20 August 2008

Dr Otmar Cloiber
Secretary General
World Medical Association
Boite Postale 63
28 Avenue des Alpes
Ferney-Voltaire
F-01212
France

Dear Dr Clobier

Declaration of Helsinki – revisions Summer 2008

The Nuffield Council on Bioethics welcomes the opportunity to contribute to the ongoing revision of the *Declaration of Helsinki* (DoH) and is grateful to the WMA for its invitation to respond to the current consultation. I hope that our Comments at Annex A will be of use to the WMA. General comments are followed by comments on specific paragraphs in the requested format.

Please do not hesitate to contact us if you require clarification on any of the information provided.

Thank you again for the opportunity to respond to the consultation.

Yours sincerely

Professor Albert Weale
Chair

Annex A

Response to the revised draft of the Declaration of Helsinki by the World Medical Association from the Nuffield Council on Bioethics

20 August 2008

1. The Nuffield Council on Bioethics welcomes the opportunity to comment on the revision of the *Declaration of Helsinki* (DoH. As in previous comments[1] we focus mainly on the implications of the DoH for the conduct of externally sponsored research in developing countries, a topic which the Council has considered in its publications on *The ethics of research related to healthcare in developing countries* of 2002 and 2005.[2]

General comments

The scope of the Declaration

2. We welcome that, in line with the mandate of the WMA, the new draft emphasises that the DoH is directed at physicians, rather than at researchers more generally.

3. We welcome that the previous proposal, which would have broadened the DoH's scope significantly from "Ethical Principles for Medical Research Involving Human Subjects" to "Ethical Principles for Biomedical Research Involving Human Beings", has not been pursued further.

4. We also welcome that the confusing reference to "human beings" has not only been removed from the title, but also from the text of the declaration. However, some ambiguity remains, in, for example the current paragraph 6 ("In medical research involving humans, the well-being of the individual research subject should take precedence over all other interests.") Some commentators might argue that embryo research involves "humans" at a very early stage of their development. But it does not seem useful to view such research as falling under the DoH. Accordingly, it would be preferable to avoid any ambiguity and to replace "humans" with, where appropriate "human subjects, materials or data". However, it seems clear that in the most recent revisions such options have already been considered. If the proposal for a

---

[1] **Commentary on the World Medical Association's current revision of paragraph 30 of the Declaration of Helsinki (2004)** available at: http://www.nuffieldbioethics.org/fileLibrary/pdf/WMA_para_30_NCOB_comment.pdf , **Response to the revision of the Declaration of Helsinki by the World Medical Association from the Nuffield Council on Bioethics (2007)** available at: http://www.nuffieldbioethics.org/fileLibrary/pdf/WMA_DoH_2007_FINAL.pdf and **Response to the revised draft of the Declaration of Helsinki by the World Medical Association from the Nuffield Council on Bioethics (2008)** http://www.nuffieldbioethics.org/fileLibrary/pdf/NCOB_comments_on_revised_DoH_Feb_2008001.pdf

[2] See: Nuffield Council on Bioethics (2002) *The Ethics of Research Related to Healthcare in Developing Countries* (London: NCOB)*;*, Nuffield Council on Bioethics (2005) *The ethics of research related to healthcare in developing countries - a follow-up Discussion Paper* (London: NCOB), available at: http://www.nuffieldbioethics.org/go/ourwork/developingcountries/introduction.html

preamble or explanatory memorandum, to which we return below, should be considered, it would be useful to clarify there that prenatal and similar early developmental forms of human life are excluded from the remit of the DoH.

The status of the Declaration

5. We also welcome that unhelpful ambiguity has been removed which arose from the fact that several key provisions differed, without obvious reason, in stipulating that certain actions "should" whereas others "must" be performed. The use of "must" invited questions about the status of the DoH, as it suggested that that the respective provisions are a set of detailed binding ethical rules that define unambiguously what is ethical and what is not. In earlier responses we have hence proposed that the WMA's proposal of 2003 should be revisited, when, in discussions around paragraph 30, it was proposed to add a preamble to the Declaration.[3]

6. It would still seem useful to add a preamble, stating, as envisaged then, that the DoH's "ethical principles provide the basis of moral reflection on the means and goals of research involving human subjects, distinct from national legal and regulatory requirements."[4] This would also seem to be supported by the current commentary on the new paragraph 7 which states "'Must' has been changed to 'should' throughout the document since it is a statement of principles, not of laws or regulations." Questions about the status of the DoH have caused considerable confusion among many of those referring to it, and while the current revisions are of considerable use in clarifying matters, addressing the status explicitly in the preamble, or a possible explanatory memorandum, would eliminate all doubt.

