The placebo and the Declaration of Pachuca: dead letters?

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Abstract

The Latin American and Caribbean Medical Confederation (CONFEMEL), an organization that brings together related organizations from countries of the region, works on behalf of the medical profession and the population's health guided by international documents. During its General Assembly (Pachuca, Mexico; 2013) the *Declaration of Pachuca* was approved with strong critics regarding the review of the *Declaration of Helsinki* that occurred in Brazil and the issue of clinical trials that use placebo in diseases with known treatment. The strong and energetic tone of this Declaration proposes that member entities condemn ethical abuses in all forums and also to administrations so that they engage against the use of placebo in these conditions. These recommendations are supported in the global movement on Integrity and Ethics in Research. The conclusion addresses the importance of the educative role of ethical supervision of Medicine warning physicians who violate these guidelines, which are also incorporated in the Code of Medical Ethics, that they will be subjected to ethical-professional process.

Keywords: Placebo. Declaration of Helsinki. Medicine. Biomedical research. Medical legislation. Integrity in research.

Resumo

O placebo e a *Declaração de Pachuca*: letras mortas?

A Confederação Médica Latino-Americana e do Caribe, organização que congrega as entidades congêneres dos países da região, atua em defesa da profissão médica e da saúde da população, guiando-se por documentos internacionais. Em sua Assembleia Geral (Pachuca, México; 2013) foi aprovada a *Declaração de Pachuca*, com severas críticas à revisão da *Declaração de Helsinki* ocorrida no Brasil e aos ensaios clínicos que usam placebo em doenças com tratamento definido. O tom duro e enérgico dessa Declaração propõe que entidades-membro denunciem os abusos éticos em todos os foros e aos governantes, e que atuem impedindo o uso do placebo nessas condições. Tais recomendações encontram respaldo no movimento mundial sobre integridade e ética na pesquisa. Conclui-se pela importância do papel educativo dos órgãos de fiscalização ética da medicina, alertando-se os médicos que infringirem essa orientação, a qual também integra o Código de Ética Médica, de que estarão sujeitos a processo ético-profissional.

Palavras-chave: Placebo. Declaração de *Helsinki*. Medicina. Pesquisa biomédica. Legislação médica. Integridade em pesquisa.

Resumen

El placebo y la *Declaración de Pachuca*: ¿letras muertas?

La Confederación Médica Latinoamericana y del Caribe (CONFEMEL), una organización que reúne a instituciones similares de los países de la región, actúa en defensa de la profesión médica y salud de la población, guiándose por los documentos internacionales. En su Asamblea General (Pachuca, México; 2013) se aprobó la *Declaración de Pachuca* con duras críticas a la revisión de la *Declaración de Helsinki* que tuvo lugar en Brasil y a los ensayos clínicos que utilizan placebo en enfermedades con tratamiento conocido. El tono duro y enérgico de tal Declaración propone que las entidades-miembros a denunciar los abusos éticos en todos los foros y a los gobernantes, y que actúen impidiendo el uso del placebo en estas circunstancias. Estas recomendaciones se apoyan en el movimiento mundial sobre Integridad y ética en la investigación. Se concluye sobre la importancia del papel educativo de los órganos de supervisión ética da medicina, alertando a los médicos que violen esta norma, que también está contemplada en el Código de Ética Médica, que estarán sujetos a proceso ético-profesional.

Palabras-clave: Placebo. Declaración de Helsinki. Medicina. Investigación biomédica. Legislación médica. Integridad en investigación.

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Declara não haver conflito de interesse.

