M11 TECHNICAL SPECIFICATION: CLINICAL ELECTRONIC STRUCTURED HARMONISED PROTOCOL (CeSHarP)

This draft guidance, when finalized, will represent the current thinking of the Food and Drug Administration (FDA or Agency) on this topic. It does not establish any rights for any person and is not binding on FDA or the public. You can use an alternative approach if it satisfies the requirements of the applicable statutes and regulations. To discuss an alternative approach, contact the FDA staff responsible for this guidance as listed on the title page. The draft guidance has been left in the original International Council for Harmonisation format. The final guidance will be reformatted and edited to conform with FDA's good guidance practice regulation and style.

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FOREWORD

The International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH) has the mission of achieving greater regulatory harmonization worldwide to ensure that safe, effective, and high-quality medicines are developed, registered, and maintained in the most resource-efficient manner. By harmonizing the regulatory expectations in regions around the world, ICH guidelines have substantially reduced duplicative clinical studies, prevented unnecessary animal studies, standardized safety reporting and marketing application submissions, and contributed to many other improvements in the quality of global drug development and manufacturing and the products available to patients.

ICH is a consensus-driven process that involves technical experts from regulatory authorities and industry parties in detailed technical and science-based harmonization work that results in the development of ICH guidelines. The commitment to consistent adoption of these consensus-based guidelines by regulators around the globe is critical to realizing the benefits of safe, effective, and high-quality medicines for patients as well as for industry. As a Founding Regulatory Member of ICH, the Food and Drug Administration (FDA) plays a major role in the development of each of the ICH guidelines, which FDA then adopts and issues as guidance to industry.

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 *Step 2* and release for public consultation (document dated 6 September 2022). *Minor editorial changes made pre-publication (document dated 14 October 2022).*	27 September 2022

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

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

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	**Value Allowed:** Yes **Relationship:** Not transferred **Concept:** Protocol title
Duplicate field in other sections	

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	**Value Allowed:** Yes **Relationship:** Not transferred **Concept:** Protocol title
Duplicate field in other sections	

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	**Value Allowed:** Yes **Relationship:** Table column heading **Concept:** 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	**Value Allowed:** Yes **Relationship:** Repeating for each new date Not transferred **Concept:** 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	**Value Allowed:** Yes **Relationship:** Table column heading Not transferred **Concept:** 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	**Value Allowed:** Yes **Relationship:** Repeating for each description of revision Not transferred **Concept:** n/a
Duplicate field in other sections	

20

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	**Value Allowed:** Yes **Relationship:** n/a **Concept:** n/a
Duplicate field in other sections	

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	**Value Allowed:** Yes **Relationship:** Not transferred **Concept:** n/a
Duplicate field in other sections	

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	**Value Allowed:** Yes **Relationship:** Not transferred **Concept:** n/a
Duplicate field in other sections	

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	**Value Allowed:** Yes **Relationship:** Not transferred **Concept:** n/a
Duplicate field in other sections	

Term (Variable)	Description of conventions
Data Type	Text
Topic, Value or Header	D
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	
Business rules	**Value Allowed:** Yes **Relationship:** Not transferred **Concept:** n/a
Duplicate field in other sections	

27

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

28

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

29

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

30

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

31

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

32

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

33

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

34

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

35

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

36

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

37 # Protocol Full Title

Term (Variable)	Protocol Full 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	Protocol Full Title
Business rules	**Value Allowed:** Yes **Relationship:** Table row heading **Concept:** n/a
Duplicate field in other sections	

38

Term (Variable)	Protocol Full Title
Data Type	Text
Topic, Value or Header	D
Definition	
User Guidance	The protocol should have a descriptive title that identifies the scientific aspects of the trial sufficiently to ensure it is immediately evident what the trial is investigating and on whom, and to allow retrieval from literature or internet searches.
Conformance	Required
Cardinality	
Relationship content from ToC representing the protocol hierarchy	Title page
Relationship (reference to high level conceptual model)	
Value	4000 Eudra characters 600 ct.gov UTF 8 - Special
Business rules	**Value Allowed:** Yes **Relationship:** n/a **Concept:** Protocol Title
Duplicate field in other sections	

39

Term (Variable)	Sponsor Confidentiality Statement
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	Sponsor confidentiality statement
Business rules	**Value Allowed:** Yes **Relationship:** Table row heading **Concept:** n/a
Duplicate field in other sections	

40

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

41

Term (Variable)	Protocol Number
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	Protocol number
Business rules	**Value Allowed:** Yes **Relationship:** Table row heading **Concept:** n/a
Duplicate field in other sections	

42

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

43

Term (Variable)	Version
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	Version
Business rules	**Value Allowed:** Yes **Relationship:** Table row heading **Concept:** n/a
Duplicate field in other sections	

44

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

45

Term (Variable)	Amendment Number
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	Amendment Number
Business rules	**Value Allowed:** Yes **Relationship:** Table row heading **Concept:** n/a
Duplicate field in other sections	

46

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

47

Term (Variable)	Amendment Scope
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	Amendment Scope
Business rules	**Value Allowed:** Yes **Relationship:** Table row heading **Concept:** n/a
Duplicate field in other sections	

48

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

49

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

50

Term (Variable)	Compound Number(s)
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	Compound Number
Business rules	**Value Allowed:** Yes **Relationship:** Table row heading **Concept:** n/a
Duplicate field in other sections	

51

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

52

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

53

Term (Variable)	Compound Name(s)
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	Compound name(s)
Business rules	**Value Allowed:** n/a **Relationship:** Table row heading **Concept:** n/a
Duplicate field in other sections	

54

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

55

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

56

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

57

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

58

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

59

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	**Value Allowed:** Yes **Relationship:** Table row heading **Concept:** 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	**Value Allowed:** Yes **Relationship:** Table row heading **Concept:**
Duplicate field in other sections	

61

Term (Variable)	Short Title
Data Type	Text
Topic, Value or Header	D
Definition	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.
User Guidance	
Conformance	Required
Cardinality	
Relationship content from ToC representing the protocol hierarchy	Title page
Relationship (reference to high level conceptual model)	
Value	300AN
Business rules	**Value Allowed:** n/a **Relationship:** n/a **Concept:** Sponsor
Duplicate field in other sections	

62

Term (Variable)	Sponsor Name and Address
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	Sponsor Name and Address
Business rules	**Value Allowed:** Yes **Relationship** Table row heading **Concept:** Sponsor
Duplicate field in other sections	

63

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

64

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

65

Term (Variable)	Local Sponsor Name and Address
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	Local Sponsor Name and Address
Business rules	**Value Allowed:** Yes **Relationship:** n/a **Concept:** n/a
Duplicate field in other sections	

66

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

67

68

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

69

Term (Variable)	Manufacturer Name and Address
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	Manufacturer Name and Address
Business rules	**Value Allowed:** Yes **Relationship:** Table row heading **Concept:** Regulatory investigational product number
Duplicate field in other sections	Repeatable

70

Term (Variable)	Device Manufacturer Name
Data Type	Text
Topic, Value or Header	D
Definition	
User Guidance	Manufacturer name and address information is required only for protocols that include investigational device(s) and should not be included for other protocols. Include the manufacturer address only if the manufacturer is different than the Sponsor listed above. Add additional fields as needed if multiple investigational devices will be used in the trial. Delete this line from the table if not applicable.
Conformance	Optional
Cardinality	
Relationship content from ToC representing the protocol hierarchy	Title Page
Relationship (reference to high level conceptual model)	
Value	
Business rules	**Value Allowed:** n/a **Relationship:** n/a **Concept:** n/a
Duplicate field in other sections	Repeatable

71

Term (Variable)	Device Manufacturer Address
Data Type	Text
Topic, Value or Header	D
Definition	
User Guidance	Manufacturer name and address information is required only for protocols that include investigational device(s) and should not be included for other protocols. Include the manufacturer address only if the manufacturer is different than the Sponsor listed above. Add additional fields as needed if multiple investigational devices will be used in the trial. Delete this line from the table if not applicable.
Conformance	Optional
Cardinality	
Relationship content from ToC representing the protocol hierarchy	Title Page
Relationship (reference to high level conceptual model)	
Value	
Business rules	**Value Allowed:** n/a **Relationship:** n/a **Concept:** n/a
Duplicate field in other sections	Repeatable

72

Term (Variable)	Regulatory Agency Identifier Number(s)
Data Type	Text
Topic, Value or Header	H
Definition	
User Guidance	Include all numbers that are applicable for the trial and available at the time of protocol or amendment finalisation. Delete prompts for numbers not available at the time of document finalisation. Delete unused fields. Add fields for "other" if more than one is needed.
Conformance	Required
Cardinality	
Relationship content from ToC representing the protocol hierarchy	Title Page
Relationship (reference to high level conceptual model)	
Value	Regulatory Agency Identifier Number(s):
Business rules	**Value Allowed:** Yes **Relationship:** Table row heading **Concept:** Regulatory investigational product number
Duplicate field in other sections	

73

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

74

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

75

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

76

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

77

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

78

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

79

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

80

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

81

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

82

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

83

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

84

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

85

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

86

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

87

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

88

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

89

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

90

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

91

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	Title Page
Relationship (reference to high level conceptual model)	
Value	Other
Business rules	**Value Allowed:** Yes **Relationship:** n/a **Concept:** Protocol approval date
Duplicate field in other sections	

92

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

93

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

94

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

95

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

96

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

97

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

98

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

99

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

100

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

101

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

102

Term (Variable)	[This protocol was approved via {describe method} as described on the approval page appended to the document]
Data Type	Text
Topic, Value or Header	D
Definition	
User Guidance	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.
Conformance	Optional
Cardinality	
Relationship content from ToC representing the protocol hierarchy	Title Page
Relationship (reference to high level conceptual model)	
Value	[This protocol was approved via {describe method} as described on the approval page appended to the document]
Business rules	**Value Allowed:** Yes **Relationship:** n/a **Concept:** n/a
Duplicate field in other sections	

103

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

104

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

105

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

106

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

107

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

108

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

109

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

110

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

111

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

112

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

113

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

114

115

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

116

Term (Variable)	History of Amendment
Data Type	Text
Topic, Value or Header	H
Definition	Heading
User Guidance	Do not include the current amendment in the table below, as final approval dates are often difficult to predict during document preparation. Previous amendments, 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. 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".
Conformance	Required
Cardinality	
Relationship content from ToC representing the protocol hierarchy	Amendment Details
Relationship (reference to high level conceptual model)	
Value	History of Amendment
Business rules	**Value Allowed:** Yes **Relationship:** n/a **Concept:** n/a
Duplicate field in other sections	

117

Term (Variable)	{#/A total of #} prior {global} amendments have occurred, as shown in the table below:
Data Type	Text
Topic, Value or Header	H
Definition	
User Guidance	Do not include the current amendment in the table below, as final approval dates are often difficult to predict during document preparation. Previous amendments should appear in reverse chronological order with the most recent at the top (for example, Amendment 3, 2, 1). Delete lines not needed, add lines as needed. Inclusion of regional-, country-, and site-specific amendments in the table is optional. If included, ensure that the scope is clearly distinguishable from global amendments. If including the column with enrollment numbers, follow the instructions below. • For global amendments, list approximate global enrollment total or percentage at the time of the amendment and select "globally". • For local amendments, list the approximate local enrollment total or percentage at the time of the amendment and select "locally".
Conformance	Required
Cardinality	
Relationship content from ToC representing the protocol hierarchy	Amendment Details
Relationship (reference to high level conceptual model)	
Value	{#/A total of #} prior {global} amendments have occurred, as shown in the table below:
Business rules	**Value Allowed:** Yes **Relationship:** n/a **Concept:** n/a
Duplicate field in other sections	

118

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

119

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

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	**Value Allowed:** Yes **Relationship:** Row title **Concept:** 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	**Value Allowed:** Yes **Relationship:** Row title **Concept:** n/a
Duplicate field in other sections	

122

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

123

Term (Variable)	X
Data Type	integer
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	
Business rules	**Value Allowed:** n/a **Relationship:** Rows content **Concept:** n/a
Duplicate field in other sections	Repeat for each amendment

124

Term (Variable)	Amendment X Date
Data Type	date dd/mmm/yyyy
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	
Business rules	**Value Allowed:** n/a **Relationship:** Rows content **Concept:** n/a
Duplicate field in other sections	Repeat for each amendment

125

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

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	**Value Allowed:** Yes **Relationship:** Rows content **Concept:** 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	**Value Allowed:** Yes **Relationship:** n/a **Concept:** n/a
Duplicate field in other sections	

128

Term (Variable)	The table below provides an overview of the current amendment
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	The table below provides an overview of the current amendment
Business rules	**Value Allowed:** Yes **Relationship:** n/a **Concept:** n/a
Duplicate field in other sections	Not included in original

