Introduction to Informed Consent

Course objectives and contents

Objectives

Upon completion of this course, you will have an understanding of:

- The events that lead to the development of universal research ethics
- Why informed consent is necessary and the guidelines that brought it about
- What is involved in taking informed consent from a potential study participant and the information they should be provided with
- Who is, and is not, eligible to sign a consent form
- Language that should not be used when asking an individual to enrol in a study
- The options that are available for non-paper based communities
- Points to be taken into account when taking consent

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References & Resources
This section provides the references used in this course which you may find useful for further reading.

- **Quiz**

This section provides questions that will allow you to test what you have learned from the course.

### Research Ethics History

The need for ethical research practices arose when infamous cases such as the Nazi’s experiments on concentration camp prisoners in WWII (1941-1945), the sale of the unlicensed drug Thalidomide to pregnant women (1957-1961) and the Tuskegee Syphilis Study (1932 –1972) on black American men, highlighted unethical or incorrectly regulated research practices where vulnerable groups were exploited, abused or inadequately protected.

The research misconduct that took place in these cases, as well as in others, involved participants:

- not being told everything (or anything) about their disease
- being bribed with incentives they could not possibly refuse
- being kept ignorant of the fact that there was treatment for their disease
- receiving insufficiently tested drugs
- being included in research that was life-threatening
- not being asked for their consent to be included in research
- being subjected to procedures which had no justifiable scientific or medical purposes

These events occurred because there was an absence, or inadequate provision, of protection for the individuals involved. This form of misconduct is more likely to occur when populations or communities:

- are poor therefore potentially reliant on others for basic necessities
- have low levels of education and literacy so that individuals cannot read and/or understand the study information or purpose
- accept authority unquestioningly e.g. where the leader’s opinion is the governing one, or where women do not question male figures
- lack health services: it is very difficult for someone to refuse when it may be the only opportunity to see a medical professional
- have no knowledge of what research encompasses: they may be unable to differentiate between research and medical care and therefore not understand that participation is completely voluntary and that they can change their mind at any time without consequences

### Development of Regulations and Guidelines

In response to the cases cited above, and the problems which they expose, guidelines for the conduct of clinical research were developed. These include the 1947 Nuremberg Code, the 1964 Declaration of Helsinki and the 1979 Belmont Report. These further led to the development of the 1996 International Conference on Harmonization Principles of Good Clinical Practice (ICH GCP) Guidelines, the 2002 Council for International Organizations of Medical Sciences (CIOMS) Guidelines, the National Bioethics Advisory Committee (NBAC) 2001 Report, the U S Code of Federal Regulation (CFR) and many others.

Three key basic ethical principles underlined in the Belmont Report are:

- Justice: no group should carry more than their fair share of the burdens of research, those who participated should have access to
the benefits of the results and no group should be unfairly excluded from research. In their paper, Minnies et al. (2008) emphasise that ‘poverty, disease, lack of education, hardship, submissiveness, the effects of war, famine, pandemics, and social insecurity prevalent in developing countries all make participants more vulnerable to research exploitation’.

- Beneficence: possible harms should be minimised and possible benefits should be maximised. To this the 2002 CIOMS guidelines added an additional principal:
  - Non-maleficence: participation in the study should result in no intentional injury or harm for the individual.
- Respect for autonomy: individuals’ freedom to choose and act must be respected and vulnerable individuals must be protected.

Abiding by these principles and complying with the agreed regulations and guidelines means that research participants:

- are not harmed (and neither are family members)
- rights are put before the needs of science
- do not have their right to choose taken away by researchers

Informed consent was developed on the principle that dictates respect for the individual’s right to choose what shall, or shall not, happen to them. The 1996 ICH-GCP guidelines define informed consent as ‘the process by which a person freely confirms their willingness to participate in clinical research after having been informed of all parts of the study that are relevant to the individual’s decision to participate’.

Informed consent protects the participant’s rights by ensuring that they are aware of every step of the study process in which they are being asked to participate and that participation is completely voluntary. Furthermore, participants should be made fully aware that they can withdraw at any point without having to provide a reason, and without fear of reprisal.

The NBAC report states that research in developing countries should address local health needs and should involve community representative throughout and ensure culturally appropriate informed consent process. The US CFR defines the Common Rule which is a rule of ethics regulating human biomedical and behavioural research and which outlines the general requirements for informed consent for all research funded by US government.

