World Health Organization

International Standards for Clinical Trial Registries

The registration of all interventional trials is a scientific, ethical and moral responsibility

International Clinical Trials Registry Platform

Version 3.0

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Contributors and acknowledgements

These standards were developed as part of the programme of work of WHO's International Clinical Trials Registry Platform (ICTRP). The mission of the ICTRP is to ensure that a complete view of research is accessible to all those involved in health-care decision-making. This will improve research transparency and will ultimately strengthen the validity and value of the scientific evidence base.

This document was updated by Lisa Askie (Australian New Zealand Clinical Trials Registry, ANZCTR), Ghassan Karam, Samantha Slattery and Vasee Moorthy (WHO, Geneva). The previous version was produced and written by Davina Ghersi (WHO, Geneva) and Lisa Askie.

The general requirements of a clinical trial registry (the WHO Registry Criteria) were developed and agreed upon by the ICTRP's Advisory Group. The starting point for these criteria were the requirements of clinical trial registries published by the International Committee of Medical Journal Editors (ICMJE) *(1)*. These requirements became the criteria that a registry must meet in order to be considered eligible for the status of Primary Registry in the WHO Registry Network.

The specific, detailed standards in this document further define the requirements of each registry criterion. These standards were reviewed by the ICTRP Secretariat and administrators of Primary Registries in the WHO Registry Network.

These standards were initially developed in consultation with the ICTRP's Best Practice Group, which was composed of the administrators of selected Primary Registries in the WHO Registry Network. Its membership changed over time and included: Hélène Faure, International Standard Randomised Controlled Trial Number registry (ISRCTN); Ambujam Nair Kapoor, Clinical Trials Registry – India (CTR-I); Abha Aggarwal, CTR-I; Ludovic Reveiz, Latin American Ongoing Clinical Trial Register (LatinRec); Taixiang Wu, Chinese Clinical Trial Registry (ChiCTR); Lisa Askie, ANZCTR; Udaya Ranawaka, Sri Lanka Clinical Trials Registry (SLCTR); Lotty Hooft, Netherlands Trials Register (NTR); Lakshmi Grama, Physician Data Query (PDQ); and Susanne Jena, German Clinical Trials Register (DRKS). Input into the development of the standards was also provided by Ghassan Karam, Chris Jones, Hazim Timimi and Maribel Gomez of the ICTRP Secretariat (WHO, Geneva).

Abbreviations

AGCTRR	Advisory Group on Clinical Trial Registration and Reporting
ANZCTR	Australia New Zealand Clinical Trials Registry
CDISC	Clinical Data Interchange Standards Consortium
HL7	Health Level 7
ICH	International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use
ICMJE	International Committee of Medical Journal Editors
ICTRP	International Clinical Trials Registry Platform
IRAMG	ICTRP Registry Application and Monitoring Group
ISRCTN	International Standard Randomised Controlled Trial Number
PI	Principal Investigator
SOP	standard operating procedure
TRDS	Trial Registration Data Set
UMLS	Unified Medical Language System
UTN	Universal Trial Number
xml	Extensible Markup Language

Introduction

The International Clinical Trials Registry Platform (ICTRP) is a global initiative that aims to make information about all clinical trials involving human beings publicly available. It was established in 2006 in response to demand from countries, through the World Health Assembly, for: "a voluntary platform to link clinical trials registers in order to ensure a single point of access and the unambiguous identification of trials with a view to enhancing access to information by patients, families, patient groups and others" *(2)*.

The ICTRP Secretariat is hosted by WHO in its headquarters in Geneva. The Secretariat performs the following roles:

- It publishes the ICTRP Search Portal *(3)*, a database that makes it possible for anyone to search, for free, data provided by clinical trial registries that meet WHO criteria for content and quality. Data on the portal is updated weekly.
- It supports the WHO Registry Network, a forum for registries to exchange information and work together to establish best practice for clinical trial registration and results reporting and the collection of high-quality data.
- It supports countries and regions wanting to establish clinical trial registries or policies on trial registration and results reporting. In some cases, these registries will be a catalyst for other capacity-building activity in clinical trial conduct and oversight – particularly ethical and regulatory oversight.

Any registry that enters clinical trials into its database prospectively (that is, before the first participant is recruited) and meets the WHO Registry Criteria, or that is working with the ICTRP towards meeting these criteria, can be part of the WHO Registry Network. The WHO Registry Criteria have been categorized into six main areas:

- content
- quality and validity
- accessibility
- unambiguous identification
- technical capacity
- administration and governance.

Primary Registries in the WHO Registry Network are those that meet all WHO Registry Criteria. Primary Registries must also meet the requirements of the International Committee of Medical Journal Editors (ICMJE) *(4)*. Partner Registries in the WHO Registry Network must meet most, but not all, of the criteria. Specifically, they are not required to have a national mandate, and they can be limited in scope (for example, to trials in a particular disease or intervention).

