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 9.2.2 |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: Identification and 9.2.2 Collection Procedures Concept: CNEW |
| Repeating and/or Reuse Rules | No |

583
584
585

| | |
|--|---|
| 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 |

586

| | |
|--|--|
| Term (Variable) | <Severity> |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C25676 For review purpose, see definition of the controlled terminology below The description of the intensity (severity) of an event. |
| User Guidance | Specify the intensity rating categories/scale. |
| Conformance | Required |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 9.2.2 |

| | |
|-------------------------------------|---|
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: Severity; 9.2.2 Collection Procedures Concept: C25676 |
| Repeating and/or Reuse Rules | No |

587

| | |
|--|--|
| 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 |

588

| | |
|--|---|
| Term (Variable) | <Causality> |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C82552 For review purpose, see definition of the controlled terminology below The description of the degree of causality (attributability) between a trial intervention and an event. |
| User Guidance | Specify: <ul style="list-style-type: none"> • The causality categories/scale • Procedures for assessing causality |
| Conformance | Required |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 9.2.2 |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: Causality; 9.2.2 Collection Procedures Concept: C82552 |
| Repeating and/or Reuse Rules | No |

589

| | |
|------------------------|-----------|
| 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 |

590

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

591

| | |
|--|--------------------------|
| 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 |

592

| | |
|--|--|
| Term (Variable) | <Follow-up> |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | CNEW For review purpose, see definition of the controlled terminology below A description of the procedures for follow-up, including the assessment tools that will be used to monitor an event and the duration of follow-up. |
| User Guidance | Specify the procedures for follow-up. Include the assessment tools that will be used to monitor the events and the duration of follow-up after appearance of the events. |
| Conformance | Required |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 9.2.2 |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: Follow-up and 9.2.2 Collection Procedures Concept: CNEW |
| Repeating and/or Reuse Rules | No |

593

594

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 |

595

| | |
|--|--|
| Term (Variable) | <Reporting> |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | CNEW For review purpose, see definition of the controlled terminology below A description of the method and timelines for reporting adverse events, serious adverse events, pregnancy and postpartum events, and medical device product complaints to the sponsor. |
| User Guidance | Specify the reporting method (e.g., an electronic data collection tool or a paper CRF.) backup reporting method if applicable and reporting timeline to the Sponsor. |
| Conformance | Required |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 9.2.3 |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: 9.2.3 Reporting Concept: CNEW |
| Repeating and/or Reuse Rules | No |

596

597

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 |

598

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

| | |
|--|---|
| | A description of the requirements for the sponsor/designee to report adverse events, serious adverse events, pregnancy and postpartum events, and medical device product complaints, including the criteria for reporting, to the relevant regulatory authority. |
| User Guidance | Specify: <ul style="list-style-type: none"> the investigators’ responsibilities for reporting to the Sponsor (and to Ethics Committees, where required), specifying timing of reporting to allow the Sponsor to meet their responsibilities the Sponsor’s legal/regulatory responsibilities to report SAEs to regulatory authorities, ethics committees, and investigators serious and unexpected adverse reaction reporting |
| Conformance | Required |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 9.2.3.1 |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: 9.2.3.1 Regulatory Reporting Requirements Concept: CNEW |
| Repeating and/or Reuse Rules | No |

599

600

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 |

601

| | |
|---|--|
| Term (Variable) | <Adverse Events of Special Interest or state “Not applicable”> |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | CNEW |

| | |
|--|--|
| | For review purpose, see definition of the controlled terminology below A description of the processes and procedures used to define, measure, confirm, and report the occurrence of adverse events that are of special interest to the specific trial, or state not applicable. |
| User Guidance | Specify any AESI: <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 occurrence |
| Conformance | Required |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 9.2.4 |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: 9.2.4 Adverse Events of Special Interest Concept: CNEW |
| Repeating and/or Reuse Rules | No |

602

603 **9.2.5 Disease-related Events or Outcomes Not Qualifying as AEs or SAEs**

604

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

605

| | |
|--|---|
| Term (Variable) | <Disease-related Events or Outcomes Not Qualifying as AEs or SAEs> |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | CNEW For review purpose, see definition of the controlled terminology below A description of events or outcomes related to the trial disease indication but not qualifying as adverse events or serious adverse events within the trial, or state not applicable. |
| User Guidance | Specify any DREs, DROs, or both that will not be reported as AEs or SAEs (e.g., seizures in anticonvulsant trials) or state “Not applicable.” |
| Conformance | Required |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 9.2.5 |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: 9.2.5 Disease-related Events or Outcomes Not Qualifying as AEs or SAEs Concept: CNEW |
| Repeating and/or Reuse Rules | No |

606

607

9.3 Pregnancy and Postpartum Information

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

608

609 **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 |

610

| | |
|---|--|
| Term (Variable) | {<Participants Who Become Pregnant During the Trial>} |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | CNEW For review purpose, see definition of the controlled terminology below A description of the processes and procedures used to collect pregnancy data for a trial participant who becomes pregnant while the participant is in the trial, as well as data collection about the child. |
| User Guidance | Specify: <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) For postpartum follow-up, include the time period (e.g., initial child development) with the justification. If exposure to trial intervention during breastfeeding is applicable, specify: <ul style="list-style-type: none"> the assessments to be performed |

| | |
|--|--|
| | <ul style="list-style-type: none"> • type and duration of monitoring • what information will be collected for both the participant and child |
| Conformance | Conditional: when collecting pregnancy data for a trial participant who becomes pregnant during the trial. |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 9.3.1 |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: 9.3.1 Participants Who Become Pregnant During the Trial Concept: CNEW |
| Repeating and/or Reuse Rules | No |

611

612 **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 |
| 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 |

613

| | |
|---|---|
| Term (Variable) | {<Participants Whose Partners Become Pregnant During the Trial>} |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | CNEW For review purpose, see definition of the controlled terminology below A description of the processes and procedures used to collect pregnancy data for a trial participant's partner, who becomes pregnant while the participant is in the trial. |
| User Guidance | Specify: |

| | |
|--|--|
| | <ul style="list-style-type: none"> if the investigator will attempt to collect pregnancy information about a participant's partner, who becomes pregnant during the specified period in the trial whether the participant whose partner becomes pregnant should be discontinued from trial intervention (refer to Section 7 Participant Discontinuation of Trial Intervention and Discontinuation or Withdrawal from Trial as applicable) the assessments to be performed, type and duration of monitoring, and the information to be collected |
| Conformance | Conditional: when collecting pregnancy data for the partner of a trial participant who becomes pregnant during the trial. |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 9.3.2 |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: 9.3.2 Participants Whose Partners Become Pregnant During the Trial Concept: CNEW |
| Repeating and/or Reuse Rules | No |

614

615

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 |

616

| | |
|---|-----------------------------|
| Term (Variable) | <Special Safety Situations> |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |

| | |
|--|---|
| Definition | CNEW For review purpose, see definition of the controlled terminology below A characterization or classification of those trial specific situations that are associated with the trial intervention(s) and require regulatory reporting, but that do not qualify as an adverse event or serious adverse event for the given trial. |
| User Guidance | Specify special safety situations associated with the trial intervention(s) that do not qualify as an AE or SAE, but require regulatory reporting. Examples include: <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 • product complaint, including falsified or counterfeit products • suspected drug-food or drug-drug interaction |
| Conformance | Required |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 9.4 |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: 9.4 Special Safety Situations Concept: CNEW |
| Repeating and/or Reuse Rules | No |

617

618

10 STATISTICAL CONSIDERATIONS

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

| | |
|-------------------------------------|---|
| Value | STATISTICAL CONSIDERATIONS |
| Business rules | Value Allowed: No Relationship: Table of Contents Concept: Heading |
| Repeating and/or Reuse Rules | No |

619

620 **10.1 General Considerations**

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

621

| | |
|--|--|
| Term (Variable) | <General Considerations> |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C164387 For review purpose, see definition of the controlled terminology below Careful thought or deliberation related to the planned conduct of statistical analyses within the context of the trial. |
| User Guidance | Provide 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 |
| Repeating and/or Reuse Rules | No |

622

623 **10.2 Analysis Sets**

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

624

| | |
|--|--|
| Term (Variable) | <Analysis Sets> |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | CNEW For review purpose, see definition of the controlled terminology below A description of the set of participants whose data are to be included in the analyses. |
| User Guidance | Describe analysis sets to be considered at the trial level, i.e., the set of participants whose data are to be included in the analyses, 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: CNEW |
| Repeating and/or Reuse Rules | No |

625

626 **10.3 Analyses of Demographics and Other Baseline Variables**

| | |
|---|--|
| Term (Variable) | 10.3 Analyses of Demographics and Other Baseline Variables |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | H |
| Definition | Heading |

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

627

| | |
|--|---|
| Term (Variable) | <Analyses of Demographics and Other Baseline Variables> |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | CNEW For review purpose, see definition of the controlled terminology below A description of analyses relevant to variables at baseline, for example demographics, related to the trial. |
| User Guidance | Describe the summary statistics that will be used to characterize the distribution of demographic and other relevant variables at baseline. Specify when the variables are 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: CNEW |
| Repeating and/or Reuse Rules | No |

628

629

10.4 Analyses Associated with Primary Objective(s)

| | |
|---|---|
| Term (Variable) | 10.4 Analyses Associated with Primary Objective(s) |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | H |
| Definition | Heading |
| User Guidance | 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 Primary Objective(s) |
| Business rules | Value Allowed: No Relationship: 10 STATISTICAL CONSIDERATIONS; Table of Contents Concept: Heading |
| Repeating and/or Reuse Rules | No |