**The Informed Consent Process**

Community sensitisation is a requirement in some cultures as an investigator may only enter a community to conduct research after obtaining permission from a community leader, a council of elders, or another designated authority. However, whilst it is very important to adhere to and respect local customs, at no point does the permission of a community leader or any other authority substitute for individual informed consent.

The process of informed consent involves explaining to the potential participant about all of the study related activities that are beyond standard care and to ask for that person’s consent to be included in the study.

Jacob et al. (2011) list the key elements to gain informed consent as:

- Information: ensuring that the individual receives full disclosure of relevant information
- Comprehension: ensuring that the individual understands what is being asked of them
- Voluntary participation: ensuring that the individual acts voluntarily in consenting

The consent taker, usually the investigator (or a nominated delegate), must assess the
individuals’ understanding of the purpose and nature of the study, what is required of them, and what the possible benefits and risks are.

The consent taker’s role is to educate and inform the participant about the study with the objective facts to allow the participant to make their own decision on whether or not to participate. Informed consent ensures that the individual has the opportunity to decide if they want to participate, or continue participation, and whether it is compatible with their goals, values and interest.

The Informed Consent Process

The following steps are those usually followed in the informed consent process:

1. The process involves the consent taker reviewing the consent form and relevant study information with the participant and verifying the participant’s comprehension of the content. It is essential to verify the person’s understanding.
2. The consent taker should relate to the participant all of the important aspects of the study, including the written information giving approval by the Research Ethics Committee (REC)/Independent Ethics Committee (IEC). They must inform and educate the potential participant about the study.
3. The consent taker is responsible for assessing whether the individual has a true understanding of what they are being told. Open ended questions tend to be the best way to test this as they require feedback from the participant. If all reasonable attempts have been made to help them understand yet it is clear they do not, even if they are willing to consent, they should not be recruited to the study; they have not fully appreciated what they are being asked to do and therefore the consent is not truly informed.
4. The consent taker must allow the individual ample time and opportunity to inquire about details of the study and to decide whether or not to participate. All questions about the study should be answered to the person’s satisfaction.
5. The 2002 CIOMS guidelines emphasis that if the consent taker does not speak or read the language of the participant they are not allowed to consent the person without an impartial witness who does understand the participant’s language.
6. The informed consent form should be signed/marked by the participant and by the consent taker before the person can take part in the study. A signed/marked copy of the consent form must be given to the participant; a copy of a blank form is not acceptable.
7. Informed consent is an on-going process (during each study visit); it begins before the informed consent form is signed/marked and continues until the participant has completed the study.
8. Informed consent must happen before any study related procedure is carried out

Key Information for Participants

ICH GCP (1996) outlines what should be included in the information a potential recruit is provided with. This includes:

- information on all applicable parts of the study such as its purpose, duration, how many will be recruited, required procedures (including randomisation, if applicable), the fact that it is research (not individualised medical treatment) and key contacts
- that they can always ask the research team for additional information throughout the study
- that if they change their mind about participation they can leave the study and are under no obligation to explain why they are leaving
- explaining the benefits and risks involved in taking part, costs involved and any compensations that may be provided
- what is expected of them in the study, how long they will be involved for, what action will be taken if they suffer a study related injury and whether there are any alternative treatments/options open to them
• who has the authority to view their personal details and how this information will be handled
• that if a better treatment was developed or if it was determined the study was unsafe, the study could be stopped and their participation would be terminated

Who Can Sign a Consent Form?

The 2002 CIOMS guidelines states that the informed consent should be signed and personally dated by the subject, or by the subject’s legally acceptable representative, and the person who conducted the informed consent discussion. There are however cases where signed consent may not be required ‘when the research design involves no more than minimal risk and a requirement of individual informed consent would make the conduct of the research impracticable (for example, where the research involves only excerpting data from subjects’ records), the ethical review committee may waive some or all of the elements of informed consent’ (CIOMS 2002).

Different regulations provide differing guidelines with regards to the age of adulthood, however these should always abide by the country’s legal age. Generally people from 18 are considered to be independent adults and can give consent to be in a study; exceptions to this include individuals with mental incapacities. Minors who are married and/or are parents may be accepted as an emancipated adult in some countries, a country’s regulatory requirement should always be followed.

