STATISTICS IN REGULATORY AFFAIRS IN WWW.WIKIPEDIA.ORG: INITIATIVE OF THE ISCB STATISTICS IN REGULATORY AFFAIRS SUBCOMMITTEE (SIRA SC)

USER GUIDE

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on behalf of ISCB SiRA SC

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(1) JOIN THE INITIATIVE IN JUST TWO STEPS

STEP 1: SIGN UP IN WIKIPEDIA

➢ Open Wikipedia and create an account to be part of a community with more than 28 million of Wikipedians.

➢Use "**Create account**" tab on the top left hand side of any Wikipedia page.

STEP 2: BE BOLD AND START EDITING

➢ The above Wikipedia expression is widely used to encourage editing: https://en.wikipedia.org/wiki/Wikipedia:Be_bold

➢There are two main ways to contribute to the SiRA Wikipedia initiative by:

- adding references in the **Wikipedia List:** https://en.wikipedia.org/wiki/List_of_Guidances_for_Statistics_in_Regulatory_Affairs

- creating articles related to regulatory guidances on the **Wikipedia Article:** https://en.wikipedia.org/wiki/Guidances_for_statistics_in_regulatory_affairs

(2) WIKIPEDIA "ARTICLE" ON "GUIDANCES FOR STATISTICS IN REGULATORY AFFAIRS"

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Guidances for statistics in regulatory affairs

From Wikipedia, the free encyclopedia

Guidances for statistics in regulatory affairs are applicable to the pharmaceutical industry and medical devices industry. These Guidances represent the current thinking of regulatory agencies on a particular subject. It is to be noted that the term "Guidances" is used in the USA, whereas the term "Guidelines" is used in Europe.

Regulatory affairs, also called government affairs, is a profession within regulated industries, such as pharmaceutical and medical devices, where professionals such as statisticians have the responsibility to comply with the regulatory guidance. Statisticians working in a regulated environment (e.g. the pharmaceutical and healthcare industry) are obliged to have a sound knowledge and understanding of the regulatory requirements that affect the design, conduct, analysis and reporting of their studies.[1]

Regulatory guidance for the pharmaceutical and medical devices industry can be found at the international level (e.g. ICH - International Council on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use), as well as at the regional/national level; for example:

- EMA - European Medicines Agency in Europe,
- MHRA - Medicines and Healthcare products Regulatory Agency in UK,
- IQWiG - Institute for Quality and Efficiency in Health Care in Germany,
- FDA - Food and Drug Administration in USA and
- PMDA - Pharmaceuticals and Medical Devices Agency in Japan.

Furthermore, statistical regulatory guidance is found under general topics (e.g. Good Clinical Practice - ICH E6(R2)[2]) and specific ones explicitly related to statistics (e.g. Statistical Principles for Clinical Trials - ICH E9 [3]) or not explicitly (e.g. Special Populations: Geriatrics [ICH E7] [4] or Clinical Trial Endpoints in Oncology [FDA][5]). This large volume and diversity of documents and information sources is subject to regular revisions.

The Wikipedia List of Guidances for Statistics in Regulatory Affairs provides links to various guidances under different topics.

Contents [hide]
1 History
2 General Guidance
2.1 Good Clinical Practice
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4 References
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History [edit source]

The pharmaceutical and medical devices industry has been highly regulated following the tragedies from Thalidomide that was marketed in 1957, Germany, without adequate testing.[6] In the US, Elixir sulfanilamide already caused some regulatory initiative in the 1930s. The Thalidomide catastrophe tightened the regulatory pressure in the US in the 1960s as well. A large volume and variety of regulatory "guidances" were initially developed by the Food and Drug Administration (FDA) in the USA and "guidelines" by the European Medicines Agency (EMA) in Europe. Also, other regions of the world issued regulatory guidance, for example, Pharmaceuticals and Medical Devices Agency (PMDA) in Japan. In 1989 a plan for harmonization of guidance across Europe, Japan and the USA was started and the first meeting of International Council on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH) was held in 1990, Brussels.

