In Brazil, the legislation that deals with the protection and rights of the research subject are Document of the Americas of Good Clinical Practices, Resolution 196/1996 of the National Health Council and Resolution RDC 39/2008 of Anvisa. Studies involving Human Beings in Brazil must follow these laws and be conducted in accordance with Good Clinical Practices.

Informed consent must be obtained from each subject prior to participation in the research in accordance with national requirements and culture. When a subject is not capable of giving free and informed consent, authorization from a legally authorized representative must be obtained in accordance with applicable legislation.

Informed consent is documented in a written, signed and dated consent form, which is called the Free and Informed Consent Form – TCLE.

When observing irregularities in studies that violate the rights of research subjects, they must contact the Research Ethics Committee -
CEP of the research center and with the National Research Ethics Commission –
CONEP (website: Conselho.saude.gov.br/web_comissoes/conep/index.html). Additionally, you can contact Anvisa through the following communication channels: Call Center 0800 642 9782 or through "Contact Us" on the ANVISA website:

(http://www.anvisa.gov.br/institucional/faleconosco/FaleConosco.asp).

Calls can be made from Monday to Friday, from 7:30 am to 7:30 pm, excluding holidays. Complaints must be directed to the Coordination of Research and Clinical Trials – COPEM.

Below are some questions and answers to guide the research subject regarding their rights in participating in studies involving Human Beings:

What is meant by "free" consent or "voluntary" participation in an investigation? How is this implemented within Good Clinical Practice?

Informed consent is based on the principle that competent individuals have the right to freely choose whether to participate in research. Free and informed consent protects individual freedom of choice and respects the individual's autonomy. The ICF must always be applied before the start of any study procedure, including diagnostic tests or others that are carried out exclusively to determine the individual's eligibility to participate in the research.

Therefore, the decision to participate in the study must be voluntary, that is, free and spontaneous. If you agree to participate in the study, the individual becomes a "research subject".

"Obtaining free and informed consent is a process that begins when initial contact is made with the research subject, and continues throughout the course of the study. By informing research subjects, by repetition and explanation, by

response to the subjects' questions, and to ensure that each individual understands each procedure, the researchers obtain their consent form, expressing respect for the subjects' dignity and autonomy. "(CIOMS, international ethical guidelines, Guidance Commentary 4)

Who can apply the TCLE?

The person conducting the consent interview must be knowledgeable about the study and able to answer the questions. Some sponsors and some ethics committees require that the clinical investigator personally conduct the consent interview.
If someone other than the clinical investigator conducts the interview and obtains consent, the clinical investigator must ensure that this responsibility is formally delegated to that individual, and that the delegated person is qualified and receives appropriate training to perform this activity. Neither the physician-researcher nor the research team should oblige, coerce or inappropriately influence a subject to participate or continue participation in a study;

How long does the research subject have to decide and sign the ICF? Is it the research subject's right to receive a copy of the ICF?

The research subject has as much time as necessary to clarify any doubts. Each individual should be given the time necessary to reach a decision, including time for consultation with family members or others.
Adequate time and resources should be reserved for informed consent procedures. Before participating in the study, the subject or his/her authorized legal representative has the right to receive a copy of the signed and dated Informed Consent Form.

How should the ICF be prepared for the research subject to understand?

The form and context in which information is transmitted is as important as the information itself. For example, presenting information in a disorganized and rapid manner, allowing too little time for analysis, or reducing opportunities for questioning can all adversely affect a subject's ability to make an informed choice. Therefore, the ICF must be clear, organized and understandable.
The TCLE must provide the telephone contact details of the main investigator or delegated professional so that the research subject can contact him in the event of unpleasant reactions with the medication he is receiving in the study.

How should the physician-investigator or delegated professional transmit information about the study for the research subject to make a decision?

The investigator must transmit the information, orally or in writing, in language according to the individual's level of understanding. The investigator must keep in mind that the prospective subject's ability to understand the information necessary to give consent depends on his or her maturity, intelligence, education, and the system

of beliefs. Therefore, the investigator must then ensure that the subject or his/her authorized legal representative has adequately understood the information. The investigator must give each person full opportunity to ask questions and must answer them honestly, promptly and completely. In some cases, the researcher may administer an oral or written test, verifying that the information has been adequately understood. No subject should be admitted to a study before clarifying all their doubts and signing the ICF.

How should possible risks and benefits be informed to research subjects?

Information about possible risks and benefits of participating in the study must be described in the ICF and explained by the investigator to the subject. Therefore,
The reasonably foreseeable risks or inconveniences to the subject and, when applicable, to an embryo, fetus or infant must be reported; the benefits reasonably expected. When there is no claim of clinical benefit to the research subject, the subject must be informed about this; the alternative procedures or treatments that may be available to the subject, and their important benefits and potential risks.

"...The investigator must give no unreasonable assurances about the benefits, risks, and drawbacks of the research, for example, or induce a close relative or a community leader to influence the subject's decision." (CIOMS, international ethical guidelines, Guidance Commentary 6)

After signing the ICF, will the research subject be able to leave the study?