129

Term (Variable)	Amendment Number
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	Amendment Number
Business rules	**Value Allowed:** Yes **Relationship:** n/a **Concept:** n/a
Duplicate field in other sections	

130

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

131

Term (Variable)	Approximate {(#/%)} enrolled
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	Approximate {(#/%)} enrolled
Business rules	**Value Allowed:** Yes **Relationship:** n/a **Concept:** n/a
Duplicate field in other sections	

132

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

133

Term (Variable)	Reason(s) for Amendment
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	Reason(s) for Amendment:
Business rules	**Value Allowed:** Yes **Relationship:** n/a **Concept:** n/a
Duplicate field in other sections	

134

Term (Variable)	Primary
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	Primary:
Business rules	**Value Allowed:** Yes **Relationship:** n/a **Concept:** n/a
Duplicate field in other sections	

135

Term (Variable)	Primary Reason for Amendment
Data Type	Pick list
Topic, Value or Header	D
Definition	
User Guidance	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".
Conformance	Required
Cardinality	Amendment Details
Relationship content from ToC representing the protocol hierarchy	
Relationship (reference to high level conceptual model)	
Value	• Regulatory agency request to amend • New regulatory guidance • IRB/IEC feedback • New safety information available • Manufacturing change • Adaptive clinical trial IMP addition • Change in strategy • Change in standard of care • New data available (other than safety data) • Investigator/site feedback • Recruitment difficulty • Inconsistency and/or error in the protocol • Protocol design error
Business rules	**Value Allowed:** Yes **Relationship:** n/a **Concept:** n/a
Duplicate field in other sections	Multiple accepted

136

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	**Value Allowed:** Yes **Relationship:** n/a **Concept:** 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	**Value Allowed:** n/a **Relationship:** n/a **Concept:** n/a
Duplicate field in other sections	

138

Term (Variable)	Primary Reason for Amendment
Data Type	Pick List
Topic, Value or Header	D
Definition	
User Guidance	
Conformance	Required / Required
Cardinality	
Relationship content from ToC representing the protocol hierarchy	Amendment Details
Relationship (reference to high level conceptual model)	
Value	• Regulatory agency request to amend • New regulatory guidance • IRB/IEC feedback • New safety information available • Manufacturing change • Adaptive clinical trial IMP addition • Change in strategy • Change in standard of care • New data available (other than safety data) • Investigator/site feedback • Recruitment difficulty • Inconsistency and/or error in the protocol • Protocol design error
Business rules	**Value Allowed:** Yes **Relationship:** n/a **Concept:** n/a
Duplicate field in other sections	Multiple accepted

139

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	**Value Allowed:** Yes **Relationship:** n/a **Concept:** 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	**Value Allowed:** n/a **Relationship:** n/a **Concept:** n/a
Duplicate field in other sections	

141

Term (Variable)	Summary of Amendment
Data Type	Text
Topic, Value or Header	H
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	Summary of Amendment
Business rules	**Value Allowed:** Yes **Relationship:** n/a **Concept:** n/a
Duplicate field in other sections	

142

Term (Variable)	Summary of Amendment
Data Type	Text
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	
Business rules	**Value Allowed:** n/a **Relationship:** n/a **Concept:** n/a
Duplicate field in other sections	

143

Term (Variable)	Question
Data Type	Text
Topic, Value or Header	H
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	Is this amendment likely to have a substantial impact on • safety or rights of the subjects, or • on the reliability and robustness of the data generated in the clinical trial?
Business rules	**Value Allowed:** Yes **Relationship:** n/a **Concept:** n/a
Duplicate field in other sections	

144

Term (Variable)	Yes/No
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	Yes No
Business rules	**Value Allowed:** Yes **Relationship:** n/a **Concept:** n/a
Duplicate field in other sections	

145

Term (Variable)	Summary of Changes in Current Amendment
Data Type	Text
Topic, Value or Header	H
Definition	Section heading
User Guidance	Follow the steps below to prepare the summary of changes. • 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. • 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). Tabular presentation is common but not required. The page can be changed to landscape orientation if necessary.
Conformance	Conditional / Required
Cardinality	
Relationship content from ToC representing the protocol hierarchy	Amendment Details
Relationship (reference to high level conceptual model)	
Value	Summary of Changes in Current Amendment
Business rules	**Value Allowed:** Yes **Relationship:** n/a **Concept:** Protocol short title
Duplicate field in other sections	

146

Term (Variable)	Section # and Name
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	Section # and Name
Business rules	**Value Allowed:** Yes **Relationship:** Rows content **Concept:** Trial purpose summary
Duplicate field in other sections	Repeat until complete

147

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

148

Term (Variable)	Description of Change
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	Description of Change
Business rules	**Value Allowed:** Yes **Relationship:** Rows content **Concept:** Primary Objective
Duplicate field in other sections	Repeat until complete

149

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

150

Term (Variable)	Brief Rationale for Change
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	Brief Rationale for Change
Business rules	**Value Allowed:** Yes **Relationship:** Rows content **Concept:** Primary endpoint
Duplicate field in other sections	Repeat until complete

151

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

152

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

153

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	**Value Allowed:** n/a **Relationship:** n/a **Concept:** 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	**Value Allowed:** Yes **Relationship:** n/a **Concept:** n/a
Duplicate field in other sections	

155

1.1 Protocol Synopsis

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

Term (Variable)	Primary Objective
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	Primary Objective
Business rules	**Value Allowed:** Yes **Relationship:** Table header **Concept:** n/a
Duplicate field in other sections	Section 3.1 replicated for primary/secondary

Term (Variable)	Objective X
Data Type	Text
Topic, Value or Header	D
Definition	
User Guidance	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).
Conformance	Required
Cardinality	
Relationship content from ToC representing the protocol hierarchy	Protocol Summary
Relationship (reference to high level conceptual model)	
Value	
Business rules	**Value Allowed:** n/a **Relationship:** Relate endpoint **Concept:** n/a
Duplicate field in other sections	Repeat as needed

159

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

160

Term (Variable)	Endpoint X
Data Type	Text
Topic, Value or Header	D
Definition	
User Guidance	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. 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.
Conformance	Conditional / Conditional
Cardinality	
Relationship content from ToC representing the protocol hierarchy	Protocol Summary
Relationship (reference to high level conceptual model)	
Value	
Business rules	**Value Allowed:** n/a **Relationship:** Relate to objective **Concept:** 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

161

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

162

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

173

Term (Variable)	Population Diagnosis or Condition
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 Diagnosis or Condition
Business rules	**Value Allowed:** Yes **Relationship:** Table cell title **Concept:** n/a
Duplicate field in other sections	

174

Term (Variable)	Population Diagnosis or Condition
Data Type	Text
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	CT: "acute lung injury," or a specific biomarker profile); indicate "N/A – Healthy" for studies in healthy volunteers
Business rules	**Value Allowed:** Yes **Relationship:** n/a **Concept:** n/a
Duplicate field in other sections	

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	**Value Allowed:** Yes **Relationship:** Table Cell title **Concept:** 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	**Value Allowed:** Yes **Relationship:** n/a **Concept:** n/a
Duplicate field in other sections	

178

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

179

Term (Variable)	Minimum
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	Minimum
Business rules	**Value Allowed:** Yes **Relationship:** Table cell entry **Concept:** n/a
Duplicate field in other sections	

180

Term (Variable)	Minimum age
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	**Value Allowed:** n/a **Relationship:** n/a **Concept:** n/a
Duplicate field in other sections	

181

Term (Variable)	Maximum
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	Maximum
Business rules	**Value Allowed:** Yes **Relationship:** Table Cell entry **Concept:** n/a
Duplicate field in other sections	

182

Term (Variable)	Maximum age
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	**Value Allowed:** n/a **Relationship:** n/a **Concept:** n/a
Duplicate field in other sections	

183

Term (Variable)	Age units
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	Weeks, months, years
Business rules	**Value Allowed:** Yes **Relationship:** n/a **Concept:** n/a
Duplicate field in other sections	

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	**Value Allowed:** Yes **Relationship:** n/a **Concept:** 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	**Value Allowed:** Yes **Relationship:** n/a **Concept:** 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	**Value Allowed:** Yes **Relationship:** Randomisation **Concept:** 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	**Value Allowed:** Yes **Relationship:** N/A **Concept:** n/a
Duplicate field in other sections	

188

189

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

190

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

191

Term (Variable)	Number of Arms
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	Number of Arms
Business rules	**Value Allowed:** Yes **Relationship:** n/a **Concept:** n/a
Duplicate field in other sections	

192

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

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	**Value Allowed:** Yes **Relationship:** n/a **Concept:** 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	**Value Allowed:** Yes **Relationship:** n/a **Concept:** n/a
Duplicate field in other sections	

195

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

196

Term (Variable)	Number of participants
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	
Business rules	**Value Allowed:** n/a **Relationship:** n/a **Concept:** n/a
Duplicate field in other sections	

197

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

198

Term (Variable)	[randomly assigned to trial intervention/enrolled]
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	Randomly assigned to Trial intervention/ enrolled
Business rules	**Value Allowed:** Yes **Relationship:** n/a **Concept:** n/a
Duplicate field in other sections	

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	**Value Allowed:** Yes **Relationship:** n/a **Concept:** 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	**Value Allowed:** Yes **Relationship:** n/a **Concept:** n/a
Duplicate field in other sections	

201

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

202

Term (Variable)	Total duration of trial intervention for each participant:
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	Total duration of trial intervention for each participant:
Business rules	**Value Allowed:** Yes **Relationship:** n/a **Concept:** n/a
Duplicate field in other sections	

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	**Value Allowed:** Yes **Relationship:** n/a **Concept:** 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	**Value Allowed:** n/a **Relationship:** n/a **Concept:** 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	**Value Allowed:** n/a **Relationship:** n/a **Concept:** 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	**Value Allowed:** Yes **Relationship:** n/a **Concept:** 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	**Value Allowed:** Yes **Relationship:** Complete **Concept:** 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	**Value Allowed:** Yes **Relationship:** n/a **Concept:** n/a
Duplicate field in other sections	

209

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

210

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

211

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

212

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

213

Term (Variable)	Committee Name
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	Data Monitoring Committee, Dose Escalation Committee, or Endpoint Adjudication Committee, other none
Business rules	**Value Allowed:** Yes **Relationship:** n/a **Concept:** n/a
Duplicate field in other sections	

214

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

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	**Value Allowed:** Yes **Relationship:** n/a **Concept:** 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	**Value Allowed:** Yes **Relationship:** n/a **Concept:** n/a
Duplicate field in other sections	Repeat as needed

217

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

218

Term (Variable)	other Committees:
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	other Committees:
Business rules	**Value Allowed:** Yes **Relationship:** n/a **Concept:** n/a
Duplicate field in other sections	

219

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

220

1.2 Trial Schema

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

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

223

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

224

1.3 Schedule of Activities

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

Term (Variable)	Schedule of Activities
Data Type	Text
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	**Value Allowed:** n/a **Relationship:** n/a **Concept:** 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	**Value Allowed:** Yes **Relationship:** n/a **Concept:** n/a
Duplicate field in other sections	

228

2.1 Purpose of Trial

Term (Variable)	Purpose 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	Introduction
Relationship (reference to high level conceptual model)	
Value	Purpose of Trial
Business rules	**Value Allowed:** Yes **Relationship:** n/a **Concept:** n/a
Duplicate field in other sections	

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

231

2.2 Summary of Benefits and Risks

Term (Variable)	Summary of Benefits and Risks
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	Summary of Benefits and Risks
Business rules	**Value Allowed:** Yes **Relationship:** n/a **Concept:** n/a
Duplicate field in other sections	

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

Term (Variable)	Benefit Summary
Data Type	Text
Topic, Value or Header	D
Definition	
User Guidance	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. Benefits to society in general may also be included but should be discussed separately.
Conformance	Required
Cardinality	
Relationship content from ToC representing the protocol hierarchy	Introduction
Relationship (reference to high level conceptual model)	
Value	
Business rules	**Value Allowed:** n/a **Relationship:** n/a **Concept:** n/a
Duplicate field in other sections	

235

Term (Variable)	Risk Summary and Mitigation Strategy
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	Risk Summary and Mitigation Strategy
Business rules	**Value Allowed:** Yes **Relationship:** n/a **Concept:** n/a
Duplicate field in other sections	

236

Term (Variable)	Trial Specific Discussion of intervention Risks and Mitigation
Data Type	Text
Topic, Value or Header	D
Definition	
User Guidance	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.
Conformance	Required
Cardinality	
Relationship content from ToC representing the protocol hierarchy	Introduction
Relationship (reference to high level conceptual model)	
Value	
Business rules	**Value Allowed:** n/a **Relationship:** n/a **Concept:** n/a
Duplicate field in other sections	