Regarding applications in Health technology assessment (HTA) a number of national guidance papers are available from the local HTA organizations: the Institute for Quality and Efficiency in Health Care (IQWiG) in Germany, the National Institute for Health and Care Excellence (NICE) in UK , the Agency for Healthcare Research and Quality (AHRQ) in USA or the Canadian Agency for Drugs and Technologies in Health (CADTH) in Canada. In Europe, the European Network for Health Technology Assessment (EUnetHTA) was established in 2005 to create an effective and sustainable network for HTA to support collaboration between European HTA organizations. EUnetHTA Guidelines have been developed to help the assessors of evidence to process, analyse and interpret the data.

General Guidance [edit source]

General guidance covers statistical topics that relate to good clinical practice; study design, monitoring and reporting, and market authorization of medical products or medical devices.

Good Clinical Practice [edit source]

The good clinical practice (GCP) [7] is an international ethical and scientific quality standard for designing, conducting, recording and reporting trials that involve the participation of human subjects. It was issued by ICH under Good Clinical Practice Directive (Directive 2005/28/EC) of 8 April 2005. A similar guideline for clinical trials of medical devices is the international standard ISO 14155, that is valid in the European Union as a harmonized standard. Compliance with the GCP standard provides public assurance that the rights, safety and well-being of trial subjects are protected, consistent with the principles that have their origin in the Declaration of Helsinki, and that the clinical trial data are credible.

See also [edit source]

- Clinical trials

(3) WIKIPEDIA "LIST OF GUIDANCES FOR STATISTICS IN REGULATORY AFFAIRS"

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List of Guidances for Statistics in Regulatory Affairs

From Wikipedia, the free encyclopedia

This List presents a comprehensive source of references for statistical guidance documents and related articles that are relevant to regulatory affairs for those statisticians that work on clinical studies. The List is associated with the Wikipedia page Guidances for statistics in regulatory affairs that aims to address the various topics of the listed guidances.

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1 References classified by statistical topic
1.1 Good clinical practice
1.2 Data monitoring committees
1.3 Adjustment by covariates
1.4 Small populations
1.5 Non-Inferiority
1.6 Subgroup analysis
1.7 Endpoints
1.8 Marketing authorization
1.9 Missing data
1.10 Multiplicity
1.11 Randomization
1.12 Reporting
1.13 Study design
1.14 Method Validation
2 References classified by special populations
2.1 Gender
2.2 Geriatrics
3 References classified by therapeutic area
3.1 Diabetes Mellitus
3.2 Oncology
4 References classified as country specific
5 See also
6 References
7 External links

References classified by statistical topic [edit source]

Good clinical practice [edit source]

- ICH E6(R2) Good clinical practice [1] is an international ethical and scientific quality standard for designing, conducting, recording and reporting trials that involve the participation of human subjects.
- FDA Good Review Practice: Clinical Review of Investigational New Drug Applications.[2] This good review practice (GRP) document was prepared to assist FDA clinical review staff in reviewing clinical submissions to an investigational new drug application (IND) from the pre-IND phase to the time of the pre-new drug application/biologics license application meeting.

Data monitoring committees [edit source]

- CHMP/EWP/5872/03 Data monitoring committees[3] (EMA) deals with independent data monitoring committees. It highlights the key issues involved when sponsors include data monitoring committees as a part of their trial management.
- FDA Establishment and Operation of Clinical Trial Data Monitoring Committees.[4] This guidance discusses the roles, responsibilities and operating procedures of Data Monitoring Committees (DMCs) (also known as Data and Safety Monitoring Boards (DSMBs) or Data andSafety Monitoring Committees (DSMCs)) that may carry out important aspects of clinical trial monitoring.

