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

15 February 2007

1. The Nuffield Council on Bioethics welcomes the opportunity to comment on the revision of the *Declaration of Helsinki* (DoH).[1] The Council has contributed to the response submitted by the British Medical Association (BMA), which sought input from the wide range of UK stakeholders, and we offer the observations below in addition to the BMA's response.

2. As in previous comments[2] 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.[3]

General comments[4]

The scope of the Declaration

3. The new draft considerably broadens the DoH's scope. The proposed revision to the title would turn the DoH from "Ethical Principles for Medical Research Involving Human Subjects" to "Ethical Principles for Biomedical Research Involving Human Beings", and corresponding changes are found throughout the text. Accordingly it is proposed, first, that the DoH no longer pertains to medical research, but to biomedical research more generally. Second, it is now meant to guide research with human beings rather than human subjects. And third, it addresses researchers rather than physicians.[5]

4. These changes have important implications for the content, authority, and acceptance of the document. For example, in principle, the scope of the Declaration appears to expand into a range of different areas of basic science.

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[1] See: http://www.wma.net/e/press/2007_14.htm

[2] 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

[3] 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

[4] Note that commenting on the paragraphs listed here does not entail endorsement of the remaining paragraphs of the DoH. We have focused our discussion on those provisions where we consider that we have carried out sufficient research to provide robust comment.

[5] With the exception of Paragraphs 2 and 3 (setting out WMA's authority on the matter) and Paragraphs 28, 31 and 32 (covering additional principles for biomedical research combined with medical care)

Some might argue that embryo research involves "human beings" at a very early stage of their development. But it seems not useful to view such research as falling under the DoH. Accordingly, it would be preferable to avoid any ambiguity and to replace "human beings" with, where appropriate "human subjects, materials or data".

5. Furthermore, the WMA's authority for issuing guidance for the biomedical researcher community at large is unclear. If it is felt that the extension in scope should be upheld it would need to be considered how the Declaration's provisions relate to those included in other relevant documents, for example, UNESCO's recent *Universal Declaration on Bioethics and Human Rights*, or the Council for Science and Technology's *Universal Ethical Code for Scientists*.

6. In view of the potential complications, and in order to secure the strongest possible standing for the DoH we would therefore recommend not to change its scope and title.

The status of the Declaration

7. Some of the changes also raise renewed questions about the status of the DoH. One the one hand, the revisions appear to suggest that the provisions are a set of detailed binding ethical rules that define unambiguously what is ethical and what is not. The use of "must" in paragraphs 13, 15, 20, 21, 22, 24-26, and 31 seems to imply that there is no scope for deviating from the provisions. Also, several of these paragraphs apply to precisely defined medical or research practices, with little room for interpretation, and many new additions (13, 14, 22a, 23) contain a level of detail that is very close to, for example, the current CIOMS guidelines. At the same time, other provisions remain very general, and paragraphs 9, 13-18, 21-24, 26-27, 29, and 31 use the softer "should", and appear to give some scope for flexibility.

8. In the review of Paragraph 30 in 2004, the WMA's working group made a proposal to add a preamble to the DoH, which would have clarified the question of whether the principles should be understood as setting out aspirational ideals, or binding rules. The proposed text would have stated that the declarations' "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."[6] The proposal has however, not been adopted. Equally, the proposed revision of Paragraph 9, which addresses related matters, does not assist in bringing clarity about the status of the DoH.

9. We comment on paragraph 9 below, and note here that renewed consideration should be given to adding a preamble to the DoH, or providing an Explanatory Memorandum. This would allow a clarification of the status[7] of the DoH's provisions. The section from the WMA's 2004 Working Group report in which

[6] 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

[7] And equally it would help clarify possible ambiguities around the use of "human beings" as it could be explained that the declarations is concerned with born human beings only.

the above quote occurs provides a very suitable starting point for this purpose.[8]

Reference to different versions of the DoH

10. 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[9] refer to the 1996 version of the DoH, although by then the 2000 revision had been published.

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

[8] "As a statement of principles, the Declaration of Helsinki is intended to establish high ethical standards that guide physicians and other participants in medical research involving human subjects. These 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. Interpreting the provisions of the Declaration regarding the design, conduct or completion of the research requires careful balancing of all of the Declaration's ethical principles. Differences in interpretation should be resolved by physicians and other participants involved in the research who are most familiar with all relevant factors, including the needs of research participants and of the host population."

