

---

---

**Clinical investigation of medical  
devices for human subjects — Good  
clinical practice**

*Investigation clinique des dispositifs médicaux pour sujets humains —  
Bonne pratique clinique*

**iTeh Standards**  
**(<https://standards.iteh.ai>)**  
**Document Preview**

[ISO 14155:2020](https://standards.iteh.ai/catalog/standards/iso/cd55c9bc-b95d-44e9-855b-bdff5d32701e/iso-14155-2020)

<https://standards.iteh.ai/catalog/standards/iso/cd55c9bc-b95d-44e9-855b-bdff5d32701e/iso-14155-2020>



**iTeh Standards**  
**(<https://standards.iteh.ai>)**  
**Document Preview**

[ISO 14155:2020](https://standards.iteh.ai/catalog/standards/iso/cd55c9bc-b95d-44e9-855b-bdff5d32701e/iso-14155-2020)

<https://standards.iteh.ai/catalog/standards/iso/cd55c9bc-b95d-44e9-855b-bdff5d32701e/iso-14155-2020>



**COPYRIGHT PROTECTED DOCUMENT**

© ISO 2020

All rights reserved. Unless otherwise specified, or required in the context of its implementation, no part of this publication may be reproduced or utilized otherwise in any form or by any means, electronic or mechanical, including photocopying, or posting on the internet or an intranet, without prior written permission. Permission can be requested from either ISO at the address below or ISO's member body in the country of the requester.

ISO copyright office  
CP 401 • Ch. de Blandonnet 8  
CH-1214 Vernier, Geneva  
Phone: +41 22 749 01 11  
Email: [copyright@iso.org](mailto:copyright@iso.org)  
Website: [www.iso.org](http://www.iso.org)

Published in Switzerland

# Contents

	Page
<b>Foreword</b> .....	<b>v</b>
<b>1 Scope</b> .....	<b>1</b>
<b>2 Normative references</b> .....	<b>1</b>
<b>3 Terms and definitions</b> .....	<b>1</b>
<b>4 Summary of good clinical practice (GCP) principles</b> .....	<b>9</b>
<b>5 Ethical considerations</b> .....	<b>10</b>
5.1 General.....	10
5.2 Improper influence or inducement.....	10
5.3 Compensation and additional health care.....	10
5.4 Registration in publicly accessible database.....	11
5.5 Responsibilities.....	11
5.6 Communication with the ethics committee (EC).....	11
5.6.1 General.....	11
5.6.2 Initial EC submission.....	11
5.6.3 Information to be obtained from the EC.....	12
5.6.4 Continuing communication with the EC.....	12
5.6.5 Continuing information to be obtained from the EC.....	12
5.7 Vulnerable populations.....	12
5.8 Informed consent.....	13
5.8.1 General.....	13
5.8.2 Process of obtaining informed consent.....	13
5.8.3 Special circumstances for informed consent.....	14
5.8.4 Information to be provided to the subject.....	15
5.8.5 Informed consent signature.....	17
5.8.6 New information.....	17
<b>6 Clinical investigation planning</b> .....	<b>17</b>
6.1 General.....	17
6.2 Risk management.....	18
6.2.1 General.....	18
6.2.2 Investigational device including clinical procedure risks and their disclosure.....	18
6.2.3 Clinical investigation process.....	18
6.3 Justification for the design of the clinical investigation.....	19
6.4 Clinical investigation plan (CIP).....	19
6.5 Investigator's brochure (IB).....	19
6.6 Case report forms (CRFs).....	20
6.7 Monitoring plan.....	20
6.8 Investigation site selection.....	21
6.9 Agreement(s).....	21
6.10 Labelling.....	21
6.11 Data monitoring committee (DMC).....	21
<b>7 Clinical investigation conduct</b> .....	<b>22</b>
7.1 General.....	22
7.2 Investigation site initiation.....	22
7.3 Investigation site monitoring.....	22
7.4 Adverse events and device deficiencies.....	22
7.4.1 Signals requiring immediate action.....	22
7.4.2 Adverse events.....	23
7.4.3 Device deficiencies.....	23
7.4.4 Risk assessment process for potentially unacceptable risks.....	23
7.5 Clinical investigation documents and documentation.....	24
7.5.1 Amendments.....	24
7.5.2 Subject identification log.....	24