237

Term (Variable)	Trial Specific discussion of Procedure (s) Risks and Mitigation
Data Type	Text
Topic, Value or Header	D
Definition	
User Guidance	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.
Conformance	Required
Cardinality	
Relationship content from ToC representing the protocol hierarchy	Introduction
Relationship (reference to high level conceptual model)	
Value	
Business rules	**Value Allowed:** n/a **Relationship:** n/a **Concept:** n/a
Duplicate field in other sections	

238

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

239

Term (Variable)	Overall Benefit: Risk Conclusion
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	Overall Benefit: Risk Conclusion
Business rules	**Value Allowed:** Yes **Relationship:** n/a **Concept:** n/a
Duplicate field in other sections	

240

Term (Variable)	Overall Benefit: Risk Conclusion
Data Type	Text
Topic, Value or Header	D
Definition	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.
User Guidance	Risks need to be weighed against the benefits for the individual participant. 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. 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.
Conformance	Required
Cardinality	
Relationship content from ToC representing the protocol hierarchy	Introduction
Relationship (reference to high level conceptual model)	
Value	
Business rules	**Value Allowed:** n/a **Relationship:** n/a **Concept:** n/a
Duplicate field in other sections	

241

3. Trial Objectives, Endpoints and Estimands

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

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

Term (Variable)	{Primary/Secondary/Exploratory} Objective + Associated Endpoint {and Estimand}
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	3.X {Primary/Secondary/Exploratory} Objective + Associated Endpoint {and Estimand}
Business rules	**Value Allowed:** Yes **Relationship:** Repeats for Primary, Secondary, Exploratory **Concept:** n/a
Duplicate field in other sections	Repeated and numbered for each objective-endpoint(s) combination

Term (Variable)	{Primary/Secondary/Exploratory} Objective
Data Type	Text
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} Objective
Business rules	**Value Allowed:** Yes **Relationship:** "Table Headers Repeats for primary, Secondary, Exploratory" **Concept:** n/a
Duplicate field in other sections	Repeated and numbered for each objective-endpoint(s) Combination

Term (Variable)	{Primary/Secondary/Exploratory} Endpoint
Data Type	Text
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	**Value Allowed:** Yes **Relationship:** Table Headers Repeats for primary, Secondary, Exploratory **Concept:** n/a
Duplicate field in other sections	Repeated and numbered for each objective-endpoint(s) Combination

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	**Value Allowed:** n/a **Relationship:** "Table Entry one per number Repeats for additional" **Concept:** n/a
Duplicate field in other sections	Multiple relates to objective Repeated and numbered for each objective-endpoint(s) combination

249

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

250

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

251

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

252

4. Trial Design

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

4.1 Description of Trial Design

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

Term (Variable)	Expected Number of Participants
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	**Value Allowed:** Yes **Relationship:** n/a **Concept:** n/a
Duplicate field in other sections	

257

Term (Variable)	Control Mechanism
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	Placebo, active comparator, low dose, historical, standard of care, sham procedure, or none [uncontrolled]
Business rules	**Value Allowed:** Yes **Relationship:** n/a **Concept:** n/a
Duplicate field in other sections	

258

Term (Variable)	Type of Trial
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	Superiority, non-inferiority, dose escalation, or equivalence
Business rules	**Value Allowed:** Yes **Relationship:** n/a **Concept:** n/a
Duplicate field in other sections	

259

Term (Variable)	Adaptive Trial
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	**Value Allowed:** Yes **Relationship:** n/a **Concept:** n/a
Duplicate field in other sections	

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	**Value Allowed:** Yes **Relationship:** n/a **Concept:** 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	**Value Allowed:** Yes **Relationship:** n/a **Concept:** n/a
Duplicate field in other sections	

262

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

263

Term (Variable)	[Description of Trial Duration]
Data Type	Text
Topic, Value or Header	D
Definition	
User Guidance	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. 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. If applicable, describe within-trial transition rules, for example, transitions involving cohorts or trial parts. Dose escalation or dose-ranging details should also be described.
Conformance	Required
Cardinality	
Relationship content from ToC representing the protocol hierarchy	Trial Design
Relationship (reference to high level conceptual model)	
Value	
Business rules	**Value Allowed:** n/a **Relationship:** n/a **Concept:** Trial Population
Duplicate field in other sections	

264

Term (Variable)	Randomisation
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	**Value Allowed:** n/a **Relationship:** n/a **Concept:**
Duplicate field in other sections	

265

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

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	**Value Allowed:** Yes **Relationship:** n/a **Concept:**
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	**Value Allowed:** Yes **Relationship:** n/a **Concept:**
Duplicate field in other sections	

268

Term (Variable)	[Method of Assignment to Trial Intervention]
Data Type	Text
Topic, Value or Header	D
Definition	
User Guidance	Discuss important aspects of trial design, including: • Geographic scope of trial (for example, single-centre, multi-centre, or multi-centre and multi-national). • Planned use of a Data Monitoring Committee, or similar review group and cross-reference Section 10.3, Committees Structure, for details. Whether an interim analysis is planned and, if so, refer to details in Section 9.7, Interim Analysis..
Conformance	Required
Cardinality	
Relationship content from ToC representing the protocol hierarchy	Trial Design
Relationship (reference to high level conceptual model)	
Value	
Business rules	**Value Allowed:** n/a **Relationship:** n/a **Concept:** n/a
Duplicate field in other sections	

269

Term (Variable)	Geographic Scope
Data Type	Text
Topic, Value or Header	D
Definition	
User Guidance	Discuss important aspects of trial design, including: • Geographic scope of trial (for example, single-centre, multi-centre, or multi-centre and multi-national). • Planned use of a Data Monitoring Committee, or similar review group and cross-reference Section 10.3, Committees Structure, for details. • Whether an interim analysis is planned and, if so, refer to details in Section 9.7, Interim Analysis.
Conformance	Required
Cardinality	
Relationship content from ToC representing the protocol hierarchy	Trial Design
Relationship (reference to high level conceptual model)	
Value	Single-centre, multi-centre, or multi-centre and multi-national
Business rules	**Value Allowed:** Yes **Relationship:** n/a **Concept:** n/a
Duplicate field in other sections	

270

Term (Variable)	Decentralise Process, Tools, or Features
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	**Value Allowed:** Yes **Relationship:** n/a **Concept:** n/a
Duplicate field in other sections	

271

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

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	**Value Allowed:** Yes **Relationship:** n/a **Concept:** 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	**Value Allowed:** Yes **Relationship:** n/a **Concept:** n/a
Duplicate field in other sections	

274

Term (Variable)	Planned Extension
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	No, planned extension Trial, long-term follow-up/registry, or post-Trial sample analysis or other data-related activities
Business rules	**Value Allowed:** Yes **Relationship:** n/a **Concept:** n/a
Duplicate field in other sections	

275

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	**Value Allowed:** Yes **Relationship:** n/a **Concept:** 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	**Value Allowed:** Yes **Relationship:** n/a **Concept:** n/a
Duplicate field in other sections	

277

Term (Variable)	Participant Input
Data Type	Text
Topic, Value or Header	D
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	
Business rules	**Value Allowed:** n/a **Relationship:** n/a **Concept:** n/a
Duplicate field in other sections	

278 ## 4.2 Rationale for Trial Design

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

279

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

280

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

281

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

282

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

283 ### 4.2.1 Rationale for Comparator

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

284

Term (Variable)	[Rationale for Comparator]
Data Type	Text
Topic, Value or Header	D
Definition	
User Guidance	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.
Conformance	Conditional
Cardinality	
Relationship content from ToC representing the protocol hierarchy	Trial Design
Relationship (reference to high level conceptual model)	
Value	
Business rules	**Value Allowed:** n/a **Relationship:** Control Mechanism **Concept:** n/a
Duplicate field in other sections	

285

4.2.2 Rationale for Adaptive or Novel Trial Design

Term (Variable)	Rationale for Adaptive or Novel Trial Design
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	Rationale for Adaptive or Novel Trial Design
Business rules	**Value Allowed:** Yes **Relationship:** n/a **Concept:** n/a
Duplicate field in other sections	

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	**Value Allowed:** n/a **Relationship:** n/a **Concept:** 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	**Value Allowed:** Yes **Relationship:** n/a **Concept:** 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	**Value Allowed:** n/a **Relationship:** n/a **Concept:** 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	**Value Allowed:** Yes **Relationship:** n/a **Concept:** n/a
Duplicate field in other sections	

291

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

4.4 Start of Trial and End of Trial

Term (Variable)	Start of Trial and 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	Start of Trial and End of Trial
Business rules	**Value Allowed:** Yes **Relationship:** n/a **Concept:** n/a
Duplicate field in other sections	

Term (Variable)	[Trial Start and End]
Data Type	Text
Topic, Value or Header	D
Definition	
User Guidance	Provide definitions of the start and end of the trial. These definitions should consider local regulatory requirements. 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.
Conformance	Required
Cardinality	
Relationship content from ToC representing the protocol hierarchy	Trial Design
Relationship (reference to high level conceptual model)	
Value	
Business rules	**Value Allowed:** n/a **Relationship:** n/a **Concept:** n/a
Duplicate field in other sections	

295

296 # 5. Trial Population

Term (Variable)	Trial Population
Data Type	Text
Topic, Value or Header	H
Definition	
User Guidance	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. • 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. • 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. • If measures to enrich the trial population for pre-specified subgroups of interest are used, these should be described
Conformance	Required
Cardinality	
Relationship content from ToC representing the protocol hierarchy	Trial Population
Relationship (reference to high level conceptual model)	
Value	Trial Population
Business rules	**Value Allowed:** Yes **Relationship:** n/a **Concept:** n/a
Duplicate field in other sections	

297

5.1 Selection of Trial Population

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

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

300

5.2 Rationale for Trial Population

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

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

303

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

5.3 Inclusion Criteria

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

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

306

Term (Variable)	# Inclusion Criteria
Data Type	Number
Topic, Value or Header	D
Definition	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.
User Guidance	
Conformance	Required
Cardinality	
Relationship content from ToC representing the protocol hierarchy	Trial Population
Relationship (reference to high level conceptual model)	
Value	
Business rules	**Value Allowed:** n/a **Relationship:** n/a **Concept:** n/a
Duplicate field in other sections	number consecutively, repeat for each inclusion criteria, if deleted do not replace, do not duplicate

307

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

5.4 Exclusion Criteria

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

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

310

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

5.5 Lifestyle Considerations

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

Term (Variable)	[Lifestyle Considerations]
Data Type	Text
Topic, Value or Header	D
Definition	
User Guidance	In the following subsections, describe any restrictions during the trial pertaining to lifestyle and/or diet, intake of caffeine, alcohol, or tobacco, or physical and other activities. If not applicable, include a statement that no restrictions are required.
Conformance	Required (at least one item and repeat for each item)
Cardinality	
Relationship content from ToC representing the protocol hierarchy	Trial Population
Relationship (reference to high level conceptual model)	
Value	
Business rules	**Value Allowed:** n/a **Relationship:** n/a **Concept:** n/a
Duplicate field in other sections	

5.5.1 Meals and Dietary Restrictions

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

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

5.5.2 Caffeine, Alcohol, Tobacco, and Other Habits

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

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

5.5.3 Physical Activity

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

Term (Variable)	[Physical Activity]
Data Type	Text
Topic, Value or Header	D
Definition	
User Guidance	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.
Conformance	Optional (repeat for each item)
Cardinality	
Relationship content from ToC representing the protocol hierarchy	Trial Population
Relationship (reference to high level conceptual model)	
Value	
Business rules	**Value Allowed:** n/a **Relationship:** n/a **Concept:** n/a
Duplicate field in other sections	

5.5.4 Other Activity

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

Term (Variable)	[Other Activity]
Data Type	Text
Topic, Value or Header	D
Definition	
User Guidance	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.
Conformance	Optional (repeat for each item)
Cardinality	
Relationship content from ToC representing the protocol hierarchy	Trial Population
Relationship (reference to high level conceptual model)	
Value	
Business rules	**Value Allowed:** n/a **Relationship:** n/a **Concept:** n/a
Duplicate field in other sections	

5.6 Screen Failures

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

Term (Variable)	[Screen Failure]
Data Type	Text
Topic, Value or Header	D
Definition	
User Guidance	Indicate how screen failure will be handled in the trial, including conditions and criteria upon which rescreening is acceptable. If applicable, indicate the circumstances and time window under which a repeat procedure is allowed for screen failure relating to specific inclusion/exclusion criteria for the trial.
Conformance	Required
Cardinality	
Relationship content from ToC representing the protocol hierarchy	Trial Population
Relationship (reference to high level conceptual model)	
Value	
Business rules	**Value Allowed:** n/a **Relationship:** n/a **Concept:** n/a
Duplicate field in other sections	