[9] http://www.opsi.gov.uk/si/si2004/20041031.htm

Comments on specific paragraphs

WORLD MEDICAL ASSOCIATION DECLARATION OF HELSINKI

Ethical Principles for ~~M~~Biomedical Research Involving Human ~~Subjects~~ Beings

Adopted by the 18th WMA General Assembly
Helsinki, Finland, June 1964
and amended by the
29th WMA General Assembly, Tokyo, Japan, October 1975
35th WMA General Assembly, Venice, Italy, October 1983
41st WMA General Assembly, Hong Kong, September 1989
48th WMA General Assembly, Somerset West, Republic of South Africa, October 1996
and the
52nd WMA General Assembly, Edinburgh, Scotland, October 2000
Note of Clarification on Paragraph 29 added by the WMA General Assembly, Washington 2002
Note of Clarification on Paragraph 30 added by the WMA General Assembly, Tokyo 2004

A. INTRODUCTION

Original DoH and WMA's suggestion for revisions	WMA's initial explanatory commentary	NCOB's critical commentary on revised paragraphs
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 **bio**medical research involving human ~~subjects~~ **beings**. ~~M~~**Biom**edical research involving human ~~subjects~~ **beings** includes research on ~~identifiable~~ human material ~~or~~ **and** ~~identifiable~~ data.	'Medical research involving human subjects' has been changed to 'biomedical research involving human beings' throughout the document. There seems to be no good reason to exclude unidentifiable human material or data from the scope of biomedical research.	See our paragraphs 4-7 above where we advise against extending the scope.
2. It is the duty of the physician to promote and safeguard the health of ~~the~~ people **who participate in biomedical research**. The physician's knowledge and conscience are dedicated to the fulfillment of this duty.	The addition makes the physician's general duty relevant to the subject of the Declaration, i.e., research. Although in other paragraphs the term 'physician' has been changed to 'researcher', here and in paragraph 3 the Declaration is addressing physicians in particular.	No comment*
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 **best** interest when providing medical care ~~which might have the effect of weakening the physical and mental~~	This change brings the Declaration into line with the current wording of the International Code that was amended in 2006.	No comment

~~condition of the patient~~."		

Original DoH and WMA's suggestion for revisions	WMA's initial explanatory commentary	NCOB's critical commentary on revised paragraphs
4. Medical progress is based on research ~~which~~ **that** ultimately must ~~rest in part on~~ **include** ~~experimentation~~ **studies** involving human ~~subjects~~ **beings**. **Populations that have previously been underrepresented in biomedical research, such as children and pregnant women, should be provided equitable access to participation in research.**	Minor grammatical changes. The added sentence incorporates the suggestions of several commentators. It fits well in this paragraph.	See our paragraphs 8-10 above where we suggest to review the use of "should" and "must", and recommend to clarify the status of the DoH.
5. In **bio**medical research on human ~~subjects~~ **beings**, considerations related to the well-being of the ~~human subject~~ **individual** should take precedence over the interests of science**,** ~~and~~ society **and the sponsors of research**.	The addition indicates that commercial interests should not outweigh those of the research participant.	See our paragraph 5 above. This provision could be interpreted as extending to different forms of embryo research and might be referred to by those opposed to it. Keeping "subjects" instead of "beings" is far less ambiguous.
6. The primary purpose of **bio**medical research involving human ~~subjects~~ **beings** is to improve prophylactic, diagnostic**,** ~~and~~ therapeutic **and palliative** procedures and the understanding of the aetiology and pathogenesis of disease. Even the best proven prophylactic, diagnostic**,** ~~and~~ therapeutic **and palliative** methods must continuously be challenged through research for their effectiveness, efficiency, accessibility and quality.	'Palliative' has been added throughout the document.	No comment
7. In current medical practice and in **bio**medical research, most prophylactic, diagnostic**,** ~~and~~ therapeutic **and palliative** procedures involve risks and burdens.		No comment
8. ~~M~~**Biom**edical 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~~ **These include** the **educationally,** economically ~~and~~ **or** 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 **medical** care.	Minor grammatical changes. The deletion near the end incorporates the idea that, by its very nature, research cannot guarantee that participants will benefit from the intervention.	No comment

9. Research**ers** ~~Investigators~~ should be aware of the ethical, legal and regulatory requirements for research on human ~~subjects~~ **beings** 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~~ **beings** set forth in this Declaration.	"be allowed to" is unnecessary.	See our paragraphs 8-10 above where we suggest to review the use of "should" and "must", and recommend to clarify the status of the DoH.