Reference to different versions of the DoH

7. As observed earlier, the DoH has now been revised five times, and several notes of clarification have been added. Nonetheless, where reference to the DoH is being made in policy documents, the different versions appear to be used in somewhat of a pick-and-choose manner. For example, there is anecdotal evidence that versions of the DoH that are annexed to commercial trial protocols predate the versions that are available at the time. Equally, the EU's clinical trials directive of 4 April 2001, and the UK's **The Medicines for Human Use (Clinical Trials) Regulations 2004**[5] refer to the 1996 version of the DoH, although by then the 2000 revision had been published.[6]

8. To prevent such eclectic use, and to ensure that the revisions the WMA feels are necessary are taken into account by those referring to it, a preamble or explanatory memorandum could also set out that only the most recent version

[3] WG/DoH/Sept2003, Workgroup report on the revision of paragraph 30 of the declaration of Helsinki, http://www.wma.net/e/pdf/wg_doh_sept2003.pdf
[4] WG/DoH/Sept2003, Workgroup report on the revision of paragraph 30 of the declaration of Helsinki, http://www.wma.net/e/pdf/wg_doh_sept2003.pdf
[5] http://www.opsi.gov.uk/si/si2004/20041031.htm
[6] Ref to Directive

of the document constitutes WMA policy, and that all earlier versions are annulled.

Comments on specific paragraphs

THE WORLD MEDICAL ASSOCIATION, INC.

WORLD MEDICAL ASSOCIATION DECLARATION OF HELSINKI

Note:
Comments have been made in the requested format, ie:

- **Bold <u>underlined</u>** print to indicate ADDITIONS to the text. Use the exact language your association proposes for the final text.
- ~~Strikethrough~~ to indicate text that should be DELETED**.**
- When re-arrangement of paragraphs or sentences is suggested, use CAPITAL LETTERS to explain which paragraph or part of the text should be moved to another location.

We have only provided comments on those paragraphs where, based on our previous work, as outlined above, we felt were able to provide useful comment. Not commenting on particular paragraphs should not be understood as an endorsement.

For ease of use we have shaded those sections on which we have commented in grey.

2004 version	**May 2008 Consultation Draft**	**Reasons for Changes**
Subtitle: Ethical Principles for Medical Research Involving Human Subjects	Subtitle: Ethical Principles for Medical Research Involving Humans	'Subjects' is used in the document where appropriate.
A. INTRODUCTION	A. INTRODUCTION	
1. The World Medical Association has developed the Declaration of Helsinki as a statement of ethical principles to provide guidance to physicians and other participants in medical research involving human subjects**.** Medical research involving human subjects includes research on identifiable human material or identifiable data.	1. The World Medical Association (WMA) has developed the Declaration of Helsinki as a statement of ethical principles for medical research involving humans**,** including research on identifiable human material and data.	This paragraph has been divided in two: the first stating the purpose and scope of the Declaration; the second specifying to whom it is addressed.
	2. Although the Declaration is addressed primarily to physicians, the World Medical Association invites other participants in medical research involving humans to adopt these principles.	Most commentators felt that the Declaration should be addressed primarily to physicians but that others should be encouraged to act according to its principles.
2. It is the duty of the	3. It is the duty of the physician	The addition makes the