324

6. Trial Intervention and Concomitant Therapy

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

6.1 Description of Trial Intervention

Term (Variable)	Description of Trial Intervention
Data Type	Text
Topic, Value or Header	H
Definition	Heading
User Guidance	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). It is suggested that the trial intervention(s) be described concisely in a table. 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. For drug/device combination products, include details on the configuration and use of the device and device manufacturer. A device user manual may be referenced in this section
Conformance	Required
Cardinality	
Relationship content from ToC representing the protocol hierarchy	Description of Trial Intervention
Relationship (reference to high level conceptual model)	
Value	Description of Trial Intervention
Business rules	**Value Allowed:** Description of Trial Intervention **Relationship:** Table row headers **Concept:** n/a
Duplicate field in other sections	

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	**Value Allowed:** Yes **Relationship:** Table header **Concept:** 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	**Value Allowed:** Yes **Relationship:** Table header **Concept:** n/a
Duplicate field in other sections	

330

Term (Variable)	Intervention 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	Intervention Name
Business rules	**Value Allowed:** Yes **Relationship:** Table Header **Concept:** n/a
Duplicate field in other sections	

331

Term (Variable)	Intervention 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	Intervention Type
Business rules	**Value Allowed:** Yes **Relationship:** Table header **Concept:** n/a
Duplicate field in other sections	

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	**Value Allowed:** Yes **Relationship:** Table header **Concept:** 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	**Value Allowed:** Yes **Relationship:** Table header **Concept:** n/a
Duplicate field in other sections	

334

Term (Variable)	Formulation
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	Formulation
Business rules	**Value Allowed:** Yes **Relationship:** Table header **Concept:** n/a
Duplicate field in other sections	

335

Term (Variable)	Unit Dose Strength
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	Unit Dose Strength
Business rules	**Value Allowed:** Yes **Relationship:** Table header **Concept:** n/a
Duplicate field in other sections	

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	**Value Allowed:** Yes **Relationship:** Table header **Concept:** 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	**Value Allowed:** Yes **Relationship:** Table Header **Concept:** 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	**Value Allowed:** Yes **Relationship:** Table Heading **Concept:** 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	**Value Allowed:** Yes **Relationship:** n/a **Concept:** 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	**Value Allowed:** Yes **Relationship:** Relates to Arm and intervention formulation dosage **Concept:** n/a
Duplicate field in other sections	Once for each arm Replicate for number of arms

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	**Value Allowed:** n/a **Relationship:** Relates to arm **Concept:** 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	**Value Allowed:** Yes **Relationship:** Relates to arm and intervention formulation dosage **Concept:** n/a
Duplicate field in other sections	Replicate for all interventions in the arm

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	**Value Allowed:** Yes **Relationship:** Relates to arm and intervention formulation dosage **Concept:** n/a
Duplicate field in other sections	Replicate for all interventions in the arm

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	**Value Allowed:** Yes **Relationship:** Relates to arm and intervention formulation dosage **Concept:** n/a
Duplicate field in other sections	Replicate for all interventions in the arm

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	**Value Allowed:** Yes **Relationship:** Relates to arm and intervention formulation dosage **Concept:** n/a
Duplicate field in other sections	Replicate for all interventions in the arm

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	**Value Allowed:** n/a **Relationship:** Relates to Arm and intervention formulation dosage **Concept:** n/a
Duplicate field in other sections	Replicate for all interventions in the arm

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	**Value Allowed:** n/a **Relationship:** Relates to arm and intervention formulation dosage **Concept:** n/a
Duplicate field in other sections	Replicate for all interventions in the arm

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	**Value Allowed:** Yes **Relationship:** Relates to arm and intervention formulation dosage **Concept:** n/a
Duplicate field in other sections	Replicate for all interventions in the arm

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	**Value Allowed:** Yes **Relationship:** Relates to arm and intervention formulation dosage **Concept:** n/a
Duplicate field in other sections	Replicate for all interventions in the arm

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	**Value Allowed:** n/a **Relationship:** n/a **Concept:** n/a
Duplicate field in other sections	

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	**Value Allowed:** Yes **Relationship:** n/a **Concept:** n/a
Duplicate field in other sections	

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

353

6.3 Dosing and Administration

Term (Variable)	Dosing and 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	Dosing and Administration
Business rules	**Value Allowed:** Yes **Relationship:** n/a **Concept:** n/a
Duplicate field in other sections	

Term (Variable)	Dosing and Administration
Data Type	Text
Topic, Value or Header	D
Definition	Describes the details of dosing and administration, schedule, as well as any specific instructions as listed below.
User Guidance	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. 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. Discussion of dose escalation or cohort expansion as part of the overall trial design should be covered in Section 4.2 (Trial Design).
Conformance	Required
Cardinality	
Relationship content from ToC representing the protocol hierarchy	Trial Intervention and Concomitant Therapy
Relationship (reference to high level conceptual model)	
Value	
Business rules	**Value Allowed:** n/a **Relationship:** n/a **Concept:** n/a
Duplicate field in other sections	

356

6.3.1 Trial Intervention Dose Modification

Term (Variable)	Trial Intervention Dose Modification
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	Trial Intervention Dose Modification
Business rules	**Value Allowed:** Yes **Relationship:** n/a **Concept:** n/a
Duplicate field in other sections	

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

359

6.4 Treatment of Overdose

Term (Variable)	Treatment of Overdose
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	Treatment of Overdose
Business rules	**Value Allowed:** Yes **Relationship:** n/a **Concept:** n/a
Duplicate field in other sections	

Term (Variable)	Treatment of Overdose
Data Type	Text
Topic, Value or Header	D
Definition	Specifies what is meant by trial intervention overdose and any known antidote or therapies.
User Guidance	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.
Conformance	Required
Cardinality	
Relationship content from ToC representing the protocol hierarchy	Trial Intervention and Concomitant Therapy
Relationship (reference to high level conceptual model)	
Value	
Business rules	**Value Allowed:** n/a **Relationship:** n/a **Concept:** n/a
Duplicate field in other sections	

362

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	**Value Allowed:** Yes **Relationship:** n/a **Concept:** n/a
Duplicate field in other sections	

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	**Value Allowed:** Yes **Relationship:** n/a **Concept:** n/a
Duplicate field in other sections	

Term (Variable)	[Trial Intervention Preparation]
Data Type	Text
Topic, Value or Header	D
Definition	Describe any preparation of the trial intervention and control product and by whom.
User Guidance	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. 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.
Conformance	Required
Cardinality	
Relationship content from ToC representing the protocol hierarchy	Trial Intervention and Concomitant Therapy
Relationship (reference to high level conceptual model)	
Value	[insert Trial Intervention Preparation text]
Business rules	**Value Allowed:** Yes **Relationship:** n/a **Concept:** n/a
Duplicate field in other sections	

366

6.5.2 Handling and Storage of Trial Intervention

Term (Variable)	Handling and Storage 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	Storage and Handling of Trial Intervention
Business rules	**Value Allowed:** Yes **Relationship:** n/a **Concept:** n/a
Duplicate field in other sections	

Term (Variable)	Trial Intervention Storage and Handling
Data Type	Text
Topic, Value or Header	D
Definition	Describes storage and handling requirements (for example, protection from light, temperature, humidity) for the trial intervention and control product.
User Guidance	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.
Conformance	Required
Cardinality	
Relationship content from ToC representing the protocol hierarchy	Trial Intervention and Concomitant Therapy
Relationship (reference to high level conceptual model)	
Value	[insert Trial Intervention Storage and Handling text]
Business rules	**Value Allowed:** Yes **Relationship:** n/a **Concept:** n/a
Duplicate field in other sections	

369

6.5.3 Accountability of Trial Intervention

Term (Variable)	Accountability 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	Accountability of Trial Intervention
Business rules	**Value Allowed:** Yes **Relationship:** n/a **Concept:** n/a
Duplicate field in other sections	

Term (Variable)	Accountability
Data Type	Text
Topic, Value or Header	D
Definition	
User Guidance	Describe the method by which the accountability will be achieved, including trial intervention will be distributed and related details, including: • how and by whom the trial intervention will be distributed • participation of a drug repository or pharmacy, if applicable, • plans for disposal or return of unused product, and • expectations for reconciliation.
Conformance	Required
Cardinality	
Relationship content from ToC representing the protocol hierarchy	Trial Intervention and Concomitant Therapy
Relationship (reference to high level conceptual model)	
Value	[Accountability Text]
Business rules	**Value Allowed:** Yes **Relationship:** n/a **Concept:** n/a
Duplicate field in other sections	

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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	**Value Allowed:** Yes **Relationship:** n/a **Concept:** 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	**Value Allowed:** Yes **Relationship:** n/a **Concept:** n/a
Duplicate field in other sections	

375

Term (Variable)	Participant Assignment
Data Type	Text
Topic, Value or Header	D
Definition	Describes the method of assigning participants to trial intervention
User Guidance	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.
Conformance	Required
Cardinality	
Relationship content from ToC representing the protocol hierarchy	Trial Intervention and Concomitant Therapy
Relationship (reference to high level conceptual model)	
Value	
Business rules	**Value Allowed:** n/a **Relationship:** n/a **Concept:** n/a
Duplicate field in other sections	

376

6.6.2 Randomisation

Term (Variable)	Randomisation
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	Randomisation
Business rules	**Value Allowed:** Yes **Relationship:** n/a **Concept:** n/a
Duplicate field in other sections	

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

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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	**Value Allowed:** Yes **Relationship:** n/a **Concept:** n/a
Duplicate field in other sections	

Term (Variable)	Blinding
Data Type	Text
Topic, Value or Header	D
Definition	Describe efforts to ensure that the trial intervention and control products are as indistinguishable as possible.
User Guidance	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.
Conformance	Required
Cardinality	
Relationship content from ToC representing the protocol hierarchy	Trial Intervention and Concomitant Therapy
Relationship (reference to high level conceptual model)	
Value	
Business rules	**Value Allowed:** n/a **Relationship:** n/a **Concept:** n/a
Duplicate field in other sections	

382

Term (Variable)	Emergency Unblinding
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	Emergency Unblinding
Business rules	**Value Allowed:** Yes **Relationship:** n/a **Concept:** n/a
Duplicate field in other sections	

383

Term (Variable)	Emergency Unblinding
Data Type	Text
Topic, Value or Header	D
Definition	Describes the criteria for breaking the trial mask (blind) or participant code.
User Guidance	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.
Conformance	Required
Cardinality	
Relationship content from ToC representing the protocol hierarchy	Trial Intervention and Concomitant Therapy
Relationship (reference to high level conceptual model)	
Value	
Business rules	**Value Allowed:** n/a **Relationship:** n/a **Concept:** n/a
Duplicate field in other sections	

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6.7 Trial Intervention Compliance

Term (Variable)	Trial Intervention Compliance
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	Trial Intervention Compliance
Business rules	**Value Allowed:** Yes **Relationship:** n/a **Concept:** n/a
Duplicate field in other sections	

Term (Variable)	Additional Trial Intervention Compliance
Data Type	Text
Topic, Value or Header	D
Definition	Describe measures to ensure and document dosing information and trial intervention compliance (for example, accountability records, diary cards, concentration measurements).
User Guidance	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
Conformance	Required
Cardinality	
Relationship content from ToC representing the protocol hierarchy	Trial Intervention and Concomitant Therapy
Relationship (reference to high level conceptual model)	
Value	
Business rules	**Value Allowed:** n/a **Relationship:** n/a **Concept:** n/a
Duplicate field in other sections	

6.8 Concomitant Therapy

Term (Variable)	Concomitant Therapy
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	Concomitant Therapy
Business rules	**Value Allowed:** Yes **Relationship:** n/a **Concept:** n/a
Duplicate field in other sections	

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

390

391 6.8.1 Prohibited Concomitant Therapy

Term (Variable)	Prohibited Concomitant Therapy
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	Prohibited Concomitant Therapy
Business rules	**Value Allowed:** Yes **Relationship:** n/a **Concept:** n/a
Duplicate field in other sections	

392

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

393 ### 6.8.2 Permitted Concomitant Therapy

Term (Variable)	Permitted Concomitant Therapy
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	Permitted Concomitant Therapy
Business rules	**Value Allowed:** Yes **Relationship:** n/a **Concept:** n/a
Duplicate field in other sections	

394

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

6.8.3 Rescue Therapy

Term (Variable)	Rescue Therapy
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	Rescue Therapy
Business rules	**Value Allowed:** Yes **Relationship:** n/a **Concept:** n/a
Duplicate field in other sections	

Term (Variable)	Rescue Therapy
Data Type	Text
Topic, Value or Header	D
Definition	Describes the circumstances under which use of rescue therapy is permitted.
User Guidance	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.
Conformance	Required
Cardinality	
Relationship content from ToC representing the protocol hierarchy	Trial Intervention and Concomitant Therapy
Relationship (reference to high level conceptual model)	
Value	
Business rules	**Value Allowed:** n/a **Relationship:** n/a **Concept:** n/a
Duplicate field in other sections	