If the research subject wishes to leave the study, he or she can do so at any time after signing the TCLE. This decision will have no repercussions on your participation in other clinical studies and will not result in any punishment or loss of benefits to which you are entitled.

Can the research subject be paid to participate in a study?

According to Brazilian legislation, paying research subjects to participate in the study is prohibited. Only compensation for transportation and food to the research subject is acceptable. Reimbursement must be defined at the beginning of the study and must be described in the Informed Consent Form. If

reimbursement has not occurred as previously established, we ask that you contact the Research Ethics Committee of the research center.

What do we mean by "vulnerable people"?

"Vulnerable people are those who are relatively (or absolutely) unable to protect their own interests. More formally, they may have insufficient power, intelligence, education, resources, strength or other attributes necessary to protect their own interests." (CIOMS, guidelines international ethics, Commentary

on Guidance 13). In general, all individuals, including healthy volunteers, who participate as research subjects should be viewed as inherently vulnerable because:

1. During the course of the study are (or may be) exposed to a medication for which the safety and efficacy are unknown or not completely understood and

2. There may be other factors - social, cultural, economic, psychological, medical - that may adversely affect an individual's ability to make rational and objective choices that protect their own interests, but that may not be readily apparent to the researcher.

Some vulnerabilities may be easily identified because they are obvious (e.g., institutionalized individuals, individuals with diminished mental capabilities) or relevant to research (e.g., children participating in a pediatric vaccine trial). Other vulnerabilities of subjects cannot be as easily identified (for example, individuals who are homeless or economically disadvantaged).

Individuals may also become more or less vulnerable over the course of a study in relation to their health status.

What special protections are needed to enable vulnerable populations to participate in research?

"For research subjects who are legally incompetent, physically or mentally incapable of giving consent, or legally incompetent minors, the investigator must obtain informed consent from the legally authorized representative in accordance with appropriate legislation. These groups should not be included in research unless it is necessary to promote the health of the population represented and such research may not instead be carried out on legally competent individuals" (Declaration of Helsinki)

Can the ICF be obtained more than once during the study?

When there are substantial changes to the conditions and procedures of a study, and also periodically, long-term studies, the researcher must once again seek the informed consent of the subjects..." (CIOMS, International ethical guidelines, Commentary on Guidance 4)

What is Anvisa’s role in ensuring the safety of research subjects?

Prior to the start of the study, Anvisa carries out an evaluation of the clinical study to verify whether it is methodologically in accordance with Good Clinical Practices to guarantee the safety and well-being of research subjects and the validity of the data provided.

will be generated by the search. Furthermore, Anvisa carries out inspections in Brazilian research centers to verify adherence to Good Clinical Practices in clinical studies.

How can the research subject know about a clinical study that will recruit or is recruiting patients?

Research subjects learn about studies being carried out through publication in the media and at the research center, which may be the hospital or clinic where the subject is receiving treatment. All such advertisements must have prior approval by the Research Ethics Committee. Furthermore, the research subject can talk to their doctor so that they can advise on possible research that they can participate in. In Brazil, there is the Brazilian Clinical Trials Registry (ReBEC), which is a platform where research subjects can search for possible studies in which they could be potential participants. To learn about some of the clinical trials being carried out in Brazil, you can access the link: http://www.ensaiosclinicos.gov.br/

Can the study doctor remove the research subject from the study for safety reasons?

The doctor, in accordance with his clinical assessment, may discontinue the treatment to protect the patient's safety. Depending on what was planned in the schedule, it is not possible to carry out other procedures foreseen in the research, as this may affect health and test results.

How should subjects who were removed from the study/treatment by the doctor or chose to leave before the end of the research be monitored?

The research subject must be monitored by a doctor after leaving the study.
This monitoring must be foreseen in the study plan. For subjects withdrawn from the study by the doctor or who choose to leave the study for safety reasons (example: occurrence of unpleasant reactions), follow-up must be aimed at complete resolution of all unpleasant reactions.

Are research subjects entitled to compensation?

Research subjects who suffer damages (whether or not foreseen in the study protocol) must be entitled to compensation, according to the Resolution of the National Health Council
196/96.

Bibliographic references:

Good Clinical Practices: Document of the Americas. Pan American Health Organization, Washington DC, 2005.

Brazil. Ministry of Health. National Health Council. Resolution n. 196 of October 10, 1996.

Declaration of Helsinki. The World Medical Association.

Handbook for good clinical research practice (GCP): Guidance for implementation. World Health Organization, Geneva 2005.

International Compilation of Human Research Protections" e *"Human Subjects Research Protections: Enhancing Protections for Research Subjects and Reducing Burden, Delay, and Ambiguity for Investigators ICH-GCP and WHO.*

Manual for Good Clinical Practice – Tripartite harmonized version (USA, Europe and Japan) prepared by the International Conference on Harmonization – *ICH.* Topic E6 – CPMP/ICH/135/95.

The Council for International Organizations of Medical Sciences (CIOMS) International Ethical Guidelines for Biomedical Research Involving Human Subjects.