630 **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 | Collection for only one primary objective 10.4.1, 10.4.2, 10.4.3, 10.4.4, 10.4.5 For more than one primary objective repeat the collection as level 4 headings where X is = to the number of Primary objectives |
| Cardinality | One to many |
| Relationship content from ToC representing the protocol hierarchy | 10.4.X |
| Value | Primary Objective <#>: # 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.X Primary Objective <#>; 10.4 Analyses Associated with Primary Objective(s); 10 STATISTICAL CONSIDERATIONS; Table of Contents Concept: Heading |
| Repeating and/or Reuse Rules | Yes, repeatable for each objective. |

631

632 **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 |

633

| | |
|-------------------------------------|--|
| Value | Statistical Analysis Method |
| Business rules | Value Allowed: No Relationship: 10.4.X Primary Objective <#>; 10.4 Analyses Associated with 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 Method of Analysis> |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | CNEW For review purpose, see definition of the controlled terminology below A description of the statistical model, hypothesis, and methods of analyses for each objective within the trial. |
| User Guidance | Describe the statistical analysis methods that will be used to evaluate the primary objective(s) and associated estimand(s) in Section 3.1 Primary Objective(s) and Associated Estimands. 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 and the factors that will be included (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: CNEW |
| Repeating and/or Reuse Rules | Yes, repeatable for each objective as a series of level 4 sections (10.4.X.1, 10.4.X.2, 10.4.X.3, 10.4.X.4, 10.4.X.5). |

634

635

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 |

636

| | |
|-------------------------------------|--|
| Value | Handling of Data in relation to Primary Estimand(s) |
| Business rules | Value Allowed: No X may be a number for the collection Relationship: 10.4.X Primary Objective(s) <#>; 10.4 Analyses Associated with Primary Objective(s); 10 STATISTICAL CONSIDERATIONS; Table of Contents Concept: Heading |
| Repeating and/or Reuse Rules | Yes, repeatable for each objective as a series of level 4 sections (10.4.X.1, 10.4.X.2, 10.4.X.3, 10.4.X.4, 10.4.X.5). |

| | |
|--|---|
| Term (Variable) | <Handling of Data in Relation to Primary Estimand(s)> |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | CNEW For review purpose, see definition of the controlled terminology below A description of how data will be handled for the statistical analysis in line with the primary estimand. |
| User Guidance | For each intercurrent event of the primary estimand(s) (Section 3.1 Primary Objective(s) and Associated Estimands), 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 Handling of Data in relation to Primary Estimand(s) |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: 10.4.X.2 Handling of Data in relation to Primary Estimand(s) Concept: CNEW |
| Repeating and/or Reuse Rules | Yes, repeatable for each objective as a series of level 4 sections (10.4.X.1, 10.4.X.2, 10.4.X.3, 10.4.X.4, 10.4.X.5). |

637

638

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

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

639

| | |
|--|---|
| | Concept: Heading |
| Repeating and/or Reuse Rules | No |
| Term (Variable) | <Handling of Missing Data in Relation to Primary Estimand> |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | CNEW For review purpose, see definition of the controlled terminology below A description of how missing data associated with the primary estimand will be handled, including the rationale for the approach. |
| User Guidance | Describe how missing data will be addressed (e.g., imputation method and model), state the underlying assumptions, and provide a rationale for the approach. |
| Conformance | Required |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 10.4.X.3 |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: 10.4.X.3 Handling of Missing Data Concept: CNEW |
| Repeating and/or Reuse Rules | Yes, repeatable for each objective as a series of level 4 sections (10.4.X.1, 10.4.X.2, 10.4.X.3, 10.4.X.4, 10.4.X.5). |

640

641 **10.4.1.4 Sensitivity Analysis**

| | |
|--|---|
| Term (Variable) | 10.4.X.4 Sensitivity Analysis |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | H |
| Definition | Heading |
| User Guidance | N/A |
| Conformance | Conditional: when there is Sensitivity Analysis for a primary objective |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 10.4.X.4 |
| Value | Sensitivity Analysis |
| Business rules | Value Allowed: No Relationship: 10.4.X Primary Objective(s); 10.4 Analyses Associated with Primary Objective(s); 10 STATISTICAL CONSIDERATIONS; 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). |

642

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

| | |
|--|---|
| | For review purpose, see definition of the controlled terminology below A description of the series of analyses conducted to explore the robustness of inferences from the main estimator to deviations from its underlying modeling assumptions and limitations in the data. |
| 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: CNEW |
| Repeating and/or Reuse Rules | Yes, repeatable for each objective as a series of level 4 sections (10.4.X.1, 10.4.X.2, 10.4.X.3, 10.4.X.4, 10.4.X.5). |

643

644

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). |

645

| | |
|---|--|
| Term (Variable) | {<Supplementary Analysis>} |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | CNEW For review purpose, see definition of the controlled terminology below A description of the analyses that are conducted in addition to the main and sensitivity analysis with the intent to provide additional insights into the understanding of the treatment effect. |

| | |
|--|--|
| User Guidance | Describe any supplementary analysis, if applicable. Supplementary analyses are conducted in addition to the main and sensitivity analysis with the intent to provide additional insights into the understanding of the treatment effect. |
| Conformance | Conditional: when there is Supplementary Analysis for a primary objective |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 10.4.X.5 |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: 10.4.X.5 Supplementary Analysis Concept: CNEW |
| Repeating and/or Reuse Rules | Yes, repeatable for each objective as a series of level 4 sections (10.4.X.1, 10.4.X.2, 10.4.X.3, 10.4.X.4, 10.4.X.5). |

646

647

10.5 Analysis Associated with the Secondary Objective(s)

| | |
|--|---|
| Term (Variable) | 10.5 Analyses Associated with the Secondary Objective(s) |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | H |
| Definition | Heading |
| User Guidance | Describe the statistical analysis methods in alignment with the secondary objectives and associated estimands in Section 3.2 Secondary Objective(s) and Associated Estimands. Use the same section structure as Section 10.4 Analyses Associated with the Primary Objective(s). 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 Secondary Objective(s) |
| Business rules | Value Allowed: No Relationship: 10 STATISTICAL CONSIDERATIONS; Table of Contents Concept: Heading |
| Repeating and/or Reuse Rules | No |

648

649

10.5.1 {Secondary Objective <#>}

| | |
|---|--------------------------------|
| Term (Variable) | 10.5.X Secondary Objective <#> |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | H |
| Definition | Data |
| User Guidance | N/A |

| | |
|--|--|
| Conformance | Conditional: secondary objective 10.5.1, 10.5.2, 10.5.3, 10.5.4, 10.5.5 For more than one secondary objective repeat the collection as level 4 headings where X is = to the number of secondary objectives |
| Cardinality | One to many |
| Relationship content from ToC representing the protocol hierarchy | 10.5.X |
| Value | Secondary Objective <#>. # 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: 10.5 Analyses Associated with Secondary Objective(s); 10 STATISTICAL CONSIDERATIONS; Table of Contents Concept: Heading |
| Repeating and/or Reuse Rules | Yes, repeatable for each objective. |

650

651 **10.5.1.1 Statistical Analysis Method**

| | |
|--|--|
| Term (Variable) | {10.5.X.1 Statistical Analysis Method} |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | H |
| Definition | Heading |
| User Guidance | N/A |
| Conformance | Conditional: when there is Secondary Objective |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 10.5.X.1 |
| Value | Statistical Analysis Method |
| Business rules | Value Allowed: No Relationship: 10.5.X Secondary Objective <#>; 10.5 Analyses Associated with Secondary Objective(s); 10 STATISTICAL CONSIDERATIONS; 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). |

652

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

| | |
|--|--|
| User Guidance | Describe the statistical analysis methods in alignment with the secondary objectives and associated estimands in Section 3.2 Secondary Objective(s) and Associated Estimands. Use the same section structure as Section 10.4 Analyses Associated with the Primary Objective(s). 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 estimand |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 10.5.X.1 |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: 10.5.X.1 Statistical Analysis Method Concept: CNEW |
| Repeating and/or Reuse Rules | Yes, repeatable for each objective as a series of level 4 sections (10.5.X.1, 10.5.X.2, 10.5.X.3, 10.5.X.4, 10.5.X.5). |

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654

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

| | |
|--|--|
| Term (Variable) | {10.5.X.2 Handling of Data in Relation to Secondary Estimand(s)} |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | H |
| Definition | Heading |
| User Guidance | N/A |
| Conformance | Conditional: when there is Secondary estimand |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 10.5.X.2 |
| Value | Statistical Method of Analysis |
| Business rules | Value Allowed: No Relationship: 10.5.X Secondary Objective <#>; 10.5 Analyses Associated with Secondary Objective(s); 10 STATISTICAL CONSIDERATIONS; 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). |

655

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

| | |
|--|---|
| | For review purpose, see definition of the controlled terminology below A description of how data will be handled for the statistical analysis in line with the secondary estimand. |
| 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 | Text |
| Business rules | Value Allowed: Yes Relationship: 10.5.X.2 Handling of Data in relation to Secondary Estimand(s) Concept: CNEW |
| Repeating and/or Reuse Rules | Yes, repeatable for each objective as a series of level 4 sections (10.5.X.1, 10.5.X.2, 10.5.X.3, 10.5.X.4, 10.5.X.5). |

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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). |

658

| | |
|--|---|
| Term (Variable) | {<Handling of Missing Data in Relation to Secondary Estimand(s)>} |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | CNEW For review purpose, see definition of the controlled terminology below A description of how missing data associated with the secondary estimand will be handled, including the rationale for the approach. |
| 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 | Text |
| Business rules | Value Allowed: Yes Relationship: 10.5.X.3 Handling of Missing Data in Relation to Secondary Estimand(s) Concept: CNEW |
| Repeating and/or Reuse Rules | Yes, repeatable for each objective as a series of level 4 sections (10.5.X.1, 10.5.X.2, 10.5.X.3, 10.5.X.4, 10.5.X.5). |

