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Revision of the CIOMS ethical guidelines for Biomedical Research

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What is CIOMS?

- Council of International Organizations of Medical Sciences
- An NGO: international, non-governmental, non-profit organization
- Forum to consider and prepare advice on contentious issues in research ethics and safety of pharmaceuticals...
- ... for WHO, public health authorities, academia, pharmaceutical industry and others.
- Established 1949 by WHO and UNESCO

Who is CIOMS?

Members:

- 45 international member organizations, representing many of the biomedical disciplines
- 18 national members mainly representing national academies of sciences and medical research councils
- Executive committee:
  - 10 member organizations

CIOMS research ethics guidelines

- Purpose: indicate how fundamental ethical principles and Declaration of Helsinki can be applied effectively in medical research world-wide in different:
  - cultures, religions, traditions, socioeconomic circumstances;
  - with special attention for low and middle income countries.

- Content: guidelines plus commentaries (!)

- 2002 Guidelines have been widely used, notably in LMICs.
  - Indication: translation into several languages, including French, Spanish, Portuguese, Chinese, Arabic, Czech, and Vietnamese.

Reasons for revision

- Changes in other relevant documents
  - UNESCO, WHO, Council of Europe, various regional institution (such as EU, MERCOSUR), European Medicines Agency (EMA), International Conference on Harmonisation (ICH), new Laws in LA etc
- Changes in the field of research
  - clinical trials in elderly (Alzheimer disease, dementia etc) and paediatric trials: areas have expanded and will expand even more in the future.
- Developments within ethics of science
  - More need for transparency about conflicts of interests, obligation to publish, register trials etc

The process of revision of ethics gIns

- Working group of 10 people (many balances)
- Collaboration with WHO (MoU)
- Advisors (WMA, UNESCO, COHRED)
- Draft posted on the web Sept 2015 – March 2016:
  - Consultation among CIOMS member organisations
  - Consultation meetings in Mexico, Phillipines, South Africa, Singapore, Edinburg
  - Comments in English and Spanish
- Many (groups of) commentators with high quality feed back

Role of evidence

- Modern demand to base guidelines on (graded) evidence
- Obviously: ethics cannot be derived solely from facts
- But facts are relevant..
- And reasoned positions of others should be taken into account
- Therefore we used systematic literature searches
- All positions are reasoned positions

Current challenges in research ethics

- Bridge valley of death in translational research (1)
- Fair research in low-resource settings (2)
- Science in transition, public engagement (7)
- Research: less a single project and more part of a system (LHS, big data) (11, 12)
- Protect participant AND ensure benefits of research (19)

How did CIOMS respond? (NB interconnectedness of guidelines!)

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This conference

1 – Scientific and social value and respect for rights

2 – Research conducted in low-resource settings

3 – Equitable distribution of benefits and burdens in the selection of groups of participants

4 – Potential benefits and risks of research

5 – Choice of control in clinical trials

6 – Caring for participants' health needs

7 – Community engagement

8 – Collaborative partnership and capacity building

9 – Individual informed consent

10 – Modifications and waivers of informed consent

11 – Collection, storage and use of biological materials and related data

12 – Collection, storage and use of data in health-related research

13 – Reimbursement and compensation for research participants

14 – Treatment and compensation for research-related harms

15 – Research involving vulnerable persons

16 – Research involving individuals who are incapable of giving informed consent

17 – Research involving children and adolescents

18 – Women as research participants

19 – Pregnant women and lactating women as research participants

20 – Research in disasters and disease outbreaks

21 – Cluster randomized trials

22 – Use of online environment and digital tools

23 – Research ethics committees and review

24 – Public accountability

25 – Conflicts of interest

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ESTABLISHED UNDER THE AUSPICES OF THE WORLDHEALTH ORGANIZATION AND UNESCO

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1 Social value

The ethical justification for undertaking health-related research involving humans is its scientific and social value: the prospect of generating the knowledge and the means necessary to protect and promote people's health. Patients, health professionals, researchers, policy-makers, public health officials, pharmaceutical companies and others rely on the results of research for activities and decisions that impact individual and public health, welfare, and the use of limited resources. (…)

1 Social value (ctnd)

Therefore, researchers, sponsors, research ethics committees, and health authorities, must ensure that proposed studies are scientifically sound, build on an adequate prior knowledge base, and are likely to generate valuable information.

Although scientific and social value are the fundamental justification for undertaking research, researchers, sponsors, research ethics committees and health authorities have a moral obligation to ensure that all research is carried out in ways that uphold human rights, and respect, protect, and are fair to study participants and the communities in which the research is conducted. Scientific and social value cannot legitimate subjecting study participants or host communities to mistreatment, or injustice.

