TriTiCon

Clinical Standards Overview

About this document

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1 Introduction

Clinical Standards are much more than CDSIC data standards for data managers and programmers. There are for example standards/best practices for which data to collect, how to collect it, how to report it, and for how documents are filed in the Trial Master file.

Historically standards have been seen as a method for ensuring that things are done in the same way all the time, and as such as a somewhat rigid approach imposing constraints to how the individual trials are done. However, today's standards are - in fact -flexible. This might sound contradictory, but most standards consist of a framework and best practices, allowing the *content* to be flexible to the specific trial needs.

Standards in itself do not have any value, but it is an excellent tool or methodology for driving a number of important objectives/benefits, such as:

Quality –As tested, proven and known best practices, standards drive quality of your trial conduct and your data.

Efficiency – Use established and existing components, and re-use what has been done before instead of re-do what has already been done or developed. Saves work and money and frees up time for more important challenges.

Flexibility – using standards, gives flexibility in use of vendors and resources, because what you have is familiar and known from the start, and do not depend on someone knowing the specific knowledge on your data-structure or way of documenting.

Compliance – There are regulatory expectations, both on how things is done (for example AE/SAE handling) and how data and documents are reported and submitted (for example CDISC SDTM and associated define-xml-file).

Phone +45 52 19 31 99 |Mail: info@triticom.com

TriTiCon | Sandvejen 30 | DK 2665, Vallensbæk Strand | Denmark

2 Clinical Standard Areas

The most common standardization areas related to clinical data and documents are listed below. Many more areas can of course be standardized, and many requirements or common practices can be seen as a standard, but we consider the ones below as the most important and most widely used in relation to clinical data and documents.

Area	Description
Industry standard instruments – standards for which data to collect.	Standards for which data to collect regarding a certain topic. Including for example validated instruments for HEOR/QoL, therapeutic area practice standards such as RECIST on oncology or Bristol Stool Scale in IBS. These are more strategic standards, important to consider early in your clinical development plan, to support endpoints, filing approval, claims and re-imbursement.
CRF-standards – standards for how to collect the data.	CDISC CDASH for best practice CRF pages, consistency with SDTM. Further, CDISC TAUGs (Therapeutic Area User Guides) are more comprehensive and detailed standards for different areas like diabetes, vaccines oncology etc. These are in constant development and thereby differently established, but worth considering.
Trial Data Standards: Data Structure and Format Standards Standards for documentation of data structure	<u>Data Structure and Format Standards</u> SDTM Data (CDISC)* – Standard for the collected data. As a starting point "raw" and underived data. ADaM Data (CDISC)* – Analysis data, with derived data and used for analysis and output tables, figures and listings. <u>Standards for documentation of data structure</u> Define.xml-file (CDISC)* - Xml-files in very specific format, defining how the SDTM and ADaM data is structured, how derivations are done etc. Annotated & blank CRFs* – Blank CRF documenting the users view when recording the data, and annotated CRF linking the collection view to the resulting SDTM data-structure. Reviewers Guide (cSDRG)* – Readme file with key comments about the data. These can be known issues in the data or comments on how the data is derived and structured, in order for a reviewer to understand the data correctly and efficiently. Expected as part of submission, but also useful for other future understanding and use of the data. * Part of FDA expected submission package. I.e. you are expected to submit your data in this structure/format and with this documentation. There are specific rules for format, bookmarking etc.

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Operational Data Standards	Operational data – such as status and quality data, for example CRF page status, query status and other "operational" aspects such as site status etc. - is not yet very standardized, but increasingly relevant to consider as it both helps you manage your trial and is a key element of data-driven risk-based monitoring. Note that some areas like protocol deviations and drug accountability, which can be seen as operational aspects are also part of the SDTM data structure and can be expected for submission. Thereby the SDTM structure might influence how you handle them operationally and which data you need to collect. See also meta-data below.
Meta data Standards	User-stamps, date/time stamps, audit-records, CRF version tags etc. can be labelled as "meta-data". As for operational data (the areas are partly overlapping), the practical implementation of standards in this field is currently limited, but the area is increasingly used for KPIs, KQIs and RBM. However, the CDISC ODM standard defines a general (and rather technical) framework for how this data can be structured.
Safety Data Standards	The E2B data standard for reporting (S)AE data to EMA and FDA, and other safety reporting requirements for periodic reporting etc. indirectly drives which data that need to be collected for (S)AEs. Note that especially E2B requirements are quite specific on which data items that are to be submitted, and thereby collected, and which options (answer-alternatives) that should be used.
TMF – Document Index Standards	There are also standards for how to file documents in the trial master file. The DIA Reference index, defines a recommended folder ("section")-structure, which document to store where and provides guidance on which meta-data to use for the document. The index is not a requirement as such, but a strong recommendation and truly beneficial standard when the amount of documents and involved people rapidly grow. It is also a great way to prepare for submission from the beginning.
Submission documents standards	Requirements for submitted documents (primarily requirements for format (pdf) fonts, margins, bookmarks etc., can be viewed as a standard, and is important to consider from start.

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