7.5.3	Source documents	25
7.6	Additional members of the investigation site team	25
7.7	Subject privacy and confidentiality of data	25
7.8	Document and data control	25
7.8.1	Traceability of documents and data	25
7.8.2	Recording of data	25
7.8.3	Electronic clinical data systems	26
7.9	Investigational device accountability	27
7.10	Accounting for subjects	27
7.11	Auditing	27
<b>8</b>	<b>Suspension, termination, and close-out of the clinical investigation</b>	<b>28</b>
8.1	Completion of the clinical investigation	28
8.2	Suspension or premature termination of the clinical investigation	28
8.2.1	Procedure for suspension or premature termination	28
8.2.2	Procedure for resuming the clinical investigation after temporary suspension	29
8.3	Routine close-out	29
8.4	Clinical investigation report	30
8.5	Risk assessment and conclusions	30
8.6	Document retention	31
<b>9</b>	<b>Responsibilities of the sponsor</b>	<b>31</b>
9.1	Clinical quality management	31
9.2	Clinical investigation planning and conduct	31
9.2.1	Selection and training of clinical personnel	31
9.2.2	Preparation of documents and materials	32
9.2.3	Conduct of clinical investigation	33
9.2.4	Monitoring	33
9.2.5	Safety evaluation and reporting	36
9.2.6	Clinical investigation close-out	37
9.3	Outsourcing of duties and functions	37
9.4	Communication with regulatory authorities	37
<b>10</b>	<b>Responsibilities of the principal investigator</b>	<b>38</b>
10.1	General	38
10.2	Qualification of the principal investigator	38
10.3	Qualification of investigation site	38
10.4	Communication with the EC	38
10.5	Informed consent process	39
10.6	Compliance with the CIP	39
10.7	Medical care of subjects	40
10.8	Safety reporting	41
	<b>Annex A (normative) Clinical investigation plan (CIP)</b>	<b>42</b>
	<b>Annex B (normative) Investigator's brochure (IB)</b>	<b>51</b>
	<b>Annex C (informative) Case report forms (CRFs)</b>	<b>54</b>
	<b>Annex D (normative) Clinical investigation report</b>	<b>56</b>
	<b>Annex E (informative) Essential clinical investigation documents</b>	<b>61</b>
	<b>Annex F (informative) Adverse event categorization</b>	<b>68</b>
	<b>Annex G (informative) EC responsibilities</b>	<b>70</b>
	<b>Annex H (informative) Application of ISO 14971 to clinical investigations</b>	<b>74</b>
	<b>Annex I (informative) Clinical development stages</b>	<b>75</b>
	<b>Annex J (informative) Clinical investigation audits</b>	<b>80</b>
	<b>Bibliography</b>	<b>83</b>

## Foreword

ISO (the International Organization for Standardization) is a worldwide federation of national standards bodies (ISO member bodies). The work of preparing International Standards is normally carried out through ISO technical committees. Each member body interested in a subject for which a technical committee has been established has the right to be represented on that committee. International organizations, governmental and non-governmental, in liaison with ISO, also take part in the work. ISO collaborates closely with the International Electrotechnical Commission (IEC) on all matters of electrotechnical standardization.

The procedures used to develop this document and those intended for its further maintenance are described in the ISO/IEC Directives, Part 1. In particular the different approval criteria needed for the different types of ISO documents should be noted. This document was drafted in accordance with the editorial rules of the ISO/IEC Directives, Part 2 (see [www.iso.org/directives](http://www.iso.org/directives)).

Attention is drawn to the possibility that some of the elements of this document may be the subject of patent rights. ISO shall not be held responsible for identifying any or all such patent rights. Details of any patent rights identified during the development of the document will be in the Introduction and/or on the ISO list of patent declarations received (see [www.iso.org/patents](http://www.iso.org/patents)).