Research article

The Confemel

The federal councils and medical colleges of Latin American and Caribbean countries created, in 1997, the Medical Confederation of Latin American and the Caribbean (Confemel), a non-governmental medical entity, nonprofit, with the objective, among others, o act in favor of the health of the populations, from the human, scientific, technological and political perspectives. The Confemel is governed by the principles of universality, comprehensiveness, equity and accessibility, that is, has as its premises that medical attention must be universal, comprehensive, equitable and egalitarian, providing access opportunity with quality and cordiality. Furthermore, its action is guided by several international documents, including the Declaration of Helsinki (DoH), from 1964, modified in Scotland in 2000 [1]. The confederation brings together medical organizations from 19 countries in the region, including the six that more conducted clinical trials in Latin America, as recorded in the international platform clinicaltrial.gov: Brazil, Mexico, Argentina, Chile, Colombia and Peru. In Brazil's party, three national medical entities integrated Confemel: the Federal Medical Council, the Brazilian Medical Association and the National Federation of Physicians.

The Confemel annually gathers in a general meeting, when deliberations are taken on acute issues of human health that affect people and physicians in the region. Thus, in its 11th Ordinary Annual Meeting, in 2008, the *Declaración de Buenos Aires sobre Investigaciones Médicas* (Declaration on Medical Investigations of Buenos Aires), with tough criticism about the DoH changes introduced in the same year in Seoul, South Korea, by the World Medical Association (WMA), especially in relation to the double standard, and in which concludes its strong commitment to act on governments of countries that are part of it, to prevent its implementation [2]. The last of these meetings, the 16th in its history of struggles and advances occurred in the Mexican city of Pachuca, in November 2013, when it was discussed a controversial topic, antique, but still current, related to the use of placebo as control in clinical trials.

The placebo and the Helsinki Declaration of 2013 - Fortaleza, Ceará, Brazil

The subject of the 16th meeting concerned, specifically, an episode from a month earlier in Fortaleza, Ceará, Brazil, when the WMA approved a new Declaration of Helsinki (DoH 2013) [3], whose text on the use of placebo inadequately became more flexible. The document creates unlimited possibilities of using placebo, camouflaged in the old and ethically questioned *compelling and scientifically solid methodological reasons*. In addition, the DoH 2013 accepts *any less effective intervention that the best proven when necessary to determine the efficacy or safety of an intervention* [3]. The final sentence on the use of placebo, recommending that an *extreme care must be taken to prevent abuse of this option*, sounds like a useless warning and relegated to oblivion. This part of the text on DoH over placebo seems to be the one that caused repulse and outrage to medical entities of Confemel present at the 16th Assembly, which has led to the terms of the Declaration of Pachuca [4].

The Declaration of Pachuca

Expression of the medical party, the Declaration of Pachuca on the revision of *Helsinki* [4] was approved on November 22nd, 2013, as part of the 16th Assembly of Confemel, and ratified, unanimously, the *Declaration of Bogotá*, issued by the same organization in 2012, when it had manisfested itself contrary to the use of placebo, as follows: *In that sense, it unconditionally opposes to Articles 32 and 33 of the Declaration of Helsinki on Human Research of the World Medical Association and understands that this type of research with placebo is contrary to the principles and values of the profession and of medical ethics* [5].

In turn, the Declaration of Pachuca was approved as follows: unanimously rejects any medical research involving human subjects using a placebo when there is a proven medication for the condition under study. The poor and vulnerable populations, discriminated by their lack of resources can not be subjected to biomedical research that have lower security levels to those applied in societies of greater development [4].

The document, by criticizing the DoH 2013, approved in Brazil, also notes that: c) In terms of point 33, the use of placebo when there are proven and effective interventions is contrary to principles and values of the profession and medical ethics. [...] e) As immediate it proposes to the respective governments not authorizing no financial support for medication that has used placebo, when existing better proven interventions. f) The member Associations commit to denounce this situation in all instances and national and international forums, as well as in

their governments, and to promote institutional actions from CONFEMEL to impede the application of this norm inn the medical investigation [4].

It is important to emphasize the strong revolt of the supervisory bodies of medical practice in Latin America and the Caribbean on the flexibilization of the use of placebo included in DoH 2013, to the point to, for the first time, propose that governments do not allow trials with this ethical bias and that this situation is denounced at all levels of government to prevent its application in our territory.

