Ethical Considerations in Research

Risks & Benefits

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“Responsible Conduct of Research (RCR) and Research Ethics”, DMR (HQ), July 2020
Outline

1. Ethical Research: What makes Research Ethical?
2. Ethical Considerations: Ethical Framework
3. Risks and Benefits: Definition, Stratification and Assessment
4. Guidelines on R & B: International, Regional, National and Institutional
5. R & B in Local Practice: DMR, UPH and Other Medical Institutions
6. Way forward: Take Home Message
Research vs Human Research

Research: for the advancement of the science

Research involving Humans
  1. For the Advancement of Science
  2. For the Protection of Human Subjects

Ethical Considerations?
  for the Protection of Human Subjects

Role (Main Function) of ERC/REC/IRB
  by Reviewing and Monitoring the Research
1. Ethical Research

JAMA. 2000; 283: 2701-2711
by Emanuel et al (2000)

Seven Ethical Requirements

1. Social Value
2. Scientific Validity
3. Fair Subject Selection
4. Favorable Risk-Benefit Ratio
5. Independent Review
6. Informed Consent
7. Human Subject Protection
1. Ethical Research

**JAMA. 2000; 283: 2701-2711**
by Emanuel et al (2000)

**The Journal of Infectious Diseases. 2004; 189:930-7**
by Emanuel et al (2004)
1. Ethical Research

*JAMA.* 2000; 283: 2701-2711

*The Journal of Infectious Disease.* 2004; 189:930-7

*Oxford University Press.*

Ethical Framework

NIH adopted
2. Ethical Considerations: Ethical Framework

1. Collaborative Partnership
2. Social Value
3. Scientific Validity
4. Fair Subject Selection
5. **Favourable Risk-Benefit Ratio**
6. Independent Review
7. Informed Consent
8. Human Subject Protection
3. Risks and Benefits: Definition, Stratification and Assessment

**Risks:** The probability of harm (physical, psychological, social, legal, or economic) occurring as a result of participation in a research study.

**Benefits:** A valued or desired outcome as a result of participation in a research study.

All research have some risks! So, a research should have favourable risk-benefit ratio!!
Stratification of Risks: Low or High?

1. **Minimal Risk:** the probability and magnitude of harm or discomfort anticipated in the research which are not greater than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests.

   **Minor Increase above Minimal Risk** (especially with Vulnerable Population)

2. **Greater Than Minimal Risk**

   **Maximal Risk ???**

Ref: US DHHS OHRP (2009) Protection of Human Subjects in 45 CFR 46 which defines only Minimal Risk in Research
Types of Research-related Risks

1. Physical

2. Psychological

3. Social

4. Legal

5. Economical

(Ref: WHO (2011) Standards and Operational Guidance for Ethics Review)
Types of Research-related Risks

1. Physical
   Any form of research related physical injuries to the participants
   (discomfort, pain, injury, illness or disease)

2. Psychological
   Any form of mental stresses
   (anxiety, depression, guilt, shock, loss of self-esteem & altered behaviour)

3. Social
   Any changes in social standing/relationship of the participant
   (in the family, work, community)

4. Legal
   Any liability for a violation of the law

5. Economical
   Any loss of income, additional costs

(Ref: WHO (2011) Standards and Operational Guidance for Ethics Review)
Risks: Assessment and Management

Assessment: Risks to Participants, Researchers, Sponsors and RECs, ...

Risk Identification, Estimation, and Evaluation by

- the Researchers
- the Sponsors
- the ERCs/RECs/IRBs

Management: Risks Protection Mechanisms

Minimizing the Risks & Maximizing the Benefits
Risks Monitoring, Reporting, Excluding and Stopping the Research !!
Benefit

Benefits to Participants, Researchers, Sponsors and RECs, ...

1. Direct medical benefit to subjects
2. Indirect benefit to subjects
3. Benefit to others

Incentives should not exceed "reimbursement" for the subject’s time and expenses!

According to minimum daily wage!!
Risks and Benefits

Risks and benefits must be "balanced" and in a favourable ratio.

