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Review Article

**Informed Consent form in Clinical Trial****Sunny Panwar*, Hemant Pal and Amrish Chandra***Department of Drug Regulatory Affairs, Amity Institute of Pharmacy, Amity University, Sector-125, Noida (UP), India***Abstract**

Informed consent form is a vital requirement for research study on the human participant. It is the consent which is given by the subject before participate in clinical trial. Informed consent mainly came in existence after the Nuremberg trial and the other guideline line like Helsinki Declaration and Belmont Report also play an important role in their evaluation. Informed consent form mainly contains the complete information about the clinical trial, protocol, duration, potential risk and benefit of the trial. Informed consent is revised from time to time, as the new information is available. In some case waiver of consent done by proper review by Institutional Ethic Committees (IEC).

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E-mail address: sunnypanwardra93@gmail.com (Sunny Panwar).**1. Introduction**

In India, the regulatory bodies and Ethic committee (EC) regulate clinical trial. The main guidelines, which are following in India, are "Schedule y" of Drug and Cosmetics Act 1945 and other guidelines like "Good clinical practice for clinical research in India by Central Drug Standardization Control Organization (CDSCO), ICH E6 guideline (good clinical practice guideline) and Ethical guideline for biomedical research on human participant by Indian council of medical research (ICMR). It all contains the guideline for the protection of right and safety of participant in clinical trial. Informed consent form is a mandatory requirement that is mention and defines in the guideline.

Patient consent form is a written legal document that contains the information of complete procedure of clinical trial in the language that is understandable by the participant. It concerns about the potential risk and benefit, complete time which taken and endorsement which is given during the study. Patient consent form is sign under the presence of an investigator and guarantor that the participant agrees for inclusion criteria.

According to ICH Guideline for Good Clinical Practice E6(R1), informed consent form is "A process by which a subject voluntarily confirms his or her

willingness to participate in a particular trial, after having been informed of all aspects of the trial that are relevant to the subject's decision to participate. Informed consent is documented by means of a written, signed and dated informed consent form."

According to World Health Organization (WHO) Guidelines for good clinical practice (GCP) for trials on pharmaceutical products, informed consent form is "A subject's voluntary confirmation of willingness to participate in a particular trial, and the documentation thereof. This consent should only be sought after all appropriate information has been given about the trial including an explanation of its status as research, its objectives, potential benefits, risks and inconveniences, alternative treatment that may be available, and of the subject's rights and responsibilities in accordance with the current revision of the Declaration of Helsinki" (1,2).

Clinical trial professional often forgets about the informed consent form. Informed consent form is an essential requirement for approval of clinical trial by the Ethical committee. Before participate in clinical trail the volunteer should sign the Patient Consent Form.

Informed consent form is a legal document which signature by participant and perform as an evidence that

- The purpose of study has been clear and understood by the subject.
- It is an open discussion between the participant and the investigator that contains all the information of the queries of clinical trial and compensation, wages that given to him.
- It is also contained statement that the privacy is maintained by the both volunteer and participant. It is the responsibility of the ethic committee as informed consent form contains all the quality information, the appropriate way in which is understood by the participant and protection of participant and their safety.