The legally acceptable representative, as described by ICH GCP (1996), is an individual, jurisdiction, or other body authorised under applicable law to consent on behalf of a prospective individual, to that person’s participation in the study. This representative gives consent on behalf of a minor or an incompetent adult. However, some developing countries do not have laws which state who this person could be. In these instances the cultural norms of that community should be respected. It should be clearly stated in the standard operating procedures (SOPs) who, for the purposes of the study, is an acceptable representative. This will usually be a parent or guardian. If a guardian is considered acceptable, who can act as a guardian must also be recorded in the SOPs, this should be in accordance with cultural practices.

Assent is the affirmative agreement to participate in an activity. Typically between the ages of 12 to 18 years young people are classed as adolescents. For this group, consent is taken from the parent/guardian and assent from the adolescent. Assent confirms voluntarily willingness to participate in the study, it does not, however, indicate full understanding and thus requires consent to be given by the parent/guardian. It is important to note that mere failure to object may not be construed as assent. Assent can never take the place of informed consent. An adolescent cannot be enrolled into the study without both assent and consent being obtained.

When studies include individuals with mental incapacities, the person should be informed and if capable, should assent and sign/mark the informed consent which will then be signed by their representative.

Who Can Sign a Consent Form?

For children less than 12 years of age, usually only consent from the parents is required as children of this age are generally considered to be too young to be fully informed. Only a parent or the legal guardian is allowed to sign the consent form. Even where the head of the house e.g. the grandmother, is supportive of the child’s participation, if the parents are not, the child is not to be included. Some children under 12 will have some understanding and may be able to give verbal assent, additionally some communities may require the child’s opinion to be considered. The country’s regulatory requirements should be followed.

An impartial witness is used if the participant, or their legally acceptable representative, is unable to read or write, or if the consent taker does not speak the local language. ICH GCP (1996) defines an impartial witness as 'a
person, who is independent of the trial, who cannot be unfairly influenced by people involved with the trial'. The role of impartial witness is to, if necessary, translate the applicable information into the participant’s language, and/or to sign the consent form to confirm that they observed the participant have the information sheet read out to them, that the participant understood the information and that they had all of their questions answered. The witness should be present during the entire informed consent discussion. The witness signs and the participant (or representative) provides their signature/thumbprint, with the person taking consent writing their name and the date.

The impartial witness should be unconnected to the study and could be

- Appointed by the community to be a representative of the potential participant
- A member of staff unrelated to the study
- A family member

The differences between research and medical care should be made clear when it comes to consent. In some cases a grandmother or other relative can make decisions with regards to medical care and procedures. However only the parents or legal guardian can give consent for involvement in research. This should follow country’s procedure of who is a guardian.

Special Circumstances for Consent

In some instances the head of household qualifies to sign consent even if they are only 16 years old. In these cases it is essential to check the country’s regulations with regards to the age of ‘majority’, the definitions of legal guardianship, the legal documentation needed to confirm head of household, etc.

If a 16 year old is simply caring for siblings while the parents are away for a few months, they are not considered the legal guardian and would not be able to consent for their siblings. If the 16 year old is the parent of the child that the researcher wishes to enrol, they may be able to give consent. However, where the mother is 16 but after several explanations of the study she does not understand, even if she is still willing to consent, (and the head of the house is in agreement) the child should not be enrolled.

Ethics guidelines outline five instances which allow for the enrolment of minors or those unable to make decisions for themselves:

1. Study objectives cannot be met using participants who are capable of giving informed consent.
2. The foreseeable risks to the participants are low.
3. The negative impact on the participant’s well-being is minimized and low.
4. The study is not prohibited by law.
5. The approval of the Research Ethics Committee/Independent Ethics Committee (REC/IEC) is expressly sought on the inclusion of such participants, and the written approval covers this aspect.

In emergency situations, when prior consent of the participant is not possible, the consent of their legally acceptable representative should be sought. When prior consent is not possible and their representative is not available, recruitment procedures should be described in the protocol and will usually involve the use of an impartial witness. This normally applies to studies that might enrol trauma victims.

Undue Influence

Consent to participate in a study must be completely voluntary and free of any coercion or undue influence:
Coercion occurs when intimidating or threatening behaviour is used to force someone into doing something e.g. “join this study or I will tell all your friends you have TB” or “your entire village is participating, they will think something is wrong with you if you don’t”.

Undue influence occurs through an offer of an excessive, unwarranted, inappropriate or improper reward or other overture in order to obtain compliance. Additionally, inducements that would ordinarily be acceptable may become undue influences if the person is from a vulnerable group. Statements from the consent taker such as “this study is observational, you may as well join”, “I really need to consent three people a day so please sign the consent form” or “you get free medical care if you join up” would be considered undue influence.

