Ministério da Saúde
Secretaria-Executiva do Conselho Nacional de Saúde
Comissão Nacional de Ética em Pesquisa

Circular Letter No. 13/2020-CONEP/SECNS/MS

Brasília, June 2, 2020.

To the Coordinators of the Research Ethics Committees,

Subject: Provides information on the processing of Adverse Events in the CEP/Conep System.

1. The Plenary of the National Research Ethics Commission (Conep) in its Ordinary Meeting in October 2019, held on October 30th and 31st and November 1st, 2019, considering the need to standardize the processing of adverse events in the System CEP/Conep; and considering the provisions of CNS Resolution No. 251 of 1997, items III.2.d and V.1.h; in CNS Resolution No. 346 of 2005, item 5; in CNS Resolution No. 466 of 2012, items V.5,
X.1.3 and XI.2; in CNS Operational Standard No. 01 of 2012, item 7; in CNS Operational Standard No. 01 of 2013, item 2.1.j; in Circular Letter No. 008/2011/Conep/CNS/GB/MS of 2011 and the associated form;
Resolve to approve the following Circular Letter.

2. This letter establishes the processing in the CEP/Conep System of adverse events occurring in Brazil and outside the country.

3. For the purposes of this letter, the following terms and definitions are adopted:

3.1. **COORDINATOR CENTER:** Brazilian institution that coordinates the activities of a uni or multicenter study, being responsible for communication with Conep, when applicable.

3.2. **PARTICIPANT CENTER:** Brazilian institution participating in a multicenter study, carrying out all stages of the protocol, without the prerogatives of the coordinating center.

3.3. **MULTICENTRIC STUDY:** study conducted according to a single protocol in several research centers and, therefore, to be carried out in its entirety by the responsible researcher in each center in the country, following the same procedures.

3.4. **SERIOUS ADVERSE EVENT (SAE):** any unfavorable occurrence with the research participant, after signing the TCLE, which results in: 1) Death; 2) Threat or risk to life;
3) Need for hospitalization; 4) Prolongation of pre-existing hospitalization; 5)
Permanent disability or damage; 6) Congenital anomaly; or 7) Significant medical occurrence that, based on appropriate medical judgment, may harm the participant and/or require medical or surgical intervention to prevent any of the other events mentioned.
Synonymy: serious adverse event.

3.5. **INDEX ADVERSE EVENT:** corresponds to the initial adverse event in the participant, which may have complete resolution or unfold in a subsequent event.

3.6. **SUBSEQUENT ADVERSE EVENT:** adverse event that occurs sequentially and as a consequence of another.

3.7. **SERIOUS ADVERSE EVENT NOTIFICATION:** report of the index and subsequent adverse events to the CEP/Conep System suffered by a research participant in Brazil.

3.8. **CONSOLIDATED REPORT OF SERIOUS ADVERSE EVENTS:** summary of adverse events occurring in Brazilian research centers or outside the country.

4. PROCESSING OF ADVERSE EVENTS OCCURRING IN THE COUNTRY:

4.1. Only adverse events considered serious occurring in the country should be notified to the CEP/Conep System.

4.1.1. Notification of non-serious adverse events is optional, and this is the prerogative of the researcher or sponsor.

4.2. The ethical analysis of the EAG is the exclusive responsibility of the CEP.

4.2.1. The occurrence of adverse events will not be assessed by Conep, except when, at the discretion of the CEP, there is a need.

4.3. Notifications about the index and subsequent events of a participant must be presented in a single document, in tabular format, and submitted to the CEP/Conep System through the Brazil Platform, through the "notification" functionality, and must be updated with each occurrence of subsequent adverse event.

4.3.1. The document must contain the study identification (research title and CAAE number), name of the research center, name of the responsible researcher, coded identification of the participant and description of the index event and subsequent events.

4.3.2. Each adverse event must be characterized according to:

I. Date of occurrence of the adverse event.

II. Participant number or code.

III. Event number or code (EAG).

IV. Classification of the adverse event (index or subsequent).

V. Discrimination of occurrence (examples: febrile neutropenia, pneumonia, among others).

SAW. Type of EAG ("death", "life threatening", "need for hospitalization", "prolonged hospitalization", "significant damage", "permanent damage", "congenital anomaly", "at the discretion of the researcher", "other ");

VII. Causality with the investigated product or research procedure ("unrelated", "possibly related", "probably related", "definitely related").

VIII. Detailed description of the assistance provided to the participant.

IX. Date of last update.

X. Participant's status on the date of the last update ("in progress", "recovered without sequelae", "recovered with sequelae" and "death").

XI. Description of the discontinuity of research participants.

4.3.3. Subsequent events must be organized chronologically, in the same document, according to the date of occurrence.

4.3.4. Notification updates must maintain the history with the event description index and subsequent ones.

4.4. It is the researcher's responsibility to periodically prepare the consolidated report of EAG that occurred in the study at his research center.

4.5. The consolidated report must be submitted to the CEP linked to the research center, through Plataforma Brasil, when submitting the partial and final reports of the study, through the "notification" functionality.

4.6. The consolidated report comprises a summary containing:

I. Absolute and relative distribution of EAG;

II. Detailed description of cases in which there are sequelae or death as a result of participation in the research (and not due to disease progression); and

III. Detailed description of cases that requested compensation or other types of legal demands.

4.7. In the case of multicenter studies, the researcher at the coordinating center must, additionally, prepare the consolidated report containing information on adverse events from all research centers and submit it to the CEP to which he is linked, via Plataforma Brasil, through the functionality "notification", when submitting the partial and final reports of the study.

4.8. In addition to the CEP linked to the coordinating center, Conep will also evaluate the consolidated report on adverse events if the protocol falls under item IX.4. of CNS Resolution No. 466 of 2012.