2 Research conducted in low-resource settings

Before instituting a plan to undertake research in a population or community in low-resource settings, the sponsor, researchers, and relevant public health authority must ensure that the research is responsive to the health needs or priorities of the communities or populations where the research will be conducted. (…)

2 low-resource settings (ctnd)

As part of their obligation, sponsors, and researchers must also:

- make every effort, in cooperation with government and other relevant stakeholders, to make available as soon as possible any intervention or product developed, and knowledge generated, for the population or community in which the research is carried out, and to assist in building local research capacity. In some cases, in order to ensure an overall fair distribution of the benefits and burdens of the research, additional benefits such as investments in the local health infrastructure should be provided to the population or community; and
- consult with and engage communities in making plans for any intervention or product developed available, including the responsibilities of all relevant stakeholders.

4 Potential individual benefits and risks of research

To justify imposing any research risks on participants in health research, the research must have social and scientific value. Before inviting potential participants to join a study, the researcher, sponsor and the research ethics committee must ensure that risks to participants are minimized and appropriately balanced in relation to the prospect of potential individual benefit and the social and scientific value of the research.

The potential individual benefits and risks of research must be evaluated in a two-step process. First, the potential individual benefits and risks of each individual research intervention or procedure in the study must be evaluated. In a second step, the aggregate risks and potential individual benefits of the entire study must be assessed and must be considered appropriate.

4 Potential individual benefits and risks of research

For research interventions or procedures that have the potential to benefit participants, risks are acceptable if they are minimized and outweighed by the prospect of potential individual benefit and the available evidence suggests that the intervention will be at least as advantageous, in the light of foreseeable risks and benefits, as any established effective alternative.

For research interventions or procedures that offer no potential individual benefits to participants, the risks must be minimized and appropriate in relation to the social and scientific value of the knowledge to be gained (expected benefits to society from the generalizable knowledge).

In general, when it is not possible or feasible to obtain the informed consent of participants, research interventions or procedures that offer no potential individual benefits must pose no more than minimal risks. However, a research ethics committee may permit a minor increase above minimal risk when it is not possible to gather the necessary data in another population or in a less risky or burdensome manner, and the social and scientific value of the research is compelling.

7 Community engagement

Researchers, sponsors, health authorities and relevant institutions should engage potential participants and communities in a meaningful participatory process that involves them in an early and sustained manner in the design, development, implementation, design of the informed consent process and monitoring of research, and in the dissemination of its results.

11 Collection, storage and use of biological materials and related data (1)

When biological materials and related data, such as health or employment records, are collected and stored, institutions must have a governance system to obtain authorization for future use of these materials in research. Researchers must not adversely affect the rights and welfare of individuals from whom the materials were collected.

When specimens are collected for research purposes, either specific informed consent for a particular use or broad informed consent for unspecified future use must be obtained from the person from whom the material originally is obtained. The ethical acceptability of broad informed consent relies on proper governance.

11 Collection, storage and use of biological materials and related data (2)

When human biological materials are left over after clinical diagnosis or treatment (so-called “residual tissue”) and are stored for future research, a specific or broad informed consent may be used or may be substituted by an informed opt-out procedure. This means that the material is stored and used for research unless the person from whom it originates explicitly objects. The informed opt-out procedure must fulfill the following conditions: 1) patients need to be aware of its existence; 2) sufficient information needs to be provided; 3) patients need to be told that they can withdraw their data; and 4) a genuine possibility to object has to be offered.

11 Collection storage and use of biological materials and related data (3)

When researchers seek to use stored materials collected for past research, clinical or other purposes without having obtained informed consent for their future use for research, the research ethics committee may waive the requirement of individual informed consent if: 1) the research would not be feasible or practicable to carry out without the waiver; and 2) the research has important social value; and 3) the research poses no more than minimal risks to participants or to the group to which the participant belongs.

11 Collection storage and use of biological materials and related data (4)

Custodians of biological materials must arrange to protect the confidentiality of the information linked to the material, by sharing only anonymized or coded data with researchers, and limiting access to the material of third parties. The key to the code must remain with the custodian of the biological material.

The transfer of biological materials must be covered by a Material Transfer Agreement (MTA).

11 Collection storage and use of biological materials and related data (5)

Biological materials and related should only be collected and stored in collaboration with local health authorities. The governance structure of such collection should have representation of the original setting. If the specimen and data are stored outside the original setting, there should be provisions to return all materials to that setting and share possible results and benefits

12 Collection, storage and use of data in health-related research (1)

When data are stored, institutions must have a governance system to obtain authorization for future use of these data in research. Researchers must not adversely affect the rights and welfare of individuals from whom the data were collected.

When data are collected and stored for research purposes, either specific informed consent for a particular use or broad informed consent for unspecified future use must be obtained from the person from whom the data are originally obtained. The ethical acceptability of broad informed consent relies on proper governance.