Adjustment by covariates [edit source]

- EMA/CHMP/295050/2013 Adjustment for baseline covariates in clinical trials[5] (EMA) provides advice on how to address important baseline covariates in designing, analysing and reporting clinical trials. It mainly focuses on confirmatory randomised trials.

Small populations [edit source]

- CHMP/EWP/83561/05 Clinical trials in small populations[6] (EMA) addresses problems associated with clinical trials when there are limited numbers of patients available to study.

Non-Inferiority [edit source]

- CPMP/EWP/2158/99 Choice of a non-inferiority[7] (EMA) provides guidance on two types of non-inferiority trials: trials with two arms, the test product and a comparator; and three-armed trials with the test product, an active comparator and placebo.
- CPMP/EWP/482/99 Switching between superiority and non-inferiority[8] (EMA) addresses the issues of superiority, non-inferiority and equivalence from the perspective of an efficacy trial with a single primary variable.

Subgroup analysis [edit source]

- EMA/CHMP/539146/2013 Investigation of subgroups in confirmatory clinical trials[9] (EMA) provides guidance for assessors in European regulatory agencies on assessment of subgroup analyses in confirmatory clinical trials.

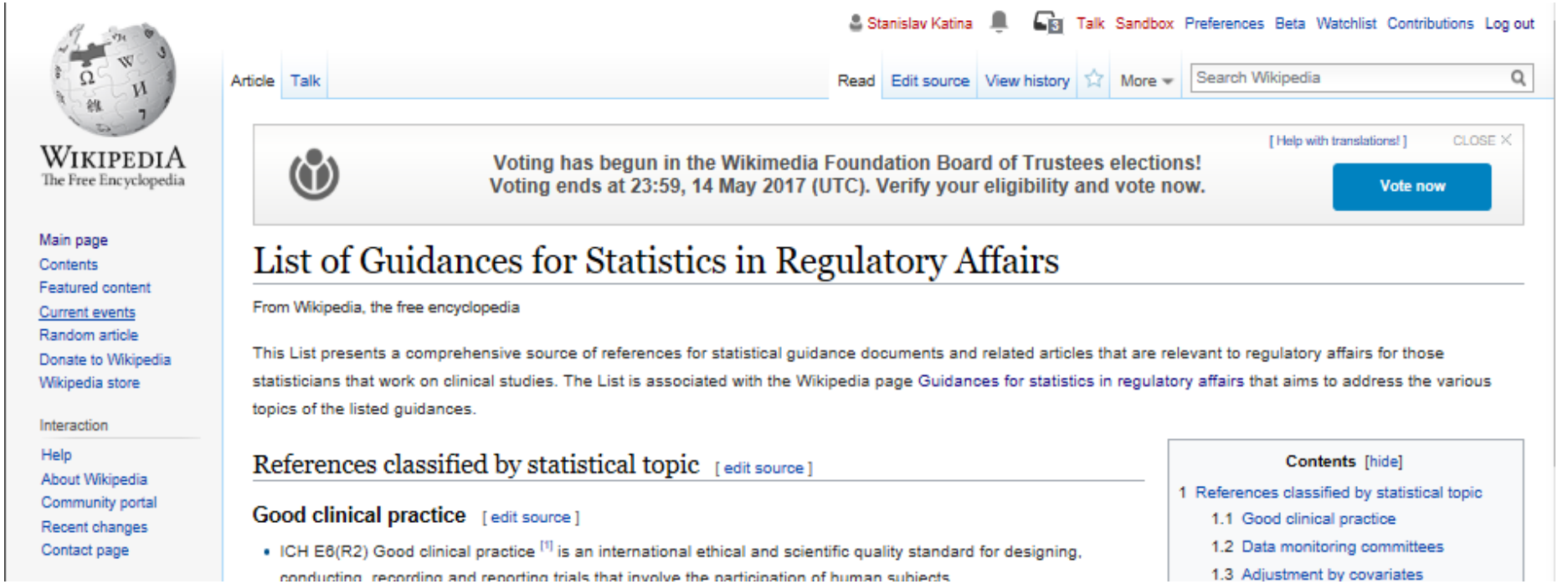
Endpoints [edit source]