659

660 **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). |

661

| | |
|--|---|
| Term (Variable) | {<Sensitivity Analysis>} |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | CNEW For review purpose, see definition of the controlled terminology below A description of the series of analyses conducted to explore the robustness of inferences from the main estimator to deviations from its underlying modeling assumptions and limitations in the data. |
| User Guidance | N/A |
| 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: CNEW |
| Repeating and/or Reuse Rules | Yes, repeatable for each objective as a series of level 4 sections (10.5.X.1, 10.5.X.2, 10.5.X.3, 10.5.X.4, 10.5.X.5). |

662

663 **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. |

664

| | |
|--|--|
| Term (Variable) | {<Supplementary Analysis>} |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | CNEW For review purpose, see definition of the controlled terminology below A description of the analyses that are conducted in addition to the main and sensitivity analysis with the intent to provide additional insights into the understanding of the treatment effect. |
| User Guidance | N/A |
| 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: CNEW |
| Repeating and/or Reuse Rules | Yes, repeatable for each objective as a series of level 4 sections (10.5.X.1, 10.5.X.2, 10.5.X.3, 10.5.X.4, 10.5.X.5). |

665

666 **10.6 Analyses Associated with Exploratory Objective(s)**

| | |
|---|--|
| Term (Variable) | 10.6 Analyses Associated with Exploratory Objective(s) |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | H |
| Definition | Heading |

| | |
|--|--|
| User Guidance | N/A |
| Conformance | Required |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 10.6 |
| Value | Analyses of Exploratory Endpoint(s) |
| Business rules | Value Allowed: No Relationship: 10 STATISTICAL CONSIDERATIONS; Table of Contents Concept: Heading |
| Repeating and/or Reuse Rules | No |

667

| | |
|--|--|
| Term (Variable) | <Analysis Associated with Exploratory Objectives(s)> |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | CNEW For review purpose, see definition of the controlled terminology below A description of the statistical model, hypothesis, and methods of analyses for each exploratory objective within the trial. |
| User Guidance | Describe any exploratory analyses, if applicable. Additional subsections 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: CNEW |
| Repeating and/or Reuse Rules | No |

668

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10.7 Safety Analyses

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

670

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

671

672

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 |

673

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

| | |
|--|---|
| Data (D), Value (V) or Heading (H) | D |
| Definition | CNEW For review purpose, see definition of the controlled terminology below A description of the analyses that are different than the one(s) previously specified or mentioned. |
| User Guidance | Describe other analyses not included in Sections 10.3-10.7, 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: CNEW |
| Repeating and/or Reuse Rules | No |

674

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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 |

676

| | |
|---|---|
| Term (Variable) | <Interim Analyses> |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C142582 For review purpose, see definition of the controlled terminology below A description of any analysis intended to compare treatment arms with respect to efficacy or safety at any time prior to the formal completion of a trial. |
| User Guidance | Describe any interim analyses and criteria for stopping or adapting the trial. Ensure alignment with Section 4.3 Trial Stopping Rules. |

| | |
|--|--|
| | <p>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 for other trial adaptations such as sample size re-estimation, alteration to the proportion of participants allocated to each trial group, or changes to eligibility criteria the applied statistical method; 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 implementation 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), for example, investigator, principal investigator, DMC, or Sponsor. |
| Conformance | Required |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 10.9 |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: 10.9 Interim Analyses Concept: C142582 |
| Repeating and/or Reuse Rules | Yes, repeatable for each interim |

677

678

10.10 Multiplicity Adjustments

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

679

| | |
|--|--|
| Repeating and/or Reuse Rules | No |
| Term (Variable) | <Multiplicity Adjustments> |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | CNEW For review purpose, see definition of the controlled terminology below A description of the statistical adjustments needed to limit the probability of false positive findings in trials where there are multiple simultaneous hypotheses. |
| User Guidance | Multiple testing procedures may be needed to limit the probability of false positive findings in a trial. Reasons for carrying out multiple statistical tests include - but are not restricted to - multiple endpoints, multiple treatment groups, multiple hypotheses, subgroups, multiple timepoints. Describe any approaches to multiplicity control for the trial. This description might go beyond the analysis of primary objectives. Specify the statistical approach to control the overall type I error rate as well as the (adjusted) significance levels to test specific hypotheses, as applicable. Clarify whether the tests/confidence intervals are one- or two-sided. State the circumstances under which a 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. For some statistical approaches it might be helpful to include a graphical depiction, as visualisation will be helpful for understanding, coupled with the clinical translation of the mathematical choices. Details regarding interim analyses should be provided in Section 10.9 Interim Analyses. |
| Conformance | Required |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 10.10 |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: 10.10 Multiplicity Adjustments Concept: CNEW |
| Repeating and/or Reuse Rules | No |

680

681

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 For review purpose, see definition of the controlled terminology below A statistical calculation to determine the number of participants required for the primary analysis, which should be large enough to provide a reliable answer to the questions addressed and should be determined by the primary objective of the trial. If the sample size is determined on some other basis, then this should be made clear and justified. |
| User Guidance | This section should detail the methods used for the determination of the sample size. The sample size calculation should be aligned with the primary estimand and the primary analysis, otherwise a justification is needed. Details of sample size calculation should include all relevant information to enable reproduction of the sample size, e.g.,: <ul style="list-style-type: none"> • referencing any prior studies on which assumptions were based • significance level (including information on the choice of one- or two-sided level) • power • assumed treatment effect and variability • how dropout rate and intercurrent events have been incorporated into sample size calculation • precision of estimator/length of confidence interval Any assumptions made should be stated and justified. Further analysis of how deviations from the assumptions will affect the sample size should be included. If complex simulations were used to calculate the sample size, consider including details in a separate simulation report as an appendix to the protocol. If the planned sample size is not derived statistically, then this should be explicitly stated along with a rationale for the intended sample size (e.g., exploratory nature of pilot trials; pragmatic considerations for trials in rare diseases). |
| Conformance | Required |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 10.11 |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: 10.11 Sample Size Determination, Concept: C115467 |
| Repeating and/or Reuse Rules | No |

683

684 **11 TRIAL OVERSIGHT AND OTHER GENERAL CONSIDERATIONS**

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

685

686 **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 |

687

| | |
|---|---|
| Term (Variable) | <Regulatory and Ethical Considerations> |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | CNEW For review purpose, see definition of the controlled terminology below Careful thought or deliberation related to the regulatory and ethical aspects of the trial. |
| User Guidance | Provide a high-level statement on the prevailing ethical, legal, and regulatory guidelines that will be applied throughout the trial. |

| | |
|--|---|
| | <p>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 |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 11.1 |
| Value | Text |
| Business rules | <p>Value Allowed: Yes Relationship: 11.1 Regulatory and Ethical Considerations Concept: CNEW</p> |
| Repeating and/or Reuse Rules | No |

688

689

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 | <p>Value Allowed: No Relationship: 11 TRIAL OVERSIGHT AND OTHER GENERAL CONSIDERATIONS; Table of Contents Concept: Heading</p> |
| Repeating and/or Reuse Rules | No |

690

| | |
|---|---|
| Term (Variable) | {<Trial Oversight>} |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | <p>CNEW For review purpose, see definition of the controlled terminology below A description of the planned processes and procedures to govern and conduct a clinical trial in order to protect the rights, safety and welfare of the trial participants.</p> |

| | |
|--|--|
| User Guidance | Concisely summarize the trial oversight listing the investigator and sponsor responsibilities not covered in other sections of the protocol which are essential for the operations of the trial, specifying the ones related to quality assurance. if not using below optional subheadings |
| Conformance | Conditional: if not using the optional subheadings Level 3 (11.2.1, 11.2.2) |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 11.2 |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: 11.2 Trial Oversight Concept: CNEW |
| Repeating and/or Reuse Rules | No |

691

692 **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 |

693

| | |
|--|--|
| Term (Variable) | <Investigator Responsibilities> |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | CNEW For review purpose, see definition of the controlled terminology below A description of the obligations of the investigator with respect to the trial. |
| User Guidance | Describe the investigator duties, including the oversight of duties delegated to a third party that may impact the trial conduct at sites, if applicable and if not addressed elsewhere. |
| Conformance | Optional |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 11.2.1 |
| Value | Text |

| | |
|-------------------------------------|--|
| Business rules | Value Allowed: Yes Relationship: 11.2.1 Investigator Responsibilities Concept: CNEW |
| Repeating and/or Reuse Rules | No |

694

695 **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 |

696

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

697

698 **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 |

699

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

700

| | |
|---|---|
| Term (Variable) | <Description of Assent Process> |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | CNEW For review purpose, see definition of the controlled terminology below A description of the assent process for those individuals unable to give informed consent on their own behalf, to participate in the trial. |
| User Guidance | N/A |

| | |
|--|---|
| Conformance | Optional |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 11.3 |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: 11.3 Informed Consent Process Concept: CNEW |
| Repeating and/or Reuse Rules | No |

701

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

702

703

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 |

704

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

705

706

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 |

707

| | |
|------------------------|---|
| Term (Variable) | {<Informed consent for Use of Remaining Samples in Exploratory Research>} |
|------------------------|---|

| | |
|--|---|
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | CNEW For review purpose, see definition of the controlled terminology below A description of the consent requirements for exploratory research using the remainder of mandatory samples. If applicable, this may include text in the original consent that address the use of remaining samples or additional text. |
| User Guidance | If participants will be asked to consent to optional exploratory research using the remainder of mandatory samples, describe the use of remaining samples for optional exploratory research. If any exploratory research is planned and additional written consent regarding the use of remaining samples for exploratory research will be obtained, describe the consent process. |
| Conformance | Conditional |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 11.3.2 |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: 11.3.2 Informed Consent for Use of Remaining Samples in Exploratory Research Concept: CNEW |
| Repeating and/or Reuse Rules | No |

