ICH M11 : A Critical Enabler for Clinical Trial Transformation

PHUSE CSS – 21 May 2025

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European Medicines Agency

Disclaimer and Acknowledgements

Disclaimer

The views expressed here are my personal views, and may not be understood or quoted as being made on behalf of the EMA or its scientific committees, or reflecting the position of the EMA

Acknowledgements

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M11 EWG

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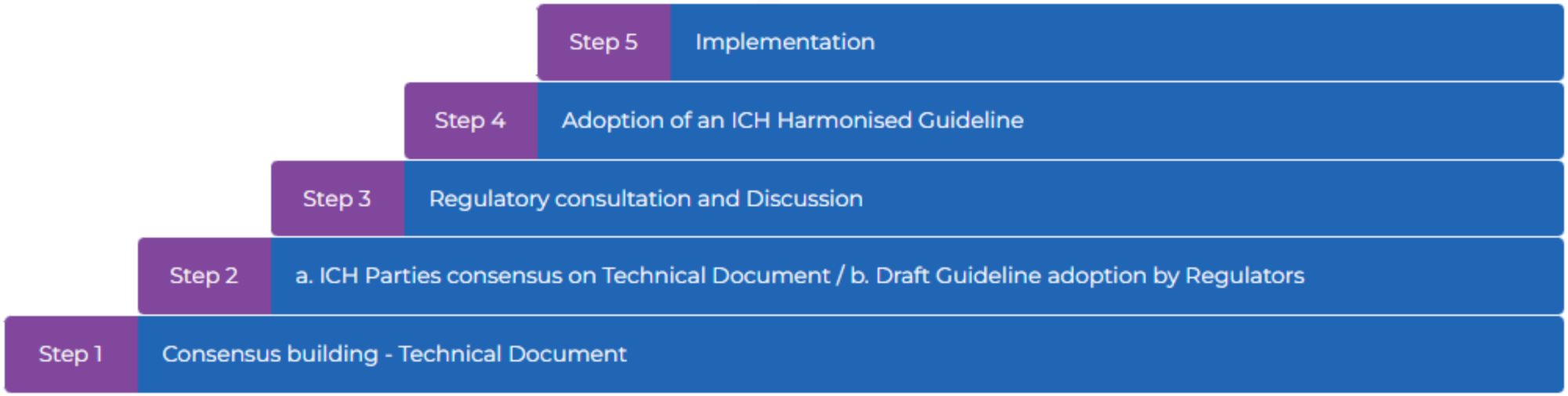
- ICH M11 Status
- ICH M11 as an enabler for clinical trial transformation

Formal ICH Procedure

- Nov 2018: Endorsement of concept paper & business plan by ICH management committee
- Sep 2022: Step 2b reached. Release for public consultation.
- Now: Step 3 ongoing. 2300 public comments were received in 2023 (400 related to statistics). Revision of documents in 2023/2024. Tech Specs currently open for public consultation.
- **Finalisation of Step 3 expected for Autumn 2025 with step 4 adoption of the guideline**
- **Step 5 Implementation by the ICH regulators**



Source: https://www.ich.org/page/formal-ich-procedure

M11 : what are the deliverables?

Guideline

Provides background, purpose, and scope as a guideline


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

ICH HARMONISED GUIDELINE

CLINICAL ELECTRONIC STRUCTURED HARMONISED PROTOCOL

(CESHARP)

M11

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.

Template

Provides written format for the Interventional Clinical Trial Protocol Template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M11 TEMPLATE

Draft version

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Technical Specifications

Provides technical representation aligned with the guideline and template


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M11 TECHNICAL SPECIFICATION

Draft version

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Guideline

- Explains the need, outlines development

Template

- Specifies headers, common text, instructions, data fields, and terminologies.

Technical Specification

- open, nonproprietary standard to enable electronic exchange of clinical protocol information

Why Clinical electronic Structured Harmonised Protocol (CeSHarP)?

Protocols

- Important document that describes the processes and procedures directing the conduct and analysis of a clinical study
- **Format and core content** of study protocols vary from sponsor to sponsor, making interpretation difficult for its users (Medical Writers, monitors, Study Sites, Regulators, ethicists…)
- Regulators receive protocols in many different formats
- In the EU, since 31 January 2022, a total of **11,081*** initial clinical trial applications, **14,210*** Substantial Modifications affecting 5,278 trials have been submitted

*Status 31 March 2025

Problem

- No internationally harmonized standard template for the format and content to support **consistency** across sponsors and **exchange of protocol information.**
- Lack of harmonisation contributes to **inefficiencies** and **difficulties** in reviewing and assessing clinical protocols by regulators, sponsors, ethical oversight bodies, investigators, and other stakeholders.

