From Helsinki to Fortaleza: a bled *Declaration*

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Abstract

The original *Declaration of Helsinki* (1964) has been subjected to numerous revisions and reformulations, supposedly necessary to keep apace with medical progress, but in fact leading to its loss of stability and authorit**y**. The Edinburgh 2000 revision made provisions for increased tolerance in the use of placebos, and loss of commitment to assure post-investigational benefits to individuals and communities involved. In spite of Argentina's and Brazil's manifest opposition, a double standard for research ethics became a *de facto* reality which has increasingly weakened the Declaration. Corporative interests of major stakeholders –researchers and sponsors- have been strongly supported as the Declaration becomes less protective of individuals and communities involved. It is therefore suggested that Latin American bioethicists would be well advised to develop a regionally pertinent normative in accordance with our social reality and the need of protecting our population.

Key words: Declaration of Helsinki. Ethics, research. Protection.

Resumo

De Helsinki à Fortaleza: uma declaração dessangrada

A *Declaração de Helsinki* de 1964 vem sendo submetida a numerosas revisões e emendas, sendo a mais recente a de Fortaleza (2013). A frequência dessas reformulações tem sido considerada necessária, dados os avanços da medicina contemporânea, mas também criticada por conferir pouca estabilidade e autoridade ao documento. A versão de Edimburgo (2000) marcou a política de tolerância ao uso de placebo e de escasso apoio aos benefícios pós-estudo aos sujeitos e à comunidade, desestimulando os esforços da Argentina e Brasil para reforçar a proteção aos participantes dos estudos. Se aceita assim – *de fato* – o duplo *standart* em ética em pesquisa, que de forma progressiva debilita a Declaração como normativa ética para a pesquisa envolvendo seres humanos. A dominação cada vez mais acentuada de interesses corporativos de investigadores e patrocinadores sugere que a bioética latino-americana deve desenvolver seu próprio documento normativo, em respeito a nossa realidade social, voltado a proteção às comunidades da região.

Palavras-chave: Declaração de Helsinki. Ética em pesquisa. Proteção.

Resumen

De Helsinki a Fortaleza: una Declaración desangrada

La *Declaración de Helsinki* 1964 ha sido sometida a numerosas revisiones y enmiendas, la más reciente siendo Fortaleza (2013), una frecuencia considerada necesaria dado los avances de la medicina contemporánea, pero también criticada por restarle estabilidad y autoridad al documento. La versión de Edimburgo (2000) enfatizó la tolerancia al uso de placebos y restó apoyo de los beneficios post-estudio para los probandos y la comunidad huésped, pese a los esfuerzos de Argentina y Brasil por robustecer la protección de las personas incorporadas a los estudios. Queda aceptado – *de hecho* – el doble estándar en la ética de investigación que debilita la Declaración como normativa ética de la investigación con seres humanos. La dominancia acentuada de los intereses corporativos de investigadores y patrocinadores sugiere que la bioética latinoamericana debiera desarrollar su propio documento normativo, en respeto a nuestra realidad social, y enfocado a la protección de las comunidades de la región.

Palabras-clave: *Declaración* de Helsinki. Ética en investigación. Protección.

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Declares not to have conflict of interest.

It Is repeated with obstinate frequency that the Declaration of Helsinki (1964) was conceived as the indignant response to the atrocities of the German fascist regime (1933-1945) disguised under the euphemism "experimentation" biological. The same justification scores the Nuremberg Code which, indeed, was the immediate reaction to the horrors of the war, the concentration camps, the brutality and medical tortures. Scientists from the post-war protest, and rightly so, that it should not approve the condemnation of torture with research ethics. This explains why Nuremberg is a single, fixed, specific code, while the Statement, presented almost 20 years later, is purposeful, changeable and, in fact, revised in seven times, the most recent, but certainly not the last, being Fortaleza (2013).

The influence of the Statement has been decreasing, mostly injured by the FDA disaffiliated from it and decided to stick by the GCP (Guidelines for Good Clinical Practice). The cutoff point was the 2000 Edinburgh Review, tenaciously resisted by the delegations of Argentina and Brazil 1, that was swayed by proposals for a more flexible and permissive use of placebos in research involving human beings and an uncertainty of post-study benefits for participants.

