AN IN-DEPTH LOOK AT INFORMED CONSENT

What is Informed Consent and Why is it Important?
The primary purpose of informed consent is to protect the prospective human subject. Informed consent provides the individual with the pertinent information regarding the research in which s/he is being asked to participate, and the opportunity to make an informed decision regarding whether or not to participate in the research. The procurement of informed consent signifies that the subject has made an informed decision and agrees to participate without coercion, force, or fraud.

Consent must also be freely given – it must be made clear to the subject that they are not required to participate and that s/he can withdraw at any time without fear of penalty or loss of benefits of any kind.

In 1974, as a result of the publicization of the Tuskegee Syphilis Study, the National Research Act was passed, leading to the publication of the Belmont Report in 1978. This report was then incorporated into the Code of Federal Regulations for the protection of human subjects in biomedical and behavioral research (45 CFR part 46).

* From 1932-1972, the US Public Health Service enrolled 400 low-income African-American males with syphilis in a research project dubbed the Tuskegee Study that studied the effects of untreated syphilis. While the men were told they were being treated for “bad blood” (the term used at that time to describe a number of ailments including anemia and fatigue, as well as syphilis), in fact, they were not: treatment was withheld throughout the study, despite the advent of penicillin and “Rapid Treatment Centers” to treat syphilis in the 1940s. In 1968 concerns were raised about the ethics of the study, however the Centers for Disease Control and Prevention (CDC), American Medical Association (AMA), and National Medical Association (NMA) continued to support the study. In 1972 the Associated Press ran a story about the Tuskegee study and the study was ended as a result of the publicity.

The Belmont Report outlined the three fundamental ethical principles by which human subjects research has since been guided:

1. **Respect for persons**, or treating individuals as autonomous agents (“capable of deliberation about personal goals and of acting under the direction of such deliberation”) and protecting persons with diminished autonomy

2. **Beneficence**, or protecting individuals from harm by maximizing potential benefits and minimizing potential for harm (risk)

3. **Justice**, or distributing the risks and potential benefits of research equally among those who may benefit from the research

The regulations codified all three of these principles in 45 CFR 46.111 (Criteria for IRB approval of research); however, respect for persons, and more specifically informed consent, receives extensive attention and is discussed in detail in sections 116 (General requirements for informed consent) and 117 (Documentation of informed consent), as well.

For more examples of research, as well as a more in-depth discussion of the Belmont Report and regulations, see An In-depth Discussion of the IRB.

Obtaining informed consent, then, is one of the cornerstones of conducting ethical human subjects research.

**Obtaining Informed Consent**
When discussing informed consent, the first thing that generally comes to mind is the informed consent form. It is important to remember, however, that informed consent is a process, not simply a form. While the
The consent form is a key document obtained in the process of informed consent, it is only a physical reference and representation of the ongoing process, as well as formal documentation.

The elements of informed consent are outlined in the consent form and include the following components:

1. Title of the study
2. Names and affiliations of the primary investigator
3. Study objectives
4. Criteria by which subjects were chosen
5. Study procedures
6. Potential risk and discomforts to the subject
7. Potential benefits to the subject, society, and/or science
8. Cost to the subject of participating in the study, and the compensation thereof
9. Whether/how the subject’s data will be used for future research
10. Confidentiality of the subject’s data
11. Rights of the subject to participate or withdraw
12. Investigator’s and relevant IRB’s contact information

The following components are used only if appropriate to the research being done:

13. An explanation of the use of incomplete disclosure
14. A description of any experimental procedures that will be used
15. A statement regarding any alternative procedures available to the subject
16. The possibility of any unforeseeable risks
17. The potential for compensation or treatment in case of injury
18. The potential for termination without regard to consent
19. Any additional costs to subjects
20. The consequences of withdrawal from the research
21. Whether the subjects will be provided with any significant new findings
22. The number of subjects participating in the research
23. The commercial use of biospecimens
24. Whether clinically relevant research results will be provided to the subject
25. Whether the research will or might include whole genome sequencing
26. Whether the research is covered by a certificate of confidentiality

The consent document may not contain exculpatory language that waives or appears to waive subjects’ rights.

To ensure informed consent, investigators must work to communicate clearly and effectively with their subjects, build trust and cooperation, openly and willingly explain their research, answer questions, and be sensitive to the needs and concerns of their subjects.