Net Risks!

Do the potential benefits to the individual participants outweigh the risks?

If not, does the knowledge gained from the study for society justify the net risks to the individual participants?

But in research with new drug, device and procedure ??
4. Guidelines on Risks and Benefits

1. International: WHO, WMA, CIOMS
2. US DHHS CFR: Research Common Rules
3. WHO SEA Region, FERCAP
4. DMR Guidelines
5. Institutional Guidelines
4. Guidelines on Risks and Benefits

International Ethical Guidelines for Health-related Research Involving Humans

Prepared by the Council for International Organizations of Medical Sciences (CIOMS) in collaboration with the World Health Organization (WHO)

Geneva 2016

INTERNATIONAL COUNCIL FOR HARMONISATION OF TECHNICAL REQUIREMENTS FOR PHARMACEUTICALS FOR HUMAN USE (ICH)

ICH Harmonised Guideline

INTEGRATED ADDENDUM TO ICH E6(R1):
GUIDELINE FOR GOOD CLINICAL PRACTICE

E6(R2)

Current Step 4 version
dated 9 November 2016

“Responsible Conduct of Research (RCR) and Research Ethics”, DMR (HQ), July 2020
International Ethical Guidelines on Risks & Benefits

1. CIOMS
2. WMA DoH

CONTENTS

Risks, Burdens and Benefits

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 risks and burdens to the research subjects.

17. All medical research involving human subjects must be preceded by careful assessment of predictable risks and burdens to the individuals and groups involved in the research in comparison with foreseeable benefits to them and to other individuals or 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.

18. Physicians may not be involved in a research study involving human subjects unless they are confident that the risks have been adequately assessed and can be satisfactorily managed.

When the risks are found to outweigh the potential benefits or when there is conclusive proof of definitive outcomes, physicians must assess whether to continue, modify or immediately stop the study.

Vulnerable Groups and Individuals

19. Some groups and individuals are particularly vulnerable and may have an increased likelihood of being wronged or of incurring additional harm.

All vulnerable groups and individuals should receive specifically considered protection.

20. Medical research with a vulnerable group is only justified if the research is responsive to the health needs or priorities of this group and the research cannot be carried out in a non-vulnerable group. In addition, this group should stand to benefit from the knowledge, practices or interventions that result from the research.
### 5. R & B in Local Practice

**Institutional Templates, Checklists:**

1. DMR Myanmar
2. UMB USA

#### 5. RISK / BENEFIT ASSESSMENT

<table>
<thead>
<tr>
<th>Questions</th>
<th>Yes</th>
<th>No</th>
<th>N/A</th>
<th>Comments</th>
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<tr>
<td>Are the following foreseeable risks present and clearly defined?</td>
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<td>- Physical risks?</td>
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<td>- Social risks?</td>
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<td>- Psychological risks?</td>
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<td>- Legal/political risks?</td>
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<td>- Economic risks?</td>
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<td>Are risks minimized as much as possible (e.g., appropriate exclusion criteria, substitution of less risky interventions, etc)?</td>
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<td>Are there potential direct benefits to individuals, and if so, are they well described? (do not consider financial incentives as direct benefits)</td>
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<td>Is the knowledge to be gained considered?</td>
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<td><strong>FINAL ASSESSMENT:</strong> Are risks to subjects reasonable when compared to anticipated direct benefits, if any, and to the knowledge to be gained?</td>
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Do we have Risks and Benefits Assessment in our Institutions?

- Investigators’ Check-list?
- Reviewer’s Check-list?
- Research Monitoring?
6. Way Forward: Take Home Message

1. Institutional Research and Research Ethics Guideline
2. Definition and Stratification of Risks and Benefits?
3. Risks and Benefits Assessment and Management?
4. Continuous Review and Research Monitoring?
5. Research Related Injuries and Legal Action ???

- Documented, Updated and Distributed SOPs !
- Research Ethics Training of Investigators and REC/IRB Members !!
Expert Comments or Discussions ??
Thank you very much!!