708

709

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 |

710

| | |
|------------------------|--------------|
| Term (Variable) | <Committees> |
| Data Type | Text |

| | |
|--|--|
| Data (D), Value (V) or Heading (H) | D |
| Definition | CNEW For review purpose, see definition of the controlled terminology below A description of the type and administrative structure of any committee associated with the trial. |
| User Guidance | Briefly describe the administrative structure of committees that will be reviewing data while the trial is ongoing, and the type of committee (e.g., Dose Escalation Committee, Data Monitoring Committee or Data Safety Monitoring Board). Note that specific details may be required depending on local law or regulation. If applicable, Committee Charters may be cross referenced. If no committees are 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: CNEW |
| Repeating and/or Reuse Rules | No |

711

712

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 |

713

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

| | |
|--|--|
| | A concise summary of the arrangements for participants insurance and indemnity as required by the applicable regulatory body. |
| User Guidance | Concisely summarize the arrangements for participants insurance and indemnity if not addressed in a separate agreement, if required by the applicable regulatory requirements. |
| Conformance | Required |
| Cardinality | One to One |
| Relationship content from ToC representing the protocol hierarchy | 11.5 |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: 11.5 Insurance and Indemnity Concept: CNEW |
| Repeating and/or Reuse Rules | No |

714

715

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 |

716

| | |
|---|--|
| Term (Variable) | <Risk-Based Quality Management> |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | CNEW For review purpose, see definition of the controlled terminology below A description of how potential risks and critical to quality factors associated with the trial will be identified and handled. |
| User Guidance | Describe the identified critical to quality factors, associated risks and risk mitigation strategies in the trial or refer to a separate document where this is described. |
| Conformance | Required |
| Cardinality | One to one |

| | |
|--|--|
| Relationship content from ToC representing the protocol hierarchy | 11.6 |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: 11.6 Risk-Based Quality Management Concept: CNEW |
| Repeating and/or Reuse Rules | No |

717

718 **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 |

719

| | |
|--|---|
| Term (Variable) | <Data Governance> |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | CNEW For review purpose, see definition of the controlled terminology below A description of the key processes to ensure data integrity, traceability and security, in order to enable accurate collection, reporting, monitoring, transfer, retention, access and publication. |
| User Guidance | Describe the key processes for critical trial integrity, traceability and security including a summary of the monitoring approaches enabling accurate collection, reporting, monitoring, transfer, retention, and access if not addressed in separate agreement(s). |
| Conformance | Required |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 11.7 |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: 11.7 Data Governance Concept: CNEW |

| | |
|-------------------------------------|----|
| Repeating and/or Reuse Rules | No |
|-------------------------------------|----|

720

721

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 |

722

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

723

724 **11.9 Source Data**

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

725

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

726

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

727

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

728

| | |
|---|---|
| Term (Variable) | <Identification of Source Data> |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C125442 For review purpose, see definition of the controlled terminology below A description of how trial-related source data will be identified. |
| User Guidance | N/A |
| Conformance | Required |
| Cardinality | One to one |

| | |
|--|---|
| Relationship content from ToC representing the protocol hierarchy | 11.9 |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: 11.9 Source Data Concept: C125442 |
| Repeating and/or Reuse Rules | No |

729

730

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 |

731

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

732

733 **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 |

734

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

735

| | |
|---|---|
| Term (Variable) | <Criteria for Early Closure> |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | CNEW For review purpose, see definition of the controlled terminology below The requirements that must be met in order to close a trial site prematurely. |
| User Guidance | List the criteria for early closure of a site by the sponsor or investigator. |
| Conformance | Required |
| Cardinality | One to one |

| | |
|--|--|
| Relationship content from ToC representing the protocol hierarchy | 11.11 |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: 11.11 Early Site Closure Concept: CNEW |
| Repeating and/or Reuse Rules | No |

736

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

737

738

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 |

739

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

740

741

12 APPENDIX: SUPPORTING DETAILS

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

742

743

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 |

744

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

745

746

12.2 Country/Region-Specific Differences

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

| | |
|-------------------------------------|-------------------------|
| | Concept: Heading |
| Repeating and/or Reuse Rules | No |

747

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

748

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

| | |
|-------------------------------------|---|
| Repeating and/or Reuse Rules | Yes, repeatable for each Country/Region |
|-------------------------------------|---|

749

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

750

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

| | |
|--|--|
| Relationship content from ToC representing the protocol hierarchy | 12.2 |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: Country /Region Identifier; 12.2 Country/Region-Specific Differences Concept: CNEW |
| Repeating and/or Reuse Rules | Yes, repeatable for each country/region |

751

752 **12.3 Prior Protocol Amendment(s)**

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

753

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

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

754

| NCI C-Code | M11 Preferred Term | Draft Definition |
|------------|---|---|
| CNEW | Not applicable. This protocol has not been amended. | Not applicable. This protocol has not been amended. |
| CNEW | Not applicable. This is the first protocol amendment. | Not applicable. This is the first protocol amendment. |
| CNEW | This protocol has been amended previously. Details of prior amendments are presented in Section 12.3 Prior Protocol Amendments. | This protocol has been amended previously. Details of prior amendments are presented in Section 12.3 Prior Protocol Amendments. |
| CNEW | This protocol has been amended previously. The Protocol Amendment Summary of Changes for the current amendment is located directly before the Table of Contents. Prior amendment(s) to this protocol are listed in the table below, beginning with the most recent. | This protocol has been amended previously. The Protocol Amendment Summary of Changes for the current amendment is located directly before the Table of Contents. Prior amendment(s) to this protocol are listed in the table below, beginning with the most recent. |

755

| | |
|---|---|
| Term (Variable) | Document |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | H |
| Definition | Table Column Heading |
| User Guidance | Previous amendments should appear in reverse chronological order with the most recent at the top (e.g., Amendment 3, 2, 1). Delete lines not needed, add lines as needed. Inclusion of regional-, country-, and site-specific amendments in the |

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

756

| | |
|---|--|
| Term (Variable) | Sponsor Approval Date |
| 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 lines not needed, add lines as needed. Inclusion of regional-, country-, and site-specific amendments in the table is optional. If included, ensure that the scope is clearly distinguishable from global amendments.</p> <p>If including the column with enrollment numbers, follow the instructions below.</p> |

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| | <ul style="list-style-type: none"> For <u>global</u> amendments to international clinical trials or amendments to a <u>single-country</u> trial, list approximate global enrollment total or percentage at the time of the amendment and select “globally”. For <u>global amendments 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, the status of all the relevant locations can be listed. For <u>country/region</u> amendments to international clinical trials, list the approximate local enrollment total or percentage at the time of the amendment and select “locally”. For <u>studies in which enrollment status by cohort is more meaningful, such as for single-site or early-phase studies</u>, listing approximate enrollment by cohort is an option. If multiple cohorts are ongoing at the time of the amendment, the status of all the ongoing cohorts can be listed. Enter the approximate number or percentage of participants enrolled as a percentage of the expected total. |
| Conformance | Required |
| Cardinality | One to many |
| Relationship content from ToC representing the protocol hierarchy | 12.3 |
| Value | Sponsor Approval Date |
| Business rules | Value Allowed: No Relationship: Table Column Heading; 12.3 Prior Protocol Amendment(s) Concept: Table Column Heading |
| Repeating and/or Reuse Rules | No |

757

| | |
|---|---|
| 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 lines not needed, add lines as needed. Inclusion of regional-, country-, and site-specific amendments in the table is optional. If included, ensure that the scope is clearly distinguishable from global amendments.</p> <p>If including the column with enrollment numbers, follow the instructions below.</p> <ul style="list-style-type: none"> For <u>global</u> amendments to international clinical trials or amendments to a <u>single-country</u> trial, list approximate global enrollment total or percentage at the time of the amendment and select “globally”. For <u>global amendments consolidating only country/region-specific requirements</u>, list approximate local enrollment total or percentage at |

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| | <p>the time of the amendment and select “locally”. If consolidating a series of local amendments, the status of all the relevant locations can be listed.</p> <ul style="list-style-type: none"> • For <u>country/region</u> amendments to international clinical trials, list the approximate local enrollment total or percentage at the time of the amendment and select “locally”. • For <u>studies in which enrollment status by cohort is more meaningful, such as for single-site or early-phase studies</u>, listing approximate enrollment by cohort is an option. If multiple cohorts are ongoing at the time of the amendment, the status of all the ongoing cohorts can be listed. • Enter the approximate number or percentage of participants enrolled as a percentage of the expected total. |
| Conformance | Optional if there is an amendment and sponsor chooses to use |
| Cardinality | One to many |
| Relationship content from ToC representing the protocol hierarchy | 12.3 |
| Value | Approximate Enrollment when Sponsor Approved Amendment |
| Business rules | <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 |

758

| | |
|---|--|
| Term (Variable) | <Amendment Identifier> |
| Data Type | Text or Universal Text “Original Protocol” |
| Data (D), Value (V) or Heading (H) | D |
| Definition | <p>CNEW</p> <p>For review purpose, see definition of the controlled terminology below</p> <p>A sequence of characters used to uniquely identify a protocol amendment.</p> |
| 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 lines not needed, add lines as needed. Inclusion of regional-, country-, and site-specific amendments in the table is optional. If included, ensure that the scope is clearly distinguishable from global amendments.</p> <p>If including the column with enrollment numbers, follow the instructions below.</p> <ul style="list-style-type: none"> • For <u>global</u> amendments to international clinical trials or amendments to a <u>single-country</u> trial, list approximate global enrollment total or percentage at the time of the amendment and select “globally”. • For <u>global amendments 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, the status of all the relevant locations can be listed. |

