ORDEM DOS MÉDICOS

WORLD MEDICAL ASSOCIATION

DECLARATION OF HELSINKI

Ethical Principles for Medical Research Involving Human Subjects

Comments on the draft version for Public Consultation

Portuguese Medical Association

The Portuguese Medical Association (PMA) congratulates the working group of the World Medical Association (WMA), which now presents for public consultation the proposed revision of the Declaration of Helsinki (DoH), for the excellent work done in the reorganization and restructuring of the entire document making it clearer.

The PMA is also in consonance with the strengthening of the principles on the protection of vulnerable groups, the establishment of a compensation for the protection of participants in trials, the achievement of more specific requirements and precise agreements on post-test, in strengthening the quality and transparency of Ethics Committees, among other changes produced.

Without prejudice to the merits of the work of the WMA and by that working group, we believe that the document can be improved with respect to:

- paragraph 15, concerning the rights that must be provided to participants in studies and trials;
- paragraph 25, regarding the informed consent and to a greater explicitness of information and consent when the placebo is used in clinical trials;
- paragraph 33 which deals with the use of placebo;

The text under analysis refers to be provided compensation and treatment for individuals who suffer damage by participating in investigations. Based on the principle of justice underlying all clinical research, we believe that it must be established that all participants can enjoy the benefits that result from a trial, at least for a period of time set previously.

Moreover, our proposal goes towards making absolutely clear what is acceptable in research done on humans when is used placebo control or when is not offered the best treatment available.

Fact is that the clinical trials using placebo has always been controversial especially when participants were randomly referenced to receive placebo and had no effective treatment.

As an alternative to a more orthodox position in which it argued that the placebo should be prohibited when there is an effective therapy, should be defended that the use of clinical trials with placebo are allowed only when:

- the methodological reasons for its use are convincing;

- an evaluation strictly ethical has made clear that participants who receive placebo will not be subject to serious damage, irreversible morbidity or disability, or who may suffer severe damage even if it is reversible or a severe discomfort.

Moreover, the placebo can only be used when procedures are adopted to minimize the risks associated with that use.

The use of placebo is therefore to be determined by its demonstrable need and for no alternative design of the trial concerned.

Among the criteria that the use of placebo must obey, **we highlight the information to be provided to participants by the investigators to be the most complete and comprehensive as possible so that informed consent be obtained after an exhaustive process of clarification**. Participants must **know the risk levels**, **understand the potentially involved damage** so they can make informed decisions effectively.

Bearing in mind what has been said it is proposed that the text underlined shall complement paragraph 15:
"*Adequate compensation and treatment for subjects who are harmed as a result in participating in the research must be ensured and it should be provided for free to all participants the beneficial treatments that results from the trial, over a period of time set in advance for each trial*."

It is also proposed to complement the paragraph 25 with the underlined text:

"*Participation by competent individuals as subjects in medical research must be voluntary. Although it may be appropriate to consult family members or community*
leaders, no competent individual may be enrolled in a research study unless he or she freely agrees. When the research involves the use of a placebo or other control different from the best proven current intervention, potential subjects

must be informed of the implications for participants assigned to each of the different study arms, including the risks of not receiving a known effective intervention.

As to paragraph 33 regarding the use of placebo, we sustain that the first part must be maintained under the terms of the document, plus the underlined phrase:

"*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 intervention is acceptable in studies where no current proven intervention exists; or
Where for compelling and scientifically sound methodological reasons the use of any intervention less effective than the best proven one, placebo or no treatment is necessary to determine the efficacy or safety of an intervention and the patients who receive any intervention less effective than the best proven one, placebo or no treatment will not be substantially more likely than those in the active-treatment group to die; to have irreversible morbidity or disability; to suffer reversible but serious harm; or to experience severe discomfort as a result of not receiving the best proven intervention."

As a minor changing of words we also suggest, in paragraph 32 the replacement of "*normally*" by "*whenever possible*".