

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

ICH HARMONISED GUIDELINE

**CLINICAL ELECTRONIC STRUCTURED HARMONISED  
PROTOCOL  
(CESHARP)**

**M11 TECHNICAL SPECIFICATION**

Draft version

Endorsed on 27 September 2022

*Currently under public consultation*

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

## M11 Technical Specification

### Document History

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

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## Technical Specification

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

NOTE: Following the public comment period, the M11 Guideline and template may be updated along with the Technical Specification. The M11 EWG recognises that the Technical Specification is at an early stage of maturity as certain terms (variables) in this version (e.g., Cardinality, Definition, Relationship to Conceptual Model) are to be addressed post the public comment period and as the M11 EWG progresses through the ICH Step process.

## Appendix 1: Detailed Descriptions of Information Components

### Overall Rules

<b>Term (Variable)</b>	Overall rules
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	H
<b>Definition</b>	
<b>User Guidance</b>	
<b>Conformance</b>	Rules
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	All document
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	REQUIRED Level 1 and Level 2 headings
<b>Business rules</b>	<b>Value Allowed:</b> Yes <b>Relationship:</b> n/a <b>Concept:</b> n/a
<b>Duplicate field in other sections</b>	

## 14 0. Foreword

Term (Variable)	Foreword
Data Type	Text
Topic, Value or Header	H
Definition	Section heading
User Guidance	
Conformance	Not required
Cardinality	
Relationship content from ToC representing the protocol hierarchy	0. Foreword
Relationship (reference to high level conceptual model)	
Value	Foreword
Business rules	<b>Value Allowed:</b> Yes <b>Relationship:</b> Not transferred <b>Concept:</b> Protocol title
Duplicate field in other sections	

## 15 0.1 Template Revision History

Term (Variable)	Template Revision History
Data Type	Text
Topic, Value or Header	H
Definition	Section heading
User Guidance	
Conformance	Not required
Cardinality	
Relationship content from ToC representing the protocol hierarchy	Foreword
Relationship (reference to high level conceptual model)	
Value	Template Revision History
Business rules	<b>Value Allowed:</b> Yes <b>Relationship:</b> Not transferred <b>Concept:</b> Protocol title
Duplicate field in other sections	

16

Term (Variable)	Date
Data Type	Text
Topic, Value or Header	H
Definition	Table column heading
User Guidance	
Conformance	Not required
Cardinality	
Relationship content from ToC representing the protocol hierarchy	Foreword
Relationship (reference to high level conceptual model)	
Value	Date
Business rules	<b>Value Allowed:</b> Yes <b>Relationship:</b> Table column heading <b>Concept:</b> n/a
Duplicate field in other sections	

17

Term (Variable)	Date of Revision
Data Type	Text
Topic, Value or Header	D
Definition	Date of Revision
User Guidance	
Conformance	Not required
Cardinality	
Relationship content from ToC representing the protocol hierarchy	Foreword
Relationship (reference to high level conceptual model)	
Value	Date
Business rules	<b>Value Allowed:</b> Yes <b>Relationship:</b> Repeating for each new date Not transferred <b>Concept:</b> n/a
Duplicate field in other sections	

18

Term (Variable)	Description of Revision
Data Type	Text
Topic, Value or Header	H
Definition	Table column heading
User Guidance	
Conformance	Not required
Cardinality	
Relationship content from ToC representing the protocol hierarchy	Foreword
Relationship (reference to high level conceptual model)	
Value	Table column heading
Business rules	<b>Value Allowed:</b> Yes <b>Relationship:</b> Table column heading Not transferred <b>Concept:</b> n/a
Duplicate field in other sections	

19

Term (Variable)	Description of Revision
Data Type	Text
Topic, Value or Header	D
Definition	Description of Revision
User Guidance	
Conformance	Not required
Cardinality	
Relationship content from ToC representing the protocol hierarchy	Foreword
Relationship (reference to high level conceptual model)	
Value	Description of revision text
Business rules	<b>Value Allowed:</b> Yes <b>Relationship:</b> Repeating for each description of revision Not transferred <b>Concept:</b> n/a
Duplicate field in other sections	

20

## 21 0.2 Intended Use of Template

Term (Variable)	Intended Use of Template
Data Type	Text
Topic, Value or Header	H
Definition	Section heading
User Guidance	
Conformance	Not required
Cardinality	
Relationship content from ToC representing the protocol hierarchy	Foreword
Relationship (reference to high level conceptual model)	
Value	Intended Use of Template
Business rules	<b>Value Allowed:</b> Yes <b>Relationship:</b> n/a <b>Concept:</b> n/a
Duplicate field in other sections	

22

Term (Variable)	Intended Use of Templates
Data Type	Text
Topic, Value or Header	D
Definition	Section heading
User Guidance	
Conformance	Not required
Cardinality	
Relationship content from ToC representing the protocol hierarchy	Foreword
Relationship (reference to high level conceptual model)	
Value	Intended Use of Template
Business rules	<b>Value Allowed:</b> Yes <b>Relationship:</b> Not transferred <b>Concept:</b> n/a
Duplicate field in other sections	

23

## 24 0.3 Template Conventions and General Instruction

Term (Variable)	Template Conventions and General Instruction
Data Type	Text
Topic, Value or Header	H
Definition	Section heading
User Guidance	
Conformance	Not required
Cardinality	
Relationship content from ToC representing the protocol hierarchy	Foreword
Relationship (reference to high level conceptual model)	
Value	0.3 Template Conventions and General Instruction
Business rules	<b>Value Allowed:</b> Yes <b>Relationship:</b> Not transferred <b>Concept:</b> n/a
Duplicate field in other sections	

25

Term (Variable)	Description of Conventions
Data Type	Text
Topic, Value or Header	H
Definition	Explains conventions and general instruction
User Guidance	
Conformance	Not required
Cardinality	
Relationship content from ToC representing the protocol hierarchy	Foreword
Relationship (reference to high level conceptual model)	
Value	Description of conventions
Business rules	<b>Value Allowed:</b> Yes <b>Relationship:</b> Not transferred <b>Concept:</b> n/a
Duplicate field in other sections	

26



<b>Term (Variable)</b>	Description of conventions
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	D
<b>Definition</b>	Explains conventions and general instruction
<b>User Guidance</b>	
<b>Conformance</b>	Not required
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Foreword
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	
<b>Business rules</b>	<b>Value Allowed:</b> Yes <b>Relationship:</b> Not transferred <b>Concept:</b> n/a
<b>Duplicate field in other sections</b>	

27

<b>Term (Variable)</b>	Heading Structure and Flexibility
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	H
<b>Definition</b>	
<b>User Guidance</b>	
<b>Conformance</b>	Not required
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Foreword
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	Heading structure and flexibility
<b>Business rules</b>	<b>Value Allowed:</b> Yes <b>Relationship:</b> Not transferred <b>Concept:</b> n/a
<b>Duplicate field in other sections</b>	

28

<b>Term (Variable)</b>	Heading Structure and Flexibility
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	D
<b>Definition</b>	
<b>User Guidance</b>	
<b>Conformance</b>	Not required
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Foreword
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	
<b>Business rules</b>	<b>Value Allowed:</b> Yes <b>Relationship:</b> Not transferred <b>Concept:</b> n/a
<b>Duplicate field in other sections</b>	

29

<b>Term (Variable)</b>	Table and Figure Numbering
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	H
<b>Definition</b>	
<b>User Guidance</b>	
<b>Conformance</b>	Not required
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Foreword
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	Table and figure numbering
<b>Business rules</b>	<b>Value Allowed:</b> Yes <b>Relationship:</b> Not transferred <b>Concept:</b> n/a
<b>Duplicate field in other sections</b>	

30

<b>Term (Variable)</b>	Table and Figure Numbering
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	D
<b>Definition</b>	
<b>User Guidance</b>	
<b>Conformance</b>	Not required
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Foreword
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	
<b>Business rules</b>	<b>Value Allowed:</b> Yes <b>Relationship:</b> Not transferred <b>Concept:</b> n/a
<b>Duplicate field in other sections</b>	

31

<b>Term (Variable)</b>	Terminology
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	H
<b>Definition</b>	
<b>User Guidance</b>	
<b>Conformance</b>	Not required
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Foreword
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	Terminology
<b>Business rules</b>	<b>Value Allowed:</b> Yes <b>Relationship:</b> Not transferred <b>Concept:</b> n/a
<b>Duplicate field in other sections</b>	

32

<b>Term (Variable)</b>	Terminology
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	D
<b>Definition</b>	
<b>User Guidance</b>	
<b>Conformance</b>	Not required
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Foreword
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	
<b>Business rules</b>	<b>Value Allowed:</b> Yes <b>Relationship:</b> Not transferred <b>Concept:</b> n/a
<b>Duplicate field in other sections</b>	

33

<b>Term (Variable)</b>	Suggestion for Publishing a Paper or PDF Document
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	H
<b>Definition</b>	
<b>User Guidance</b>	
<b>Conformance</b>	Not required
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Foreword
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	Suggestion for publishing a paper or PDF document
<b>Business rules</b>	<b>Value Allowed:</b> Yes <b>Relationship:</b> Not transferred <b>Concept:</b> n/a
<b>Duplicate field in other sections</b>	

34

<b>Term (Variable)</b>	Suggestion for Publishing a Paper or PDF Document
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	D
<b>Definition</b>	
<b>User Guidance</b>	
<b>Conformance</b>	Not required
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Foreword
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	
<b>Business rules</b>	<b>Value Allowed:</b> Yes <b>Relationship:</b> Not transferred <b>Concept:</b> n/a
<b>Duplicate field in other sections</b>	

35

<b>Term (Variable)</b>	Abbreviations Used in this Template
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	H
<b>Definition</b>	
<b>User Guidance</b>	
<b>Conformance</b>	Not required
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Foreword
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	Abbreviations Used in this Template
<b>Business rules</b>	<b>Value Allowed:</b> Yes <b>Relationship:</b> Not transferred <b>Concept:</b> n/a
<b>Duplicate field in other sections</b>	

36

<b>Term (Variable)</b>	Abbreviations Used in this Template
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	D
<b>Definition</b>	
<b>User Guidance</b>	
<b>Conformance</b>	Not required
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Foreword
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	
<b>Business rules</b>	<b>Value Allowed:</b> Yes <b>Relationship:</b> Not transferred <b>Concept:</b> n/a
<b>Duplicate field in other sections</b>	

### 37 Protocol Full Title

<b>Term (Variable)</b>	Protocol Full Title
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	H
<b>Definition</b>	Heading
<b>User Guidance</b>	
<b>Conformance</b>	Required
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Title Page
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	Protocol Full Title
<b>Business rules</b>	<b>Value Allowed:</b> Yes <b>Relationship:</b> Table row heading <b>Concept:</b> n/a
<b>Duplicate field in other sections</b>	

38

<b>Term (Variable)</b>	Protocol Full Title
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	D
<b>Definition</b>	
<b>User Guidance</b>	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.
<b>Conformance</b>	Required
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Title page
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	4000 Eudra characters 600 ct.gov UTF 8 - Special
<b>Business rules</b>	<b>Value Allowed:</b> Yes <b>Relationship:</b> n/a <b>Concept:</b> Protocol Title
<b>Duplicate field in other sections</b>	

39

<b>Term (Variable)</b>	Sponsor Confidentiality Statement
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	H
<b>Definition</b>	Heading
<b>User Guidance</b>	
<b>Conformance</b>	Optional
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Title Page
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	Sponsor confidentiality statement
<b>Business rules</b>	<b>Value Allowed:</b> Yes <b>Relationship:</b> Table row heading <b>Concept:</b> n/a
<b>Duplicate field in other sections</b>	

40

<b>Term (Variable)</b>	Sponsor Confidentiality Statement
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	D
<b>Definition</b>	
<b>User Guidance</b>	Insert a sponsor confidentiality statement, if applicable, otherwise delete.
<b>Conformance</b>	Optional
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Title page
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	
<b>Business rules</b>	<b>Value Allowed:</b> n/a <b>Relationship:</b> n/a <b>Concept:</b> n/a
<b>Duplicate field in other sections</b>	

41

<b>Term (Variable)</b>	Protocol Number
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	H
<b>Definition</b>	Heading
<b>User Guidance</b>	
<b>Conformance</b>	Required
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Title Page
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	Protocol number
<b>Business rules</b>	<b>Value Allowed:</b> Yes <b>Relationship:</b> Table row heading <b>Concept:</b> n/a
<b>Duplicate field in other sections</b>	

42



<b>Term (Variable)</b>	Protocol Number
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	D
<b>Definition</b>	A unique alphanumeric identifier for the trial.
<b>User Guidance</b>	A unique alphanumeric identifier for the trial, designated by the sponsor, is a standard part of trial data, and should be included for most studies. Some exceptions may exist, however, so this is an optional field.
<b>Conformance</b>	Required
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Title page
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	AN
<b>Business rules</b>	<b>Value Allowed:</b> Yes <b>Relationship:</b> n/a <b>Concept:</b> Protocol identifying number  Note: May be blank (null)
<b>Duplicate field in other sections</b>	

43

<b>Term (Variable)</b>	Version
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	H
<b>Definition</b>	Heading
<b>User Guidance</b>	
<b>Conformance</b>	Optional
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Title Page
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	Version
<b>Business rules</b>	<b>Value Allowed:</b> Yes <b>Relationship:</b> Table row heading <b>Concept:</b> n/a
<b>Duplicate field in other sections</b>	

44

<b>Term (Variable)</b>	Version
<b>Data Type</b>	Number
<b>Topic, Value or Header</b>	D
<b>Definition</b>	
<b>User Guidance</b>	An optional field for use by the sponsor at their discretion.
<b>Conformance</b>	Optional
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Title page
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	10N
<b>Business rules</b>	<b>Value Allowed:</b> Yes <b>Relationship:</b> n/a <b>Concept:</b> Amendment number
<b>Duplicate field in other sections</b>	

45

<b>Term (Variable)</b>	Amendment Number
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	H
<b>Definition</b>	Heading
<b>User Guidance</b>	
<b>Conformance</b>	Required
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Title page
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	Amendment Number
<b>Business rules</b>	<b>Value Allowed:</b> Yes <b>Relationship:</b> Table row heading <b>Concept:</b> n/a
<b>Duplicate field in other sections</b>	

46

<b>Term (Variable)</b>	Amendment Number
<b>Data Type</b>	Number
<b>Topic, Value or Header</b>	D
<b>Definition</b>	
<b>User Guidance</b>	Enter the version, number, or amendment number. If this is the original instance of the protocol, indicate Not Applicable.
<b>Conformance</b>	Conditional
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Title page
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	10N
<b>Business rules</b>	<b>Value Allowed:</b> n/a <b>Relationship:</b> n/a <b>Concept:</b> Amendment number
<b>Duplicate field in other sections</b>	

47

<b>Term (Variable)</b>	Amendment Scope
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	H
<b>Definition</b>	Heading
<b>User Guidance</b>	
<b>Conformance</b>	Required
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Title Page
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	Amendment Scope
<b>Business rules</b>	<b>Value Allowed:</b> Yes <b>Relationship:</b> Table row heading <b>Concept:</b> n/a
<b>Duplicate field in other sections</b>	

48

<b>Term (Variable)</b>	Amendment Scope
<b>Data Type</b>	Pick list
<b>Topic, Value or Header</b>	D
<b>Definition</b>	
<b>User Guidance</b>	Acceptable entries for amendment scope are: "Global" or "Country-specific/Regional"
<b>Conformance</b>	Required
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Title page
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	Global or Country-specific/Regional
<b>Business rules</b>	<b>Value Allowed:</b> Yes <b>Relationship:</b> n/a <b>Concept:</b> n/a
<b>Duplicate field in other sections</b>	

49

<b>Term (Variable)</b>	Country/Region or Local Identifier
<b>Data Type</b>	Pick list
<b>Topic, Value or Header</b>	D
<b>Definition</b>	
<b>User Guidance</b>	Use the ISO-3166 region or local identifier (i.e., DE or EU). For global trials delete the Region or Local Identifier field.
<b>Conformance</b>	Required/Conditional
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Title page
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	ISO 3166 for country and region blank for global
<b>Business rules</b>	<b>Value Allowed:</b> Yes <b>Relationship:</b> n/a <b>Concept:</b> n/a
<b>Duplicate field in other sections</b>	Repeatable

50

<b>Term (Variable)</b>	Compound Number(s)
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	H
<b>Definition</b>	Heading
<b>User Guidance</b>	
<b>Conformance</b>	Required
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Title Page
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	Compound Number
<b>Business rules</b>	<b>Value Allowed:</b> Yes <b>Relationship:</b> Table row heading <b>Concept:</b> n/a
<b>Duplicate field in other sections</b>	

51

<b>Term (Variable)</b>	Compound Number
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	D
<b>Definition</b>	Enter the Sponsor's unique identifier for investigational compound(s) in the trial. Add or delete additional fields as needed.
<b>User Guidance</b>	
<b>Conformance</b>	Optional
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Title Page
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	AN
<b>Business rules</b>	<b>Value Allowed:</b> Yes <b>Relationship:</b> n/a <b>Concept:</b> n/a
<b>Duplicate field in other sections</b>	Repeatable

52

<b>Term (Variable)</b>	Compound Number
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	D
<b>Definition</b>	Enter the Sponsor's unique identifier for investigational compound(s) in the trial. Add or delete additional fields as needed.
<b>User Guidance</b>	
<b>Conformance</b>	Optional
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Title Page
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	AN
<b>Business rules</b>	<b>Value Allowed:</b> Yes <b>Relationship:</b> n/a <b>Concept:</b> n/a
<b>Duplicate field in other sections</b>	Repeatable

53

<b>Term (Variable)</b>	Compound Name(s)
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	H
<b>Definition</b>	Heading
<b>User Guidance</b>	
<b>Conformance</b>	Optional
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Title Page
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	Compound name(s)
<b>Business rules</b>	<b>Value Allowed:</b> n/a <b>Relationship:</b> Table row heading <b>Concept:</b> n/a
<b>Duplicate field in other sections</b>	

54

<b>Term (Variable)</b>	Nonproprietary Name
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	D
<b>Definition</b>	
<b>User Guidance</b>	Delete this line if a nonproprietary name has not yet been assigned. Omit proprietary name fields if not yet established.
<b>Conformance</b>	Optional
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Title Page
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	300AN
<b>Business rules</b>	<b>Value Allowed:</b> n/a <b>Relationship:</b> n/a <b>Concept:</b> n/a
<b>Duplicate field in other sections</b>	Repeatable

55

<b>Term (Variable)</b>	Proprietary Name
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	D
<b>Definition</b>	
<b>User Guidance</b>	Omit proprietary name fields if not yet established.
<b>Conformance</b>	Optional / Conditional
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Title Page
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	
<b>Business rules</b>	<b>Value Allowed:</b> n/a <b>Relationship:</b> n/a <b>Concept:</b> Clinical trial phase
<b>Duplicate field in other sections</b>	

56

<b>Term (Variable)</b>	Additional Proprietary Name
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	D
<b>Definition</b>	
<b>User Guidance</b>	Omit proprietary name fields if not yet established.
<b>Conformance</b>	Optional / Conditional
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Title Page
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	
<b>Business rules</b>	<b>Value Allowed:</b> n/a <b>Relationship:</b> n/a <b>Concept:</b> n/a
<b>Duplicate field in other sections</b>	Repeatable

57

<b>Term (Variable)</b>	Trial Phase
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	H
<b>Definition</b>	Heading
<b>User Guidance</b>	
<b>Conformance</b>	
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Title Page
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	Trial phase
<b>Business rules</b>	<b>Value Allowed:</b> Yes <b>Relationship:</b> Table row heading <b>Concept:</b>
<b>Duplicate field in other sections</b>	

58



<b>Term (Variable)</b>	Trial Phase
<b>Data Type</b>	Pick list
<b>Topic, Value or Header</b>	D
<b>Definition</b>	
<b>User Guidance</b>	For trials combining investigational drugs or vaccines with devices, classify according to the phase of drug development.
<b>Conformance</b>	Required
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Title Page
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	Early Phase 1 Phase 1 Phase 1/Phase 2 Phase 2 Phase 2/Phase 3 Phase 3 Phase 4 Other
<b>Business rules</b>	<b>Value Allowed:</b> yes <b>Relationship:</b> n/a <b>Concept:</b> Protocol short title
<b>Duplicate field in other sections</b>	

Term (Variable)	Acronym
Data Type	Text
Topic, Value or Header	H
Definition	Heading
User Guidance	
Conformance	Optional
Cardinality	
Relationship content from ToC representing the protocol hierarchy	Title Page
Relationship (reference to high level conceptual model)	
Value	Acronym
Business rules	<b>Value Allowed:</b> Yes <b>Relationship:</b> Table row heading <b>Concept:</b> n/a
Duplicate field in other sections	

60

Term (Variable)	Short Title
Data Type	Text
Topic, Value or Header	H
Definition	Heading
User Guidance	
Conformance	Required
Cardinality	
Relationship content from ToC representing the protocol hierarchy	Title Page
Relationship (reference to high level conceptual model)	
Value	Short Title
Business rules	<b>Value Allowed:</b> Yes <b>Relationship:</b> Table row heading <b>Concept:</b>
Duplicate field in other sections	

61

<b>Term (Variable)</b>	Short Title
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	D
<b>Definition</b>	Explains in plain language what the trial is about and is suitable for use as "Brief Title" or "Title in Plain Language" in global clinical trial registries. It can also be suitable for use with informed consents and ethics committee submissions.
<b>User Guidance</b>	
<b>Conformance</b>	Required
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Title page
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	300AN
<b>Business rules</b>	<b>Value Allowed:</b> n/a <b>Relationship:</b> n/a <b>Concept:</b> Sponsor
<b>Duplicate field in other sections</b>	

62

<b>Term (Variable)</b>	Sponsor Name and Address
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	H
<b>Definition</b>	Heading
<b>User Guidance</b>	
<b>Conformance</b>	Required
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Title page
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	Sponsor Name and Address
<b>Business rules</b>	<b>Value Allowed:</b> Yes <b>Relationship:</b> Table row heading <b>Concept:</b> Sponsor
<b>Duplicate field in other sections</b>	

63

<b>Term (Variable)</b>	Sponsor Name
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	D
<b>Definition</b>	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.
<b>User Guidance</b>	If more than one sponsor, list the Primary Sponsor in this field.
<b>Conformance</b>	Required
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Title Page
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	
<b>Business rules</b>	<b>Value Allowed:</b> n/a <b>Relationship:</b> n/a <b>Concept:</b> n/a
<b>Duplicate field in other sections</b>	

64

<b>Term (Variable)</b>	Sponsor Legal Address
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	D
<b>Definition</b>	Legal address
<b>User Guidance</b>	The legal address of the individual or pharmaceutical or medical device company, governmental agency, academic institution, private organisation, or other organisation who takes primary responsibility for and initiates a clinical investigation.
<b>Conformance</b>	Required
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Title Page
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	
<b>Business rules</b>	<b>Value Allowed:</b> n/a <b>Relationship:</b> n/a <b>Concept:</b> n/a
<b>Duplicate field in other sections</b>	

65

<b>Term (Variable)</b>	Local Sponsor Name and Address
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	H
<b>Definition</b>	Heading
<b>User Guidance</b>	
<b>Conformance</b>	Optional
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Title Page
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	Local Sponsor Name and Address
<b>Business rules</b>	<b>Value Allowed:</b> Yes <b>Relationship:</b> n/a <b>Concept:</b> n/a
<b>Duplicate field in other sections</b>	

66

<b>Term (Variable)</b>	Sponsor Local Name
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	D
<b>Definition</b>	In some countries, the clinical trial Sponsor may be the local affiliate company (or designee). In such cases, indicate in the Sponsor Local Name.
<b>User Guidance</b>	If more than one sponsor, list the Primary Sponsor in this field.
<b>Conformance</b>	Optional
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Title page
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	
<b>Business rules</b>	<b>Value Allowed:</b> n/a <b>Relationship:</b> n/a <b>Concept:</b> n/a
<b>Duplicate field in other sections</b>	

67

68

<b>Term (Variable)</b>	Sponsor Local Address
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	D
<b>Definition</b>	Sponsor local registered address
<b>User Guidance</b>	In some countries, the clinical trial Sponsor may be the local affiliate company (or designee). In such cases, indicate in the Sponsor Local Address Field.
<b>Conformance</b>	Optional
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Title page
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	
<b>Business rules</b>	<b>Value Allowed:</b> n/a <b>Relationship:</b> n/a <b>Concept:</b> n/a
<b>Duplicate field in other sections</b>	

69

<b>Term (Variable)</b>	Manufacturer Name and Address
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	H
<b>Definition</b>	Heading
<b>User Guidance</b>	
<b>Conformance</b>	Optional
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Title Page
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	Manufacturer Name and Address
<b>Business rules</b>	<b>Value Allowed:</b> Yes <b>Relationship:</b> Table row heading <b>Concept:</b> Regulatory investigational product number
<b>Duplicate field in other sections</b>	Repeatable

70

<b>Term (Variable)</b>	Device Manufacturer Name
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	D
<b>Definition</b>	
<b>User Guidance</b>	<p>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.</p> <p>Add additional fields as needed if multiple investigational devices will be used in the trial. Delete this line from the table if not applicable.</p>
<b>Conformance</b>	Optional
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Title Page
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	
<b>Business rules</b>	<p><b>Value Allowed:</b> n/a</p> <p><b>Relationship:</b> n/a</p> <p><b>Concept:</b> n/a</p>
<b>Duplicate field in other sections</b>	Repeatable

<b>Term (Variable)</b>	Device Manufacturer Address
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	D
<b>Definition</b>	
<b>User Guidance</b>	<p>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.</p> <p>Add additional fields as needed if multiple investigational devices will be used in the trial. Delete this line from the table if not applicable.</p>
<b>Conformance</b>	Optional
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Title Page
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	
<b>Business rules</b>	<p><b>Value Allowed:</b> n/a</p> <p><b>Relationship:</b> n/a</p> <p><b>Concept:</b> n/a</p>
<b>Duplicate field in other sections</b>	Repeatable



<b>Term (Variable)</b>	Regulatory Agency Identifier Number(s)
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	H
<b>Definition</b>	
<b>User Guidance</b>	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.
<b>Conformance</b>	Required
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Title Page
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	Regulatory Agency Identifier Number(s):
<b>Business rules</b>	<b>Value Allowed:</b> Yes <b>Relationship:</b> Table row heading <b>Concept:</b> Regulatory investigational product number
<b>Duplicate field in other sections</b>	

73

<b>Term (Variable)</b>	EUDAMED
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	H
<b>Definition</b>	
<b>User Guidance</b>	
<b>Conformance</b>	Optional /
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Title Page
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	EUDAMED
<b>Business rules</b>	<b>Value Allowed:</b> Yes <b>Relationship:</b> n/a <b>Concept:</b> Protocol approval date
<b>Duplicate field in other sections</b>	

74

<b>Term (Variable)</b>	EUDAMED Number
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	D
<b>Definition</b>	
<b>User Guidance</b>	
<b>Conformance</b>	Optional / Conditional
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Title Page
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	
<b>Business rules</b>	<b>Value Allowed:</b> n/a <b>Relationship:</b> n/a <b>Concept:</b> n/a
<b>Duplicate field in other sections</b>	

75

<b>Term (Variable)</b>	EudraCT Number
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	H
<b>Definition</b>	
<b>User Guidance</b>	
<b>Conformance</b>	Optional
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Title Page
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	EudraCT Number
<b>Business rules</b>	<b>Value Allowed:</b> Yes <b>Relationship:</b> n/a <b>Concept:</b> Protocol approval date
<b>Duplicate field in other sections</b>	

76

<b>Term (Variable)</b>	EudraCT Number
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	D
<b>Definition</b>	
<b>User Guidance</b>	
<b>Conformance</b>	Optional / Conditional
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Title Page
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	
<b>Business rules</b>	<b>Value Allowed:</b> n/a <b>Relationship:</b> n/a <b>Concept:</b> n/a
<b>Duplicate field in other sections</b>	

77

<b>Term (Variable)</b>	EU Trial Number
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	H
<b>Definition</b>	
<b>User Guidance</b>	
<b>Conformance</b>	Optional
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Title Page
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	EU Trial Number
<b>Business rules</b>	<b>Value Allowed:</b> Yes <b>Relationship:</b> n/a <b>Concept:</b> Protocol approval date
<b>Duplicate field in other sections</b>	

78

<b>Term (Variable)</b>	EU Trial Number
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	D
<b>Definition</b>	
<b>User Guidance</b>	
<b>Conformance</b>	Optional / Conditional
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Title Page
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	
<b>Business rules</b>	<b>Value Allowed:</b> n/a <b>Relationship:</b> n/a <b>Concept:</b> n/a
<b>Duplicate field in other sections</b>	

79

<b>Term (Variable)</b>	IDE
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	H
<b>Definition</b>	
<b>User Guidance</b>	
<b>Conformance</b>	Optional
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Title page
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	IDE
<b>Business rules</b>	<b>Value Allowed:</b> Yes <b>Relationship:</b> n/a <b>Concept:</b> Protocol approval date
<b>Duplicate field in other sections</b>	

80

<b>Term (Variable)</b>	IDE Number
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	D
<b>Definition</b>	
<b>User Guidance</b>	
<b>Conformance</b>	Optional / Conditional
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Title Page
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	
<b>Business rules</b>	<b>Value Allowed:</b> n/a <b>Relationship:</b> n/a <b>Concept:</b> n/a
<b>Duplicate field in other sections</b>	