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| | <ul style="list-style-type: none"> For <u>country/region</u> amendments to international clinical trials, list the approximate local enrollment total or percentage at the time of the amendment and select “locally”. For <u>studies in which enrollment status by cohort is more meaningful, such as for single-site or early-phase studies</u>, listing approximate enrollment by cohort is an option. If multiple cohorts are ongoing at the time of the amendment, the status of all the ongoing cohorts can be listed. Enter the approximate number or percentage of participants enrolled as a percentage of the expected total. |
| Conformance | Required |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 12.3 |
| Value | Text or Universal Text “Original Protocol” |
| Business rules | Value Allowed: Yes Relationship: Table Column Heading “Document” Concept: CNEW |
| Repeating and/or Reuse Rules | Yes, reuse from the title page or other previous amendment |

759

| | |
|---|--|
| Term (Variable) | <Sponsor Approval Date> |
| Data Type | Date |
| Data (D), Value (V) or Heading (H) | D |
| Definition | CNEW For review purpose, see definition of the controlled terminology below The date that the sponsor approved the current or prior version of the protocol. |
| User Guidance | Previous amendments should appear in reverse chronological order with the most recent at the top (e.g., Amendment 3, 2, 1). Delete lines not needed, add lines as needed. Inclusion of regional-, country-, and site-specific amendments in the table is optional. If included, ensure that the scope is clearly distinguishable from global amendments. If including the column with enrollment numbers, follow the instructions below. <ul style="list-style-type: none"> For <u>global</u> amendments to international clinical trials or amendments to a <u>single-country</u> trial, list approximate global enrollment total or percentage at the time of the amendment and select “globally”. For <u>global amendments 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, the status of all the relevant locations can be listed. For <u>country/region</u> amendments to international clinical trials, list the approximate local enrollment total or percentage at the time of the amendment and select “locally”. |

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|--|---|
| | <ul style="list-style-type: none"> For <u>studies in which enrollment status by cohort is more meaningful, such as for single-site or early-phase studies</u>, listing approximate enrollment by cohort is an option. If multiple cohorts are ongoing at the time of the amendment, the status of all the ongoing cohorts can be listed. Enter the approximate number or percentage of participants enrolled as a percentage of the expected total. |
| Conformance | Required |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 12.3 |
| Value | Date |
| Business rules | Value Allowed: Yes Relationship: Table Column Heading “Amendment Identifier “Sponsor Approval Date” Concept: CNEW |
| Repeating and/or Reuse Rules | Yes, reuse from the title page or other previous amendment |

760

| | |
|---|---|
| Term (Variable) | <# or %> enrolled <globally/locally/per cohort> |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | CNEW For review purpose, see definition of the controlled terminology below The value (expressed either numerically or as a percentage) for the estimated number of participants enrolled at the time of the protocol amendment. |
| User Guidance | Previous amendments should appear in reverse chronological order with the most recent at the top (e.g., Amendment 3, 2, 1). Delete lines not needed, add lines as needed. Inclusion of regional-, country-, and site-specific amendments in the table is optional. If included, ensure that the scope is clearly distinguishable from global amendments. If including the column with enrollment numbers, follow the instructions below. <ul style="list-style-type: none"> For <u>global</u> amendments to international clinical trials or amendments to a <u>single-country</u> trial, list approximate global enrollment total or percentage at the time of the amendment and select “globally”. For <u>global amendments 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, the status of all the relevant locations can be listed. For <u>country/region</u> amendments to international clinical trials, list the approximate local enrollment total or percentage at the time of the amendment and select “locally”. For <u>studies in which enrollment status by cohort is more meaningful, such as for single-site or early-phase studies</u>, listing approximate |

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|--|---|
| | <p>enrollment by cohort is an option. If multiple cohorts are ongoing at the time of the amendment, the status of all the ongoing cohorts can be listed.</p> <ul style="list-style-type: none"> Enter the approximate number or percentage of participants enrolled as a percentage of the expected total. |
| Conformance | Optional: when there is an amendment and sponsor chooses |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 12.3 |
| Value | <# or %> enrolled <globally/locally/per cohort> |
| Business rules | <p>Value Allowed: Yes</p> <p>Relationship: Amendment Identifier; Sponsor Approval Date</p> <p>Concept: CNEW</p> |
| Repeating and/or Reuse Rules | Yes, reuse from the title page or other previous amendment |

761

| | |
|--|--|
| Term (Variable) | <# or %> |
| Data Type | Number |
| Data (D), Value (V) or Heading (H) | D |
| Definition | <p>CNEW</p> <p>For review purpose, see definition of the controlled terminology below</p> <p>The numeric value (expressed as an absolute value or percentage) for the estimated number of participants enrolled at the time of the protocol amendment.</p> |
| 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 | <p>Value Allowed: Yes</p> <p>Relationship: Amendment Identifier; Sponsor Approval Date</p> <p>Concept: CNEW</p> |
| Repeating and/or Reuse Rules | Yes, reuse from the title page or other previous amendment |

762

| | |
|--|---|
| Term (Variable) | {The Overview of Changes from each prior protocol amendment is {provided below} or <specify alternative location>} |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | Universal text and V, D |
| Definition | N/A |
| User Guidance | Move the Overview of Changes table from the previous amendments to this section in reverse chronological order (most recent first). |
| Conformance | Conditional: if not original protocol or first amendment |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 12.3 |
| Value | The Overview of Changes from each prior protocol amendment is |

| | |
|-------------------------------------|--|
| | Choose provided below or <specify alternative location>. |
| Business rules | Value Allowed: Yes Relationship: 12.3 Prior Protocol Amendment(s) {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 |

763

| | |
|--|--|
| Term (Variable) | <specify alternative location> |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | CNEW For review purpose, see definition of the controlled terminology below The physical or virtual location of the overview of changes from each prior amendment. |
| User Guidance | N/A |
| Conformance | Conditional: when a specify alternative location is selected |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 12.3 |
| Value | Text Location where information can be found |
| Business rules | Value Allowed: Yes Relationship: Location for previous amendments Concept: CNEW |
| Repeating and/or Reuse Rules | Yes, reuse from the title page. |

764

| | |
|--|---|
| Term (Variable) | {The Overview of Changes in Amendment <amendment number> (<date>)} |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | H |
| Definition | Heading |
| User Guidance | Move the Overview of Changes table from the previous amendments to this section in reverse chronological order (most recent first). |
| Conformance | Conditional: when there is an amendment |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 12.3 |
| Value | Overview of Changes in Amendment: |
| Business rules | Value Allowed: No Relationship: 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 |

765

| | |
|--|---|
| Term (Variable) | <amendment Identifier> |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | CNEW For review purpose, see definition of the controlled terminology below A sequence of characters used to uniquely identify a protocol amendment. |
| User Guidance | 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: Overview of Changes from each prior protocol amendment is {provided below} or <specify alternative location>. Concept: CNEW |
| Repeating and/or Reuse Rules | Yes, repeatable one table per amendment identifier |

766

| | |
|--|---|
| Term (Variable) | <Sponsor Approval Date> |
| Data Type | Date |
| Data (D), Value (V) or Heading (H) | D |
| Definition | CNEW For review purpose, see definition of the controlled terminology below The date that the sponsor approved the current or prior version of the protocol. |
| User Guidance | Move the Overview of Changes table from the previous amendments to this section in reverse chronological order (most recent first). |
| Conformance | Conditional: if amendment |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 12.3 |
| Value | Date |
| Business rules | Value Allowed: Yes Relationship: {The Overview of Changes from each prior protocol amendment is {provided below} or <specify alternative location>}. Concept: CNEW |
| Repeating and/or Reuse Rules | Yes, repeatable one table per amendment |

767

| | |
|---|---|
| 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 |

768

| | |
|--|---|
| Term (Variable) | <Description of Change> |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | CNEW For review purpose, see definition of the controlled terminology below A description of the change introduced in the current or prior version of the protocol. |
| User Guidance | N/A |
| Conformance | Conditional: if there is a previous amendment. Table optional |
| Cardinality | Column Heading Row Content |
| Relationship content from ToC representing the protocol hierarchy | 12.3 |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: Table Column Heading “Description of Change”; 12.3 Prior Protocol Amendment(s) Concept: CNEW |
| Repeating and/or Reuse Rules | Yes, repeatable for every description of change |

769

| | |
|--|--|
| 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 |

770

| | |
|--|---|
| Term (Variable) | <Brief Rationale for Change> |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | CNEW For review purpose, see definition of the controlled terminology below The brief reason for the change introduced in the current or prior version of the protocol. |
| User Guidance | N/A |
| Conformance | Conditional: if there is a previous amendment. Table optional |
| Cardinality | One to Column Heading Row description of change Section# and Name |
| Relationship content from ToC representing the protocol hierarchy | 12.3 |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: Table Column Heading {Brief Rationale for Change} and <Description of Change> Concept: CNEW |
| Repeating and/or Reuse Rules | Yes, repeatable for every description of change |

771

| | |
|--|--|
| 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 |

772

| | |
|---|--|
| Term (Variable) | <Section # and Name of Change> |
| Data Type | Valid Value |
| Data (D), Value (V) or Heading (H) | V |
| Definition | CNEW For review purpose, see definition of the controlled terminology below The protocol section number and name containing the change introduced in the current or prior version of the protocol. |

| | |
|--|---|
| User Guidance | N/A |
| Conformance | Conditional: if there is a previous amendment. Table optional |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 12.3 |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: Table Column Heading {Section # and Name} and <Description of Change> |
| Repeating and/or Reuse Rules | Yes, repeatable for every Description of Change |