In 2008, coinciding with the recent revision at the time (Seoul, 2008), the FDA (Food and Drug Administration) officially denied its support for the Statement and welcomed to the GPC that while pays homage to Helsinki, is more likely to respect corporate interests of the pharmaceutical industry and researchers at the expense of maximum protection of probands. FDA's stance was criticized as a move of dubious ethical value for its tolerance of the use of placebos, which would lead to the paradoxical conclusion that would be unethical to do researches in Africa, South America or Indonesia, and contrary to ethical standards in the U.S., Europe or Japan 2 and, a disappointing example for many nations 3 .

The review of the Declaration of Helsinki in Seoul (2008) was followed with great attention and generally criticized by strengthening ethically reprehensible positions by delineating and eventually ratifying the ethics of "double standard" 4 : A "aspirational" or maximum applied in more economically developed countries, and one or pragmatic context that downplays the ethical rigor to poor corruptible, less educated countries of "vulnerable" population in the sense of being "unable to defend their own interests " 5.6 . The Statement loses influence by progressive weakness of what is, or should be its nuclear purpose: recommend the welfare of research subjects [that] must always be protected and not suffer subordination to the interests of thirds 7 .

It deals with the paradox that the same researchers who denigrate Statement invest huge efforts to bring it to increasingly unfavorable reviews for the individual test and the host communities, strengthening, however, support for sponsors and investigators linked to transnational corporations and powerful institutions such as the NIH (National Institutes of Health) 8 . Helsinki is diluted and denigrated, distorted by the establishment of a factual [bio] ethics of human research based on protocols that in their country of origin would be ethically unacceptable.

In various opinions expressed against the impending revision of 2013 were put forward the same arguments that still remain unpaid: the use of placebos, the management of the control group of the existing best medical means vs. the locally available, the commitment post-study, the appropriateness that the researcher and the physician were the same person, the utilitarianism as relevant of an ethical research in general, to the Declaration of Helsinki in particular.

A regrettable extinction: therapeutic / non-therapeutic trials

The Declaration of Helsinki (1964) consists of a page, which the fourth paragraph reads: In the field of clinical research a fundamental distinction must be recognized between clinical research in which the aim is essentially therapeutic for a patient, and clinical research the essential object of which is purely scientific and without therapeutic value to the persons subjected to the research 9 .

The doctor, specifies the document, can combine research with professional care, in order to gain new medical knowledge, only to the extent that clinical research is justified by its therapeutic value for the patient 10, a distinction emphatically required by Hans Jonas 20 years before 11. The Statement underwent five revisions over 36 years, the Edinburgh (2000) preceded by a long debate on convenience, the urgency according to some, and the need for a thorough review, against the caution prompted by others concerned that these reviews could take a detour to improperly centered in efficiency and weaken the moral principles of the researcher committed to the research subject and the fair allocation of benefits and charges 12. The distinction between therapeutic and non-therapeutic study eventually disappeared, suffocated by the argument that the class of activities covered by the term "therapeutic

research" is in turn problematic because all clinical trials of therapeutic agents include some components that can be therapeutic (or intended as such) and others that are clearly non-therapeutic 13 .

The extinction of the original and explicit distinction between therapeutic and nontherapeutic clinical trials, led to two conclusions clearly increasing the vulnerability of patients enrolled as probands: 1) The "similarity position" that considers the ethics of the clinical research as merely a special case or the application of relevant clinical ethics of the medical practice, and the position of difference, whereby the research and the clinical practice are distinct activities with different goals - gathering of knowledge to benefit future patients vs. therapeutic benefit for the individual patient 14. In another publication, these same authors, promoting the difference between clinical ethics and research ethics, recognized that in independence of the motivations of the researcher, voluntary patients are at risk of seeing their well-being committed in the course of scientific research 15.

The dispute is hidden when using the phrasing of section 16 of the review of Fortaleza in 2013: Medical research that includes human subjects may only be performed if the importance of the objective outweighs the risks and loads to the research subjects 16 . For various reasons, it is an empty proposal, subject to arbitrary interpretations of what is an important goal, and the evaluation of risks and loads, that in no way ensures the protection of patients involved in clinical trials. The review of Fortaleza is the requiem to the Declaration of Helsinki 1964.