When using an informed consent form, the investigator reviews each component of the form, encourages and answers any questions the subject has, and allows ample time for the subject to deliberate on whether s/he would like to participate in the study. It is important that, when the investigator presents the information, the subjects’ ability to comprehend is taken into account. In addition, the investigator must ensure that the subject knows his/her participation is completely voluntary and that they may withdraw from the research at any time.

For consent forms that are complicated and/or long – as are used with clinical/biomedical research – the form must begin with a concise and focused presentation of the key information that is most likely to assist a prospective subject in understanding the reasons why one might or might not want to participate in the research.

Note that the consent form is not a substitute for discussion; it is a summary of what was discussed. Once the subject agrees to participate and the investigator is confident the subject’s decision to participate is an informed one, the subject’s signature on the form is obtained and the subject is provided with a copy of the consent document.
Waivers of Documented Informed Consent

There are times when the use of an informed consent form would be impractical or detrimental to the study. In these cases, a waiver of documented informed consent may be requested of the IRB. Such waivers may be granted under three conditions:

1. If the consent document would provide the only link to the subject and the principal risk of the research would be a breach of confidentiality
2. If the risk to the subjects is minimal and consent would not be required outside the research context
3. If the subjects are members of a distinct cultural group or community in which signing forms is not the norm

In cases where a waiver of documented informed consent is granted, it is important for the investigator to understand that the waiver involves only the documentation of informed consent, not the process, and active consent must still be obtained.

Oftentimes when documented informed consent is waived, the investigator will use an information sheet in its place. An information sheet follows the same format as the consent form and includes all the same elements. In lieu of the consent form, the investigator reviews and discusses the information sheet and obtains the subject’s verbal consent.

In either case, the consent process is not over once consent has been obtained, but it continues throughout the subject’s involvement in the research. Subjects should continually be encouraged to ask questions and request clarifications, and be reminded that they may withdraw from the research at any time. Maintaining consent is particularly important in cases where the subject’s participation in the research is ongoing.

Note: The IRB may approve an alteration of documented informed consent, as well, where one or more of the elements of informed consent are not included in the informed consent form.

Waivers and Alterations of Informed Consent

In exceptional circumstances the principal investigator may request a waiver or alteration of informed consent. The IRB may waive the requirements of informed consent if all the following stipulations are met:

1. The research involves no more than minimal risk to the participants
2. The waiver or alteration will not adversely affect the rights and welfare of the participants
3. The research could not practically be carried out without the waiver or alteration
4. Whenever appropriate, the participants will be provided with additional pertinent information after participation
5. If the research involves using identifiable private information or identifiable biospecimens, the research could not practically be carried out without using such information or biospecimens in an identifiable format

Deception and Informed Consent

Fully informed consent is not possible without all relevant information pertaining to the subjects’ participation in research; therefore, the use of deception in human subjects research necessitates a waiver or alteration of informed consent.

Informed Consent and Assent of Children

Children (defined in Massachusetts as persons under the age of 18, but vary state to state and country to country – investigator must discuss the different state/national rules if they apply) are considered by the Federal Code of Regulations to be a “vulnerable Population” due to their (assumed) inability to fully
understand how to weigh the risks and potential benefits of research (or what they are), as well as their susceptibility to undue influence.

Legally, children are not able to provide informed consent on their own behalf; therefore, obtaining informed consent for the involvement of children as research subjects is a two-step process: the investigator must obtain informed consent from the child’s parent(s)/guardian(s), or legally authorized representative (LAR), as well as assent from the child, assuming s/he is capable.

Obtaining informed consent from a child’s LAR involves the same process as does obtaining informed consent from an adult on their own behalf. The pertinent information regarding the research is reviewed with the LAR, and the LAR is encouraged to ask questions to ensure an informed decision is made. When appropriate, the LAR should discuss the research with the child.

After documented informed consent has been obtained from the LAR, the investigator must, assuming the child is capable, also obtain informed assent (the active affirmation of a desire to participate in the research) from the child. In determining whether a child is capable of assenting, the investigator should take into account the age, maturity, and psychological state of child. This judgment may be made for all children to be involved in research under a particular protocol, or for each child. When a child is capable of providing assent, s/he should be given an explanation of the proposed research procedures in language that is appropriate to the child’s age, experience, maturity, and condition.