81

<b>Term (Variable)</b>	IND Number
<b>Data Type</b>	
<b>Topic, Value or Header</b>	H
<b>Definition</b>	
<b>User Guidance</b>	
<b>Conformance</b>	Optional
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Title Page
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	IND
<b>Business rules</b>	<b>Value Allowed:</b> Yes <b>Relationship:</b> n/a <b>Concept:</b> Protocol approval date
<b>Duplicate field in other sections</b>	

82

<b>Term (Variable)</b>	IND Number
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	D
<b>Definition</b>	
<b>User Guidance</b>	
<b>Conformance</b>	Optional / Conditional
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Title page
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	
<b>Business rules</b>	<b>Value Allowed:</b> n/a <b>Relationship:</b> n/a <b>Concept:</b> n/a
<b>Duplicate field in other sections</b>	

83

<b>Term (Variable)</b>	jRCT
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	H
<b>Definition</b>	
<b>User Guidance</b>	
<b>Conformance</b>	Optional /
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Title Page
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	jRCT
<b>Business rules</b>	<b>Value Allowed:</b> Yes <b>Relationship:</b> n/a <b>Concept:</b> Protocol approval date
<b>Duplicate field in other sections</b>	

84

<b>Term (Variable)</b>	jRCT Number
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	D
<b>Definition</b>	
<b>User Guidance</b>	
<b>Conformance</b>	Optional / Conditional
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Title Page
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	
<b>Business rules</b>	<b>Value Allowed:</b> n/a <b>Relationship:</b> n/a <b>Concept:</b> n/a
<b>Duplicate field in other sections</b>	

85

<b>Term (Variable)</b>	NCT
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	H
<b>Definition</b>	
<b>User Guidance</b>	
<b>Conformance</b>	Optional /
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Title page
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	NTC
<b>Business rules</b>	<b>Value Allowed:</b> Yes <b>Relationship:</b> n/a <b>Concept:</b> Protocol approval date
<b>Duplicate field in other sections</b>	

86

<b>Term (Variable)</b>	NCT Number
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	D
<b>Definition</b>	
<b>User Guidance</b>	
<b>Conformance</b>	Optional / Conditional
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Title Page
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	
<b>Business rules</b>	<b>Value Allowed:</b> n/a <b>Relationship:</b> n/a <b>Concept:</b> n/a
<b>Duplicate field in other sections</b>	

87

<b>Term (Variable)</b>	NMPA IND
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	H
<b>Definition</b>	
<b>User Guidance</b>	
<b>Conformance</b>	Optional
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Title Page
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	NMPA IND
<b>Business rules</b>	<b>Value Allowed:</b> Yes <b>Relationship:</b> n/a <b>Concept:</b> Protocol approval date
<b>Duplicate field in other sections</b>	

88



<b>Term (Variable)</b>	NMPA IND Number
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	D
<b>Definition</b>	
<b>User Guidance</b>	
<b>Conformance</b>	Optional / Conditional
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Title Page
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	
<b>Business rules</b>	<b>Value Allowed:</b> n/a <b>Relationship:</b> n/a <b>Concept:</b> Protocol approval date
<b>Duplicate field in other sections</b>	

89

<b>Term (Variable)</b>	WHO
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	H
<b>Definition</b>	
<b>User Guidance</b>	
<b>Conformance</b>	Optional /
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Title Page
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	WHO
<b>Business rules</b>	<b>Value Allowed:</b> Yes <b>Relationship:</b> n/a <b>Concept:</b> Protocol approval date
<b>Duplicate field in other sections</b>	

90

<b>Term (Variable)</b>	WHO Number
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	D
<b>Definition</b>	
<b>User Guidance</b>	
<b>Conformance</b>	Optional / Conditional
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Title Page
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	
<b>Business rules</b>	<b>Value Allowed:</b> n/a <b>Relationship:</b> n/a <b>Concept:</b> n/a
<b>Duplicate field in other sections</b>	

91

<b>Term (Variable)</b>	Other
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	H
<b>Definition</b>	
<b>User Guidance</b>	
<b>Conformance</b>	Optional
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Title Page
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	Other
<b>Business rules</b>	<b>Value Allowed:</b> Yes <b>Relationship:</b> n/a <b>Concept:</b> Protocol approval date
<b>Duplicate field in other sections</b>	

92

<b>Term (Variable)</b>	Other Number
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	D
<b>Definition</b>	
<b>User Guidance</b>	
<b>Conformance</b>	Optional / Conditional
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Title Page
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	
<b>Business rules</b>	<b>Value Allowed:</b> n/a <b>Relationship:</b> n/a <b>Concept:</b> n/a
<b>Duplicate field in other sections</b>	Repeatable

93

<b>Term (Variable)</b>	Sponsor Approval Date
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	H
<b>Definition</b>	Heading
<b>User Guidance</b>	
<b>Conformance</b>	Required / Required
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Title page
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	Sponsor Approval Date
<b>Business rules</b>	<b>Value Allowed:</b> Yes <b>Relationship:</b> Table row heading <b>Concept:</b> n/a
<b>Duplicate field in other sections</b>	

94

<b>Term (Variable)</b>	Approval Date
<b>Data Type</b>	Date
<b>Topic, Value or Header</b>	D
<b>Definition</b>	
<b>User Guidance</b>	All versions should be uniquely identifiable. Use the date format (dd/mmm/yyyy, for example 07/JUN/2015) to indicate the date the protocol (or amendment) was approved by the Sponsor.
<b>Conformance</b>	Required Choice
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Title Page
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	dd/mmm/yyyy date format
<b>Business rules</b>	<b>Value Allowed:</b> Yes <b>Relationship:</b> n/a <b>Concept:</b> n/a
<b>Duplicate field in other sections</b>	

95

<b>Term (Variable)</b>	The approval date is included with the electronic signature, located {describe location}
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	D
<b>Definition</b>	
<b>User Guidance</b>	
<b>Conformance</b>	Required / Choice
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Title page
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	
<b>Business rules</b>	<b>Value Allowed:</b> n/a <b>Relationship:</b> n/a <b>Concept:</b> Sponsor representative
<b>Duplicate field in other sections</b>	

96

<b>Term (Variable)</b>	Sponsor Signatory
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	H
<b>Definition</b>	Function(s) and roles authorised by the sponsor to sign the protocol and any substantial amendments.
<b>User Guidance</b>	
<b>Conformance</b>	Conditional
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Title Page
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	Sponsor Signatory
<b>Business rules</b>	<b>Value Allowed:</b> Yes <b>Relationship:</b> IF "CHOICE, THEN approval date is included with the electronic signature <b>Concept:</b> n/a
<b>Duplicate field in other sections</b>	

97

<b>Term (Variable)</b>	Wet Signature image
<b>Data Type</b>	Image
<b>Topic, Value or Header</b>	D
<b>Definition</b>	
<b>User Guidance</b>	Where allowed, an electronic/digital signature may be used for approval rather than a wet signature. In such cases, replace the signature block with appropriate description of the electronic/digital approval and the location of relevant information for traceability.
<b>Conformance</b>	Optional
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Title Page
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	
<b>Business rules</b>	<b>Value Allowed:</b> n/a <b>Relationship:</b> n/a <b>Concept:</b> n/a
<b>Duplicate field in other sections</b>	

98

<b>Term (Variable)</b>	Digital Signature
<b>Data Type</b>	Image
<b>Topic, Value or Header</b>	D
<b>Definition</b>	
<b>User Guidance</b>	
<b>Conformance</b>	Optional
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Title Page
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	
<b>Business rules</b>	<b>Value Allowed:</b> n/a <b>Relationship:</b> n/a <b>Concept:</b> n/a
<b>Duplicate field in other sections</b>	

99

<b>Term (Variable)</b>	Name
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	D
<b>Definition</b>	
<b>User Guidance</b>	
<b>Conformance</b>	Optional
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Title page
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	
<b>Business rules</b>	<b>Value Allowed:</b> n/a <b>Relationship:</b> n/a <b>Concept:</b> n/a
<b>Duplicate field in other sections</b>	

100

<b>Term (Variable)</b>	Title of Sponsor Signatory
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	D
<b>Definition</b>	
<b>User Guidance</b>	
<b>Conformance</b>	Optional
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Title Page
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	
<b>Business rules</b>	<b>Value Allowed:</b> n/a <b>Relationship:</b> n/a <b>Concept:</b> n/a
<b>Duplicate field in other sections</b>	

101

<b>Term (Variable)</b>	Sponsor Signatory Date
<b>Data Type</b>	Date
<b>Topic, Value or Header</b>	D
<b>Definition</b>	
<b>User Guidance</b>	
<b>Conformance</b>	Optional
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Title Page
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	dd/mmm/yyyy date format
<b>Business rules</b>	<b>Value Allowed:</b> Yes <b>Relationship:</b> n/a <b>Concept:</b> n/a
<b>Duplicate field in other sections</b>	

102

<b>Term (Variable)</b>	[This protocol was approved via {describe method} as described on the approval page appended to the document]
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	D
<b>Definition</b>	
<b>User Guidance</b>	Where allowed, an electronic/digital signature may be used for approval rather than a wet signature. In such cases, replace the signature block with appropriate description of the electronic/digital approval and the location of relevant information for traceability.
<b>Conformance</b>	Optional
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Title Page
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	[This protocol was approved via {describe method} as described on the approval page appended to the document]
<b>Business rules</b>	<b>Value Allowed:</b> Yes <b>Relationship:</b> n/a <b>Concept:</b> n/a
<b>Duplicate field in other sections</b>	

103

<b>Term (Variable)</b>	{describe method}
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	D
<b>Definition</b>	
<b>User Guidance</b>	Where allowed, an electronic/digital signature may be used for approval rather than a wet signature. In such cases, replace the signature block with appropriate description of the electronic/digital approval and the location of relevant information for traceability.
<b>Conformance</b>	Optional / Conditional
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Investigator Signature Page
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	
<b>Business rules</b>	Not transferred during IND/CTA process
<b>Duplicate field in other sections</b>	

104



<b>Term (Variable)</b>	Medical Monitor Name and Contact Information
<b>Data Type</b>	
<b>Topic, Value or Header</b>	
<b>Definition</b>	
<b>User Guidance</b>	
<b>Conformance</b>	
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Investigator Signature Page
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	
<b>Business rules</b>	
<b>Duplicate field in other sections</b>	

105

<b>Term (Variable)</b>	Medical Monitor Institution Name
<b>Data Type</b>	
<b>Topic, Value or Header</b>	
<b>Definition</b>	
<b>User Guidance</b>	
<b>Conformance</b>	
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Investigator Signature Page
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	
<b>Business rules</b>	Not transferred during IND/CTA process
<b>Duplicate field in other sections</b>	

106

<b>Term (Variable)</b>	Medical Monitor Institution Address
<b>Data Type</b>	
<b>Topic, Value or Header</b>	
<b>Definition</b>	
<b>User Guidance</b>	
<b>Conformance</b>	
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Investigator Signature Page
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	
<b>Business rules</b>	
<b>Duplicate field in other sections</b>	

107

<b>Term (Variable)</b>	Provided Separately/can be found {describe location}]
<b>Data Type</b>	
<b>Topic, Value or Header</b>	
<b>Definition</b>	
<b>User Guidance</b>	
<b>Conformance</b>	
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Investigator Signature Page
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	
<b>Business rules</b>	Not transferred during IND/CTA process
<b>Duplicate field in other sections</b>	

108

<b>Term (Variable)</b>	{describe location}
<b>Data Type</b>	
<b>Topic, Value or Header</b>	
<b>Definition</b>	
<b>User Guidance</b>	
<b>Conformance</b>	
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Investigator Signature Page
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	
<b>Business rules</b>	Not transferred during IND/CTA process
<b>Duplicate field in other sections</b>	

109

<b>Term (Variable)</b>	Report Serious Adverse Events within 24 hours {via E-mail/fax provided in the site manual. /per the options below:}
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	H
<b>Definition</b>	Heading
<b>User Guidance</b>	
<b>Conformance</b>	Required / Required
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Investigator Signature Page
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	Report Serious Adverse Events within 24 hours {via E-mail/fax provided in the site manual. /per the options below:}
<b>Business rules</b>	<b>Value Allowed:</b> Not transferred during IND/CTA process <b>Relationship:</b> n/a <b>Concept:</b> n/a
<b>Duplicate field in other sections</b>	

110

<b>Term (Variable)</b>	Email
<b>Data Type</b>	
<b>Topic, Value or Header</b>	
<b>Definition</b>	
<b>User Guidance</b>	
<b>Conformance</b>	
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Investigator Signature Page
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	Email:
<b>Business rules</b>	Not transferred during IND/CTA process
<b>Duplicate field in other sections</b>	

111

<b>Term (Variable)</b>	{Rapid Alert email address}
<b>Data Type</b>	
<b>Topic, Value or Header</b>	
<b>Definition</b>	
<b>User Guidance</b>	
<b>Conformance</b>	
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Investigator Signature Page
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	
<b>Business rules</b>	Not transferred during IND/CTA process
<b>Duplicate field in other sections</b>	

112

<b>Term (Variable)</b>	Fax
<b>Data Type</b>	
<b>Topic, Value or Header</b>	
<b>Definition</b>	
<b>User Guidance</b>	
<b>Conformance</b>	
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Investigator Signature Page
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	
<b>Business rules</b>	Not transferred during IND/CTA process
<b>Duplicate field in other sections</b>	

113

<b>Term (Variable)</b>	{Rapid Alert Fax Number"
<b>Data Type</b>	
<b>Topic, Value or Header</b>	
<b>Definition</b>	
<b>User Guidance</b>	
<b>Conformance</b>	
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Investigator Signature Page
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	
<b>Business rules</b>	Not transferred during IND/CTA process
<b>Duplicate field in other sections</b>	

114

115

<b>Term (Variable)</b>	Amendment Details
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	H
<b>Definition</b>	
<b>User Guidance</b>	Delete this entire section if this is the original protocol.
<b>Conformance</b>	Required / Required
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Amendment Details
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	Amendment Details
<b>Business rules</b>	<b>Value Allowed:</b> Yes <b>Relationship:</b> n/a <b>Concept:</b> n/a
<b>Duplicate field in other sections</b>	Not required for original

<b>Term (Variable)</b>	History of Amendment
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	H
<b>Definition</b>	Heading
<b>User Guidance</b>	<p>Do not include the current amendment in the table below, as final approval dates are often difficult to predict during document preparation. Previous amendments, including regional amendments, should appear in reverse chronological order with the most recent at the top (for example, Amendment 3, 2, 1). Delete lines not needed, add lines as needed.</p> <p>Some regulatory agencies find the approximate number or percent of enrollment at the time of each amendment to be helpful, and the information can be repurposed in final trial reports; however, it is neither a protocol requirement of any agency nor expected universally. If including the column with enrollment numbers, list approximate global enrollment total or percentage at the time of the amendment and select "globally". For local amendments, list the approximate local enrollment total or percentage at the time of the amendment and select "locally".</p>
<b>Conformance</b>	Required
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Amendment Details
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	History of Amendment
<b>Business rules</b>	<b>Value Allowed:</b> Yes <b>Relationship:</b> n/a <b>Concept:</b> n/a
<b>Duplicate field in other sections</b>	

<b>Term (Variable)</b>	{#/A total of #} prior {global} amendments have occurred, as shown in the table below:
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	H
<b>Definition</b>	
<b>User Guidance</b>	<p>Do not include the current amendment in the table below, as final approval dates are often difficult to predict during document preparation. Previous amendments should appear in reverse chronological order with the most recent at the top (for example, Amendment 3, 2, 1). Delete lines not needed, add lines as needed. Inclusion of regional-, country-, and site-specific amendments in the table is optional. If included, ensure that the scope is clearly distinguishable from global amendments. If including the column with enrollment numbers, follow the instructions below.</p> <ul style="list-style-type: none"> <li>• For global amendments, list approximate global enrollment total or percentage at the time of the amendment and select "globally".</li> <li>• For local amendments, list the approximate local enrollment total or percentage at the time of the amendment and select "locally".</li> </ul>
<b>Conformance</b>	Required
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Amendment Details
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	{#/A total of #} prior {global} amendments have occurred, as shown in the table below:
<b>Business rules</b>	<p><b>Value Allowed:</b> Yes</p> <p><b>Relationship:</b> n/a</p> <p><b>Concept:</b> n/a</p>
<b>Duplicate field in other sections</b>	



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

119

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

120

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

121

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

122

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

123

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

124

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

125

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

126

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

127

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

128

<b>Term (Variable)</b>	The table below provides an overview of the current amendment
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	H
<b>Definition</b>	
<b>User Guidance</b>	
<b>Conformance</b>	Optional
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Amendment Details
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	The table below provides an overview of the current amendment
<b>Business rules</b>	<b>Value Allowed:</b> Yes <b>Relationship:</b> n/a <b>Concept:</b> n/a
<b>Duplicate field in other sections</b>	Not included in original

129

<b>Term (Variable)</b>	Amendment Number
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	H
<b>Definition</b>	
<b>User Guidance</b>	
<b>Conformance</b>	Required
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Amendment Details
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	Amendment Number
<b>Business rules</b>	<b>Value Allowed:</b> Yes <b>Relationship:</b> n/a <b>Concept:</b> n/a
<b>Duplicate field in other sections</b>	

130

<b>Term (Variable)</b>	Amendment Number
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	D
<b>Definition</b>	
<b>User Guidance</b>	
<b>Conformance</b>	Required
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Amendment Details
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	
<b>Business rules</b>	<b>Value Allowed:</b> n/a <b>Relationship:</b> n/a <b>Concept:</b> n/a
<b>Duplicate field in other sections</b>	Row 23 in BoR

131

<b>Term (Variable)</b>	Approximate {(#/%)} enrolled
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	H
<b>Definition</b>	
<b>User Guidance</b>	
<b>Conformance</b>	Required
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Amendment Details
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	Approximate {(#/%)} enrolled
<b>Business rules</b>	<b>Value Allowed:</b> Yes <b>Relationship:</b> n/a <b>Concept:</b> n/a
<b>Duplicate field in other sections</b>	

132

<b>Term (Variable)</b>	Number or %
<b>Data Type</b>	Integer
<b>Topic, Value or Header</b>	D
<b>Definition</b>	Estimated # of participants enrolled as a percentage of the expected total.
<b>User Guidance</b>	Good estimates are adequate, as precise enrolment figures will likely be changing while an amendment is being prepared.
<b>Conformance</b>	Required
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Amendment Details
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	
<b>Business rules</b>	<b>Value Allowed:</b> n/a <b>Relationship:</b> n/a <b>Concept:</b> n/a
<b>Duplicate field in other sections</b>	Row 101 of BoR

133

<b>Term (Variable)</b>	Reason(s) for Amendment
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	H
<b>Definition</b>	
<b>User Guidance</b>	
<b>Conformance</b>	Required
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Amendment Details
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	Reason(s) for Amendment:
<b>Business rules</b>	<b>Value Allowed:</b> Yes <b>Relationship:</b> n/a <b>Concept:</b> n/a
<b>Duplicate field in other sections</b>	

134



<b>Term (Variable)</b>	Primary
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	H
<b>Definition</b>	
<b>User Guidance</b>	
<b>Conformance</b>	Required
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Amendment Details
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	Primary:
<b>Business rules</b>	<b>Value Allowed:</b> Yes <b>Relationship:</b> n/a <b>Concept:</b> n/a
<b>Duplicate field in other sections</b>	

<b>Term (Variable)</b>	Primary Reason for Amendment
<b>Data Type</b>	Pick list
<b>Topic, Value or Header</b>	D
<b>Definition</b>	
<b>User Guidance</b>	Choose from the available categories as the primary reason for the amendment. Select the closest match among the choices. Changes to key measures or endpoints should be listed as a change of strategy/objective. If none apply, choose "other" and provide a description. Categories are derived from Getz, et al., DIA TIRS, 2016 "The Impact of Protocol Amendments on Clinical Trial Performance and Cost".
<b>Conformance</b>	Required
<b>Cardinality</b>	Amendment Details
<b>Relationship content from ToC representing the protocol hierarchy</b>	
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	<ul style="list-style-type: none"> <li>• Regulatory agency request to amend</li> <li>• New regulatory guidance</li> <li>• IRB/IEC feedback</li> <li>• New safety information available</li> <li>• Manufacturing change</li> <li>• Adaptive clinical trial IMP addition</li> <li>• Change in strategy</li> <li>• Change in standard of care</li> <li>• New data available (other than safety data)</li> <li>• Investigator/site feedback</li> <li>• Recruitment difficulty</li> <li>• Inconsistency and/or error in the protocol</li> <li>• Protocol design error</li> </ul>
<b>Business rules</b>	<b>Value Allowed:</b> Yes <b>Relationship:</b> n/a <b>Concept:</b> n/a
<b>Duplicate field in other sections</b>	Multiple accepted

Term (Variable)	Other
Data Type	Text
Topic, Value or Header	H
Definition	
User Guidance	
Conformance	Optional
Cardinality	
Relationship content from ToC representing the protocol hierarchy	Amendment Details
Relationship (reference to high level conceptual model)	
Value	Other:
Business rules	<b>Value Allowed:</b> Yes <b>Relationship:</b> n/a <b>Concept:</b> n/a
Duplicate field in other sections	

137

Term (Variable)	Other description
Data Type	Text
Topic, Value or Header	D
Definition	
User Guidance	
Conformance	Optional
Cardinality	
Relationship content from ToC representing the protocol hierarchy	Amendment Details
Relationship (reference to high level conceptual model)	
Value	
Business rules	<b>Value Allowed:</b> n/a <b>Relationship:</b> n/a <b>Concept:</b> n/a
Duplicate field in other sections	

138

<b>Term (Variable)</b>	Primary Reason for Amendment
<b>Data Type</b>	Pick List
<b>Topic, Value or Header</b>	D
<b>Definition</b>	
<b>User Guidance</b>	
<b>Conformance</b>	Required / Required
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Amendment Details
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	<ul style="list-style-type: none"> <li>• Regulatory agency request to amend</li> <li>• New regulatory guidance</li> <li>• IRB/IEC feedback</li> <li>• New safety information available</li> <li>• Manufacturing change</li> <li>• Adaptive clinical trial IMP addition</li> <li>• Change in strategy</li> <li>• Change in standard of care</li> <li>• New data available (other than safety data)</li> <li>• Investigator/site feedback</li> <li>• Recruitment difficulty</li> <li>• Inconsistency and/or error in the protocol</li> <li>• Protocol design error</li> </ul>
<b>Business rules</b>	<b>Value Allowed:</b> Yes <b>Relationship:</b> n/a <b>Concept:</b> n/a
<b>Duplicate field in other sections</b>	Multiple accepted

Term (Variable)	Other
Data Type	Text
Topic, Value or Header	H
Definition	
User Guidance	
Conformance	Conditional / Optional
Cardinality	
Relationship content from ToC representing the protocol hierarchy	Amendment Details
Relationship (reference to high level conceptual model)	
Value	Other:
Business rules	<b>Value Allowed:</b> Yes <b>Relationship:</b> n/a <b>Concept:</b> n/a
Duplicate field in other sections	

140

Term (Variable)	Other description
Data Type	Text
Topic, Value or Header	D
Definition	
User Guidance	
Conformance	Conditional / Optional
Cardinality	
Relationship content from ToC representing the protocol hierarchy	Amendment Details
Relationship (reference to high level conceptual model)	
Value	
Business rules	<b>Value Allowed:</b> n/a <b>Relationship:</b> n/a <b>Concept:</b> n/a
Duplicate field in other sections	

141

<b>Term (Variable)</b>	Summary of Amendment
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	H
<b>Definition</b>	
<b>User Guidance</b>	
<b>Conformance</b>	Conditional / Required
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Amendment Details
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	Summary of Amendment
<b>Business rules</b>	<b>Value Allowed:</b> Yes <b>Relationship:</b> n/a <b>Concept:</b> n/a
<b>Duplicate field in other sections</b>	

142

<b>Term (Variable)</b>	Summary of Amendment
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	D
<b>Definition</b>	
<b>User Guidance</b>	
<b>Conformance</b>	Conditional / Required
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Amendment Details
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	
<b>Business rules</b>	<b>Value Allowed:</b> n/a <b>Relationship:</b> n/a <b>Concept:</b> n/a
<b>Duplicate field in other sections</b>	

143

<b>Term (Variable)</b>	Question
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	H
<b>Definition</b>	
<b>User Guidance</b>	
<b>Conformance</b>	Conditional / Required
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Amendment Details
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	Is this amendment likely to have a substantial impact on <ul style="list-style-type: none"> <li>• safety or rights of the subjects, or</li> <li>• on the reliability and robustness of the data generated in the clinical trial?</li> </ul>
<b>Business rules</b>	<b>Value Allowed:</b> Yes <b>Relationship:</b> n/a <b>Concept:</b> n/a
<b>Duplicate field in other sections</b>	

144

<b>Term (Variable)</b>	Yes/No
<b>Data Type</b>	Pick list
<b>Topic, Value or Header</b>	D
<b>Definition</b>	
<b>User Guidance</b>	
<b>Conformance</b>	Conditional / Required
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Amendment Details
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	Yes No
<b>Business rules</b>	<b>Value Allowed:</b> Yes <b>Relationship:</b> n/a <b>Concept:</b> n/a
<b>Duplicate field in other sections</b>	

145

<b>Term (Variable)</b>	Summary of Changes in Current Amendment
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	H
<b>Definition</b>	Section heading
<b>User Guidance</b>	<p>Follow the steps below to prepare the summary of changes.</p> <ul style="list-style-type: none"> <li>• If a Summary of Changes already exists from a prior amendment, move it to Section 12.5, History of Previous Amendments, and populate a clean summary table for the present amendment.</li> <li>• List the changes that apply to the current amendment. Provide a brief description of the change(s) and a brief scientific rationale for specific changes (for example, change to individual inclusion/exclusion criteria).</li> </ul> <p>Tabular presentation is common but not required. The page can be changed to landscape orientation if necessary.</p>
<b>Conformance</b>	Conditional / Required
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Amendment Details
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	Summary of Changes in Current Amendment
<b>Business rules</b>	<p><b>Value Allowed:</b> Yes</p> <p><b>Relationship:</b> n/a</p> <p><b>Concept:</b> Protocol short title</p>
<b>Duplicate field in other sections</b>	



<b>Term (Variable)</b>	Section # and Name
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	H
<b>Definition</b>	
<b>User Guidance</b>	
<b>Conformance</b>	Required
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Amendment Details
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	Section # and Name
<b>Business rules</b>	<b>Value Allowed:</b> Yes <b>Relationship:</b> Rows content <b>Concept:</b> Trial purpose summary
<b>Duplicate field in other sections</b>	Repeat until complete

147

<b>Term (Variable)</b>	Location of Change
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	D
<b>Definition</b>	
<b>User Guidance</b>	
<b>Conformance</b>	Required
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Amendment Details
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	
<b>Business rules</b>	<b>Value Allowed:</b> n/a <b>Relationship:</b> Rows content <b>Concept:</b> Trial purpose summary
<b>Duplicate field in other sections</b>	Repeat until complete

148

<b>Term (Variable)</b>	Description of Change
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	H
<b>Definition</b>	
<b>User Guidance</b>	
<b>Conformance</b>	Required
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Amendment Details
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	Description of Change
<b>Business rules</b>	<b>Value Allowed:</b> Yes <b>Relationship:</b> Rows content <b>Concept:</b> Primary Objective
<b>Duplicate field in other sections</b>	Repeat until complete

149

<b>Term (Variable)</b>	Description of Change
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	D
<b>Definition</b>	
<b>User Guidance</b>	
<b>Conformance</b>	Required
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Amendment Details
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	
<b>Business rules</b>	<b>Value Allowed:</b> n/a <b>Relationship:</b> Rows content <b>Concept:</b> Primary endpoint
<b>Duplicate field in other sections</b>	Repeat until complete

150

<b>Term (Variable)</b>	Brief Rationale for Change
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	H
<b>Definition</b>	
<b>User Guidance</b>	
<b>Conformance</b>	Required
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Amendment Details
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	Brief Rationale for Change
<b>Business rules</b>	<b>Value Allowed:</b> Yes <b>Relationship:</b> Rows content <b>Concept:</b> Primary endpoint
<b>Duplicate field in other sections</b>	Repeat until complete

151

<b>Term (Variable)</b>	Brief Rationale for Change
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	D
<b>Definition</b>	
<b>User Guidance</b>	
<b>Conformance</b>	Required
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Amendment Details
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	
<b>Business rules</b>	<b>Value Allowed:</b> n/a <b>Relationship:</b> Rows content <b>Concept:</b> n/a
<b>Duplicate field in other sections</b>	Repeat until complete

152

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

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

154 **1. Protocol Summary**

Term (Variable)	Protocol Summary
Data Type	Text
Topic, Value or Header	H
Definition	
User Guidance	No text is intended here (header only)
Conformance	Required
Cardinality	
Relationship content from ToC representing the protocol hierarchy	Protocol Summary
Relationship (reference to high level conceptual model)	
Value	1. Protocol Summary
Business rules	<b>Value Allowed:</b> Yes <b>Relationship:</b> n/a <b>Concept:</b> n/a
Duplicate field in other sections	

155

156 **1.1 Protocol Synopsis**

<b>Term (Variable)</b>	1.1 Protocol Synopsis
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	H
<b>Definition</b>	Header
<b>User Guidance</b>	The protocol synopsis is a short summary of the key points of the trial. No text is intended here (header only).
<b>Conformance</b>	Required
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Protocol Summary
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	1.1 Protocol Synopsis
<b>Business rules</b>	<b>Value Allowed:</b> Yes <b>Relationship:</b> n/a <b>Concept:</b> Secondary endpoint(s)
<b>Duplicate field in other sections</b>	