5. THE PROCESSING OF ADVERSE EVENTS OCCURRING OUTSIDE THE COUNTRY:

5.1. It is up to the researcher at the coordinating center to prepare the consolidated report on SAEs that occurred outside the country.

5.2. The consolidated report must be submitted via Plataforma Brasil to the linked CEP to the coordinating center, at any time, through the "notification" functionality

5.3. The consolidated report comprises a summary containing:

I. Absolute and relative distribution of EAG;

II. Detailed description of cases in which there are sequelae or death as a result of participation in the research (and not due to disease progression);

5.4. The submission of standard forms of individual notification such as "CIOMS", "FDA/Medwatch", among others.

5.5. The consolidated report of EAGs occurring outside the country will not be assessed by Conep, except when, at the discretion of the CEP linked to the coordinating center, there is a need.

5.6. The researcher at the coordinating center is responsible for sending the consolidated reports to the participating and co-participating centers.

6. DELIBERATIONS

6.1. In view of notifications and consolidated reports of adverse events and aiming to protect research participants, the CEP must deliberate on the need to adapt the protocol, including modification of the free and informed consent form and change in the study design or even its interruption .

6.2. If the CEP decides to interrupt the protocol in the center to which it is linked as a result of the EAG, such measure must be immediately communicated to the CEP of the coordinating center by means of an official letter.

6.3. If the CEP of the coordinating center interrupts the study in the country due to adverse events, Conep must be immediately communicated by official letter.

7. After the publication of this letter, the contents of Circular Letter no. 008/2011/Conep/CNS/GB/MS of 2011 and the associated form;

8. The procedure provided for in this Circular Letter will be in force until the implementation of the "Serious Adverse Events" (EAG) functionality in the future version of PlataformaBrasil.

Yours sincerely,

JORGE ALVES DE ALMEIDA VENANCIO
COORDENADOR DA COMISSÃO NACIONAL DE ÉTICA EM PESQUISA

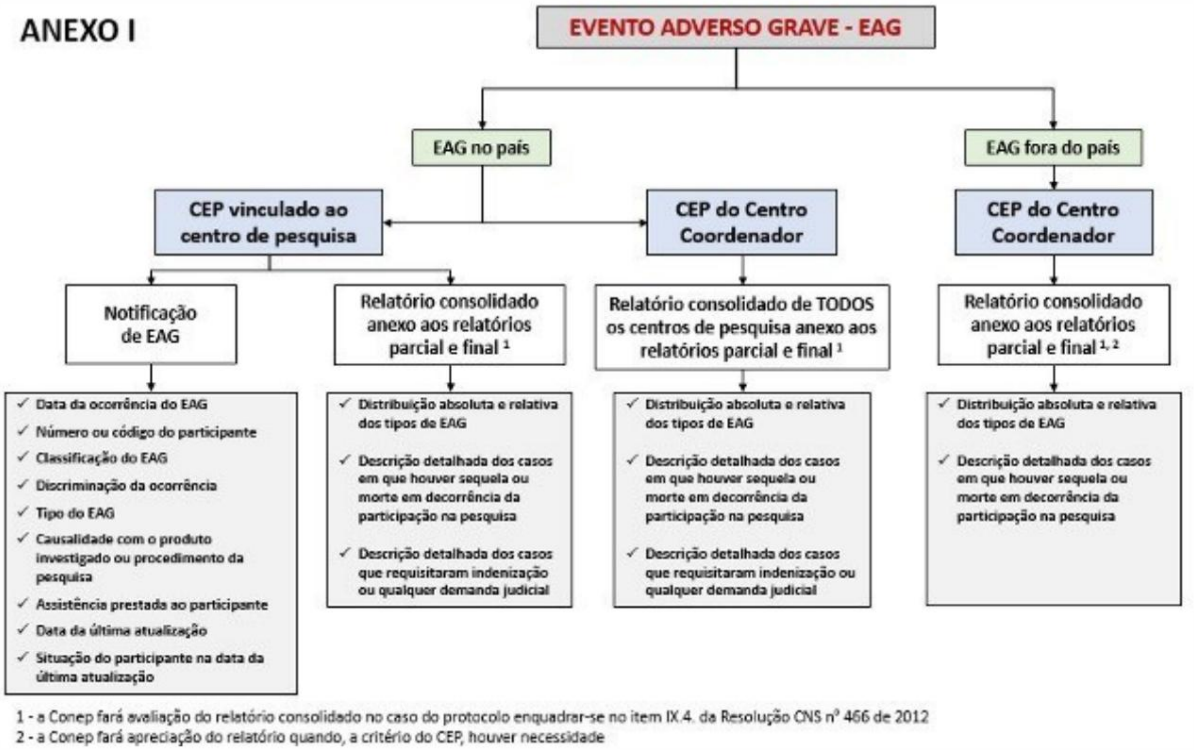

Table model for reporting serious adverse events.

EAG opening date	Participant code	Code of EAG	Classification your EAG	Breakdown of occurrence	Type of EAG	Causality with the investigated product or procedure of the search	Assistance provided to the participant	Data yes last update	Participant's situation on the date of last update
01/01/2019	9999	XXXX	Index	Febrile neutropenia	need of hospitalization	probably related	Hospitalization and use of antibiotics	17/01/2019	death
15/01/2019	9999	XXXX	Subsequent	Pneumonia	threat to life	probably related	Hospitalization and use of antibiotics intravenous	17/01/2019	death
16/01/2019	9999	XXXX	Subsequent	Leak Pleural	threat to life	probably related	Drainage surgical	17/01/2019	death
17/01/2019	9999	XXXX	Subsequent	BECAUSE	death	probably related	Hospitalization and UTI	17/01/2019	death