773

| NCI C-code | M11 Preferred Term | Draft Definition |
|-------------------|---|--|
| CNEW | 1 PROTOCOL SUMMARY | Section 1 of the ICH M11 Protocol standard, PROTOCOL SUMMARY. |
| CNEW | 1.1 Protocol Synopsis | Section 1.1 of the ICH M11 Protocol standard, Protocol Synopsis. |
| CNEW | 1.1.1 Primary and Secondary Objectives and Estimands | Section 1.1.1 of the ICH M11 Protocol standard, Primary and Secondary Objectives and Estimands. |
| CNEW | 1.1.2 Overall Design | Section 1.1.2 of the ICH M11 Protocol standard, Overall Design. |
| CNEW | 1.2 Trial Schema | Section 1.2 of the ICH M11 Protocol standard, Trial Schema. |
| CNEW | 1.3 Schedule of Activities | Section 1.3 of the ICH M11 Protocol standard, Schedule of Activities. |
| CNEW | 2 INTRODUCTION | Section 2 of the ICH M11 Protocol standard, INTRODUCTION. |
| CNEW | 2.1 Purpose of Trial | Section 2.1 of the ICH M11 Protocol standard, Purpose of Trial. |
| CNEW | 2.2 Assessment of Risks and Benefits | Section 2.2 of the ICH M11 Protocol standard, Assessment of Risks and Benefits. |
| CNEW | 2.2.1 Risk Summary and Mitigation Strategy | Section 2.2.2 of the ICH M11 Protocol standard, Risk Summary and Mitigation Strategy. |
| CNEW | 2.2.2 Benefit Summary | Section 2.2.1 of the ICH M11 Protocol standard, Benefit Summary. |
| CNEW | 2.2.3 Overall Benefit-Risk Assessment | Section 2.2.3 of the ICH M11 Protocol standard, Overall Benefit:Risk Assessment. |
| CNEW | 3 TRIAL OBJECTIVES AND ASSOCIATED ESTIMANDS | Section 3 of the ICH M11 Protocol standard, TRIAL OBJECTIVES AND ASSOCIATED ESTIMANDS. |
| CNEW | 3.1 Primary Objective(s) and Associated Estimand(s) | Section 3.1 of the ICH M11 Protocol standard, Primary Objective(s) and Associated Estimand(s). |
| CNEW | 3.1.1 Primary Objective # | Section 3.1.1 of the ICH M11 Protocol standard, Primary Objective. |
| CNEW | 3.2 Secondary Objective(s) and Associated Estimand(s) | Section 3.2 of the ICH M11 Protocol standard, Secondary Objective(s) and Associated Estimand(s). |
| CNEW | 3.2.1 Secondary Objective # | Section 3.2.1 of the ICH M11 Protocol standard, Secondary Objective. |
| CNEW | 3.3 Exploratory Objective(s) | Section 3.3 of the ICH M11 Protocol standard, Exploratory Objective(s). |

| | | |
|------|--|---|
| CNEW | 3.3.1 Exploratory Objective # | Section 3.3.1 of the ICH M11 Protocol standard, Exploratory Objective. |
| CNEW | 4 TRIAL DESIGN | Section 4 of the ICH M11 Protocol standard, TRIAL DESIGN. |
| CNEW | 4.1 Description of Trial Design | Section 4.1 of the ICH M11 Protocol standard, Description of Trial Design. |
| CNEW | 4.1.1 Stakeholder Input into Design | Section 4.1.1 of the ICH M11 Protocol standard, Stakeholder Input into Design. |
| CNEW | 4.2 Rationale for Trial Design | Section 4.2 of the ICH M11 Protocol standard, Rationale for Trial Design. |
| CNEW | 4.2.1 Rationale for Estimand(s) | Section 4.2.1 of the ICH M11 Protocol standard, Rationale for Estimand(s). |
| CNEW | 4.2.2 Rationale for Intervention Model | Section 4.2.2 of the ICH M11 Protocol standard, Rationale for Intervention Model. |
| CNEW | 4.2.3 Rationale for Control Type | Section 4.2.3 of the ICH M11 Protocol standard, Rationale for Control Type. |
| CNEW | 4.2.4 Rationale for Trial Duration | Section 4.2.4 of the ICH M11 Protocol standard, Rationale for Trial Duration. |
| CNEW | 4.2.3 Rationale for Estimand Attributes | Section 4.2.3 of the ICH M11 Protocol standard, Rationale for Estimand Attributes. |
| CNEW | 4.2.5 Rationale for Adaptive or Novel Trial Design | Section 4.2.5 of the ICH M11 Protocol standard, Rationale for Adaptive or Novel Trial Design. |
| CNEW | 4.2.6 Rationale for Interim Analysis | Section 4.2.6 of the ICH M11 Protocol standard, Rationale for Interim Analysis. |
| CNEW | 4.2.7 Rationale for Other Trial Design Aspects | Section 4.2.7 of the ICH M11 Protocol standard, Rationale for Other Trial Design Aspects. |
| CNEW | 4.3 Trial Stopping Rules | Section 4.3 of the ICH M11 Protocol standard, Trial Stopping Rules. |
| CNEW | 4.4 Start of Trial and End of Trial | Section 4.4 of the ICH M11 Protocol standard, Start of Trial and End of Trial. |
| CNEW | 4.5 Access to Trial Intervention After End of Trial | Section 4.5 of the ICH M11 Protocol standard, Access to Trial Intervention After End of Trial. |
| CNEW | 5 TRIAL POPULATION | Section 5 of the ICH M11 Protocol standard, TRIAL POPULATION. |
| CNEW | 5.1 Description of Trial Population and Rationale | Section 5.1 of the ICH M11 Protocol standard, Description of Trial Population and Rationale. |
| CNEW | 5.2 Inclusion Criteria | Section 5.2 of the ICH M11 Protocol standard, Inclusion Criteria. |
| CNEW | 5.3 Exclusion Criteria | Section 5.3 of the ICH M11 Protocol standard, Exclusion Criteria. |
| CNEW | 5.4 Contraception | Section 5.4 of the ICH M11 Protocol standard, Contraception. |
| CNEW | 5.4.1 Definitions Related to Childbearing Potential | Section 5.4.1 of the ICH M11 Protocol standard, Definitions Related to Childbearing Potential. |
| CNEW | 5.4.2 Contraception Requirements | Section 5.4.2 of the ICH M11 Protocol standard, Contraception Requirements. |
| CNEW | 5.5 Lifestyle Restrictions | Section 5.5 of the ICH M11 Protocol standard, Lifestyle Restrictions. |
| CNEW | 5.5.1 Meals and Dietary Restrictions | Section 5.5.1 of the ICH M11 Protocol standard, Meals and Dietary Restrictions. |
| CNEW | 5.5.2 Caffeine, Alcohol, Tobacco, and Other Restrictions | Section 5.5.2 of the ICH M11 Protocol standard, Caffeine, Alcohol, Tobacco, and Other Restrictions. |

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| CNEW | 5.5.3 Physical Activity Restrictions | Section 5.5.3 of the ICH M11 Protocol standard, Physical Activity Restrictions. |
| CNEW | 5.5.4 Other Activity Restrictions | Section 5.5.4 of the ICH M11 Protocol standard, Other Activity Restrictions. |
| CNEW | 5.6 Screen Failure and Rescreening | Section 5.6 of the ICH M11 Protocol standard, Screen Failure and Rescreening. |
| CNEW | 6 TRIAL INTERVENTION AND CONCOMITANT THERAPY | Section 6 of the ICH M11 Protocol standard, TRIAL INTERVENTION AND CONCOMITANT THERAPY. |
| CNEW | 6.1 Description of Investigational Trial Intervention | Section 6.1 of the ICH M11 Protocol standard, Description of Investigational Trial Intervention. |
| CNEW | 6.2 Rationale for Investigational Trial Intervention Dose and Regimen | Section 6.2 of the ICH M11 Protocol standard, Rationale for Investigational Trial Intervention Dose and Regimen. |
| CNEW | 6.3 Investigational Trial Intervention Administration | Section 6.3 of the ICH M11 Protocol standard, Investigational Trial Intervention Administration. |
| CNEW | 6.4 Investigational Trial Intervention Dose Modification | Section 6.4 of the ICH M11 Protocol standard, Investigational Trial Intervention Dose Modification. |
| CNEW | 6.5 Management of Investigational Trial Intervention Overdose | Section 6.5 of the ICH M11 Protocol standard, Management of Investigational Trial Intervention Overdose. |
| CNEW | 6.6 Preparation, Storage, Handling and Accountability of Investigational Trial Intervention | Section 6.6 of the ICH M11 Protocol standard, Preparation, Storage, Handling and Accountability of Investigational Trial Intervention. |
| CNEW | 6.6.1 Preparation of Investigational Trial Intervention | Section 6.6.1 of the ICH M11 Protocol standard, Preparation of Investigational Trial Intervention. |
| CNEW | 6.6.2 Storage and Handling of Investigational Trial Intervention | Section 6.6.2 of the ICH M11 Protocol standard, Storage and Handling of Investigational Trial Intervention. |
| CNEW | 6.6.3 Accountability of Investigational Trial Intervention | Section 6.6.3 of the ICH M11 Protocol standard, Accountability of Investigational Trial Intervention. |
| CNEW | 6.7 Investigational Trial Intervention Assignment, Randomisation and Blinding | Section 6.7 of the ICH M11 Protocol standard, Investigational Trial Intervention Assignment, Randomisation and Blinding. |
| CNEW | 6.7.1 Participant Assignment to Investigational Trial Intervention | Section 6.7.1 of the ICH M11 Protocol standard, Participant Assignment to Investigational Trial Intervention. |
| CNEW | 6.7.2 Randomisation | Section 6.7.2 of the ICH M11 Protocol standard, Randomisation. |
| CNEW | 6.7.3 Measures to Maintain Blinding | Section 6.7.3 of the ICH M11 Protocol standard, Measures to Maintain Blinding. |