157

<b>Term (Variable)</b>	Primary Objective
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	H
<b>Definition</b>	Heading
<b>User Guidance</b>	
<b>Conformance</b>	Required
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Protocol Summary
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	Primary Objective
<b>Business rules</b>	<b>Value Allowed:</b> Yes <b>Relationship:</b> Table header <b>Concept:</b> n/a
<b>Duplicate field in other sections</b>	Section 3.1 replicated for primary/secondary

158

<b>Term (Variable)</b>	Objective X
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	D
<b>Definition</b>	
<b>User Guidance</b>	Define the primary objective(s) and the rationale for the objective(s). Where applicable, provide information about the relevance of the objective. For multi-arm studies, ensure that each objective clarifies the way in which all of the intervention groups will be compared (e.g., A versus B, A versus C).
<b>Conformance</b>	Required
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Protocol Summary
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	
<b>Business rules</b>	<b>Value Allowed:</b> n/a <b>Relationship:</b> Relate endpoint <b>Concept:</b> n/a
<b>Duplicate field in other sections</b>	Repeat as needed

159

<b>Term (Variable)</b>	Primary Endpoint
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	H
<b>Definition</b>	Section Heading
<b>User Guidance</b>	
<b>Conformance</b>	Required
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Protocol Summary
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	Primary Endpoint
<b>Business rules</b>	<b>Value Allowed:</b> Yes <b>Relationship:</b> n/a <b>Concept:</b> n/a
<b>Duplicate field in other sections</b>	

160

<b>Term (Variable)</b>	Endpoint X
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	D
<b>Definition</b>	
<b>User Guidance</b>	<p>Define each primary endpoint(s) and the rationale for each endpoint(s). The endpoint is the variable of interest that will be obtained for each participant. The endpoint should be a clear, unambiguous, quantitative measure directly related to the corresponding objective.</p> <p>It may be pertinent to list the additional time points at which the endpoint/outcome will be measured if it is possible to be measured more than once during the trial.</p>
<b>Conformance</b>	Conditional / Conditional
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Protocol Summary
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	
<b>Business rules</b>	<p><b>Value Allowed:</b> n/a</p> <p><b>Relationship:</b> Relate to objective</p> <p><b>Concept:</b> n/a</p>
<b>Duplicate field in other sections</b>	<p>Must be at least one endpoint per objective</p> <p>May be more than one endpoint per objective</p> <p>Repeat as needed</p>



<b>Term (Variable)</b>	Secondary Objective
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	H
<b>Definition</b>	Heading
<b>User Guidance</b>	
<b>Conformance</b>	Required / Required
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Protocol Summary
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	Secondary Objective
<b>Business rules</b>	<b>Value Allowed:</b> Yes <b>Relationship:</b> Table header <b>Concept:</b> n/a
<b>Duplicate field in other sections</b>	Section 3.1 replicated for primary/secondary

162

<b>Term (Variable)</b>	Objective X
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	D
<b>Definition</b>	
<b>User Guidance</b>	Define the secondary objective(s) and the rationale for the objective(s). Where applicable, provide information about the relevance of the objective.
<b>Conformance</b>	Required / Required
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Protocol Summary
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	
<b>Business rules</b>	<b>Value Allowed:</b> n/a <b>Relationship:</b> Relate endpoint <b>Concept:</b> n/a
<b>Duplicate field in other sections</b>	Repeat as needed

163

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

164

Term (Variable)	Endpoint X
Data Type	Text
Topic, Value or Header	D
Definition	
User Guidance	Define each secondary endpoint(s) and the rationale for each endpoint(s).
Conformance	Conditional / Conditional
Cardinality	
Relationship content from ToC representing the protocol hierarchy	Protocol Summary
Relationship (reference to high level conceptual model)	
Value	
Business rules	<b>Value Allowed:</b> n/a <b>Relationship:</b> Relate to object <b>Concept:</b> n/a
Duplicate field in other sections	Must be at least one endpoint per objective May be more than one endpoint per objective repeat as needed

165

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

166

Term (Variable)	Several key aspects of the trial design are summarised below
Data Type	Text
Topic, Value or Header	H
Definition	
User Guidance	
Conformance	Required
Cardinality	
Relationship content from ToC representing the protocol hierarchy	Protocol Summary
Relationship (reference to high level conceptual model)	
Value	Several key aspects of the trial design are summarised below
Business rules	<b>Value Allowed:</b> Yes <b>Relationship:</b> n/a <b>Concept:</b> n/a
Duplicate field in other sections	

167

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

168

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

169

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

170

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

171

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

172

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

173

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

174

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

175

176

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

177

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

178



<b>Term (Variable)</b>	Population Age
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	H
<b>Definition</b>	
<b>User Guidance</b>	Population age range (for example 0-3 mos, 18-80 years old). List N/A if a maximum or minimum age limit does not apply. For trials in which multiple age ranges may be eligible (for example, a younger cohort and an older cohort), indicate the minimum and maximum ages for the trial overall, with an additional comment for any excluded age ranges.
<b>Conformance</b>	Required
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Protocol Summary
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	Population Age
<b>Business rules</b>	<b>Value Allowed:</b> Yes <b>Relationship:</b> Table cell title <b>Concept:</b> n/a
<b>Duplicate field in other sections</b>	

179

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

180

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

181

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

182

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

183

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

184

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

185

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

186

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

187

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

188

189

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

190

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

191

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

192

<b>Term (Variable)</b>	Number of Arms
<b>Data Type</b>	integer
<b>Topic, Value or Header</b>	D
<b>Definition</b>	
<b>User Guidance</b>	Enter the numeric value for the number of arms in the trial. For trials with a different number of arms in different periods, populate this field based on the period with the greatest number of arms.
<b>Conformance</b>	Required
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Protocol Summary
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	Greatest number of arms
<b>Business rules</b>	<b>Value Allowed:</b> Yes <b>Relationship:</b> n/a <b>Concept:</b> n/a
<b>Duplicate field in other sections</b>	

193

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

194

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

195



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

196

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

197

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

198

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

199

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

200

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

201

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

202

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

203

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

204

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

205

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

206

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

207

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

208

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

209

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

210

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

211



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

<b>Term (Variable)</b>	Committee
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	H
<b>Definition</b>	
<b>User Guidance</b>	Indicate whether any committee(s) will be reviewing data while the trial is ongoing, and the type of committee. Common examples include Data Monitoring Committee, Dose Escalation Committee, or Endpoint Adjudication Committee; describe others, if applicable. List independent committees in the space indicated. Other committees may be included at the Sponsor's discretion in the separate space provided. Committees listed here should be fully described in Section 10.3, Committees Structure.
<b>Conformance</b>	Required
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Protocol Summary
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	Committee
<b>Business rules</b>	<b>Value Allowed:</b> Yes <b>Relationship:</b> n/a <b>Concept:</b> n/a
<b>Duplicate field in other sections</b>	

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

214

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

215

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

216

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

217

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

218

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

219

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

221 **1.2 Trial Schema**

<b>Term (Variable)</b>	Trial Schema
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	H
<b>Definition</b>	Heading
<b>User Guidance</b>	The purpose of this section is to provide a visual depiction of the trial design, orienting users of the protocol to the key features of the trial design. The schema depicts the trial arms, the flow of individual participants through the progression of trial period(s)/epochs (such as screening, washout/run-in, intervention, and key milestones [for example, randomisation, cross-over, end of treatment]). For complex trials, additional schemas may be added to describe activities or trial periods in greater detail.
<b>Conformance</b>	Required
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Protocol Summary
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	Trial Schema
<b>Business rules</b>	<b>Value Allowed:</b> Yes <b>Relationship:</b> n/a <b>Concept:</b> n/a
<b>Duplicate field in other sections</b>	

222

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



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

225 **1.3 Schedule of Activities**

<b>Term (Variable)</b>	Schedule of Activities
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	H
<b>Definition</b>	Heading
<b>User Guidance</b>	The schedule of activities must capture the procedures that will be accomplished at each trial visit, and all contact with trial participants, for example, telephone contacts. This includes any tests that are used for eligibility, participant randomisation or stratification, or decisions on trial intervention discontinuation. Allowable windows should be stated for all visits.
<b>Conformance</b>	Required
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Protocol Summary
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	Schedule of Activities
<b>Business rules</b>	<b>Value Allowed:</b> Yes <b>Relationship:</b> n/a <b>Concept:</b> n/a
<b>Duplicate field in other sections</b>	

226

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

227      **2. Introduction**

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

228

229     **2.1     Purpose of Trial**

<b>Term (Variable)</b>	Purpose of Trial
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	H
<b>Definition</b>	Heading
<b>User Guidance</b>	
<b>Conformance</b>	Required
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Introduction
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	Purpose of Trial
<b>Business rules</b>	<b>Value Allowed:</b> Yes <b>Relationship:</b> n/a <b>Concept:</b> n/a
<b>Duplicate field in other sections</b>	

230

<b>Term (Variable)</b>	Purpose of Trial
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	D
<b>Definition</b>	Clear explanation of the research question/hypothesis and the justification of the trial i.e. why the question is worth asking and, through consultation with public and patient groups, why answering this question is worthwhile to patients.
<b>User Guidance</b>	Explain why the trial is needed, why the research questions being asked are important and, where applicable, why closely related questions are not being covered. Do not restate the IB.
<b>Conformance</b>	Required
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Introduction
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	
<b>Business rules</b>	<b>Value Allowed:</b> n/a <b>Relationship:</b> n/a <b>Concept:</b> n/a
<b>Duplicate field in other sections</b>	

232 **2.2 Summary of Benefits and Risks**

<b>Term (Variable)</b>	Summary of Benefits and Risks
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	H
<b>Definition</b>	Heading
<b>User Guidance</b>	
<b>Conformance</b>	Required
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Introduction
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	Summary of Benefits and Risks
<b>Business rules</b>	<b>Value Allowed:</b> Yes <b>Relationship:</b> n/a <b>Concept:</b> n/a
<b>Duplicate field in other sections</b>	

233

<b>Term (Variable)</b>	Benefit Summary
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	H
<b>Definition</b>	
<b>User Guidance</b>	
<b>Conformance</b>	Required
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Introduction
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	Benefit Summary
<b>Business rules</b>	<b>Value Allowed:</b> Yes <b>Relationship:</b> n/a <b>Concept:</b> n/a
<b>Duplicate field in other sections</b>	

234

<b>Term (Variable)</b>	Benefit Summary
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	D
<b>Definition</b>	
<b>User Guidance</b>	<p>The benefit summary should be written from the perspective of an individual participant, and should describe any physical, psychological, social, legal, 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 studies such as Phase 1, benefits for an individual participant (other than those of altruism) are expected to be minimal.</p> <p>Benefits to society in general may also be included but should be discussed separately.</p>
<b>Conformance</b>	Required
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Introduction
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	
<b>Business rules</b>	<p><b>Value Allowed:</b> n/a</p> <p><b>Relationship:</b> n/a</p> <p><b>Concept:</b> n/a</p>
<b>Duplicate field in other sections</b>	

<b>Term (Variable)</b>	Risk Summary and Mitigation Strategy
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	H
<b>Definition</b>	Heading
<b>User Guidance</b>	
<b>Conformance</b>	Required
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Introduction
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	Risk Summary and Mitigation Strategy
<b>Business rules</b>	<b>Value Allowed:</b> Yes <b>Relationship:</b> n/a <b>Concept:</b> n/a
<b>Duplicate field in other sections</b>	

236

<b>Term (Variable)</b>	Trial Specific Discussion of intervention Risks and Mitigation
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	D
<b>Definition</b>	
<b>User Guidance</b>	Trial Intervention – Discuss risks related to trial-specific treatments and interventions. For the protocol, focus discussion only 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.
<b>Conformance</b>	Required
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Introduction
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	
<b>Business rules</b>	<b>Value Allowed:</b> n/a <b>Relationship:</b> n/a <b>Concept:</b> n/a
<b>Duplicate field in other sections</b>	

237



<b>Term (Variable)</b>	Trial Specific discussion of Procedure (s) Risks and Mitigation
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	D
<b>Definition</b>	
<b>User Guidance</b>	Trial Procedures – Consider risks associated with the trial design and procedures specific to THIS trial (for example, biopsies) or design (for example, placebo arm), and any measures to control 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.
<b>Conformance</b>	Required
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Introduction
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	
<b>Business rules</b>	<b>Value Allowed:</b> n/a <b>Relationship:</b> n/a <b>Concept:</b> n/a
<b>Duplicate field in other sections</b>	

<b>Term (Variable)</b>	Trial specific Discussion of other Risks and Mitigations
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	D
<b>Definition</b>	
<b>User Guidance</b>	Other – Consider risks associated with other items (for example, comparators, challenge agents, imaging agents, medical devices). Insert a line for each, as needed.
<b>Conformance</b>	Required
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Introduction
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	
<b>Business rules</b>	<b>Value Allowed:</b> n/a <b>Relationship:</b> n/a <b>Concept:</b> n/a
<b>Duplicate field in other sections</b>	

239

<b>Term (Variable)</b>	Overall Benefit: Risk Conclusion
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	H
<b>Definition</b>	Heading
<b>User Guidance</b>	
<b>Conformance</b>	Required
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Introduction
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	Overall Benefit: Risk Conclusion
<b>Business rules</b>	<b>Value Allowed:</b> Yes <b>Relationship:</b> n/a <b>Concept:</b> n/a
<b>Duplicate field in other sections</b>	

240

<b>Term (Variable)</b>	Overall Benefit: Risk Conclusion
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	D
<b>Definition</b>	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.
<b>User Guidance</b>	<p>Risks need to be weighed against the benefits for the individual participant.</p> <p>Clinical trials should generally pose only minimal risks to incapacitated subjects, minors, pregnant or breastfeeding women, and clinical trials conducted in emergency situations. Refer to local guidelines for specific requirements or benefit/risk thresholds in these populations and ensure that these are addressed here, if applicable.</p> <p>Outcomes of discussions with regulatory authorities as related to benefit/risk and reporting may be summarised here if it provides useful insights for the investigator.</p>
<b>Conformance</b>	Required
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Introduction
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	
<b>Business rules</b>	<b>Value Allowed:</b> n/a <b>Relationship:</b> n/a <b>Concept:</b> n/a
<b>Duplicate field in other sections</b>	

### 242 3. Trial Objectives, Endpoints and Estimands

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

243

244 **3.1 {Primary/Secondary/Exploratory} Objective + Associated**  
 245 **Endpoint {and Estimand}**

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

246

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

247

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

248

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

249

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

250

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

251

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



253 **4. Trial Design**

<b>Term (Variable)</b>	Trial Design
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	H
<b>Definition</b>	Heading
<b>User Guidance</b>	In this section, describe the trial design with specific mention, as applicable, of the components of an adequate and well-controlled trial. The description of the trial design should be concise and consistent across Section 1.1, Protocol Synopsis and Section 1.2, Trial Schema.
<b>Conformance</b>	Required
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Trial Design
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	Trial Design
<b>Business rules</b>	<b>Value Allowed:</b> Yes <b>Relationship:</b> n/a <b>Concept:</b> n/a
<b>Duplicate field in other sections</b>	

254

255 **4.1 Description of Trial Design**

<b>Term (Variable)</b>	Description of Trial Design
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	H
<b>Definition</b>	heading
<b>User Guidance</b>	<p>Describe the trial intervention model (for example, single group, parallel group, cross-over, factorial, sequential), the expected number of participants, and the control method (for example, placebo, active comparator, low dose, historical, standard of care, sham procedure, or none [uncontrolled]).</p> <p>If applicable, indicate the type of trial (for example, superiority, non-inferiority, dose escalation, or equivalence).</p> <p>If the trial will have an adaptive or novel design (for example, the trial will be conducted under a master protocol), provide a summary of these design aspects.</p>
<b>Conformance</b>	Required /
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Trial Design
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	Description of Trial Design
<b>Business rules</b>	<p><b>Value Allowed:</b> Yes</p> <p><b>Relationship:</b> n/a</p> <p><b>Concept:</b> n/a</p>
<b>Duplicate field in other sections</b>	

256

<b>Term (Variable)</b>	Expected Number of Participants
<b>Data Type</b>	Number
<b>Topic, Value or Header</b>	D
<b>Definition</b>	
<b>User Guidance</b>	
<b>Conformance</b>	Required
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Trial Design
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	
<b>Business rules</b>	<b>Value Allowed:</b> Yes <b>Relationship:</b> n/a <b>Concept:</b> n/a
<b>Duplicate field in other sections</b>	

257

<b>Term (Variable)</b>	Control Mechanism
<b>Data Type</b>	List
<b>Topic, Value or Header</b>	D
<b>Definition</b>	
<b>User Guidance</b>	
<b>Conformance</b>	Required
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Trial Design
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	Placebo, active comparator, low dose, historical, standard of care, sham procedure, or none [uncontrolled]
<b>Business rules</b>	<b>Value Allowed:</b> Yes <b>Relationship:</b> n/a <b>Concept:</b> n/a
<b>Duplicate field in other sections</b>	

258

<b>Term (Variable)</b>	Type of Trial
<b>Data Type</b>	List
<b>Topic, Value or Header</b>	D
<b>Definition</b>	
<b>User Guidance</b>	
<b>Conformance</b>	Required
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Trial Design
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	Superiority, non-inferiority, dose escalation, or equivalence
<b>Business rules</b>	<b>Value Allowed:</b> Yes <b>Relationship:</b> n/a <b>Concept:</b> n/a
<b>Duplicate field in other sections</b>	

259

<b>Term (Variable)</b>	Adaptive Trial
<b>Data Type</b>	List
<b>Topic, Value or Header</b>	D
<b>Definition</b>	
<b>User Guidance</b>	
<b>Conformance</b>	Required
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Trial Design
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	Boolean (Yes/No)
<b>Business rules</b>	<b>Value Allowed:</b> Yes <b>Relationship:</b> n/a <b>Concept:</b> n/a
<b>Duplicate field in other sections</b>	

260

Term (Variable)	Novel Design
Data Type	List
Topic, Value or Header	D
Definition	
User Guidance	
Conformance	Required
Cardinality	
Relationship content from ToC representing the protocol hierarchy	Trial Design
Relationship (reference to high level conceptual model)	
Value	Boolean (Yes/No)
Business rules	<b>Value Allowed:</b> Yes <b>Relationship:</b> n/a <b>Concept:</b> n/a
Duplicate field in other sections	

261

Term (Variable)	Under Master
Data Type	List
Topic, Value or Header	D
Definition	
User Guidance	
Conformance	Required
Cardinality	
Relationship content from ToC representing the protocol hierarchy	Trial Design
Relationship (reference to high level conceptual model)	
Value	Boolean (Yes/No)
Business rules	<b>Value Allowed:</b> Yes <b>Relationship:</b> n/a <b>Concept:</b> n/a
Duplicate field in other sections	

262

<b>Term (Variable)</b>	[Description of Intervention Model]
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	D
<b>Definition</b>	
<b>User Guidance</b>	Describe the trial duration with reference to Section 1.2, Trial Schema. Explain what the overall trial 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 10.3, Committees Structure.
<b>Conformance</b>	Required
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Trial Design
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	
<b>Business rules</b>	<b>Value Allowed:</b> n/a <b>Relationship:</b> n/a <b>Concept:</b> n/a
<b>Duplicate field in other sections</b>	

<b>Term (Variable)</b>	[Description of Trial Duration]
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	D
<b>Definition</b>	
<b>User Guidance</b>	<p>Describe the method of assignment to trial intervention (for example, stratified randomisation). If assignment to trial intervention is by randomisation, describe when randomisation occurs relative to screening.</p> <p>Describe the level and method of blinding, for example, single-blind, double-blind, [including Sponsor unblinded], matching placebo, double-dummy, or open-label). Include mention of measures taken to minimise bias on the part of participants, investigators, and analysts.</p> <p>If applicable, describe within-trial transition rules, for example, transitions involving cohorts or trial parts. Dose escalation or dose-ranging details should also be described.</p>
<b>Conformance</b>	Required
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Trial Design
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	
<b>Business rules</b>	<p><b>Value Allowed:</b> n/a</p> <p><b>Relationship:</b> n/a</p> <p><b>Concept:</b> Trial Population</p>
<b>Duplicate field in other sections</b>	

<b>Term (Variable)</b>	Randomisation
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	D
<b>Definition</b>	
<b>User Guidance</b>	
<b>Conformance</b>	Required
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Trial Design
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	
<b>Business rules</b>	<b>Value Allowed:</b> n/a <b>Relationship:</b> n/a <b>Concept:</b>
<b>Duplicate field in other sections</b>	

265

<b>Term (Variable)</b>	Method and Level of Blinding
<b>Data Type</b>	List
<b>Topic, Value or Header</b>	D
<b>Definition</b>	
<b>User Guidance</b>	
<b>Conformance</b>	Required/Multiple
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Trial Design
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	Single-blind, double-blind, [including Sponsor unblinded], matching placebo, double-dummy, or open-label
<b>Business rules</b>	<b>Value Allowed:</b> Yes <b>Relationship:</b> n/a <b>Concept:</b>
<b>Duplicate field in other sections</b>	

266



Term (Variable)	Measures to Minimise Bias
Data Type	Text
Topic, Value or Header	D
Definition	
User Guidance	
Conformance	Required
Cardinality	
Relationship content from ToC representing the protocol hierarchy	Trial Design
Relationship (reference to high level conceptual model)	
Value	
Business rules	<b>Value Allowed:</b> Yes <b>Relationship:</b> n/a <b>Concept:</b>
Duplicate field in other sections	

267

Term (Variable)	Trial Transition Rules
Data Type	Text
Topic, Value or Header	D
Definition	
User Guidance	
Conformance	Optional
Cardinality	
Relationship content from ToC representing the protocol hierarchy	Trial Design
Relationship (reference to high level conceptual model)	
Value	
Business rules	<b>Value Allowed:</b> Yes <b>Relationship:</b> n/a <b>Concept:</b>
Duplicate field in other sections	

268

<b>Term (Variable)</b>	[Method of Assignment to Trial Intervention]
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	D
<b>Definition</b>	
<b>User Guidance</b>	<p>Discuss important aspects of trial design, including:</p> <ul style="list-style-type: none"> <li>• Geographic scope of trial (for example, single-centre, multi-centre, or multi-centre and multi-national).</li> <li>• Planned use of a Data Monitoring Committee, or similar review group and cross-reference Section 10.3, Committees Structure, for details.</li> </ul> <p>Whether an interim analysis is planned and, if so, refer to details in Section 9.7, Interim Analysis..</p>
<b>Conformance</b>	Required
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Trial Design
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	
<b>Business rules</b>	<p><b>Value Allowed:</b> n/a</p> <p><b>Relationship:</b> n/a</p> <p><b>Concept:</b> n/a</p>
<b>Duplicate field in other sections</b>	

<b>Term (Variable)</b>	Geographic Scope
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	D
<b>Definition</b>	
<b>User Guidance</b>	<p>Discuss important aspects of trial design, including:</p> <ul style="list-style-type: none"> <li>• Geographic scope of trial (for example, single-centre, multi-centre, or multi-centre and multi-national).</li> <li>• Planned use of a Data Monitoring Committee, or similar review group and cross-reference Section 10.3, Committees Structure, for details.</li> <li>• Whether an interim analysis is planned and, if so, refer to details in Section 9.7, Interim Analysis.</li> </ul>
<b>Conformance</b>	Required
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Trial Design
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	Single-centre, multi-centre, or multi-centre and multi-national
<b>Business rules</b>	<p><b>Value Allowed:</b> Yes</p> <p><b>Relationship:</b> n/a</p> <p><b>Concept:</b> n/a</p>
<b>Duplicate field in other sections</b>	

<b>Term (Variable)</b>	Decentralise Process, Tools, or Features
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	D
<b>Definition</b>	
<b>User Guidance</b>	
<b>Conformance</b>	Optional
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Trial Design
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	
<b>Business rules</b>	<b>Value Allowed:</b> Yes <b>Relationship:</b> n/a <b>Concept:</b> n/a
<b>Duplicate field in other sections</b>	

271

<b>Term (Variable)</b>	Committees
<b>Data Type</b>	List
<b>Topic, Value or Header</b>	D
<b>Definition</b>	
<b>User Guidance</b>	
<b>Conformance</b>	Required/Multiple
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Trial Design
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	No, Data Monitoring Committee
<b>Business rules</b>	<b>Value Allowed:</b> Yes <b>Relationship:</b> n/a <b>Concept:</b> n/a
<b>Duplicate field in other sections</b>	

272

Term (Variable)	Interim Analyses
Data Type	List
Topic, Value or Header	D
Definition	
User Guidance	
Conformance	Required
Cardinality	
Relationship content from ToC representing the protocol hierarchy	Trial Design
Relationship (reference to high level conceptual model)	
Value	Yes, No
Business rules	<b>Value Allowed:</b> Yes <b>Relationship:</b> n/a <b>Concept:</b> n/a
Duplicate field in other sections	

273

Term (Variable)	Number if Interim Analyses
Data Type	Number
Topic, Value or Header	D
Definition	
User Guidance	
Conformance	Required
Cardinality	
Relationship content from ToC representing the protocol hierarchy	Trial Design
Relationship (reference to high level conceptual model)	
Value	
Business rules	<b>Value Allowed:</b> Yes <b>Relationship:</b> n/a <b>Concept:</b> n/a
Duplicate field in other sections	

274

<b>Term (Variable)</b>	Planned Extension
<b>Data Type</b>	List
<b>Topic, Value or Header</b>	D
<b>Definition</b>	
<b>User Guidance</b>	
<b>Conformance</b>	Required
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Trial Design
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	No, planned extension Trial, long-term follow-up/registry, or post-Trial sample analysis or other data-related activities
<b>Business rules</b>	<b>Value Allowed:</b> Yes <b>Relationship:</b> n/a <b>Concept:</b> n/a
<b>Duplicate field in other sections</b>	

Term (Variable)	[Additional Description of Trial Design]
Data Type	Text
Topic, Value or Header	D
Definition	
User Guidance	
Conformance	Required
Cardinality	
Relationship content from ToC representing the protocol hierarchy	Trial Design
Relationship (reference to high level conceptual model)	
Value	
Business rules	<b>Value Allowed:</b> Yes <b>Relationship:</b> n/a <b>Concept:</b> n/a
Duplicate field in other sections	Protocol Synopsis / Overall Design

#### 276 4.1.1 Participant Input into Design

Term (Variable)	Participant Input into Design
Data Type	Text
Topic, Value or Header	H
Definition	Heading
User Guidance	If applicable, describe any participant involvement in the design of the clinical trial and any participant suggestions implemented.
Conformance	Required
Cardinality	
Relationship content from ToC representing the protocol hierarchy	Trial Design
Relationship (reference to high level conceptual model)	
Value	Participant Input into Design
Business rules	<b>Value Allowed:</b> Yes <b>Relationship:</b> n/a <b>Concept:</b> n/a
Duplicate field in other sections	

277

<b>Term (Variable)</b>	Participant Input
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	D
<b>Definition</b>	Heading
<b>User Guidance</b>	If applicable, describe any participant involvement in the design of the clinical trial and any participant suggestions implemented.
<b>Conformance</b>	Required
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Trial Design
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	
<b>Business rules</b>	<b>Value Allowed:</b> n/a <b>Relationship:</b> n/a <b>Concept:</b> n/a
<b>Duplicate field in other sections</b>	

## 278 4.2 Rationale for Trial Design

<b>Term (Variable)</b>	Rationale for Trial Design
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	H
<b>Definition</b>	
<b>User Guidance</b>	
<b>Conformance</b>	Required
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Trial Design
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	Rationale for Trial Design
<b>Business rules</b>	<b>Value Allowed:</b> Yes <b>Relationship:</b> n/a <b>Concept:</b> n/a
<b>Duplicate field in other sections</b>	

279



<b>Term (Variable)</b>	[Rationale for Intervention Model]
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	D
<b>Definition</b>	
<b>User Guidance</b>	Provide a rationale for the trial intervention model selected in Section 4.1, Description of Trial Design. A rationale for the choice of comparator, if applicable, should be described separately in Section 4.2.1, Rationale for Comparator.
<b>Conformance</b>	Required
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Trial Design
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	
<b>Business rules</b>	<b>Value Allowed:</b> n/a <b>Relationship:</b> n/a <b>Concept:</b> n/a
<b>Duplicate field in other sections</b>	

280

<b>Term (Variable)</b>	[Rationale for Trial Duration]
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	D
<b>Definition</b>	
<b>User Guidance</b>	Provide a rationale that the trial duration is appropriate to show a reliable and relevant effect of the trial intervention per the trial objective(s).
<b>Conformance</b>	Required
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Trial Design
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	
<b>Business rules</b>	<b>Value Allowed:</b> n/a <b>Relationship:</b> n/a <b>Concept:</b> n/a
<b>Duplicate field in other sections</b>	

281

<b>Term (Variable)</b>	[Rationale for Trial Duration]
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	D
<b>Definition</b>	
<b>User Guidance</b>	Provide a rationale that the trial endpoint(s) described in Section 3, Trial Objectives, Endpoints, and Estimands, are clinically relevant and provide a reliable and valid measurement of the intended intervention effect.
<b>Conformance</b>	Required
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Trial Design
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	
<b>Business rules</b>	<b>Value Allowed:</b> n/a <b>Relationship:</b> n/a <b>Concept:</b> n/a
<b>Duplicate field in other sections</b>	

