

These materials were developed for a course in International Bioethics offered in early 2012 as part of the Advanced Certificate Program for Research Ethics in Central and Eastern Europe, a collaborative project between Union Graduate College and Vilnius University. They are free for use, distribution and modification with proper attribution.

International Research Ethics 1

Week 1: Conceptual and Regulatory Aspects of Human Subjects Research

INTRODUCTION

We will start the second course of this Advanced Certificate Program with a module examining research ethics committees (RECs). This first week will focus on the scope of ethical review carried on by RECs, one of the most important issues of research ethics.

First of all, it is important to explore the research versus non-research distinction. Research involving human subjects is subject to stricter regulatory requirements than other health related activities. For example, such studies must not only undergo independent review by an ethics committee, but there are also strict requirements regarding the express and written consent of study participants, the types of benefits that can be offered, the level of risk to which subjects can be exposed, etc. By contrast, ethics committees are not required to review activities as routine medical practice, auditing of health care institutions, or other sorts of clinical monitoring activities. Thus, distinguishing between what is research and not research is not only interesting from a theoretical perspective, but also has important practical implications.

An in-depth analysis of the concept of research, as distinguished, from other activities is provided by Bortolotti and Heinrichs (2007). Some of the other readings assigned for this week explore the distinction between research and clinical practice, a topic that has been of central importance when dealing with such issues as clinical equipoise and therapeutic misconception (Levine [2003]).

An example of a working definition of research that reflects current US regulations (45 CFR 46) is provided in the policy guidelines that make up part of your assigned reading. These guidelines state that research is the “systematic investigation, including research development, testing and evaluation, designed to contribute to generalizable knowledge.” This is a very expansive definition, and research ethics committees in the US (called Institutional Review Boards, or IRBs) are uniformly required to review a wide range of research projects involving human participants.

By contrast, in Europe and other regions of the world not all research involving human subjects must undergo independent ethical review. Furthermore, the level of review that

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different types of human subjects research must undergo can vary. In some European countries, the ethical review of non-biomedical research employing social science methodologies (e.g. the use of surveys and questionnaires) is not always legally required. For example, in the Nordic countries of Norway, Denmark and Finland, recommendations about the independent ethical review of social science research are rather advisory nature (see the Eurecnet webpage, part of the assigned readings). This “asymmetry” in ethical review of different types of human research is particularly striking in some of the Central and Eastern European countries.

To help understand this asymmetry, let’s distinguish between the following different types of research:

- Human research (which includes both biomedical and non-biomedical studies involving human subjects);
- Widely defined biomedical research;
- Narrowly defined biomedical research; and
- Clinical drug trials.

This typology is particularly relevant for understanding the international context. It shows the relationship between different types of human research and the international regulatory framework that shapes the ethical review procedures. It is also helping for understanding the “asymmetries” or “non-equivalences” that exist in countries where different types of human research are subject to different levels of ethical review.

Regulatory frameworks like these, found in many European countries, seems to leave some gaps in the ethical review of non-biomedical research. This does not seem to be a problem in the US (and in the UK) where regulations employ a broader definition of the term “human subject research” and where the stringency of ethical review is based on to the level of risk to which study participants are exposed.

LEARNING OBJECTIVES

At the end of this week, students will be able to:

1. Define the concept of research;
2. Distinguish between different types of human subjects research;
3. Describe different types of non-research activities that might be confused with human subjects research;
4. Evaluate different international guidelines on human subjects research;
5. Explore existing asymmetries in the review of different types of human subjects research; and
6. Develop a strategy to address existing asymmetries and introduce a more balanced system of ethical review.

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TOPICS

1. Human subjects research;
2. Criteria for defining an activity as biomedical research;
3. Activities that overlap with or are confused with research;
4. Existing international guidelines and legal regulations on human subjects research; and
5. Non-equivalent stringency of ethical review.

REQUIRED READINGS, AUDIO AND VIDEO

1. Holm S. (2007). A Rose By Any Other Name: Is the Research/Non-Research Distinction Still Important and Relevant? *Theoretical Medicine and Bioethics* 28(3): 153-5. [COPYRIGHTED]
2. Bortolotti L, Heinrichs B. (2007). Delimiting the Concept of Research: An Ethical Perspective. *Theoretical Medicine and Bioethics* 28(3): 157-79. [COPYRIGHTED]
3. Emanuel EJ, Crouch RA, Arras JD, Moreno JA, Grady C. (2003). The Ethics of Clinical Trial Design. In Emanuel EJ, Crouch RA, Arras JD, Moreno JA, Grady C (eds). *Ethical and Regulatory Aspects of Clinical Research: Readings and Commentary*. Baltimore, MD: The Johns Hopkins University Press. pp. 95-102.
4. Levine RJ. (2003). The Distinction Between Research and Treatment. In Emanuel EJ, Crouch RA, Arras JD, Moreno JA, Grady C (eds). *Ethical and Regulatory Aspects of Clinical Research: Readings and Commentary*. Baltimore, MD: The Johns Hopkins University Press. pp. 103-7.
5. Gefenas E, Dranseika V, Čekanauskaitė A, Hug K, Mezinska S, Peicius E, Silis V, Soosaar A, Strosberg M. (2010) Non-equivalent Stringency of Ethical Review in the Baltic States: A Sign of a Systematic Problem in Europe? *Journal of Medical Ethics* 36(7): 435-9. Available online at: <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3072805/?tool=pubmed>.
6. Florida State University Human Subjects Committee – Human Subjects Research Committee Webpage. Available online at: <http://www.research.fsu.edu/humansubjects/index.html>.
7. European Network of Research Ethics Committees – EUREC Website. Available online at: <http://www.eurecnet.org/index.html>
8. University of Sheffield (UK) Ethics Policy. Available online at: http://www.shef.ac.uk/content/1/c6/07/21/09/ethics_POLICY.pdf.