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| CNEW | 6.7.4 Emergency Unblinding at the Site | Section 6.7.4 of the ICH M11 Protocol standard, Emergency Unblinding at the Site. |
| CNEW | 6.8 Investigational Trial Intervention Adherence | Section 6.8 of the ICH M11 Protocol standard, Investigational Trial Intervention Adherence. |
| CNEW | 6.9 Description of Noninvestigational Trial Intervention | Section 6.9 of the ICH M11 Protocol standard, Description of Noninvestigational Trial Intervention. |
| CNEW | 6.9.1 Background Trial Intervention | Section 6.9.1 of the ICH M11 Protocol standard, Background Trial Intervention. |
| CNEW | 6.9.2 Rescue Therapy | Section 6.9.2 of the ICH M11 Protocol standard, Rescue Therapy. |
| CNEW | 6.9.3 Other Noninvestigational Trial Intervention | Section 6.9.3 of the ICH M11 Protocol standard, Other Noninvestigational Trial Intervention. |
| CNEW | 6.10 Concomitant Therapy | Section 6.10 of the ICH M10 Protocol standard, Concomitant Therapy. |
| CNEW | 6.10.1 Prohibited Concomitant Therapy | Section 6.10.1 of the ICH M10 Protocol standard, Prohibited Concomitant Therapy. |
| CNEW | 6.10.2 Permitted Concomitant Therapy | Section 6.10.2 of the ICH M10 Protocol standard, Permitted Concomitant Therapy. |
| CNEW | 7 PARTICIPANT DISCONTINUATION OF TRIAL INTERVENTION AND DISCONTINUATION OR WITHDRAWAL FROM TRIAL | Section 7 of the ICH M11 Protocol standard, PARTICIPANT DISCONTINUATION OF TRIAL INTERVENTION AND DISCONTINUATION OR WITHDRAWAL FROM TRIAL. |
| CNEW | 7.1 Discontinuation of Trial Intervention for Individual Participants | Section 7.1 of the ICH M11 Protocol standard, Discontinuation of Trial Intervention for Individual Participants. |
| CNEW | 7.1.1 Permanent Discontinuation of Trial Intervention | Section 7.1.1 of the ICH M11 Protocol standard, Permanent Discontinuation of Trial Intervention. |
| CNEW | 7.1.2 Temporary Discontinuation of Trial Intervention | Section 7.1.2 of the ICH M11 Protocol standard, Temporary Discontinuation of Trial Intervention. |
| CNEW | 7.1.3 Rechallenge | Section 7.1.3 of the ICH M11 Protocol standard, Rechallenge. |
| CNEW | 7.2 Participant Discontinuation or Withdrawal from the Trial | Section 7.2 of the ICH M11 Protocol standard, Participant Discontinuation or Withdrawal from the Trial. |
| CNEW | 7.3 Lost to Follow-Up | Section 7.3 of the ICH M11 Protocol standard, Lost to Follow-Up. |
| CNEW | 8 TRIAL ASSESSMENTS AND PROCEDURES | Section 8 of the ICH M11 Protocol standard, TRIAL ASSESSMENTS AND PROCEDURES. |
| CNEW | 8.1 Trial Assessments and Procedures Considerations | Section 8.1 of the ICH M11 Protocol standard, Trial Assessments and Procedures Considerations. |
| CNEW | 8.2 Screening/Baseline Assessments and Procedures | Section 8.2 of the ICH M11 Protocol standard, Screening/Baseline Assessments and Procedures. |
| CNEW | 8.3 Efficacy Assessments and Procedures | Section 8.3 of the ICH M11 Protocol standard, Efficacy Assessments and Procedures. |

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| CNEW | 8.4 Safety Assessments and Procedures | Section 8.4 of the ICH M11 Protocol standard, Safety Assessments and Procedures. |
| CNEW | 8.4.1 Physical Examination | Section 8.4.1 of the ICH M11 Protocol standard, Physical Examination. |
| CNEW | 8.4.2 Vital Signs | Section 8.4.2 of the ICH M11 Protocol standard, Vital Signs. |
| CNEW | 8.4.3 Electrocardiograms | Section 8.4.3 of the ICH M11 Protocol standard, Electrocardiograms. |
| CNEW | 8.4.4 Clinical Laboratory Assessments | Section 8.4.4 of the ICH M11 Protocol standard, Clinical Laboratory Assessments. |
| CNEW | 8.4.5 Pregnancy Testing | Section 8.4.5 of the ICH M11 Protocol standard, Pregnancy Testing. |
| CNEW | 8.4.6 Suicidal Ideation and Behaviour Risk Monitoring | Section 8.4.6 of the ICH M11 Protocol standard, Suicidal Ideation and Behaviour Risk Monitoring. |
| CNEW | 8.5 Pharmacokinetics | Section 8.5 of the ICH M11 Protocol standard, Pharmacokinetics. |
| CNEW | 8.6 Biomarkers | Section 8.6 of the ICH M11 Protocol standard, Biomarkers. |
| CNEW | 8.6.1 Genetics and Pharmacogenomics | Section 8.6.1 of the ICH M11 Protocol standard, Genetics and Pharmacogenomics. |
| CNEW | 8.6.2 Pharmacodynamic Biomarkers | Section 8.6.2 of the ICH M11 Protocol standard, Pharmacodynamic Biomarkers. |
| CNEW | 8.6.3 Other Biomarkers | Section 8.6.3 of the ICH M11 Protocol standard, Other Biomarkers. |
| CNEW | 8.7 Immunogenicity Assessments | Section 8.7 of the ICH M11 Protocol standard, Immunogenicity Assessments. |
| CNEW | 8.8 Medical Resource Utilisation and Health Economics | Section 8.8 of the ICH M11 Protocol standard, Medical Resource Utilisation and Health Economics. |
| CNEW | 9 ADVERSE EVENTS, SERIOUS ADVERSE EVENTS, PRODUCT COMPLAINTS, PREGNANCY AND POSTPARTUM INFORMATION, AND SPECIAL SAFETY SITUATIONS | Section 9 of the ICH M11 Protocol standard, ADVERSE EVENTS, SERIOUS ADVERSE EVENTS, PRODUCT COMPLAINTS, PREGNANCY AND POSTPARTUM INFORMATION, AND SPECIAL SAFETY SITUATIONS. |
| CNEW | 9.1 Definitions | Section 9.1 of the ICH M11 Protocol standard, Definitions. |
| CNEW | 9.1.1 Definitions of Adverse Events | Section 9.1.1 of the ICH M11 Protocol standard, Definitions of Adverse Events. |
| CNEW | 9.1.2 Definitions of Serious Adverse Events | Section 9.1.2 of the ICH M11 Protocol standard, Definitions of Serious Adverse Events. |
| CNEW | 9.1.3 Definitions of Product Complaints | Section 9.1.3 of the ICH M11 Protocol standard, Definitions of Product Complaints. |
| CNEW | 9.1.3.1 Definitions of Medical Device Product Complaints | Section 9.1.3.1 of the ICH M11 Protocol standard, Definitions of Medical Device Product Complaints. |
| CNEW | 9.2 Timing and Procedures for | Section 9.2 of the ICH M11 Protocol standard, Timing and Procedures for Collection and Reporting. |

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| | Collection and Reporting | |
| CNEW | 9.2.1 Timing | Section 9.2.1 of the ICH M11 Protocol standard, Timing. |
| CNEW | 9.2.2 Collection Procedures | Section 9.2.2 of the ICH M11 Protocol standard, Collection Procedures. |
| CNEW | 9.2.3 Reporting | Section 9.2.3 of the ICH M11 Protocol standard, Reporting. |
| CNEW | 9.2.3.1 Regulatory Reporting Requirements | Section 9.2.3.1 of the ICH M11 Protocol standard, Regulatory Reporting Requirements. |
| CNEW | 9.2.4 Adverse Events of Special Interest | Section 9.2.4 of the ICH M11 Protocol standard, Adverse Events of Special Interest. |
| CNEW | 9.2.5 Disease-related Events or Outcomes Not Qualifying as AEs or SAEs | Section 9.2.5 of the ICH M11 Protocol standard, Disease-related Events or Outcomes Not Qualifying as AEs or SAEs. |
| CNEW | 9.3 Pregnancy and Postpartum Information | Section 9.3 of the ICH M11 Protocol standard, Pregnancy and Postpartum Information. |
| CNEW | 9.3.1 Participants Who Become Pregnant During the Trial | Section 9.3.1 of the ICH M11 Protocol standard, Participants Who Become Pregnant During the Trial. |
| CNEW | 9.3.2 Participants Whose Partners Become Pregnant During the Trial | Section 9.3.2 of the ICH M11 Protocol standard, Participants Whose Partners Become Pregnant During the Trial. |
| CNEW | 9.4 Special Safety Situations | Section 9.4 of the ICH M11 Protocol standard, Special Safety Situations. |
| CNEW | 10 STATISTICAL CONSIDERATIONS | Section 10 of the ICH M11 Protocol standard, STATISTICAL CONSIDERATIONS. |
| CNEW | 10.1 General Considerations | Section 10.1 of the ICH M11 Protocol standard, General Considerations. |
| CNEW | 10.2 Analysis Sets | Section 10.2 of the ICH M11 Protocol standard, Analysis Sets. |
| CNEW | 10.3 Analyses of Demographics and Other Baseline Variables | Section 10.3 of the ICH M11 Protocol standard, Analyses of Demographics and Other Baseline Variables. |
| CNEW | 10.4 Analyses Associated with the Primary Objective(s) | Section 10.4 of the ICH M11 Protocol standard, Analyses Associated with the Primary Objective(s). |
| CNEW | 10.4.1 Primary Objective # | Section 10.4.1 of the ICH M11 Protocol standard, Primary Objective. |
| CNEW | 10.4.1.1 Statistical Analysis Method | Section 10.4.1.1 of the ICH M11 Protocol standard, Statistical Analysis Method. |
| CNEW | 10.4.1.2 Handling of Data in Relation to Primary Estimand(s) | Section 10.4.1.2 of the ICH M11 Protocol standard, Handling of Data in Relation to Primary Estimand(s). |
| CNEW | 10.4.1.3 Handling of Missing Data in Relation to Primary Estimand(s) | Section 10.4.1.3 of the ICH M11 Protocol standard, Handling of Missing Data in Relation to Primary Estimand(s) |
| CNEW | 10.4.1.4 Sensitivity Analysis | Section 10.4.1.4 of the ICH M11 Protocol standard, Sensitivity Analysis. |
| CNEW | 10.4.1.5 Supplementary Analysis | Section 10.4.1.5 of the ICH M11 Protocol standard, Supplementary Analysis. |

