

Recommendations on Unreasonable Confidentiality/Non-publication Clauses: Art 7.6

The following outlines the thinking of the Working Committee regarding a corollary issue to the recommendations on investigator's/REB's TCPS duty to share new information that arises in the clinical trials setting (new article 7.5). Before turning to the corollary issue, it should be noted that much of the literature agrees that an investigator's duty to share new risk information on a timely basis is grounded on a paramount concern for patient safety, autonomy, informed consent, associated principles of doing no harm, a researcher's fiduciary duty and/or the principles of scientific integrity. Many also agree that the duty is overriding – that is, it tends to override contractual agreements that prevent the sharing or reporting of risk information.

To complement the Working Committee's recommendation for a clearer and more explicit investigator's duty to share information via a new article 7.5 in the TCPS, an important question arises: should the TCPS also directly address so-called “gag rules” – that is, confidentiality clauses or publication bans in industry/researcher contracts, which have come into prominence in recent years, as illustrated by the Olivieri affair?

After considering the rationales for and against doing so, the Working Committee recommends that the TCPS directly address this issue. Doing so would further the rationales behind an investigator's and REB's duty to share information, and would be directly responsive to recommendations in some of the Olivieri reports. It would provide important guidance to investigators, REBs and universities addressing such issues. It may contribute to policy development by other players such as government regulators and industry. Doing so would also likely enhance participants' welfare, rights and safety.

I. Existing TCPS Guidance

The existing guidance on this issue is found in the commentary to the Clinical Trials section. As the following excerpt indicates, the TCPS notes related issues and encourages researchers and REBs to resist efforts to hamper communications.

TCPS, Clinical Trials, Section 7, Subsection E

E. Analysis and Dissemination of Results of Clinical Trials (TCPS, p.7.5):

In many clinical trials, the sponsors obtain contractual rights to the initial analysis and interpretation of the resultant data. Researchers and REBs must ensure, however, that final analysis and interpretation of such data remain with the researchers, whose duty it is to ensure the integrity of their research....

Equally important, though sometimes difficult to achieve, is the researchers' duty to disseminate the analysis and interpretation of their results to the research community. Unfortunately, negative results and outcomes of research frequently are not published or disseminated. Silence on such results may foster inappropriate and potentially harmful clinical practices or needless and wasteful duplication. Researchers and REBs may exert pressure to alleviate this deficiency in the dissemination of research results by resisting publication bans proposed in research protocols, on the basis of ethical obligations of truthfulness and the integrity of research.

II. Points of Convergence and Commentary from Selected Reports

Our analysis of the different reports that have responded to the Olivieri affair indicate the following points of convergence. One of those points is that confidentiality clauses and publication restrictions may be acceptable, if they contain reasonable, justified, and not absolute restrictions.

- Primacy of patient safety and ensuring continuing consent
- Duty to disclose risks/information in the clinical trial setting
- Dissemination of research results to the scientific community
- Confidentiality clauses: acceptable if limited in time and scope
- Role of REBs: with respect to contracts
- Institutional support.

Excerpts from relevant related Canadian commentary on publication restrictions/confidentiality clauses:

CAUT Report, 2001

1..... Certain circumscribed confidentiality restrictions may be appropriate, for example, those pertaining to information on the chemical structure, or synthesis of a drug, or its method of encapsulation. ... Restrictions on disclosures of risks to patients are not appropriate.

Naimark Report, 1998 (Statements or Recommendations)

Part II *Introduction: University policies on contract research and conflict of interest* "...recognize both the primacy of the principle of free communication of research findings and the legitimate interests of industrial sponsors in protecting commercially valuable intellectual property." These two conflicting interests can be reconciled by providing a delay in publication sufficient to give the sponsor the opportunity to seek patent protection. "The University's policy states that the delay should never be longer than 12 months."

The Hospital for Sick Children Research and Policy Review Task Force Report, 1999

3.1.3: "The confidentiality provisions in contracts should be proportionate to the need for confidentiality."

3.1.4: "Contracts should include a provision which specifically allows the Hospital's REB to share and discuss information relating to multi-centre trials with other REBs reviewing the same protocol."

III. Selected Provisions from International Documents

A selected survey of leading international documents was conducted to collect relevant provisions regarding publication limitations and confidentiality clauses. They indicate that some of the documents address publication bans in a manner similar to the current TCPS, but with perhaps more force. We have identified two international policies that address the confidentiality clauses of investigator contracts, as done by Canadian reports in recent years. The International Conference on Harmonization and the new Directive on Clinical Trials from the European Union are silent on the issue. The U.S. FDA needs to be confirmed.