<b>Term (Variable)</b>	[Interim Analysis]
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	D
<b>Definition</b>	
<b>User Guidance</b>	If applicable, provide a rationale for any interim analysis planned with respect to its purpose (for example, stopping the trial early for efficacy or futility) and timing.
<b>Conformance</b>	Required
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Trial Design
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	
<b>Business rules</b>	<b>Value Allowed:</b> n/a <b>Relationship:</b> n/a <b>Concept:</b> n/a
<b>Duplicate field in other sections</b>	

#### 283 4.2.1 Rationale for Comparator

<b>Term (Variable)</b>	Rationale for Comparator
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	H
<b>Definition</b>	
<b>User Guidance</b>	
<b>Conformance</b>	Optional
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Trial Design
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	Rationale for Comparator
<b>Business rules</b>	<b>Value Allowed:</b> Yes <b>Relationship:</b> n/a <b>Concept:</b> n/a
<b>Duplicate field in other sections</b>	

284

<b>Term (Variable)</b>	[Rationale for Comparator]
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	D
<b>Definition</b>	
<b>User Guidance</b>	If applicable, provide a rationale for the type of control selected for the trial (for example, placebo, active drug, combination, historical). Discuss 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. Describe prior studies that support the dose and/or dose regimen.
<b>Conformance</b>	Conditional
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Trial Design
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	
<b>Business rules</b>	<b>Value Allowed:</b> n/a <b>Relationship:</b> Control Mechanism <b>Concept:</b> n/a
<b>Duplicate field in other sections</b>	

286 **4.2.2 Rationale for Adaptive or Novel Trial Design**

<b>Term (Variable)</b>	Rationale for Adaptive or Novel Trial Design
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	H
<b>Definition</b>	Heading
<b>User Guidance</b>	
<b>Conformance</b>	Optional
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Trial Design
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	Rationale for Adaptive or Novel Trial Design
<b>Business rules</b>	<b>Value Allowed:</b> Yes <b>Relationship:</b> n/a <b>Concept:</b> n/a
<b>Duplicate field in other sections</b>	

287

Term (Variable)	[Rationale for Adaptive or Novel Trial Design]
Data Type	Text
Topic, Value or Header	D
Definition	
User Guidance	If applicable, provide a rationale for the use of an adaptive or novel trial design.
Conformance	Conditional
Cardinality	
Relationship content from ToC representing the protocol hierarchy	Trial Design
Relationship (reference to high level conceptual model)	
Value	
Business rules	<b>Value Allowed:</b> n/a <b>Relationship:</b> n/a <b>Concept:</b> n/a
Duplicate field in other sections	

#### 288 4.2.3 Other Trial Design Considerations

Term (Variable)	Other Trial Design Considerations
Data Type	Text
Topic, Value or Header	H
Definition	Heading
User Guidance	
Conformance	Optional
Cardinality	
Relationship content from ToC representing the protocol hierarchy	Trial Design
Relationship (reference to high level conceptual model)	
Value	Other Trial Design Considerations
Business rules	<b>Value Allowed:</b> Yes <b>Relationship:</b> n/a <b>Concept:</b> n/a
Duplicate field in other sections	

289

Term (Variable)	[Other Trial Design Considerations]
Data Type	Text
Topic, Value or Header	D
Definition	
User Guidance	Discuss any additional aspects of trial design not addressed above.
Conformance	Conditional
Cardinality	
Relationship content from ToC representing the protocol hierarchy	Trial Design
Relationship (reference to high level conceptual model)	
Value	
Business rules	<b>Value Allowed:</b> n/a <b>Relationship:</b> n/a <b>Concept:</b> n/a
Duplicate field in other sections	

### 290 4.3 Access to Trial Intervention After End of Trial

Term (Variable)	Access to Trial Intervention After End of Trial
Data Type	Text
Topic, Value or Header	H
Definition	Heading
User Guidance	
Conformance	Required
Cardinality	
Relationship content from ToC representing the protocol hierarchy	Trial Design
Relationship (reference to high level conceptual model)	
Value	Access to Trial Intervention After End of Trial
Business rules	<b>Value Allowed:</b> Yes <b>Relationship:</b> n/a <b>Concept:</b> n/a
Duplicate field in other sections	

291

<b>Term (Variable)</b>	Access to Trial Intervention After End of Trial
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	D
<b>Definition</b>	
<b>User Guidance</b>	If applicable, describe any possibilities for access to trial intervention, if any, beyond completion of the trial. Planned extension trials, if described above in Section 4.1 do not need to be repeated.
<b>Conformance</b>	Required
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Trial Design
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	
<b>Business rules</b>	<b>Value Allowed:</b> n/a <b>Relationship:</b> n/a <b>Concept:</b> n/a
<b>Duplicate field in other sections</b>	

292

#### 293 4.4 Start of Trial and End of Trial

<b>Term (Variable)</b>	Start of Trial and End of Trial
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	H
<b>Definition</b>	Heading
<b>User Guidance</b>	
<b>Conformance</b>	Required
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Trial Design
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	Start of Trial and End of Trial
<b>Business rules</b>	<b>Value Allowed:</b> Yes <b>Relationship:</b> n/a <b>Concept:</b> n/a
<b>Duplicate field in other sections</b>	

294



<b>Term (Variable)</b>	[Trial Start and End]
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	D
<b>Definition</b>	
<b>User Guidance</b>	<p>Provide definitions of the start and end of the trial. These definitions should consider local regulatory requirements.</p> <p>If applicable, describe any planned extension trial, long-term follow-up/registry, or post-trial sample analysis or other data-related activities. Refer to Section 7.5, Access to Trial Intervention, for a description of plans for post-trial access to trial intervention.</p>
<b>Conformance</b>	Required
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Trial Design
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	
<b>Business rules</b>	<p><b>Value Allowed:</b> n/a</p> <p><b>Relationship:</b> n/a</p> <p><b>Concept:</b> n/a</p>
<b>Duplicate field in other sections</b>	

296 **5. Trial Population**

<b>Term (Variable)</b>	Trial Population
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	H
<b>Definition</b>	
<b>User Guidance</b>	<p>In this section, describe the trial population. Use the following guidance when developing participant eligibility criteria to be listed in Section 5.3, Inclusion Criteria, and Section 5.4, Exclusion Criteria.</p> <ul style="list-style-type: none"> <li>• List the criteria necessary for participation in the trial. Ensure that each criterion can be easily assessed on the basis of measurable data and answered with yes/no responses.</li> <li>• If participants require screening, distinguish between screening vs enrolling participants. Identify specific laboratory tests or clinical characteristics that will be used as criteria for enrollment or exclusion. If permitting existing medical diagnosis, imaging, genetic tests, or laboratory results, state any required window or acceptable test type.</li> <li>• If measures to enrich the trial population for pre-specified subgroups of interest are used, these should be described</li> </ul>
<b>Conformance</b>	Required
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Trial Population
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	Trial Population
<b>Business rules</b>	<p><b>Value Allowed:</b> Yes</p> <p><b>Relationship:</b> n/a</p> <p><b>Concept:</b> n/a</p>
<b>Duplicate field in other sections</b>	

297

298 **5.1 Selection of Trial Population**

<b>Term (Variable)</b>	Selection of Trial Population
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	H
<b>Definition</b>	Heading
<b>User Guidance</b>	
<b>Conformance</b>	Required
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Trial Population
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	Selection of Trial Population
<b>Business rules</b>	<b>Value Allowed:</b> Yes <b>Relationship:</b> n/a <b>Concept:</b> n/a
<b>Duplicate field in other sections</b>	

299

<b>Term (Variable)</b>	[Selection of Trial Population]
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	D
<b>Definition</b>	
<b>User Guidance</b>	Describe the trial population selected (for example, healthy volunteers, adult participants, paediatric participants). Specify the population age range (for example, 0 to 3 months, 18 to 80 years old) and any key diagnostic criteria for the population (for example, "acute lung injury", or a specific biomarker profile). If applicable, describe similar conditions or diseases and their differential diagnosis.
<b>Conformance</b>	Required
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Trial Population
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	
<b>Business rules</b>	<b>Value Allowed:</b> n/a <b>Relationship:</b> n/a <b>Concept:</b> n/a
<b>Duplicate field in other sections</b>	

## 301 5.2 Rationale for Trial Population

<b>Term (Variable)</b>	Rationale for Trial Population
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	H
<b>Definition</b>	Heading
<b>User Guidance</b>	
<b>Conformance</b>	Required
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Trial Population
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	Rationale for Trial Population
<b>Business rules</b>	<b>Value Allowed:</b> Yes <b>Relationship:</b> n/a <b>Concept:</b> n/a
<b>Duplicate field in other sections</b>	

302

<b>Term (Variable)</b>	[Rationale for Trial Population]
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	D
<b>Definition</b>	
<b>User Guidance</b>	Provide a rationale for the trial population ensuring that the trial population selected is well defined and clinically recognisable. Justify whether the trial intervention is to be evaluated in children, in adults unable to consent for themselves, other vulnerable participant populations, or those that may respond to the trial intervention differently (for example, females, elderly, hepatic or renally impaired, or immunocompromised participants).
<b>Conformance</b>	Required
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Trial Population
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	
<b>Business rules</b>	<b>Value Allowed:</b> n/a <b>Relationship:</b> n/a <b>Concept:</b> n/a
<b>Duplicate field in other sections</b>	

303

<b>Term (Variable)</b>	Individuals who do not meet criteria for trial eligibility must not be enrolled via protocol waivers or exemptions
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	H
<b>Definition</b>	
<b>User Guidance</b>	
<b>Conformance</b>	Required
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Trial Population
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	Individuals who do not meet criteria for trial eligibility must not be enrolled via protocol waivers or exemptions
<b>Business rules</b>	<b>Value Allowed:</b> Yes <b>Relationship:</b> n/a <b>Concept:</b> n/a
<b>Duplicate field in other sections</b>	

### 304 5.3 Inclusion Criteria

<b>Term (Variable)</b>	Inclusion Criteria
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	H
<b>Definition</b>	Heading
<b>User Guidance</b>	
<b>Conformance</b>	Required
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Trial Population
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	Inclusion Criteria
<b>Business rules</b>	<b>Value Allowed:</b> Yes <b>Relationship:</b> n/a <b>Concept:</b> n/a
<b>Duplicate field in other sections</b>	

305

<b>Term (Variable)</b>	To be eligible to participate in this trial, an individual must meet all the following criteria:
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	H
<b>Definition</b>	
<b>User Guidance</b>	
<b>Conformance</b>	Required
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Trial Population
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	To be eligible to participate in this trial, an individual must meet all the following criteria:
<b>Business rules</b>	<b>Value Allowed:</b> Yes <b>Relationship:</b> n/a <b>Concept:</b> n/a
<b>Duplicate field in other sections</b>	

306

<b>Term (Variable)</b>	# Inclusion Criteria
<b>Data Type</b>	Number
<b>Topic, Value or Header</b>	D
<b>Definition</b>	Inclusion criteria are characteristics that define the population under trial, for example, those criteria that every potential participant must satisfy, to qualify for trial entry.
<b>User Guidance</b>	
<b>Conformance</b>	Required
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Trial Population
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	
<b>Business rules</b>	<b>Value Allowed:</b> n/a <b>Relationship:</b> n/a <b>Concept:</b> n/a
<b>Duplicate field in other sections</b>	number consecutively, repeat for each inclusion criteria, if deleted do not replace, do not duplicate

307



<b>Term (Variable)</b>	Inclusion Criteria
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	
<b>Definition</b>	Inclusion criteria are characteristics that define the population under trial, for example, those criteria that every potential participant must satisfy, to qualify for trial entry.
<b>User Guidance</b>	
<b>Conformance</b>	Required
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Trial Population
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	
<b>Business rules</b>	<b>Value Allowed:</b> n/a <b>Relationship:</b> n/a <b>Concept:</b> n/a
<b>Duplicate field in other sections</b>	

## 308 5.4 Exclusion Criteria

<b>Term (Variable)</b>	Exclusion Criteria
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	H
<b>Definition</b>	Heading
<b>User Guidance</b>	
<b>Conformance</b>	Required
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Trial Population
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	Exclusion Criteria
<b>Business rules</b>	<b>Value Allowed:</b> Yes <b>Relationship:</b> n/a <b>Concept:</b> n/a
<b>Duplicate field in other sections</b>	

309

<b>Term (Variable)</b>	An individual who meets any of the following criteria will be excluded from participation in this trial:
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	H
<b>Definition</b>	
<b>User Guidance</b>	
<b>Conformance</b>	Required
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Trial Population
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	An individual who meets any of the following criteria will be excluded from participation in this trial:
<b>Business rules</b>	<b>Value Allowed:</b> Yes <b>Relationship:</b> n/a <b>Concept:</b> n/a
<b>Duplicate field in other sections</b>	

<b>Term (Variable)</b>	# Exclusion Criteria
<b>Data Type</b>	Number
<b>Topic, Value or Header</b>	D
<b>Definition</b>	Exclusion criteria are characteristics that make an individual ineligible for trial participation
<b>User Guidance</b>	
<b>Conformance</b>	Required
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Trial Population
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	
<b>Business rules</b>	<b>Value Allowed:</b> n/a <b>Relationship:</b> n/a <b>Concept:</b> n/a
<b>Duplicate field in other sections</b>	Number consecutively, repeat for each inclusion criteria, if deleted do not replace, do not duplicate

## 311 5.5 Lifestyle Considerations

<b>Term (Variable)</b>	Lifestyle Considerations
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	H
<b>Definition</b>	Heading
<b>User Guidance</b>	
<b>Conformance</b>	Required
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Trial Population
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	Lifestyle Considerations
<b>Business rules</b>	<b>Value Allowed:</b> Yes <b>Relationship:</b> n/a <b>Concept:</b> n/a
<b>Duplicate field in other sections</b>	

<b>Term (Variable)</b>	[Lifestyle Considerations]
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	D
<b>Definition</b>	
<b>User Guidance</b>	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.
<b>Conformance</b>	Required (at least one item and repeat for each item)
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Trial Population
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	
<b>Business rules</b>	<b>Value Allowed:</b> n/a <b>Relationship:</b> n/a <b>Concept:</b> n/a
<b>Duplicate field in other sections</b>	

### 313 5.5.1 Meals and Dietary Restrictions

<b>Term (Variable)</b>	Meals and Dietary Restrictions
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	H
<b>Definition</b>	Heading
<b>User Guidance</b>	
<b>Conformance</b>	Required
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Trial Population
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	Meals and Dietary Restrictions
<b>Business rules</b>	<b>Value Allowed:</b> Yes <b>Relationship:</b> n/a <b>Concept:</b> n/a
<b>Duplicate field in other sections</b>	

314

<b>Term (Variable)</b>	[Meals and Dietary Restrictions]
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	D
<b>Definition</b>	
<b>User Guidance</b>	If applicable, describe any restrictions on diet (for example, food and drink restrictions, timing of meals relative to dosing).
<b>Conformance</b>	Optional (repeat for each item)
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Trial Population
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	
<b>Business rules</b>	<b>Value Allowed:</b> n/a <b>Relationship:</b> n/a <b>Concept:</b> n/a
<b>Duplicate field in other sections</b>	

### 315 5.5.2 Caffeine, Alcohol, Tobacco, and Other Habits

<b>Term (Variable)</b>	Caffeine, Alcohol, Tobacco, and Other Habits
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	H
<b>Definition</b>	Heading
<b>User Guidance</b>	
<b>Conformance</b>	Required
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Trial Population
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	Caffeine, Alcohol, Tobacco, and Other Habits
<b>Business rules</b>	<b>Value Allowed:</b> Yes <b>Relationship:</b> n/a <b>Concept:</b> n/a
<b>Duplicate field in other sections</b>	

316

<b>Term (Variable)</b>	[Caffeine, Alcohol, Tobacco, and Other Habits]
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	D
<b>Definition</b>	
<b>User Guidance</b>	If applicable, describe any restrictions on the intake of caffeine, alcohol, tobacco, or other restrictions.
<b>Conformance</b>	Optional (repeat for each item)
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Trial Population
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	
<b>Business rules</b>	<b>Value Allowed:</b> n/a <b>Relationship:</b> n/a <b>Concept:</b> n/a
<b>Duplicate field in other sections</b>	

### 317 5.5.3 Physical Activity

<b>Term (Variable)</b>	Physical Activity
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	H
<b>Definition</b>	
<b>User Guidance</b>	
<b>Conformance</b>	Required
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Trial Population
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	Physical Activity
<b>Business rules</b>	<b>Value Allowed:</b> Yes <b>Relationship:</b> n/a <b>Concept:</b> n/a
<b>Duplicate field in other sections</b>	

318

<b>Term (Variable)</b>	[Physical Activity]
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	D
<b>Definition</b>	
<b>User Guidance</b>	If applicable, describe any restrictions on activity (for example, in first-in-human studies, activity may be restricted by ensuring participants remain in bed for 4 to 6 hours after dosing); or any other activity restrictions, such as on driving, heavy machinery use, or sun exposure.
<b>Conformance</b>	Optional (repeat for each item)
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Trial Population
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	
<b>Business rules</b>	<b>Value Allowed:</b> n/a <b>Relationship:</b> n/a <b>Concept:</b> n/a
<b>Duplicate field in other sections</b>	

319

#### 320 5.5.4 Other Activity

<b>Term (Variable)</b>	Other Activity
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	H
<b>Definition</b>	Heading
<b>User Guidance</b>	
<b>Conformance</b>	Required
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Trial Population
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	Other Activity
<b>Business rules</b>	<b>Value Allowed:</b> Yes <b>Relationship:</b> n/a <b>Concept:</b> n/a
<b>Duplicate field in other sections</b>	

321

<b>Term (Variable)</b>	[Other Activity]
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	D
<b>Definition</b>	
<b>User Guidance</b>	If applicable, describe restrictions on any other activity (for example, blood or tissue donation); or any other activity restrictions, such as on driving, heavy machinery use, or sun exposure.
<b>Conformance</b>	Optional (repeat for each item)
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Trial Population
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	
<b>Business rules</b>	<b>Value Allowed:</b> n/a <b>Relationship:</b> n/a <b>Concept:</b> n/a
<b>Duplicate field in other sections</b>	

## 322 5.6 Screen Failures

<b>Term (Variable)</b>	Screen failures
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	H
<b>Definition</b>	Heading
<b>User Guidance</b>	
<b>Conformance</b>	Required
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Trial Population
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	Screen failures
<b>Business rules</b>	<b>Value Allowed:</b> n/a <b>Relationship:</b> n/a <b>Concept:</b> n/a
<b>Duplicate field in other sections</b>	

323



<b>Term (Variable)</b>	[Screen Failure]
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	D
<b>Definition</b>	
<b>User Guidance</b>	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.
<b>Conformance</b>	Required
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Trial Population
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	
<b>Business rules</b>	<b>Value Allowed:</b> n/a <b>Relationship:</b> n/a <b>Concept:</b> n/a
<b>Duplicate field in other sections</b>	

325 **6. Trial Intervention and Concomitant Therapy**

<b>Term (Variable)</b>	Trial Intervention and Concomitant Therapy
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	H
<b>Definition</b>	Heading
<b>User Guidance</b>	In this section, describe the trial intervention being tested and any control product being used. If multiple trial interventions are to be evaluated, Section 6.1, Description of Trial Intervention, Section 6.3, Dosing and Administration, and Section 6.5, Preparation, Handling, Storage, and Accountability should differentiate between each product.
<b>Conformance</b>	Required
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Trial Intervention and Concomitant Therapy
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	Trial Intervention and Concomitant Therapy
<b>Business rules</b>	<b>Value Allowed:</b> Yes <b>Relationship:</b> n/a <b>Concept:</b> n/a
<b>Duplicate field in other sections</b>	

326

327 **6.1 Description of Trial Intervention**

<b>Term (Variable)</b>	Description of Trial Intervention
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	H
<b>Definition</b>	Heading
<b>User Guidance</b>	<p>Describe the 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, packaging, labelling, and storage conditions. Include information for all trial interventions (experimental, placebo, active comparator, sham comparator). The trial intervention should be designated as an investigational medicinal product (IMP) or non-investigational medicinal product (NIMP)/auxiliary medicinal product (AxMP).</p> <p>It is suggested that the trial intervention(s) be described concisely in a table.</p> <p>Indicate whether an additional product will be provided as part of the trial and its intended use (background intervention, challenge agent, rescue medication, diagnostic, or other). If use of an additional product is planned, include dosing information. Refer to approved regional labelling or describe any differences.</p> <p>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</p>
<b>Conformance</b>	Required
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Description of Trial Intervention
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	Description of Trial Intervention
<b>Business rules</b>	<p><b>Value Allowed:</b> Description of Trial Intervention</p> <p><b>Relationship:</b> Table row headers</p> <p><b>Concept:</b> n/a</p>
<b>Duplicate field in other sections</b>	

328

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

329

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

330

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

331

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

332

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

333

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

334

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

335

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

336

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

337

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

338



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

339

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

340

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

341

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

342

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

343

Term (Variable)	Use
Data Type	Pick List
Topic, Value or Header	D
Definition	
User Guidance	
Conformance	Required
Cardinality	
Relationship content from ToC representing the protocol hierarchy	Trial Intervention and Concomitant Therapy
Relationship (reference to high level conceptual model)	
Value	Experimental, Placebo, rescue medicine, background treatment, challenge agent, diagnostic, systemic, all prescribed
Business rules	<b>Value Allowed:</b> Yes <b>Relationship:</b> Relates to arm and intervention formulation dosage <b>Concept:</b> n/a
Duplicate field in other sections	Replicate for all interventions in the arm

344

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

345

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

346

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

347

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

348

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

349

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

350

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

## 351 6.2 Rationale for Trial Intervention

Term (Variable)	Rationale for Trial intervention
Data Type	Text
Topic, Value or Header	H
Definition	
User Guidance	
Conformance	Required
Cardinality	
Relationship content from ToC representing the protocol hierarchy	Trial Intervention and Concomitant Therapy
Relationship (reference to high level conceptual model)	
Value	Rationale for Trial intervention
Business rules	<b>Value Allowed:</b> Yes <b>Relationship:</b> n/a <b>Concept:</b> n/a
Duplicate field in other sections	

352

<b>Term (Variable)</b>	Rationale for Trial intervention
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	D
<b>Definition</b>	
<b>User Guidance</b>	Provide a rationale for the selection of the dose(s) or dose range, the route of administration, and dosing regimen (including starting dose, dose titration, dose interval) of the trial intervention and any control product. This rationale should include relevant results from previous preclinical and clinical studies that support selection of the dose and regimen. Include any information about age or sex-based pharmacokinetic or pharmacodynamic differences known from previous studies. If applicable, justify any differences in specifications, dose regimen, or therapeutic use relative to approved labelling. Include a rationale for prospective dose adjustments incorporated in the trial, if any; for example, as a result of interim analysis.
<b>Conformance</b>	Required
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Trial Intervention and Concomitant Therapy
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	
<b>Business rules</b>	<b>Value Allowed:</b> n/a <b>Relationship:</b> n/a <b>Concept:</b> n/a
<b>Duplicate field in other sections</b>	



### 354 6.3 Dosing and Administration

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

355

<b>Term (Variable)</b>	Dosing and Administration
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	D
<b>Definition</b>	Describes the details of dosing and administration, schedule, as well as any specific instructions as listed below.
<b>User Guidance</b>	<p>Describe the detailed procedures for administration of each participant's dose of trial intervention and control product. This may include the timing of dosing (for example, time of day, interval), the duration (for example, the length of time trial participants will be administered the trial intervention), the planned route of administration (for example, oral, nasal, intramuscular), 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.</p> <p>For an individual participant, describe dose modifications allowed. 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.</p> <p>Discussion of dose escalation or cohort expansion as part of the overall trial design should be covered in Section 4.2 (Trial Design).</p>
<b>Conformance</b>	Required
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Trial Intervention and Concomitant Therapy
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	
<b>Business rules</b>	<p><b>Value Allowed:</b> n/a</p> <p><b>Relationship:</b> n/a</p> <p><b>Concept:</b> n/a</p>
<b>Duplicate field in other sections</b>	

357 **6.3.1 Trial Intervention Dose Modification**

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

358

<b>Term (Variable)</b>	Dose Modification
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	D
<b>Definition</b>	Describes the conditions under which a dose modification will be made, particularly with regard to failure to respond or to toxic or untoward changes in stipulated indicators.
<b>User Guidance</b>	If applicable, the protocol should state the conditions under which a dose modification will be made for an individual participant, particularly regarding failure to respond or to toxic or untoward changes in stipulated indicators. This section can also include discussion of dose titration. Do not include information on stopping trial intervention for individual participants due to safety/other reasons as this is detailed in Section 7, Discontinuation of Trial Intervention and Participant Discontinuation/Withdrawal from the Trial.
<b>Conformance</b>	Required
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Trial Intervention and Concomitant Therapy
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	
<b>Business rules</b>	<b>Value Allowed:</b> n/a <b>Relationship:</b> n/a <b>Concept:</b> n/a
<b>Duplicate field in other sections</b>	

359

## 360 6.4 Treatment of Overdose

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

361

<b>Term (Variable)</b>	Treatment of Overdose
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	D
<b>Definition</b>	Specifies what is meant by trial intervention overdose and any known antidote or therapies.
<b>User Guidance</b>	Although clinical experience with overdose is often limited in early phases of development, provide any available project-specific guidance and information; however, ensure consistency with and avoid unnecessary duplication with any overdose information in the Investigator's Brochure /package insert. Cross-reference these documents if appropriate. Refer to the approved product label of the comparator (as applicable) for advice on overdose.
<b>Conformance</b>	Required
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Trial Intervention and Concomitant Therapy
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	
<b>Business rules</b>	<b>Value Allowed:</b> n/a <b>Relationship:</b> n/a <b>Concept:</b> n/a
<b>Duplicate field in other sections</b>	

363

## 6.5 Preparation, Handling, Storage and Accountability

Term (Variable)	Preparation, Handling, Storage, and Accountability
Data Type	Text
Topic, Value or Header	H
Definition	
User Guidance	
Conformance	Required
Cardinality	
Relationship content from ToC representing the protocol hierarchy	Trial Intervention and Concomitant Therapy
Relationship (reference to high level conceptual model)	
Value	Preparation, Handling, Storage, and Accountability
Business rules	<b>Value Allowed:</b> Yes <b>Relationship:</b> n/a <b>Concept:</b> n/a
Duplicate field in other sections	

364

### 6.5.1 Preparation of Trial Intervention

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

365

<b>Term (Variable)</b>	[Trial Intervention Preparation]
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	D
<b>Definition</b>	Describe any preparation of the trial intervention and control product and by whom.
<b>User Guidance</b>	<p>Discuss the maximum hold time once thawed/mixed, if appropriate, before administration. Include thawing, diluting, mixing, and reconstitution/preparation instructions in this section, as applicable. For drug/device combination products, include any relevant assembly or use instructions.</p> <p>If the instructions are lengthy or complicated, it is acceptable to reference the label (if applicable) or include them as a separate document(s) provided to the site (for example, a pharmacy manual). If instructions are provided to the site as a separate document(s), this should be noted in here.</p>
<b>Conformance</b>	Required
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Trial Intervention and Concomitant Therapy
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	[insert Trial Intervention Preparation text]
<b>Business rules</b>	<p><b>Value Allowed:</b> Yes</p> <p><b>Relationship:</b> n/a</p> <p><b>Concept:</b> n/a</p>
<b>Duplicate field in other sections</b>	



## 367 6.5.2 Handling and Storage of Trial Intervention

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

368

<b>Term (Variable)</b>	Trial Intervention Storage and Handling
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	D
<b>Definition</b>	Describes storage and handling requirements (for example, protection from light, temperature, humidity) for the trial intervention and control product.
<b>User Guidance</b>	For studies in which multi-dose vials are utilised, provide additional information regarding stability and expiration time after initial use (for example, the seal is broken). [Trial Intervention Storage and Handling] State how the trial intervention and control product will be provided to the Investigator. If applicable, describe the kits, packaging, or other material of the trial intervention for blinding purposes.
<b>Conformance</b>	Required
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Trial Intervention and Concomitant Therapy
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	[insert Trial Intervention Storage and Handling text]
<b>Business rules</b>	<b>Value Allowed:</b> Yes <b>Relationship:</b> n/a <b>Concept:</b> n/a
<b>Duplicate field in other sections</b>	

370 **6.5.3 Accountability of Trial Intervention**

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

371

<b>Term (Variable)</b>	Accountability
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	D
<b>Definition</b>	
<b>User Guidance</b>	<p>Describe the method by which the accountability will be achieved, including trial intervention will be distributed and related details, including:</p> <ul style="list-style-type: none"> <li>• how and by whom the trial intervention will be distributed</li> <li>• participation of a drug repository or pharmacy, if applicable,</li> <li>• plans for disposal or return of unused product, and</li> <li>• expectations for reconciliation.</li> </ul>
<b>Conformance</b>	Required
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Trial Intervention and Concomitant Therapy
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	[Accountability Text]
<b>Business rules</b>	<p><b>Value Allowed:</b> Yes</p> <p><b>Relationship:</b> n/a</p> <p><b>Concept:</b> n/a</p>
<b>Duplicate field in other sections</b>	

## 373 6.6 Participant Assignment, Randomisation and Blinding

Term (Variable)	Participant Assignment, Randomisation and Blinding
Data Type	Text
Topic, Value or Header	H
Definition	
User Guidance	
Conformance	Required
Cardinality	
Relationship content from ToC representing the protocol hierarchy	Trial Intervention and Concomitant Therapy
Relationship (reference to high level conceptual model)	
Value	Participant Assignment, Randomisation and Blinding
Business rules	<b>Value Allowed:</b> Yes <b>Relationship:</b> n/a <b>Concept:</b> n/a
Duplicate field in other sections	