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| CNEW | 10.5 Analyses Associated with the Secondary Objective(s) | Section 10.5 of the ICH M11 Protocol standard, Analyses Associated with the Secondary Objective(s). |
| CNEW | 10.5.1 Secondary Objective # | Section 10.5.1 of the ICH M11 Protocol standard, Secondary Objective. |
| CNEW | 10.5.1.1 Statistical Analysis Method | Section 10.5.1.1 of the ICH M11 Protocol standard, Statistical Analysis Method. |
| CNEW | 10.5.1.2 Handling of Data in Relation to Secondary Estimand(s) | Section 10.5.1.2 of the ICH M11 Protocol standard, Handling of Data in Relation to Secondary Estimand(s). |
| CNEW | 10.5.1.3 Handling of Missing Data in Relation to Secondary Estimand(s) | Section 10.5.1.3 of the ICH M11 Protocol standard, Handling of Missing Data in Relation to Secondary Estimand(s). |
| CNEW | 10.5.1.4 Sensitivity Analysis | Section 10.5.1.4 of the ICH M11 Protocol standard, Sensitivity Analysis. |
| CNEW | 10.5.1.5 Supplementary Analysis | Section 10.5.1.5 of the ICH M11 Protocol standard, Supplementary Analysis. |
| CNEW | 10.6 Analysis Associated with the Exploratory Objective(s) | Section 10.6 of the ICH M11 Protocol standard, Analysis Associated with the Exploratory Objective(s). |
| CNEW | 10.7 Safety Analyses | Section 10.7 of the ICH M11 Protocol standard, Safety Analyses. |
| CNEW | 10.8 Other Analyses | Section 10.8 of the ICH M11 Protocol standard, Other Analyses. |
| CNEW | 10.9 Interim Analyses | Section 10.9 of the ICH M11 Protocol standard, Interim Analyses. |
| CNEW | 10.10 Multiplicity Adjustments | Section 10.10 of the ICH M11 Protocol standard, Multiplicity Adjustments. |
| CNEW | 10.11 Sample Size Determination | Section 10.11 of the ICH M11 Protocol standard, Sample Size Determination. |
| CNEW | 11 TRIAL OVERSIGHT AND OTHER GENERAL CONSIDERATIONS | Section 11 of the ICH M11 Protocol standard, TRIAL OVERSIGHT AND OTHER GENERAL CONSIDERATIONS. |
| CNEW | 11.1 Regulatory and Ethical Considerations | Section 11.1 of the ICH M11 Protocol standard, Regulatory and Ethical Considerations. |
| CNEW | 11.2 Trial Oversight | Section 11.2 of the ICH M11 Protocol standard, Trial Oversight. |
| CNEW | 11.2.1 Investigator Responsibilities | Section 11.2.1 of the ICH M11 Protocol standard, Investigator Responsibilities. |
| CNEW | 11.2.2 Sponsor Responsibilities | Section 11.2.2 of the ICH M11 Protocol standard, Sponsor Responsibilities. |
| CNEW | 11.3 Informed Consent Process | Section 11.3 of the ICH M11 Protocol standard, Informed Consent Process. |
| CNEW | 11.3.1 Informed Consent for Rescreening | Section 11.3.1 of the ICH M11 Protocol standard, Informed Consent for Rescreening. |
| CNEW | 11.3.2 Informed Consent for Use of Remaining Samples in Exploratory Research | Section 11.3.2 of the ICH M11 Protocol standard, Informed Consent for Use of Remaining Samples in Exploratory Research. |
| CNEW | 11.4 Committees | Section 11.4 of the ICH M11 Protocol standard, Committees. |
| CNEW | 11.5 Insurance and Indemnity | Section 11.5 of the ICH M11 Protocol standard, Insurance and Indemnity. |

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| CNEW | 11.6 Risk-Based Quality Management | Section 11.6 of the ICH M11 Protocol standard, Risk-Based Quality Management. |
| CNEW | 11.7 Data Governance | Section 11.7 of the ICH M11 Protocol standard, Data Governance. |
| CNEW | 11.8 Data Protection | Section 11.8 of the ICH M11 Protocol standard, Data Protection. |
| CNEW | 11.9 Source Data | Section 11.9 of the ICH M11 Protocol standard, Source Data. |
| CNEW | 11.10 Protocol Deviations | Section 11.10 of the ICH M11 Protocol standard, Protocol Deviations. |
| CNEW | 11.11 Early Site Closure | Section 11.11 of the ICH M11 Protocol standard, Early Site Closure. |
| CNEW | 11.12 Data Dissemination | Section 11.12 of the ICH M11 Protocol standard, Data Dissemination. |
| CNEW | 12 APPENDIX: SUPPORTING DETAILS | Section 12 of the ICH M11 Protocol standard, APPENDIX: SUPPORTING DETAILS. |
| CNEW | 12.1 Clinical Laboratory Tests | Section 12.1 of the ICH M11 Protocol standard, Clinical Laboratory Tests. |
| CNEW | 12.2 Country/Region-Specific Differences | Section 12.2 of the ICH M11 Protocol standard, Country/Region-Specific Differences. |
| CNEW | 12.3 Prior Protocol Amendment(s) | Section 12.3 of the ICH M11 Protocol standard, Prior Protocol Amendment(s). |
| CNEW | 13 APPENDIX: GLOSSARY OF TERMS AND ABBREVIATIONS | Section 13 of the ICH M11 Protocol standard, APPENDIX: GLOSSARY OF TERMS AND ABBREVIATIONS. |
| CNEW | 14 APPENDIX: REFERENCES | Section 14 of the ICH M11 Protocol standard, APPENDIX: REFERENCES. |

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| Term (Variable) | 12.X Additional Appendices |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | H |
| Definition | Heading |
| User Guidance | N/A |
| Conformance | Optional |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 12 X where X is a unique number for each Additional Appendix |
| Value | Title of Appendix |
| Business rules | Value Allowed: Yes Relationship: 12 APPENDIX: SUPPORTING DETAILS and Table of content Concept: Heading |
| Repeating and/or Reuse Rules | Yes, repeatable for each additional Appendix |

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| Term (Variable) | <Enter Appendix> |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | N/A |
| User Guidance | N/A |
| Conformance | Optional |
| Cardinality | One to one |

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| Relationship content from ToC representing the protocol hierarchy | 12 X where X is a unique number for each Additional Appendix |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: 12.X Additional Appendices Concept: CNEW |
| Repeating and/or Reuse Rules | Yes, repeatable for each additional Appendix |

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13 APPENDIX: GLOSSARY OF TERMS AND ABBREVIATIONS

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| 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 |

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|--|--|
| Term (Variable) | <Glossary of Terms and Abbreviations> |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | CNEW For review purpose, see definition of the controlled terminology below A list of terms with their abbreviations and/or definitions. |
| User Guidance | Define abbreviations and other terms used in the protocol. A tabular presentation is common and may serve as the definition at first use. |
| Conformance | Required |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 13 |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: 13 APPENDIX: GLOSSARY OF TERMS AND ABBREVIATIONS Concept: CNEW |
| Repeating and/or Reuse Rules | No |

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| Term (Variable) | 14 APPENDIX: REFERENCES |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | H |
| Definition | Heading |
| User Guidance | N/A |
| Conformance | Required |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 14 |
| Value | APPENDIX: REFERENCES |
| Business rules | Value Allowed: No Relationship: Table of Contents Concept: Heading |
| Repeating and/or Reuse Rules | No |

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|--|--|
| Term (Variable) | <References> |
| Data Type | Text |
| Data (D), Value (V) or Heading (H) | D |
| Definition | C184397 For review purpose, see definition of the controlled terminology below The curated list of sources that are cited within the reference section of the document. |
| User Guidance | References should be listed in a common format that includes all relevant information to identify the source and date published. If not published, this should be clearly indicated. |
| Conformance | Required |
| Cardinality | One to one |
| Relationship content from ToC representing the protocol hierarchy | 14 |
| Value | Text |
| Business rules | Value Allowed: Yes Relationship: 14 APPENDIX: REFERENCES Concept: C184397 |
| Repeating and/or Reuse Rules | No |

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