The leadership of Brazil and the role of the Federal Council of Medicine on the ethical use of placebo

The Brazil, while ago, has the recognition of the national and international community connected to the DoH, in particular by its strong and permanent performance of the Federal Council of Medicine (FCM) in defending the ethical use of placebo [6]. In Brazil, the WMA always found acceptance of the DoH as the FCM was the first national organization to support it, transforming its guidelines on a professional ethics norm to be followed by the medical category under its jurisdiction in respect of clinical research, through Resolution 671/1975 [7].

However, the 2008 DoH review was not supported by FCM, since alternatives have been created to the unethical use of placebo. The solid and contrary position happened during the assembly of the WMA in Seoul, when the then president of the Federal Council of Medical critically and forcefully expressed himself against the approved text, which allowed the flexibility of placebo use [8]. Due to this strong and opportune demonstration against the DoH 2008 regarding the flexibilization of using placebo, it is understood being important to register it for the story in your words in the official language of the WMA, as follows:

Esteemed Colleagues,

Today we are here together and at the point of ending two years of work on the modification of the Declaration of Helsinki. This key document is for us the most important manifestation of our commitment in the field of human ethics. There are other documents, which are part of our tradition, but none have the dimensions, the impact, and the level of acceptance as the Declaration of Helsinki. The Declaration of Helsinki is a liberating document, which puts the World Medical Association in the forefront of the defense of human rights by demanding that the highest ethical and scientific standards be used when research takes place in human subjects. The Declaration of Helsinki protects not only those who participate in research, but also all human beings because it demands that the results from this research be of quality. The Declaration of Helsinki, as a protector, keeps the beautiful structure of medicine on a firm foundation, strengthening it to be what it must be – able to offer care based on science and ethical conduct. This is my message which comes to you from my heart, and I say this without concern for the emotion that I feel, because I cannot understand medicine without compassion or the provision of care unaccompanied by love, and I ask you "What are the scientific reasons that can justify the ethical-scientific use of placebo in research with human beings that have not been discussed by Professor Dr. José Luis Gomes do Amaral and which we are defending in the forum of this Association? What is the scientific evidence for change? Where are the irrefutable voices of scientific knowledge leading us to impose change without having to weaken the structure of our beautiful profession? There is only silence. There are no voices, because this evidence does not exist. We cannot rest here. Brazil proposes to this illustrious Assembly that, with no scientific evidence to modify, justify, or relax the ethical standards governing the use of placebo in research with human subjects, and with the necessity of maintaining the highest level of our professional ethics in defending human interest – which is the only justification for the practice of medicine - we do not approve the modifications to Article 29 of the Declaration of Helsinki as they have been presented to us by the Director of the World Medical Association, and we retain the professional standing that deserves the respect of humanity.

Signed: Edson de Oliveira Andrade, President of the FCM [9].

As a result, four days later, the FCM issued the Resolution 1.885/2008 [10] with the ethical restrictions necessary to the use of placebo, prohibiting Brazilian physicians to participate in clinical trials when there is effective treatment for the studied disease. For the vehemence of the reasons and importance of its historical value, it is worthy to reproduce the entire content of ethical document condemning the abuse of placebo in trials of new drugs:

Considering the decided in the General Assembly in 2008 of the World Medical Association, held on Oc-

tober 15-18th in Seoul - South Korea, which amended Article 29 of the Declaration of Helsinki, allowing the use of placebo even being a recognized effective treatment, for methodological reasons; Whereas there are no scientific evidences to justify the ethical complacency adopted in the use of placebo by changing the current Declaration of Helsinki; Considering the non-approval by the Brazilian medical representation of the proposed amendments to the new wording of Article 29 of the Declaration of Helsinki (2004 revision), renumbered as Article 32 in the Assembly in Seoul, South Korea; Whereas the decided in plenary on October 23rd, 2008, Resolves: Art. 1 It is prohibited to the physician connection of any nature with medical research involving human subjects, using placebo in their experiments, when there is efficient and effective treatment for the disease studied [10].