### 374 6.6.1 Participant Assignment

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

375

<b>Term (Variable)</b>	Participant Assignment
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	D
<b>Definition</b>	Describes the method of assigning participants to trial intervention
<b>User Guidance</b>	Describe the method of assigning participants to trial intervention without being so specific that blinding or randomisation might be compromised. If assignment to trial intervention is by randomisation, describe when randomisation occurs relative to screening. If participants will be assigned to intervention sequences as in a cross-over trial, then describe these sequences. If adaptive randomisation or other methods of covariate balancing/minimisation are employed, include a cross-reference to the methods of analysis in Section 9, Statistical Considerations. As applicable, details regarding the implementation of procedures to minimise bias should be described.
<b>Conformance</b>	Required
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Trial Intervention and Concomitant Therapy
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	
<b>Business rules</b>	<b>Value Allowed:</b> n/a <b>Relationship:</b> n/a <b>Concept:</b> n/a
<b>Duplicate field in other sections</b>	

377 **6.6.2 Randomisation**

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

378

<b>Term (Variable)</b>	Randomisation
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	D
<b>Definition</b>	Describe the randomisation procedures (for example, central randomisation procedures), the method used to generate the randomisation schedule (for example, computer generated), the source of the randomisation schedule (for example, Sponsor, Investigator, or other), and whether or not IVRS/IWRS will be used.
<b>User Guidance</b>	To maintain the integrity of the blinding, do not include the block size. Describe the use and validation of any computer systems or programs in randomisation, stratification, and unblinding.
<b>Conformance</b>	Required
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Trial Intervention and Concomitant Therapy
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	
<b>Business rules</b>	<b>Value Allowed:</b> n/a <b>Relationship:</b> n/a <b>Concept:</b> n/a
<b>Duplicate field in other sections</b>	



### 380 6.6.3 Blinding and Unblinding

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

381

<b>Term (Variable)</b>	Blinding
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	D
<b>Definition</b>	Describe efforts to ensure that the trial intervention and control products are as indistinguishable as possible.
<b>User Guidance</b>	Plans for the maintenance of trial randomisation codes and appropriate blinding for the trial should be discussed. Procedures for planned and unplanned breaking of randomisation codes should be provided. If the trial allows for some investigators or other designated staff to remain unmasked (for example, to allow them to adjust medication), the means of maintaining the blinding for other investigators or staff should be explained. Measures to prevent unblinding by laboratory measurements, if used, should be described.
<b>Conformance</b>	Required
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Trial Intervention and Concomitant Therapy
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	
<b>Business rules</b>	<b>Value Allowed:</b> n/a <b>Relationship:</b> n/a <b>Concept:</b> n/a
<b>Duplicate field in other sections</b>	

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

383

<b>Term (Variable)</b>	Emergency Unblinding
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	D
<b>Definition</b>	Describes the criteria for breaking the trial mask (blind) or participant code.
<b>User Guidance</b>	Discuss the circumstances in which the blinding would be broken for an individual or for all participants (for example, for SAEs) and who has responsibility. Include the procedure for emergency unblinding such as via IVRS/IWRS or code envelopes as well as documentation of unblinding. Indicate to whom the intentional and unintentional unblinding should be reported.
<b>Conformance</b>	Required
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Trial Intervention and Concomitant Therapy
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	
<b>Business rules</b>	<b>Value Allowed:</b> n/a <b>Relationship:</b> n/a <b>Concept:</b> n/a
<b>Duplicate field in other sections</b>	

384

385 **6.7 Trial Intervention Compliance**

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

386

<b>Term (Variable)</b>	Additional Trial Intervention Compliance
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	D
<b>Definition</b>	Describe measures to ensure and document dosing information and trial intervention compliance (for example, accountability records, diary cards, concentration measurements).
<b>User Guidance</b>	Include a discussion of what documents are mandatory to complete (for example, participant drug log) and what source data/records will be used to document trial intervention compliance
<b>Conformance</b>	Required
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Trial Intervention and Concomitant Therapy
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	
<b>Business rules</b>	<b>Value Allowed:</b> n/a <b>Relationship:</b> n/a <b>Concept:</b> n/a
<b>Duplicate field in other sections</b>	

387

## 388 6.8 Concomitant Therapy

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

389

<b>Term (Variable)</b>	Concomitant Therapy
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	D
<b>Definition</b>	Describes how allowed concomitant therapy might affect the outcome (for example, drug-drug interaction, direct effects on the trial endpoints) and how the independent effects of concomitant and trial interventions could be ascertained.
<b>User Guidance</b>	This section should be consistent with the medication restrictions in the inclusion/exclusion criteria previously listed. Describe the data (for example, dose and frequency, and any changes) that will be recorded related to permitted concomitant medications, supplements, complementary and alternative therapies, treatments, and/or procedures, and include details about when the information will be collected (for example, screening, all trial visits).
<b>Conformance</b>	Required
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Trial Intervention and Concomitant Therapy
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	
<b>Business rules</b>	<b>Value Allowed:</b> n/a <b>Relationship:</b> n/a <b>Concept:</b> n/a
<b>Duplicate field in other sections</b>	

## 391 6.8.1 Prohibited Concomitant Therapy

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

392

<b>Term (Variable)</b>	Prohibited Concomitant Therapy
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	D
<b>Definition</b>	Describes any prohibited concomitant therapy.
<b>User Guidance</b>	Include content in this section if applicable, otherwise note as not applicable.
<b>Conformance</b>	Required
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Trial Intervention and Concomitant Therapy
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	
<b>Business rules</b>	<b>Value Allowed:</b> n/a <b>Relationship:</b> n/a <b>Concept:</b> n/a
<b>Duplicate field in other sections</b>	

## 393 6.8.2 Permitted Concomitant Therapy

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

394



<b>Term (Variable)</b>	Permitted Concomitant Therapy
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	D
<b>Definition</b>	Describes any permitted concomitant therapy.
<b>User Guidance</b>	Include content in this section if applicable, otherwise note as not applicable.
<b>Conformance</b>	Required
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Trial Intervention and Concomitant Therapy
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	
<b>Business rules</b>	<b>Value Allowed:</b> n/a <b>Relationship:</b> n/a <b>Concept:</b> n/a
<b>Duplicate field in other sections</b>	

### 395 6.8.3 Rescue Therapy

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

396

<b>Term (Variable)</b>	Rescue Therapy
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	D
<b>Definition</b>	Describes the circumstances under which use of rescue therapy is permitted.
<b>User Guidance</b>	List all medications, treatments, and/or procedures which may be provided during the trial for rescue therapy and provide relevant instructions about the administration of rescue medications. Describe the circumstances under which use of rescue therapy is permitted. 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, Discontinuation of Trial Intervention and Participant Discontinuation/Withdrawal from the Trial.
<b>Conformance</b>	Required
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Trial Intervention and Concomitant Therapy
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	
<b>Business rules</b>	<b>Value Allowed:</b> n/a <b>Relationship:</b> n/a <b>Concept:</b> n/a
<b>Duplicate field in other sections</b>	

398 **6.8.4 Other Therapy**

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

399

<b>Term (Variable)</b>	Other Therapy
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	D
<b>Definition</b>	Describes the circumstances under which use of other noninvestigational or auxiliary therapy are permitted, e.g. challenge agents.
<b>User Guidance</b>	Include content in this section if applicable.
<b>Conformance</b>	Required
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Trial Intervention and Concomitant Therapy
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	
<b>Business rules</b>	<b>Value Allowed:</b> n/a <b>Relationship:</b> n/a <b>Concept:</b> n/a
<b>Duplicate field in other sections</b>	

400

## 7. Discontinuation of Trial Intervention and Participant Withdrawal from Trial

<b>Term (Variable)</b>	Discontinuation of Trial Intervention and Participant Withdrawal from Trial
<b>Data Type</b>	
<b>Topic, Value or Header</b>	H
<b>Definition</b>	
<b>User Guidance</b>	This section must align with the intercurrent events introduced in Section 3, Trial Objectives, Endpoints, and Estimands, and the treatment described in Section 6 Trial Intervention and Concomitant Therapy.
<b>Conformance</b>	Required
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Discontinuation of Trial Intervention
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	Discontinuation of Trial Intervention and Participant Withdrawal from Trial
<b>Business rules</b>	<b>Value Allowed:</b> Yes <b>Relationship:</b> n/a <b>Concept:</b> n/a
<b>Duplicate field in other sections</b>	

## 404 7.1 Discontinuation of Trial Intervention

<b>Term (Variable)</b>	Discontinuation of Trial Intervention
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	H
<b>Definition</b>	
<b>User Guidance</b>	Discontinuation of trial intervention for a participant occurs when trial intervention is stopped earlier than the protocol planned duration
<b>Conformance</b>	Required
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Discontinuation of Trial Intervention
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	Discontinuation of Trial Intervention
<b>Business rules</b>	<b>Value Allowed:</b> Yes <b>Relationship:</b> n/a <b>Concept:</b> n/a
<b>Duplicate field in other sections</b>	

### 405 7.1.1 Criteria for Permanent Discontinuation of Trial Intervention

<b>Term (Variable)</b>	Criteria for Discontinuation of Trial Intervention
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	H
<b>Definition</b>	
<b>User Guidance</b>	
<b>Conformance</b>	Required
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Discontinuation of Trial Intervention
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	Criteria for Discontinuation of Trial Intervention
<b>Business rules</b>	<b>Value Allowed:</b> Yes <b>Relationship:</b> n/a <b>Concept:</b> n/a
<b>Duplicate field in other sections</b>	

406

<b>Term (Variable)</b>	Criteria for Permanent Discontinuation of Trial Intervention
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	D
<b>Definition</b>	Criteria's for discontinuation of a participant from trial intervention.
<b>User Guidance</b>	Describe the criteria for discontinuation of a participant from trial intervention, carefully evaluating which are appropriate for the participant population and therapy being studied. Specify whether participants who discontinue trial intervention can or cannot continue the trial (continue trial visits). Refer to the SoA for assessments to be performed at the time of and following discontinuation of trial intervention
<b>Conformance</b>	Required
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Discontinuation of Trial Intervention
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	
<b>Business rules</b>	<b>Value Allowed:</b> n/a <b>Relationship:</b> n/a <b>Concept:</b> n/a
<b>Duplicate field in other sections</b>	

408 **7.1.2 Temporary Discontinuation or Interruption of Trial Intervention**

<b>Term (Variable)</b>	Temporary Discontinuation or Interruption of Trial Intervention
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	H
<b>Definition</b>	
<b>User Guidance</b>	
<b>Conformance</b>	Required
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Discontinuation of Trial Intervention
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	Temporary Discontinuation or Interruption of Trial Intervention
<b>Business rules</b>	<b>Value Allowed:</b> Yes <b>Relationship:</b> n/a <b>Concept:</b> n/a
<b>Duplicate field in other sections</b>	

409

<b>Term (Variable)</b>	Temporary Discontinuation/Interruption of Trial Intervention
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	D
<b>Definition</b>	Specifics criteria for interrupting trial intervention
<b>User Guidance</b>	<p>Describe</p> <ul style="list-style-type: none"> <li>the criteria for temporary discontinuation or interruption of trial intervention for an individual participant</li> <li>what to do and which restrictions still apply if the participant needs to temporarily discontinue or interrupt trial intervention</li> <li>whether they will continue in the trial, and</li> <li>whether all, or specify which, assessments will be performed for the stated duration of the trial.</li> </ul> <p>Details of any rechallenge or restart after a safety-related event should be included in Section 7.1.3, Rechallenge.</p>
<b>Conformance</b>	Required
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Discontinuation of Trial Intervention
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	
<b>Business rules</b>	<p><b>Value Allowed:</b> n/a</p> <p><b>Relationship:</b> n/a</p> <p><b>Concept:</b> n/a</p>
<b>Duplicate field in other sections</b>	



411 **7.1.3 Rechallenge**

<b>Term (Variable)</b>	Rechallenge
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	H
<b>Definition</b>	
<b>User Guidance</b>	
<b>Conformance</b>	Required
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Discontinuation of Trial Intervention
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	Rechallenge
<b>Business rules</b>	<b>Value Allowed:</b> Yes <b>Relationship:</b> n/a <b>Concept:</b> n/a
<b>Duplicate field in other sections</b>	

412

<b>Term (Variable)</b>	Rechallenge
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	D
<b>Definition</b>	
<b>User Guidance</b>	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.
<b>Conformance</b>	Required
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Discontinuation of Trial Intervention
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	
<b>Business rules</b>	<b>Value Allowed:</b> n/a <b>Relationship:</b> n/a <b>Concept:</b> n/a
<b>Duplicate field in other sections</b>	

413

## 414 7.2 Participant Withdrawal from the Trial

<b>Term (Variable)</b>	Participant Withdrawal from Trial
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	H
<b>Definition</b>	
<b>User Guidance</b>	
<b>Conformance</b>	Required
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Discontinuation of Trial Intervention
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	Participant Withdrawal from Trial
<b>Business rules</b>	<b>Value Allowed:</b> Yes <b>Relationship:</b> n/a <b>Concept:</b> n/a
<b>Duplicate field in other sections</b>	

415

<b>Term (Variable)</b>	Participant Withdrawal from Trial
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	D
<b>Definition</b>	
<b>User Guidance</b>	Describe the criteria for participant withdrawal from the trial.
<b>Conformance</b>	Required
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Discontinuation of Trial Intervention
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	
<b>Business rules</b>	<b>Value Allowed:</b> n/a <b>Relationship:</b> n/a <b>Concept:</b> n/a
<b>Duplicate field in other sections</b>	

416

### 417 7.3 Lost to Follow-Up

Term (Variable)	Lost to Follow-Up
Data Type	Text
Topic, Value or Header	H
Definition	
User Guidance	
Conformance	Required
Cardinality	
Relationship content from ToC representing the protocol hierarchy	Discontinuation of Trial Intervention
Relationship (reference to high level conceptual model)	
Value	Lost to Follow-Up
Business rules	<b>Value Allowed:</b> Yes <b>Relationship:</b> n/a <b>Concept:</b> n/a
Duplicate field in other sections	

418

Term (Variable)	Lost to Follow-Up
Data Type	Text
Topic, Value or Header	D
Definition	
User Guidance	Describe how the trial will define and address participants who are lost to follow-up to help limit the amount and impact of missing data. Describe the nature and duration of follow-up, as appropriate.
Conformance	Required
Cardinality	
Relationship content from ToC representing the protocol hierarchy	Discontinuation of Trial Intervention
Relationship (reference to high level conceptual model)	
Value	
Business rules	<b>Value Allowed:</b> Yes <b>Relationship:</b> n/a <b>Concept:</b> n/a
Duplicate field in other sections	

419

## 420 7.4 Trial Stopping Rules

Term (Variable)	Trial Stopping Rules
Data Type	Text
Topic, Value or Header	H
Definition	
User Guidance	
Conformance	Required
Cardinality	
Relationship content from ToC representing the protocol hierarchy	Discontinuation of Trial Intervention
Relationship (reference to high level conceptual model)	
Value	Trial Stopping Rules
Business rules	<b>Value Allowed:</b> Yes <b>Relationship:</b> n/a <b>Concept:</b> n/a
Duplicate field in other sections	

421

Term (Variable)	Trial Stopping Rules
Data Type	Text
Topic, Value or Header	D
Definition	
User Guidance	If applicable, describe or refer to any trial-specific stopping rules described in the protocol, including guidance on when the trial should be stopped for safety reasons, when a cohort or dose escalation should be terminated, and/or when a given treatment arm should be terminated.
Conformance	Required
Cardinality	
Relationship content from ToC representing the protocol hierarchy	Discontinuation of Trial Intervention
Relationship (reference to high level conceptual model)	
Value	
Business rules	<b>Value Allowed:</b> n/a <b>Relationship:</b> n/a <b>Concept:</b> n/a
Duplicate field in other sections	

422

423 **8. Trial Assessments and Procedures**

<b>Term (Variable)</b>	Trial Assessments and Procedures
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	H
<b>Definition</b>	
<b>User Guidance</b>	<ul style="list-style-type: none"> <li>• Describe the assessments and procedures required during each phase of the trial. Provide details that are not already presented in the SoA, taking care not to duplicate information.</li> <li>• Describe methods, training, tools, instruments/questionnaires, calibration methods, etc. that will be used to record and assess data and ensure consistency across centres and participants. Include instructions on timing/conditions of assessments and if a specifically qualified person should be performing these assessments. Describe whether centralised readings and measurements will be utilised. Describe procedures to be used to maintain the blind.</li> <li>• Reference the literature for the validation of scales/instruments/questionnaires/assays.</li> <li>• Instructions or protocols for specialised tests may be presented in an appendix or a separate document and cross-referenced.</li> <li>• If the trial includes qualitative interviews, describe these evaluations.</li> <li>• If COA measures are utilised, include instructions for the investigators per local guidance. All COA parameters should be fully integrated into the appropriate sections of the protocol; separate COA sections should not be created in the protocol.</li> <li>• Include minimums and limits for procedures (for example, volume of blood draws, number of imaging procedures/biopsies, radiation exposure, etc.) if appropriate to the trial.</li> </ul>
<b>Conformance</b>	Required
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Trial Assessments and Procedures
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	Trial Assessments and Procedures
<b>Business rules</b>	<b>Value Allowed:</b> Yes <b>Relationship:</b> n/a <b>Concept:</b> n/a
<b>Duplicate field in other sections</b>	

424

425 **8.1 Screening/Baseline Assessments and Procedures**

<b>Term (Variable)</b>	Screening/Baseline Assessments and Procedures
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	H
<b>Definition</b>	
<b>User Guidance</b>	This section describes assessments and procedures that are unique to screening/baseline (for example, collection of data on participant characteristics, assessments/procedures performed for the purpose of determining eligibility or for stratification) in this section.
<b>Conformance</b>	Required
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Trial Assessment and Procedures
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	Screening/Baseline Assessments and Procedures
<b>Business rules</b>	<b>Value Allowed:</b> Yes <b>Relationship:</b> n/a <b>Concept:</b> n/a
<b>Duplicate field in other sections</b>	

426

<b>Term (Variable)</b>	Screening/Baseline Assessments and Procedures
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	D
<b>Definition</b>	
<b>User Guidance</b>	This section describes assessments and procedures that are unique to screening/baseline (for example, collection of data on participant characteristics, assessments/procedures performed for the purpose of determining eligibility or for stratification) in this section.
<b>Conformance</b>	Optional/Repeated
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Screening/Baseline Assessments and Procedures Link to objective endpoint or estimand
<b>Relationship (reference to high level conceptual model)</b>	Trial Assessment and Procedures
<b>Value</b>	
<b>Business rules</b>	<b>Value Allowed:</b> potential controlled terminology <b>Relationship:</b> n/a <b>Concept:</b> n/a
<b>Duplicate field in other sections</b>	Repeat for each procedure

## 427 8.2 Efficacy Assessments and Procedures

<b>Term (Variable)</b>	Efficacy Assessments and Procedures
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	H
<b>Definition</b>	
<b>User Guidance</b>	This section describes efficacy assessments and procedures
<b>Conformance</b>	Required
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Trial Assessment and Procedures
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	Efficacy Assessments and Procedures
<b>Business rules</b>	<b>Value Allowed:</b> Yes <b>Relationship:</b> n/a <b>Concept:</b> n/a
<b>Duplicate field in other sections</b>	

428

<b>Term (Variable)</b>	Efficacy Assessments and Procedures
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	D
<b>Definition</b>	
<b>User Guidance</b>	This section describes efficacy assessments and procedures
<b>Conformance</b>	Optional/Repeated
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Trial Assessment and Procedures
<b>Relationship (reference to high level conceptual model)</b>	Efficacy Assessments and Procedures Link to objective endpoint or estimand
<b>Value</b>	
<b>Business rules</b>	<b>Value Allowed:</b> potential controlled terminology <b>Relationship:</b> n/a <b>Concept:</b> n/a
<b>Duplicate field in other sections</b>	Repeat for each procedure



### 430 8.3 Safety Assessments and Procedures

<b>Term (Variable)</b>	Safety Assessments and Procedures
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	H
<b>Definition</b>	
<b>User Guidance</b>	<p>This section describes safety assessments and procedures in this section. Level 3 headings can be added as needed.</p> <ul style="list-style-type: none"> <li>• Identify any non-investigator party responsible for evaluation of laboratory or other safety assessments (for example, Sponsor or external Independent Data Monitoring Committee).</li> <li>• Include guidelines for the management of relevant laboratory or other safety assessment abnormalities.</li> </ul>
<b>Conformance</b>	Required
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Trial Assessment and Procedures
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	Efficacy Assessments and Procedures
<b>Business rules</b>	<p><b>Value Allowed:</b> Yes</p> <p><b>Relationship:</b> n/a</p> <p><b>Concept:</b> n/a</p>
<b>Duplicate field in other sections</b>	

431

<b>Term (Variable)</b>	Safety Assessments and Procedures
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	D
<b>Definition</b>	
<b>User Guidance</b>	<p>This section describes safety assessments and procedures in this section. Level 3 headings can be added as needed.</p> <ul style="list-style-type: none"> <li>Identify any non-investigator party responsible for evaluation of laboratory or other safety assessments (for example, Sponsor or external Independent Data Monitoring Committee).</li> <li>Include guidelines for the management of relevant laboratory or other safety assessment abnormalities.</li> </ul>
<b>Conformance</b>	Optional/ Repeated
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Trial Assessment and Procedures
<b>Relationship (reference to high level conceptual model)</b>	Safety Assessments and Procedures Link to objective endpoint or estimand
<b>Value</b>	
<b>Business rules</b>	<p><b>Value Allowed:</b> Potential controlled terminology</p> <p><b>Relationship:</b> n/a</p> <p><b>Concept:</b> n/a</p>
<b>Duplicate field in other sections</b>	Repeat for each procedure

433 **8.3.1 Physical Examination**

<b>Term (Variable)</b>	Physical Examination
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	H
<b>Definition</b>	Section heading
<b>User Guidance</b>	
<b>Conformance</b>	Required
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Trial Assessments and Procedures
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	Physical Examination
<b>Business rules</b>	<b>Value Allowed:</b> Yes <b>Relationship:</b> n/a <b>Concept:</b> n/a
<b>Duplicate field in other sections</b>	

434

<b>Term (Variable)</b>	Physical Examination
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	D
<b>Definition</b>	
<b>User Guidance</b>	Include any specific instructions with respect to the collection and interpretation of physical examinations.
<b>Conformance</b>	Optional/Repeated
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Trial Assessments and Procedures
<b>Relationship (reference to high level conceptual model)</b>	Physical Examination Link to objective endpoint or estimand
<b>Value</b>	
<b>Business rules</b>	<b>Value Allowed:</b> Potential controlled terminology <b>Relationship:</b> n/a <b>Concept:</b> n/a
<b>Duplicate field in other sections</b>	Repeat for each procedure

### 435 8.3.2 Vital Signs

<b>Term (Variable)</b>	Vital Signs
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	H
<b>Definition</b>	Section Heading
<b>User Guidance</b>	
<b>Conformance</b>	Required
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Trial Assessments and Procedures
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	Vital Signs
<b>Business rules</b>	<b>Value Allowed:</b> Yes <b>Relationship:</b> n/a <b>Concept:</b> n/a
<b>Duplicate field in other sections</b>	

436

<b>Term (Variable)</b>	Vital Signs
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	D
<b>Definition</b>	
<b>User Guidance</b>	<ul style="list-style-type: none"> <li>Carefully consider which vital signs (if any) should be measured to ensure that only essential data are collected</li> <li>Include any specific instructions with respect to the collection and interpretation of vital signs (for example, order). If orthostatic vital signs will be assessed, include instructions for supine and standing blood pressure and pulse measurements</li> <li>Select the standard methods of vital sign collection as appropriate for the countries in which the trial will be conducted</li> <li>For studies requiring sensitive blood pressure monitoring (for example, if blood pressure decrease or increase is an anticipated effect), include details on device calibration requirements or frequency of measuring.</li> </ul>
<b>Conformance</b>	Optional/Repeated
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Trial Assessments and Procedures
<b>Relationship (reference to high level conceptual model)</b>	Vital signs Link to objective endpoint or estimand
<b>Value</b>	
<b>Business rules</b>	<b>Value Allowed:</b> potential controlled terminology <b>Relationship:</b> n/a <b>Concept:</b> n/a
<b>Duplicate field in other sections</b>	Repeat for each procedure

438 **8.3.3 Electrocardiograms**

<b>Term (Variable)</b>	Electrocardiograms
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	H
<b>Definition</b>	Section Heading
<b>User Guidance</b>	
<b>Conformance</b>	Required
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Trial Assessments and Procedures
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	Electrocardiograms
<b>Business rules</b>	<b>Value Allowed:</b> Yes <b>Relationship:</b> n/a <b>Concept:</b> n/a
<b>Duplicate field in other sections</b>	

439

<b>Term (Variable)</b>	Electrocardiograms
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	D
<b>Definition</b>	
<b>User Guidance</b>	<ul style="list-style-type: none"> <li>Specify if the ECG is for screening purposes only.</li> <li>Include any specific instructions for the collection, interpretation, and archiving of ECGs (for example, time points relative to dosing with trial treatment or other evaluations).</li> <li>Indicate whether single or triplicate ECGs will be collected at each time point. If triplicate ECGs will be collected, provide necessary details.</li> <li>Indicate whether ECGs will be analysed at a central or local laboratory.</li> </ul> <p>High-quality ECG data should be collected if the goal is to assess the effects of trial treatment on ECG intervals such as the QT interval. Such ECG data may be required to meet regulatory authority expectations for a thorough ECG assessment (for example, as outlined in ICH E14) or to better assess a cardiac conduction signal from previous nonclinical or clinical studies.</p>
<b>Conformance</b>	Optional/Repeated
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Trial Assessments and Procedures
<b>Relationship (reference to high level conceptual model)</b>	Electrocardiograms Link to objective endpoint or estimand
<b>Value</b>	
<b>Business rules</b>	<p><b>Value Allowed:</b> Potential controlled terminology</p> <p><b>Relationship:</b> n/a</p> <p><b>Concept:</b> n/a</p>
<b>Duplicate field in other sections</b>	Repeat for each procedure

#### 441 8.3.4 Clinical Laboratory Assessments

<b>Term (Variable)</b>	Clinical Laboratory Assessments
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	H
<b>Definition</b>	Section Heading
<b>User Guidance</b>	
<b>Conformance</b>	Required
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Trial Assessments and Procedures
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	Clinical Laboratory Assessments
<b>Business rules</b>	<b>Value Allowed:</b> Yes <b>Relationship:</b> n/a <b>Concept:</b> n/a
<b>Duplicate field in other sections</b>	

442



<b>Term (Variable)</b>	Clinical Laboratory Assessments
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	D
<b>Definition</b>	
<b>User Guidance</b>	<ul style="list-style-type: none"> <li>• For multicenter studies in participants who are patients, make every effort to ensure routine laboratory safety assessments are performed by a central laboratory. If local laboratory assessments are required, these must be stated clearly in the protocol. Provisions should be in place to allow for the acceptance of local laboratory data (even if a central laboratory is used). Sponsor databases should be set up appropriately for the reporting of data from both central and local laboratories. Consult with the data management representative for language to be included on how data should be reported to the sponsor if a local laboratory is used.</li> <li>• Specify if the use of local laboratories is allowed in cases where initiation of trial treatment or safety follow-up is time-sensitive and the central laboratory results will not be available before the need to begin trial treatment or other actions that need to be taken for safety reasons.</li> <li>• Specify any special instructions for screening samples.</li> <li>• Specify which laboratory parameters should be included in each panel (for example, for hematology, chemistry, urinalysis). List only those that will be analysed for the trial. Confirm lists and blood volumes before finalising the protocol.</li> </ul>
<b>Conformance</b>	Optional/Repeated
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Trial Assessments and Procedures
<b>Relationship (reference to high level conceptual model)</b>	Clinical Laboratory Assessments Link to objective endpoint or estimand
<b>Value</b>	
<b>Business rules</b>	<b>Value Allowed:</b> potential controlled terminology <b>Relationship:</b> n/a <b>Concept:</b> n/a
<b>Duplicate field in other sections</b>	Repeat for each procedure

444 **8.3.5 Suicidal Ideation and Behaviour Risk Monitoring**

<b>Term (Variable)</b>	Suicidal Ideation and Behaviour Risk Monitoring
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	H
<b>Definition</b>	Section Heading
<b>User Guidance</b>	
<b>Conformance</b>	Required
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Trial Assessments and Procedures
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	Suicidal Ideation and Behaviour Risk Monitoring
<b>Business rules</b>	<b>Value Allowed:</b> Yes <b>Relationship:</b> n/a <b>Concept:</b> n/a
<b>Duplicate field in other sections</b>	