- FDA Clinical trial endpoints for the approval of cancer drugs and biologics[10] provides recommendations to applicants on endpoints for cancer clinical trials submitted to the Food and Drug Administration (FDA) to support effectiveness claims in new drug applications (NDAs), biologics license applications (BLAs), or

(4) WIKIPEDIA “TALK” PAGE

“TALK” PAGE IS RELATED TO “ARTICLE”

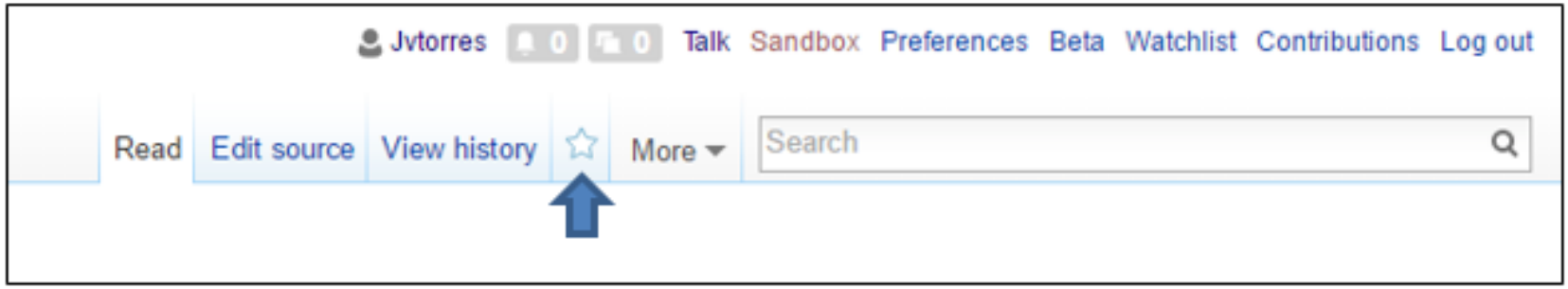
- “Talk” page provides space for editors of an article discuss changes associated with it.
- Talk Page(s) related to the SiRA initiative shows information about the format that the Articles must follow, a “To-Do List” for anyone interested to collaborate, and a space for open discussion.



(5) WIKIPEDIA "WATCHLIST"

FOLLOW ARTICLES

- Follow Articles of your interest by including them in your "Watchlist".
- You will be notified anytime there is a change on the Articles you follow.
- This might be very useful to keep you updated about any new document included in the *List of Guidances for Statistics in Regulatory Affairs.*



Click on the start to active the Watchlist.

(6) PROPOSED MAIN SECTIONS FOR THE ARTICLE: "GUIDANCES FOR STATISTICS IN REGULATORY AFFAIRS" (I/II)

HEADERS (LEVEL-2) IN WIKIPEDIA

Contents

Leading text

1. History
2. General guidance
3. Specific statistical guidance
4. Special populations guidance
5. Therapeutic areas guidance
6. Country specific guidance
7. See also
8. Notes
9. References
10. Furhter reading
11. External links

Note:

1. Level-1 header in Wikipedia is reserved for the page title.

2. Further proposed sub-section headers are available in a separate document (see Wikipedia ISCB Conference Poster, 2017).

(7) BASIC EDITING TIPS IN WIKIPEDIA (I/II)

(Adapted from https://en.wikipedia.org/wiki/Help:Cheatsheet)

Description	What you type	What you get
Italics, bold, and both	''italics'', '''bold''', and '''''both'''''	*italics*, **bold**, and ***both***
Underline	<u>Underline this</u>	Underline this
Strike	<s>Strike this</s>	~~Strike this~~
Link to another article within Wikipedia	Link to [[Mean]]	Link to Mean
Change the link's text	Link to [[Mean|Average]]	Link to Average
Link to a section	[[Mean#Truncated_mean Truncated mean]]	Truncated mean
Link to a website	[http://www.wikipedia.org Wikipedia]	Wikipedia
References	`FDA,<ref name=”fda”>[fda.gov FDA website]</ref>`	FDA[1]
References (subsequent uses)	`FDA again<ref name="fda" />`	FDA again[1]
Add comments within the text	`<!—Invisible comment-->`	

