The Objectives For This Module Are:

* To identify the three principles of ethical human subjects research identified in the Belmont Report
* To comprehend the current HHS regulations, including:
  + Risks associated with participation in research and appropriate protections against risks
  + Vulnerable populations that need specific protections
  + Situations in which research involving humans is exempt from regulatory requirements

The Belmont Report

Following the public outrage over the Syphilis Study at Tuskegee, Congress established the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research in 1974. The National Commission was charged with:

1. Identifying the ethical principles to guide all research involving human subjects
2. Developing guidelines for the conduct of ethical research involving human subjects



In 1979, the National Commission drafted [**The Belmont Report – Ethical Principles and Guidelines for the Protection of Human Subjects of Research**](http://www.hhs.gov/ohrp/humansubjects/guidance/belmont.html).

The Belmont Report identified **three principles** essential to the ethical conduct of research with humans:

1. **Respect for persons**
2. **Beneficence**
3. **Justice**

**These three basic principles serve as the foundation of the current HHS regulations and guidelines for the ethical conduct of human subjects research supported by HHS.**

Respect for Persons



The principle of respect for persons can be broken down into two basic ideas:

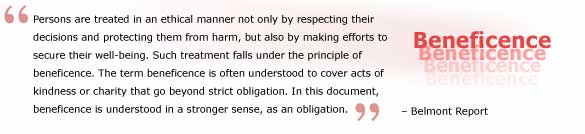
**1. Individuals should be treated as autonomous agents**

**2. Persons with diminished autonomy are entitled to additional protections**

The challenges in applying the **Belmont principle of respect for persons** are in:

* Making sure that potential participants comprehend the risks and potential benefits of participating in research
* Avoiding influencing potential participants’ decisions either through explicit or implied threats ([***coercion***](https://phrp.nihtraining.com/glossary.php#coercion)) or through excessive [***compensation***](https://phrp.nihtraining.com/glossary.php#compensation) ([***undue influence***](https://phrp.nihtraining.com/glossary.php#undue_influence))

Beneficence



Two general rules have been articulated as complementary expressions of beneficent actions:

1. Do no harm
2. Maximize possible benefits and minimize possible harms

The challenge inherent in applying the **Belmont principle of beneficence** is how to determine when potential benefits outweigh considerations of risks and vice versa.