Informed assent may be written or it may be verbal, depending on the age of the child and the appropriateness of requiring the child to give written assent. Either way, informed assent, as with informed consent, is an ongoing process.

Note that for children who turn 18 during the course of the research, they must be re-consented, or give informed consent as an adult, and be given the opportunity to withdraw their participation in the research.

Waiver of Assent
An IRB may waive the requirements for obtaining subject assent in circumstances in which the subject population does not have the capacity to comprehend the research or associated procedures. This judgment may be made for all subjects involved in the research or for each child individually. If the IRB determines either of the following to be true, then the assent of the child is not a necessary condition for proceeding with the research:

- The capability of some or all of the subjects is so limited that they cannot reasonably be consulted
- When the research offers the subject the possibility of a direct benefit that is important to the health or well-being of the subject and is available only in the context of the research

The IRB will take into account the age, maturity, and psychological state of the subjects involved in determining whether a waiver of assent is appropriate.

Waiver of Consent
An IRB may, for the protection of the subjects, waive the requirements for obtaining parental or LAR consent if the IRB determines that a research protocol is designed for conditions or for a subject population for which parental or LAR permission is not a reasonable requirement (for example, neglected or abused children). In such cases, there must be another mechanism in place for the protection of the subjects.

Third Party Consent
When an investigator conducting research obtains identifiable private information about a living individual, that individual becomes a research subject, regardless of whether that person is the individual with whom the investigator is having an interaction. For example, if the research involves asking the primary subject to provide identifiable private information about a third party, that third party then becomes a subject in the research. As such, all of the regulatory requirements for protecting that individual obtain.
The IRB can determine whether informed consent needs to be sought from third party subjects, or whether it can be waived. In making this determination, the IRB relies on both the requirements for a waiver (noted earlier in this section) and the importance of the information to the research. Investigators whose research may involve so-called "secondary subjects" are encouraged to contact the IRB Staff to discuss how to best protect the rights and welfare of these subjects in a given project.

**Language Barriers to Informed Consent**

Much social research being done today involves subjects whose primary language is not that of the investigator and special precautions must be taken in these cases. (For simplicity purposes, we will assume the investigator’s primary language is English.) However, informed consent must always be obtained in a language in which the subject is comfortably fluent. In those instances where the subjects do not speak English, the informed consent form should be translated into the primary language spoken and understood by the subjects and an interpreter hired to translate throughout the informed consent process.

It is important that you not rely on family members or friends of the subjects. Instead, you should hire a professional with whom you can discuss the study in detail. It is important that the interpreter fully understands your research or s/he may not communicate the information accurately. In addition, it is important that the subjects feel comfortable answering and/or asking questions freely.

In those instances where a subject has some competency in English, the investigator may be tempted to forgo the use of an interpreter. The investigator must be careful, however, to be sure the subject is truly proficient in English. There are often times when a subject believes s/he is proficient “enough” and so does not inform the investigator – or even realize – that both s/he and the researcher would be better served by the use of an interpreter.

**Cultural Barriers to Informed Consent**

Even when language is not an issue in the informed consent process, cultural barriers may still exist in both local and international research. When dealing with subjects whose culture, for example, reveres education, the subjects’ inclination may be to agree to participate in the research simply out of respect for the investigator. The investigator should be aware, therefore, of the potential for cultural differences between his/her subjects and him/herself.

**International Research and Informed Consent**

When conducting research internationally, the Brandeis IRB may require the investigator to obtain approval from the local equivalent of the IRB where the research is to take place. In cases where there is no local equivalent, investigators may be required to obtain approval from local experts or community leaders in lieu of a local IRB. In such cases the investigator should be cognizant of local culture, mores, and attitudes that may affect subjects’ informed consent. For example, the local IRB equivalent may be a council of elders whose own approval of the research may imply to the subjects a requirement to participate in the research.

**References**

Code of Federal Regulations 45 CFR part 46
http://www.ecfr.gov/cgi-bin/text-idx?tpl=/ecfrbrowse/Title45/45cfr46_main_02.tpl

Centers for Disease Control and Prevention US Public Health Service Syphilis Study at Tuskegee
http://www.cdc.gov/tuskegee/index.html

The Belmont Report
http://www.hhs.gov/ohrp/policy/belmont.html

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