

21 August 2007

Dear Dr Tamber,

Thank you for this opportunity to provide suggestions for the revision of the Declaration of Helsinki. Besides being the regional editor of the Croatian Medical Journal, I am also leading the Ottawa group on trial registration – <http://ottawagroup.ohri.ca>

Attached please find the Ottawa group recommendations for the revision of the Declaration of Helsinki.

I hope that WAME will include the trial registration requirement in its official recommendations, considering that since July 2005 it has been advising its member editors to require prior registration of all trials published in their journal when suitable registries are available. In the meantime not only have suitable registries become available, but the WHO trial registration platform has been creating the network of registries. Furthermore, it established the global portal. These efforts are part of the WHO International Standards for trial registration, <http://www.who.int/ictip/en/>, developed by WHO in 2006.

The WHO international standards have been supported by the ICMJE, and numerous other medical journal editors.

If you have any questions, or need any additional information, please feel free to contact me. I would appreciate to learn about the WAME recommendations.

Thank you for your attention,

Sincerely

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Recommendations regarding the Sixth Revision of the Declaration of Helsinki

Introduction

Subjects entering clinical trials do so with a mixture of motives, but they share two related expectations regarding the common good and knowledge management. They expect that the information provided to them at the time of recruitment will be based on the entirety of the knowledge base at that time, and they expect that the knowledge gained from their experiences will be available to guide others.

An increasing body of research leads to the conclusion that such expectations are ill-founded. For references please consult the <http://ottawagroup.ohri.ca>. An increasing atmosphere of commercialisation and competition has led to selective and incomplete publication, incomplete knowledge of past and ongoing related research, and an inability to optimally synthesise knowledge into unbiased practice guidelines. Although a failure to publish has been described as scientific misconduct, the problem persists.

These issues are currently addressed in paragraphs 16 and 27 of the DOH, referring to disclosure and publication respectively.

These issues have been addressed concurrently by the drive for mandatory clinical trials registration, a work in progress, in which details of clinical trials would need to be publicly disclosed in an internationally approved and accessible database prior to commencement of recruitment and as a condition of regulatory and ethical approval and for publication. We have spearheaded this initiative in conjunction with the World Health Organisation (WHO) and the International Committee of Medical Journal Editors (ICMJE). The process is evolving as more journals and ethics committees adopt the concept, while the WHO has set minimal standards for and coordinated such databases (registries) by the International standards, launched in May 2006. Both the scope of human research covered and the degree of disclosure continues to evolve. The Ottawa Group recommends that all trial documents be disclosed together with results and publications once available – <http://ottawagroup.ohri.ca>. Ideally this should include the complete data set for use in systematic reviews and hence clinical guidelines, as well as pooled analyses of safety data.

There is an ethical obligation to both subjects and to society to ensure that the design, details, data and results of all medical research are publicly available and accessible through publication, disclosure and deposition in an internationally approved registry.

The Ottawa group Recommendations for the revision of DOH

1. Add the prospective registration of trials to item # 16. Details are defined by Ottawa Statements (<http://ottawagroup.ohri.ca>) and by the International Standards for Trial Registration launched by the WHO, supported by the ICMJE- the International Committee of Medical Journal Editors.

We propose that the revised item # 16 reads:

“Every medical research project involving human should be preceded by careful assessment of predictable risks and burdens in comparison with foreseeable benefits to the subject or to others. Such an assessment should be based on the systematic review of literature on the issues under study. This does not preclude the participation of healthy volunteers in medical research. The design of all studies should be publicly available, and selected trial elements should be registered prior to the onset of the recruitment in accordance with the international standards, launched by the WHO in 2006.”

2. Add the registration and public disclosure of the cleaned, meaningfully coded, anonymised, and unidentifiable individual participant level dataset to the item #27. Individual data can be disclosed as per the Health Insurance Portability and Accountability Act, and EU standards. This proposal is in accordance with the Ottawa statement p3, and with the Budapest and Berlin declarations of access to research results.

We propose that the revised item # 27 reads:

“Both investigators and publishers have ethical obligations. In publication of the results of research, the investigators are obliged to preserve the accuracy of the results. Negative, neutral, as well as positive results should be published or otherwise made publicly available. This should include a summary of results, publications when available, and the unidentifiable individual participant level dataset. Sources of funding, institutional affiliations and any possible conflicts of interest should be declared in the publication. Reports of experimentation not in accordance with the principles laid down in this Declaration should not be accepted for publication.”

3. Also we suggest that the word “subject” is replaced by the word “study participant”.

Respectfully submitted,

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20th August 2007