The review of Fortaleza

Why is the term "peoples" was replaced preferring to speak of "groups"? The deontic vocabulary (should, must, may) has a fluctuating and seemingly arbitrary use. In section "informed consent" is overridden "competent" by "capable of giving informed consent": Maybe in a hypercritical reading it could be argued that the "competition" is objectively measurable, being more comfortable talking about "the capacity of", which lends itself to a more subjective and biased assessment.

The reference to placebos (now n. 33) remains favorable to an interpretation by the researchers; the subtle change of "any risk of serious or irreversible harm" by "additional risk of serious or irreversible harm as a result of not receiving the best proven intervention" 16 creates a greater uncertainty when talking about risks - which are potential-instead of recognizing harmful side effects actually occurred. It is manifested, also, the difficulty to prove a direct causality of the harm by omission of the best medical means tested (should say existing).

The other point of contention regarding "post-study provisions" now refers to "provisions prior to the study for all participants" 16. There is no binding Statement that the probands would receive the benefits that are medically necessary for them, only a vague commitment to the participants still requiring an identifiable intervention study (n. 34) 16 is validated.

Reviewing the reviews

Unfinished the debate and their unsatisfactory results, Edinburgh (2000) were followed by two explanatory notes (Washington 2002, Tokyo 2004), and two reviews (Seoul 2008, Fortaleza 2013) and various explanatory notes, with a periodicity of five years, signaling that the Statement is constantly in the crosshairs of criticism and controversy:

The frequency with the Declaration of Helsinki has been revised - about every 6 years - is itself a problem ... This process of revision raises doubts about whether the Declaration's guidance is really well reasoned and authoritative; it encourages researchers not to take the Declaration seriously. Genuine ethical obligations do not change every few years 17.

Just proclaimed the first Declaration of Helsinki, it was recognized as a document that will remain controversial that, at very least and suddenly, proves the concern of the global medical profession by the ethical issues involved [on human experimentation] 9. It is an acknowledgment of the inefficiency and an invitation to reviews which have proved endless. Researchers committed to strengthening the position of a research ethics that replaces the clinical ethics when a patient is recruited as testing, have insisted on the need to review "bad" aspects of the Statement 18.

At the same time, the World Medical Association (WMA) recognized that studies on the use of zidovudine to prevent perinatal transmission of HIV infection, were creating pressure to correct the principles of research involving human subjects 19. The proposed revisions weaken the commitment to moral principle of the investigator with the research subject protection and reduce the rights of [such] subject. The utilitarian efficiency, together with the market values, is more prominent, and these values are applied to any socio-economic context 19.

It is possible that the Statement requires modernization ... but must keep their goals (to protect human subjects) and set an ideal standard 20; review which is contested on the grounds that ethical codes and guidelines should be very practical assertions of what researchers believe can and should do today 21. And must be utilitarian, in as much the utilitarianism is simply a method of ethical analysis that evaluates the ethical propriety of human conduct in relation to the anticipated consequences 21 .

Non lead, this is an overly utilitarian position of utilitarianism, in the sense of obviating all references to the definition and distribution of the utility and the costs which means to get it. In sum, the recent update of the Declaration of Helsinki shows a similar pattern to the others, resolving a few issues raised in earlier versions, introducing minor semantic variations without clarifying controversial points, continuing to weaken the protection of probands, individual and collective, and choking those who continue in the struggle to ensure their autonomy.

Fallen trees, burnt forests

The process of construction / deconstruction of the Declaration of Helsinki is a desolate field of debilitating disputes and lost battles that have wrecked efforts to regulate the [bio] ethics of the research with human beings in a respectful manner of the weakest and regulative of the insatiable corporate interests. The WMA is proud to revise [their] documents regularly, modifying them when it seems appropriate to address current and future challenges. The Declaration of Helsinki is, therefore, a living document that has been adapted over time in response to the developments in medical research 22. More than justify flexibility and present, the impression remains that the frequency of these reviews are due to external pressures and denotes a process of heteronomy weakness and unresponsive to new developments in biomedicine, as alleged, but a reformulation of issues which remain under controversy and tensions that are resolved inadequately and temporarily.