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398 ### 6.8.4 Other Therapy

Term (Variable)	Other Therapy
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	Other Therapy
Business rules	**Value Allowed:** Yes **Relationship:** n/a **Concept:** n/a
Duplicate field in other sections	

399

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

400

7. Discontinuation of Trial Intervention and Participant Withdrawal from Trial

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

7.1 Discontinuation of Trial Intervention

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

7.1.1 Criteria for Permanent Discontinuation of Trial Intervention

Term (Variable)	Criteria for Discontinuation 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	Discontinuation of Trial Intervention
Relationship (reference to high level conceptual model)	
Value	Criteria for Discontinuation of Trial Intervention
Business rules	**Value Allowed:** Yes **Relationship:** n/a **Concept:** n/a
Duplicate field in other sections	

Term (Variable)	Criteria for Permanent Discontinuation of Trial Intervention
Data Type	Text
Topic, Value or Header	D
Definition	Criteria's for discontinuation of a participant from trial intervention.
User Guidance	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
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	**Value Allowed:** n/a **Relationship:** n/a **Concept:** n/a
Duplicate field in other sections	

407

7.1.2 Temporary Discontinuation or Interruption of Trial Intervention

Term (Variable)	Temporary Discontinuation or Interruption 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	Discontinuation of Trial Intervention
Relationship (reference to high level conceptual model)	
Value	Temporary Discontinuation or Interruption of Trial Intervention
Business rules	**Value Allowed:** Yes **Relationship:** n/a **Concept:** n/a
Duplicate field in other sections	

Term (Variable)	Temporary Discontinuation/Interruption of Trial Intervention
Data Type	Text
Topic, Value or Header	D
Definition	Specifics criteria for interrupting trial intervention
User Guidance	Describe • the criteria for temporary discontinuation or interruption of trial intervention for an individual participant • what to do and which restrictions still apply if the participant needs to temporarily discontinue or interrupt trial intervention • whether they will continue in the trial, and • whether all, or specify which, assessments will be performed for the stated duration of the trial. Details of any rechallenge or restart after a safety-related event should be included in Section 7.1.3, Rechallenge.
Conformance	Required
Cardinality	
Relationship content from ToC representing the protocol hierarchy	Discontinuation of Trial Intervention
Relationship (reference to high level conceptual model)	
Value	
Business rules	**Value Allowed:** n/a **Relationship:** n/a **Concept:** n/a
Duplicate field in other sections	

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411 ### 7.1.3 Rechallenge

Term (Variable)	Rechallenge
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	Rechallenge
Business rules	**Value Allowed:** Yes **Relationship:** n/a **Concept:** n/a
Duplicate field in other sections	

412

Term (Variable)	Rechallenge
Data Type	Text
Topic, Value or Header	D
Definition	
User Guidance	Describe the criteria for rechallenge/restarting trial intervention, how to perform rechallenge, number of rechallenges allowed during the trial, and whether all, or specify which, assessments will be performed for the stated duration of the trial. If rechallenge is not allowed, state this.
Conformance	Required
Cardinality	
Relationship content from ToC representing the protocol hierarchy	Discontinuation of Trial Intervention
Relationship (reference to high level conceptual model)	
Value	
Business rules	**Value Allowed:** n/a **Relationship:** n/a **Concept:** n/a
Duplicate field in other sections	

413

7.2 Participant Withdrawal from the Trial

Term (Variable)	Participant Withdrawal from Trial
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	Participant Withdrawal from Trial
Business rules	**Value Allowed:** Yes **Relationship:** n/a **Concept:** n/a
Duplicate field in other sections	

Term (Variable)	Participant Withdrawal from Trial
Data Type	Text
Topic, Value or Header	D
Definition	
User Guidance	Describe the criteria for participant withdrawal from the trial.
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	**Value Allowed:** n/a **Relationship:** n/a **Concept:** n/a
Duplicate field in other sections	

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	**Value Allowed:** Yes **Relationship:** n/a **Concept:** n/a
Duplicate field in other sections	

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	**Value Allowed:** Yes **Relationship:** n/a **Concept:** n/a
Duplicate field in other sections	

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	**Value Allowed:** Yes **Relationship:** n/a **Concept:** n/a
Duplicate field in other sections	

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	**Value Allowed:** n/a **Relationship:** n/a **Concept:** n/a
Duplicate field in other sections	

8. Trial Assessments and Procedures

Term (Variable)	Trial Assessments and Procedures
Data Type	Text
Topic, Value or Header	H
Definition	
User Guidance	• 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. • 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. • Reference the literature for the validation of scales/instruments/questionnaires/assays. • Instructions or protocols for specialised tests may be presented in an appendix or a separate document and cross-referenced. • If the trial includes qualitative interviews, describe these evaluations. • 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. • 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.
Conformance	Required
Cardinality	
Relationship content from ToC representing the protocol hierarchy	Trial Assessments and Procedures
Relationship (reference to high level conceptual model)	
Value	Trial Assessments and Procedures
Business rules	**Value Allowed**: Yes **Relationship**: n/a **Concept**: n/a
Duplicate field in other sections	

8.1 Screening/Baseline Assessments and Procedures

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

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

8.2 Efficacy Assessments and Procedures

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

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

429

8.3 Safety Assessments and Procedures

Term (Variable)	Safety Assessments and Procedures
Data Type	Text
Topic, Value or Header	H
Definition	
User Guidance	This section describes safety assessments and procedures in this section. Level 3 headings can be added as needed. • Identify any non-investigator party responsible for evaluation of laboratory or other safety assessments (for example, Sponsor or external Independent Data Monitoring Committee). • Include guidelines for the management of relevant laboratory or other safety assessment abnormalities.
Conformance	Required
Cardinality	
Relationship content from ToC representing the protocol hierarchy	Trial Assessment and Procedures
Relationship (reference to high level conceptual model)	
Value	Efficacy Assessments and Procedures
Business rules	**Value Allowed:** Yes **Relationship:** n/a **Concept:** n/a
Duplicate field in other sections	

Term (Variable)	Safety Assessments and Procedures
Data Type	Text
Topic, Value or Header	D
Definition	
User Guidance	This section describes safety assessments and procedures in this section. Level 3 headings can be added as needed. • Identify any non-investigator party responsible for evaluation of laboratory or other safety assessments (for example, Sponsor or external Independent Data Monitoring Committee). • Include guidelines for the management of relevant laboratory or other safety assessment abnormalities.
Conformance	Optional/ Repeated
Cardinality	
Relationship content from ToC representing the protocol hierarchy	Trial Assessment and Procedures
Relationship (reference to high level conceptual model)	Safety Assessments and Procedures Link to objective endpoint or estimand
Value	
Business rules	**Value Allowed:** Potential controlled terminology **Relationship:** n/a **Concept:** n/a
Duplicate field in other sections	Repeat for each procedure

8.3.1 Physical Examination

Term (Variable)	Physical Examination
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	Physical Examination
Business rules	**Value Allowed:** Yes **Relationship:** n/a **Concept:** n/a
Duplicate field in other sections	

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

8.3.2 Vital Signs

Term (Variable)	Vital Signs
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	Vital Signs
Business rules	**Value Allowed:** Yes **Relationship:** n/a **Concept:** n/a
Duplicate field in other sections	

Term (Variable)	Vital Signs
Data Type	Text
Topic, Value or Header	D
Definition	
User Guidance	• Carefully consider which vital signs (if any) should be measured to ensure that only essential data are collected • 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 • Select the standard methods of vital sign collection as appropriate for the countries in which the trial will be conducted • 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.
Conformance	Optional/Repeated
Cardinality	
Relationship content from ToC representing the protocol hierarchy	Trial Assessments and Procedures
Relationship (reference to high level conceptual model)	Vital signs Link to objective endpoint or estimand
Value	
Business rules	**Value Allowed:** potential controlled terminology **Relationship:** n/a **Concept:** n/a
Duplicate field in other sections	Repeat for each procedure

437

8.3.3 Electrocardiograms

Term (Variable)	Electrocardiograms
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	Electrocardiograms
Business rules	**Value Allowed:** Yes **Relationship:** n/a **Concept:** n/a
Duplicate field in other sections	

Term (Variable)	Electrocardiograms
Data Type	Text
Topic, Value or Header	D
Definition	
User Guidance	• Specify if the ECG is for screening purposes only. • 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). • Indicate whether single or triplicate ECGs will be collected at each time point. If triplicate ECGs will be collected, provide necessary details. • Indicate whether ECGs will be analysed at a central or local laboratory. 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.
Conformance	Optional/Repeated
Cardinality	
Relationship content from ToC representing the protocol hierarchy	Trial Assessments and Procedures
Relationship (reference to high level conceptual model)	Electrocardiograms Link to objective endpoint or estimand
Value	
Business rules	**Value Allowed:** Potential controlled terminology **Relationship:** n/a **Concept:** n/a
Duplicate field in other sections	Repeat for each procedure

441 ### 8.3.4 Clinical Laboratory Assessments

Term (Variable)	Clinical Laboratory Assessments
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	Clinical Laboratory Assessments
Business rules	**Value Allowed:** Yes **Relationship:** n/a **Concept:** n/a
Duplicate field in other sections	

442

Term (Variable)	Clinical Laboratory Assessments
Data Type	Text
Topic, Value or Header	D
Definition	
User Guidance	• 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. • 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. • Specify any special instructions for screening samples. • 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.
Conformance	Optional/Repeated
Cardinality	
Relationship content from ToC representing the protocol hierarchy	Trial Assessments and Procedures
Relationship (reference to high level conceptual model)	Clinical Laboratory Assessments Link to objective endpoint or estimand
Value	
Business rules	**Value Allowed**: potential controlled terminology **Relationship**: n/a **Concept**: n/a
Duplicate field in other sections	Repeat for each procedure

443

8.3.5 Suicidal Ideation and Behaviour Risk Monitoring

Term (Variable)	Suicidal Ideation and Behaviour Risk Monitoring
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	Suicidal Ideation and Behaviour Risk Monitoring
Business rules	**Value Allowed:** Yes **Relationship:** n/a **Concept:** n/a
Duplicate field in other sections	

Term (Variable)	Suicidal Ideation and Behaviour Risk Monitoring
Data Type	Text
Topic, Value or Header	D
Definition	
User Guidance	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.
Conformance	Required
Cardinality	
Relationship content from ToC representing the protocol hierarchy	Trial Assessments and Procedures
Relationship (reference to high level conceptual model)	
Value	[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. OR [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.
Business rules	**Value Allowed:** Potential controlled terminology **Relationship:** n/a **Concept:** n/a
Duplicate field in other sections	

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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	**Value Allowed:** Yes **Relationship:** n/a **Concept:** n/a
Duplicate field in other sections	

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	**Value Allowed:** Yes **Relationship:** n/a **Concept:** n/a
Duplicate field in other sections	

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	**Value Allowed:** Yes **Relationship:** n/a **Concept:** n/a
Duplicate field in other sections	

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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	**Value Allowed:** Yes **Relationship:** n/a **Concept:** 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	**Value Allowed:** Yes **Relationship:** n/a **Concept:** 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	**Value Allowed:** Yes **Relationship:** n/a **Concept:** n/a
Duplicate field in other sections	

Term (Variable)	Time period and frequency for collecting AEs and SAEs
Data Type	Text
Topic, Value or Header	D
Definition	
User Guidance	Specify the start and ending time periods for collecting AEs and SAEs. Consider the following factors when deciding on the collection time period: • Available information on how long the trial intervention remains active in the participant • How long it may remain active/inactive in the participant and potentially be transferable to a fetus • 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) • Known late effects (e.g. secondary malignancies that will require active monitoring) • Trial design • If collection will start when the ICF is signed to capture baseline rates
Conformance	Required
Cardinality	
Relationship content from ToC representing the protocol hierarchy	Trial Assessments and Procedures
Relationship (reference to high level conceptual model)	
Value	
Business rules	**Value Allowed:** n/a **Relationship:** n/a **Concept:** n/a
Duplicate field in other sections	

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8.4.3 Identifying AEs and SAEs

Term (Variable)	Identifying AEs and 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	Identifying AEs and SAEs
Business rules	**Value Allowed:** Yes **Relationship:** n/a **Concept:** n/a
Duplicate field in other sections	

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

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	**Value Allowed:** Yes **Relationship:** n/a **Concept:** n/a
Duplicate field in other sections	

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	**Value Allowed:** n/a **Relationship:** n/a **Concept:** n/a
Duplicate field in other sections	

Term (Variable)	Further details on assessing severity and causality of AEs and SAEs are in Appendices 12.3 and 12.4
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	Further details on assessing severity and causality of AEs and SAEs are in Appendices 12.3 and 12.4
Business rules	**Value Allowed:** n/a **Relationship:** n/a **Concept:** n/a
Duplicate field in other sections	

