Outline

• The World Medical Association
• Declaration of Helsinki: history and status
• 2007-2008 revision process
• Changes
  – Scope
  – Placebo use
  – Access to benefits
  – Other proposed changes
• The DoH, FDA and GCP
• Conclusion
The World Medical Association

- Established after WW2, mainly in reaction to reports of atrocities involving physicians
- Global representative body for physicians
- 85 National Medical Associations, approximately 7 million physicians
WMA’S Legitimacy

• No legal authority
• Sources of its moral authority
  - Pioneer in guidelines development (DoH)
  - Members’ experience in ethics and research
  - Extensive consultation/consensus building
  - Quality of its policies
How Does the WMA Decide What is Ethical?

- Considers existing principles of medical ethics
- Extensive consultation on proposed new policies or amendments to existing policies
- Discussion at Medical Ethics Committee meetings; recommendations to Council and General Assembly
- 75% majority vote at Assembly to adopt or amend ethics policies
Roles of the WMA in Medical Research

• Establishment of high-level global ethical standards for medical research (*Declaration of Helsinki*)

• Bridge between physicians and researchers

• Advocate for patients serving as research subjects

• Participant in capacity-building and education initiatives (NEBRA, TREEE for Africa project, Strengthening the Capacity of Research Ethics Committees in Africa project, Clinical Trials talking book)
Declaration of Helsinki

Brief History

- First adopted in 1964
- Significant additions in 1975
- Major revision and reorganization in 2000
- ‘Notes of clarification’ in 2002 and 2004
- Latest revision begun in 2007 and completed in October 2008
Declaration of Helsinki - Influence

- CIOMS Guidelines follow the DoH quite closely
- ICH-GCP Guidelines require adherence to “the principles that have their origin in the DoH”
- EC Directive on Clinical Trials and the U.S. FDA (until recently) require adherence to the principles of the DoH (not the current version, however)
- The UNESCO Declaration on Bioethics and Human Rights cites the DoH
Declaration of Helsinki - Influence

• DoH is by far the most cited research ethics document by research ethics committees in Central and Western Africa (NEBRA, 2006)

• Standing Committee of European Doctors (CPME) “urges EMEA and national pharmaceutical authorities to no longer accept clinical trial data that are not in accordance with the Declaration of Helsinki.” (15 March 2008)
2007-2008 Revision Process

- May 2007  WMA council decision to begin a review
- Identify gaps, avoid complete re-opening
- Use the review process to promote the DoH.
- A formal working group appointed - members are the Medical Associations of Brazil, Germany, Japan, South Africa and Sweden
2007-2008 Revision Process

- Three stakeholder workshops: in Helsinki, Cairo and Sao Paulo
- Four sets of WMA meetings: May and October 2007, May and October 2008
- Final approval at 2008 WMA General Assembly in Seoul
Principal Changes from 2004 Version

- Integration of notes of clarification in the text
- Many editorial and terminology changes
- Some reorganization of paragraphs
- Addition of requirement to include clinical trials in a publicly accessible database (para. 19)
Principal Changes from 2004 Version (cont.)

- Additional requirements for informed consent (paras. 22-29)
- Different requirements for research on human material and data (para. 25)
- Acknowledgment of other health care professionals in supervising medical research (para. 16)
- Rewording of controversial paragraphs 29 and 30 of 2004 version
Scope of DoH – physicians or all researchers?

• “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” (paragraph 1)
Scope of DoH – Physicians or all Researchers?

- New paragraph 2 – “Although the Declaration is addressed primarily to physicians, the WMA encourages other participants in medical research involving human subjects to adopt these principles.”
Scope of DoH

• A statement of general principles or should it provide some detailed information about how the principles are to be applied?
• Subtitle: “Ethical Principles for Medical Research Involving Human Subjects”
• Former paragraphs 13 and 22 already quite detailed
• Many suggestions for additional details
• Conclusion – no change
Placebos

• Former paragraph 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.”
Rewording of Paragraph 29 (new 32)

“The benefits, risks, burdens and effectiveness of a new intervention must be tested against those of the best current proven intervention, except in the following circumstances:

- The use of placebo, or no treatment, is acceptable in studies where no current proven intervention exists; or
- Where for compelling and scientifically sound methodological reasons the use of placebo is necessary to determine the efficacy or safety of an intervention and the patients who receive placebo or no treatment will not be subject to any risk of serious or irreversible harm. Extreme care must be taken to avoid abuse of this option.”
Access to Benefits

- Former paragraph 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.”
Rewording of Paragraph 30 (new 33)

• “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.”

• Addition to paragraph 14: “The protocol should describe arrangements for post-study access by study subjects to interventions identified as beneficial in the study or access to other appropriate care or benefits.”
Other Proposed Changes

• “For medical research using identifiable human material or data, physicians must normally seek consent for their collection, analysis, storage and/or reuse. 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 may be done only after consideration and approval of a research ethics committee.” (new paragraph 25)
Other Proposed Changes

- Researchers should be required to explain *how* the principles of the DoH have been addressed in the research protocol rather than simply confirm *that* their proposed research complies with these principles (paragraph 14)
The DoH, FDA and GCP

• FDA regulations on acceptance of foreign clinical studies not conducted under an investigational new drug application (IND) as support for an IND or application for marketing approval for a drug or biological product

• Until last year (October 27) – FDA required such studies to be conducted in accordance with ethical principles stated in the Declaration of Helsinki issued by the World Medical Association, specifically the 1989 version

• Henceforth, just compliance with GCP
Ethics vs. Good Clinical Practice

• ICH (1996) defines GCP as “A standard for the design, conduct, performance, monitoring, auditing, recording, analyses, and reporting of clinical trials that provides assurance that the data and reported results are credible and accurate, and that the rights, integrity, and confidentiality of trial subjects are protected.”

• Ethics has a narrower scope and generally higher standards than GCP. It also involves consideration of how these standards should be applied in specific circumstances.
Regulation vs. Ethics

• Regulation: what *must* be done (legal and other sanctions)

• Ethics: what *should* be done, even if not required (non-binding guidelines)

• Why do more than what is required:
  - Values (altruism, compassion, justice, etc.)
  - Reputation
Conclusion

• Many different, and often conflicting, interests in research ethics
• Interests of research subjects should prevail over those of researchers, research institutions and commercial enterprises, sponsors and funders, etc
• All stakeholders, but especially RECs, should aim for the highest ethical standards.
Thank You !!

www.wma.net

John R. Williams, Ph.D.
University of Ottawa, Canada
jrewms@yahoo.com