THE WORLD MEDICAL ASSOCIATION, INC.

Document no: **Title:**	**MEC 195/DoH & COM/Oct2013/Rev2** **WMA DECLARATION OF HELSINKI WORKING GROUP - FINAL REVISED VERSION & COMMENTS**	Original: English
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Note	The table below presents the final draft produced at WMA workgroup meeting in Washington DC (August 2013), with comments. This document was revised to reflect an amendment made by the Council prior to the General Assembly.	

	Revised text	Comments
	Preamble	New heading
1	The World Medical Association (WMA) has developed the Declaration of Helsinki as a statement of ethical principles for medical research involving human subjects**,** including research on identifiable human material and data. The Declaration is intended to be read as a whole and each of its constituent paragraphs should ~~not~~ be applied with~~out~~ consideration of all other relevant paragraphs.	Double negative removed.
2	~~Although~~ **Consistent with the mandate of the WMA,** the Declaration is addressed primarily to physicians~~,~~**.** **T**~~t~~he WMA encourages other**s** ~~participants in~~**who are involved in** medical research involving human subjects to adopt these principles.	Clarifies why the DoH is addressed to physicians. Clarifies what is meant by "participants" to avoid confusion.
	General Principles	New heading
3	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."	Old Paragraph 4, no changes.
4	It is the duty of the physician to promote and safeguard the health ~~and~~**, well-being and rights** of patients, including those who are involved in medical research. The physician's knowledge and conscience are dedicated to the fulfilment of this duty.	Old Paragraph 3 Introduces the concept of patient and subject well-being and rights early in the document.

5	Medical progress is based on research that ultimately must include studies involving human subjects.	Old Paragraph 5 separated into two parts; this is the first part (no changes), second part is in Paragraph 13.
6	The primary purpose of medical research involving human subjects is to understand the causes, development and effects of diseases and improve preventive, diagnostic and therapeutic interventions (methods, procedures and treatments). Even the best ~~current~~ **proven** interventions must be evaluated continually through research for their safety, effectiveness, efficiency, accessibility and quality.	Old Paragraph 7 Change made for terminology consistency.
7	Medical research is subject to ethical standards that promote **and ensure** respect for all human subjects and protect their health and rights.	Old Paragraph 9, divided into 2 parts; this is the first part, the second part of old Paragraph 9 is now in Paragraph 19. Change to this paragraph provides for a higher level of ethical standards.
8	~~**In medical research involving human subjects, the well-being of the individual research subject must take precedence over all other interests.**~~ **While the primary purpose of medical research is to generate new knowledge, this goal can never take precedence over the rights and interests of individual research subjects.**	Old Paragraph 6 Better clarifies the intent of this paragraph and still provides for the same level of protection of individual research subjects. Should mitigate some of the concerns regarding conflicts between this paragraph and other parts of the Declaration.
9	It is the duty of physicians who ~~**participate in**~~ **are involved in** medical research to protect the life, health, dignity, integrity, right to self-determination, privacy, and confidentiality of personal information of research subjects. The responsibility for the protection of research subjects must always rest with the physician or other health care professionals and never with the research subjects, even though they have given consent.	Old Paragraph 11 Last sentence moved up from the last part of old Paragraph 16. First part of old Paragraph 16 is now Paragraph 12. Avoids using the term “participate” which has been felt to be ambiguous. “Involved in” denotes the same level of involvement as “participate in” without the potential ambiguity.
10	Physicians ~~**should**~~ **must** consider the ethical, legal and regulatory norms and standards for research involving human subjects in their own countries as well as applicable international norms and standards. No national or international ethical, legal or regulatory requirement should reduce or eliminate any of the protections for research subjects set forth in this Declaration.	Old Paragraph 10 Higher standard of requirement.
11	~~**Appropriate caution must be exercised in the conduct of medical research that may harm the environment.**~~**Medical research should be conducted in a manner that minimises possible harm to the environment.**	Old Paragraph 13 Provides increased specificity around minimization of harm to the environment.
12	Medical research involving human subjects must be conducted only by individuals with the appropriate **ethics and** scientific **education,** training and qualifications. Research on patients or healthy volunteers requires the supervision of a competent and appropriately qualified physician or other health care professional.	First part of old Paragraph 16, second part of old Paragraph 16 is moved to end of Paragraph 9. Requires appropriate *ethics* education, training and qualifications (not just scientific) for those conducting research.

