**June 14, 2013**

**To the World Medical Association Secretariat:**

The following are the comments from the Executive Committee of the Latin American and Caribbean Network of Bioethics UNESCO[1] to the draft of the proposed modifications to the Declaration of Helsinki submitted for public consultation.

Sincerely,

Victor B. Penchaszadeh, MD
President

## 1 – General considerations

1.1. It is sad to note that the trend of weakening of the Declaration of Helsinki, which has taken place over the last revisions, is continuing in force in the proposed modifications. As we observe in the following paragraphs of this commentary, provisions to protect the rights of research subjects have been significantly watered down. At the same time, obligations of researchers and sponsors are been relaxed. This two-way trend is seen in the flexibilization of the use of placebos, the relaxation of the requirement of informed consent for studies on biological specimens, the post-trial benefits for participants and their communities, and others. Any intelligent observer will see the pressures from the pharmaceutical and biotechnology industries behind many of the proposed modifications.

1.2. It is of note that precisely because of the flexibilization in the use of placebos and the lack of commitment with research participants at the end of trials on the part of researchers and commercial sponsors, countries like Brazil and Uruguay have ceased to rely on the Helsinki Declaration as ethical normative in research. The Latin American and Caribbean Network of Bioethics UNESCO reaffirms its commitment to the preservation of ethical principles enacted in the Universal Declaration of Bioethics and Human Rights and its recommendation to our member countries to enact their own rules of conduct in the field of research ethics.

1.3. We find improper that a draft document produced in a process that took 18 months, be given only 2 months of public consultation. Furthermore, we find improper that English be the only language in which the draft is written and the comments are accepted, in spite (a) that the WMA has three official languages (English, Spanish and French), (b) that the document is short and (c) that the WMA counts with official translators. Both improprieties have no justification, particularly since the next meeting of the WMA Council will take place only in April 2014.

1.4. While we are in disagreement with the annotated weakening trend of ethical guidelines of the Declaration of Helsinki and the pitfalls of the revision process, we proceed in the following paragraphs to make specific observations and suggestions for improvement of the proposed modifications.

[1] Disclaimer: The opinions expressed in this document are of the exclusive responsibility of the Executive Committee of the Latin American and Caribbean Network of Bioethics UNESCO, and not necessarily reflect the opinions of UNESCO and in no way express its official policies.

**2 – Specific comments**

**2.2. Proposed paragraph 5**

Given that in Latin America it is costumary that participation in research is offered by physicians who also provide medical care for participants, we propose an additional sentence (underlined), meant to monitor this practice and avoid coercion.

*"The physician may combine medical research with medical care only to the extent that the research is justified by its potential preventive, diagnostic or therapeutic value and if the physician has good reason to believe that participation in the research study will not adversely affect the health of the patients who serve as research subjects. Extreme care must be taken to avoid abuse of this option and the research protocol needs an exhaustive revision by ethics committee."*

**2.3. Proposed paragraph 15**

We would like to see more precision in the provision of this paragraph, specifying that "adequate treatment" should adhere to proven and effective therapies.
The suggested wording includes an inserted text (underlined):

*"Adequate compensation and treatment with proven and effective therapies for subjects who are harmed as a result of participating in the research must be ensured".*

**2.4. Proposed paragraph 16.**

We suggest the insertion of the word *clearly* (underlined):

*"In medical practice and in medical research, most interventions involve risks and burdens.*
*Medical research involving human subjects may only be conducted if the importance of the objective **clearly** outweighs the inherent risks and burdens to the research subjects".*

**2.5. Proposed paragraph 18.**

The obligation must be strengthened substituting the word ***must*** (underlined) for *may*.

*"Physicians **must** not participate in a research study involving human subjects unless they are confident that the risks involved have been adequately assessed and can be satisfactorily managed. Physicians must immediately stop a study when the risks are found to outweigh the potential benefits or when there is conclusive proof of positive and beneficial result"s*

**2.6. Proposed paragraph 30.**

We suggest strengthening the provision by adding a last sentence (underlined):

*Research involving subjects who are physically or mentally incapable of giving consent, for example, unconscious patients, may be done only if the physical or mental condition*

*that prevents giving informed consent is a necessary characteristic of the research population. In such circumstances the physician should seek informed consent from the legally authorized representative. If no such representative is available and if the research cannot be delayed, the study may proceed without informed consent provided that the specific reasons for involving subjects with a condition that renders them unable to give informed consent have been stated in the research protocol and the study has been approved by a research ethics committee.*
*Consent to remain in the research should be obtained as soon as possible from the subject or a legally authorized representative.*
***Extreme care must be taken to avoid abuse of this option and such cases must be reported to the ethics committee.***

**2.7. Proposed paragraph 32**

The proposed changes introduce an unacceptable relaxation of provisions of current p. 25, namely that (a) the requirement of informed consent for collection of human samples is annulled; (b) by only requiring informed consent for identifiable samples, it reduces the ethical issues to an individual problem of donor identification, neglecting to address the major issue of benefit sharing of samples flowing from poor to rich countries; (c) attaching the term "normally" to the requirement of informed consent implies that there may be situations in which it may not be required. Furthermore, since researchers may include professionals other than physicians, the appropriate term to refer to them is **"*researchers*".**

The use of biological samples in repositories and biobanks requires special ethical treatment with the perspective of justice and human rights, given the strong asymmetries between poor and rich countries, that allow the latter to obtain patents whose royalties the former will have to pay. In order to avoid abuse and conflict with ethics committees, particularly in view of the proliferation of commercial enterprises, it is preferable to eliminate the provision of "exceptional circumstances", knowing that informed consent should not be an obstacle for research.