B. BASIC PRINCIPLES FOR ~~ALL~~ BIOMEDICAL RESEARCH

Original DoH and WMA's suggestion for revisions	WMA's initial explanatory commentary	NCOB's critical commentary on revised paragraphs
10. It is the duty of ~~the physician in~~ **bio**medical research**ers** to protect the life, health, **dignity, right to self-determination,** privacy, and **confidentiality of information** ~~dignity~~ of ~~the human subject~~ **research participants**.	All researchers have this duty, which includes protection of the right to self-determination and confidentiality of personal health information. 'Research subject(s)' has been changed to 'research participant(s)' throughout the document.	The addition relating to "confidentiality" is useful. If the proposed idea of an Explanatory Memorandum is taken up we suggest that this should also clarify important differences between privacy and confidentiality of information. First, privacy rights are recognised in relation to both informational and non-informational matters and so are much broader than confidentiality. Secondly, regarding the context of health-related information, privacy concerns a person's right to prevent others knowing about a special class of personal information. If person A chooses to disclose such information to person B, there is no breach of A's privacy right. However, if B is told by A that the information is intended just for B, then should B disclose that information, to a person C, B breaches A's confidentiality right. Privacy therefore gives the right-holder control over the outward flow of sensitive personal information; and confidentiality gives the right-holder control over the onward transmission (or exploitation) of information that has been disclosed.
11. ~~M~~**Biom**edical research involving human ~~subjects~~ **beings** must conform to generally accepted scientific principles,	Minor grammatical changes.	No comment

be based on a thorough knowledge of the scientific literature, other relevant sources of information, and ~~on~~ adequate laboratory and, ~~where~~ **as** appropriate, animal experimentation.		
12. Appropriate caution must be exercised in the conduct of research ~~which~~ **that** may affect the environment~~, and the welfare of animals used for research must be respected~~.	Minor grammatical change. This paragraph has been divided into two because of the different topics covered.	See comment below
12A. The welfare of animals used for research must be respected.		Separating this paragraph from the previous paragraph 12 gives it more importance. One the one hand, this is to be welcomed, if the new DoH is indeed addressed to the wide community of biomedical scientists. Although we advise in our paragraphs 4-7 against such an extension in scope, we suggest that if the WMA nonetheless aims to pursue this project the following wording be added at the end of the sentence: "…this should include application of the concept of the Three Rs (Refine, Reduce, Replace). The principle of the 3Rs is acknowledged explicitly by all major funders of animal research in the UK and features prominently in UK law and EU policy (see also our 2004 Report The ethics of animal research[10]).
13. The design and performance of each ~~experimental~~ **research** procedure involving human ~~subjects~~ **beings** should be clearly formulated in a~~n experimental~~ **research** protocol. This protocol should be submitted for consideration, comment, guidance, and ~~where appropriate,~~ approval to a**n** ~~specially appointed~~ ethical review committee, which must be independent of the ~~investigator~~ **researcher**, the sponsor ~~or~~ **and** 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 **to be** performed. The committee has the right to monitor ongoing ~~trials~~ **studies**. The researcher has the obligation to provide monitoring information to the committee, especially any serious adverse events. The researcher should also submit to the	All ethical review committees should have the authority to approve, or not approve, research proposals. Such committees should exist wherever biomedical research is conducted and therefore should not have to be specially appointed to deal with specific proposals.	In order to ensure usefulness of the DoH in the context of healthcare related research being carried out in developing countries we propose to add a separate sentence at the end of this paragraph: "Where the funding of a study comes from outside of the country where it is to be carried out, review should take place in both the sponsoring country(ies) and the host country(ies)" See also our paragraphs 8-10 above where we suggest to review the use of "should" and "must", and recommend to clarify the status of the DoH. Concerning information about incentives for subjects, it would be useful to specify

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

committee, for review, information regarding funding, sponsors, institutional affiliations, other potential conflicts of interest and incentives for subjects **and provisions for treating participants who suffer injury as a consequence of research interventions**.	This addition was recommended by a commentator and seems to be quite appropriate here.	that this information should be specific with regard to the size and type of incentives that might be appropriate. The word 'subject' remains in this paragraph, and should perhaps be changed to 'participant' as elsewhere.