445

<b>Term (Variable)</b>	Suicidal Ideation and Behaviour Risk Monitoring
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	D
<b>Definition</b>	
<b>User Guidance</b>	If clinical trials meet any of the criteria requiring suicidal ideation and behavior risk monitoring by the guidance/guideline in each region, include any specific instructions with respect to the collection and interpretation of the assessment.
<b>Conformance</b>	Required
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Trial Assessments and Procedures
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	<p>[Trial Intervention] is considered to be central nervous system (CNS)-active. In addition, there have been some reports of {suicidal ideation or behavior as reported in the product label} when it has been given to some participants with {certain conditions}. The sponsor considers it important to monitor for such events before and during this clinical trial.</p> <p>OR</p> <p>[Trial Intervention] is considered to be an {antidepressant/ antiepileptic/ CNS-active trial treatment}. There has been some concern that {antidepressants/ antiepileptics/ some CNS-active trial treatments} may be associated with an increased risk of suicidal ideation or behavior when given to some participants with {major depressive disorder/ bipolar disorder/ epilepsy/ certain conditions}. Although this trial treatment or other similar drugs in this class have not been shown to be associated with an increased risk of suicidal thinking or behavior when given to {healthy volunteers/this participant population}, the sponsor considers it important to monitor for such events before or during this clinical trial.</p>
<b>Business rules</b>	<p><b>Value Allowed:</b> Potential controlled terminology</p> <p><b>Relationship:</b> n/a</p> <p><b>Concept:</b> n/a</p>
<b>Duplicate field in other sections</b>	

## 447 8.4 Adverse Events and Serious Adverse Events

Term (Variable)	Adverse Events and Serious Adverse Events
Data Type	Text
Topic, Value or Header	H
Definition	
User Guidance	
Conformance	Required
Cardinality	
Relationship content from ToC representing the protocol hierarchy	Trial Assessments and Procedures
Relationship (reference to high level conceptual model)	
Value	Adverse Events and Serious Adverse Events
Business rules	<b>Value Allowed:</b> Yes <b>Relationship:</b> n/a <b>Concept:</b> n/a
Duplicate field in other sections	

### 448 8.4.1 Definitions of AE and SAE

Term (Variable)	Definition of Adverse Events and Serious Adverse Events
Data Type	Text
Topic, Value or Header	H
Definition	
User Guidance	
Conformance	Required
Cardinality	
Relationship content from ToC representing the protocol hierarchy	
Relationship (reference to high level conceptual model)	
Value	Definition of Adverse Events and Serious Adverse Events
Business rules	<b>Value Allowed:</b> Yes <b>Relationship:</b> n/a <b>Concept:</b> n/a
Duplicate field in other sections	

449

Term (Variable)	[AE Definition]
Data Type	Text
Topic, Value or Header	D
Definition	
User Guidance	
Conformance	Required
Cardinality	
Relationship content from ToC representing the protocol hierarchy	
Relationship (reference to high level conceptual model)	
Value	Definition of Adverse Event
Business rules	<b>Value Allowed:</b> Yes <b>Relationship:</b> n/a <b>Concept:</b> n/a
Duplicate field in other sections	

450

Term (Variable)	[SAE Definition]
Data Type	Text
Topic, Value or Header	D
Definition	
User Guidance	
Conformance	Required
Cardinality	
Relationship content from ToC representing the protocol hierarchy	
Relationship (reference to high level conceptual model)	
Value	Definition of Serious Adverse Event
Business rules	<b>Value Allowed:</b> Yes <b>Relationship:</b> n/a <b>Concept:</b> n/a
Duplicate field in other sections	

451

Term (Variable)	Additional details and clarifications for AEs and SAEs are in Appendices 12.1 and 12.2
Data Type	Text
Topic, Value or Header	H
Definition	
User Guidance	
Conformance	Required
Cardinality	
Relationship content from ToC representing the protocol hierarchy	
Relationship (reference to high level conceptual model)	
Value	Additional details and clarifications for AEs and SAEs are in Appendices 12.1 and 12.2
Business rules	<b>Value Allowed:</b> Yes <b>Relationship:</b> n/a <b>Concept:</b> n/a
Duplicate field in other sections	

#### 8.4.2 Time Period and Frequency for Collecting AE and SAE Information

Term (Variable)	Time Period and Frequency for collection AE and SAE Information
Data Type	Text
Topic, Value or Header	H
Definition	
User Guidance	
Conformance	Required
Cardinality	
Relationship content from ToC representing the protocol hierarchy	Trial Assessments and Procedures
Relationship (reference to high level conceptual model)	
Value	Time Period and Frequency for collection AE and SAE Information
Business rules	<b>Value Allowed:</b> Yes <b>Relationship:</b> n/a <b>Concept:</b> n/a
Duplicate field in other sections	

<b>Term (Variable)</b>	Time period and frequency for collecting AEs and SAEs
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	D
<b>Definition</b>	
<b>User Guidance</b>	<p>Specify the start and ending time periods for collecting AEs and SAEs. Consider the following factors when deciding on the collection time period:</p> <ul style="list-style-type: none"> <li>• Available information on how long the trial intervention remains active in the participant</li> <li>• How long it may remain active/inactive in the participant and potentially be transferable to a fetus</li> <li>• How long it takes for AEs and SAEs to peak (e.g. is there an anticipated cumulative effect of dosing and when is this likely to occur)</li> <li>• Known late effects (e.g. secondary malignancies that will require active monitoring)</li> <li>• Trial design</li> <li>• If collection will start when the ICF is signed to capture baseline rates</li> </ul>
<b>Conformance</b>	Required
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Trial Assessments and Procedures
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	
<b>Business rules</b>	<p><b>Value Allowed:</b> n/a</p> <p><b>Relationship:</b> n/a</p> <p><b>Concept:</b> n/a</p>
<b>Duplicate field in other sections</b>	

456 **8.4.3 Identifying AEs and SAEs**

<b>Term (Variable)</b>	Identifying AEs and SAEs
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	H
<b>Definition</b>	
<b>User Guidance</b>	
<b>Conformance</b>	Required
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Trial Assessments and Procedures
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	Identifying AEs and SAEs
<b>Business rules</b>	<b>Value Allowed:</b> Yes <b>Relationship:</b> n/a <b>Concept:</b> n/a
<b>Duplicate field in other sections</b>	

457

<b>Term (Variable)</b>	Identifying AEs and SAEs
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	D
<b>Definition</b>	Specifies the method(s) used to identify AEs and SAEs.
<b>User Guidance</b>	To avoid bias, Open-ended and non leading verbal questioning of the participant is the preferred method. However, for studies in which the participants are not always able to provide valid verbal responses to open ended questions, another method may be required.
<b>Conformance</b>	Required
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Trial Assessments and Procedures
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	
<b>Business rules</b>	<b>Value Allowed:</b> n/a <b>Relationship:</b> n/a <b>Concept:</b> n/a
<b>Duplicate field in other sections</b>	

458



#### 459 8.4.4 Recording of AEs and SAEs

Term (Variable)	Recording of AEs and SAEs
Data Type	Text
Topic, Value or Header	H
Definition	
User Guidance	
Conformance	Required
Cardinality	
Duplicate field in other sections	
Relationship content from ToC representing the protocol hierarchy	Trial Assessments and Procedures
Relationship (reference to high level conceptual model)	
Value	Recording of AEs and SAEs
Business rules	<b>Value Allowed:</b> Yes <b>Relationship:</b> n/a <b>Concept:</b> n/a
Duplicate field in other sections	

460

Term (Variable)	Recording of AEs and SAEs
Data Type	Text
Topic, Value or Header	D
Definition	Specifies the Investigator's actions for recording AEs, including the final AE outcome.
User Guidance	
Conformance	Required
Cardinality	
Duplicate field in other sections	
Relationship content from ToC representing the protocol hierarchy	Trial Assessments and Procedures
Relationship (reference to high level conceptual model)	
Value	
Business rules	<b>Value Allowed:</b> n/a <b>Relationship:</b> n/a <b>Concept:</b> n/a
Duplicate field in other sections	

461

<b>Term (Variable)</b>	Further details on assessing severity and causality of AEs and SAEs are in Appendices 12.3 and 12.4
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	D
<b>Definition</b>	Specifies the Investigator's actions for recording AEs, including the final AE outcome.
<b>User Guidance</b>	
<b>Conformance</b>	Required
<b>Cardinality</b>	
<b>Duplicate field in other sections</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Trial Assessments and Procedures
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	Further details on assessing severity and causality of AEs and SAEs are in Appendices 12.3 and 12.4
<b>Business rules</b>	<b>Value Allowed:</b> n/a <b>Relationship:</b> n/a <b>Concept:</b> n/a
<b>Duplicate field in other sections</b>	

#### 462 8.4.5 Follow-up of AEs and SAEs

<b>Term (Variable)</b>	Follow-up of AEs and SAEs
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	H
<b>Definition</b>	
<b>User Guidance</b>	
<b>Conformance</b>	Required
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Trial Assessments and Procedures
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	Follow-up of AEs and SAEs
<b>Business rules</b>	<b>Value Allowed:</b> Yes <b>Relationship:</b> n/a <b>Concept:</b> n/a
<b>Duplicate field in other sections</b>	

463

<b>Term (Variable)</b>	Follow-up of AEs and SAEs
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	D
<b>Definition</b>	
<b>User Guidance</b>	Specify the procedures for follow-up of AEs and SAEs until they are resolved or considered stable. Include the assessment tools that will be used to monitor the events and the duration of follow-up after appearance of the events. Specify any procedures to be used for studies in which death is not an endpoint.
<b>Conformance</b>	Required
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Trial Assessments and Procedures
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	
<b>Business rules</b>	<b>Value Allowed:</b> n/a <b>Relationship:</b> n/a <b>Concept:</b> n/a
<b>Duplicate field in other sections</b>	

465 **8.4.6 Reporting of SAEs**

<b>Term (Variable)</b>	Reporting of SAEs
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	H
<b>Definition</b>	
<b>User Guidance</b>	
<b>Conformance</b>	Required
<b>Cardinality</b>	
<b>Duplicate field in other sections</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Trial Assessments and Procedures
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	Reporting of SAEs
<b>Business rules</b>	<b>Value Allowed:</b> Yes <b>Relationship:</b> n/a <b>Concept:</b> n/a
<b>Duplicate field in other sections</b>	

466

Term (Variable)	Reporting of SAEs
Data Type	Text
Topic, Value or Header	D
Definition	
User Guidance	Specify the SAE reporting method (e.g., an electronic data collection tool or a paper CRF).
Conformance	Required
Cardinality	
Duplicate field in other sections	
Relationship content from ToC representing the protocol hierarchy	Trial Assessments and Procedures
Relationship (reference to high level conceptual model)	
Value	
Business rules	<b>Value Allowed:</b> n/a <b>Relationship:</b> n/a <b>Concept:</b> n/a
Duplicate field in other sections	

#### 467 8.4.7 Regulatory Reporting Requirements for SAEs

Term (Variable)	Regulatory Reporting Requirements for SAEs
Data Type	Text
Topic, Value or Header	H
Definition	
User Guidance	
Conformance	Required
Cardinality	
Relationship content from ToC representing the protocol hierarchy	Trial Assessments and Procedures
Relationship (reference to high level conceptual model)	
Value	Regulatory Reporting Requirements for SAEs
Business rules	<b>Value Allowed:</b> Yes <b>Relationship:</b> n/a <b>Concept:</b> n/a
Duplicate field in other sections	

468

<b>Term (Variable)</b>	Regulatory Reporting
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	D
<b>Definition</b>	
<b>User Guidance</b>	Specify: <ul style="list-style-type: none"> <li>• The Sponsor's legal/regulatory responsibilities to report SAEs to regulatory authorities, ethics committees, and investigators.</li> <li>• The investigators' responsibilities for promptly reporting SAEs to the Sponsor to allow the Sponsor to meet their responsibilities.</li> </ul>
<b>Conformance</b>	Required
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Trial Assessments and Procedures
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	
<b>Business rules</b>	<b>Value Allowed:</b> n/a <b>Relationship:</b> n/a <b>Concept:</b> n/a
<b>Duplicate field in other sections</b>	

469

## 470 8.4.8 Serious and Unexpected Adverse Reaction Reporting

<b>Term (Variable)</b>	Serious and Unexpected Adverse Reaction Reporting
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	H
<b>Definition</b>	
<b>User Guidance</b>	
<b>Conformance</b>	Required
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Trial Assessment and Procedures
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	Serious and Unexpected Adverse Reaction Reporting
<b>Business rules</b>	<b>Value Allowed:</b> Yes <b>Relationship:</b> n/a <b>Concept:</b> n/a
<b>Duplicate field in other sections</b>	

471

<b>Term (Variable)</b>	Serious and Unexpected Adverse Reaction Reporting
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	D
<b>Definition</b>	
<b>User Guidance</b>	Include this section, if applicable.
<b>Conformance</b>	Required
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Trial Assessment and Procedures
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	
<b>Business rules</b>	<b>Value Allowed:</b> n/a <b>Relationship:</b> n/a <b>Concept:</b> n/a
<b>Duplicate field in other sections</b>	

#### 472 8.4.9 Adverse Events of Special Interest

<b>Term (Variable)</b>	Adverse Events of Special Interest
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	H
<b>Definition</b>	
<b>User Guidance</b>	
<b>Conformance</b>	Required
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Trial Assessment and Procedures
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	Adverse Events of Special Interest
<b>Business rules</b>	<b>Value Allowed:</b> Yes <b>Relationship:</b> n/a <b>Concept:</b> n/a
<b>Duplicate field in other sections</b>	

473

<b>Term (Variable)</b>	Adverse Events of Special Interest
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	D
<b>Definition</b>	
<b>User Guidance</b>	<p>Include this section, if applicable.</p> <p>Specify any Adverse Events of Special Interest (AESI):</p> <ul style="list-style-type: none"> <li>• Other events that merit reporting to the Sponsor, trial leadership, IRB, and regulatory agencies (for example, secondary malignancies in oncology studies).</li> <li>• Other reportable events not already included in the previous sections, such as cardiovascular and death events, medical device incidents (including malfunctions), laboratory test abnormalities, and trial intervention overdose.</li> </ul> <p>Include the following for each AESI:</p> <ul style="list-style-type: none"> <li>• The definition of the event. Specify the MedDRA preferred terms to use to report the AESI.</li> <li>• If it is a measurable quantity, specify how will the measurement be done.</li> </ul> <p>If it is a clinical event, specify how will it be confirmed.</p>
<b>Conformance</b>	Required
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Trial Assessment and Procedures
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	
<b>Business rules</b>	<p><b>Value Allowed:</b> n/a</p> <p><b>Relationship:</b> n/a</p> <p><b>Concept:</b> n/a</p>
<b>Duplicate field in other sections</b>	



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

<b>Term (Variable)</b>	Disease-related Events or Outcomes Not Qualifying as AEs or SAEs
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	H
<b>Definition</b>	
<b>User Guidance</b>	
<b>Conformance</b>	Required
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Trial Assessments and Procedures
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	Disease-related Events or Outcomes Not Qualifying as AEs or SAEs
<b>Business rules</b>	<b>Value Allowed:</b> Yes <b>Relationship:</b> n/a <b>Concept:</b> n/a
<b>Duplicate field in other sections</b>	

<b>Term (Variable)</b>	Disease-related Events or Outcomes Not Qualifying as AEs or SAEs
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	D
<b>Definition</b>	
<b>User Guidance</b>	Specify any Disease-Related Events (DREs), disease-related outcomes, or both that will not be reported as AEs or SAEs (for example, seizures in anticonvulsant studies).
<b>Conformance</b>	Required
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Trial Assessment and Procedures
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	
<b>Business rules</b>	<b>Value Allowed:</b> n/a <b>Relationship:</b> n/a <b>Concept:</b> n/a
<b>Duplicate field in other sections</b>	

## 479 8.5 Pregnancy and Postpartum Information

Term (Variable)	Pregnancy and Postpartum Information
Data Type	Text
Topic, Value or Header	H
Definition	
User Guidance	
Conformance	Required
Cardinality	
Relationship content from ToC representing the protocol hierarchy	Trial Assessments and Procedures
Relationship (reference to high level conceptual model)	
Value	Pregnancy and Postpartum Information
Business rules	<b>Value Allowed:</b> Yes <b>Relationship:</b> n/a <b>Concept:</b> n/a
Duplicate field in other sections	

### 480 8.5.1 Participants Who Become Pregnant During the Trial

Term (Variable)	Participants Who Become Pregnant During Trial
Data Type	Text
Topic, Value or Header	H
Definition	
User Guidance	
Conformance	Optional
Cardinality	
Relationship content from ToC representing the protocol hierarchy	Trial Assessment and Procedures
Relationship (reference to high level conceptual model)	
Value	Participants Who Become Pregnant During Trial
Business rules	<b>Value Allowed:</b> Yes <b>Relationship:</b> n/a <b>Concept:</b> n/a
Duplicate field in other sections	

481

<b>Term (Variable)</b>	Participants Who Become Pregnant During Trial
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	D
<b>Definition</b>	
<b>User Guidance</b>	<p>Specify the assessments to be performed, type and duration of monitoring, and what information will be collected for a participant who becomes pregnant during the trial (for example, 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 (for example, initial child development) with the justification.</p> <p>If exposure to trial intervention during breastfeeding is applicable, specify the assessments to be performed, type and duration of monitoring, and what information will be collected for both the participant and child.</p> <p>Specify that pregnancy is not an AE, unless a negative or consequential outcome occurs in the participant or child/foetus. If the negative event meets the seriousness criteria, then this is considered an SAE (for example, spontaneous abortion, foetal death, stillbirth, congenital anomalies, ectopic pregnancy, or pre-eclampsia) and reported per Section 8.1.5, Reporting of SAEs.</p>
<b>Conformance</b>	Optional
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Trial Assessments and Procedures
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	
<b>Business rules</b>	<p><b>Value Allowed:</b> n/a</p> <p><b>Relationship:</b> n/a</p> <p><b>Concept:</b> n/a</p>
<b>Duplicate field in other sections</b>	

483 **8.5.2 Participants Whose Partners Become Pregnant**

<b>Term (Variable)</b>	Participants Whose Partners Become Pregnant
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	H
<b>Definition</b>	
<b>User Guidance</b>	
<b>Conformance</b>	Optional
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Trial Assessments and Procedures
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	Participants Whose Partners Become Pregnant
<b>Business rules</b>	<b>Value Allowed:</b> Yes <b>Relationship:</b> n/a <b>Concept:</b> n/a
<b>Duplicate field in other sections</b>	

484

<b>Term (Variable)</b>	Participants Whose Partners Become Pregnant
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	D
<b>Definition</b>	
<b>User Guidance</b>	Specify: <ul style="list-style-type: none"> <li>• If the Investigator will attempt to collect pregnancy information for a participant's partner, who becomes pregnant while the participant is in the trial.</li> <li>• The assessments to be performed, type and duration of monitoring, and what information will be collected.</li> </ul>
<b>Conformance</b>	Optional
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Trial Assessments and Procedures
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	
<b>Business rules</b>	<b>Value Allowed:</b> n/a <b>Relationship:</b> n/a <b>Concept:</b> n/a
<b>Duplicate field in other sections</b>	

485

## 8.6 Medical Device Product Complaints for Drug/Device Combination Products

<b>Term (Variable)</b>	Medical Device Product Complaints for Drug/Device Combination Products
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	H
<b>Definition</b>	
<b>User Guidance</b>	
<b>Conformance</b>	Required
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Trial Assessments and Procedures
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	Medical Device Product Complaints for Drug/Device Combination Products
<b>Business rules</b>	<b>Value Allowed:</b> Yes <b>Relationship:</b> n/a <b>Concept:</b> n/a
<b>Duplicate field in other sections</b>	

### 8.6.1 Definition of Medical Device Product Complaints

<b>Term (Variable)</b>	Definition of Medical Device Complaints
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	H
<b>Definition</b>	
<b>User Guidance</b>	
<b>Conformance</b>	Optional
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Trial Assessment and Procedures
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	
<b>Business rules</b>	<b>Value Allowed:</b> Yes <b>Relationship:</b> n/a <b>Concept:</b> n/a
<b>Duplicate field in other sections</b>	

<b>Term (Variable)</b>	Definition of Medical Device Compliance
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	D
<b>Definition</b>	
<b>User Guidance</b>	Add this section for drug/device combination products; otherwise, omit it.
<b>Conformance</b>	Optional
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Trial Assessments and Procedures
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	The definitions and procedures in this section comply with ISO 14155 and European Medical Device Regulation (MDR) 2017/745 for clinical device research (if applicable). Both the Investigator and the Sponsor will comply with all local medical device product complaint reporting requirements.
<b>Business rules</b>	<b>Value Allowed:</b> Yes <b>Relationship:</b> n/a <b>Concept:</b> n/a
<b>Duplicate field in other sections</b>	

491

## 492 8.6.2 Recording of Medical Device Product Complaints

<b>Term (Variable)</b>	Recording of medical Device Product Complaints
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	H
<b>Definition</b>	
<b>User Guidance</b>	
<b>Conformance</b>	Optional
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Trial Assessments and Procedures
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	Recording of Medical Device Product Complaints
<b>Business rules</b>	<b>Value Allowed:</b> Yes <b>Relationship:</b> n/a <b>Concept:</b> n/a
<b>Duplicate field in other sections</b>	

493

<b>Term (Variable)</b>	Recording of Medical Device Product Complaints
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	D
<b>Definition</b>	
<b>User Guidance</b>	
<b>Conformance</b>	Optional
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Trial Assessments and Procedures
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	When a product complaint occurs, the Investigator will review relevant documentation (for example, diary cards, memory aids, hospital progress notes, laboratory reports, and diagnostics reports) related to the event.
<b>Business rules</b>	<b>Value Allowed:</b> Yes <b>Relationship:</b> n/a <b>Concept:</b> n/a
<b>Duplicate field in other sections</b>	



### 8.6.3 Time Period and Frequency for Collecting Medical Device Product Complaints

<b>Term (Variable)</b>	Time Period and Frequency for Collecting Medical Device Product Complaints
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	H
<b>Definition</b>	
<b>User Guidance</b>	
<b>Conformance</b>	Optional
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Trial Assessments and Procedures
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	Time Period and Frequency for Collecting Medical Device Product Complaints
<b>Business rules</b>	<b>Value Allowed:</b> Yes <b>Relationship:</b> n/a <b>Concept:</b> n/a
<b>Duplicate field in other sections</b>	

<b>Term (Variable)</b>	Time Period and Frequency for Collection Medical Device Product Complaints
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	D
<b>Definition</b>	
<b>User Guidance</b>	
<b>Conformance</b>	Optional
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Trial Assessments and Procedures
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	Time Period and Frequency for Collection Medical Device Product Complaints
<b>Business rules</b>	<b>Value Allowed:</b> Yes <b>Relationship:</b> n/a <b>Concept:</b> n/a
<b>Duplicate field in other sections</b>	

499

#### 8.6.4 Follow-Up of Medical Device Product Complaints

<b>Term (Variable)</b>	Follow-up of Medical Device Product Complaints
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	H
<b>Definition</b>	
<b>User Guidance</b>	
<b>Conformance</b>	Optional
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Trial Assessments and Procedures
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	Follow-up of Medical Device Product Complaints
<b>Business rules</b>	<b>Value Allowed:</b> Yes <b>Relationship:</b> n/a <b>Concept:</b> n/a
<b>Duplicate field in other sections</b>	

500

<b>Term (Variable)</b>	Follow-up of Medical Device Product Complaints
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	D
<b>Definition</b>	
<b>User Guidance</b>	Specify how medical device product complaints will be followed until resolved or considered stable. Specify the procedures for their follow-up, including what assessment tools will be used to monitor the events and the duration of follow-up after appearance of the events.
<b>Conformance</b>	Optional
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Trial Assessments and Procedures
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	
<b>Business rules</b>	<b>Value Allowed:</b> <b>Relationship:</b> n/a <b>Concept:</b> n/a
<b>Duplicate field in other sections</b>	

501

502 **8.6.5 Regulatory Reporting Requirements for Medical Device Product**  
503 **Complaints**

<b>Term (Variable)</b>	Regulatory Reporting Requirements for Medical Device Product Complaints
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	H
<b>Definition</b>	
<b>User Guidance</b>	
<b>Conformance</b>	Optional
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Trial Assessment and Procedures
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	Regulatory Reporting Requirements for Medical Device Product Complaints
<b>Business rules</b>	<b>Value Allowed:</b> Yes <b>Relationship:</b> n/a <b>Concept:</b> n/a
<b>Duplicate field in other sections</b>	

504

Term (Variable)	Regulatory Reporting Requirements for Medical Device Product Complaints
Data Type	Text
Topic, Value or Header	D
Definition	
User Guidance	This section addresses the Investigators' responsibilities for reporting Medical Device Product Complaints (e.g., within 24 hours). Sponsors have additional regulatory responsibilities that are not described in this template.
Conformance	Optional
Cardinality	
Relationship content from ToC representing the protocol hierarchy	Trial Assessment and Procedures
Relationship (reference to high level conceptual model)	
Value	
Business rules	<b>Value Allowed:</b> n/a <b>Relationship:</b> n/a <b>Concept:</b> n/a
Duplicate field in other sections	

505

## 506 8.7 Pharmacokinetics

Term (Variable)	Pharmacokinetics
Data Type	Text
Topic, Value or Header	H
Definition	Section Heading
User Guidance	
Conformance	Required
Cardinality	
Relationship content from ToC representing the protocol hierarchy	Trial Assessments and Procedures
Relationship (reference to high level conceptual model)	
Value	Pharmacokinetics
Business rules	<b>Value Allowed:</b> Yes <b>Relationship:</b> n/a <b>Concept:</b> n/a
Duplicate field in other sections	

507

<b>Term (Variable)</b>	Pharmacokinetics
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	D
<b>Definition</b>	
<b>User Guidance</b>	<ul style="list-style-type: none"> <li>• Insert text as appropriate for this trial. If population PK will be included, provide appropriate text. If PK will not be part of the trial, include a statement to this effect.</li> <li>• Describe any trial treatment concentrations to be measured and the sample collection times relative to dosing. Samples of plasma, urine, or other fluids may be taken for the purpose of measuring compliance, adjusting dose, or determining if a therapeutic “window” exists. This section of the protocol will be written in collaboration with the appropriate PK representatives and will contain information about sampling times, sample volume, sample handling procedures, assay methods, etc. Specific sample collection and processing including retention time instructions can be described in an Appendix and cross-referenced.</li> <li>• Indicate definitions for the PK parameters (for example, area under the curve [AUC], maximum observed concentration [C<sub>max</sub>], time to C<sub>max</sub> [T<sub>max</sub>], half-life [T<sub>1/2</sub>], volume of distribution [V<sub>d</sub>], clearance [CL]) of interest and how they will be calculated. Consult with the PK representative for this information</li> <li>• Describe sampling time relative to ingestion of food, posture, and possible effects of concomitant medications/alcohol/cafeine/nicotine.</li> <li>• Describe the biological sample(s) collected (blood, urine, or other such as breath, saliva, biopsies, etc.), the handling of samples, and the assay method including references to published and/or internal assay validation documentation.</li> <li>• Specify other factors that are important in assessing the PK of the trial treatment (for example, soluble circulating receptors, renal or hepatic function) and the plan for measuring these factors.</li> </ul>
<b>Conformance</b>	Optional/Repeated
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Trial Assessments and Procedures
<b>Relationship (reference to high level conceptual model)</b>	Pharmacokinetics Assessments and Procedures Link to objective endpoint or estimand
<b>Value</b>	
<b>Business rules</b>	<b>Value Allowed:</b> potential controlled terminology <b>Relationship:</b> n/a <b>Concept:</b> n/a
<b>Duplicate field in other sections</b>	Repeat for each assessment

509      **8.8      Genetics**

<b>Term (Variable)</b>	Genetics
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	H
<b>Definition</b>	Section Heading
<b>User Guidance</b>	
<b>Conformance</b>	Required
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Trial Assessments and Procedures
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	Genetics
<b>Business rules</b>	<b>Value Allowed:</b> Yes <b>Relationship:</b> n/a <b>Concept:</b> n/a
<b>Duplicate field in other sections</b>	

510

<b>Term (Variable)</b>	Genetics
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	D
<b>Definition</b>	
<b>User Guidance</b>	<p>Refer to ICH E15 and E18 as needed.</p> <p>Contact the appropriate sponsor functional area representatives to ensure that appropriate pharmacogenomic trial design text is included throughout the protocol.</p> <p>See the appropriate guidelines/templates from the sponsor functional area representatives (for example, standard attachments for shipping and handling of laboratory samples). Dependent upon the volume of these attachments, they may be added to the protocol in an additional section or provided in supplementary documents that will accompany the protocol.</p>
<b>Conformance</b>	Optional/Repeated
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Trial Assessments and Procedures
<b>Relationship (reference to high level conceptual model)</b>	Genetic Assessments and Procedures Link to objective endpoint or estimand
<b>Value</b>	
<b>Business rules</b>	<p><b>Value Allowed:</b> potential controlled terminology</p> <p><b>Relationship:</b> n/a</p> <p><b>Concept:</b> n/a</p>
<b>Duplicate field in other sections</b>	Repeat for each analysis

513 **8.9 Biomarkers**

<b>Term (Variable)</b>	Biomarkers
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	H
<b>Definition</b>	Section Heading
<b>User Guidance</b>	
<b>Conformance</b>	Required
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Trial Assessments and Procedures
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	Biomarkers
<b>Business rules</b>	<b>Value Allowed:</b> Yes <b>Relationship:</b> n/a <b>Concept:</b> n/a
<b>Duplicate field in other sections</b>	