Suggested writing for proposed p. 32:

*"For medical research using identifiable human material or data, such as research on material or data contained in biobanks or similar repositories, researchers must seek consent for its collection, analysis, storage and/or reuse".*

**2.8. Proposed paragraph 33**

For the past five years, the Latin American and Caribbean Network of Bioethics UNESCO has taken the position and argued publicly that the relaxation of the restriction for the use of placebos (Seul, 2008) amounts to condoning an unethical double standard differentially applicable to countries and populations according to their socioeconomic status. The new language does not improve the situation and continues to use words that are either confusing (such as "compelling") or redundant (such as "scientifically sound") which leave the door open to widely diverse interpretations by researchers and sponsors. There is no doubt in our minds that in this paragraph the WMA has yielded to the pressure of the pharmaceutical industry and the regulatory agencies of rich countries that put the earnings of big corporations above the health needs of the people.

**We suggest the following wording of proposed paragraph 33:**

*"The benefits, risks, burdens and effectiveness of a new intervention must be tested against those of the best proven intervention(s), except in the following circumstances:*

*"The use of placebo, or no treatment intervention is acceptable in studies where no current proven intervention exists; or*

"*the patients who receive any intervention less effective than the best proven one, placebo or no treatment, will not be subject to any additional risks of harm more than minimal as a result of not receiving the best proven intervention; or*

*"the placebo will be added to the best proven intervention, without any significant increase in the risk for patients.*

*"Extreme care must be taken to avoid abuse of this option".*

**2.9. Proposed paragraph 34.**

The proposed wording of this paragraph unfortunately restricts the provisions of current p. 33, which asserts the rights of participants to "share any benefits" that result from the study, substituting it by the "post-trial access for all participants who still need an intervention identified as beneficial in the study". In current p. 33 the latter is only an example of possible benefit entitlements, which may also include "other appropriate care or benefits" (such as commercial benefits, patents, etc) , which is clearly more inclusive.

**Suggested wording:**

*"At the conclusion of the study, patients entered into the study are entitled to be informed about the outcome of the study and to share any benefits that result from it, for example, access to interventions identified as beneficial in the study, patents, and other benefits. This arrangement should be defined before the study starts, in a benefit-sharing agreement".*

**Additional comment and suggested new paragraph**

When in the course of a particular study, researchers or sponsors decide to collect biological specimens to study biomarkers, genes or similar elements, they should not present the collection as a "substudy", but instead they should develop an independent research protocol, in which it should be demonstrated that it is a specific research with specific objectives and not simply a collection of specimens for repositories or biobanks for undefined future uses. Furthermore, it should be made explicit that no samples, whether isolated or anonymized in a pool, or data dervived from the samples will be used for commercial or for profit purposes.

**2.10. Proposed paragraph 36.**

We suggest to strengthen this paragraph with the following additions (underlined):

*"Researchers, authors, sponsors, editors and publishers all have ethical obligations with regard to the publication of the results of research. Protocol studies lacking publication planning details, and/or claiming data exclusive property by sponsors, should be rejected by research ethics committees. Authors 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. They should adhere to accepted guidelines for ethical reporting. Negative and inconclusive as well as positive results should be published or otherwise made publicly available, both as elaborated and raw data. Sources of funding, institutional affiliations and conflicts of interest should be declared in the publication. Reports of research not in accordance with the principles of this Declaration should not be accepted for publication".*

**2.11. Proposed paragraph 37.**

We suggest to strengthen the obligation by deleting "Where possible" and substituting "must" for "should", as follows:

*"In the treatment of an individual patient, where proven interventions do not exist or have been ineffective, the physician, after seeking expert advice, with informed consent from the patient or a legally authorized representative, may use an unproven intervention if in the physician's judgement it offers hope of saving life, re-establishing health or alleviating suffering. ~~Where possible, t~~**T**his intervention ~~should~~ **must** subsequently be made the object of research, designed to evaluate its safety and efficacy. In all cases, new information should be recorded and, where appropriate, made publicly available.*

**3. Final remarks.**

As we state at the beginning of this commentary, we see a trend of weakening of the Declaration of Helsinki taking place over the last revisions, and continuing in force in the proposed modifications. As we observe in the precedent paragraphs of this commentary, provisions to protect the human rights and wellbeing of research subjects have been significantly watered down. At the same time, obligations of researchers and sponsors are been relaxed (as in the use of placebos, the requirement of informed consent for studies on biological specimens, and the post-trial benefits for participants and their communities). Any intelligent observer will see the pressures from the pharmaceutical and biotechnology industries behind many of the proposed modifications.

It is of note that precisely because of the relaxation of the rules for the use of placebos and the condoning of the lack of commitment with research participants at the end of trials on the part of researchers and commercial sponsors, countries like Brazil and Uruguay have ceased to rely on the Helsinki Declaration as ethical normative in research. The Latin American and Caribbean Network of Bioethics UNESCO reaffirms its commitment to the preservation of ethical principles enacted in the Universal Declaration of Bioethics and Human Rights.

Sincerely,
Victor B. Penchaszadeh, MD
President,
On behalf of the Executive Committee of the Latin American and Caribbean Network of Bioethics UNESCO