2. Ethical point which is considered during complete process of consent (1, 3)

- Language used in the informed consent form should be easily understandable to subject. There should be low level of complexity and scientific language.
 - Subject, their guardian, relative, legal representative have an ample opportunity to explore about complete information of the trial and research.
 - There should be clear information that trial is a procedure and volunteer is free to refuse the participation or withdrawn from the trial at any stage.
 - Subject must be allowed enough time to determine whether they want to participate or not.
 - Subject must be aware that their personal information kept confidential and it is carefully handled and examined by authorized person only.
 - The sponsor about insurance, compensation and wages informs to subject and treatment shall he or she get in case of any injury or disability by participating in clinical trial.
 - If a subject consent to take in clinical trial after complete explanation of study which includes:
 - Aim and objective of the trial.
 - Time frame of complete clinical trial.
 - The mode of treatment used.
 - Expected benefit
 - Potential risk and inconvenience.
 The complete consent recorded.
 - If the subject is incapable of giving personal consent (i.e. minor, mentally challenged) there consent in the trial accepted when it permitted by the local law and regulation and their legal representative gives consent form or participation.
 - The written information in the informed consent form be revised whenever important new information available. Any revised informed consent form should receive the approval from the IEC's/IRB.
 - Nobody, neither the investigator/sponsor nor trial staff should pressurize a subject to participate in clinical trial or continue trial.
- If a subject participates in clinical trial, Informed consent form should be signed and dated by the subject or subject legally accepted representative and it also signed by the person who conducted informed consent session.
 - If a person is unable to read or legally accepted representative is also unable to read informed consent form, an impartial witness should be present there during the complete consent discussion. All the written informed should be read and explained to the subject or subject legal representative. Then the subject or legal representative has signed the informed consent, the witness should also sign and personally dated the informed consent form.
 - Prior to participation in clinical trial, the subject and legally accepted representative should receive a copy of the signed and dated written informed consent and any other information regarding to trial.
 - In a non-therapeutic trial (i.e. trial in which there is no direct clinical benefit to the subject), the consent of subject is taken by giving complete information that there is no direct clinical benefit to subject takes place. Subject should sign personally and dated consent form.

Why informed consent is required

In the Second World War, German medical practitioner had done a number of trials on the people of Germany without their consent or willingness. In this, trial millions of people died and suffered from extreme injury or permanent disabilities. Thus, the first international statement on the safety and ethics of medical research using human subject was formulated in 1947, which is known as "Nuremberg Code" (4).

In 1964 Council for international organization of medical science (CIOMS) at Helsinki, the World Medical Association formulated general principal and specific guidelines on use of human subject in the medical research, known as Helsinki Declaration (5), which is revised time to time.

Belmont report (1978) was published in 1978, which promoted the problem arising from the Tuskegee Syphilis study (1932-1972). It is one of the major projects towards ethics of healthcare research. It arises the ethics for protection of participants in the clinical trial and research (5).

The fundamental principal for using any human subject for research purpose:

1. Safety of human participant.
2. It should be beneficial for human being. Benefit is high and risk is low.
3. Respect of the person
4. There should be fair justice, non-exploitation of participant.
5. Moral value of humanities is follows (5, 6).

Condition for taking re-consent form

1. If there is new information which would necessary for the deviation of protocol.
2. When a participant gains its consciousness from unconscious state and a mentally challenged patient able to understand study.
3. If a study is planned to extended for a long term.
4. If there is any change in treatment modality, procedure and site (6).
5. Confidentiality record i.e., patient identity and their any disease.
6. Number of subjects participate in the clinical trial.
7. Compensation for injury or death during the clinical trial.
8. Time for questions to be asked and answered by the participant and their legal accepted representative.
9. Brief detail of the participant's decision.
10. Contact details of the participant and their alternative contact detail.
11. Travel reimbursement and their day wages.
12. Subject responsibilities and subject satisfaction.
13. Use understandable language which is non-scientific
14. One signed Copy of ICF was given to the participant.
15. Subject should sign personally and dated consent form

Essential Element of Informed Consent Form (7, 8)

1. Aim and objective of the study
2. Purpose of the study.
3. Protocol and Period of study.
4. A testimonial that the protocol and the informed consent were revised with the participant, as well as the risks and benefits of the study.
5. Alternative treatment options discussed such as placebo.