In the following year, in 2009, recognizing the importance of maintaining this ethical brake to medical researchers in clinical trials in the country, the content of this document has been fully maintained in Code of Medical Ethics (CEM), embodied in the FCM Resolution 1.931/2009 [11], confirming its previous position on restrictions on the use of placebo.

Alongside the permanent performance of FCM, other entities such as the National Health Council (CNS), the National Ethics Commission in Research (Conep), and the Brazilian Society of Bioethics, also have always been present in the most delicate moments, either by editing normative resolutions, or by the approval of motions of unrestricted support for the fight against the ethical failure in uncontrolled use of placebo. This action should be permanent by the growing increase in research on new drugs in Brazil, since it was demonstrated that the country has a promising future in research and development in the pharmaceutical area [12].

The use of placebo and the disregard for ethical standards in Brazil

However, despite the duration of the CEM and other ethical standards, it seems that some medical researchers insist to ignore them and continue to use placebo in diseases for which there is a huge range of effective drugs available. In a survey of the clinical trials phase III drugs for any disease, and registered in clinicaltrials.gov platform for ten years, being five before and five after 2008, it was concluded by the ineffectiveness of ethical constraints determined by the FCM, as well as those contained from the resolutions of the National Health Council (CNS), given that the placebo percentage usage, when comparing the two periods was similar and that in studies with sponsorship of university institutions, national companies and others, there was a significant increase after 2008 [13].

Most decisive example of the failure to comply with the CEM was observed in phase III clinical trials in patients with type 2 diabetes, registered in clinicaltrials.gov, sponsored by the pharmaceutical industry and which in 51.6% (93/48) of the studies conducted in Brazil, between 2003 and 2013, placebo was used as control arm. Needless to emphasize the range of drugs available for the treatment of this disease, and yet, in more than half of the studies, the control-arm contained placebo, which sets ethical infraction. Unimaginable that this is happening with Brazilian participants, who should also be equally supported by the resolutions of the National Health Council.

These data were collected in the cited online platform, in where it was possible to obtain the total intervention by drugs in diabetes 2 in the reference period by the insertion of descriptors in Find Studies and Advanced Search icons: “drug”; “excluded Unknown”; “Interventional Studies”; “diabetes 2”; “Brazil”; “Child, Adult, Senior”; “Phase 3”; “Industry”; “received from 01/01/2003 to 31/12/2013.” In turn, to obtain the number of such tests with placebo, this word was inserted in the same Advanced Search and Find Studies icons, “drug”; “Excluded Unknown”; “Interventional Studies”; “2 diabetes”; “Placebo”; “Brazil”; “Child, Adult, Senior”; “Phase 3”; “Industry”; “Received from 1/1/2003 to 31/12/2013.”

It is also alerted that research in diabetes, due to the chronic course of the disease, presents several years of use of placebo in the control arm. The data from these surveys of clinicaltrials.gov, especially the studies on diabetes 2, frontally oppose to the view that the prohibition of FCM would cast researches with placebo in Brazil since the adoption of FCM´s Resolution 1885/2008, as argued by some research groups [14]. It is interesting that the justification for this argument states that *if the placebo is unethical, such researches are, from October 23rd 2008, not viable, since they can not use data obtained unethically for a scientific publication* [15].

As it is known, studies sponsored by multinational industries have their protocols developed abroad, being up to the specialist physicians in Brazil to accept or not to participate when asked. By these numbers, it seems that many agree to participate as

responsible in their clinical research centers, ignoring the prohibitions of CEM, which is receiving close monitoring by regional councils of medicine, particularly those with jurisdiction in large urban centers, with the largest number of research centers.