13	~~Populations~~ Groups that are underrepresented in medical research should be provided appropriate access to participation in research.	From old Paragraph 5, second sentence. First part of old Paragraph 5 is now the new Paragraph 5. Terminology change – use the term "groups" instead of "populations" or "communities" in most circumstances to ensure consistency and avoid confusion.
14	~~The p~~Physicians ~~may~~ who combine medical research with medical care ~~only to the extent that the~~ should involve their patients in research only to the extent that this 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.	Old paragraph 31 The old heading "Additional principles for medical research combined with medical care" has been removed as it is captured in this principle. Terminology now consistent with Paragraph 16 with respect to risks and burdens. Will help mitigate potential conflicts with other paragraphs.
15	**Appropriate compensation and treatment for subjects who are harmed as a result of participating in research must be ensured.**	New paragraph. It reflects the obligation to ensure that subjects who are harmed will receive compensation and treatment.
	Risks, Burdens and Benefits	New heading
16	In medical practice and in medical research, most interventions involve risks and burdens. Medical research involving human subjects may only be conducted if the importance of the objective outweighs the ~~inherent~~ risks and burdens to the research subjects.	Combines two previous Paragraphs (old Paragraphs 8 and 21). Editorial change.
17	~~Every~~ All medical research ~~study~~ involving human subjects must be preceded by careful assessment of predictable risks and burdens to the individuals and ~~communities~~ groups involved in the research in comparison with foreseeable benefits to them and to other individuals or ~~communities~~ groups affected by the condition under investigation. **Measures to minimise the risks must be implemented. The risks must be continuously monitored, assessed and documented by the researcher.~~The risks must always be monitored by the researcher throughout the trial.~~**	First part is old Paragraph 18. Applies to all medical research. Terminology changed from "communities" to "groups". New addition to the Paragraph. Clarifies the obligations of the researcher with respect to risks.
18	Physicians may not ~~participate in~~be involved in a research study involving human subjects unless they are confident that the risks ~~involved~~ have been adequately assessed and can be satisfactorily managed. ~~Physicians must immediately stop a study when~~ When the risks are found to outweigh the potential benefits or when there is conclusive proof of ~~positive~~ definitive outcomes ~~and beneficial results~~, physicians must assess whether to continue, modify or immediately stop the study.	Old Paragraph 20 Terminology consistency – from "participate" to "be involved in". Clarification of when the physician must assess the trial and expansion of options for action.
	Vulnerable Groups and Individuals	New heading

19	Some ~~research populations~~ groups and individuals are particularly vulnerable and ~~need special protection~~ may have an increased likelihood of being wronged or of incurring additional ~~and greater~~ harm. ~~These include those who cannot give or refuse consent for themselves and those who may be vulnerable to coercion or undue influence.~~ All vulnerable groups and individuals ~~need~~ should receive specifically considered protection.	Second part of old Paragraph 9. First part of old Paragraph 9 is now part of Paragraph 7. Terminology changes. Deletion of examples. Changes made for terminology consistency ("groups" instead of "populations/communities") and "vulnerable *individuals*" added.
20	Medical research ~~involving~~ with a ~~disadvantaged or~~ vulnerable ~~population or community~~group is only justified if the research is responsive to the health needs ~~and~~ or priorities of this ~~population or community~~group and the research cannot be carried out in a non-vulnerable ~~population~~ group. In addition, ~~and if there is a reasonable likelihood that~~ this ~~population or community~~group should stand~~s~~ to benefit from the knowledge, practices or interventions that result from the ~~results of the~~ research.	Old Paragraph 17 Use of "group" for consistency Clarification of requirements for carrying out research in a vulnerable population.
	Scientific Requirements and Research Protocols	New heading
21	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 adequate laboratory and, as appropriate, animal experimentation. The welfare of animals used for research must be respected.	Old Paragraph 12 with no changes.
22	The design and performance of each research study involving human subjects must be clearly described and justified in a research protocol. ~~The research protocol should discuss and justify the chosen study design.~~ 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 information regarding provisions for treating and/or compensating subjects who are harmed as a consequence of participation in the research study. In clinical trials, t~~T~~he protocol ~~should~~ must also describe appropriate arrangements for post-trial provisions ~~study access by study subjects to interventions identified as beneficial in the study or access to other appropriate care or benefits.~~	Old Paragraph 14 Editorial revision Editorial revisions Must be read in conjunction with Paragraph 34. Avoids repetition and ambiguity.
	Research Ethics Committees	New heading
23	The research protocol must be submitted for consideration, comment, guidance and approval to ~~a~~ the concerned research ethics committee before the study begins. This committee must be transparent in its functioning, must be independent of the researcher, the sponsor and any other undue influence and must be duly qualified. It must take into consideration the laws	Old Paragraph 15 Specifies which REC should be involved. Requires transparency in functioning and qualifications for committee members.

