Clinical Research

The importance of standard operating procedures (SOPs) for clinical research centers

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Standard operating procedures (SOPs) are detailed instructions described to attain homogeneity when carrying out a specific function[1,2]. Basically, the importance of establishing SOPs in a clinical research center lies in: better preparation when conducting clinical studies, organization of clinical research processes at the research center, training, professionalism, credibility and quality assurance through process standardization and traceability in auditing and inspections[3]. The Normative Statute #4 of the *Agência Nacional de Vigilância Sanitária* (ANVISA) addresses the Inspection Guide for Good Clinical Practices (GCPs), which registers some SOPs that will be required during the inspection of the clinical study in the research center[4].

The inspections have as main objectives to verify the degree of adherence to the current Brazilian law and the GCPs[4,5], protection and well-being of the research individuals[2,6]. The GCPs constitute a standard for the planning, conduction, performance and monitoring of clinical studies. To correctly perform a clinical research project, systems must be implemented, with procedures that will ensure the quality of each aspect of the study[1,2], with the creation of specific SOPs for each phase of the research performance[7], being of the utmost importance for the development of a standard format, that is, a SOP on how to create a SOP[3]. Each phase of the SOP creation must have the participation of the involved team, which will be able to evaluate and validate their procedures and, if necessary, will be able to hire specialized personnel for this purpose. In these cases, it is important that the team have the sector knowledge and interact with the center group, being acquainted with each one of the processes and discussing each new SOP that is created.

The SOP must be written down in details to achieve homogeneity, both in production or service delivery. Each document must be part of a standard list[7]. Some items must be considered regarding their format, such as: heading containing the type of document, title, code, company or institution logo, area in charge, individual in charge, dates of creation, approval and authorization, objectives, field of application, reach or applicability, responsibilities, abbreviations, description of the procedures, references and appendices. The pagination, version and number of the last review can be disclosed as footnotes[3,7]. The access to SOPs, either in print or electronic format, must be controlled and limited to the users and eventual reviews and updates must be appropriately approved before their implementation[3].

The inspection process carried out by ANVISA will consist of the following phases: communication of inspection to the sponsor/ clinical research representative organizations and Main Investigator of the clinical study, opening meeting, interview with the study team, visit to the facilities, document analysis and closing meeting. At the document analysis phase, availability of essential documents in the clinical study phases will be verified. Among them, the following SOPs for critical procedures of the research center:

- Training and refresher courses for the study team;
- Recruiting and selection of research subjects;
- Free and Informed Consent Form use;
- Filling out of clinical files;
- Data correction in clinical files;
- Verification of source-documents and clinical files;
- Validated methodologies that have been used;
- Use and calibration of equipment/ instruments;
- Administration, preparation and transportation of the investigational product;
- Reception, control and accounting of the investigational product;
- Destruction/ Return of the investigational product;
- Electricity failure in the storage area of the investigational product;

- Collection, transportation, preparation, identification and analysis of laboratory samples;
- Disposal of biological and non-biological material;
- Breach of study blindness;
- Notification of adverse events and severe adverse events;
- File creation and maintenance;
- Other SOPs can be requested.

Depending on the inspection report and the sponsor's manifestation, ANVISA might declare, at the end of the Final Inspection Report that the study is or is not being conducted according to the GCPs. In cases of nonconformity, it can determine the temporary interruption of the research, discontinuation of the clinical research activities of the involved investigator or even the definitive termination of a clinical research in that specific center or in all centers in Brazil[4].

We conclude that the creation of and adherence to SOPs through training are essential to guarantee the quality and homogeneity of all processes involved in study conduction and that clinical research centers must prepare their services by creating these SOPs, which will be required during ANVISA inspections.

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