World Medical Association, Declaration of Helsinki, 1964, as revised and clarified in 2002

27. Both authors and publishers have ethical obligations. In publication of the results of research, the investigators are obliged to preserve the accuracy of the results. Negative as well as positive results should be published or otherwise publicly available. Sources of funding, institutional affiliations and any possible conflicts of interests 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.

Council of Europe, *Additional Protocol to the Convention on Human Rights and Biomedicine Concerning Biomedical Research* (2005)

“Art. 28 Availability of results

... 3. The researcher shall take appropriate measures to make public results of research in reasonable time.”

The scope and intent of this article is discussed in the *Explanatory Report to the Draft Additional Protocol to the Convention on Human Rights and Biomedicine Concerning Biomedical Research* (2004).

Article 28 Availability of results

135. Accountability is implicit in the relationship between the researcher and the participant. For this reason, this Article requires that the conclusions of the research be made available on request to research participants in a form comprehensible to them.

136. The Article requires researchers to submit a summary or report of the research to the ethics committee or competent body, and *to make public the results of their research even if the outcome is negative. Such results must be published or made otherwise available in a manner accessible to other researchers. The aim of the Article is to prevent the needless repetition of research using persons due to the non-publication of previous results, and to prevent the suppression of negative or positive results for commercial or other non-scientific reasons. It is stated that this be done “in reasonable time” so as to not prejudice a patent application or scientific publication. This obligation to publish cannot be restricted by contractual obligations* (emphasis added). However, under the terms of Article 26, paragraph 1, of the Convention, the obligation to publish research results would be waived if publication would potentially compromise, for example, public health or safety or the rights and freedoms of others. An example of such research could be that concerning counter-measures to the use of biological weapons, the publication of which could compromise public safety.

World Health Organization, *Operational Guidelines for Ethics Committees that Review Biomedical Research, TDR/PRD/ETHICS/2000.1, Geneva* (2000)

6.2 Elements of the Review

The primary task of an EC lies in the review of research proposals and their supporting documents, with special attention given to the informed consent process, documentation, and the suitability and feasibility of the protocol. ECs need to take into account prior scientific reviews, if any, and the requirements of applicable laws and regulations. The following should be considered, as applicable:

6.2.1 Scientific Design and Conduct of the Study

...

6.2.1.8 The manner in which the results of the research will be reported and published; ...

International Committee of Medical Journal Editors (ICMJE), *Statement on Conflicts of Interest* (2001)

Scientists have an ethical obligation to submit credible research results for publication. As the persons directly responsible for their work, researchers should not enter into agreements that interfere with their access to data independently, to prepare manuscripts and to publish them.

Pharmaceutical Research and Manufacturers Association (United States), *Principles on Conduct of Clinical Trials and Communication of Clinical Trial Results*, (2002)

Sponsors commit to “... not suppress or veto publications or other appropriate means of communication (in rare cases it may be necessary to delay publication and/or communication for a short time to protect intellectual property)...”

American Association of Medical Colleges/Baer I, Feiler ME, Regulski A, Switzer SS. *Clinical Trial Contracts: A Discussion of Four Selected Provisions*, (2004, pp. 7-8)

Publication is necessary for the Academic institution to fulfill its academic mission and disseminate the fruits of research. Research integrity is the cornerstone of the academic endeavor, and Academic institutions must demonstrate that research is being conducted in an unbiased manner, irrespective of the funding source... Some argue that research on human subjects that is not published is unethical; first, by needlessly exposing subjects to risk without benefit to general knowledge and second, by risking exposure of others because the research results are not available.

IV. Basic Options and Points to Consider for Framing a Recommendation

The Working Committee identified at least three options for addressing confidentiality and publication clauses within the current section 7 of the TCPS. They include (i) preserving the status quo; (ii) amending the existing commentary; or (iii) adopting a new article that addresses the matter. The merits of the issues and developments since 1998 persuaded the Committee to move beyond the status quo text of the TCPS in favour of the third option of a new article.

It was thus agreed that, consistent with the themes from the Olivieri reports noted in section II above, amongst the points to be included in a new TCPS article and accompanying commentary are the following:

- That confidentiality clauses or publication bans that impose absolute or unduly broad limitations should be presumed to be ethically unacceptable; and
- That institutions and REBs should develop an explicit written policy on confidentiality and publication bans affecting clinical trials