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

Term (Variable)	Follow-up of AEs and 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	Follow-up of AEs and SAEs
Business rules	**Value Allowed:** Yes **Relationship:** n/a **Concept:** n/a
Duplicate field in other sections	

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

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8.4.6 Reporting of SAEs

Term (Variable)	Reporting of 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	Reporting of SAEs
Business rules	**Value Allowed:** Yes **Relationship:** n/a **Concept:** n/a
Duplicate field in other sections	

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	**Value Allowed:** n/a **Relationship:** n/a **Concept:** n/a
Duplicate field in other sections	

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	**Value Allowed:** Yes **Relationship:** n/a **Concept:** n/a
Duplicate field in other sections	

Term (Variable)	Regulatory Reporting
Data Type	Text
Topic, Value or Header	D
Definition	
User Guidance	Specify: • The Sponsor's legal/regulatory responsibilities to report SAEs to regulatory authorities, ethics committees, and investigators. • The investigators' responsibilities for promptly reporting SAEs to the Sponsor to allow the Sponsor to meet their responsibilities.
Conformance	Required
Cardinality	
Relationship content from ToC representing the protocol hierarchy	Trial Assessments and Procedures
Relationship (reference to high level conceptual model)	
Value	
Business rules	**Value Allowed:** n/a **Relationship:** n/a **Concept:** n/a
Duplicate field in other sections	

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470 8.4.8 Serious and Unexpected Adverse Reaction Reporting

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

471

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

8.4.9 Adverse Events of Special Interest

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

Term (Variable)	Adverse Events of Special Interest
Data Type	Text
Topic, Value or Header	D
Definition	
User Guidance	Include this section, if applicable. Specify any Adverse Events of Special Interest (AESI): • Other events that merit reporting to the Sponsor, trial leadership, IRB, and regulatory agencies (for example, secondary malignancies in oncology studies). • 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. Include the following for each AESI: • The definition of the event. Specify the MedDRA preferred terms to use to report the AESI. • If it is a measurable quantity, specify how will the measurement be done. If it is a clinical event, specify how will it be confirmed.
Conformance	Required
Cardinality	
Relationship content from ToC representing the protocol hierarchy	Trial Assessment and Procedures
Relationship (reference to high level conceptual model)	
Value	
Business rules	**Value Allowed:** n/a **Relationship:** n/a **Concept:** n/a
Duplicate field in other sections	

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

Term (Variable)	Disease-related Events or Outcomes Not Qualifying as AEs or 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	Disease-related Events or Outcomes Not Qualifying as AEs or SAEs
Business rules	**Value Allowed:** Yes **Relationship:** n/a **Concept:** n/a
Duplicate field in other sections	

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

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	**Value Allowed:** Yes **Relationship:** n/a **Concept:** n/a
Duplicate field in other sections	

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	**Value Allowed:** Yes **Relationship:** n/a **Concept:** n/a
Duplicate field in other sections	

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

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8.5.2 Participants Whose Partners Become Pregnant

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

Term (Variable)	Participants Whose Partners Become Pregnant
Data Type	Text
Topic, Value or Header	D
Definition	
User Guidance	Specify: • If the Investigator will attempt to collect pregnancy information for a participant's partner, who becomes pregnant while the participant is in the trial. • The assessments to be performed, type and duration of monitoring, and what information will be collected.
Conformance	Optional
Cardinality	
Relationship content from ToC representing the protocol hierarchy	Trial Assessments and Procedures
Relationship (reference to high level conceptual model)	
Value	
Business rules	**Value Allowed:** n/a **Relationship:** n/a **Concept:** n/a
Duplicate field in other sections	

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8.6 Medical Device Product Complaints for Drug/Device Combination Products

Term (Variable)	Medical Device Product Complaints for Drug/Device Combination Products
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	Medical Device Product Complaints for Drug/Device Combination Products
Business rules	**Value Allowed:** Yes **Relationship:** n/a **Concept:** n/a
Duplicate field in other sections	

8.6.1 Definition of Medical Device Product Complaints

Term (Variable)	Definition of Medical Device Complaints
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	
Business rules	**Value Allowed:** Yes **Relationship:** n/a **Concept:** n/a
Duplicate field in other sections	

Term (Variable)	Definition of Medical Device Compliance
Data Type	Text
Topic, Value or Header	D
Definition	
User Guidance	Add this section for drug/device combination products; otherwise, omit it.
Conformance	Optional
Cardinality	
Relationship content from ToC representing the protocol hierarchy	Trial Assessments and Procedures
Relationship (reference to high level conceptual model)	
Value	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.
Business rules	**Value Allowed:** Yes **Relationship:** n/a **Concept:** n/a
Duplicate field in other sections	

8.6.2 Recording of Medical Device Product Complaints

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

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

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8.6.3 Time Period and Frequency for Collecting Medical Device Product Complaints

Term (Variable)	Time Period and Frequency for Collecting Medical Device Product Complaints
Data Type	Text
Topic, Value or Header	H
Definition	
User Guidance	
Conformance	Optional
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 Collecting Medical Device Product Complaints
Business rules	**Value Allowed:** Yes **Relationship:** n/a **Concept:** n/a
Duplicate field in other sections	

Term (Variable)	Time Period and Frequency for Collection Medical Device Product Complaints
Data Type	Text
Topic, Value or Header	D
Definition	
User Guidance	
Conformance	Optional
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 Medical Device Product Complaints
Business rules	**Value Allowed**: Yes **Relationship**: n/a **Concept**: n/a
Duplicate field in other sections	

8.6.4 Follow-Up of Medical Device Product Complaints

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

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

8.6.5 Regulatory Reporting Requirements for Medical Device Product Complaints

Term (Variable)	Regulatory Reporting Requirements for Medical Device Product Complaints
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	Regulatory Reporting Requirements for Medical Device Product Complaints
Business rules	**Value Allowed:** Yes **Relationship:** n/a **Concept:** n/a
Duplicate field in other sections	

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	**Value Allowed:** n/a **Relationship:** n/a **Concept:** n/a
Duplicate field in other sections	

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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	**Value Allowed:** Yes **Relationship:** n/a **Concept:** n/a
Duplicate field in other sections	

507

Term (Variable)	Pharmacokinetics
Data Type	Text
Topic, Value or Header	D
Definition	
User Guidance	• 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. • 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. • Indicate definitions for the PK parameters (for example, area under the curve [AUC], maximum observed concentration [Cmax], time to Cmax [Tmax], half-life [T½], volume of distribution [Vd], clearance [CL]) of interest and how they will be calculated. Consult with the PK representative for this information • Describe sampling time relative to ingestion of food, posture, and possible effects of concomitant medications/alcohol/caffeine/nicotine. • 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. • 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.
Conformance	Optional/Repeated
Cardinality	
Relationship content from ToC representing the protocol hierarchy	Trial Assessments and Procedures
Relationship (reference to high level conceptual model)	Pharmacokinetics Assessments and Procedures Link to objective endpoint or estimand
Value	
Business rules	**Value Allowed:** potential controlled terminology **Relationship:** n/a **Concept:** n/a
Duplicate field in other sections	Repeat for each assessment

508

8.8 Genetics

Term (Variable)	Genetics
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	Genetics
Business rules	**Value Allowed:** Yes **Relationship:** n/a **Concept:** n/a
Duplicate field in other sections	

511

Term (Variable)	Genetics
Data Type	Text
Topic, Value or Header	D
Definition	
User Guidance	Refer to ICH E15 and E18 as needed. Contact the appropriate sponsor functional area representatives to ensure that appropriate pharmacogenomic trial design text is included throughout the protocol. 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.
Conformance	Optional/Repeated
Cardinality	
Relationship content from ToC representing the protocol hierarchy	Trial Assessments and Procedures
Relationship (reference to high level conceptual model)	Genetic Assessments and Procedures Link to objective endpoint or estimand
Value	
Business rules	**Value Allowed:** potential controlled terminology **Relationship:** n/a **Concept:** n/a
Duplicate field in other sections	Repeat for each analysis

512

8.9 Biomarkers

Term (Variable)	Biomarkers
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	Biomarkers
Business rules	**Value Allowed:** Yes **Relationship:** n/a **Concept:** n/a
Duplicate field in other sections	

Term (Variable)	Biomarkers
Data Type	Text
Topic, Value or Header	D
Definition	
User Guidance	Refer to ICH E15 and E18 as needed. If biomarkers will be evaluated: • Include analyses (e.g, ribonucleic acid [RNA], serum, plasma, or other soluble markers). • Indicate any additional analyses, such as flow cytometry, histology, serology, immunogenicity, or histochemical analyses. • 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. • If instructions for collection of samples are complex, then consider including them in an appendix rather than the main text of protocol. • Specify whether optional or required (both here and in the SoA). Required samples must be based on a protocol objective. • To distinguish between different types of biomarker samples, include the following for each sample, as appropriate: o Indicate if residual samples. 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 o Indicate the purpose of the sample (e.g., participant eligibility, exploratory research, RNA analysis). 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. o Indicate the biomarkers that will be studied.
Conformance	Optional/Repeated
Cardinality	
Relationship content from ToC representing the protocol hierarchy	Trial Assessments and Procedures
Relationship (reference to high level conceptual model)	Biomarker Assessments and Procedures Link to objective endpoint or estimand
Value	
Business rules	**Value Allowed:** potential controlled terminology **Relationship:** n/a **Concept:** n/a
Duplicate field in other sections	Repeat for each biomarker

515

8.10 Immunogenicity Assessments

Term (Variable)	Immunogenicity Assessments
Data Type	Text
Topic, Value or Header	H
Definition	Section Heading
User Guidance	Include any specific instructions for the collection of samples and interpretation of immunogenicity. If immunogenicity assessments are included within Efficacy Assessments or Safety Assessments, cross-reference to that section.
Conformance	Required
Cardinality	
Relationship content from ToC representing the protocol hierarchy	Trial Assessments and Procedures
Relationship (reference to high level conceptual model)	
Value	Immunogenicity Assessments
Business rules	**Value Allowed:** Yes **Relationship:** n/a **Concept:** n/a
Duplicate field in other sections	

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

8.11 Medical Resource Utilisation and Health Economics

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

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

520

9. Statistical Considerations

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

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

523

9.1 Analysis Sets

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

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

9.2 Analyses Supporting Primary Objective(s)

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

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

529

9.2.1 Statistical Model, Hypothesis, and Method of Analysis

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

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

532

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

533

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

534

9.2.2 Handling of Intercurrent Events of Primary Estimand(s)

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

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

537

9.2.3 Handling of Missing Data

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

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

9.2.4 Sensitivity Analysis

Term (Variable)	Sensitivity Analysis
Data Type	Text
Topic, Value or Header	H
Definition	
User Guidance	Sensitivity analyses are a series of analyses conducted with the intent to explore the robustness of inferences from the main estimator to deviations from its underlying modelling assumptions and limitations in the data.
Conformance	Required
Cardinality	
Relationship content from ToC representing the protocol hierarchy	Statistical Considerations/Analyses Supporting Primary Objective(s)/Sensitivity Analysis
Relationship (reference to high level conceptual model)	
Value	

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

541

Term (Variable)	Sensitivity Analysis
Data Type	Text
Topic, Value or Header	D
Definition	
User Guidance	Sensitivity analyses are a series of analyses conducted with the intent to explore the robustness of inferences from the main estimator to deviations from its underlying modelling assumptions and limitations in the data.
Conformance	Required
Cardinality	
Relationship content from ToC representing the protocol hierarchy	Statistical Considerations/Analyses Supporting Primary Objective(s)/Sensitivity Analysis
Relationship (reference to high level conceptual model)	
Value	
Business rules	**Value Allowed**: n/a **Relationship**: n/a **Concept**: n/a
Duplicate field in other sections	

542

9.2.5 Supplementary Analysis

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

Duplicate field in other sections	

543

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

544

9.3 Analysis Supporting Secondary Objective(s)

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

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

547

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

548

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

549

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

550

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

551

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

552

9.4 Analysis of Exploratory Objective(s)

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

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

555

9.5 Safety Analyses

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

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

9.6 Other Analyses

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

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

9.7 Interim Analyses

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

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

9.8 Sample Size Determination

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

9.9 Protocol Deviations

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

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

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

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

10.1 Regulatory and Ethical Considerations

Term (Variable)	Regulatory and Ethical Considerations
Data Type	Text
Topic, Value or Header	H
Definition	Section Heading
User Guidance	List the prevailing ethical, legal, and regulatory guidelines that will be applied throughout the trial. This trial will be conducted in accordance with the protocol and with the following: • Consensus ethical principles derived from international guidelines including the Declaration of Helsinki and Council for International Organizations of Medical Sciences (CIOMS) International Ethical Guidelines • ICH Good Clinical Practice (GCP) Guidelines • Applicable laws and regulations • {insert additional as needed} List the investigators' and sponsor's responsibilities in this regard. **Investigator Responsibilities** [Investigator Responsibilities] **Sponsor Responsibilities** [Sponsor Responsibilities]
Conformance	Required
Cardinality	
Relationship content from ToC representing the protocol hierarchy	General Considerations: Regulatory, Ethical, and Trial Oversight Considerations
Relationship (reference to high level conceptual model)	
Value	Regulatory and Ethical Considerations
Business rules	**Value Allowed:** n/a **Relationship:** n/a **Concept:** n/a
Duplicate field in other sections	