12 Collection, storage and use of data in health-related research (2)

When data are used that were collected in the context of routine clinical care, an informed opt-out procedure must be used. This means that the data may be stored and used for research unless a person explicitly objects. However, a person's objection is not applicable when it is mandatory to include data in population-based registries. The informed opt-out procedure must fulfill the following conditions: 1) patients need to be aware of its existence; 2) sufficient information needs to be provided; 3) patients need to be informed that they can withdraw their data; and 4) a genuine possibility to object has to be offered.

12 Collection, storage and use of data in health-related research (3)

When researchers seek to use stored data collected for past research, clinical or other purposes without having obtained informed consent for their future use for research, the research ethics committee may consider to waive the requirement of individual informed consent if: 1) the research would not be feasible or practicable to carry out without the waiver; and 2) the research has important social value; and 3) the research poses no more than minimal risks to participants or to the group to which the participant belongs.

12 Collection, storage and use of data in health-related research (4)

Custodians of the data must arrange to protect the confidentiality of the information linked to the data, by sharing only anonymised or coded data with researchers, and limiting access to the material of third parties. The key to the code must remain with the custodian of the data.

Data from low-resource settings should only be collected and stored in collaboration with local health authorities. The governance structure of such a databank must have representation of the original setting. If the collection is stored outside the original setting there should be provisions to return all data to that setting and share possible results and benefits

12 Collection, storage and use of data in health-related research (4)

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17 Research involving children and adolescents (1)

Children and adolescents must be included in health-related research unless a good scientific reason justifies their exclusion. As children and adolescents have distinctive physiologies and health needs, they merit special consideration by researchers and research ethics committees. However, their distinctive physiologies and emotional development may also place children and adolescents at increased risk of being harmed in the conduct of research. Moreover, without appropriate support, they may not be able to protect their own interests due to their evolving capacity to give informed consent. Specific protections to safeguard children's rights and welfare in the research are therefore necessary.

17 Research involving children and adolescents (2)

Before undertaking research involving children and adolescents, the researcher and the research ethics committee must ensure that:

- a parent or a legally authorized representative of the child or adolescent has given permission; and
- the agreement (assent) of the child or adolescent has been obtained in keeping with the child's or adolescent's capacity, after having been provided with adequate information about the research tailored to the child's or adolescent's level of maturity.

If children reach the legal age of maturity during the research, their consent to continued participation should be obtained.

In general, the refusal of a child or adolescent to participate or continue in the research must be respected, unless, in exceptional circumstances, research participation is considered the best medical option for a child or adolescent.

17 Research involving children and adolescents (3)

For research interventions or procedures that have the potential to benefit children or adolescents, the risks must be minimized and outweighed by the prospect of potential individual benefit.

For research interventions or procedures that have no potential individual benefits for participants, two conditions apply:

- the interventions and procedures should be studied in adults first, when these interventions and procedures target conditions that affect adults as well as children and adolescents, unless the necessary data cannot be obtained without participation of children or adolescents; and
- the risks must be minimized and no more than minimal.

When the social value of the studies with such research interventions and procedures is compelling, and these studies cannot be conducted in adults, a research ethics committee may permit a minor increase above minimal risk.

17 Research involving children and adolescents (1)

19 Pregnant and lactating women

- Pregnant and breastfeeding women have distinctive physiologies and health needs. Research designed to obtain knowledge relevant to the health needs of the pregnant and breastfeeding woman must be promoted. Research in pregnant women must be initiated only after careful consideration of the best available relevant data.
- In no case must the permission of another person replace the requirement of individual informed consent by the pregnant or breastfeeding woman.
- For research interventions or procedures that have the potential to benefit either pregnant or breastfeeding women or their fetus or infant, risks must be minimized and outweighed by the prospect of potential individual benefit (…)

19 Pregnant and lactating women (contd)

For research interventions or procedures that have no potential individual benefits for pregnant and breastfeeding women:

- the risks must be minimized and no more than minimal; and
- the purpose of the research must be to obtain knowledge relevant to the particular health needs of pregnant or breastfeeding women or their fetuses or infants.

When the social value of the research for pregnant or breastfeeding women or their fetus or infant is compelling, and the research cannot be conducted in non-pregnant or non-breastfeeding women, a research ethics committee may permit a minor increase above minimal risk.

19 Pregnant and lactating women (contd)

Short-term and long-term follow-up of the fetus and the child may be required in research involving pregnant and breastfeeding women depending upon the study intervention and its potential risks.

As a general rule, health-related research involving pregnant women that has the potential for harm to the fetus should be conducted only in settings where women can be guaranteed access to a safe, timely and legal abortion in the event that participation in the research makes the pregnancy unwanted.

Conclusion

- Almost all guidelines are newly drafted
- Collaboration with WHO very useful
- Transparent process with open consultation, strengthening credibility
- Revised (2016) Guidelines:
  - available on the web for free: *www.cioms.ch*
  - Printed version available against shipping costs

Conclusion

- We want to keep the CIOMS guidelines
  - *a living document*
  - *based on thorough ethical reflection*
  - *ready to meet future challenges of research*