	and regulations of the country or countries in which the research is to be performed as well as applicable international norms and standards but these must not be allowed to reduce or eliminate any of the protections for research subjects set forth in this Declaration. The committee must have the right to monitor ongoing studies. The researcher must provide monitoring information to the committee, especially information about any serious adverse events. No **amendment** ~~**change**~~ to the protocol may be made without consideration and approval by the committee. **After the end of the study, the researchers must submit a final report to the committee containing a summary of the study's findings and conclusions.**	Small/editorial changes to the protocol do not need REC approval. New requirement that a report be submitted to the REC at the end of the study. This will also enhance transparency and accountability.
	Privacy and Confidentiality	New heading
24	Every precaution must be taken to protect the privacy of research subjects and the confidentiality of their personal information ~~**and to minimize the impact of the study on their physical, mental and social integrity.**~~	Old Paragraph 23 The second part of the sentence does not address the issue of privacy and confidentiality and is already addressed in paragraph 17.
	Informed Consent	New heading
25	Participation by ~~**competent**~~ individuals **capable of giving informed consent** as subjects in medical research must be voluntary. Although it may be appropriate to consult family members or community leaders, no ~~**competent**~~ individual **capable of giving informed consent** may be enrolled in a research study unless he or she freely agrees.	Old Paragraph 22 Clarification of meaning of "competence" in research context.
26	In medical research involving ~~**competent**~~ human subjects **capable of giving informed consent**, 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, **post-~~trial access~~study provisions** and any other relevant aspects of the study. The potential subject must 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 or another appropriately qualified individual must 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 must be formally documented and witnessed. **All medical research subjects should be given the option of being informed about the general outcome and results of the study.**	Old Paragraph 24 Clarification of meaning of "competence" in research context. Clarification of terminology. Part of old Paragraph 33 with changes to clarify that subjects have the choice of whether or not to be informed about the results.
27	When seeking informed consent for participation in a	Old Paragraph 26

	research study the physician ~~should~~ **must** be particularly cautious if the potential subject is in a dependent relationship with the physician or may consent under duress. In such situations the informed consent ~~should~~ **must** be sought by an appropriately qualified individual who is completely independent of this relationship.	Increased level of obligation – from should to must.
28	For a potential research subject who is ~~incompetent~~**incapable of giving informed consent**, the physician must seek informed consent from the legally authori~~s~~**z**ed representative. These individuals must not be included in a research study that has no likelihood of benefit for them unless it is intended to promote the health of the ~~population~~ **group** represented by the potential subject, the research cannot instead be performed with ~~competent~~ persons **capable of providing informed consent**, and the research entails only minimal risk and minimal burden.	Old Paragraph 27 Clarification of meaning of "competence" in research context. Terminology consistency.
29	When a potential research subject who is deemed **incapable of giving informed consent**~~incompetent~~ is able to give assent to decisions about participation in research, the physician must seek that assent in addition to the consent of the legally authori~~s~~**z**ed representative. The potential subject's dissent should be respected.	Old Paragraph 28 Clarification of meaning of "competence" in research context.
30	Research involving subjects who are physically or mentally incapable of giving consent, for example, unconscious patients, may be done only if the physical or mental condition that prevents giving informed consent is a necessary characteristic of the research ~~population~~ **group**. In such circumstances the physician ~~should~~ **must** seek informed consent from the legally authori~~s~~**z**ed 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~~ **must** be obtained as soon as possible from the subject or a legally authori~~s~~**z**ed representative.	Old Paragraph 29 Terminology consistency. Increased level of obligation – from should to must. Increased level of obligation – from should to must.
31	The physician must fully inform the patient which aspects of the**ir** 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 must never ~~interfere~~ **adversely affect** ~~with~~ the patient-physician relationship.	Old Paragraph 34 Editorial change Better terminology
32	For medical research using identifiable human material or data, **such as research on material or data contained in biobanks or similar repositories,** physicians must ~~normally~~ seek **informed** consent for ~~the~~ **its** collection, storage and/or reuse. There may be **exceptional** situations where consent would be impossible or **impracticable** ~~impractical~~ to obtain for such research ~~or would pose a threat to the validity of the research~~. In such situations the research may be done only after consideration and approval of a research ethics committee.	Old Paragraph 25 Introduces the issue of biobanks and similar repositories. Clarifies that consent must be informed. Terminology changes.