For a pregnant mother from an impoverished community, the promise of free healthcare or baby formula would probably convince her to enrol her child as a study participant. As Ready and Riker (2008) discuss, for a community without healthcare the opportunity to see a healthcare professional may be too much to turn down; for the very poor the offer of money means they could buy essentials supplies. Compensatory payments must be handled with care when dealing with vulnerable populations. The information must be presented carefully, the use of a phrase like “how would you like to get free baby formula, all you have to do is sign up for this study” is very different from explaining about the study and then mentioning about the compensation for the time spent to take part in the study at the end of the consent process.

Compensation for time and inconvenience, expenses for the likes of travel or work days missed are allowable. However anything which may be offered to a study participant must be approved by the REC/IEC before it is used.

Re-consenting

There are occasions when you may have to re-consent a participant who has already been through the informed consent process and is participating in the study. Chin and Lee (2008) explain that if new information becomes available or there is a significant change in the protocol which may impact upon the participant’s willingness to continue being involved they must be informed in a timely manner. It may mean they have to be re-consented once approval for the change has been received from the REC/IEC. A participant is free to refuse when being re-consented even if they have signed/marked the consent form the first time.

If a participant wants to withdraw it is helpful for the research team to know a) that they are withdrawing; and b) why the person is withdrawing, as it may be something that is affecting other participants e.g. unpleasant side effects, too expensive to travel to the research site, etc. However, remember that the participant is not obliged to give a reason for discontinuing their participation.

In the case of children it is best that both parents are informed and that the same parent signs if re-consenting is required. If it is not possible to have the same parent, then the reasons why should be documented in the child’s records.

Documentation

As Machin & Fayers (2010) point out that ‘an integral part of the consent process is providing the individual with full information about the study’. For most studies, together with a consent form, there will be an information sheet or leaflet summarising key information about the study. This information (which may be verbal, on audio tape, written, on video tape, on DVD or be pictorial) should be given to the person when they are approached about participating. All oral and written communication and information must be in a non-technical and understandable format. It must also be in the preferred language of the participant.

In developing countries it is often the case that signing a form is not considered appropriate as many impoverished communities are illiterate. Additionally, Creed-Kanashiro et al. (2005) cite
examples of nutritional studies run in the highlands of Peru where “the rural community were suspicious of signing a document as they were unable to read and because they had lost land by signing a document”. In this case the REC/IEC felt signed forms were unsuitable and consent was based on the verbal consent of the individuals. In other cases an impartial witness is involved.

Other methods used for non-paper based societies include taking an audio or video recording of the consent process. The 2002 CIOMS guidelines state that: “Informed consent should be obtained according to the legal requirements and cultural standards of the community in which the intervention is carried out.”

Care must be taken in designing consent forms as a common error in consent forms is mixing research only processes and with standard care procedures. This can risk those who decline to participate being opted out of a procedure they should receive regardless of the research. At no point during the study does the participant lose or waive their rights. A consent form is not a legal contract that binds the participant to the study. The informed consent form is simply written confirmation that the process of informed consent has occurred.

**Considerations when Consenting**

The challenges around gaining fully informed consent is one of the most highly discussed and important elements (particularly from an ethics perspective) in the conduct of clinical research. In their paper, Mystakidou et al. (2009) emphasize that the process of obtaining consent should be an on-going process, that it is not a single event (i.e. reading and signing a consent form) and it is not just based on the information and the form. There should be a wider consideration of what information should be conveyed, when and by whom. The aim being to have a study-specific consent process, including a training plan and operating procedures, which often are as important as the consent form itself.

When thinking through an appropriate consent process you should consider factors such as:

- the benefits or risks for the individuals or groups (do benefits outweigh risks)
- the length and level of participation required
- the vulnerability of the proposed study population (e.g. impoverished, low education level, children)
- the perception of the community (will approval of the research activity from community leaders be required before the individual members of the community consider being involved)
- whether the compensations for participation (if any) might have any undue influence.

**Key Points to Remember**

- Research misconduct is more likely to occur in populations or communities who are poor, have little education, don’t challenge authority, lack health services and have no understanding of research.
- Four key basic principles for the protection of participants of clinical research are justice, beneficence, non-maleficence and respect for autonomy.
- Informed consent involves explaining to the potential participant about all of the study related activities that are beyond standard care and to ask for that person’s consent to be included in the study.
- The key elements of informed consent are information, comprehension and voluntary participation.
- The consent taker must assess the individual’s understanding of the purpose of the study, what their involvement entails and what benefits and risks may exist for them.
- The consent taker must help the person to understand the information they
are given, encourage them to ask questions, test how much the person comprehends, give adequate time for them to consider their answer and, if they consent, provided them with a signed/marketed copy of the consent form.

