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25 August 2008

The World Medical Association
13, ch. du Levant
CIB - Bâtiment A
01210 Ferney-Voltaire
France

Re: DoH Call for Comments 08/2008

Dear Sir or Madam:

The Biotechnology Industry Organization (BIO) appreciates the opportunity to comment on the World Medical Association's (WMA's) Declaration of Helsinki.

BIO represents more than 1,200 biotechnology companies, academic institutions, state biotechnology centers and related organizations across the United States and in more than 30 other nations. BIO members are involved in the research and development of innovative healthcare, agricultural, industrial and environmental biotechnology technologies, thereby expanding the boundaries of science to benefit humanity by providing better healthcare, enhanced agriculture, and a cleaner and safer environment.

We very much appreciate the opportunity to provide input. Please do not hesitate to contact me for more information or clarification of our comments.

Sincerely,

/s/

Sara Radcliffe
Vice President, Science and Regulatory Affairs
Biotechnology Industry Organization

WORLD MEDICAL ASSOCIATION DECLARATION OF HELSINKI

2004 version	May 2008 Consultation Draft	BIO Changes	BIO Comments on May 2008 Consultation Draft
Subtitle: Ethical Principles for Medical Research Involving Human Subjects	Subtitle: Ethical Principles for Medical Research Involving Humans	Title Revision: We suggest retaining the original subtitle of the Declaration of Helsinki, with the exception of the change from "medical" to "biomedical", *i.e.*, "Ethical Principles for Biomedical Research Involving Human **Subjects**."	The proposed change is inconsistent with language used in the Good Clinical Practice (GCP) guidelines of the International Conference on Harmonisation (ICH) and the United States' Food and Drug Administration (FDA) regulations. The phrase "human subjects" should be retained throughout the Declaration because it is widely used and well-understood.
SUBTITLE	SUBTITLE		
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.		No comment

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	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.		No comment
2. It is the duty of 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.	3. It is the duty of the physician 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.	3. We suggest the alternate wording, "It is the duty of the physician to promote and safeguard the health of ~~people~~ **humans**, including ~~those~~ **human subjects** who are involved in medical research **conducted by that physician**."	The language is confusing whether this document is targeted primarily at treating physicians or physician/biomedical researchers.
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."		No comment

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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.	5. We suggest the alternate wording, "Populations that are underrepresented in medical research should be provided ~~appropriate~~ access to participation in research **when appropriate."**	BIO's February 8th, 2008 comments suggested that the statement be revised to include addition of "when appropriate" to the end of the statement. WMA revised the statement, but added the word "appropriate" before access to research instead of at the end of the sentence. We think this could be misread as promoting a double-standard – *i.e.*, that populations that are underrepresented are entitled to a lesser level of access to research – rather than what was intended, which is that depending on the hypothesis being tested and study design, it may or may not be possible to include and enrol an underrepresented population in the study. Therefore, BIO recommends that the placement of "appropriate" should be moved to modify the participation in the research not the access to participation, as shown.
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.		No comment

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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 effectiveness, efficiency, accessibility and quality.	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.		No comment
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.		No comment

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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.	9. We suggest the alternate wording, "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."	It is unclear what "educationally… disadvantaged" means. The other text in this paragraph relating to consent is clear and appropriate, and may cover whatever was intended by the reference to education.
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 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.		No comment
B. BASIC PRINCIPLES FOR ALL MEDICAL RESEARCH	B. PRINCIPLES FOR ALL MEDICAL RESEARCH		

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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 information of research subjects.	11. We suggest the alternate wording, "It is the duty of physicians who participate in medical research to protect the life, health, dignity, integrity, ~~right to self-determination,~~ and privacy~~, and confidentiality of personal information~~ of research subjects."	The previous language was redundant, because "the right to self determination" and "confidentiality of information" are covered by other words in this sentence.
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.	12. We suggest that this sentence be deleted: ~~The welfare of animals used for research must be respected.~~	While we fully support and endorse this statement, it is misplaced in a document on the ethical principles for medical research involving human subjects.
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		No comment

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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 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.	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 to methods identified as beneficial in the study or access to other appropriate care or benefits.	14. We suggest the alternate wording, "The protocol should contain a statement of the ethical considerations involved and should indicate ~~how~~ **that** the principles **arising out of** ~~in this~~ **the** 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~~ **identify whether there are** arrangements for post-study access by study subjects to methods ~~identified~~ **proven** as beneficial in the study or access to other appropriate care or benefits."	BIO recommends that the statement be revised to clarify acceptance of the principles rather than imply specific enumeration of how the principles have been addressed. The third sentence in the May draft provokes prescriptive details that are not possible to include in most protocols. Institutional affiliations for trial sites are usually not known when the protocol is finalized and incentives for subjects are addressed in each informed consent. This may be specific to an investigative site and Ethics Committees, and should not be a part of the protocol. Also, BIO recommends revision to the section on post-trial access to clarify that post-trial access will not apply to every study, but should be referenced in the protocol when applicable. The availability of post-trial access to the study drug will vary widely depending on the nature of the study and other factors, and cannot be an underlying expectation for every research study. To that same end, BIO recommends the phrase "methods proven as beneficial" rather than "methods identified as beneficial" to clarify that a method must be recognized as beneficial by established standards. In addition, use of "proven" is consistent with Paragraph 35 (May 2008 version).

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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.	15. We suggest the alternate wording, "~~No c~~Changes in the protocol should be made with~~out~~ consideration and approval by the committee**, as appropriate.**"	BIO recommends changes to the last sentence to reflect that certain minor changes to a protocol may require notification to but not approval by the ethics committee.