Any trade name used in this document is information given for the convenience of users and does not constitute an endorsement.

For an explanation of the voluntary nature of standards, the meaning of ISO specific terms and expressions related to conformity assessment, as well as information about ISO's adherence to the World Trade Organization (WTO) principles in the Technical Barriers to Trade (TBT) see the following URL: [www.iso.org/iso/foreword.html](http://www.iso.org/iso/foreword.html).

This document was prepared by Technical Committee ISO/TC 194, *Biological and clinical evaluation of medical devices*, in collaboration with the European Committee for Standardization (CEN) Technical Committee CEN/TC 206, *Biological and clinical evaluation of medical devices*, in accordance with the Agreement on technical cooperation between ISO and CEN (Vienna Agreement).

This third edition cancels and replaces the second edition (ISO 14155:2011), which has been technically revised. The main changes to the previous edition are as follows:

- inclusion of a summary section of GCP principles (see [Clause 4](#));
- reference to registration of the clinical investigation in a publicly accessible database (see [5.4](#));
- inclusion of clinical quality management (see [9.1](#));
- inclusion of risk-based monitoring (see [6.7](#));
- inclusion of statistical considerations in [Annex A](#);
- inclusion of guidance for ethics committees in [Annex G](#);
- reinforcement of risk management throughout the process of a clinical investigation (planning to consideration of results) including [Annex H](#);
- clarification of applicability of the requirements of this document to the different clinical development stages (see [Annex I](#));
- inclusion of guidance on clinical investigation audits (see [Annex J](#)).

Any feedback or questions on this document should be directed to the user's national standards body. A complete listing of these bodies can be found at [www.iso.org/members.html](http://www.iso.org/members.html).



# Clinical investigation of medical devices for human subjects — Good clinical practice

## 1 Scope

This document addresses good clinical practice for the design, conduct, recording and reporting of clinical investigations carried out in human subjects to assess the clinical performance or effectiveness and safety of medical devices.

For post-market clinical investigations, the principles set forth in this document are intended to be followed as far as relevant, considering the nature of the clinical investigation (see [Annex I](#)).

This document specifies general requirements intended to

- protect the rights, safety and well-being of human subjects,
- ensure the scientific conduct of the clinical investigation and the credibility of the clinical investigation results,
- define the responsibilities of the sponsor and principal investigator, and
- assist sponsors, investigators, ethics committees, regulatory authorities and other bodies involved in the conformity assessment of medical devices.

NOTE 1 Users of this document need to consider whether other standards and/or national requirements also apply to the investigational device(s) under consideration or the clinical investigation. If differences in requirements exist, the most stringent apply.

NOTE 2 For Software as a Medical Device (SaMD) demonstration of the analytical validity (the SaMD's output is accurate for a given input), and where appropriate, the scientific validity (the SaMD's output is associated to the intended clinical condition/physiological state), and clinical performance (the SaMD's output yields a clinically meaningful association to the target use) of the SaMD, the requirements of this document apply as far as relevant (see Reference [4]). Justifications for exemptions from this document can consider the uniqueness of indirect contact between subjects and the SaMD.

This document does not apply to *in vitro* diagnostic medical devices. However, there can be situations, dependent on the device and national or regional requirements, where users of this document might consider whether specific sections and/or requirements of this document could be applicable.

## 2 Normative references

The following documents are referred to in the text in such a way that some or all of their content constitutes requirements of this document. For dated references, only the edition cited applies. For undated references, the latest edition of the referenced document (including any amendments) applies.

ISO 14971, *Medical devices — Application of risk management to medical devices*

## 3 Terms and definitions

For the purposes of this document, the following terms and definitions apply.

ISO and IEC maintain terminological databases for use in standardization at the following addresses:

- ISO Online browsing platform: available at <http://www.iso.org/obp>
- IEC Electropedia: available at <http://www.electropedia.org/>