Term (Variable)	Regulatory and Ethical Considerations
Data Type	Text
Topic, Value or Header	D
Definition	
User Guidance	List the prevailing ethical, legal, and regulatory guidelines that will be applied throughout the trial. This trial will be conducted in accordance with the protocol and with the following: • Consensus ethical principles derived from international guidelines including the Declaration of Helsinki and Council for International Organizations of Medical Sciences (CIOMS) International Ethical Guidelines • ICH Good Clinical Practice (GCP) Guidelines • Applicable laws and regulations • {insert additional as needed} List the investigators' and sponsor's responsibilities in this regard. **Investigator Responsibilities** [Investigator Responsibilities] **Sponsor Responsibilities** [Sponsor Responsibilities]
Conformance	Required/Repeatable Required/Repeatable
Cardinality	
Relationship content from ToC representing the protocol hierarchy	General Considerations: Regulatory, Ethical, and Trial Oversight Considerations / Regulatory and Ethical Considerations
Relationship (reference to high level conceptual model)	
Value	
Business rules	**Value Allowed:** Yes **Relationship:** n/a **Concept:** n/a Note: This field can contain a text value
Duplicate field in other sections	

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Term (Variable)	Investigator Responsibilities
Data Type	Text
Topic, Value or Header	H
Definition	
User Guidance	List the prevailing ethical, legal, and regulatory guidelines that will be applied throughout the trial. This trial will be conducted in accordance with the protocol and with the following: • Consensus ethical principles derived from international guidelines including the Declaration of Helsinki and Council for International Organizations of Medical Sciences (CIOMS) International Ethical Guidelines • ICH Good Clinical Practice (GCP) Guidelines • Applicable laws and regulations • {insert additional as needed} List the investigators' and sponsor's responsibilities in this regard. **Investigator Responsibilities** [Investigator Responsibilities]
Conformance	Required
Cardinality	
Relationship content from ToC representing the protocol hierarchy	General Considerations: Regulatory, Ethical, and Trial Oversight Considerations / Regulatory and Ethical Considerations
Relationship (reference to high level conceptual model)	
Value	Investigator Responsibilities
Business rules	**Value Allowed:** Yes **Relationship:** n/a **Concept:** n/a
Duplicate field in other sections	

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Term (Variable)	Investigator Responsibilities
Data Type	Text
Topic, Value or Header	D
Definition	
User Guidance	List the prevailing ethical, legal, and regulatory guidelines that will be applied throughout the trial. This trial will be conducted in accordance with the protocol and with the following: • Consensus ethical principles derived from international guidelines including the Declaration of Helsinki and Council for International Organizations of Medical Sciences (CIOMS) International Ethical Guidelines • ICH Good Clinical Practice (GCP) Guidelines • Applicable laws and regulations • {insert additional as needed} List the investigators' and sponsor's responsibilities in this regard. **Investigator Responsibilities** [Investigator Responsibilities]
Conformance	Required
Cardinality	
Relationship content from ToC representing the protocol hierarchy	General Considerations: Regulatory, Ethical, and Trial Oversight Considerations / Regulatory and Ethical Considerations
Relationship (reference to high level conceptual model)	
Value	
Business rules	**Value Allowed:** Yes **Relationship:** n/a **Concept:** n/a
Duplicate field in other sections	

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Term (Variable)	Sponsor Responsibilities
Data Type	Text
Topic, Value or Header	H
Definition	
User Guidance	List the prevailing ethical, legal, and regulatory guidelines that will be applied throughout the trial. This trial will be conducted in accordance with the protocol and with the following: • Consensus ethical principles derived from international guidelines including the Declaration of Helsinki and Council for International Organizations of Medical Sciences (CIOMS) International Ethical Guidelines • ICH Good Clinical Practice (GCP) Guidelines • Applicable laws and regulations • {insert additional as needed} List the investigators' and sponsor's responsibilities in this regard. **Sponsor Responsibilities** [Sponsor Responsibilities]
Conformance	Required
Cardinality	
Relationship content from ToC representing the protocol hierarchy	General Considerations: Regulatory, Ethical, and Trial Oversight Considerations / Regulatory and Ethical Considerations
Relationship (reference to high level conceptual model)	
Value	Sponsor Responsibilities
Business rules	**Value Allowed:** Yes **Relationship:** n/a **Concept:** n/a
Duplicate field in other sections	

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Term (Variable)	Sponsor Responsibilities
Data Type	Text
Topic, Value or Header	D
Definition	
User Guidance	List the prevailing ethical, legal, and regulatory guidelines that will be applied throughout the trial. This trial will be conducted in accordance with the protocol and with the following: • Consensus ethical principles derived from international guidelines including the Declaration of Helsinki and Council for International Organizations of Medical Sciences (CIOMS) International Ethical Guidelines • ICH Good Clinical Practice (GCP) Guidelines • Applicable laws and regulations • {insert additional as needed} List the investigators' and sponsor's responsibilities in this regard. **Sponsor Responsibilities** [Sponsor Responsibilities]
Conformance	Required
Cardinality	
Relationship content from ToC representing the protocol hierarchy	General Considerations: Regulatory, Ethical, and Trial Oversight Considerations / Regulatory and Ethical Considerations
Relationship (reference to high level conceptual model)	
Value	
Business rules	**Value Allowed:** Yes **Relationship:** n/a **Concept:** n/a
Duplicate field in other sections	

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10.2 Committees

Term (Variable)	Committees
Data Type	Text
Topic, Value or Header	H
Definition	
User Guidance	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. [Committees Structure]
Conformance	Required
Cardinality	
Relationship content from ToC representing the protocol hierarchy	General Considerations: Regulatory, Ethical, and Trial Oversight Considerations / Committees Structure
Relationship (reference to high level conceptual model)	
Value	Committees
Business rules	**Value Allowed:** n/a **Relationship:** n/a **Concept:** n/a Specific details are not required
Duplicate field in other sections	

Term (Variable)	Committees Structure
Data Type	Text
Topic, Value or Header	D
Definition	
User Guidance	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. [Committees Structure]
Conformance	Required/Repeated
Cardinality	
Relationship content from ToC representing the protocol hierarchy	General Considerations: Regulatory, Ethical, and Trial Oversight Considerations / Committees Structure
Relationship (reference to high level conceptual model)	
Value	
Business rules	**Value Allowed:** Yes **Relationship**: n/a **Concept**: n/a Specific details are not required
Duplicate field in other sections	For each committee

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10.3 Informed Consent Process

Term (Variable)	Informed Consent Process
Data Type	Text
Topic, Value or Header	H
Definition	Section Heading
User Guidance	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). **[Informed Consent Process]** 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. **[Emergency Consent Process]** 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. **[Consent Requirements for Rescreening]** 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. **[Additional ICF text for Use of Remaining Samples in Optional Exploratory Research]**
Conformance	Required
Cardinality	
Relationship content from ToC representing the protocol hierarchy	General Considerations: Regulatory, Ethical, and Trial Oversight Considerations / Informed Consent Process
Relationship (reference to high level conceptual model)	
Value	Informed Consent Process
Business rules	**Value Allowed:** n/a **Relationship:** n/a **Concept:** n/a
Duplicate field in other sections	

Term (Variable)	Informed Consent Process
Data Type	Text
Topic, Value or Header	D
Definition	
User Guidance	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). **[Informed Consent Process]-Required/Required** 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. **[Emergency Consent Process]-Required/Required** **[Rescreening]-Required/Required** **Value-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. **[Consent Requirements for Rescreening]Required/Required** 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. **[Additional ICF text for Use of Remaining Samples in Optional Exploratory Research]**
Conformance	Required
Cardinality	
Relationship content from ToC representing the protocol hierarchy	General Considerations: Regulatory, Ethical, and Trial Oversight Considerations / Informed Consent Process
Relationship (reference to high level conceptual model)	
Value	
Business rules	**Value Allowed:** yes **Relationship:** n/a **Concept:** n/a Note: This field can contain a text value
Duplicate field in other sections	

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10.4 Data Protection

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

10.5 Early Site Closure or Trial Termination

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

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

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

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

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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	**Value Allowed:** Yes **Relationship:** n/a **Concept:** n/a
Duplicate field in other sections	

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	**Value Allowed:** Yes **Relationship:** n/a **Concept:** n/a
Duplicate field in other sections	

Term (Variable)	Quality Tolerance Limits
Data Type	Text
Topic, Value or Header	D
Definition	
User Guidance	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. **[QTL]**
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	
Business rules	**Value Allowed:** n/a **Relationship:** n/a **Concept:** n/a Note: This field can contain a text value
Duplicate field in other sections	

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11.2 Data Quality Assurance

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

Term (Variable)	Data Quality Assurance
Data Type	Text
Topic, Value or Header	H
Definition	
User Guidance	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]
Conformance	Required
Cardinality	
Relationship content from ToC representing the protocol hierarchy	General Considerations: Risk Management and Quality Assurance /Data Quality Assurance
Relationship (reference to high level conceptual model)	
Value	Data Quality Assurance
Business rules	**Value Allowed**: n/a **Relationship**: n/a **Concept**: n/a Note: This field can contain a text value
Duplicate field in other sections	

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Term (Variable)	Data Quality Assurance
Data Type	Text
Topic, Value or Header	D
Definition	
User Guidance	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]**
Conformance	Required
Cardinality	
Relationship content from ToC representing the protocol hierarchy	General Considerations: Risk Management and Quality Assurance /Data Quality Assurance
Relationship (reference to high level conceptual model)	
Value	
Business rules	**Value Allowed:** n/a **Relationship:** n/a **Concept:** n/a Note: This field can contain a text value
Duplicate field in other sections	

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11.3 Source Data

Term (Variable)	Source Data
Data Type	Text
Topic, Value or Header	H
Definition	Section Heading
User Guidance	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). **[Source Data Introduction]- Required/Required** **[Investigator Expectations for Source Data]- Required/Required** **[Trial Monitor Expectations for Source Data]- Required/Required** **[Definition of Source Data]- Required/Required**
Conformance	Required
Cardinality	
Relationship content from ToC representing the protocol hierarchy	General Considerations: Risk Management and Quality Assurance /Source Data
Relationship (reference to high level conceptual model)	
Value	Source Data
Business rules	**Value Allowed:** Yes **Relationship:** n/a **Concept:** n/a
Duplicate field in other sections	

Term (Variable)	Source Data Introduction
Data Type	Text
Topic, Value or Header	D
Definition	Procedures for the identification of data to be recorded directly on the CRF considered as source data.
User Guidance	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). **[Source Data Introduction]- Required/Required** **[Investigator Expectations for Source Data]- Required/Required** **[Trial Monitor Expectations for Source Data]- Required/Required** **[Definition of Source Data]- Required/Required**
Conformance	Required
Cardinality	
Relationship content from ToC representing the protocol hierarchy	General Considerations: Risk Management and Quality Assurance /Source Data
Relationship (reference to high level conceptual model)	
Value	
Business rules	**Value Allowed:** n/a **Relationship:** n/a **Concept:** n/a Note: This field can contain a text value
Duplicate field in other sections	

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Term (Variable)	Investigator Expectations for Source Data
Data Type	Text
Topic, Value or Header	D
Definition	Procedures for the identification of data to be recorded directly on the CRF considered as source data.
User Guidance	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). **[Source Data Introduction]- Required/Required** **[Investigator Expectations for Source Data]- Required/Required** **[Trial Monitor Expectations for Source Data]- Required/Required** **[Definition of Source Data]- Required/Required**
Conformance	Required
Cardinality	
Relationship content from ToC representing the protocol hierarchy	General Considerations: Risk Management and Quality Assurance /Source Data
Relationship (reference to high level conceptual model)	
Value	
Business rules	**Value Allowed:** n/a **Relationship:** n/a **Concept:** n/a Note: This field can contain a text value
Duplicate field in other sections	

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Term (Variable)	Trial Monitor Expectations for Source Data
Data Type	Text
Topic, Value or Header	D
Definition	Procedures for the identification of data to be recorded directly on the CRF considered as source data.
User Guidance	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). **[Source Data Introduction]- Required/Required** **[Investigator Expectations for Source Data]- Required/Required** **[Trial Monitor Expectations for Source Data]- Required/Required** **[Definition of Source Data]- Required/Required**
Conformance	Required
Cardinality	
Relationship content from ToC representing the protocol hierarchy	General Considerations: Risk Management and Quality Assurance /Source Data
Relationship (reference to high level conceptual model)	
Value	
Business rules	**Value Allowed:** n/a **Relationship:** n/a **Concept:** n/a Note: This field can contain a text value
Duplicate field in other sections	