Table 1 Origin and evaluation of consent form

Origin and evaluation of consent form

Informed consent for participation in research was recorded in 1900

<i>Nuremberg Code in 1948</i>	Nuremberg code is the set of ethical guide which come in existence after the world war 2.It contains guideline for safety of human subject, participate in research study.
<i>sIndian Council of Medical Research (ICMR) in 1949</i>	ICMR is an apex body of India, which form the guideline for safety, and protection of human participant, which take part participation in biomedical research.
<i>Council for International Organisations of Medical Sciences (CIOMS) in 1964 give Helsinki Declaration</i>	Helsinki Declaration is a set of the ethical guideline for the protection human participant for the medical community by World Medical Association (WMA).
<i>The Belmont Report-1979</i>	The Belmont Report is a report created by National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research. It is containing fundamental principal of human safety in research study.
<i>The World Health Organisation (WHO) and the CIOMS in 1982, issued the 'Proposed International Guidelines for Biomedical Research involving Human Subjects.'</i>	CIOMS and WHO give the joint guideline for the ethic of human participant. They giving the 21 core guideline for the physician, which are, engage in the medical and non-medical research.
<i>International conference on harmonization ICH CGP-1996</i>	Ich GCP is guideline is provided by ich. It is containing the standard for good clinical practice which is made by the joint of three tripartite region of US, Japan and European Union.
<i>"Universal Declaration on Bioethics and Human Rights" in 2005</i>	In 2005 The United Nation Educational, Scientific and Culture Organization (UNESCO) give the bioethical Guideline for the protection of vulnerable population and human subject in developing country.

Table 2 Type of consent form (7, 8)

Type of informed consent form	
Assent	It is a child's agreeing agreement to participate in research. If the subject is 7-17 years of age, assent must be obtained. The assent form must be written at the appropriate reading level of the youngest subject in the age range and use simple terminology.
Consent	The adult able to gives this type of consent. The subject must be 18 years of age and competent to make the decision to participate in the clinical trial.
Parental Permission	If minor or children are participant in trial there, parent/guardian must sign a parental permission consent document.
Active consent	Participants indicate their willingness to participate by agreeing to a specific statement, and then are included in the study. This is the most common, and recommended, form of consent for research.
Explicit consent	In this type of consent the participant, answer specific question about their willingness to participate in trial.
Short Form	A "short form" is usually used when there is a language barrier and an English approved consent is verbally translated in the subject's native language.
Passive consent	In this type of consent assuming that the participant is, agree to participate unless they specifically decline to be participate in study like in school form are send to parent asking to allow student to participant.
Information/Fact Sheet	An information sheet many be used as a form of consent in certain circumstances where a signature could compromise the participant or in studies where signed consent is not required by regulations (research procedures involving minimal/ no risk).

3. Waiver of consent (8)

Informed consent always vital for every research study but in certain situation informed consent is waived. If there is any justify reason is involved, if the research involved not more than the minimal risk or when the participant and researcher does not come in contact with each other, if there is any emerging situation is taken place and there is necessity to start trail (9).

1. In case of HIV/AIDS, their needs to be make confidentiality for such diseases so in that case waive occur in informed consent.
2. Research on publicly available information, documents, records, works, performances, reviews, quality assurance studies service programs for benefit of public having a bearing on public health programs, and consumer acceptance studies.

3. Research on anonymized biological samples from deceased individuals, DNA or RNA from recognized institutions or qualified investigators, samples or data from repositories or registries etc.
4. In emergency situations when no surrogate consent can be taken.

4. Challenge of Informed consent form in clinical Trail

In India the volunteer is easily available but there are several barriers that is limited the rate of clinical trial. The barrier is: (9)

- Language Barrier
- Religious influence
- Perception of subject
- False expectation
- Vulnerable people and group

The recruit of the volunteer in the clinical trial is done by interviews (9). The interview conducted by the investigator and sometime by the sponsor for the recruitment of the patient investigator paid by incentive. It creates an unethical practice. Many of the patient participant in clinical trial as it is suggested by their physician. When the physician is also investigator sometime, they force and misguide the patient to participate in the clinical trial for incentive and other cause.