(7) BASIC EDITING TIPS IN WIKIPEDIA (II/II)

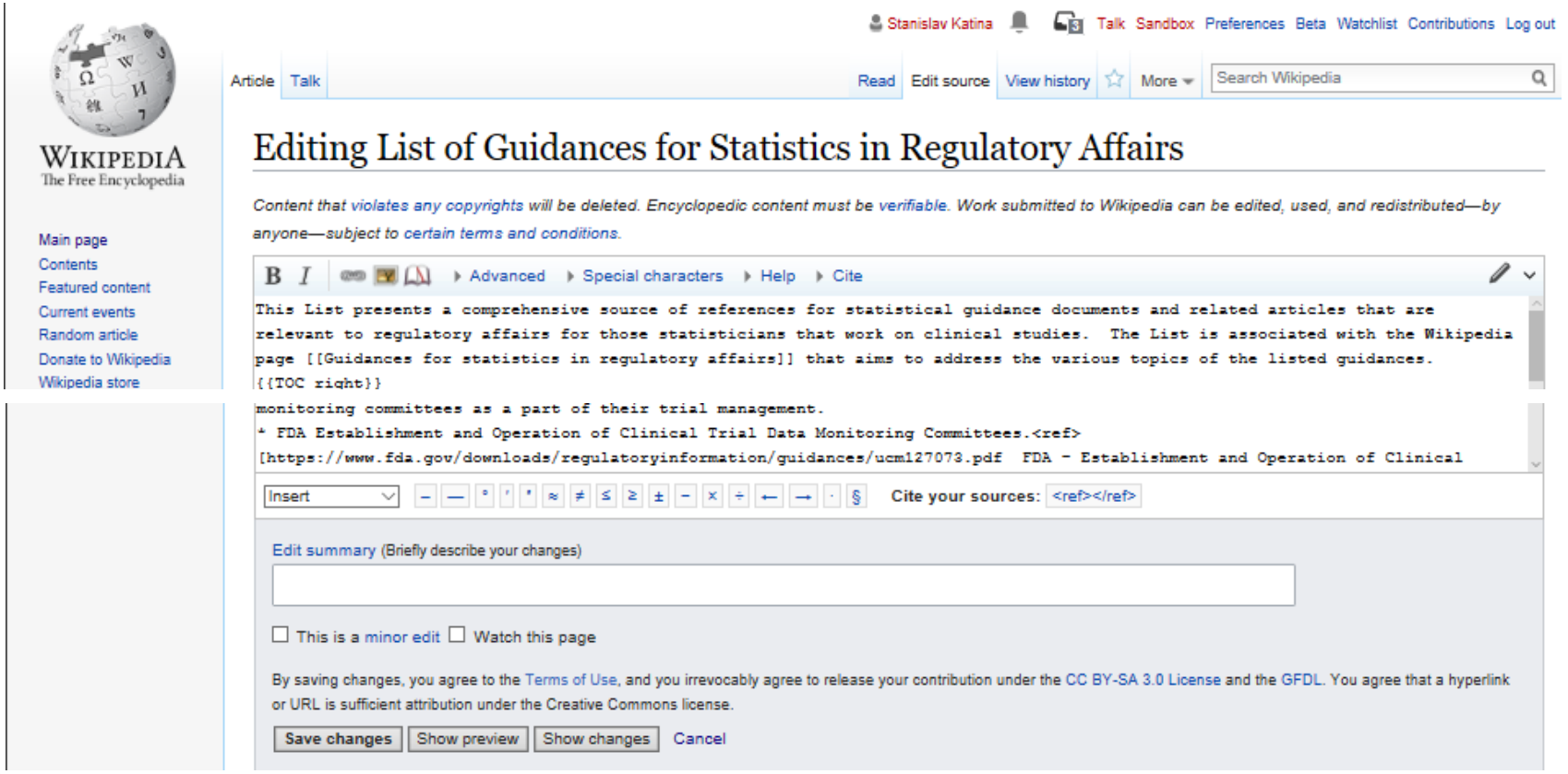
(Adapted from https://en.wikipedia.org/wiki/Help:Cheatsheet)