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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 research, even though the subject has given consent.	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 consent.	16. We suggest the alternate wording, "Medical research involving humans should be conducted ~~only~~ by scientifically qualified persons under the supervision of a competent and appropriately qualified physician **and/or a medical researcher**. The responsibility for the protection of research subjects should ~~always~~ rest with the physician **and/or a medical researcher** and never the research subjects, even though they have given consent."	Paragraph 1 of the Declaration includes medical research utilizing identifiable human material or data and includes this under the scope of medical research on human subjects. There may be instances in which a physician/healthcare professional (*i.e.*, one who directly provides healthcare) may not be involved in such a study and thus, "the supervision of a competent and appropriately qualified physician" may not be required. In addition, the responsibility for protection rests with the medical researcher, not necessarily a physician, even though a physician may be available as part of the team (e.g., a pharmacologist may conduct a bioavailability study but a physician may be available to assess adverse events, should they occur).
	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.		No comment

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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.	18. We suggest the alternate wording, "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 the subject or to others.** ~~to them and to other individuals or communities affected by the condition under investigation~~. **This does not preclude the participation of healthy volunteers in medical research."**	WMA's proposed wording removes the explicit note that participation of healthy volunteers is not precluded, and the end of this paragraph, "…affected by the condition under investigation" could be read as excluding healthy subjects.

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	19. Every clinical trial should be registered in a publicly accessible database before recruitment of the first subject.	19. We suggest the alternate wording, "**Controlled clinical investigations other than Phase I trials** should be registered in a publicly accessible database ~~before recruitment of the first subject~~."	BIO supports the goal of this proposed new section, namely to promote the transparency of and ease of access to clinical trial information by health care professionals and the general public. However, it is generally recognized that not every clinical trial should be registered in a publicly available database. For example, clinical trials that are exploratory or hypothesis-generating are of little guidance to prescribers and patients since they are preliminary, have statistical limitations, and are not intended or designed to provide conclusive information on safety or efficacy. In addition, these clinical trials are often highly proprietary, and disclosure of them at such an early stage could violate property rights and frustrate research and development efforts. Notably, recent laws passed in the United States (Title VIII of the Food and Drug Administration Amendments Act of 2007 (FDAAA)) and guidance issued in the EU (Public Consultation on list of fields to be made public from EudraCT for Paediatric Clinical Trials) both exclude Phase 1 trials from disclosure on public databases. BIO therefore encourages the WMA to reflect this rationale here, and modify the text to allow for the fact that not every clinical trial should or must be registered.

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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.		No comment
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.		No comment
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.			

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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.	22. We suggest the alternate wording, "Participation by legally competent individuals in medical research involving humans must be voluntary. Although it may be appropriate to consult **with** family members or community leaders **in certain situations about an individual's participation in a research study**, no competent individual should be enrolled in **such** a research study unless he or she freely agrees."	BIO recommends that this be revised as indicated to clarify the purpose of the consultation and emphasize that the decision by the individual is required for participation.
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.	23. We suggest the alternate wording, "Every **practical** 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."	BIO recommends the additional language as there may be many ways to protect privacy which may not be practical or are unnecessary with other measures.

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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.	24. We suggest the alternate wording, "After ensuring that the potential subject has understood the information, the physician should then **obtain** ~~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."	We ask that WMA reconsider its suggested change from "obtain" to "seek." This change would mean that the paragraph no longer implies that consent should be obtained, only that it should be sought.

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	25. For medical research using human tissues or data, physicians 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.		No comment
23. When obtaining informed consent for the research 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.	26. When seeking informed consent for participation in the 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.		No comment

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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.		No comment
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.		No comment

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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.		No comment

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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 this Declaration should not be accepted for publication	30. We suggest the alternate wording, "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 **that can improve patient care** ~~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 **arising out** of this Declaration should not be accepted for publication."	We are concerned that unless WMA specifies to which trials this language applies, this paragraph can be interpreted to mean that results from *all* trials should be made public. (Please see comments to 19.) That would include Phase I trials as well as trials for products that were not approved. This is not consistent with United States law. In addition, it is not clear what purpose it would serve to publish the results of Phase I trials, because such trials typically have limited statistical power and serve primarily to generate hypotheses for possible future trials. BIO supports public disclosure of the analysis of the results of confirmatory trials for marketed drugs within one year of the completion of the analysis. In addition, BIO recommends revisions to emphasize the intent of the Declaration rather than the specifics.
C. ADDITIONAL PRINCIPLES FOR MEDICAL RESEARCH COMBINED WITH MEDICAL CARE	C. ADDITIONAL PRINCIPLES FOR MEDICAL RESEARCH COMBINED WITH MEDICAL CARE		

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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.		No comment

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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, 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	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.	32. We suggest the alternate wording, "The benefits, risks, burdens and effectiveness of a new method should be tested against those of the ~~best~~ **an effective and well tolerated** 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."	BIO recommends the following language because the "best" should be considered in terms of efficacy and safety. Further, it is often not possible to identify unequivocally the best method.

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- 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.			

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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.		No comment
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.		No comment

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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.	35. We suggest the alternate wording, "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."	BIO recommends returning to the original text. Introduction of "expert advice" is vague and justification of an "expert" can be subjective. It can be expected that the physician would seek appropriate input as needed. In addition, it is also unclear how and by whom experts would be compensated in these situations.