Original DoH and WMA's suggestion for revisions	WMA's initial explanatory commentary	NCOB's critical commentary on revised paragraphs
14. The research protocol should always contain a statement of the ethical considerations involved and should indicate ~~that there is compliance~~ **how the proposed research complies** with the principles enunciated in this Declaration. **The protocol should identify arrangements for post-trial access by study participants to prophylactic, diagnostic, therapeutic and palliative procedures identified as beneficial in the study or access to other appropriate care.**	The first change strengthens the obligation of the researcher to demonstrate compliance with the Declaration. The second change (additional sentence) has been transferred from the note of clarification to paragraph 30, since it belongs more appropriately here.	We welcome this addition which is in line with our earlier comments on the issue of post-trial access, and, in the context of research carried out in developing countries, takes up one of the key issues in the ethical debate. Another element of this debate could be incorporated if "and the wider community, where appropriate" would be added after "study participants", and we strongly recommend this amendment. However, see also our paragraphs 8-10 above where we suggest to review the use of "should" and "must", and recommend to clarify the status of the DoH. Depending on how WMA intends to resolve this issue we would urge that in the present context the obligation be specified in a way that sets it out as a strong obligation (whether in the declaration itself, or in a separate explanatory memorandum). The current wording could be read as if providing information about post-trial access is an merely an option.

Original DoH and WMA's suggestion for revisions	WMA's initial explanatory commentary	NCOB's critical commentary on revised paragraphs
15. ~~Medical~~ **Clinical** research involving human ~~subjects~~ **beings** should be conducted only by scientifically qualified persons ~~and~~ under the supervision of a ~~clinically~~	The term 'clinical research' is introduced here to distinguish the type of research described in this paragraph from other types (non-clinical epidemiological,	See our paragraphs 8-10 above where we suggest to review the use of "should" and "must", and recommend to clarify the status of the DoH.

competent ~~medical person~~ **health professional**. The responsibility for the **protection of** human ~~subject~~ **research participants** must always rest with ~~a medically qualified person~~ **the researcher** and never ~~rest~~ on ~~the subject of~~ the research **participants**, even though ~~the subject has~~ **they have** given consent.	observational, etc.) that do not require supervision by health professionals. The term 'clinically competent medical person' is unclear. In any case, other health professionals besides physicians (dentists, nurses, etc.) do conduct clinical research. Every researcher is responsible for protecting those who are involved in the research study.	
15 A. Former 19. ~~M~~**Biom**edical research **involving vulnerable populations as research participants** 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.	This addition allows for phase one clinical trials on diseases that affect developing countries to be conducted in developed countries.	No comment

Original DoH and WMA's suggestion for revisions	WMA's initial explanatory commentary	NCOB's critical commentary on revised paragraphs
16. Every **bio**medical research project involving human ~~subjects~~ **beings** 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 ~~the subject~~ **them** or to other~~s~~ **individuals or communities affected by the condition under investigation**. ~~This does not preclude the participation of healthy volunteers in medical research.~~ The design of all studies should be publicly available. **In particular, before recruitment of the first participant, each clinical trial should be included in a database register that is freely accessible by members of the public.**	The first addition recognizes the importance of communities in determining the risks and benefits of a research study. The second addition is meant to exclude benefits to researchers and sponsors. The deleted sentence is unnecessary and moreover does not fit in here. The last addition was recommended by several commentators and seems quite appropriate here.	See our paragraphs 8-10 above where we suggest to review the use of "should" and "must", and recommend to clarify the status of the DoH.
17. ~~Physicians~~ **Researchers** should abstain from engaging in research projects involving human ~~subjects~~ **beings** unless they ~~are confident~~ **can demonstrate** that the risks involved have been adequately assessed and can be satisfactorily managed. ~~Physicians~~	These requirements apply to all researchers, not just physicians. Researchers must demonstrate to the ethical review committee that they have taken all necessary measures to protect the research	See our paragraphs 8-10 above where we suggest to review the use of "should" and "must", and recommend to clarify the status of the DoH.