For the most part, these centers are located in São Paulo (37), Porto Alegre (13), Rio de Janeiro (10), Belo Horizonte (10), Campinas (9) and Curitiba (7), according to data from 2005 to 2009 [12]. In turn, clinical trials with placebo-controlled group are cheaper because they require less sample and a less costly infrastructure than trials in which the control group is treated with medications already available on the market [9].

It should be added that both the 2008 DoH as the 2013 DoH deserved serious restrictions on the text on the placebo, not only by the Federal Council of Medicine, but also of the National Research Ethics Comission (Conep) of the National Health Council, through the Resolution 404/2008 [16] (repealed by the Resolution CNS 466/2012), of the Brazilian Society of Bioethics and prestigious Latino American bioethicists [17-19]. One of them [19], expanding its indignation against the 2013DoH, proposed that Latin America abandons the DoH and creates its own ethical document, facing our reality.

Nothing illogical in this proposal, if we considere that the United States, through the Food and Drug Administration (FDA) abandoned the DoH in October 2008, replacing it with the Good Clinical Practices/International Conference on Harmonization (GCP/ICH), 1996 . As known, this document is intended to harmonize the methodological procedures between the US, Europe and Japan, to facilitate the mutual acceptance of clinical trials by its regulatory agencies [18], not being, therefore, an ethical document, reason why it can not be a substitute for the DoH.

In Brazil, however, not all parties share the same view held by FCM and Conep, given that the Brazilian Medical Association (BMA) approved the text of the DoH 2008 adopted at the Seoul meeting, in concluding that: *We have, therefore, a document solid enough, updated and available to the ethical beacon* [20]. Similarly, in reviewing the DoH of Fortaleza (2013), the representative of BMA assessed that: *The BMA recognizes the importance of the DoH as a set of ethical principles accomplished by medical societies from around the world and believes that Brazil needs to be aligned with all countries where researches are done* [21]. It is clear, therefore, that there is a historical national divergence between the position of the BMA, aligned and signatory to the DoH, and that adopted throughout the years by FCM and Conep [15].

The Declaration of Pachuca and the worldwide movement for integrity and ethics in research

An interesting connection may be established between the *Declaration of Pachuca* and the global movement initiated by researchers from several countries concerned about the ethical, moral and honesty issues growing alarmingly in the sciences. Resulted from these concerns, the 1st World Conference on Research Integrity was held in Portugal in 2007; the 2nd in Singapore in 2010; the 3rd in Canada, in 2012; and the 4th Conference will take place in Brazil, more precisely in the city of Rio de Janeiro, in 2015 [22].

In Brazil, the first initiatives to establish a forum for discussion and debate on the subject of integrity, ethics and responsibility in research were the 1st Brazilian Meeting on Research Integrity , Science and Publication Ethics - BRISPE [23], in 2010, and the 2nd BRISPE [24], carried out in 2012, having the first one the support of the Brazilian Society of Bioethics in promoting the event. Both had as a guideline the promotion of the release of the topic of ethics and integrity with research institutions and education process of researchers, especially students and young researchers.

To further clarify this issue of integrity, it is worthy to reproduce the words of Santos, who very well summarize the real meaning of this theme: *The term "research integrity" has been used to mark a particular field within the professional ethics of the scientist, understood as the total sphere of ethical duties to which the scientist is subject to properly perform their scientific activities. Within this sphere, it may be distinguished, on the one hand, the set of duties derived from ethical values more universal than that specifically scientific. Are from this nature those that make up the field of what is named Bioethics, derived, for example, from the value (not specifically scientific) that is the respect for the physical, psychological and moral integrity of human beings* [25].

However, by addressing a specific field of professional ethics of the researcher, nothing more logical that the subject to be included in the range of ethical codes from the various health professions, by involving ethical values as beneficence, the non-maleficence, recklessness and the negligence, directly related to the use of placebo in clinical trials. Add to them the principle of justice, since everyone in-

volved in the study should be offered the same rights of access to the best possible treatments.