Data providers are responsible for a database that is used by one or more registries.

- Data providers provide data to WHO for inclusion in the ICTRP Search Portal.
- The ICTRP will accept trial records from data providers if it is satisfied that those trial records have been created and managed in a manner that is consistent with the WHO Registry Criteria.

Why standards are necessary

The registries in the WHO Registry Network are disparate in remit and functionality. In order to promote harmonization in the way in which data are collected and validated by these registries, and thus ensure a baseline level of data quality, minimum standards need to be determined and implemented. In doing so, participating registries will improve the usability of the ICTRP Search Portal and ultimately benefit all those looking for and using information about clinical trials.

How these standards will be used by the ICTRP

The standards contained in this document are based on the criteria that clinical trial registries must attain in order to be recognized as a Primary Registry in the WHO Registry Network, and that they must maintain in order to retain that recognition. They are minimum standards and individual registries may choose to impose stricter requirements than those defined in this document. In some instances, ideal standards have also been suggested.

All registries in the WHO Registry Network, and registries applying for Primary or Partner Registry status, must be able to demonstrate that they comply with the standards by:

- having documented, registry-specific standard operating procedures (SOPs) in place (see also sections 2.2 and 9);
- providing a written commitment to comply with the standards;
- updating that commitment on an annual basis along with an update of the WHO Registry Profile;
- agreeing to site visits and random audits by the ICTRP Secretariat and/or delegated auditors.

How registries will use these standards

These standards outline the broad criteria that Primary Registries in the WHO Registry Network must fulfil in six main areas: content, quality and validity, accessibility, unambiguous identification, technical capacity, and administration and governance.

Primary and Partner Registries in the WHO Registry Network must adapt these broad standards into registry-specific SOPs which detail the way in which each of these standards are operationalized within each registry.

Translation of these standards

These standards have been developed, and will be maintained, in English. Registries may choose to translate these standards into the language/s used by registry staff; however, the registry must take responsibility for any translation, and ensure that at least two people have checked and confirmed the accuracy of the translation.

Updating these standards

The intention is to update this standards document every five years. Individual standards may be updated on ad hoc basis, depending on need. Any proposed modifications, revisions or additions made in the interim will be discussed at WHO Registry Network meetings. Once a new or modified standard is agreed upon it will be posted on the ICTRP's website. Registries are advised to regularly check the ICTRP website to make sure they are part of the discussion around new standards and are using current information.

Other standards

Several other organizations have developed standards that relate either directly or indirectly to those contained in this document. These include the ICMJE updated statement on trial registration requirements *(5)*; the Declaration of Helsinki *(6)*; and data interchange standards initiatives such as the Clinical Data Interchange Standards Consortium (CDISC), Health Level 7 (HL7) and others. The standards contained in this document are in accordance with the ICMJE requirements for trial registration.

Responsibilities

Several parties have responsibilities for ensuring that we all have access to complete and meaningful information about clinical trials being conducted throughout the world.

Responsibilities of the registry
A registry accepting trials for registration must make all reasonable efforts to ensure that an individual who is submitting a trial for registration (known as the Responsible Registrant):

- is a real person;
- is the appropriate person to be registering the trial;
- provides complete, accurate and meaningful data for each item in the WHO Trial Registration Data Set (TRDS) at the time of initial registration (see section 7).

Registries are also responsible for ensuring they have quality control processes and procedures in place to ensure compliance with all of the minimum international standards defined in this document.

Responsibilities of the Responsible Registrant
The Responsible Registrant is an appropriate representative of the trial's primary sponsor.[1] The Responsible Registrant is responsible for making sure that the data submitted for each item in the TRDS for a trial are complete, accurate and meaningful at the time the trial is initially registered. They are also responsible for keeping that data up to date and compliant with the trial registration and results reporting recommendations and/or requirements within their own jurisdiction(s).

The Responsible Registrant will make every reasonable effort to ensure that a trial is registered once, and only once, in any one register, and that the trial is registered in the fewest number of registers necessary to meet applicable regulations (see section 4). If a trial is, by necessity, registered in more than one registry then the Responsible Registrant is responsible for ensuring that all known identifiers for the trial are included in each registry's record as secondary identifiers to facilitate unambiguous identification of the trial.

Other stakeholders with responsibilities
Comprehensive prospective trial registration and subsequent results reporting is a global effort that requires the assistance of more parties that just Responsible Registrants and the registries to which they submit their data. Journal editors, ethics committees/institutional review boards (IRBs), regulatory authorities and funding agencies can all play a major role in ensuring complete research transparency by requiring trials under their auspices to be prospectively registered. In this way, we ensure that everybody involved in research in humans accepts that the registration of all interventional trials is a scientific, ethical and moral responsibility.