Clinical Trials Registry - India
National Institute of Medical Statistics (ICMR)

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Inside

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"We welcome the agreement of International standards for reporting time-frames that everyone can work towards"

Dr Soumya Swaminathan, Director General, ICMR and Secretary Department of Health Research holds many professional memberships such as International Union Against Tuberculosis and Lung Diseases;International Scientific Advisory Expert Group for the All-Party Parliamentary Group on Global Tuberculosis (APPG TB), UK.
Dr Soumya Swaminathan also serves as a Member, UNAIDS, Scientific and Technical Advisory Group, WHO Stop TB department. In addition, she serves on national committees of the health ministry, DBT, DST and national institutes like AIIMS and IISC.

Prospective Trial Registration

* The CTRI currently has 8950 trials registered (as on 30th June 2017) out of which 3318 are prospective and 5604 are retrospective registrations.
* The mandate of CTRI is prospective registration i.e. registration before enrolment of first patient.
* Upon registration all trials are flagged according to the status at the time of registration
* For Prospective Registration at the time of trial submission, patient enrolment should not have begun i.e..
  - Date of first Enrolment is an anticipated future date and
  - Status of trial is Not Yet Recruiting
* Otherwise, trial will be flagged as Trial Registered Retrospectively
* Once a trial is registered, flagging cannot be changed.

Coming soon: Clinical trials transparency

Big Funders Decide To Make Results Public

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New Delhi: Some of the world's largest funders of medical research, including Indian Council of Medical Research (ICMR), UK Medical Research Council and international organisations like PATH and Bill and Melinda Gates Foundation, have decided to make public results of all clinical trials funded and supported by them.

This assumes significance as almost half of clinical trials go unreported currently. Moreover, the move will enhance access to crucial data which can be useful in advancement of medical research. The decision is part of an agreement on standards, framed by the World Health Organisation (WHO), signed by the agencies at the ongoing United Nations' World Health Assembly in Geneva. Health Minister J P Nadda and senior officials from the health ministry are attending the Assembly where delegates from health groups and civil society from across the world are present.

The research institutes and other funding agencies agreed to develop and implement policies within the next 12 months that require all trials they fund, co-fund, sponsor or support to be registered in a publicly-availa-

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agreed that all results would be disclosed within specified time-frames on the registry or by publication in a scientific journal.

"We need timely clinical trial results to inform clinical care practices as well as make decisions about allocation of resources for future research," said Dr Soumya Swaminathan, DG of ICMR. "We welcome the agreement of international standards for reporting time-frames that everyone can work towards."

Most of these trials and their results will be accessible through WHO's International Clinical Trials Registry Platform, a unique global database of clinical trials that compiles data from 17 registries around the world, including the US' clinicaltrials.gov, the EU's Clinical Trials Register, the Chinese and Indian Clinical Trial Registries and many others.

Experts say unreported trial results leave an incomplete and potentially misleading picture of the risks and benefits of vaccines, drugs and medical devices, and can lead to use of suboptimal or even harmful products. A common registry is expected to solve this problem. "Research funders are making a strong statement that there will be no more excuses on why some clinical trials remain unreported long after they have been completed," said Dr Marie-Paule Kieny, Assistant Director-General for Health Systems and Innovation at WHO.

Problems in trial registration? Visit e-tutorial on CTRI Home Page

New Developments

In the last meeting of the World Medical Association[1] held in 2013, the policy statement the Declaration of Helsinki clearly states that:
"*Every research study involving human subjects must be registered in a publicly accessible database before recruitment of the first subject*."

Moreover, it emphasizes that: "*Researchers, authors, sponsors, editors and publishers all have ethical obligations with regard to the publication and dissemination of the results of research. Researchers have a duty to make publicly available the results of their research on human subjects and are accountable for the completeness and accuracy of their reports. All parties should adhere to accepted guidelines for ethical reporting. Negative and inconclusive as well as positive results must be published or otherwise made publicly available. Sources of funding, institutional affiliations and conflicts of interest must be declared in the publication. Reports of research not in accordance with the principles of this Declaration should not be accepted for publication*."

In keeping with these directions, in May this year, under the aegis of WHO a joint statement signed by global non-industry research funders, including ICMR, was released. This statement makes clearly defined commitments to results disclosure[2]. The key features of the Joint Statement are described below:

Prospective registration

To implement mandatory prospective registration for all interventional trials.