OPTIONAL READINGS, AUDIO AND VIDEO

1. Holm S, Bortolotti L. (2007). Large Scale Surveys for Policy Formation and Research – A Study in Inconsistency. *Theoretical Medicine and Bioethics* 28(3): 205-20. [COPYRIGHTED]

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2. Hofmann B. (2007). That's Not Science! The Role of Moral Philosophy in the Science/Non-Science Divide. *Theoretical Medicine and Bioethics* 28(3): 243-56. [COPYRIGHTED]
3. Cave E, Nichols C. (2007). Clinical Audit and Reform of the UK Research Ethics Review System. *Theoretical Medicine and Bioethics* 28(3): 181-203. [COPYRIGHTED]
4. Council of Europe Guide for Research Ethics Committee Members. Available online at: [http://www.coe.int/t/dg3/healthbioethic/source/INF\(2011\)_en.pdf](http://www.coe.int/t/dg3/healthbioethic/source/INF(2011)_en.pdf)
5. US Department of Health and Human Services 45 Code of Federal Regulations 46 (aka the Common rule). Available online at: <http://www.hhs.gov/ohrp/humansubjects/guidance/45cfr46.html#46.101>

DISCUSSION FORUMS

The Discussion Forums are the main vehicle for promoting interaction among the students. All students are expected to participate in each Discussion Forum by answering questions, challenging assumptions, posing new questions, and sharing concerns and insights. Timely participation is expected, as each Forum will remain active for only a two-week window.

There are two Discussion Forums for this week, each worth 30 points:

Forum 1.1: THE DRUID PROJECT (30 points).

The European Union (EU)-sponsored DRUID (Driving Under the Influence of Drugs, Alcohol and Medicine) project is designed to combat driving under the influence of drugs, alcohol and medicine in 21 European countries. It comes under the thematic priority "Sustainable Surface Transport" of the EU framework programme. The intention is that DRUID will describe the extent and nature of the impaired driving problem. The actual incidence of impaired driving will also be compared with accident rates so that a measure of the risk may be obtained. The project will also examine how police surveillance can be designed for maximum effectiveness, and how driver training, information campaigns and rehabilitation programs can be formulated so that the problem may be prevented right from the beginning (c.f. VTI, the Swedish National Road and Transport Research Institute, http://www.druid-project.eu/cln_031/nn_107542/Druid/EN/home/homepage_node.html?_nnn=true)

The goals of the DRUID project include:

1. Determining prevalence rates of driving under influence (DUI) and to compare Member States;
2. Estimating risks and defining thresholds for the most relevant

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- psychoactive substances;
- 3. Defining best practice of controls and countermeasures;
- 4. Establishing an applicable classification system for psychoactive medicaments; and
- 5. Developing guidelines and disseminating information.

There are 3 **different components** of the project. Participating countries could be involved in all 3 or just in one or two of the mentioned components:

1. Drivers will be randomly stopped on the road and asked to fill in the anonymous questionnaire (to collect some basic information about age, experience of driving but also information dealing with their habits of using psychoactive substances).
2. In addition to filling in the questionnaire some drivers will be asked to give saliva (in some countries - blood) the project description indicates that participation in this component of the study is also voluntary and anonymous.
3. Blood samples will be also collected from the dead drivers in the emergency rooms or autopsy departments (the researchers will only get unidentifiable blood samples).

Please consider the following discussion questions:

- Could all 3 mentioned components of the DRUID project be regarded as biomedical research?
- Should all 3 components of the DRUID project be reviewed by the REC?
- To answer questions 1 and 2, does it matter what kind of biological material is going to be collected – saliva or blood?
- What kind of consent is needed (if any) when taking a blood sample from the dead driver (the third component)?

Forum 1.2: *COMPARING US AND EUROPEAN REGULATIONS (30 points).*

Please consider the following discussion questions:

- How does the Additional Protocol (and its Explanatory Report) on Biomedical Research of the Council of Europe Bioethics Convention define the scope of the instrument? What are the key concepts used for these purposes?
- How does the scope of the Additional Protocol compare with that presented on Florida State University's Human Subjects Committee webpage?
- Which activities other than research might be candidates for ethical review and oversight, as suggested by Bortolotti and Heinrichs (2007)?

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WRITING ASSIGNMENT (40 points):

To be submitted electronically by the end of week 2. For assignments submitted within a week after the expected deadline, students will receive an automatic 10% grade deduction. Assignments received greater than 7 days after the expected deadline will not be accepted.

In 1000 words or less, describe how human/biomedical research is defined in your country? Where does the definition appear (e.g. in which legal texts or guidelines)? What types of human research have to be approved by ethics committees? What other types of research are not required to undergo ethical review?

Try to answer these questions in the context of so-called non-equivalences or asymmetries of ethical review of human research using the framework developed by Gefenas et al. (2010).