physician to promote and safeguard the health of the people. The physician's knowledge and conscience are dedicated to the fulfillment of this duty.	to promote and safeguard the health of people, including those who are involved in medical research. The physician's knowledge and conscience are dedicated to the fulfilment of this duty.	physician's general duty relevant to the subject of the Declaration, i.e., research.
3. The Declaration of Geneva of the World Medical Association binds the physician with the words, "The health of my patient will be my first consideration," and the International Code of Medical Ethics declares that, "A physician shall act only in the patient's interest when providing medical care which might have the effect of weakening the physical and mental condition of the patient."	4. The Declaration of Geneva of the WMA binds the physician with the words, "The health of my patient will be my first consideration," and the International Code of Medical Ethics declares that, "A physician shall act in the patient's best interest when providing medical care."	This change brings the Declaration into line with the current wording of the International Code that was amended in 2006.
4. Medical progress is based on research which ultimately must rest in part on experimentation involving human subjects.	5. Medical progress is based on research that ultimately must include studies involving humans. Populations that are underrepresented in medical research should be provided appropriate access to participation in research.	The additional sentence incorporates the suggestions of commentators. It fits well in this paragraph.
5. In medical research on human subjects, considerations related to the well-being of the human subject should take precedence over the interests of science and society.	6. In medical research involving humans, the well-being of the individual research subject should take precedence over all other interests.	Minor editorial changes.
6. The primary purpose of medical research involving human subjects is to improve prophylactic, diagnostic and therapeutic procedures and the understanding of the aetiology and pathogenesis of disease. Even the best proven prophylactic, diagnostic, and therapeutic methods must continuously be challenged through research for their	7. The primary purpose of medical research involving humans is to understand the aetiology and pathogenesis of disease and improve preventive, diagnostic and therapeutic methods. Even the best current methods should continually be evaluated through research for their safety, effectiveness, efficiency, accessibility and quality.	Minor editorial changes including elimination of unnecessary repetition. 'Must' has been changed to 'should' throughout the document since it is a statement of principles, not of laws or regulations.

effectiveness, efficiency, accessibility and quality.		
7. In current medical practice and in medical research, most prophylactic, diagnostic and therapeutic procedures involve risks and burdens.	8. In medical practice and in medical research, most methods involve risks and burdens.	Minor editorial changes.

8. Medical research is subject to ethical standards that promote respect for all human beings and protect their health and rights. Some research populations are vulnerable and need special protection. The particular needs of the economically and medically disadvantaged must be recognized. Special attention is also required for those who cannot give or refuse consent for themselves, for those who may be subject to giving consent under duress, for those who will not benefit personally from the research and for those for whom the research is combined with care.	9. Medical research is subject to ethical standards that promote respect for all humans and protect their health and rights. Some research populations are particularly vulnerable and need special protection. These include the educationally, economically or medically disadvantaged, those who cannot give or refuse consent for themselves, those who may be subject to giving consent under duress, and those who may be vulnerable to coercion or undue influence.	Minor editorial changes. The deletion of "for those who will not benefit personally from the research" incorporates the idea that, by its very nature, research cannot guarantee that subjects will benefit from the research intervention.
9. Investigators should be aware of the ethical, legal and regulatory requirements for research on human subjects in their own countries as well as applicable international requirements. No national ethical, legal or regulatory requirement should be allowed to reduce or eliminate any of the protections for human subjects set forth in this Declaration.	10. ~~Physicians~~ Investigators should consider the ethical, legal and regulatory norms and standards for research involving humans in their own countries as well as applicable international norms and standards. No national ethical, legal or regulatory requirement should reduce or eliminate any of the protections for research subjects set forth in this Declaration.	Minor editorial changes. NCOB: "Physician" should be replaced with "Investigator" to include the non-clinical scientific personnel involved in designing and setting up the trials. This is a rather general point about considering matters including "regulatory norms and standards" and it would hence appear more appropriate to request all relevant investigators, rather than just physicians, to do so. Another option might be to address this paragraph to: "Physicians and scientists".

B. BASIC PRINCIPLES FOR ALL MEDICAL RESEARCH	B. PRINCIPLES FOR ALL MEDICAL RESEARCH	'Basic' is unnecessary.
10. It is the duty of the physician in medical research to protect the life, health, privacy, and dignity of the human subject.	11. It is the duty of physicians who participate in medical research to protect the life, health, dignity, integrity, right to self-determination, privacy, and confidentiality of personal	The additions bring together concepts that formerly were scattered throughout this section.

	information of research subjects.	