Results disclosure

This includes the addition of two data set points to be filled by the Registrant once a trial is Completed (defined as last patient, last visit):

- Date of actual study completion
- Final enrolment number achieved

Once a trial is completed, it will make its results publicly available no later than one year after trial completion by posting to the results section of the primary clinical trial registry. In case a results database is not available, the results should be posted on a free-to-access, publicly available, searchable institutional website of the Regulatory Sponsor, Funder or Principal Investigator. The format of the results has been predefined as

Participant Flow:This includes a summary of the progress of participants through each stage of a study, by study arm or comparison group. It will include the numbers of participants who started, completed, and dropped out of each period of the study based on the sequence in which interventions were assigned.

Signatories to Joint Statement

Indian Council of Medical Research
Research Council of Norway
UK Medical Research Council
Médecins Sans Frontières
Epicentre
CEPI
PATH
Institut Pasteur
Bill and Melinda Gates Foundation
Wellcome Trust

Why is Trial Registration Important?

Prospective trial registration would help to:

- Prevent selective reporting and publication of positive results
- Prevent unnecessary duplication of research efforts
- Empower patients and the public about planned or ongoing trials and if necessary enrol in them.
- Give ethics committees and researchers access to studies being conducted and compare them to research that is under their consideration or is being planned.

Baseline Characteristics: A tabular summary of the data collected at the beginning of a study for all participants, by study arm or comparison group. These data include demographics, such as age and gender, and study-specific measures (for example, systolic blood pressure, prior antidepressant treatment).

***Outcome Measures and Statistical Analyses*:** A tabular summary of outcome measure values, by study arm or comparison group. It includes tables for each pre-specified Primary Outcome and Secondary Outcome and may also include other pre-specified outcomes, post hoc outcomes, and any appropriate statistical analyses.

***Adverse Events*:** A tabular summary of all anticipated and unanticipated serious adverse events and a tabular summary of anticipated and unanticipated other adverse events exceeding a frequency threshold. For each serious or other adverse event the summary includes the adverse event term, affected organ system, number of participants at risk, and number of participants affected, by study arm or comparison group.

In addition to the above, the protocol, along with its amendments, would also be made available publicly.

Publication

Within 24 months of trial completion, trial findings should be published in a peer-reviewed open access journal. If necessary, fund allocation for publication should be included in the clinical trial budget for publication in an open access journal.

Trial Identification Number

The Trial Registration Number assigned after the final registration needs to be mentioned at the time of publication. This is essential for linking journal publications with registry records.

IPD Sharing

The feasibility of implementing individual patient data (IPD) sharing is being explored. Consensus and policy formation regarding the same might take some time to be implemented after sharing the concerns with all stakeholders.

Concluding Remarks

The implementation of the objectives of the joint statement would help make research findings more discoverable, reduce bias and raise research standards in the country. Currently, modalities are being worked out in consultation with stakeholders as to how best to implement these changes in the CTRI platform.

References

1. https://www.wma.net/policies-post/wma-declaration-of-helsinki-ethical-principles-for-medical-research-involving-human-subjects/
2. http://who.int/ictrp/results/ICTRP_JointStatement_2017.pdf?__ua=1

How to Register a Trial

Trial registration in the CTRI is an online process and free of cost.
The trial registration dataset of the CTRI is given in Table 1.

Process of trial registration is discussed in detail in the E- tutorial on the home page of CTRI [http://10.1.75.7:8079/ctri/]

Steps to trial registration is described briefly below:

- Register in the CTRI by clicking on NEW APPLICANT on the CTRI Home Page.
- Fill the form online and click on Submit button.
- Login to CTRI and upload trial data by clicking on "ADD NEW TRIAL".
- The form must be filled online only and may be filled in parts as per Registrant convenience.
- Please present information in proper sentence format using proper upper and lower case alphabets with proper spacing as all information is viewable globally.
- Upload Ethics and DCGI approval (if applicable).
- Once the form is filled, click on the SUBMIT button (in Part 8).
- In case all fields are not filled, the trial will not be submitted and fields requiring attention would be highlighted with a cross.
- If all trial data set form items are filled, an acknowledgment number (REF number) is assigned to the trial, which should be quoted in all trial related correspondence.
- Once a trial is submitted the trial is viewable but not editable by Registrant.
- After review by the CTRI scientists, the trial may be sent back in case any changes or additional information
- Verification mails will be sent to all mentioned *contact persons* other than trial registrant.
- A trial will registered upon satisfaction of all clarifications/modifications requested, submission of documents and receipt of confirmation mail from *contact persons*.