Researchers 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.	participants.	
18. ~~M~~**Biom**edical research involving human ~~subjects~~ **beings** should only be conducted if the importance of the objective outweighs the inherent risks and burdens to the ~~subject~~ **research participants**. ~~This is especially important when the human subjects~~ **participants** ~~are healthy volunteers.~~	The principle applies equally to all participants in research. Healthy volunteers are no different in this respect.	See our paragraphs 8-10 above where we suggest to review the use of "should" and "must", and recommend to clarify the status of the DoH.
~~19. M~~**Biom**~~edical research~~ ~~**involving vulnerable populations as research participants** 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 just after para. 15 where it is more appropriate.	No comment

Original DoH and WMA's suggestion for revisions	WMA's initial explanatory commentary	NCOB's critical commentary on revised paragraphs
20. ~~The subjects must be volunteers and informed participants in the research project~~ **Participation by competent individuals in biomedical research involving human beings must be voluntary. Although it may be appropriate to consult family members or community leaders, no competent individual may be enrolled in a research study unless he or she freely agrees to do so.**	The first change allows for involuntary participation in research by incompetent individuals as governed by paragraphs 24-26. 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.	We welcome this addition which is in line with comments we made in our previous submission. The addition helps ensure relevance of the DoH in the context of research carried out in developing countries. See also our paragraphs 8-10 above where we suggest to review the use of "should" and "must", and recommend to clarify the status of the DoH.

Original DoH and WMA's suggestion for revisions	WMA's initial explanatory commentary	NCOB's critical commentary on revised paragraphs
21. The ~~right of research subjects to safeguard their~~ **dignity and** integrity **of human participants in biomedical research** must always be respected. Every precaution should be taken to respect the**ir** privacy ~~of the subject,~~ **and** the confidentiality of ~~the patient's~~ **their** information and to minimize the impact of the study on ~~the subject's~~ **their** physical and mental integrity and	Minor grammatical changes.	See our paragraphs 8-10 above where we suggest to review the use of "should" and "must", and recommend to clarify the status of the DoH.

~~on the~~ personality ~~of the subject~~.		
22. In any **clinical** research ~~on~~ **involving competent** human beings, each **potential** ~~subject~~ **participant** 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**, and any other relevant details of the study**. The ~~subject~~ **potential participant** should be informed of the right to abstain from participation 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 participants, as well as to the methods used to deliver the information. Potential research participants should be informed that secondary/chance findings or information on genetic disease dispositions may impact their personal or professional lives**. After ensuring that the ~~subject~~ **potential participant** has understood the information, the ~~physician~~ **researcher** should then ~~obtain~~ **seek** the ~~subject's~~ **potential participant'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.	These requirements do not apply equally to non-clinical epidemiological research. Incompetent potential research participants are dealt with in paragraphs 24-26. The term 'potential participant' is used to indicate that an individual does not become a 'participant' until consent is given. Additions suggested by the several commentators. 'Obtain' has been changed to 'seek' to emphasize the potential participant's right to either refuse or agree to take part in the research.	We welcome the new addition on considering " specific information needs" which is especially relevant in the context of research carried out in developing countries. See also our paragraphs 8-10 above where we suggest to review the use of "should" and "must", and recommend to clarify the status of the DoH.
22A. In observational epidemiological research, conducted by examining large databases, there may be situations where informed consent is impossible, difficult, or unethical to obtain or poses a threat to the validity of research. Such research should be done only after consideration and approval of an ethical review committee.	New paragraph to deal with informed consent in non-clinical epidemiological research.	No comment

Original DoH and WMA's suggestion for revisions	WMA's initial explanatory commentary	NCOB's critical commentary on revised paragraphs

23. When ~~obtaining~~ **seeking** informed consent for **participation in** the research project the ~~physician~~ **researcher** should be particularly cautious if the ~~subject~~ **potential participant** is in a dependent relationship with the ~~physician~~ **researcher** or may consent under duress. In that case the informed consent should be ~~obtained~~ **sought** by ~~a well-informed physician~~ **an appropriately qualified individual** who is not engaged in the investigation and who is completely independent of this relationship.	These requirements apply to all researchers, not just physicians.	See our paragraphs 8-10 above where we suggest to review the use of "should" and "must", and recommend to clarify the status of the DoH.