11. Medical research involving human subjects must conform to generally accepted scientific principles, be based on a thorough knowledge of the scientific literature, other relevant sources of information, and on adequate laboratory and, where appropriate, animal experimentation.	12. Medical research involving humans should conform to generally accepted scientific principles, be based on a thorough knowledge of the scientific literature, other relevant sources of information, and adequate laboratory and, as appropriate, animal experimentation. The welfare of animals used for research should be respected and **this should include application of the concept of the Three Rs (Refine, Reduce, Replace).**	The last sentence has been moved from former para. 12 since it fits more appropriately here. NCOB: The principle of the 3Rs is acknowledged explicitly by all major funders of animal research in the UK, features prominently in UK law and EU policy, and is recognised internationally (see also our 2004 Report The ethics of animal research[7]).
12. Appropriate caution must be exercised in the conduct of research which may affect the environment, and the welfare of animals used for research must be respected.	13. Appropriate caution should be exercised in the conduct of research that may affect the environment	Moved to para. 11
13. The design and performance of each experimental procedure involving human subjects should be clearly formulated in an experimental protocol. This protocol should be submitted for consideration, comment, guidance, and where appropriate, approval to a specially appointed ethical review committee, which must be independent of the investigator, the sponsor or any other kind of undue influence. This independent committee should be in conformity with the laws and regulations of the country in which the research experiment is performed. The committee has the right to monitor ongoing trials. The researcher has the obligation to provide monitoring information to the	14. The design and performance of each research study involving humans should be clearly described in a research protocol. The protocol should contain a statement of the ethical considerations involved and should indicate how the principles in this Declaration have been addressed. The protocol should include information regarding funding, sponsors, institutional affiliations, other potential conflicts of interest, incentives for subjects and provisions for treating and/or compensating subjects who are harmed as a consequence of participation in the research study. The protocol should describe arrangements for post-study access by study subjects **and the wider community** to methods identified as beneficial in the	Current paragraphs 13 and 14 have been reorganized so that the protocol is dealt with in new 14 and the research ethics committee in new 15. The change from "that there is compliance with the principles enunciated in this Declaration" to "how the principles in this Declaration have been addressed" is intended to encourage researchers to consider carefully the ethical aspects of their research. The last sentence has been transferred from the note of clarification to paragraph 30, since it belongs more appropriately here. NCOB: we welcome the inclusion of the issue of post-trial access here. adding "and the wider community" would bring the DoH in line with much current thinking

[7] http://www.nuffieldbioethics.org/go/ourwork/animalresearch/introduction

committee, especially any serious adverse events. The researcher should also submit to the committee, for review, information regarding funding, sponsors, institutional affiliations, other potential conflicts of interest and incentives for subjects.	study or access to other appropriate care or benefits.	in this area and would moreover be consistent with the new paragraph 18, which refers to "individuals or communities affected by the condition under investigation"
14. The research protocol should always contain a statement of the ethical considerations involved and should indicate that there is compliance with the principles enunciated in this Declaration.	15. The research protocol should be submitted for consideration, comment, guidance and approval to a research ethics committee, which should be independent of the researcher, the sponsor and any kind of undue influence. This committee should take into consideration the laws and regulations of the country or countries in which the research is to be performed. The committee should have the right to monitor ongoing studies. The researcher should provide monitoring information to the committee, especially information about any serious adverse events. No change in the protocol should be made without consideration and approval by the committee. **In the case of research carried out in developing countries with funding coming from outside of the country, review should take place in both the sponsoring country(ies) and the host country(ies)**	All research ethics committees (a more widely used term than 'ethical review committees') should have the authority to approve, or not approve, research protocols. If the research is to be conducted in a country or countries other than that where committee approval is sought, the committee should ensure that the research is not in conflict with the laws and regulations of the host country or countries. Such committees should exist wherever medical research is conducted and therefore should not have to be specially appointed to deal with specific protocols. NCOB: The added text ensures usefulness of the DoH in the context of healthcare related research being carried out in developing countries.
15. Medical research involving human subjects should be conducted only by scientifically qualified persons and under the supervision of a clinically competent medical person. The responsibility for the human subject must always rest with a medically qualified person and never rest on the subject of the	16. Medical research involving humans should be conducted only by scientifically qualified persons under the supervision of a competent and appropriately qualified physician. The responsibility for the protection of research subjects should always rest with the physician and never the research subjects, even though they have given	Minor editorial changes.

research, even though the subject has given consent.	consent.	