	Use of Placebo	New heading
33	The benefits, risks, burdens and effectiveness of a new intervention must be tested against those of the best ~~current~~ proven intervention**(s)**, except in the following circumstances: ~~**The use of placebo, or no treatment is acceptable in studies where no current proven intervention exists**~~**Where no proven intervention exists, the use of placebo, or no intervention, is acceptable**; or Where for compelling and scientifically sound methodological reasons the use of **any intervention less effective than the best proven one, the use of** placebo**, or no intervention** is necessary to determine the efficacy or safety of an intervention and the patients who receive **any intervention less effective than the best proven one,** placebo**,** or no ~~**treatment**~~ **intervention** will not be subject to ~~**any**~~ **additional** risk**s** of serious or irreversible harm **as a result of not receiving the best proven intervention**. Extreme care must be taken to avoid abuse of this option.	Old Paragraph 32 Rewording for consistency with rest of Paragraph. Terminology changes as previously discussed by WMA Council. Terminology changes as previously discussed by WMA Council.
	Post-Trial Provisions	New heading
34	**In advance of a clinical trial, sponsors, researchers and host country governments should make provisions for post-trial access for all participants who still need an intervention identified as beneficial in the trial. This information must also be disclosed to participants during the informed consent process.** ~~**At the conclusion of the study, patients entered into the study are entitled to be informed about the outcome of the study and to share any benefits that result from it, for example, access to interventions identified as beneficial in the study or to other appropriate care or benefits.**~~	Old Paragraph 33 Reworded based on stakeholder meetings and feedback and discussions of the Working Group. Higher level of onus on sponsors, researchers and host country governments. Part of this Paragraph is now included at the end of Paragraph 26.
	Research Registration and Publication and Dissemination of Results	New heading
35	Every ~~**clinical trial**~~**research study involving human subjects** must be registered in a publicly accessible database before recruitment of the first subject.	Old Paragraph 18 Expands the obligation for the registration of research studies.
36	**Researchers,** ~~**A**~~**a**uthors, **sponsors,** editors and publishers all have ethical obligations with regard to the publication **and dissemination** of the results of research. ~~**Authors**~~ **Researchers** have a duty to make publicly available the results of their research on human subjects and are accountable for the completeness and accuracy of their reports. ~~**They**~~ **All parties** should adhere to accepted guidelines for ethical reporting. Negative and inconclusive as well as positive results ~~**should**~~ **must** be published or otherwise made publicly available. Sources of funding, institutional affiliations and conflicts of interest ~~**should**~~ **must** be declared in the publication.	Old Paragraph 30 Adds researchers and sponsors to those who have ethical obligations. The duty to make the results publicly available best rests with researchers rather than authors. Editorial change. Increased level of obligations (“should” to “must”). Increased level of obligations (“should” to “must”).

	Reports of research not in accordance with the principles of this Declaration should not be accepted for publication.	
	Unproven Interventions in Clinical Practice	New heading
37	In the treatment of a**n individual** patient, where proven interventions do not exist or **other known interventions** have been ineffective, the physician, after seeking expert advice, with informed consent from the patient or a legally authori**s~~z~~**ed representative, may use an unproven intervention if in the physician's judgement it offers hope of saving life, re-establishing health or alleviating suffering. **~~Where possible, t~~**This intervention should **subsequently** be made the object of research, designed to evaluate its safety and efficacy. In all cases, new information **~~should~~ must** be recorded and, where appropriate, made publicly available.	Old Paragraph 35 Editorial changes for clarification of intent of Paragraph. Increased level of obligation. Increased level of obligation.

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18.10.2013