In the mentioned article, whose authors are members of the working group World Medical Association Declaration of Helsinki, insist in the public consultation process to discuss the draft of the revised and the convening of eminent bioethicists, whose recommendations, however, are partially adopted, to the point of retaining many flaws - and contradictions - ... and add new faults 23. As a result, the new Statement is likely to lead to further discussions by certain sponsors research ... [leading] to significant stakeholders [interest groups] to preferentially adhere to earlier versions of the Declaration, to obviate the confrontation with certain provisions included in recent versions 24.

Disturbing is the comment posted just a month after the filing of Fortaleza 2013 review, subtitled Progress but Many Remaining Challenges Remaining - whereby missing to acknowledge the possibility of obviating the informed consent in some cases of research with competent adults, develop advice to obtain "broader" consents for future use of biological material, noting that they are limiting barriers for the science the efforts to protect research in subjects unable to consent to studies not related to their impairment, and as it would be inconsistent the objections to studies "not beneficial" when the net risks to the interests of the participant are low and the benefits to society large enough 25. The text continues by noting that the Declaration is confusing and wrong as far as vulnerability and adequate protection concerns 25 and suggests the need to revise paragraph 34 regarding post-study benefits and paragraph 33 concerning placebos. Faced with an agenda as proposed, it is feared that a new and even more prompt review messes even more the autonomy and protection of probands and populations declared "vulnerable".

In short, the status of the Statement is changing, its status goes into decline, the immediate reaction to the latest revision recognizes as unresolved the outstanding issues and adds new points of debate, being very sensitive, necessarily leading to lengthy discussions and continuing the process of destabilization of the Statement, conditioning and neutralizing even more the efforts to protect the probands and subordinate, as it should be, the clinical ethics to the research ethics, assuming accepted, at least the fact, the double standard of ethics of clinical research.

Translation to Spanish

Forty-eight hours after the publication of the recent revision of the Statement, the Spanish translation appears, causing immediate alarmed reaction of Luis Justo, who sends a brief e-mail entitled "Watch Out Latin America: Grave mistranslation of the Helsinki 2013 to Spanish": when no proven intervention exists that is misrepresented to Spanish as "When there is an unproven intervention." Following his suggestion that the Spanish version "is badly translated, very poorly translated", you may find, in-

deed, at least 50 translated excerpts which are imprecise or incorrect, such as: developed = "Promulgated" rather than developed, each paragraph = "A paragraph" instead of each paragraph, burden = "Costs" instead of loads, sponsors = "Sponsors" instead of sponsors; patients who serve as research subjects = " patients as part of the investigation, "rather than patients who serve as research subjects; repositories = "Like tanks" instead of repositories; Individual research subjects = "The person involved in the investigation," instead of individual research subjects.

Perhaps it is not the place to evaluate the translation commits trivial errors or euphemistic interpretations, but only to show arbitrary semantic which correction may differ from the one suggested here, but does not deny that the Spanish version is improper. The original document is far from a stylistic delicacy, but the translation is even more defective in that regard.

Final Thoughts

This paper does not intend to discuss the conceptual content of the recent Declaration of Helsinki nor the stress or disappointment felt by Latin American bioethicists with each new revision. The purpose is rather to clarify the rhetorical and relevant mechanisms that are influencing this document, to the point of taking an already consolidated discredit that seriously affects the work of the regional bioethics and complicates the work of the [bio] ethics Committees of human research. The bioethical institutions, including teaching, no longer are able to trust the Statement of Helsinki, have less and less influence to rectify it, and should be wary of other guides research ethics that claim to be based in Helsinki.

The conclusion, which has been hinted several times unfortunately without much significance, is that the Latin American bioethics would do well to abandon the sterile debate about the Statement, and seriously seek to build your own guiding instrument for clinical research, respectful and relevant to the social reality in which our nations live, creating a potent immunity against the colonization by corporate interests and bioethics "utilitarian" that is subordinated to them. We must take seriously the task of counseling and guidance in defending and protecting our population, from a vision committed to the needs of the region 26,27.

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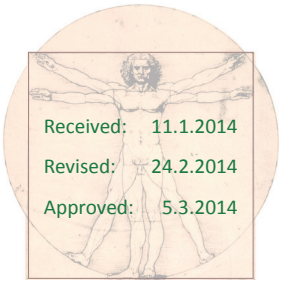

Received: 11.1.2014
Revised: 24.2.2014
Approved: 5.3.2014