Review Article

Importance of Informed Consent Form and Use of Electronic Informed Consent Form

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ABSTRACT

Informed consent is an ethical and legal requirement for research involving human participants. In this process the participants is informed about all the aspects of the trials, which are important for the participants to make a decision and after studying all aspects of the trial the participant voluntarily confirms his/her willingness to participate in a particular clinical trial and significance of the research for the advancement of medical knowledge and social welfare. Obtaining consent involves informing the subject about his/her rights, purpose of study, procedure to be undertaken, potential risk and benefits of the patients, expected duration of the study, extend of confidentiality of personal identification and demographic data so that the participation of the subject in the study is voluntary. It discusses about the basic elements of informed consent and the process to be followed while obtaining the informed consent. The use of electronic informed consent has also been discussed that how conveniently and easily the information is passed on to participant in the form of movie, picture, video clip, graphics and spoken words which provide and interacting media session on their device.

Keywords: Informed consent, Human subject, e-consent, Institutional Review Board.

INTRODUCTION

In 1964 Declaration of Helsinki in Finland has adopted 12 principles to guide physicians on ethical considerations related to biomedical research. It emphasizes the distinction between medical care that directly benefits the patient and research that may or may not provide direct benefit.

For the drug to get approval and enter into market it has to undergo clinical trail. Clinical trial in terms describe all research related activities which involves humans as subjects. As no individual has right to infract the fundamental rights of person for the sake of fulfilling their purpose so as an important tool informed consent came into existence. Informed consent is documented dated and signed by the participant who's taking part in clinical trial. The informed consent should be signed prior the start of clinical trial and should get approved from institutional review board.

Informed consent is purely based on safety, right and well being of human subjects. The goal of informed consent is to provide complete details of the research in convenient language which subject can easily understand and voluntary make decision regarding "to" or "to not" participate into trail.

CLASSIFICATION OF INFORMED CONSENT

Consent

An adult who is capable of giving his/her willingness to participate in research study, can provide consent the subject should be 18 years of age and competent to make decision to participate.

Parental consent:

When children's are included in the research, parent/guardian must sign the parental permission consent document. In some situation only one parent permission is required, while in other situation both parent permission is required. In some cases, it is necessary to waive the requirement to obtain parental permission.

Assent:

It is child's affirmative agreement to participate in research. If the subject is 7-17 years of age, assent must be obtained. The assent form must be written in appropriate reading level of the youngest subject in the age range and use simple terminology.

Verbal:

Verbal consent contains all the elements of the trail, the participant is verbally read the elements and verbally agrees to participate.

Short Form:

A "short form" is generally used when there is a language barrier and an IRB'S approved consent is orally translated in the subject's native language.

CHALLENGES IN OBTAINING INFORMED CONSENT FORM

Language barriers

It is assumed that the individual who signs the consent form does with full understanding of whatever is given in the informed consent form. However, it is very difficult to evaluate their degree of understanding as there is no established method to measure the level of understanding

regarding the information provided. Many individuals sign the consent form without being fully aware of what they are signing, which results in withdrawal of subject at later stages of ongoing clinical studies[1].

False expectations

Some participants fear of being treated as an "experimental model" for the studies while others refuse to take part because of historical events of clinical trial fraud and misconducts known to them[2,3].

Participants perception

Most of the participants are afraid of unwanted side effects of new treatment. Convincing and receiving an informed consent from such participants is most difficult. In some cases, disclosing information regarding the potential side-effects may unnecessarily scare the participant[2,3].

Religious influence

The informed consent process is designed in such a way that every participant has the right to decide whether to accept or refuse the recommended medical treatment. Sometimes their decision for participating in researcher projects is influenced by the religious beliefs[2,3].

Children

Where research involves children (under the age of 18) consent/permission has to be obtained from parents. If the child is above 7 years of age then "child assent" is also mandatory. Difficulty arises when parents give their consent while child refuses to assent[4].

Vulnerable groups

Vulnerable groups include the person who is absolutely or relatively incapable of protecting their rights. Obtaining informed consent is critical when working with them, specifically with some groups like people with learning disabilities. There may be potential problems of understanding what the research is about, what will be their role in the research and how the research will be used.Hence, obtaining informed consent can be difficult and special care needs to be taken to develop the appropriate strategies for communicating the implications of involvement in research[5,6].