Original DoH and WMA's suggestion for revisions	WMA's initial explanatory commentary	NCOB's critical commentary on revised paragraphs
24. For a **potential** research ~~subject~~ **participant** who is legally incompetent~~,~~ **or is** physically or mentally incapable of giving consent ~~or is a legally incompetent minor~~, the ~~investigator~~ **researcher** must obtain informed consent from the legally authorized representative in accordance with applicable law. These ~~groups~~ **individuals** should not be included in **a** research **study** unless ~~the research~~ **it** is ~~necessary~~ **intended** to promote the health of the population represented **by the potential participant** and this research cannot instead be performed ~~on~~ **with** legally competent persons. **Benefits and risks need to be adequately and carefully assessed in the best interest of the legally incompetent potential research participant.**	Minor changes for clarification. The repetition of 'legally incompetent' is unnecessary. The additional sentence provides extra protection for incompetent research participants.	See our paragraphs 8-10 above where we suggest to review the use of "should" and "must", and recommend to clarify the status of the DoH.
25. When a **potential** research ~~subject~~ **participant** deemed legally incompetent, such as a minor child, is able to give assent to decisions about participation in research, the ~~investigator~~ **researcher** must obtain that assent in addition to the consent of the legally authorized representative.		See our paragraphs 8-10 above where we suggest to review the use of "should" and "must", and recommend to clarify the status of the DoH.

Original DoH and WMA's suggestion for revisions	WMA's initial explanatory commentary	NCOB's critical commentary on revised paragraphs
26. **Clinical** ~~R~~**r**esearch on individuals	This does not apply to non-clinical	See our paragraphs 8-10 above where we

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 **and the research cannot be delayed**. The specific reasons for involving ~~research subjects~~ **individuals** with a condition that renders them unable to give informed consent ~~should~~ **must** be stated in the ~~experimental~~ **research** protocol for consideration and approval of the review committee. **Benefits and risks need to be adequately and carefully assessed in the best interest of the potential research participants.** The protocol ~~should~~ **must** state that consent to remain in the research should be obtained as soon as possible from the individual or a legally authorized surrogate.	epidemiological research. The additional requirement seems appropriate, as do the changes of 'should' to 'must'. The additional sentence provides extra protection for these research participants.	suggest to review the use of "should" and "must", and recommend to clarify the status of the DoH.
26A. In addition to obtaining appropriate informed consent for sample collection and investigation of samples, researchers should also ensure that when samples are stored for future use, consent is sought for storage. In addition, if the samples are then reused for a different purpose from that for which consent was originally obtained, appropriate consent and/or approval of the ethical review committee should be obtained for such reuse.	New paragraph.	See our paragraphs 8-10 above where we suggest to review the use of "should" and "must", and recommend to clarify the status of the DoH.
26B. Re-exposure of 'professional participant' patients to clinical trials should be actively discouraged. Guidance as to the number of exposures of patients per time, or in clinical trials, should be developed by regulatory authorities, in consultation with ethics committees.	New paragraph.	See our paragraphs 8-10 above where we suggest to review the use of "should" and "must", and recommend to clarify the status of the DoH.

Original DoH and WMA's suggestion for revisions	WMA's initial explanatory commentary	NCOB's critical commentary on revised paragraphs
27. ~~Both a~~**A**uthors**, editors** and publishers **all** have ethical obligations~~.~~ ~~In~~ **with regard to the** publication of the results of research. ~~, the~~	Minor changes as suggested by commentators.	See our paragraphs 8-10 above where we suggest to review the use of "should" and "must", and recommend to clarify the status of the DoH.

~~investigators~~ **Researchers** are ~~obliged to preserve~~ **accountable for** the accuracy of the results. **They have a duty to make publicly available the results of research on human participants. 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 any possible conflicts of interest should be declared in the publication. Reports of ~~experimentation~~ **research** not in accordance with the principles laid down in this Declaration should not be accepted for publication.	Clarification and expansion of the requirement.	