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Term (Variable)	Definition of Source Data
Data Type	Text
Topic, Value or Header	D
Definition	Procedures for the identification of data to be recorded directly on the CRF considered as source data.
User Guidance	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). **[Source Data Introduction]- Required** **[Investigator Expectations for Source Data]- Required** **[Trial Monitor Expectations for Source Data]- Required** **[Definition of Source Data]- Required**
Conformance	Required
Cardinality	
Relationship content from ToC representing the protocol hierarchy	General Considerations: Risk Management and Quality Assurance /Source Data
Relationship (reference to high level conceptual model)	
Value	
Business rules	**Value Allowed:** n/a **Relationship:** n/a **Concept:** n/a Note: This field can contain a text value
Duplicate field in other sections	

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

Term (Variable)	Appendix / Appendix 12 Adverse Events and Serious Adverse Events-Definitions, Severity, and Causality
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 / Appendix 12 Adverse Events and Serious Adverse Events-Definitions, Severity, and Causality
Relationship (reference to high level conceptual model)	
Value	Appendix / Appendix 12 Adverse Events and Serious Adverse Events-Definitions, Severity, and Causality
Business rules	**Value Allowed:** Yes **Relationship:** n/a **Concept:** n/a
Duplicate field in other sections	

12.1 Further Details and Clarifications on the AE Definition

Term (Variable)	Further Details and Clarifications on the AE Definition
Data Type	Text
Topic, Value or Header	H
Definition	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).
User Guidance	Specify: • 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. • Any relevant regional requirements. • Events that meet and do not meet the AE definition. • Any trial-specific clarifications.
Conformance	Required
Cardinality	
Relationship content from ToC representing the protocol hierarchy	Appendix / Appendix 12 Adverse Events and Serious Adverse Events-Definitions, Severity, and Causality/Definition of Adverse Event
Relationship (reference to high level conceptual model)	
Value	Further Details and Clarifications on the AE Definition
Business rules	**Value Allowed**: Yes **Relationship**: n/a **Concept**: n/a
Duplicate field in other sections	

Term (Variable)	Further Details and Clarifications on the AE Definition
Data Type	Text
Topic, Value or Header	D
Definition	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).
User Guidance	Specify: • 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. • Any relevant regional requirements. • Events that meet and do not meet the AE definition. • Any trial-specific clarifications.
Conformance	Required
Cardinality	
Relationship content from ToC representing the protocol hierarchy	Appendix / Appendix 12 Adverse Events and Serious Adverse Events-Definitions, Severity, and Causality/Definition of Adverse Event
Relationship (reference to high level conceptual model)	
Value	
Business rules	**Value Allowed**: Yes **Relationship**: n/a **Concept**: n/a
Duplicate field in other sections	

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12.2 Further Details and Clarifications on the SAE Definition

Term (Variable)	Further Details and Clarifications on the SAE Definition
Data Type	Text
Topic, Value or Header	H
Definition	Section heading
User Guidance	Specify: • The SAE definition. The standard definition is in ICH E2A. • Any relevant regional requirements. • Events that meet and do not meet the SAE definition. • Any trial-specific clarifications. **[Further Details and Clarifications on the SAE Definition]**
Conformance	Required
Cardinality	
Relationship content from ToC representing the protocol hierarchy	Appendix / Appendix 12 Adverse Events and Serious Adverse Events-Definitions, Severity, and Causality/Further Details and Clarifications on the SAE Definition
Relationship (reference to high level conceptual model)	
Value	Further Details and Clarifications on the SAE Definition
Business rules	**Value Allowed:** Yes **Relationship:** n/a **Concept:** n/a
Duplicate field in other sections	

Term (Variable)	Further Details and Clarifications on the SAE Definition
Data Type	Text
Topic, Value or Header	D
Definition	A SAE is any untoward medical occurrence that, at any dose: a. Results in death b. Is life-threatening c. Requires hospitalisation or prolongation of existing hospitalisation d. Results in persistent disability or incapacity e. Is a congenital anomaly or birth defect f. 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.
User Guidance	Specify: • The SAE definition. The standard definition is in ICH E2A. • Any relevant regional requirements. • Events that meet and do not meet the SAE definition. • Any trial-specific clarifications. **[Further Details and Clarifications on the SAE Definition]**
Conformance	Required
Cardinality	
Relationship content from ToC representing the protocol hierarchy	Appendix / Appendix 12 Adverse Events and Serious Adverse Events-Definitions, Severity, and Causality/Further Details and Clarifications on the SAE Definition
Relationship (reference to high level conceptual model)	

Value	A SAE is any untoward medical occurrence that, at any dose: • Results in death • Is life-threatening a. Requires hospitalisation or prolongation of existing hospitalisation b. Results in persistent disability or incapacity c. Is a congenital anomaly or birth defect 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. 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. Clarifications of the SAE definition: 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. 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. 3) Hospitalisation for elective treatment of a pre-existing condition that did not worsen from baseline is not an AE. 4) Disability is a substantial or significant disruption of a person's ability to conduct normal life functions. 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
Business rules	**Value Allowed:** n/a **Relationship:** n/a **Concept:** n/a
Duplicate field in other sections	

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12.3 Severity

Term (Variable)	Severity
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 / Appendix 12 Adverse Events and Serious Adverse Events-Definitions, Severity, and Causality/Severity
Relationship (reference to high level conceptual model)	
Value	Severity
Business rules	**Value Allowed:** Yes **Relationship:** n/a **Concept:** n/a
Duplicate field in other sections	

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

12.4 Causality

Term (Variable)	Causality
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 / Appendix 12 Adverse Events and Serious Adverse Events-Definitions, Severity, and Causality/Severity
Relationship (reference to high level conceptual model)	
Value	Causality
Business rules	**Value Allowed:** Yes **Relationship:** n/a **Concept:** n/a
Duplicate field in other sections	

Term (Variable)	Causality
Data Type	Text
Topic, Value or Header	D
Definition	Defines the relationship of an AE to a trial intervention
User Guidance	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. **[Causality]**
Conformance	Required
Cardinality	
Relationship content from ToC representing the protocol hierarchy	Appendix / Appendix 12 Adverse Events and Serious Adverse Events-Definitions, Severity, and Causality/Severity
Relationship (reference to high level conceptual model)	
Value	
Business rules	**Value Allowed:** n/a **Relationship:** n/a **Concept:** n/a
Duplicate field in other sections	

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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	**Value Allowed:** n/a **Relationship:** n/a **Concept:** n/a
Duplicate field in other sections	

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	**Value Allowed:** Yes **Relationship:** n/a **Concept:** n/a
Duplicate field in other sections	

13.1.1 Definitions Related to Childbearing Potential

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

13.1.2 Contraception

Term (Variable)	Contraception
Data Type	Text
Topic, Value or Header	H
Definition	
User Guidance	Optional section to specify the: • Contraceptive methods required • Duration of use **[Contraception]**
Conformance	Required
Cardinality	
Relationship content from ToC representing the protocol hierarchy	Appendix 13: Definitions and Supporting Operational Details/ Contraception and Pregnancy Testing/Contraception
Relationship (reference to high level conceptual model)	
Value	Contraception
Business rules	**Value Allowed:** Yes **Relationship:** n/a **Concept:** n/a
Duplicate field in other sections	

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

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13.1.3 Pregnancy Testing

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

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

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13.2 Clinical Laboratory Tests

Term (Variable)	Clinical Laboratory Tests
Data Type	Text
Topic, Value or Header	H
Definition	Section Heading
User Guidance	Provide additional information, if needed, about clinical laboratory tests, such as • whether they will be performed by a central or local laboratory (if important to distinguish) • specific analytes or parameters included in a panel • equations and references for locally calculated labs • acceptability of additional tests deemed necessary by the Investigator or local regulations • instructions for situations in which central laboratory results are not available in time for trial intervention and/or response evaluation, or in the event of a severe disruption (for example, a pandemic or natural disaster) • treatment algorithms for results out of normal range. A tabular presentation for such information is common. **[Clinical Laboratory Tests]**
Conformance	Required
Cardinality	
Relationship content from ToC representing the protocol hierarchy	Appendix: Definitions and Supporting Operational Details/Clinical Laboratory Tests
Relationship (reference to high level conceptual model)	
Value	Clinical Laboratory Tests
Business rules	**Value Allowed:** Yes **Relationship:** n/a **Concept:** n/a
Duplicate field in other sections	Repeat for lab values

Term (Variable)	Clinical Laboratory Tests
Data Type	Text
Topic, Value or Header	D
Definition	
User Guidance	Provide additional information, if needed, about clinical laboratory tests, such as • whether they will be performed by a central or local laboratory (if important to distinguish) • specific analytes or parameters included in a panel • equations and references for locally calculated labs • acceptability of additional tests deemed necessary by the Investigator or local regulations • instructions for situations in which central laboratory results are not available in time for trial intervention and/or response evaluation, or in the event of a severe disruption (for example, a pandemic or natural disaster) • treatment algorithms for results out of normal range. A tabular presentation for such information is common. **[Clinical Laboratory Tests]**
Conformance	Required/Repeatable (for lab values)
Cardinality	
Relationship content from ToC representing the protocol hierarchy	Appendix: Definitions and Supporting Operational Details/Clinical Laboratory Test
Relationship (reference to high level conceptual model)	
Value	
Business rules	**Value Allowed:** n/a **Relationship:** n/a **Concept:** n/a
Duplicate field in other sections	

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13.3 Country/Region-Specific Differences

Term (Variable)	Country-Specific Differences
Data Type	Text
Topic, Value or Header	H
Definition	
User Guidance	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). 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. **[Country-specific Differences]**
Conformance	Required
Cardinality	
Relationship content from ToC representing the protocol hierarchy	Appendix: Definitions and Supporting Operational Details/Country-Specific Differences
Relationship (reference to high level conceptual model)	
Value	Country-Specific Differences
Business rules	**Value Allowed:** Yes **Relationship:** 0 to many **Concept:** n/a
Duplicate field in other sections	

Term (Variable)	Country
Data Type	Text
Topic, Value or Header	H
Definition	
User Guidance	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). 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. **[Country]**
Conformance	Required/Repeatable
Cardinality	
Relationship content from ToC representing the protocol hierarchy	Appendix: Definitions and Supporting Operational Details/Country-Specific Differences/Country
Relationship (reference to high level conceptual model)	
Value	Country
Business rules	**Value Allowed:** n/a **Relationship:** 0 to many **Concept:** n/a
Duplicate field in other sections	

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Term (Variable)	Header of Protocol Section to be Changed for the Country
Data Type	Text
Topic, Value or Header	H
Definition	
User Guidance	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). 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. **[Header of Protocol Section to be Changed for the Country]**
Conformance	Required/Repeatable
Cardinality	
Relationship content from ToC representing the protocol hierarchy	Appendix: Definitions and Supporting Operational Details/Country-Specific Differences/Country/Header of Protocol Section to be Changed for the Country
Relationship (reference to high level conceptual model)	
Value	Header of Protocol Section to be Changed for the Country
Business rules	**Value Allowed:** n/a **Relationship:** 0 to many **Concept:** n/a
Duplicate field in other sections	

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Term (Variable)	[Change-depends on Section]
Data Type	Text
Topic, Value or Header	D
Definition	
User Guidance	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). 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. **[Header of Protocol Section to be Changed for the Country]**
Conformance	Optional (follows original section)
Cardinality	
Relationship content from ToC representing the protocol hierarchy	Appendix: Definitions and Supporting Operational Details/Country-Specific Differences/Country/Header of Protocol Section to be Changed for the Country
Relationship (reference to high level conceptual model)	
Value	
Business rules	**Value Allowed:** n/a **Relationship:** 0 to many **Concept:** n/a
Duplicate field in other sections	

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13.4 Prior Protocol Amendments

Term (Variable)	Prior Protocol Amendments
Data Type	Text
Topic, Value or Header	H
Definition	
User Guidance	Choose the appropriate text. {This protocol has not been amended.} or {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}. 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). **Amendment {amendment number}: ({date})** **{Amendment details from this amendment}** **Add additional amendments/details as protocol amendments accrue.** **Amendment {amendment number}: ({date})** **{Amendment details from this amendment}**
Conformance	Required
Cardinality	
Relationship content from ToC representing the protocol hierarchy	Appendix: Definitions and Supporting Operational Details/Prior Protocol Amendments
Relationship (reference to high level conceptual model)	
Value	Prior Protocol Amendments
Business rules	**Value Allowed:** Yes **Relationship:** 0 to many **Concept:** n/a
Duplicate field in other sections	

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

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

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