Barriers for participation in the clinical trials[7]:

Barrier	Reason
Lack of knowledge	Limited information about clinical trials
Fear of new treatment	Uncertainties about side effects Concern over quality of life
Psychological issues	Depression
Financial burden	Concern that insurance will not cover in the treatment

E-Consent

Researchers are showing keen interest on e-consent as with developing technology the subjects are provided with the website which is approved by the IRB and is secure with the software which provides confidentiality to subjects data. E-consent provides the information of all aspects related to clinical trail in the form of picture, movie, video clip, graphics and speaker provided with different languages in which the subject is comfortable. Here, e-consent helps in enrolling larger number of subjects. The subject can take is own time to study the inform consent can take help, advice or suggestions from friends and family if in case he/she is illiterate or elderly person. The interactive presentation of the study procedures and commitments should make this informed process not only easier to understand In detail but also more comprehensive.

Investigator

The sponsor will design the informed consent, investigator should make sure that it includes all the elements required by the regulatory body, that is to be informed to enrolled subjects submit the designed cosent form to IRB for approval. Changes are to be made if any should be done in form as required by IRB. Use IRB approved form to discuss and explain trail related risks, benefits and other aspects with the potential participants and if required, the participant legal representative, before the trail begins.

Give potential participant ample time to discuss with family, answer all the questions related to trails which the participant ask do not force him/her to participate or to continue to participate in trail. If the participant is interested in involving trail date and sign the documented informed from the participant which indicates that the participant is voluntary willing to participate. Inform the participant about their right to withdraw from the ongoing study at any time without loss in compensation. Ensure that the information will be presented to prospective subjects in language that they easily understood.

IRB

Institutional review board is an administrative body established to protect the rights, wellbeing of human subjects recruited to participate in research activities conducted under the auspices of the institute which it is affiliated. IRB is responsible in reviewing , prior to the trail initiation. IRB is concerned with the safety, rights, welfare and privacy of human subjects

IRB has the authority to approve, disapprove, monitor and require modification in all research activities that fall under its jurisdiction as specified by federal regulation and institutional policy.

USE OF ELECTRONIC INFORMED CONSENT

In March 2015, US Food and Drug Administration (USFDA) released a draft guidance document with recommendation for clinical investigators, sponsors, and Institutional

Review Boards (IRBs) on the use of electronic media and processes to obtain informed consent for clinical investigations of medicinal products[8].As per this guidance, electronic informed consent (eIC) refers to using electronic systems and processes that may employ multiple electronic media including text, graphics, audio, video, podcasts and interactive web sites, and card readers etc., to communicate information related to the study and to obtain and document informed consent.

The aim of implementing e-ICF is to improve the understanding of study participants. The guidance also recommends on procedures to ensure protection of rights, safety and well-being of the human subjects. This also helps in reducing the regulatory burden.

As per the guidance, whenever an e-ICF is used, it must be properly secured with restricted access. This process must also ensure the confidentiality regarding the patients identity. This also recommends that subjects information within the system must be properly encrypted unless it is documented why encrypting is not necessary in specific cases.

An e-ICF process often uses interactive interface, which helps in enhancing the subject's ability to understand, retain, and comprehend the study information. The use of technology brings immense strength, insight, and integrity to the consenting process.

An e-ICF process which uses web applications or electronic devices is growing in popularity. Three key stakeholders in developing e-IC include sponsor, vendor, and IRB. Vendor plays an important role in making the tool simple and easy for the patients enrolled in clinical research. Electronic products which are to be used in electronic consenting process have to be validated for compliance with United States of America's Code of Federal Regulation 21 Code of Federal Regulations part 11 requirements for electronic records and signatures[9].Sponsors and investigators considering E-consenting option have to obtain IRB/Ethics Committee approval of the consent document text prior to developing the electronic consent tool.

Comparing the e-consent over paper across several categories:

	Paper informed consent	Electronic informed consent
Patient site interaction	Patient is given form to sign and site personnel should make sure that the patient understands the ICF and answers all questions	Patient engages in interactive session with videos, dictionary definition, site personnel answer question that are prompted by patient with in software application. patient retention info is documented
Patient comprehension	Limited due to extend of documents and medical and legal terminology	Enhanced due to video assistance in native language
Multiple languages	Paper translation is difficult and not up to par	Video assistance if provide high quality translation
IRB and EC review	Multiple copies varying by IRB/EC and by different country is required	Standard process with web protocol for review
Storage, asses and site monitoring	Cumbersome review of all documents and charts to be done	All form of data can be easily accessible in a web portal
Fraud protection	Complete reliance on documents	Complete audit trail showing when all parties signing documents
Site consistency	Process varies consistently from site to site	Standard process is followed at all trail site
Version control and new signatures for protocol amendments	Poorly done with paper, with a significant no of patients and receiving updated information	Strict version control with notification to sites and patients when a form is updated and requires a signature

Benefits of e-consent for participants:

- Convenience: Do not have to go to research site
- Less pressure and anxiety: Can review the consent form and consult with family members without any anxiety and pressure
- More informed: Participants can review the consent with more leisure, allowing them to make more informed decision. In addition, supplementing with electronic technologies could help the participant to better understand the research.
- More engaged: e-consent can more engage the participant than paper consent document.