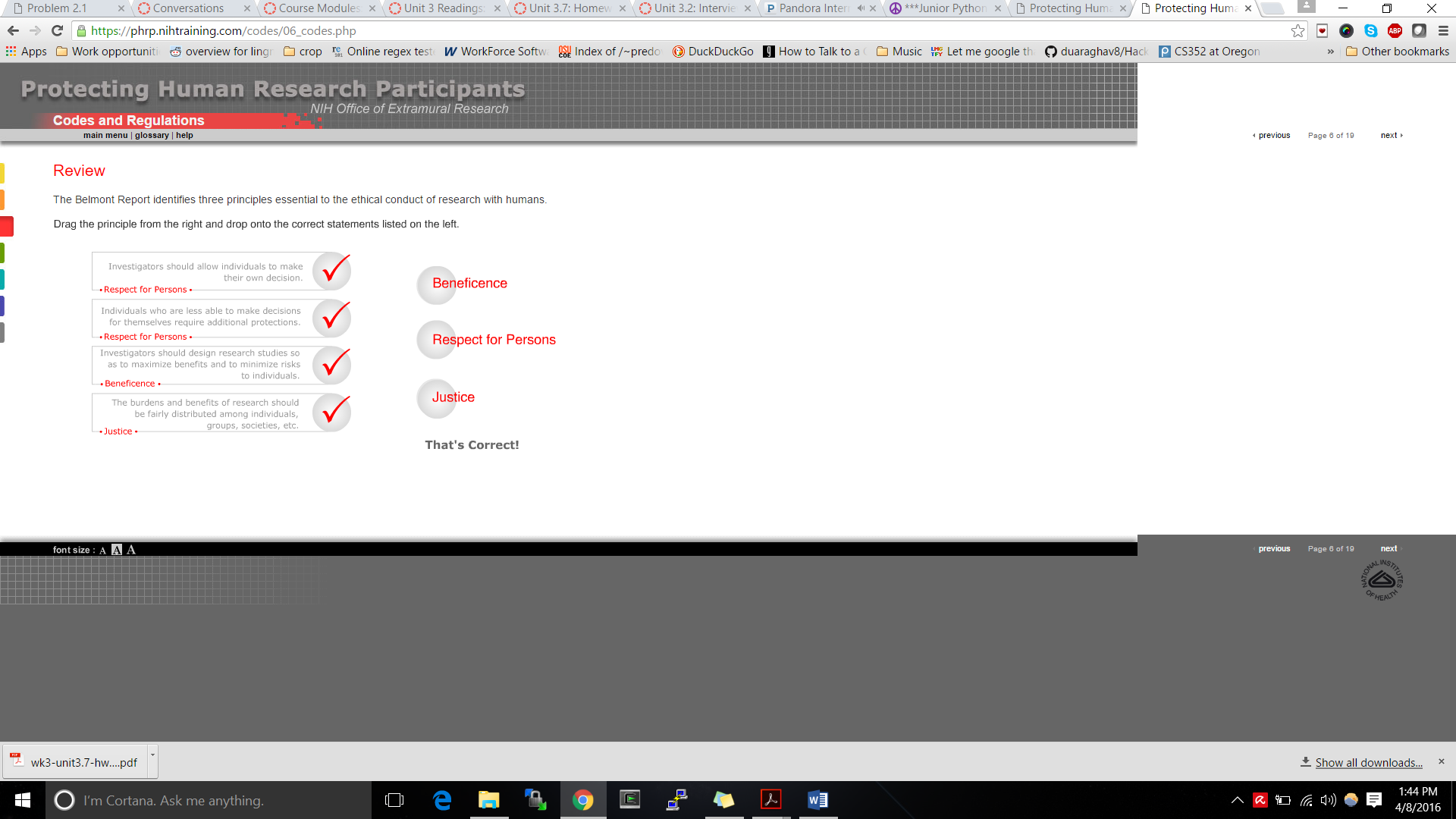
## Justice

Justice requires that individuals and groups be treated fairly and equitably in terms of bearing the burdens and receiving the benefits of research.

The principle of justice may arise in decisions about inclusion and exclusion criteria for participation in research and requires [***investigators***](https://phrp.nihtraining.com/glossary.php#investigator) to question whether groups are considered for inclusion simply because of their availability, their compromised position, or their vulnerability — rather than for reasons directly related to the problem being studied.

The challenge of applying the **Belmont principle of justice**is how to decide which criteria should be used to ensure that harms and benefits of research are equitably distributed to individuals and populations.



The ethical principles for research involving human subjects described in the Belmont Report are codified in the Code of Federal Regulations, [**45 CFR 46**](http://www.hhs.gov/ohrp/humansubjects/guidance/45cfr46.html). The NIH follows all Subparts of the HHS regulations:

[**Subpart A**](http://www.hhs.gov/ohrp/humansubjects/guidance/45cfr46.html#subparta) – Basic HHS Policy for Protection of Human Research Subjects

[**Subpart B**](http://www.hhs.gov/ohrp/humansubjects/guidance/45cfr46.html#subpartb) – Additional Protections for [***Pregnant***](https://phrp.nihtraining.com/glossary.php#pregnancy) Women, Human [***Fetuses***](https://phrp.nihtraining.com/glossary.php#fetus) and [***Neonates***](https://phrp.nihtraining.com/glossary.php#neonates) Involved in Research

[**Subpart C**](http://www.hhs.gov/ohrp/humansubjects/guidance/45cfr46.html#subpartc) – Additional Protections Pertaining to Biomedical and Behavioral Research Involving [***Prisoners***](https://phrp.nihtraining.com/glossary.php#prisoner) as Subjects

[**Subpart D**](http://www.hhs.gov/ohrp/humansubjects/guidance/45cfr46.html#subpartd) – Additional Protections for Children Involved as Subjects in Research

[**Subpart E**](http://www.hhs.gov/ohrp/humansubjects/guidance/45cfr46.html#subparte) – Registration of Institutional Review Boards (effective July 14, 2009)

Subpart A - Basic HHS Policy for Protection of Human Research Subjects

[**Subpart A**](http://www.hhs.gov/ohrp/humansubjects/guidance/45cfr46.html#subparta), also called **“The Common Rule”**, describes the required protections for all human subjects.

**Subpart A** defines a ***human subject*** as “a living individual about whom an [***investigator***](https://phrp.nihtraining.com/glossary.php#investigator)...conducting research obtains:

1. Data through intervention or interaction with the individual, or
2. Identifiable private information.”

**Subpart A** defines ***research*** as “a systematic investigation...designed to develop or contribute to generalizable knowledge.”