	17. Medical research involving a disadvantaged population or community is only justified if the research is responsive to the health needs and priorities of this population or community and if there is a reasonable likelihood that this population or community stands to benefit from the results of the research.	Moved from current 19. The addition of "a disadvantaged population or community" allows for phase one clinical trials on diseases that primarily affect developing countries (e.g., malaria) to be conducted in developed countries.
16. Every medical research project involving human subjects should be preceded by careful assessment of predictable risks and burdens in comparison with foreseeable benefits to the subject or to others. This does not preclude the participation of healthy volunteers in medical research. The design of all studies should be publicly available.	18. Every medical research study involving humans should be preceded by careful assessment of predictable risks and burdens to the individuals and communities involved in the research in comparison with foreseeable benefits to them and to other individuals or communities affected by the condition under investigation.	The addition of communities recognizes their importance in determining the risks and benefits of a research study. The deleted sentence is unnecessary and in any case does not fit in here. The last sentence has been moved to the following paragraph.
	19. Every clinical trial should be registered in a publicly accessible database before recruitment of the first subject.	Expansion of the last sentence of the previous paragraph, as suggested by commentators.
17. Physicians should abstain from engaging in research projects involving human subjects unless they are confident that the risks involved have been adequately assessed and can be satisfactorily managed. Physicians should cease any investigation if the risks are found to outweigh the potential benefits or if there is conclusive proof of positive and beneficial results.	20. Physicians should not participate in a research study involving humans unless they are confident that the risks involved have been adequately assessed and can be satisfactorily managed. Physicians should cease any investigation as soon as the risks are found to outweigh the potential benefits or as soon as there is conclusive proof of positive and beneficial results.	Minor editorial changes.

18. Medical research involving human subjects should only be conducted if the importance of the objective outweighs the inherent risks and burdens to the subject. This is especially important when the human subjects are healthy volunteers.	21. Medical research involving humans should only be conducted if the importance of the objective outweighs the inherent risks and burdens to the research subjects.	The principle applies equally to all research subjects. Healthy volunteers are no different in this respect.
19. Medical research is only justified if there is a reasonable likelihood that the populations in which the research is carried out stand to benefit from the results of the research.		Moved to 17.
20. The subjects must be volunteers and informed participants in the research project.	22. Participation by legally competent individuals in medical research involving humans must be voluntary. Although it may be appropriate to consult family members or community leaders, no competent individual should be enrolled in a research study unless he or she freely agrees.	The first change allows for involuntary participation in research by incompetent individuals as governed by paragraphs 27-29. The additional sentence addresses the custom in some populations whereby the competent individual's agreement to participate in research may need to be supplemented, but never replaced, by the agreement of another person.
21. The right of research subjects to safeguard their integrity must always be respected. Every precaution should be taken to respect the privacy of the subject, the confidentiality of the patient's information and to minimize the impact of the study on the subject's physical and mental integrity and on the personality of the subject.	23. Every precaution should be taken to protect the privacy and confidentiality of personal information of research subjects and to minimize the impact of the study on their physical, mental and social integrity.	Minor editorial changes. The deleted sentence is covered in para.10.