Benefits of e-consent for researchers:

- Higher enrollment: Large no of subjects can lead to higher enrollment, though there is not much data on subjects
- True informed consent: e-consent can help participant to be more informed, in turn allowing researchers to be more compliant and more ethical.
- More compliant participants: Participants can be more engaged and higher engagement greater compliance
- Convenience: No in person appointment scheduling
- No travel reimbursement: No travelling expenses

- Paperless: Data can be managed electronically
- Increased capability: Can conduct studies on wider picture with varied type of researches due to ability to consent participants electronically

Challenges of e-consent for participants:

- Consent decision: Limited consent decision with research staff
- Confidentiality: Access to consent documents

Challenges of e-consent for researchers:

- Expenses: Expense for infrastructure and technology to manage online documents
- Verification: Confirming identity and legitimacy of participant
- Compliance: Acceptability to auditors and in compliance, where applicable, with 21 CRF part 11

Audio-video recording of the informed consent process in India:

In recent years, there has been significant debate about the ethics of the research in developing countries. The quality of the informed consent process is identified as one of the major issue[10]. India's clinical trials system has come under intense scrutiny after a series of events involving alleged malpractices which resulted in widespread public protests. Concerns have been raised about the lack of ethical oversight, and there have also been allegations that vulnerable patients are routinely recruited to clinical trials without proper informed consent.

Central government in consultation with Drugs Technical Advisory Board (DTAB), Central Drug Standard Control Organization (CDSCO) released the Gazette of India notification dated 7 th June 2013 proposed to make draft rule that audio-video (AV) recording of the informed consent process of individual participant by an investigator including procedure of providing information to the subject and his understanding on such consent shall be maintained by the investigator for record while conducting clinical trials in India[11]. Once the Ministry makes the necessary amendments in this regard, the AV recording of informed consent will become mandatory in India.

Advantages of audio video consenting process:

- Simplification of the process
- Good reliability
- Transparency

Challenges of audio video consenting process:

Indian culture: India is a land of diverse culture. Indian culture has a tradition in which women use burkha (outer garment worn by many of the Islamic women to cover their body and face) and in most of the rural areas, women avoid eye contact with men.in such cases, it becomes difficult to obtain informed consent by audio video process.

Willingness to discuss regarding their disease in front of camera: Participants may feel uncomfortable to discuss regarding their disease especially in case of sexually transmitted diseases such as HIV. In some cases, such as patients with depression, they are to be dealt carefully. Investigator should provide assurance about the confidentiality of the patient identity and their data is secured properly.

Language barrier: During audits and inspections, it will be challenging to the auditors to know whether the process was conducted according to the guidliness and may need a translator.

Infrastructure: The minimum required infrastructure would be a separate room for consent with minimal background noise and an equipment to record the consent process, which could be a simple camera. Consideration should be given for patients who are immobile, as there may be need for a movable set-up to record their consent.

Interpretation of behaviour on camera:

It seems to be a big problem how the body language or the facial expressions of the participant or the investigator providing information are interpreted, since it is very subjective. In some of the conditions, it may seem that the participant is forced to take part in the trial based on his/her body language or vice versa.

Increased financial burden: The activity of audio video consent process has a potential to increase the clinical trial budget significantly. Consider in a study with large sample size and high screen failure rate, each and every informed consent discussion will have to be recorded, irrespective of whether the participant agrees or refuses to consent at the end of the discussion. In addition, the records of all participants who have consented but screen failed due to any inclusion and exclusion criteria will have to be archived, which adds to the cost.

Risk of tampering the records: With advancement in technology, tampering of the audio video recording may become easier and difficult to detect. Hence, ensuring controlled access and robust IT policies will be required in order to be in place to avoid any misuse of the records. How long would this information be stored for and what happens at the end of a trial would need to be defined and discussed with the regulators.

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