Description	What you type	What you get
Section headings	==Level 2== ===Level 3=== ====Level 4==== =====Level 5===== ======Level 6====== `=Level 1=` is reserved for the page title	**Level 2** **Level 3** **Level 4** **Level 5** **Level 6**
Bulleted list	* One * Two ** Two point one * Three	• One • Two • Two point one • Three
Numbered list	# One # Two ## Two point one # Three	1. One 2. Two 1. Two point one 3. Three

(8) EXAMPLE 1: INSERTING A HEADER IN THE "LIST" (I/II)

GO TO THE "LIST" PAGE AND CLICK ON THE "EDIT SOURCE" TAB ON THE TOP LEFT HAND SIDE

An "Edit Source" screen opens up. The top and the bottom of the editor has important tabs.



(8) EXAMPLE 1: INSERTING A HEADER IN THE "LIST" (II/II)

GO TO THE "LIST" PAGE AND CLICK ON THE "EDIT" TAB ON THE TOP LEFT HAND SIDE

1) To add a new level-3 header, e.g. "Cardiovascular" go to the appropriate position on the page and insert :

=== Cardiovascular ===

2) Click on "Show preview" tab for a preview that will appear on the top part of the screen.

3) Top of the screen says:
This is only a preview; your changes have not yet been saved! → Go to editing area.

4) Click on "Go to editing area" to return to the "Edit Source" mode.

5) Add some text in the field "Edit summary (Briefly describe your changes)".

6) Click on "Save changes" at the bottom of the screen.

(9) EXAMPLE 2: ADDING A REFERENCE TO THE "LIST" (I/II)

GO TO THE "LIST" PAGE AND CLICK ON THE "EDIT" TAB ON THE TOP LEFT HAND SIDE

- Let us insert the ICH-E9 Guideline in the by firstly going to the appropriate position on the "Edit Source" screen and typing the following:

  *ICH E9 Statistical principles for clinical trials<ref>[http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/general/general_content_001228.jsp&mid= ICH E9 - Statistical Principles for Clinical Trials]</ref> (EMA) section III provides a general overview of common designs in clinical trials.

- The resulting text in the list is as follows:
  - ICH E9 Statistical principles for clinical trials[22] (EMA) section III provides a general overview of common designs in clinical trials.

- The automatically numbered reference will appear at the bottom in the "Reference" section of the page as follows:

  22. ICH E9 - Statistical Principles for Clinical Trials

(9) EXAMPLE 2: ADDING A REFERENCE IN THE "LIST" (II/II)

NOTES ABOUT THE INSERTED REFERENCE

i. The Edit Source text is *ICH E9 Statistical principles for clinical trials<ref>[http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/general/general_content_001228.jsp&mid= ICH E9 - Statistical Principles for Clinical Trials]</ref> (EMA) section III provides a general overview of common designs in clinical trials.

ii. The URL of the guidance appears in the between: <ref>[ ]</ref>.

iii. Inserting "*ICH E9 Statistical principles for clinical trials" before <ref>[gives a bullet point to the name of the guidance.

iv. Inserting "(EMA) section III provides a general overview of common designs in clinical trials." after]</ref> is the ending of the sentence.

v. The text "ICH E9 - Statistical Principles for Clinical Trials" appears in the automatically numbered "Reference" section on the bottom of the page.

END

THANK YOU!