In that regard, it is interessing the journal's editorial of the Brazilian Medical Association [26], that by treating the placebo use, states that the therapeutic concealment, in principle, will bring no direct benefit to those using it and questions the reason why the physician would include in his study patients that will not get direct benefit of the research. The editorial also suggests that, in the event of damage to the patient using placebo, it is possible that there was recklessness or negligence on the part of the professional, because doctors know the risks of using placebo in diseases whose treatment is known.

In this case, one can assume that the physician would be infringing the Code of Medical Ethics (CME), which in its Article 1st of Chapter III, which deals with the professional responsibility of the CEM, seals: *Causing harm to the patient, by act or omission, characterized as malpractice, recklessness or negligence.* Besides, would certainly be also disrespecting Article 106, which prohibits the physician: *Keep relationship of any nature with medical research involving human subjects, that use placebo in their experiments, when there is efficient and effective treatment for the disease researched* [11].

The ethical sanction in this case would seek to maintain the high ethical standards of medicine, with respect and defend the rights of patients, the sole and true reason for belonging to medicine. On the other hand, in where the clear ethical infraction by Brazilian physicians who participate in clinical trials involving the use of placebo in the treatments of recognized diseases, what is known, there is no record of any denunciation or establishment of ethical-professional process by not respecting the care in the use of placebo in regional or federal councils of Medicine. The actions of the researcher that, by intention or negligence, contradict these assumptions represent an ethically improper conduct from the point of view of research integrity [25]. In other words, in tests involving the use of placebo in clear disregard of national and international standards, it can be consider that the researcher and the sponsors of these studies are making a mistake that, besides being unethical, can be classified as not righteous conduct.

Thus, it appears that there is a perfect interaction of the *Declaration of Pachuca* terms with the theme of integrity and ethics in research. In Brazil, besides the two BRISPE, it happened, for the first time, the formal manifestation of the National Counsel of Technological and Scientific Development (CNPq) to create a Special Committee to make recommendations and ethical guidelines on the subject. From the various guidelines proposed by the agency, the last of which summarizes all the ethical needs of scientific research: *All research work must be conducted within ethical standards in its performance, either with animals or humans* [27].

Similarly, the The State of São Paulo Research Foundation (FAPESP), which also joined this movement of ethics and integrity, being the first Brazilian agency for research support to approve a Code of Good Practices in Research, clearly describes *the scientific misconduct* [as] *all conduct of a researcher who, by intent or negligence, violates the values and principles that define the ethical integrity of scientific research* [28]. It is hence understood that the deliberate and conscious use of placebo in clinical trials in the above situations can be considered scientific misconduct by disregard of ethical standards identified above.

In continuation to this educational process, Spink [29], in an insightful analysis on ethics in scientific research, points out that the first challenge to be faced arises from the increasing subordination of science to powerful private economic groups, which have the means to guide their results as their interests. The author cites, among others, that the use of vulnerable populations in clinical trials is related to the growing concern about ethical issues in science. This is a frequent practice in trials conducted in Brazil [9].

Final Considerations

Given the orientation of the Declaration of Pachuca that their affiliated institutions should act more strictly to prevent the conduct of clinical trials with placebo ethically unjustifiable, it is expected that - if this directive is put into practice by the institutions that signed it, as is the case of entities in Brazil - from now, the current situation of scientific freedom, but of questionable ethical conduct, will be monitored, and the physicians better oriented.

It is believed that the range of activities may place these actions in three levels of the medical field: a) educational activities, with the implementation of preventive and educational measures to be started with researchers, academic and clinical research centers in the country, either by events, standards or other similar activities; b) enforcement actions in clinical research centers; c) discourage actions to theunethical use of placebo, including

opening of ethical and disciplinary proceedings, if it is the case.