Table 1:Registration Data Set of the CTRI

1. Registration Number
2. Trial Registration Date
3. Public Title of Study*
4. Scientific Title of Study* Acronym, if any
5. Secondary IDs, (UTN, Protocol No etc.)*
6. Principal Investigator's Name and Address
7. Contact Person (Scientific Query)*
8. Contact Person (Public Query)*
9. Source/s of Material or Monetary Support*
10. Primary Sponsor*
11. Secondary Sponsor*
12. Countries of Recruitment*
13. Site/s of study*
14. Name of Ethics Committee and approval status *
15. Regulatory Clearance obtained from DCGI*
16. Health Condition/Problem studied*
17. Study Type*
18. Intervention and Comparator agent*
19. Key inclusion/Exclusion Criteria*
20. Method of generating randomization sequence
21. Method of allocation concealment
22. Blinding and masking
23. Primary Outcome/s*
24. Secondary Outcome/s*
25. Target sample size*
26. Phase of Trial*
27. Date of first enrollment*
28. Estimated duration of trial
29. Status of Trial*
30. Publication
31. Brief Summary*
32. Date of actual study completion
33. Final enrolment number achieved

Footnote:

Underlined items are assigned by the CTRI software upon trial registration.

*Items marked with an * are mandatory items i.e. without these items the trial will not be submitted*

Items in Blue are WHO Data Set items.

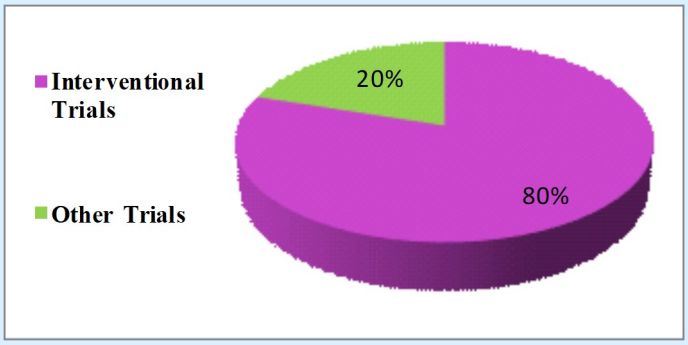
Items in Green are additional requirements in the CTRI.

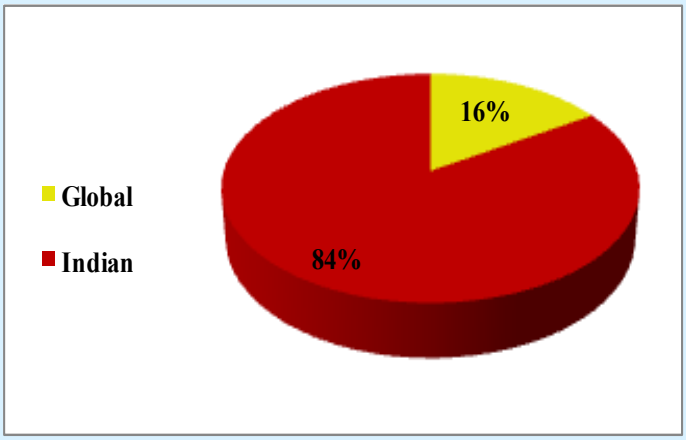
Items in Red are New Data Set Items for Completed /Terminated trials

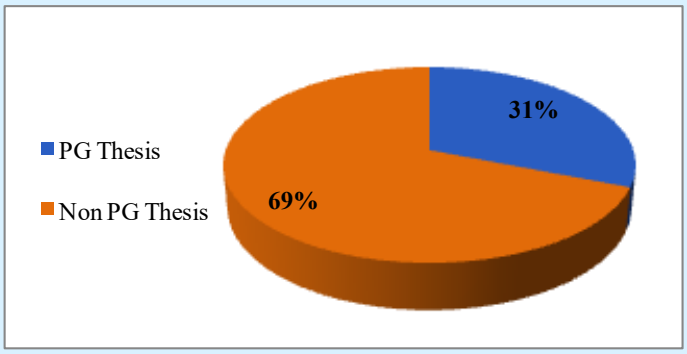
CTRI Facts and Figures

(Total Registered trials=8950)