514



<b>Term (Variable)</b>	Biomarkers
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	D
<b>Definition</b>	
<b>User Guidance</b>	<p>Refer to ICH E15 and E18 as needed.</p> <p>If biomarkers will be evaluated:</p> <ul style="list-style-type: none"> <li>• Include analyses (e.g, ribonucleic acid [RNA], serum, plasma, or other soluble markers).</li> <li>• Indicate any additional analyses, such as flow cytometry, histology, serology, immunogenicity, or histochemical analyses.</li> <li>• Ensure language describing how long the samples will be stored and how they will be destroyed is included in an ICF and any sample handling manuals.</li> <li>• If instructions for collection of samples are complex, then consider including them in an appendix rather than the main text of protocol.</li> <li>• Specify whether optional or required (both here and in the SoA). Required samples must be based on a protocol objective.</li> <li>• To distinguish between different types of biomarker samples, include the following for each sample, as appropriate: <ul style="list-style-type: none"> <li>o Indicate if residual samples.</li> <li>o Indicate the type of sample (e.g., serum, plasma, tissue, bone marrow aspirate) and volume of fluid or sample amount required and any other special instructions</li> <li>o Indicate the purpose of the sample (e.g., participant eligibility, exploratory research, RNA analysis).</li> <li>o Indicate the timing of collection (e.g., screening, disease progression); do not give specific time points (e.g., Week 4 or Cycle 4) as this information will be provided in the SoA.</li> <li>o Indicate the biomarkers that will be studied.</li> </ul> </li> </ul>
<b>Conformance</b>	Optional/Repeated
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Trial Assessments and Procedures
<b>Relationship (reference to high level conceptual model)</b>	Biomarker Assessments and Procedures Link to objective endpoint or estimand
<b>Value</b>	
<b>Business rules</b>	<p><b>Value Allowed:</b> potential controlled terminology</p> <p><b>Relationship:</b> n/a</p> <p><b>Concept:</b> n/a</p>
<b>Duplicate field in other sections</b>	Repeat for each biomarker

## 516 8.10 Immunogenicity Assessments

<b>Term (Variable)</b>	Immunogenicity Assessments
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	H
<b>Definition</b>	Section Heading
<b>User Guidance</b>	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.
<b>Conformance</b>	Required
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Trial Assessments and Procedures
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	Immunogenicity Assessments
<b>Business rules</b>	<b>Value Allowed:</b> Yes <b>Relationship:</b> n/a <b>Concept:</b> n/a
<b>Duplicate field in other sections</b>	

517

<b>Term (Variable)</b>	Immunogenicity Assessments
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	D
<b>Definition</b>	
<b>User Guidance</b>	
<b>Conformance</b>	Optional/Repeated
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Trial Assessments and Procedures
<b>Relationship (reference to high level conceptual model)</b>	Immunogenicity Assessments and Procedures Link to objective endpoint and estimand
<b>Value</b>	
<b>Business rules</b>	<b>Value Allowed:</b> n/a <b>Relationship:</b> n/a <b>Concept:</b> n/a
<b>Duplicate field in other sections</b>	Repeat for each procedure

## 518 8.11 Medical Resource Utilisation and Health Economics

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

519

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

521 **9. Statistical Considerations**

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

522

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

524 **9.1 Analysis Sets**

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

525

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

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527 **9.2 Analyses Supporting Primary Objective(s)**

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

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

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

<b>Term (Variable)</b>	Statistical Model, Hypothesis, and Method of Analysis
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	H
<b>Definition</b>	
<b>User Guidance</b>	<p>Ensure that the statistical hypothesis/model (and corresponding assumptions)/analysis is aligned with the primary estimand(s). For all applicable objectives (e.g. primary, secondary), under the appropriate header, state the null and alternative hypotheses, including the pre-planned type 1 error, or alternative criteria to define trial success and relevant operating characteristics if appropriate. Describe the statistical model used and the factors that will be included (covariates and interactions) and any rules for handling these factors (for example, pooling of centres). If applicable, state and discuss any adjustments to account for multiplicity.</p> <p>If modelling and simulation methods are to be used, please describe the model (inputs and outputs), the underlying assumptions, and the method of model fitting.</p>
<b>Conformance</b>	Required
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Statistical Considerations/Analyses Supporting Primary Objective(s)/Statistical Model, Hypothesis, and Method of Analysis
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	
<b>Business rules</b>	<b>Value Allowed:</b> yes <b>Relationship:</b> n/a <b>Concept:</b> n/a
<b>Duplicate field in other sections</b>	

<b>Term (Variable)</b>	Statistical Model, Hypothesis, and Method of Analysis
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	D
<b>Definition</b>	
<b>User Guidance</b>	<p>Ensure that the statistical hypothesis/model (and corresponding assumptions)/analysis is aligned with the primary estimand(s). For all applicable objectives (e.g. primary, secondary), under the appropriate header, state the null and alternative hypotheses, including the pre-planned type 1 error, or alternative criteria to define trial success and relevant operating characteristics if appropriate. Describe the statistical model used and the factors that will be included (covariates and interactions) and any rules for handling these factors (for example, pooling of centres). If applicable, state and discuss any adjustments to account for multiplicity.</p> <p>If modelling and simulation methods are to be used, please describe the model (inputs and outputs), the underlying assumptions, and the method of model fitting.</p>
<b>Conformance</b>	Required/Repeated
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Statistical Considerations/Analyses Supporting Primary Objective(s)/Statistical Model, Hypothesis, and Method of Analysis
<b>Relationship (reference to high level conceptual model)</b>	For each primary estimand as related to secondary endpoint combination
<b>Value</b>	Statistical Model, Hypothesis, and Method of Analysis
<b>Business rules</b>	<p><b>Value Allowed:</b> n/a</p> <p><b>Relationship:</b> n/a</p> <p><b>Concept:</b> n/a</p>
<b>Duplicate field in other sections</b>	

<b>Term (Variable)</b>	Statistical Model, Hypothesis, and Method of Analysis
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	D
<b>Definition</b>	
<b>User Guidance</b>	<p>Ensure that the statistical hypothesis/model (and corresponding assumptions)/analysis is aligned with the primary estimand(s). For all applicable objectives (e.g. primary, secondary), under the appropriate header, state the null and alternative hypotheses, including the pre-planned type 1 error, or alternative criteria to define trial success and relevant operating characteristics if appropriate. Describe the statistical model used and the factors that will be included (covariates and interactions) and any rules for handling these factors (for example, pooling of centres). If applicable, state and discuss any adjustments to account for multiplicity.</p> <p>If modelling and simulation methods are to be used, please describe the model (inputs and outputs), the underlying assumptions, and the method of model fitting.</p>
<b>Conformance</b>	Required/Repeated
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Statistical Considerations/Analyses Supporting Primary Objective(s)/Statistical Model, Hypothesis, and Method of Analysis
<b>Relationship (reference to high level conceptual model)</b>	For all applicable primary objectives state the null and alternative hypotheses, including the pre-planned type 1 error, or alternative criteria to define Trial success and relevant operating characteristics if appropriate. Describe the statistical model used and the factors that will be included (covariates and interactions) and any rules for handling these factors (for example, pooling of centres). If applicable, state and discuss any adjustments to account for multiplicity.
<b>Value</b>	Statistical Model, Hypothesis, and Method of Analysis
<b>Business rules</b>	<p><b>Value Allowed:</b> n/a</p> <p><b>Relationship:</b> n/a</p> <p><b>Concept:</b> n/a</p>
<b>Duplicate field in other sections</b>	

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

535 **9.2.2 Handling of Intercurrent Events of Primary Estimand(s)**

<b>Term (Variable)</b>	Handling of Intercurrent Events of Primary Estimand(s)
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	H
<b>Definition</b>	
<b>User Guidance</b>	<p>For each intercurrent event of the primary estimand(s) (Section 3.1, Estimand[s] for the Primary Objective[s]), explain how data will be handled for the statistical analysis in line with the primary estimand. The handling of intercurrent events in statistical analysis should be aligned with the specific estimand strategies being used.</p> <p>This section should avoid repetition with prior sections with more detail here on rationale and handling the data rather than repeating the guidance from the preceding sections.</p>
<b>Conformance</b>	Required
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Statistical Considerations/Analyses Supporting Primary Objective(s) / Handling of Intercurrent Events of Primary Estimand(s)
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	
<b>Business rules</b>	<b>Value Allowed:</b> Yes <b>Relationship:</b> n/a <b>Concept:</b> n/a
<b>Duplicate field in other sections</b>	

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<b>Term (Variable)</b>	Handling of Intercurrent Events of Primary Estimand(s)
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	D
<b>Definition</b>	
<b>User Guidance</b>	<p>For each intercurrent event of the primary estimand(s) (Section 3.1, Estimand[s] for the Primary Objective[s]), explain how data will be handled for the statistical analysis in line with the primary estimand. The handling of intercurrent events in statistical analysis should be aligned with the specific estimand strategies being used.</p> <p>This section should avoid repetition with prior sections with more detail here on rationale and handling the data rather than repeating the guidance from the preceding sections.</p>
<b>Conformance</b>	Required/Repeated
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Statistical Considerations/Analyses Supporting Primary Objective(s / Handling of Intercurrent Events of Primary Estimand(s)
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	
<b>Business rules</b>	<b>Value Allowed:</b> n/a <b>Relationship:</b> n/a <b>Concept:</b> n/a
<b>Duplicate field in other sections</b>	

538 **9.2.3 Handling of Missing Data**

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

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

#### 540 9.2.4 Sensitivity Analysis

<b>Term (Variable)</b>	Sensitivity Analysis
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	H
<b>Definition</b>	
<b>User Guidance</b>	<p>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.</p>
<b>Conformance</b>	Required
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Statistical Considerations/Analyses Supporting Primary Objective(s)/Sensitivity Analysis
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	

<b>Business rules</b>	<b>Value Allowed:</b> yes <b>Relationship:</b> n/a <b>Concept:</b> n/a
<b>Duplicate field in other sections</b>	

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

## 542 9.2.5 Supplementary Analysis

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

<b>Duplicate field in other sections</b>	
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543

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

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545 **9.3 Analysis Supporting Secondary Objective(s)**

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

546

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

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

548

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

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



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

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

553 **9.4 Analysis of Exploratory Objective(s)**

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

554

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

555

556 **9.5 Safety Analyses**

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

557

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

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559 **9.6 Other Analyses**

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

560

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

561

562 **9.7 Interim Analyses**

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

563

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

564

565 **9.8 Sample Size Determination**

<b>Term (Variable)</b>	Sample Size Determination
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	H
<b>Definition</b>	
<b>User Guidance</b>	<p>This section should detail the methods used for the determination of the sample size and a reference to tables or statistical software used to carry out the calculation. Sufficient information should be provided so that the sample size calculation can be reproduced or described.</p> <p>If the planned sample size is not derived statistically, then this should be explicitly stated along with a rationale for the intended sample size (for example, exploratory nature of pilot studies; pragmatic considerations for trials in rare diseases).</p>
<b>Conformance</b>	Required
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Statistical Considerations / Sample Size Determination
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	Sample Size Determination
<b>Business rules</b>	<p><b>Value Allowed:</b> yes</p> <p><b>Relationship:</b> n/a</p> <p><b>Concept:</b> n/a</p>
<b>Duplicate field in other sections</b>	

566



567 **9.9 Protocol Deviations**

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

568

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

569

570 **10. General Considerations: Regulatory, Ethical, and Trial Oversight**

<b>Term (Variable)</b>	General Considerations: Regulatory, Ethical, and Trial Oversight Considerations
<b>Data Type</b>	
<b>Topic, Value or Header</b>	
<b>Definition</b>	
<b>User Guidance</b>	
<b>Conformance</b>	
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	
<b>Business rules</b>	<b>Value Allowed:</b> <b>Relationship:</b> <b>Concept:</b>
<b>Duplicate field in other sections</b>	

571

572 **10.1 Regulatory and Ethical Considerations**

<b>Term (Variable)</b>	Regulatory and Ethical Considerations
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	H
<b>Definition</b>	Section Heading
<b>User Guidance</b>	<p>List the prevailing ethical, legal, and regulatory guidelines that will be applied throughout the trial.</p> <p>This trial will be conducted in accordance with the protocol and with the following:</p> <ul style="list-style-type: none"> <li>• Consensus ethical principles derived from international guidelines including the Declaration of Helsinki and Council for International Organizations of Medical Sciences (CIOMS) International Ethical Guidelines</li> <li>• ICH Good Clinical Practice (GCP) Guidelines</li> <li>• Applicable laws and regulations</li> <li>• {insert additional as needed}</li> </ul> <p>List the investigators' and sponsor's responsibilities in this regard.</p> <p><b>Investigator Responsibilities</b></p> <p>[Investigator Responsibilities]</p> <p><b>Sponsor Responsibilities</b></p> <p>[Sponsor Responsibilities]</p>
<b>Conformance</b>	Required
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	General Considerations: Regulatory, Ethical, and Trial Oversight Considerations
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	Regulatory and Ethical Considerations
<b>Business rules</b>	<p><b>Value Allowed:</b> n/a</p> <p><b>Relationship:</b> n/a</p> <p><b>Concept:</b> n/a</p>
<b>Duplicate field in other sections</b>	

573

<b>Term (Variable)</b>	Regulatory and Ethical Considerations
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	D
<b>Definition</b>	
<b>User Guidance</b>	<p>List the prevailing ethical, legal, and regulatory guidelines that will be applied throughout the trial.</p> <p>This trial will be conducted in accordance with the protocol and with the following:</p> <ul style="list-style-type: none"> <li>• Consensus ethical principles derived from international guidelines including the Declaration of Helsinki and Council for International Organizations of Medical Sciences (CIOMS) International Ethical Guidelines</li> <li>• ICH Good Clinical Practice (GCP) Guidelines</li> <li>• Applicable laws and regulations</li> <li>• {insert additional as needed}</li> </ul> <p>List the investigators' and sponsor's responsibilities in this regard.</p> <p><b>Investigator Responsibilities</b></p> <p>[Investigator Responsibilities]</p> <p><b>Sponsor Responsibilities</b></p> <p>[Sponsor Responsibilities]</p>
<b>Conformance</b>	Required/Repeatable Required/Repeatable
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	General Considerations: Regulatory, Ethical, and Trial Oversight Considerations / Regulatory and Ethical Considerations
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	
<b>Business rules</b>	<p><b>Value Allowed:</b> Yes  <b>Relationship:</b> n/a  <b>Concept:</b> n/a</p> <p>Note: This field can contain a text value</p>
<b>Duplicate field in other sections</b>	

<b>Term (Variable)</b>	Investigator Responsibilities
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	H
<b>Definition</b>	
<b>User Guidance</b>	<p>List the prevailing ethical, legal, and regulatory guidelines that will be applied throughout the trial.</p> <p>This trial will be conducted in accordance with the protocol and with the following:</p> <ul style="list-style-type: none"> <li>• Consensus ethical principles derived from international guidelines including the Declaration of Helsinki and Council for International Organizations of Medical Sciences (CIOMS) International Ethical Guidelines</li> <li>• ICH Good Clinical Practice (GCP) Guidelines</li> <li>• Applicable laws and regulations</li> <li>• {insert additional as needed}</li> </ul> <p>List the investigators' and sponsor's responsibilities in this regard.</p> <p><b>Investigator Responsibilities</b></p> <p>[Investigator Responsibilities]</p>
<b>Conformance</b>	Required
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	General Considerations: Regulatory, Ethical, and Trial Oversight Considerations / Regulatory and Ethical Considerations
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	Investigator Responsibilities
<b>Business rules</b>	<p><b>Value Allowed:</b> Yes</p> <p><b>Relationship:</b> n/a</p> <p><b>Concept:</b> n/a</p>
<b>Duplicate field in other sections</b>	

<b>Term (Variable)</b>	Investigator Responsibilities
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	D
<b>Definition</b>	
<b>User Guidance</b>	<p>List the prevailing ethical, legal, and regulatory guidelines that will be applied throughout the trial.</p> <p>This trial will be conducted in accordance with the protocol and with the following:</p> <ul style="list-style-type: none"> <li>• Consensus ethical principles derived from international guidelines including the Declaration of Helsinki and Council for International Organizations of Medical Sciences (CIOMS) International Ethical Guidelines</li> <li>• ICH Good Clinical Practice (GCP) Guidelines</li> <li>• Applicable laws and regulations</li> <li>• {insert additional as needed}</li> </ul> <p>List the investigators' and sponsor's responsibilities in this regard.</p> <p><b>Investigator Responsibilities</b></p> <p>[Investigator Responsibilities]</p>
<b>Conformance</b>	Required
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	General Considerations: Regulatory, Ethical, and Trial Oversight Considerations / Regulatory and Ethical Considerations
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	
<b>Business rules</b>	<p><b>Value Allowed:</b> Yes</p> <p><b>Relationship:</b> n/a</p> <p><b>Concept:</b> n/a</p>
<b>Duplicate field in other sections</b>	

<b>Term (Variable)</b>	Sponsor Responsibilities
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	H
<b>Definition</b>	
<b>User Guidance</b>	<p>List the prevailing ethical, legal, and regulatory guidelines that will be applied throughout the trial.</p> <p>This trial will be conducted in accordance with the protocol and with the following:</p> <ul style="list-style-type: none"> <li>• Consensus ethical principles derived from international guidelines including the Declaration of Helsinki and Council for International Organizations of Medical Sciences (CIOMS) International Ethical Guidelines</li> <li>• ICH Good Clinical Practice (GCP) Guidelines</li> <li>• Applicable laws and regulations</li> <li>• {insert additional as needed}</li> </ul> <p>List the investigators' and sponsor's responsibilities in this regard.</p> <p><b>Sponsor Responsibilities</b></p> <p>[Sponsor Responsibilities]</p>
<b>Conformance</b>	Required
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	General Considerations: Regulatory, Ethical, and Trial Oversight Considerations / Regulatory and Ethical Considerations
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	Sponsor Responsibilities
<b>Business rules</b>	<p><b>Value Allowed:</b> Yes</p> <p><b>Relationship:</b> n/a</p> <p><b>Concept:</b> n/a</p>
<b>Duplicate field in other sections</b>	

<b>Term (Variable)</b>	Sponsor Responsibilities
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	D
<b>Definition</b>	
<b>User Guidance</b>	<p>List the prevailing ethical, legal, and regulatory guidelines that will be applied throughout the trial.</p> <p>This trial will be conducted in accordance with the protocol and with the following:</p> <ul style="list-style-type: none"> <li>• Consensus ethical principles derived from international guidelines including the Declaration of Helsinki and Council for International Organizations of Medical Sciences (CIOMS) International Ethical Guidelines</li> <li>• ICH Good Clinical Practice (GCP) Guidelines</li> <li>• Applicable laws and regulations</li> <li>• {insert additional as needed}</li> </ul> <p>List the investigators' and sponsor's responsibilities in this regard.</p> <p><b>Sponsor Responsibilities</b></p> <p>[Sponsor Responsibilities]</p>
<b>Conformance</b>	Required
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	General Considerations: Regulatory, Ethical, and Trial Oversight Considerations / Regulatory and Ethical Considerations
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	
<b>Business rules</b>	<p><b>Value Allowed:</b> Yes</p> <p><b>Relationship:</b> n/a</p> <p><b>Concept:</b> n/a</p>
<b>Duplicate field in other sections</b>	



579 **10.2 Committees**

<b>Term (Variable)</b>	Committees
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	H
<b>Definition</b>	
<b>User Guidance</b>	<p>Briefly describe the administrative structure for the trial (for example, Internal Review Committee/Internal Review Forum, Steering Committee, Expert Advisory Committee, Data Monitoring Committee or Data Safety Monitoring Board). Note that specific details are not required.</p> <p>[Committees Structure]</p>
<b>Conformance</b>	Required
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	General Considerations: Regulatory, Ethical, and Trial Oversight Considerations / Committees Structure
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	Committees
<b>Business rules</b>	<p><b>Value Allowed:</b> n/a  <b>Relationship:</b> n/a  <b>Concept:</b> n/a</p> <p>Specific details are not required</p>
<b>Duplicate field in other sections</b>	

580

<b>Term (Variable)</b>	Committees Structure
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	D
<b>Definition</b>	
<b>User Guidance</b>	<p>Briefly describe the administrative structure for the trial (for example, Internal Review Committee/Internal Review Forum, Steering Committee, Expert Advisory Committee, Data Monitoring Committee or Data Safety Monitoring Board). Note that specific details are not required.</p> <p>[Committees Structure]</p>
<b>Conformance</b>	Required/Repeated
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	General Considerations: Regulatory, Ethical, and Trial Oversight Considerations / Committees Structure
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	
<b>Business rules</b>	<p><b>Value Allowed:</b> Yes  <b>Relationship:</b> n/a  <b>Concept:</b> n/a</p> <p>Specific details are not required</p>
<b>Duplicate field in other sections</b>	For each committee

581

582 **10.3 Informed Consent Process**

<b>Term (Variable)</b>	Informed Consent Process
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	H
<b>Definition</b>	Section Heading
<b>User Guidance</b>	<p>Include the primary ethical concerns of this trial. Consider the key elements of the informed consent process, including any special concerns and how addressed (for example, assent, capacity, legally acceptable representative).</p> <p><b>[Informed Consent Process]</b>            If enrolment in the trial may occur during an emergency in which the participant or their legally authorised representative is not able or available to give consent, describe the consent process.</p> <p><b>[Emergency Consent Process]</b>            Rescreening            If participants can be rescreened, add the text to state whether the participant needs to complete a new consent. Screen failure and rescreening should be clearly defined in the protocol, with cross-reference to those definitions.</p> <p><b>[Consent Requirements for Rescreening]</b>            If participants will be asked to consent to optional exploratory research using the remainder of mandatory samples, include text that addresses the use of remaining samples for optional exploratory research.</p> <p><b>[Additional ICF text for Use of Remaining Samples in Optional Exploratory Research]</b></p>
<b>Conformance</b>	Required
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	General Considerations: Regulatory, Ethical, and Trial Oversight Considerations / Informed Consent Process
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	Informed Consent Process
<b>Business rules</b>	<p><b>Value Allowed:</b> n/a</p> <p><b>Relationship:</b> n/a</p> <p><b>Concept:</b> n/a</p>
<b>Duplicate field in other sections</b>	

583

<b>Term (Variable)</b>	Informed Consent Process
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	D
<b>Definition</b>	
<b>User Guidance</b>	<p>Include the primary ethical concerns of this trial. Consider the key elements of the informed consent process, including any special concerns and how addressed (for example, assent, capacity, legally acceptable representative).</p> <p><b>[Informed Consent Process]-Required/Required</b>  If enrollment in the trial may occur during an emergency in which the participant or their legally authorised representative is not able or available to give consent, describe the consent process.</p> <p><b>[Emergency Consent Process]-Required/Required</b></p> <p><b>[Rescreening]-Required/Required</b>  <b>Value-Rescreening</b>  If participants can be rescreened, add the text to state whether the participant needs to complete a new consent. Screen failure and rescreening should be clearly defined in the protocol, with cross-reference to those definitions.</p> <p><b>[Consent Requirements for Rescreening]Required/Required</b>  If participants will be asked to consent to optional exploratory research using the remainder of mandatory samples, include text that addresses the use of remaining samples for optional exploratory research.</p> <p><b>[Additional ICF text for Use of Remaining Samples in Optional Exploratory Research]</b></p>
<b>Conformance</b>	Required
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	General Considerations: Regulatory, Ethical, and Trial Oversight Considerations / Informed Consent Process
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	
<b>Business rules</b>	<p><b>Value Allowed:</b> yes  <b>Relationship:</b> n/a  <b>Concept:</b> n/a</p> <p>Note: This field can contain a text value</p>
<b>Duplicate field in other sections</b>	

585 **10.4 Data Protection**

<b>Term (Variable)</b>	Data Protection
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	H
<b>Definition</b>	
<b>User Guidance</b>	<p>Include all measures to be taken to comply with the applicable rules on protection of personal data and any relevant information on measures to be taken in case of a data security breach</p> <p><b>[Data Protection]</b></p>
<b>Conformance</b>	Optional
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	General Considerations: Regulatory, Ethical, and Trial Oversight Considerations / Data Protection
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	Data Protection
<b>Business rules</b>	<p><b>Value Allowed:</b> Yes</p> <p><b>Relationship:</b> n/a</p> <p><b>Concept:</b> n/a</p> <p>Note: This field can contain a text value</p>
<b>Duplicate field in other sections</b>	

586

587 **10.5 Early Site Closure or Trial Termination**

<b>Term (Variable)</b>	Early Site Closure or Trial Termination
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	H
<b>Definition</b>	
<b>User Guidance</b>	
<b>Conformance</b>	Required
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	General Considerations: Regulatory, Ethical, and Trial Oversight Considerations / Data Protection
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	
<b>Business rules</b>	<b>Value Allowed:</b> n/a <b>Relationship:</b> n/a <b>Concept:</b> n/a Note: This field can contain a text value
<b>Duplicate field in other sections</b>	
<b>Duplicate field in other sections</b>	

588

<b>Term (Variable)</b>	Decision Rights for Site Closure and Trial Termination
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	D
<b>Definition</b>	
<b>User Guidance</b>	
<b>Conformance</b>	Required
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	General Considerations: Regulatory, Ethical, and Trial Oversight Considerations / Data Protection
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	
<b>Business rules</b>	<b>Value Allowed:</b> n/a <b>Relationship:</b> n/a <b>Concept:</b> n/a Note: This field can contain a text value
<b>Duplicate field in other sections</b>	
<b>Duplicate field in other sections</b>	

589

<b>Term (Variable)</b>	Criteria for Early Closure
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	D
<b>Definition</b>	
<b>User Guidance</b>	
<b>Conformance</b>	Required
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	General Considerations: Regulatory, Ethical, and Trial Oversight Considerations / Data Protection
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	
<b>Business rules</b>	<b>Value Allowed:</b> n/a <b>Relationship:</b> n/a <b>Concept:</b> n/a Note: This field can contain a text value
<b>Duplicate field in other sections</b>	
<b>Duplicate field in other sections</b>	

590

<b>Term (Variable)</b>	Responsibilities Following Termination or Suspension
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	D
<b>Definition</b>	
<b>User Guidance</b>	
<b>Conformance</b>	Required
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	General Considerations: Regulatory, Ethical, and Trial Oversight Considerations / Data Protection
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	
<b>Business rules</b>	<b>Value Allowed:</b> n/a <b>Relationship:</b> n/a <b>Concept:</b> n/a Note: This field can contain a text value
<b>Duplicate field in other sections</b>	
<b>Duplicate field in other sections</b>	



## 592 11. General Considerations: Risk Management and Quality Assurance

Term (Variable)	General Considerations: Risk Management and Quality Assurance
Data Type	Text
Topic, Value or Header	H
Definition	Section Heading
User Guidance	
Conformance	Required
Cardinality	
Relationship content from ToC representing the protocol hierarchy	General Considerations: Risk Management and Quality Assurance
Relationship (reference to high level conceptual model)	
Value	General Considerations: Risk Management and Quality Assurance
Business rules	<b>Value Allowed:</b> Yes <b>Relationship:</b> n/a <b>Concept:</b> n/a
Duplicate field in other sections	

### 593 11.1 Quality Tolerance Limits

Term (Variable)	Quality Tolerance Limits
Data Type	Text
Topic, Value or Header	H
Definition	Section Heading
User Guidance	
Conformance	Required
Cardinality	
Relationship content from ToC representing the protocol hierarchy	General Considerations: Risk Management and Quality Assurance /Quality by Design and Quality Tolerance Limits
Relationship (reference to high level conceptual model)	
Value	Quality Tolerance Limits
Business rules	<b>Value Allowed:</b> Yes <b>Relationship:</b> n/a <b>Concept:</b> n/a
Duplicate field in other sections	

594

<b>Term (Variable)</b>	Quality Tolerance Limits
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	D
<b>Definition</b>	
<b>User Guidance</b>	<p>Indicate aspects of the trial design which attend to the principles of Quality by Design, such as clear trial objectives, meaningful endpoints, and selection of appropriate trial population. Indicate where Quality Tolerance Limits will be predefined, how they will be monitored during the trial, and expected discussion in the clinical trial report.</p> <p><b>[QTL]</b></p>
<b>Conformance</b>	Required
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	General Considerations: Risk Management and Quality Assurance /Quality by Design and Quality Tolerance Limits
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	
<b>Business rules</b>	<p><b>Value Allowed:</b> n/a</p> <p><b>Relationship:</b> n/a</p> <p><b>Concept:</b> n/a</p> <p>Note: This field can contain a text value</p>
<b>Duplicate field in other sections</b>	

596 **11.2 Data Quality Assurance**

<b>Term (Variable)</b>	Data Quality Assurance
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	H
<b>Definition</b>	Section Heading
<b>User Guidance</b>	<p>Delineate the responsibilities of the Sponsor and Investigator with respect to data quality assurance.</p> <p><b>[Sponsor or Designee Responsibilities for Data Quality Assurance]</b></p> <p><b>[Investigator Responsibilities for Data Quality Assurance]</b></p>
<b>Conformance</b>	Required
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	General Considerations: Risk Management and Quality Assurance /Data Quality Assurance
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	Data Quality Assurance
<b>Business rules</b>	<p><b>Value Allowed:</b> Yes</p> <p><b>Relationship:</b> n/a</p> <p><b>Concept:</b> n/a</p>
<b>Duplicate field in other sections</b>	

597

<b>Term (Variable)</b>	Data Quality Assurance
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	H
<b>Definition</b>	
<b>User Guidance</b>	Delineate the responsibilities of the Sponsor and Investigator with respect to data quality assurance. [Sponsor or Designee Responsibilities for Data Quality Assurance] [Investigator Responsibilities for Data Quality Assurance]
<b>Conformance</b>	Required
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	General Considerations: Risk Management and Quality Assurance /Data Quality Assurance
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	Data Quality Assurance
<b>Business rules</b>	<b>Value Allowed:</b> n/a <b>Relationship:</b> n/a <b>Concept:</b> n/a Note: This field can contain a text value
<b>Duplicate field in other sections</b>	