Benefits of a structured, harmonized document

- Some advantages…
  - Efficient searching of information
  - Searchable content and metadata
  - Machine-readable
  - Content reuse
  - Makes information easily accessible for years to come

European Commission's new Datacentre in Luxembourg

Regulators receiving documents…

Chemist Lee Geismer looking over an NDA in the 1960s. Source: https://www.fda.gov/about-fda/histories-fda-regulated-products/summary-nda-approvals-receipts-1938-present

The ICH M11 initiative : an enabler

Reinforcing efficiency of planning, evaluation, conduct, and supervision of clinical trials with:

- Integration with the Single **e-submission** via the Clinical Trial Information System (CTIS)
- **Coordinated assessment** between Member States Concerned facilitating decision making
- **Interoperability** with other systems and processes
- High **transparency** of clinical trials information
- Consistency amongst ICH regulators once implemented

ICH harmonisation for better health

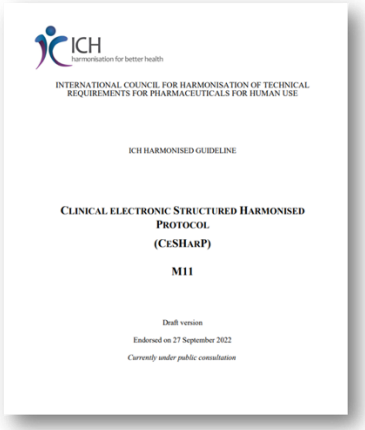
cdisc

Home / Standards / Terminology / Controlled Terminology

Controlled Terminology

M11 Template can be exchanged using many formats

Guideline & Template → **Tech Spec** → **Technical Implementation Guide** → **FHIR Profiles**


ICH harmonisation for better health

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

ICH HARMONISED GUIDELINE

CLINICAL ELECTRONIC STRUCTURED HARMONISED PROTOCOL
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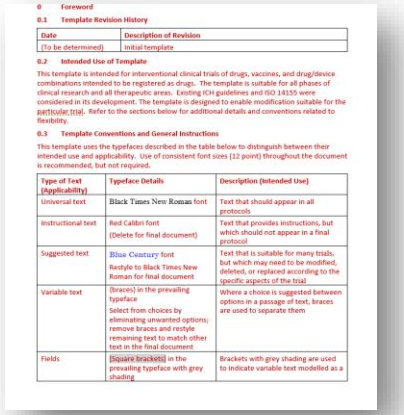

0 Foreword

0.1 Template Revision History

Date	Description of Revision
(To be determined)	Initial template

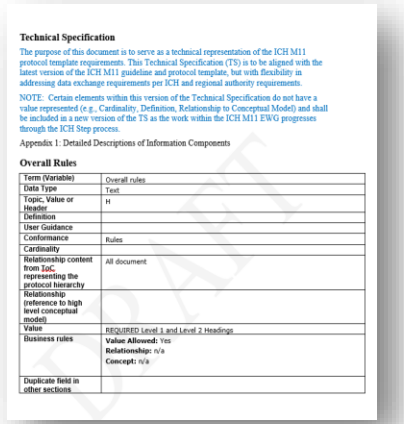
0.2 Intended Use of Template

This template is intended for interventional clinical trials of drugs, vaccines, and drug/device combinations intended to be registered as drugs. The template is suitable for all phases of clinical research and all therapeutic areas. Existing ICH guidelines and ISO 14155 were considered in its development. The template is designed to enable modification suitable for the particular trial. Refer to the sections below for additional details and conventions related to flexibility.

0.3 Template Conventions and General Instructions

This template uses the typefaces described in the table below to distinguish between their intended use and applicability. Use of consistent font sizes (12 point) throughout the document is recommended, but not required.

Type of Text (Applicability)	Typeface Details	Description (Intended Use)
Universal text	Black Times New Roman font	Text that should appear in all protocols
Instructional text	Red Calibri font (Delete for final document)	Text that provides instructions, but which should not appear in a final protocol
Suggested text	Blue Century font Restyle to Black Times New Roman for final document	Text that is suitable for many trials, but which may need to be modified, deleted, or replaced according to the specific aspects of the trial
Variable text	[braces] in the prevailing typeface Select from choices by eliminating unwanted options; remove braces and restyle remaining text to match other text in the final document	Where a choice is suggested between options in a passage of text, braces are used to separate them
Fields	[Square brackets] in the prevailing typeface with grey shading	Brackets with grey shading are used to indicate variable text modelled as a


Technical Specification

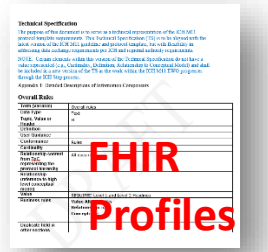
The purpose of this document is to serve as a technical representation of the ICH M11 protocol template requirements. This Technical Specification (TS) is to be aligned with the latest version of the ICH M11 guideline and protocol template, but with flexibility in addressing data exchange requirements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

NOTE: Certain elements within this version of the Technical Specification do not have a value represented (e.g., Cardinality, Definition, Relationship to Conceptual Model) and shall be included in a new version of the TS as the work within the ICH 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 IoC 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	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FHIR Profiles

Regulators implementation (ICH Step 5)

