Comment Form: WHO Statement on Public Disclosure of Clinical Trial Results

Comment as individual or on behalf of agency or institution?: Institution

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Locator (Page & Line No or section heading, footnote number)	**Comment**	**Suggested Amendment**	**Internal Use Only [blank]**
General comment	IQWiG strongly supports the improved publication of and access to clinical trial information described in the WHO Statement on Public Disclosure of Clinical Trial Results. Full trial information and results are needed for HTA agencies such as IQWiG to be able to provide appropriate and meaningful benefit assessments within their remit. As benefit assessments conducted by HTA agencies support evidence-based decision making in health care systems, improved access to clinical trial data is in the interest of public health. Previous research has shown that trial data so far publicly available are often insufficient to provide a complete and unbiased picture of a given health care intervention (see citations below). Therefore		

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	HTA also needs additional independent and high-quality data sources. HTA performed by IQWiG and other agencies specifically aims to describe comparative effectiveness. The methodology used by HTA requires • information on all trials conducted with the intervention under assessment • full information on clinical trial methods, e.g. for risk of bias assessment • full information on clinical trial results, e.g. for meta-analysis • extended information on patient populations included in clinical trials In addition, comparative effectiveness research increasingly uses indirect comparisons. For this type of analysis, full information on study methods (including, e.g., operationalization of study endpoints) and on patient populations is required to allow the assessment of similarity assumptions for studies included in a network for indirect comparisons.		
Page 1, line 10-11	“However, concerns have been raised that there may be selective publication of trials dependent on	However, there is a well-established association between the publication of trials and the nature	

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	their results" The wording seems rather cautious – numerous analyses have shown that there is a well-established association between the publication or non-publication of a trial (or outcomes of published trials) and the nature of the trial results.	of results; trial results viewed as "negative" are less likely to be submitted, or accepted, for publication in the scientific literature or made public in other ways [1, 2]. In addition, published trials are often affected by selective outcome reporting [3].	
Page 1, line 13,14	"Notification of trials to clinical trial registries has become more widespread"" This is also due to mandatory registration in ClinicalTrials.gov following the FDA-AA Amendments Act. We suggest including the citation.	Notification of trials to clinical trial registries has become more widespread, which is also due to legal requirements [4], ……	
Page 1, line 25-28	To be able to compare new treatments to currently available treatments (e.g. using indirect comparisons) and thus to determine the best available treatment in current health care, not only the full results of future trials are required, but also the results of all past trials on treatments in current use. The statement therefore should also call for full reporting of all results from all trials on all interventions in current use.	The aim should therefore be to make available all results from all past trials on interventions in current use, as well as all results from all future trials.	
Page 2; line 33-36	The date of actual study completion ("last subject last visit") is an important date for users as it indicates that study results can soon be expected. It therefore should be specified within which period	The date of actual study completion should be updated within 3 months of study completion.	

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	this date should be updated.		
Page 2, line 37 - 52	Journal publications do not seem to be the most appropriate reporting format of clinical trials any more. Research has shown that journal publications only include very limited information on study methods and results [5-8]. Similar limitations have been shown for trial (results) registries [6-9]. The primary reporting format should be the full clinical trial protocol (including any amendments and analysis plans), the full clinical study report according to ICH E3 (where available), and a standardized full presentation of all trial results in a database. These materials should be available within 12 months after study completion (also defined in the WHO statement as “last subject last visit”).	Reporting timeframes for clinical trials and information required Clinical trial information (methods and results) is to be reported within 12 months of the study completion date as defined above. Reporting should include the following: - the full clinical trial protocol (including any amendments and analysis plans) - the full clinical study report according to ICH E3 (where available), and - a standardized full presentation of all trial results in a database (see Footnote 4 below for the minimum results data set) This data set for study information should be extended to include links to any journal publications of the trial when these become available.	
Page 2; line 44-47; Footnote 4 on Key outcomes	Registration of study outcomes should not be restricted to primary and secondary outcomes. Tertiary outcomes can often also be relevant for the assessment of an intervention (e.g., health-related quality of life or other patient-reported outcomes are often defined as tertiary outcomes in clinical trials).	Minimum results data set: participant flow, baseline characteristics, concomitant diseases and concomitant medication, all outcome measures (including primary, secondary and other outcome measures), all adverse events, withdrawals due to adverse events, and serious adverse events; any pre-specified subgroup analyses.	
Page 2; line 44-	It is not stated that the trial registry entry should	If trial information is provided in sources other	

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47	include links; in our opinion this should be specified.	than the trial registry, the clinical trial registry site record should be linked to the corresponding documents (e.g. relevant journal publications).	
Page 3, line 67	We suggest extending the reference list	(see citations above)	
Additional comment	The statement does not contain information on how the described requirements will precisely be implemented. For example, we recommend that the ICTRP Search Portal requires that the clinical trial registries listed in the Portal endorse the statement; this could be achieved by extending the WHO Registry Criteria.	WHO Registry Criteria Primary registries in the WHO Registry Network will:….. - endorse the WHO Statement on Public Disclosure of Clinical Trial Results - implement the technical requirements for publishing clinical trial results by XX/XX/2015.	

References

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4. Food and Drug Administration. *Clinicaltrials.gov protocol registration system: US public law 110-85. 2010. http://prsinfo.clinicaltrials.gov/fdaaa.html*. 11.2013 11.03.2014]; Available from: http://clinicaltrials.gov/ct2/manage-recs/fdaaa.
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