22. In any research on human beings, each potential subject must be adequately informed of the aims, methods, sources of funding, any possible conflicts of interest, institutional affiliations of the researcher, the anticipated benefits and potential risks of the study and the discomfort it may entail. The subject should be informed of the right to abstain from participation in the study or to withdraw consent to participate at any time without reprisal. After ensuring that the subject has understood the information, the physician should then obtain the subject's freely-given informed consent, preferably in writing. If the consent cannot be obtained in writing, the non-written consent must be formally documented and witnessed.	24. In medical research involving legally competent human subjects, each potential subject should be adequately informed of the aims, methods, sources of funding, any possible conflicts of interest, institutional affiliations of the researcher, the anticipated benefits and potential risks of the study and the discomfort it may entail, and any other relevant aspects of the study. The potential subject should be informed of the right to refuse to participate in the study or to withdraw consent to participate at any time without reprisal. Special attention should be given to the specific information needs of individual potential subjects as well as to the methods used to deliver the information. After ensuring that the potential subject has understood the information, the physician should then seek the potential subject's freely-given informed consent, preferably in writing. If the consent cannot be expressed in writing, the non-written consent should be formally documented and witnessed.	Incompetent potential research subjects are dealt with in paragraphs 27-29. The term 'potential subject' is used to indicate that an individual does not become a 'subject' until consent is given. This addition was suggested by commentators. 'Obtain' has been changed to 'seek' to emphasize the potential subject's right to either refuse or agree to take part in the research.
	25. For medical research using human tissues or data, ~~physicians~~ investigators should seek consent for the collection, investigation, storage and reuse of samples. There may be situations where consent would be impossible or impractical to obtain for such research or would pose a threat to the validity of the research. In such situations the research should be done only after consideration and approval of a research ethics committee.	New paragraph to deal with informed consent in research using human tissues or data. NCOB: "Physician" should be replaced with "Investigator" to include other relevant staff Another option might be to address this paragraph to: "Physicians and scientists".
23. When obtaining informed consent for the research	26. When seeking informed consent for participation in the	Minor editorial changes.

project the physician should be particularly cautious if the subject is in a dependent relationship with the physician or may consent under duress. In that case the informed consent should be obtained by a well-informed physician who is not engaged in the investigation and who is completely independent of this relationship.	research study the physician should be particularly cautious if the potential subject is in a dependent relationship with the physician or may consent under duress. In that case the informed consent should be sought by an appropriately qualified individual who is completely independent of this relationship.	Another physician may not be available to perform this task.
24. For a research subject who is legally incompetent, physically or mentally incapable of giving consent or is a legally incompetent minor, the investigator must obtain informed consent from the legally authorized representative in accordance with applicable law. These groups should not be included in research unless the research is necessary to promote the health of the population represented and this research cannot instead be performed on legally competent persons.	27. For a potential research subject who is legally incompetent, the physician should seek informed consent from the legally authorized representative in accordance with applicable law. These individuals should not be included in a research study unless it is intended to promote the health of the population represented by the potential subject, the research cannot instead be performed with legally competent persons, and the research entails only minimal risk and minimal burden in the absence of benefit for the potential subject.	Potential research subjects who are physically or mentally incapable of giving consent but who are not legally incompetent are dealt with in para. 29. Additional protection for these individuals while allowing higher risk research interventions that can benefit the research subjects.
25. When a subject deemed legally incompetent, such as a minor child, is able to give assent to decisions about participation in research, the investigator must obtain that assent in addition to the consent of the legally authorized representative.	28. When a potential research subject deemed legally incompetent, such as a minor child, is able to give assent to decisions about participation in research, the physician should seek that assent in addition to the consent of the legally authorized representative.	Minor editorial changes.

26. Research on individuals from whom it is not possible to obtain consent, including proxy or advance consent, should be done only if the physical/mental condition that prevents obtaining informed consent is a necessary characteristic of the research population. The specific reasons for involving research subjects with a condition that renders them unable to give informed consent should be stated in the experimental protocol for consideration and approval of the review committee. The protocol should state that consent to remain in the research should be obtained as soon as possible from the individual or a legally authorized surrogate	29. Research involving subjects who are physically or mentally incapable of giving consent, for example, unconscious patients, should 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.	Rewording for the purpose of clarification.
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 interest 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.	30. Authors, editors and publishers all have ethical obligations with regard to the publication of the results of research. Authors are accountable for the accuracy of the results. They have a duty to make publicly available the results of their research on humans. In so doing they should adhere to accepted guidelines for ethical reporting. Negative as well as positive results should be published or otherwise made publicly available. 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	Rewording for the purpose of clarification.

	this Declaration should not be accepted for publication.	