C. ADDITIONAL PRINCIPLES FOR BIOMEDICAL RESEARCH COMBINED WITH MEDICAL CARE

Original DoH and WMA's suggestion for revisions	WMA's initial explanatory commentary	NCOB's critical commentary on revised paragraphs
28. The physician may combine **bio**medical research with medical care~~,~~ only to the extent that the research is justified by its potential prophylactic, diagnostic**,** ~~or~~ therapeutic or **palliative** value **and if he or she is convinced that participation in the research study will not adversely affect the care of the patient**. When **bio**medical research is combined with medical care, additional standards apply to protect the**se** patients ~~who are research subjects~~.	The physician's primary responsibility is the well-being of the patient rather than the advancement of science.	

Original DoH and WMA's suggestion for revisions	WMA's initial explanatory commentary	NCOB's critical commentary on revised paragraphs
29. The benefits, risks, burdens and effectiveness of a new method should be tested against those of the best current prophylactic, diagnostic**,** ~~and~~ therapeutic **and palliative** methods**, except in the following circumstances:**	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.	It is not clear how the formal process of integrating the note of clarification into the paragraph resolves the issue of substantive disagreement. Moreover, disagreement about the standard of care to be provided concerns not only the use of placebo. We therefore

- . This does not exclude t**T**he use of placebo, or no treatment, **is permitted** in studies where no proven prophylactic, diagnostic**,** and therapeutic **or palliative** method exists.**;**		recommend to add, as a first bullet point, the following provision: "Provision of the best globally available methods cannot always be made available in developing countries. Where, for compelling reasons (which need to be justified to review boards in both the sponsoring country(ies) and the country(ies) where research takes place) research should nonetheless be carried out, the standard of care in the control group should be the same level as that which would otherwise be provided in the region where research takes place."
Note of clarification on paragraph 29 of the WMA Declaration of Helsinki 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, under the following circumstances:	Unnecessary. Minor change for clarification.	See our paragraphs 8-10 above where we suggest to review the use of "should" and "must", and recommend to clarify the status of the DoH.
- Where for compelling and scientifically sound methodological reasons its **the** use **of placebo** is necessary to determine the efficacy or safety of a prophylactic, diagnostic**,** and therapeutic **or palliative** method**;** or **and**	Removal of apparent discrepancy between former para. 29 and note of clarification.	
- Where a prophylactic, diagnostic**,** and therapeutic **or palliative** method is being investigated for a minor condition**, the use of placebo is permitted if** the patients who receive placebo will not be subject to any additional risk of serious or irreversible harm.	Unnecessary.	
All other provisions of the Declaration of Helsinki must be adhered to, especially the need for appropriate ethical and scientific review.		

Original DoH and WMA's suggestion for revisions	WMA's initial explanatory commentary	NCOB's critical commentary on revised paragraphs
30. At the conclusion of the study, ~~every~~ patient**s** entered into the study ~~should be assured of~~ **are entitled to be informed about the outcome of the study and to share any benefits that result from it, for example,** access to ~~the best proven~~ prophylactic, diagnostic**,** ~~and~~ therapeutic **or palliative** ~~methods~~ **treatments** identified by the study. ~~**Note of clarification on paragraph 30 of the WMA Declaration of Helsinki**~~ ~~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.~~	This change reinforces the ethical principle of entitlement without specifying the details of which benefits should be provided and who should provide them. Moved to paragraph 14.	We consider that this matter has been addressed more clearly in the new addition 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.		See our paragraphs 8-10 above where we suggest to review the use of "should" and "must", and recommend to clarify the status of the DoH.
32. In the treatment of a patient, where proven prophylactic, diagnostic**,** ~~and~~ therapeutic **and palliative** methods do not exist or have been ineffective, the physician**, after seeking expert advice**, with informed consent from the patient **or a legally authorized surrogate**, ~~must be free to~~ **may** use **an** unproven or new prophylactic, diagnostic**,** ~~and~~ therapeutic **or palliative** ~~measures,~~ **method** if in the physician's judgement it offers hope of saving life, re-establishing health or alleviating suffering. Where possible, ~~these~~ **this** measure~~s~~ should be made the object of research, designed to evaluate ~~their~~ **its** safety and efficacy. In all cases, new information should be recorded and, where appropriate,	Minor grammatical changes. Additional protections for patients.	

~~published~~ **made publicly available**. The other relevant guidelines of this Declaration should be followed.		