- Consent is a process that should be continued throughout the length of the study to ensure the individual is still happy to participate.
- Key information which should be provided to participants includes: information on the study’s purpose, duration, sample size, procedures, benefits, costs and risks, their role and its’ duration, study related injury procedures, what happens to their details, that if found to be unsafe or if a better treatment emerges the study could be stopped, and that they are free to ask questions at any time and can withdraw without reason.
- Generally those over 18 years of age are free to given consent, adolescents give their assent together with their parent’s consent and for those under 12, consent is given by the parents. Countries' regulations and customs may have variations to these age guidelines.
- Researchers are not permitted to use coercion or undue influence when trying to consent individuals to research studies.
- Occasionally re-consenting is necessary if there is a change to the protocol which would affect the participant. The participant is absolutely free to opt out of participation at this, or any other point.
- Any information given to the participant may be verbal, written, or pictorial. All oral and written communication and information must be in a non-technical and understandable format. It must also be in the preferred language of the participant.
- In societies that are non-paper based, methods such as impartial witnesses, thumb printing, audio and video recordings, are used in place of signing a consent form.
- A consent form is not a legal contract that binds the participant to the study. The informed consent form is simply written confirmation that the process of informed consent has occurred.

References and Resources

References


Resources

1. 1947 Nuremberg Code
2. 1964 Declaration of Helsinki
3. 1979 Belmont Report
4. ICH GCP guidelines 1996
5. CIOMS guidelines 2002
6. NBAC Ethical & Policy Issues in International Research: Clinical Trials in Developing
Quiz

Summary

1. Which of the following would not be regarded as research misconduct?
   - Not being told everything (or anything) about their disease
   - Being offered suitable compensation for time spent on the study
   - Being kept ignorant of the fact that there was treatment for their disease
   - Receiving insufficiently tested drugs
   - Being included in research that was life-threatening
   - Not being asked for their consent to be included in experiments
   - Being subjected to procedures which had no justifiable scientific or medical reasons

2. You are not classed as a vulnerable group if you:
   - Are poor
   - Have low levels of education and literacy
   - Are concerned with finding better treatment than your current one
   - Have an unquestioning acceptance of authority

3. Non-maleficence is ensuring that an individual’s freedom to choose and act is respected.
   - True
   - False

4. Guidelines and regulations have been developed throughout the last several decades in order to ensure that:
   - Studies will be allowed to include everyone they invite to participate in the research
   - Everyone is treated as equal and no special considerations are given when consenting to research
   - Individual’s needs come before the needs of science

5. The consent taker assesses the individuals understanding of the information provided during the consent process so as to:
   - Find out how likely they are to agree to participate
   - To decide which arm of the study they will be placed in
   - Establish if they truly understand what they are being asked to do

6. It is important to give the potential participate adequate time to think about and ask questions on the study before they decided to consent because if they agree they cannot later change their mind.
   - True
   - False

7. Informed consent is:
   - An on-going process for the duration of the study
   - Only necessary for certain types of studies like clinical trials
   - Simply a procedure of getting someone to sign a form before they are enrolled in a study

8. Which of the following should not be done?
   - Obtaining a community leader’s agreement before approaching individuals
   - Complying with the country’s regulations and guidelines
   - Enrolling someone to the study on the consent of the head of the household

9. The key facts that an individual should receive when being asked to consent includes which
of the following study information:
- Duration
- Sample size
- Procedures
- Benefits, costs & risks
- Study related injury procedures
- The right to withdraw at any time
- All of the above

10. Assent is taken from:
- Parents when the child understands what the study is about
- Adults when participation in a study is for a very short duration
- Individuals who participate in studies that don't offer compensations
- Adolescents and those with mental incapacities

11. Those under the age of 18 are never allowed to give consent.
- True
- False

12. Undue influence occurs when an individual:
- Is offered expenses to cover their travel costs
- Is promised treatment after the study, if the outcome is successful
- Is reassured that there is no risk and it is safe to join

13. Which statement is false: Study information must...
- Use simple words
- Be in a format the person can understand
- Be in written format only
- Be in a language the person can understand