C. ADDITIONAL PRINCIPLES FOR MEDICAL RESEARCH COMBINED WITH MEDICAL CARE	C. ADDITIONAL PRINCIPLES FOR MEDICAL RESEARCH COMBINED WITH MEDICAL CARE	
28. The physician may combine medical research with medical care, only to the extent that the research is justified by its potential prophylactic, diagnostic or therapeutic value. When medical research is combined with medical care, additional standards apply to protect the patients who are research subjects.	31. 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. When medical research is combined with medical care, the following additional standards apply to protect these patients.	Additional protection for research subjects.
29. The benefits, risks, burdens and effectiveness of a new method should be tested against those of the best current prophylactic, diagnostic, and therapeutic methods. This does not exclude the use of placebo, or no treatment, in studies where no proven prophylactic, diagnostic or therapeutic method exists. **Note of clarification** The WMA hereby reaffirms its position that extreme care must be taken in making use of a placebo-controlled trial and that in general this methodology should only be used in the absence of existing proven therapy. However, a placebo-controlled trial may be ethically acceptable, even if proven therapy is available,	32. The benefits, risks, burdens and effectiveness of a new method should be tested against those of the best proven current method, except in the following circumstances: - The use of placebo, or no treatment, is acceptable in studies where no proven current method exists; or - Where for compelling and scientifically sound methodological reasons the use of placebo is necessary to determine the efficacy or safety of a method and the patients who receive placebo or no treatment will not be subject to any additional risk of serious or irreversible harm. **Where the best proven current method is not generally available in a country, is unlikely to become so during**	The contents of the note of clarification have been incorporated in the paragraph with no changes to the requirements. In this way, the apparent contradiction between the paragraph and the note, that some commentators allege, disappears. The inconsistency between ‘best current’ and ‘proven’ method has been resolved by using the term, ‘best proven current method’. NCOB The suggested addition concerns the fact that disagreement about the standard of care to be provided concerns not only the use of placebo. The added provision ensures the usefulness of the declaration in the context of research in developing countries.

under the following circumstances: - Where for compelling and scientifically sound methodological reasons its use is necessary to determine the efficacy or safety of a prophylactic, diagnostic or therapeutic method; or - Where a prophylactic, diagnostic or therapeutic method is being investigated for a minor condition and the patients who receive placebo will not be subject to any additional risk of serious or irreversible harm. All other provisions of the Declaration of Helsinki must be adhered to, especially the need for appropriate ethical and scientific review.	**the duration of the study, and where its use in the context of a research investigation would compromise the evaluation of a locally relevant experimental intervention. The intervention provided to the control group should comprise the best available to the health services in the country in which the study is conducted** **And add:** **All exceptions need to be justified explicitly to the relevant review boards.**	
30. At the conclusion of the study, every patient entered into the study should be assured of access to the best proven prophylactic, diagnostic and therapeutic methods identified by the study. Note of clarification The WMA hereby reaffirms its position that it is necessary during the study planning process to identify post-trial access by study participants to prophylactic, diagnostic and therapeutic procedures identified as beneficial in the study or access to other appropriate care. Post-trial access arrangements or other care must be described in the study protocol so the ethical review committee may consider such arrangements during its review.	33. At the conclusion of the study, patients entered into the study are entitled to be informed about the outcome of the study.	The requirement in the current paragraph is covered by the last sentence of paragraph 14. The last sentence of the note of clarification has been moved to paragraph 14.

31. The physician should fully inform the patient which aspects of the care are related to the research. The refusal of a patient to participate in a study must never interfere with the patient-physician relationship.	34. The physician should fully inform the patient which aspects of the care are related to the research. The refusal of a patient to participate in a study or the patient's decision to withdraw from the study should never interfere with the patient-physician relationship.	Addition suggested by commentators.
32. In the treatment of a patient, where proven prophylactic, diagnostic and therapeutic methods do not exist or have been ineffective, the physician, with informed consent from the patient, must be free to use unproven or new prophylactic, diagnostic and therapeutic measures, if in the physician's judgement it offers hope of saving life, re-establishing health or alleviating suffering. Where possible, these measures should be made the object of research, designed to evaluate their safety and efficacy. In all cases, new information should be recorded and, where appropriate, published. The other relevant guidelines of this Declaration should be followed.	35. In the treatment of a patient, where proven methods 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 or new method if in the physician's judgement it offers hope of saving life, re-establishing health or alleviating suffering. Where possible, this method should 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. The other relevant guidelines of this Declaration should be followed.	Addition suggested by commentators.

♣♣♣

30.05.08