<b>Term (Variable)</b>	Data Quality Assurance
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	D
<b>Definition</b>	
<b>User Guidance</b>	<p>Delineate the responsibilities of the Sponsor and Investigator with respect to data quality assurance.</p> <p><b>[Sponsor or Designee Responsibilities for Data Quality Assurance]</b></p> <p><b>[Investigator Responsibilities for Data Quality Assurance]</b></p>
<b>Conformance</b>	Required
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	General Considerations: Risk Management and Quality Assurance /Data Quality Assurance
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	
<b>Business rules</b>	<p><b>Value Allowed:</b> n/a</p> <p><b>Relationship:</b> n/a</p> <p><b>Concept:</b> n/a</p> <p>Note: This field can contain a text value</p>
<b>Duplicate field in other sections</b>	

600 **11.3 Source Data**

<b>Term (Variable)</b>	Source Data
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	H
<b>Definition</b>	Section Heading
<b>User Guidance</b>	<p>Establish the importance of source data and expectation for traceability of transcribed information back to source. Delineate expectations for Investigators and trial monitors. Define what constitutes source data and its origin or provide a reference to the location of these definitions, if contained in a separate document, such as a monitoring guideline or source data acknowledgement).</p> <p><b>[Source Data Introduction]- Required/Required</b></p> <p><b>[Investigator Expectations for Source Data]- Required/Required</b></p> <p><b>[Trial Monitor Expectations for Source Data]- Required/Required</b></p> <p><b>[Definition of Source Data]- Required/Required</b></p>
<b>Conformance</b>	Required
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	General Considerations: Risk Management and Quality Assurance /Source Data
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	Source Data
<b>Business rules</b>	<p><b>Value Allowed:</b> Yes</p> <p><b>Relationship:</b> n/a</p> <p><b>Concept:</b> n/a</p>
<b>Duplicate field in other sections</b>	

601

<b>Term (Variable)</b>	Source Data Introduction
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	D
<b>Definition</b>	Procedures for the identification of data to be recorded directly on the CRF considered as source data.
<b>User Guidance</b>	<p>Establish the importance of source data and expectation for traceability of transcribed information back to source. Delineate expectations for Investigators and trial monitors. Define what constitutes source data and its origin or provide a reference to the location of these definitions, if contained in a separate document, such as a monitoring guideline or source data acknowledgement).</p> <p><b>[Source Data Introduction]- Required/Required</b></p> <p><b>[Investigator Expectations for Source Data]- Required/Required</b></p> <p><b>[Trial Monitor Expectations for Source Data]- Required/Required</b></p> <p><b>[Definition of Source Data]- Required/Required</b></p>
<b>Conformance</b>	Required
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	General Considerations: Risk Management and Quality Assurance /Source Data
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	
<b>Business rules</b>	<p><b>Value Allowed:</b> n/a</p> <p><b>Relationship:</b> n/a</p> <p><b>Concept:</b> n/a</p> <p>Note: This field can contain a text value</p>
<b>Duplicate field in other sections</b>	

602

<b>Term (Variable)</b>	Investigator Expectations for Source Data
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	D
<b>Definition</b>	Procedures for the identification of data to be recorded directly on the CRF considered as source data.
<b>User Guidance</b>	<p>Establish the importance of source data and expectation for traceability of transcribed information back to source. Delineate expectations for Investigators and trial monitors. Define what constitutes source data and its origin or provide a reference to the location of these definitions, if contained in a separate document, such as a monitoring guideline or source data acknowledgement).</p> <p><b>[Source Data Introduction]- Required/Required</b></p> <p><b>[Investigator Expectations for Source Data]- Required/Required</b></p> <p><b>[Trial Monitor Expectations for Source Data]- Required/Required</b></p> <p><b>[Definition of Source Data]- Required/Required</b></p>
<b>Conformance</b>	Required
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	General Considerations: Risk Management and Quality Assurance /Source Data
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	
<b>Business rules</b>	<p><b>Value Allowed:</b> n/a</p> <p><b>Relationship:</b> n/a</p> <p><b>Concept:</b> n/a</p> <p>Note: This field can contain a text value</p>
<b>Duplicate field in other sections</b>	

603



<b>Term (Variable)</b>	Trial Monitor Expectations for Source Data
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	D
<b>Definition</b>	Procedures for the identification of data to be recorded directly on the CRF considered as source data.
<b>User Guidance</b>	<p>Establish the importance of source data and expectation for traceability of transcribed information back to source. Delineate expectations for Investigators and trial monitors. Define what constitutes source data and its origin or provide a reference to the location of these definitions, if contained in a separate document, such as a monitoring guideline or source data acknowledgement).</p> <p><b>[Source Data Introduction]- Required/Required</b></p> <p><b>[Investigator Expectations for Source Data]- Required/Required</b></p> <p><b>[Trial Monitor Expectations for Source Data]- Required/Required</b></p> <p><b>[Definition of Source Data]- Required/Required</b></p>
<b>Conformance</b>	Required
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	General Considerations: Risk Management and Quality Assurance /Source Data
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	
<b>Business rules</b>	<p><b>Value Allowed:</b> n/a</p> <p><b>Relationship:</b> n/a</p> <p><b>Concept:</b> n/a</p> <p>Note: This field can contain a text value</p>
<b>Duplicate field in other sections</b>	

<b>Term (Variable)</b>	Definition of Source Data
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	D
<b>Definition</b>	Procedures for the identification of data to be recorded directly on the CRF considered as source data.
<b>User Guidance</b>	<p>Establish the importance of source data and expectation for traceability of transcribed information back to source. Delineate expectations for Investigators and trial monitors. Define what constitutes source data and its origin or provide a reference to the location of these definitions, if contained in a separate document, such as a monitoring guideline or source data acknowledgement).</p> <p><b>[Source Data Introduction]- Required</b></p> <p><b>[Investigator Expectations for Source Data]- Required</b></p> <p><b>[Trial Monitor Expectations for Source Data]- Required</b></p> <p><b>[Definition of Source Data]- Required</b></p>
<b>Conformance</b>	Required
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	General Considerations: Risk Management and Quality Assurance /Source Data
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	
<b>Business rules</b>	<p><b>Value Allowed:</b> n/a</p> <p><b>Relationship:</b> n/a</p> <p><b>Concept:</b> n/a</p> <p>Note: This field can contain a text value</p>
<b>Duplicate field in other sections</b>	

606 **12. Appendix: Adverse Events and Serious Adverse Events-Definitions,**  
607 **Severity, and Causality**

<b>Term (Variable)</b>	Appendix / Appendix 12 Adverse Events and Serious Adverse Events-Definitions, Severity, and Causality
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	H
<b>Definition</b>	Section Heading
<b>User Guidance</b>	
<b>Conformance</b>	Required
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Appendix / Appendix 12 Adverse Events and Serious Adverse Events-Definitions, Severity, and Causality
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	Appendix / Appendix 12 Adverse Events and Serious Adverse Events-Definitions, Severity, and Causality
<b>Business rules</b>	<b>Value Allowed:</b> Yes <b>Relationship:</b> n/a <b>Concept:</b> n/a
<b>Duplicate field in other sections</b>	

608

## 12.1 Further Details and Clarifications on the AE Definition

<b>Term (Variable)</b>	Further Details and Clarifications on the AE Definition
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	H
<b>Definition</b>	Any untoward medical occurrence in a patient or clinical investigation subject administered a pharmaceutical product and which does not necessarily have a causal relationship with this treatment. An adverse event (AE) can therefore be any unfavourable and unintended sign (including an abnormal laboratory finding), symptom, or disease temporally associated with the use of a medicinal (investigational) product, whether or not related to the medicinal (investigational) product (see the ICH Guideline for Clinical Safety Data Management: Definitions and Standards for Expedited Reporting).
<b>User Guidance</b>	Specify: <ul style="list-style-type: none"> <li>• The AE definition. The standard definition is below is from ICH E2A Clinical Safety Data Management: Definitions and Standards for Expedited Reporting. Note that clarifications of events that do and do not meet the definition are not standard and may need to be customised for the trial.</li> <li>• Any relevant regional requirements.</li> <li>• Events that meet and do not meet the AE definition.</li> <li>• Any trial-specific clarifications.</li> </ul>
<b>Conformance</b>	Required
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Appendix / Appendix 12 Adverse Events and Serious Adverse Events-Definitions, Severity, and Causality/Definition of Adverse Event
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	Further Details and Clarifications on the AE Definition
<b>Business rules</b>	<b>Value Allowed:</b> Yes <b>Relationship:</b> n/a <b>Concept:</b> n/a
<b>Duplicate field in other sections</b>	

<b>Term (Variable)</b>	Further Details and Clarifications on the AE Definition
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	D
<b>Definition</b>	Any untoward medical occurrence in a patient or clinical investigation subject administered a pharmaceutical product and which does not necessarily have a causal relationship with this treatment. An adverse event (AE) can therefore be any unfavourable and unintended sign (including an abnormal laboratory finding), symptom, or disease temporally associated with the use of a medicinal (investigational) product, whether or not related to the medicinal (investigational) product (see the ICH Guideline for Clinical Safety Data Management: Definitions and Standards for Expedited Reporting).
<b>User Guidance</b>	Specify: <ul style="list-style-type: none"> <li>• The AE definition. The standard definition is below is from ICH E2A Clinical Safety Data Management: Definitions and Standards for Expedited Reporting. Note that clarifications of events that do and do not meet the definition are not standard and may need to be customised for the trial.</li> <li>• Any relevant regional requirements.</li> <li>• Events that meet and do not meet the AE definition.</li> <li>• Any trial-specific clarifications.</li> </ul>
<b>Conformance</b>	Required
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Appendix / Appendix 12 Adverse Events and Serious Adverse Events- Definitions, Severity, and Causality/Definition of Adverse Event
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	
<b>Business rules</b>	<b>Value Allowed:</b> Yes <b>Relationship:</b> n/a <b>Concept:</b> n/a
<b>Duplicate field in other sections</b>	

612 **12.2 Further Details and Clarifications on the SAE Definition**

<b>Term (Variable)</b>	Further Details and Clarifications on the SAE Definition
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	H
<b>Definition</b>	Section heading
<b>User Guidance</b>	Specify: <ul style="list-style-type: none"> <li>• The SAE definition. The standard definition is in ICH E2A.</li> <li>• Any relevant regional requirements.</li> <li>• Events that meet and do not meet the SAE definition.</li> <li>• Any trial-specific clarifications.</li> </ul> <b>[Further Details and Clarifications on the SAE Definition]</b>
<b>Conformance</b>	Required
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Appendix / Appendix 12 Adverse Events and Serious Adverse Events-Definitions, Severity, and Causality/Further Details and Clarifications on the SAE Definition
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	Further Details and Clarifications on the SAE Definition
<b>Business rules</b>	<b>Value Allowed:</b> Yes <b>Relationship:</b> n/a <b>Concept:</b> n/a
<b>Duplicate field in other sections</b>	

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<b>Term (Variable)</b>	Further Details and Clarifications on the SAE Definition
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	D
<b>Definition</b>	<p>A SAE is any untoward medical occurrence that, at any dose:</p> <ol style="list-style-type: none"> <li>Results in death</li> <li>Is life-threatening</li> <li>Requires hospitalisation or prolongation of existing hospitalisation</li> <li>Results in persistent disability or incapacity</li> <li>Is a congenital anomaly or birth defect</li> <li>Is another important medical event that may not result in death, be life-threatening, or require hospitalisation, but is considered serious when, based upon appropriate medical judgment, it may jeopardise the participant and may require medical or surgical intervention to prevent one of the outcomes listed above.</li> </ol>
<b>User Guidance</b>	<p>Specify:</p> <ul style="list-style-type: none"> <li>The SAE definition. The standard definition is in ICH E2A.</li> <li>Any relevant regional requirements.</li> <li>Events that meet and do not meet the SAE definition.</li> <li>Any trial-specific clarifications.</li> </ul> <p><b>[Further Details and Clarifications on the SAE Definition]</b></p>
<b>Conformance</b>	Required
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Appendix / Appendix 12 Adverse Events and Serious Adverse Events-Definitions, Severity, and Causality/Further Details and Clarifications on the SAE Definition
<b>Relationship (reference to high level conceptual model)</b>	

<b>Value</b>	<p>A SAE is any untoward medical occurrence that, at any dose:</p> <ul style="list-style-type: none"> <li>• Results in death</li> <li>• Is life-threatening</li> </ul> <ol style="list-style-type: none"> <li>a. Requires hospitalisation or prolongation of existing hospitalisation</li> <li>b. Results in persistent disability or incapacity</li> <li>c. Is a congenital anomaly or birth defect</li> <li>d. Is another important medical event that may not result in death, be life-threatening, or require hospitalisation, but is considered serious when, based upon appropriate medical judgment, it may jeopardise the participant and may require medical or surgical intervention to prevent one of the outcomes listed above.</li> </ol> <p>Examples include intensive treatment in an emergency room or at home for allergic bronchospasm, blood dyscrasias or convulsions that do not result in hospitalisation, or development of drug dependency or drug abuse.</p> <p>Clarifications of the SAE definition:</p> <ol style="list-style-type: none"> <li>1) An event is life-threatening if its occurrence places the participant at immediate risk of death. It does not include an event that, had it occurred in a more severe form, might have caused death.</li> <li>2) An event is serious if it is not appropriate to administer treatment in a physician's office or an outpatient setting, and it requires hospitalisation. An event is also serious if it prolongs hospitalisation. When in doubt as to whether "hospitalisation" occurred or was necessary, the event is considered serious.</li> <li>3) Hospitalisation for elective treatment of a pre-existing condition that did not worsen from baseline is not an AE.</li> <li>4) Disability is a substantial or significant disruption of a person's ability to conduct normal life functions.</li> <li>5) The investigator may deem as an SAE any other important medical event that did not result in any of the outcomes listed in this section due to medical or surgical intervention</li> </ol>
<b>Business rules</b>	<p><b>Value Allowed:</b> n/a</p> <p><b>Relationship:</b> n/a</p> <p><b>Concept:</b> n/a</p>
<b>Duplicate field in other sections</b>	



615 **12.3 Severity**

<b>Term (Variable)</b>	Severity
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	H
<b>Definition</b>	Section heading
<b>User Guidance</b>	
<b>Conformance</b>	Required
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Appendix / Appendix 12 Adverse Events and Serious Adverse Events-Definitions, Severity, and Causality/Severity
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	Severity
<b>Business rules</b>	<b>Value Allowed:</b> Yes <b>Relationship:</b> n/a <b>Concept:</b> n/a
<b>Duplicate field in other sections</b>	

616

<b>Term (Variable)</b>	Severity
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	D
<b>Definition</b>	
<b>User Guidance</b>	Specify the rating categories/scale to be used in the trial to assess severity. Example scales are in [document name]. Considerations for assessing severity are discussed in ICH E2A. <b>[Severity]</b>
<b>Conformance</b>	Required
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Appendix / Appendix 12 Adverse Events and Serious Adverse Events-Definitions, Severity, and Causality/Severity
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	
<b>Business rules</b>	<b>Value Allowed:</b> n/a <b>Relationship:</b> n/a <b>Concept:</b> n/a
<b>Duplicate field in other sections</b>	

617

618 **12.4 Causality**

<b>Term (Variable)</b>	Causality
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	H
<b>Definition</b>	Section heading
<b>User Guidance</b>	
<b>Conformance</b>	Required
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Appendix / Appendix 12 Adverse Events and Serious Adverse Events-Definitions, Severity, and Causality/Severity
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	Causality
<b>Business rules</b>	<b>Value Allowed:</b> Yes <b>Relationship:</b> n/a <b>Concept:</b> n/a
<b>Duplicate field in other sections</b>	

619

<b>Term (Variable)</b>	Causality
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	D
<b>Definition</b>	Defines the relationship of an AE to a trial intervention
<b>User Guidance</b>	<p>Specify the causality categories/scale that the investigator will use for his/her assessment. Considerations for assessing causality are discussed in ICH E2A. Evaluation of relatedness must consider temporality and biologic plausibility as well as etiologies such as natural history of the underlying disease, concurrent illness, concomitant therapy, trial-related procedures, accidents, and other external factors. In a clinical trial, the trial intervention must always be suspect. The Investigator's assessment of an AE's relationship to trial intervention is not a factor in determining what is or is not reported in the trial. If there is any doubt as to whether a clinical observation is an AE, the event should be reported.</p> <p><b>[Causality]</b></p>
<b>Conformance</b>	Required
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Appendix / Appendix 12 Adverse Events and Serious Adverse Events-Definitions, Severity, and Causality/Severity
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	
<b>Business rules</b>	<p><b>Value Allowed:</b> n/a</p> <p><b>Relationship:</b> n/a</p> <p><b>Concept:</b> n/a</p>
<b>Duplicate field in other sections</b>	

### 621 13. Appendix: Definitions and Supporting Operational Details

Term (Variable)	Appendix: Definitions and Supporting Operational Details
Data Type	Text
Topic, Value or Header	H
Definition	Section Heading
User Guidance	
Conformance	Required
Cardinality	
Relationship content from ToC representing the protocol hierarchy	Appendix: Definitions and Supporting Operational Details
Relationship (reference to high level conceptual model)	
Value	Appendix: Definitions and Supporting Operational Details
Business rules	<b>Value Allowed:</b> n/a <b>Relationship:</b> n/a <b>Concept:</b> n/a
Duplicate field in other sections	

### 622 13.1 Contraception and Pregnancy Testing

Term (Variable)	Contraception and Pregnancy Testing
Data Type	Text
Topic, Value or Header	H
Definition	Section Heading
User Guidance	
Conformance	Required
Cardinality	
Relationship content from ToC representing the protocol hierarchy	Appendix 13: Definitions and Supporting Operational Details/ Contraception and Pregnancy Testing
Relationship (reference to high level conceptual model)	
Value	Contraception and Pregnancy Testing
Business rules	<b>Value Allowed:</b> Yes <b>Relationship:</b> n/a <b>Concept:</b> n/a
Duplicate field in other sections	

### 623 13.1.1 Definitions Related to Childbearing Potential

<b>Term (Variable)</b>	Definitions for Contraception and Pregnancy Testing
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	D
<b>Definition</b>	
<b>User Guidance</b>	
<b>Conformance</b>	Required
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Appendix: Definitions and Supporting Operational Details/ Contraception and Pregnancy Testing/Definitions for Contraception and Pregnancy Testing
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	
<b>Business rules</b>	<b>Value Allowed:</b> n/a <b>Relationship:</b> n/a <b>Concept:</b> n/a
<b>Duplicate field in other sections</b>	

### 624 13.1.2 Contraception

<b>Term (Variable)</b>	Contraception
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	H
<b>Definition</b>	
<b>User Guidance</b>	Optional section to specify the: <ul style="list-style-type: none"> <li>• Contraceptive methods required</li> <li>• Duration of use</li> </ul> <b>[Contraception]</b>
<b>Conformance</b>	Required
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Appendix 13: Definitions and Supporting Operational Details/ Contraception and Pregnancy Testing/Contraception
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	Contraception
<b>Business rules</b>	<b>Value Allowed:</b> Yes <b>Relationship:</b> n/a <b>Concept:</b> n/a
<b>Duplicate field in other sections</b>	

625

<b>Term (Variable)</b>	Contraception
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	D
<b>Definition</b>	
<b>User Guidance</b>	<p>Optional section to specify the:</p> <ul style="list-style-type: none"> <li>• Contraceptive methods required</li> <li>• Duration of use</li> </ul> <p><b>[Contraception]</b></p>
<b>Conformance</b>	Required
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Appendix: Definitions and Supporting Operational Details/ Contraception and Pregnancy Testing/Contraception
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	
<b>Business rules</b>	<p><b>Value Allowed:</b> n/a</p> <p><b>Relationship:</b> n/a</p> <p><b>Concept:</b> n/a</p>
<b>Duplicate field in other sections</b>	

626

627 **13.1.3 Pregnancy Testing**

<b>Term (Variable)</b>	Pregnancy Testing
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	H
<b>Definition</b>	
<b>User Guidance</b>	Optional section to specify pregnancy testing requirements. <b>[Pregnancy Testing]</b>
<b>Conformance</b>	Required
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Appendix: Definitions and Supporting Operational Details/ Contraception and Pregnancy Testing/Pregnancy Testing
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	Pregnancy Testing
<b>Business rules</b>	<b>Value Allowed:</b> Yes <b>Relationship:</b> n/a <b>Concept:</b> n/a
<b>Duplicate field in other sections</b>	

628

<b>Term (Variable)</b>	Pregnancy Testing
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	D
<b>Definition</b>	
<b>User Guidance</b>	Optional section to specify pregnancy testing requirements. <b>[Pregnancy Testing]</b>
<b>Conformance</b>	Required
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Appendix: Definitions and Supporting Operational Details/ Contraception and Pregnancy Testing/Pregnancy Testing
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	
<b>Business rules</b>	<b>Value Allowed:</b> n/a <b>Relationship:</b> n/a <b>Concept:</b> n/a
<b>Duplicate field in other sections</b>	

629



630 **13.2 Clinical Laboratory Tests**

<b>Term (Variable)</b>	Clinical Laboratory Tests
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	H
<b>Definition</b>	Section Heading
<b>User Guidance</b>	<p>Provide additional information, if needed, about clinical laboratory tests, such as</p> <ul style="list-style-type: none"> <li>• whether they will be performed by a central or local laboratory (if important to distinguish)</li> <li>• specific analytes or parameters included in a panel</li> <li>• equations and references for locally calculated labs</li> <li>• acceptability of additional tests deemed necessary by the Investigator or local regulations</li> <li>• instructions for situations in which central laboratory results are not available in time for trial intervention and/or response evaluation, or in the event of a severe disruption (for example, a pandemic or natural disaster)</li> <li>• treatment algorithms for results out of normal range.</li> </ul> <p>A tabular presentation for such information is common.</p> <p><b>[Clinical Laboratory Tests]</b></p>
<b>Conformance</b>	Required
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Appendix: Definitions and Supporting Operational Details/Clinical Laboratory Tests
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	Clinical Laboratory Tests
<b>Business rules</b>	<p><b>Value Allowed:</b> Yes</p> <p><b>Relationship:</b> n/a</p> <p><b>Concept:</b> n/a</p>
<b>Duplicate field in other sections</b>	Repeat for lab values

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<b>Term (Variable)</b>	Clinical Laboratory Tests
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	D
<b>Definition</b>	
<b>User Guidance</b>	<p>Provide additional information, if needed, about clinical laboratory tests, such as</p> <ul style="list-style-type: none"> <li>• whether they will be performed by a central or local laboratory (if important to distinguish)</li> <li>• specific analytes or parameters included in a panel</li> <li>• equations and references for locally calculated labs</li> <li>• acceptability of additional tests deemed necessary by the Investigator or local regulations</li> <li>• instructions for situations in which central laboratory results are not available in time for trial intervention and/or response evaluation, or in the event of a severe disruption (for example, a pandemic or natural disaster)</li> <li>• treatment algorithms for results out of normal range.</li> </ul> <p>A tabular presentation for such information is common.</p> <p><b>[Clinical Laboratory Tests]</b></p>
<b>Conformance</b>	Required/Repeatable (for lab values)
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Appendix: Definitions and Supporting Operational Details/Clinical Laboratory Test
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	
<b>Business rules</b>	<p><b>Value Allowed:</b> n/a</p> <p><b>Relationship:</b> n/a</p> <p><b>Concept:</b> n/a</p>
<b>Duplicate field in other sections</b>	

### 633 13.3 Country/Region-Specific Differences

<b>Term (Variable)</b>	Country-Specific Differences
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	H
<b>Definition</b>	
<b>User Guidance</b>	<p>Although global clinical trial practices are increasingly harmonised, some country- and region-specific differences in requirements do exist (for example, document retention periods, contraception requirements). Where differences in requirements cannot be reconciled, sponsors should explain how they will document and communicate country-specific differences (for example, by country-specific amendments or addenda).</p> <p>An alternative to country- or region-specific amendments is to list the specific differences by country or countries in this section, including a reference to the relevant section of the protocol where the differing requirement applies.</p> <p><b>[Country-specific Differences]</b></p>
<b>Conformance</b>	Required
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Appendix: Definitions and Supporting Operational Details/Country-Specific Differences
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	Country-Specific Differences
<b>Business rules</b>	<p><b>Value Allowed:</b> Yes</p> <p><b>Relationship:</b> 0 to many</p> <p><b>Concept:</b> n/a</p>
<b>Duplicate field in other sections</b>	

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<b>Term (Variable)</b>	Country
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	H
<b>Definition</b>	
<b>User Guidance</b>	<p>Although global clinical trial practices are increasingly harmonised, some country- and region-specific differences in requirements do exist (for example, document retention periods, contraception requirements). Where differences in requirements cannot be reconciled, sponsors should explain how they will document and communicate country-specific differences (for example, by country-specific amendments or addenda).</p> <p>An alternative to country- or region-specific amendments is to list the specific differences by country or countries in this section, including a reference to the relevant section of the protocol where the differing requirement applies.</p> <p><b>[Country]</b></p>
<b>Conformance</b>	Required/Repeatable
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Appendix: Definitions and Supporting Operational Details/Country-Specific Differences/Country
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	Country
<b>Business rules</b>	<p><b>Value Allowed:</b> n/a</p> <p><b>Relationship:</b> 0 to many</p> <p><b>Concept:</b> n/a</p>
<b>Duplicate field in other sections</b>	

<b>Term (Variable)</b>	Header of Protocol Section to be Changed for the Country
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	H
<b>Definition</b>	
<b>User Guidance</b>	<p>Although global clinical trial practices are increasingly harmonised, some country- and region-specific differences in requirements do exist (for example, document retention periods, contraception requirements). Where differences in requirements cannot be reconciled, sponsors should explain how they will document and communicate country-specific differences (for example, by country-specific amendments or addenda).</p> <p>An alternative to country- or region-specific amendments is to list the specific differences by country or countries in this section, including a reference to the relevant section of the protocol where the differing requirement applies.</p> <p><b>[Header of Protocol Section to be Changed for the Country]</b></p>
<b>Conformance</b>	Required/Repeatable
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Appendix: Definitions and Supporting Operational Details/Country-Specific Differences/Country/Header of Protocol Section to be Changed for the Country
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	Header of Protocol Section to be Changed for the Country
<b>Business rules</b>	<p><b>Value Allowed:</b> n/a</p> <p><b>Relationship:</b> 0 to many</p> <p><b>Concept:</b> n/a</p>
<b>Duplicate field in other sections</b>	

<b>Term (Variable)</b>	[Change-depends on Section]
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	D
<b>Definition</b>	
<b>User Guidance</b>	<p>Although global clinical trial practices are increasingly harmonised, some country- and region-specific differences in requirements do exist (for example, document retention periods, contraception requirements). Where differences in requirements cannot be reconciled, sponsors should explain how they will document and communicate country-specific differences (for example, by country-specific amendments or addenda).</p> <p>An alternative to country- or region-specific amendments is to list the specific differences by country or countries in this section, including a reference to the relevant section of the protocol where the differing requirement applies.</p> <p><b>[Header of Protocol Section to be Changed for the Country]</b></p>
<b>Conformance</b>	Optional (follows original section)
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Appendix: Definitions and Supporting Operational Details/Country-Specific Differences/Country/Header of Protocol Section to be Changed for the Country
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	
<b>Business rules</b>	<p><b>Value Allowed:</b> n/a</p> <p><b>Relationship:</b> 0 to many</p> <p><b>Concept:</b> n/a</p>
<b>Duplicate field in other sections</b>	

638 **13.4 Prior Protocol Amendments**

<b>Term (Variable)</b>	Prior Protocol Amendments
<b>Data Type</b>	Text
<b>Topic, Value or Header</b>	H
<b>Definition</b>	
<b>User Guidance</b>	<p>Choose the appropriate text.</p> <p>{This protocol has not been amended.}</p> <p>or</p> <p>{The Protocol Amendment Summary of Changes for the current amendment is located directly before the Table of Contents. Details of prior amendments are presented below, beginning with the most recent}.</p> <p>See the instructions in the Protocol Amendment Summary of Changes located before the Table of Contents. Move all Protocol Amendment Summaries of Changes for previous amendments to this section in reverse chronological order (most recent first).</p> <p><b>Amendment {amendment number}: ({date})</b></p> <p><b>{Amendment details from this amendment}</b></p> <p><b>Add additional amendments/details as protocol amendments accrue.</b></p> <p><b>Amendment {amendment number}: ({date})</b></p> <p><b>{Amendment details from this amendment}</b></p>
<b>Conformance</b>	Required
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Appendix: Definitions and Supporting Operational Details/Prior Protocol Amendments
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	Prior Protocol Amendments
<b>Business rules</b>	<p><b>Value Allowed:</b> Yes</p> <p><b>Relationship:</b> 0 to many</p> <p><b>Concept:</b> n/a</p>
<b>Duplicate field in other sections</b>	

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<b>Term (Variable)</b>	[Statement]
<b>Data Type</b>	List
<b>Topic, Value or Header</b>	D
<b>Definition</b>	
<b>User Guidance</b>	
<b>Conformance</b>	Required
<b>Cardinality</b>	
<b>Relationship content from ToC representing the protocol hierarchy</b>	Appendix: Definitions and Supporting Operational Details/Prior Protocol Amendments/Statement
<b>Relationship (reference to high level conceptual model)</b>	
<b>Value</b>	
<b>Business rules</b>	<b>Value Allowed:</b> n/a <b>Relationship:</b> n/a <b>Concept:</b> n/a
<b>Duplicate field in other sections</b>	

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

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