The first one should be the most feasible and easier, given the many mechanisms of access to physicians, either through e-mail, newsletters, magazines and other forms. However, to develop the second level of action, it is nnecessary to refer to the recent FCM Resolution 2.056/2013, which establishes criteria for the authorization of medical services operation of any nature and establishes a minimum criteria for its ethical operation [30].

In addition, the FCM Resolution 2.056/2013 assigns to medical directors invested in administrative functions the co-responsibility, when properly aware, if the practice of medicine is in disagreement with this standard. The sole paragraph of Article 21 is explicit in determining that: *The commitment reaches the inertia to allow the persistence of degrading conditions to patient care, to research procedures in patients without authorization of the Research Ethics Committee and the use of procedures considered invalid by the Federal Council of Medicine* [30].

In other words, when it comes to the use of placebo in situations not authorized by the CEM, these medical directors, in fulfilling their obligations, should act on the prevention and monitoring of ethical practice of the profession in clinical trials, since this is a medical activity. Therefore, the FCM Resolution 2.056/2013 represents a new and important ethical instrument to control the indiscriminate and unjustifiable use of placebo.

Finally, it is understood, also, that the *Declaration of Pachuca*, when proposing global actions with the public and private sectors responsible for financing the studies and the ethical system of approval of clinical trials, such sum in the effort to protect the participants of clinical trials should be echoed by its affiliates. It is expected that the words of the *Declaration of Pachuca* and the Article 106 of the Code of Medical Ethics do not become dead letters, failing to waste the huge effort expended over the past years by Brazilian authorities in the defense of the participants and the ethical exercise of doctors in clinical researches, particularly in the care and requirement of appropriate placebo use.

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Declaration of Pachuca on the revision of Helsinki

The Latin American and Caribbean Medical Confederation

The Latin American and Caribbean Medical Confederation, meeting in its Sixteenth Ordinary General Assembly in the city of Pachuca on 20, 21, 22 and 23 November 2013, attended by representatives of medical organizations of Argentina, Bolivia, Brazil, Costa Rica, El Salvador, Guatemala, Honduras, Panama, Paraguay, Peru, Mexico, Uruguay, Venezuela and Spain as the guest organization; in relation to the revision of the Declaration of Helsinki approved by the Annual Assembly of the World Medical Association where the ethical criteria that should guide research on human beings have been updated,

Declares unanimously:

a) Despite the work of Member Associations CONFEMEL and FIEM in the working group on the revision of the Declaration of Helsinki and recognition to some modifications achieved, is reaffirmed in all aspects of the Declaration of Bogotá, adopted by the XV Assembly ordinary CONFEMEL where *unanimously rejected outright any medical research involving human subjects using a placebo when there is a proven medication for the condition under study. The poor and vulnerable populations, discriminated by their lack of resources can not be subjected to biomedical research that have lower security levels to those applied to societies with greater development levels*;

b) In regard to item 28, related to informed consent, it is understood that the ethical principle of consent and its legal reality is compromised, not guaranteeing the respect for fundamental principles and rights such as dignity, freedom and intimacy of human beings;

c) In terms of point 33, the use of placebo when there are proven and effective interventions is contrary to the principles and values of the profession and medical ethics;

d) It is for the previously stated that deeply regrets the statement above and assumes as his own the writing of paragraphs 28 and 33 of the 7th edition of the *Declaration of Helsinki*;

e) As an immediate action to the respective governments not to authorize or fund drugs that have been used placebo in its assessment if existing better proven interventions;

f) The member Associations pledge to denounce this situation at all levels and national and international forums, and to perform all institutional actions of CONFEMEL to prevent the application of this standard in Medical Research;

g) We are committed to continue working towards changing the current wording of the *Declaration of Helsinki*.

México, 22 de Noviembre de 2013.
Argentina, Bolivia, Brasil, Costa Rica, Guatemala, Honduras,
México, Panamá, Paraguay, Perú, El Salvador, Uruguay, Venezuela y España

Research article