Standard Message Exchange Formats*

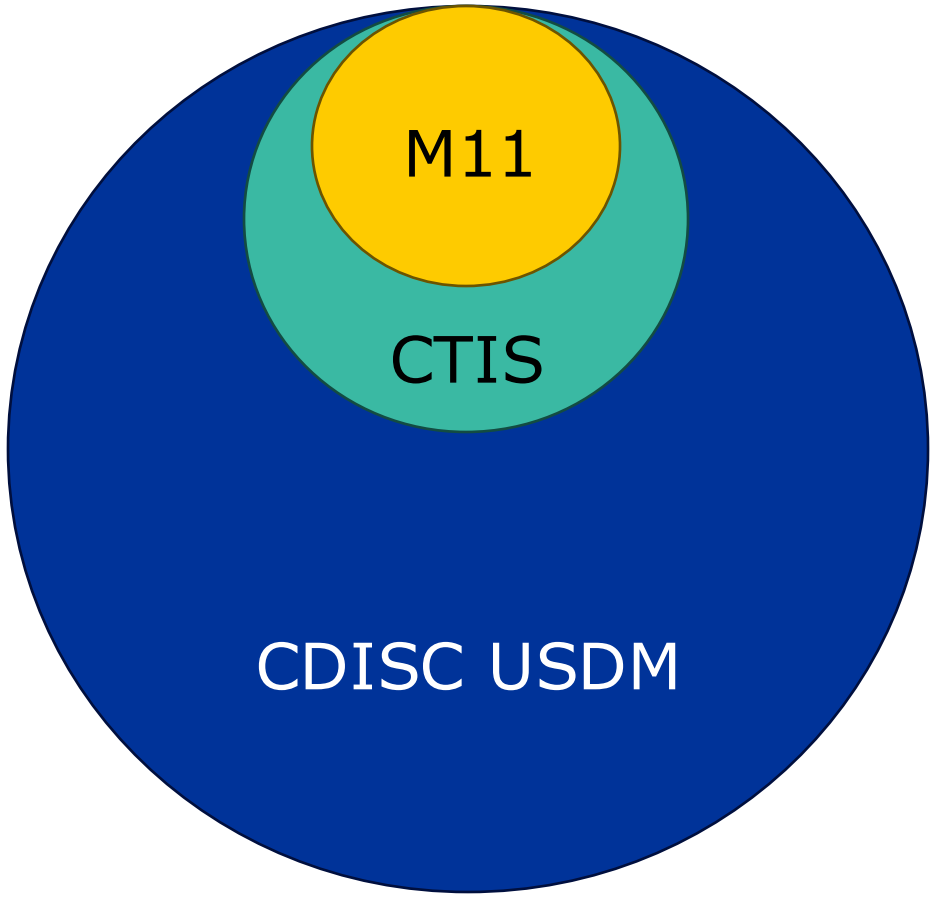
Per ICH Regional Requirements

Machine - Readable Form

PDF · Docx · XML · {JSON} · VULCAN HL7 FHIR · cdisc

*** Technical Implementation Guides may be needed for various use cases**

Link Between M11, CTIS Data and USDM*



- Areas to be aligned
  - Data elements
  - Definitions
  - Code lists
- EU CTIS has data requirements in addition to M11
- CDISC USDM accommodates the M11 elements and their semantics and create an ICH M11 model specific view
- In the future structured study results

*Unified Study Definition Model (USDM), is a Class diagram that functions as the Study Definitions Logical Data Model (LDM).

Clinical Trial Protocols

The structured data defined by ICH M11 provides key metadata and helps start the process of standardizing data format

Clinical Trial Raw data

Individual Patient Data (IPD)/raw data are collected from sites.
IPD enable detailed analysis.

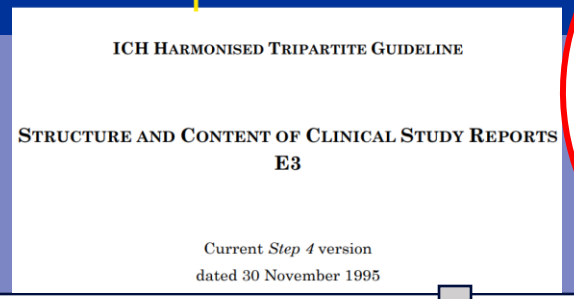
data collection & Analysis

Study Reporting

Summary Results (SR)

Aggregate data:
Summary results data combine individual data points into an overall summary

Clinical Study Report (CSR)


ICH HARMONISED TRIPARTITE GUIDELINE

STRUCTURE AND CONTENT OF CLINICAL STUDY REPORTS
E3

Current *Step 4* version
dated 30 November 1995

M11 to enhance data submission with ICH standardisation

CTA submission **SR submission** **CSR submission**

CTIS Submissions

Take-home messages

- M11 will provide a new structure for protocols (truly electronic and in terms of content)
- Standardisation is essential for structuring and for visualisation
- Efficiency gains through harmonization

Next steps:

- ICH Sign-off Step 3 and step 4 in Q4 2025 with regulatory implementation in step 5
- Supporting modernisation effort for sponsors with planning data exchange mechanism to CTIS
- Structure of summary results for clinical trials

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Thank you

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