Till 30th June 2017





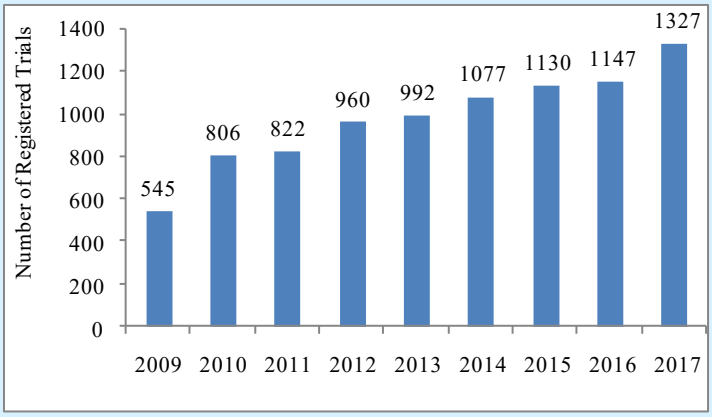


Checklist for Prospective Trial Registration

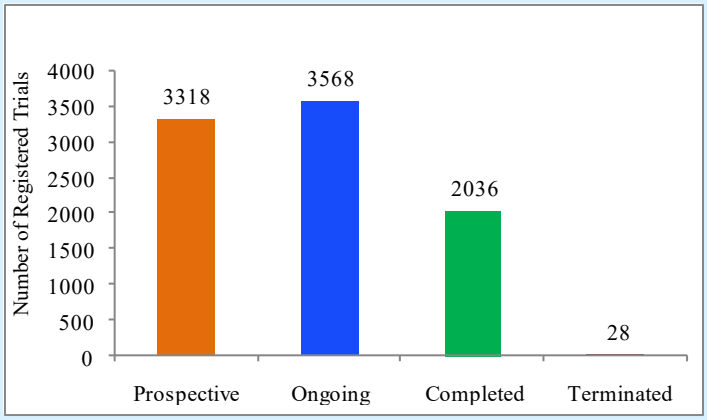
- ☐ Online trial registration form submitted?
- ☐ REF number allotted?
- ☐ Status of trial is Not Yet Recruiting
- ☐ Date of first enrolment a future date?
- ☐ Ethics and DCGI approval (if applicable) uploaded?
- ☐ Trial verification* completed?

Questions ? Send an email to ctri@gov.in

Trials Registration Trend in CTRI



Break up of Registered Trials



Publications

1. Pandey A, Aggarwal A, Maulik M, Gupta J, Juneja A. Challenges in Administering a Clinical Trials Registry: Lessons from the Clinical Trials Registry-India. *Pharm. Med*. 2013; Vol 27 (2): 83-93.
2. Pandey A, Aggarwal A, Maulik, M, Gupta J, Juneja A, Seth SD. The upgraded Clinical Trials Registry India: a summary of changes. *Ind. J. Med. Ethics* Vol VIII No 3 July-September 2011, 186
3. Pandey A, Aggarwal A, Seth SD, Maulik, M, Juneja A. Strenghtening ethics in clinical research. *Indian J Med Res [Letter to Editor] 2011; 133:339-340.* IF: 1.88
4. Pandey A, Aggarwal AR, Seth SD, Maulik, M. Clinical Trials Registry – India: Raising the veil. *Natl Med J India [Letter to Editor]2010; 23 (3):187 -188.*
5. Pandey A, Aggarwal A, Maulik, M, Seth SD. Clinical trial registration gains momentum in India. *Indian J Med Res [Letter to Editor] 2009; 130: 85-86.* IF: 1.88
6. Pandey A, Aggarwal AR, Seth SD, Maulik, M, Bano R. Juneja A. Clinical Trials Registry – India: Redefining the conduct of clinical trials. *Indian J Cancer 2008; 45 (3): 79-82.*

[*Links to each are available under Publication button at* www.ctri.nic.in]

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*What is Trial Verification?

An email is sent from CTRI to all contact persons mentioned in the trial registration form (except to the trial registrant). Once all the trial contact persons respond, trial verification process is considered complete.