The main barrier in India is linguistic. The participants that are illiterate in clinical trial are suffering more. There may be a chance of misunderstanding of information that translated. Many people sign the consent form without prior proper understanding and they withdraw at the later stage of trail. Therefore, it is responsibilities of investigator to perform informed consent form in many languages.

Many newspaper and TV program dimness the entire clinical trial. They only show the negative side of clinical trial. They only are showing the bad effect of trail not the beneficial effect. Some NGO also have gone to court and made the stay in some of clinical trial. Some people that alertly do not follow their duties do not mean the completely clinical industry is offender.

5. Conclusion

India is one of the largest populations carrying country. India has burden of poverty and diseases. Due to this every pharmaceutical company wanted to launch their product in India. For the safety of drug more clinical trial were held in India. Human which participate in clinical trial for those Informed consent forms is very vital part for their safety and their rights. India has regulatory for clinical trial, which involve Informed consent form as mandatory tool without Informed consent form no clinical trial will takes place. Informed consent form required very minor to major information of the clinical trial and their consequences with signature of senior most authority and participant and their legal

accepted representatives. Institutional ethics committee (IEC) has empowered to surveillance whether the Informed consent form is filled and verify properly by the authorized person with very reliability or not. If not then they have supremacy to take hasty and relentless action against them. Informed consent form is complex and somewhere delicate assignment to do because in India approx. 30% of the population is illiterate and unemployed. So, India's most of the population participate in clinical trial for money and better treatment without knowing the course of action and stipulations and circumstance. Informed consent form is the foremost and extremely imperative part of the clinical trial at every stage or phase. So, we should have to make sure that there is 100% transparency between the Informed consent and their phases and participant. We should more work on the human's benefits, which participate in clinical trial not only for our benefit. We should clearly share every minute information with the participant and with very persuasive language so it will be easy for both sides to take decision and held clinical trial without conspiracy.

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Conflict of interest

The authors declare that there is no conflict of interest.

References

1. Guidelines for good clinical practice (GCP) for trials on pharmaceutical products, World Health Organization WHO Technical Report Series, No. 850, 1995, Annex 3 [Internet]. APPS; 2011 Apr 20 [cited 2019 Mar 07]. Available from: apps.who.int/medicinedocs/pdf/whozip13e/whozip13e.pdf
2. Understanding Informed Consent [Internet]. 2017 Feb 02 [cited 2019 Mar 10]. Available from: <http://www.centerwatch.com/clinical-trials/understanding-informed-consent.aspx>
3. Dalla-Vorgia P, Lascaratos J, Skiadas P, Garanis-Papadatos T. Is consent in medicine a concept only of modern times? *Journal of Medical Ethics*. 2001 Feb; 27(1):59-61.
4. Ethical Guidelines for Biomedical Research on Human Subjects. New Delhi: Indian Council of Medical Research, The Nuremberg code (1947); [Internet]. 2000. [cited 2019 Jan 10]; *British Medical Journal* No 7070 vol. 313:1448. Available from: <http://www.cirp.org/library/ethics/nuremberg/>
5. World Medical Association declaration of Helsinki. Ethical principles for medical research involving human subjects) [Internet]. 2017 Jan 18. [cited 2019 Jan 11]. Available from: <http://www.ohsr.od.nih.gov/guidelines/helsinki.html>
6. Kharawala S, Dalal J. Challenges in conducting psychiatry studies in India. *Perspect Clin Res*. 2011; 2:8-12.
7. DeCosta A, D'souza N, Krishnan S, Chhabra MS, Shihaam I, Goswami K. Community based trials and

- informed consent in rural north India. J Med Ethics. 2004; 30:318-23.
8. Kegley K. Ann J, Challenges to informed consent, EMBO Report. 2004 sep; p.65.
 9. Levine RJ. Michigan: Urban and Schwarzenberg. The Ethics and Regulation of Clinical Research; 1981.