

1 WHO Statement on Public Disclosure of Clinical Trial Results

2 Background

3 Following a ministerial summit on Health Research in 2004, a World Health Assembly Resolution
4 passed in 2005 called for unambiguous identification of all interventional clinical trials. This led to
5 the establishment of the WHO International Clinical Trials Registry Platform, which collates
6 information on trials that have been notified in a network of clinical trial registries
7 (who.int/ictrp/network). WHO's existing position on registration is available at who.int/ictrp: "The
8 registration of all interventional trials is a scientific, ethical and moral responsibility". Deposition of
9 information on trials in such registries, prior to their initiation, is a condition for publishing the
10 results of trials in many leading medical journals¹. However, concerns have been raised that there
11 may be selective publication of trials dependent on their results, with particular concern that trial
12 results which may be viewed as "negative", are less likely to be submitted, or accepted, for
13 publication in the scientific literature or made public in other ways. Notification of trials to clinical
14 trial registries has become more widespread, and it is possible to evaluate what proportions of
15 recorded trials have not reported results at different times after the planned end dates of the trials.
16 Multiple analyses have confirmed that a substantial number of clinical trials remain unreported
17 several years after study completion, even in the case of large randomized clinical trials (Jones,
18 Handler et al. 2013).

19 An analysis published in May 2014 (Manzoli, Flacco et al. 2014) reported that a substantial number
20 of Randomized Controlled Trials of vaccines remained unreported 48 months post study completion.

21 In the latest version of the Declaration of Helsinki it is stated that "Every research study involving
22 human subjects must be registered in a publicly accessible database before recruitment of the first
23 subject." and that "Researchers have a duty to make publicly available the results of their research
24 Negative and inconclusive as well as positive results must be published or otherwise made
25 publicly available". There is an ethical imperative to report the results of all clinical trials.
26 Furthermore poor allocation of resources for product development and financing of available
27 interventions, and suboptimal regulatory and public health recommendations may occur where
28 decisions are based on only a subset of all completed clinical trials.

29 *Reiteration of WHO position on clinical trial registry sites*

30 Before any clinical trial² is initiated (at any Phase) its details are to be registered in a publicly
31 available, free to access, searchable clinical trial registry. The clinical trial registry entry should be
32 made before the first subject receives the first medical intervention in the trial.

¹ www.icmje.org/recommendations/browse/publishing-and-editorial-issues/clinical-trial-registration.html

² A clinical trial is defined as any experimental study which prospectively allocates humans to a medical intervention. While randomised assignments are considered of highest value for assessing the safety and efficacy of an intervention, the WHO definition of a clinical trial for reporting purposes also includes non-randomised assignments, for example in Phase I trials. As safety problems may occur in Phase I trials, it is critical that the same disclosure mechanisms apply for non-randomised Phase I trials as apply to randomised Phase I, II or III trials. Phase IV or post-licensure trials of health products are considered clinical trials if they involve prospective designs (with or without randomisation). Clinical trials have pre-specified research or

33 *Updating clinical trial registry entries*

34 All clinical trial registry sites are to be updated as necessary to include final enrolment numbers
35 achieved, and the date of actual study completion (defined as the last data collection timepoint for
36 the last subject for the primary outcome measure, often called “last subject last visit”).

37 *Reporting timeframes for clinical trials*

38 Clinical trial results are to be reported within 30 months of the study completion date as defined
39 above. Reporting is to occur in BOTH of the following two modalities.

- 40 1. The main findings of clinical trials³ ~~to be submitted for publication in a peer reviewed journal~~
41 ~~within 18 months of study completion and~~ are to be published through an open access
42 mechanism ~~unless there is a specific reason why open access cannot be used~~, or otherwise
43 made available publicly ~~at most within 30 months of study completion~~.
44 2. In addition the key outcomes⁴ are to be made publicly available by posting to the results
45 section of the primary clinical trial registry. ~~Where a registry is used without a results~~
46 ~~database available, the results should be posted on a free-to-access, publicly available,~~
47 ~~searchable institutional website of the Regulatory Sponsor, Funder or Principal Investigator.~~

48 It is noted that journals such as *Public Library of Science (PLoS)* journals and *Trials* allow open
49 access publication of the findings of all clinical trials without any prejudice against the
50 publication of negative trials. ~~These 18 month and 30 month timeframes~~ represent the longest
51 possible acceptable timeframe for reporting and shorter timeframes are strongly encouraged. It
52 should be possible in most instances for reporting to occur in shorter timeframes.

53 *Inclusion of Trial ID in clinical trial publication*

54 The Trial ID or registry identifier code/number is always to be included in all publications of clinical
55 trials, and should be provided as part of the abstract to PubMed and other bibliographic search
56 databases for easy linking of trial reports with clinical trial registry site records. Bibliographic search
57 databases such as PubMed are encouraged to make Trial IDs easily available by inclusion in the
58 abstract of each clinical trial record.

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product development objectives, and so routine use of health interventions without specified research objectives are not considered to be within the definition of a clinical trial.

³ See www.consort-statement.org for broadly accepted standards on presentation of results in peer reviewed manuscripts reporting clinical trials

⁴ “Key outcomes” here is defined as including the following as a minimum: participant flow, baseline characteristics, primary and secondary outcome measures, and adverse events including all serious adverse events and important anticipated or unanticipated adverse events. An example of a format for providing results: <https://clinicaltrials.gov/ct2/about-site/results>. Note that “key outcomes” refers to analyses conducted on data, not to primary data disclosure itself.

60 **Note on Data Sharing Initiatives**

61 The benefit of sharing research data and the facilitation of research through greater access to
62 primary datasets is a principle which WHO sees as important. This statement is not directed towards
63 sharing of primary data. However WHO is actively engaged with multiple initiatives related to data
64 sharing, and supports sharing of health research datasets whenever appropriate. WHO will continue
65 to engage with partners in support of an enabling environment to allow data sharing to maximise
66 the value of health research data.

67 **References**

- 68 Jones, C. W., L. Handler, et al. (2013). "Non-publication of large randomized clinical trials: cross
69 sectional analysis." BMJ **347**: f6104.
- 70 Manzoli, L., M. E. Flacco, et al. (2014). "Non-publication and delayed publication of randomized trials
71 on vaccines: survey." BMJ **348**: g3058.

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