This definition includes:

* Research development
* Testing
* Evaluation
* Read the study description below and determine if **Subparts B, C or D** of HHS Regulations require additional protections for the study”s participants:
* A study proposes to examine the effectiveness of a medical treatment and prevention program for adolescents in a location where the legal age for consent to such treatment is 12. The adolescents involved range from ages 12 to 17.
* **Do Subparts B, C or D require that participants in this study receive additional protections?**
* Text: What Do You Think?
* **Yes, additional protections for participants in this study are required under Subparts B, C or D**
* **The correct answer is No.**
* The regulatory definition of children depends both on the local laws and on the specific treatments or procedures that will be involved in the research. Because the location in which the research will be conducted allows 12-year-olds to consent to the treatment, the participants in this research are not considered children under the HHS regulations and can provide informed consent to participate in the study. While the regulations do not require the additional protections of ***Subpart D*** for children in this study, the IRB may require some additional protections if they feel that the adolescents who will be involved in the study are vulnerable.
* **No, additional protections for participants in this study are not required under Subparts B, C or D**
* **Correct!**
* The regulatory definition of children depends both on the local laws and on the specific treatments or procedures that will be involved in the research. Because the location in which the research will be conducted allows 12-year-olds to consent to the treatment, the participants in this research are not considered children under the HHS regulations and can provide informed consent to participate in the study. While the regulations do not require the additional protections of ***Subpart D*** for children in this study, the IRB may require some additional protections if they feel that the adolescents who will be involved in the study are vulnerable.

The HHS regulations ([**45 CFR 46.120**](http://www.hhs.gov/ohrp/humansubjects/guidance/45cfr46.html#46.120)) require that Federal Departments and Agencies that conduct or support human subjects research must evaluate all applications for research using the following criteria:

* Risks to the subjects
* Adequacy of protection against these risks
* Potential benefits of the research to the subjects and others
* Importance of the knowledge gained or to be gained
* When research covered by the HHS regulations takes place in countries other than the United States, the HHS regulations ([**45 CFR 46.101(h)**](http://www.hhs.gov/ohrp/humansubjects/guidance/45cfr46.html#46.101)) allow a department or agency head to approve the substitution of alternative polices, codes, or regulations to protect human subjects in lieu of the requirements of 45 CFR 46 as long as the alternatives afford protections that are at least equivalent to those provided in 45 CFR 46.
* 
* In a [**Federal Register Notice**](http://edocket.access.gpo.gov/2006/E6-10511.htm) on July 7, 2006, HHS clarified that the requirements of the HHS regulations (45 CFR 46) must be satisfied for all HHS-conducted or -supported research covered by the [**Federalwide Assurance**](http://www.hhs.gov/ohrp/assurances/assurances/index.html), regardless of whether the research is conducted domestically or internationally. As of the publication of that Notice, HHS had not deemed any other procedural standards equivalent to 45 CFR 46.

Engagement in Human Subjects Research

Each institution that is engaged in NIH-funded human subjects research must:

* Obtain or hold a current [**Federalwide Assurance**](http://www.hhs.gov/ohrp/assurances/assurances/index.html) (FWA), assuring that an institution will comply with HHS regulatory requirements for the protection of human subjects (this is obtained from the HHS Office for Human Subjects Protections (OHRP)); and
* Certify to NIH that grant applications and contract proposals describing research involving human subjects has been reviewed and approved by an Institutional Review Board (IRB) designated in the FWA, and will be subject to continuing review by an IRB.

IRBs are committees that consist of 5 or more members with varying expertise and diversity that are responsible for reviewing and approving human subjects research activities on behalf of institutions.

The Common Rule specifies:

* IRB membership ([**45 CFR 46.107**](http://www.hhs.gov/ohrp/humansubjects/guidance/45cfr46.html#46.107))
* IRB functions & operations ([**45 CFR 46.108**](http://www.hhs.gov/ohrp/humansubjects/guidance/45cfr46.html#46.108))
* IRB review of research ([**45 CFR 46.109**](http://www.hhs.gov/ohrp/humansubjects/guidance/45cfr46.html#46.109) and [**45 CFR 46.110**](http://www.hhs.gov/ohrp/humansubjects/guidance/45cfr46.html#46.110))
* Criteria for IRB approval of research ([**45 CFR 46.111**](http://www.hhs.gov/ohrp/humansubjects/guidance/45cfr46.html#46.111))
* The HHS regulations describe categories of human subjects research that may be exempt from requirements described in the HHS regulations including IRB oversight.
* 
* Studies proposing only research that falls under one or more of the exempt categories of research do not require IRB review and approval, but the HHS Office for Human Research Protections (OHRP) has stated that: “[**Institutions should have a clear policy in place on who shall determine what research is exempt under 46.101(b)**](http://www.hhs.gov/ohrp/policy/hsdc95-02.html)” and that [***investigators***](https://phrp.nihtraining.com/glossary.php#investigator) should not be able to determine whether or not their own research is exempt. This authority should rest with the IRB or other entity designated by the institution.
* The exemptions can be found at [**45 CFR 46.101(b)**](http://www.hhs.gov/ohrp/humansubjects/guidance/45cfr46.html#46.101).