• **ACCREDITATION PROJECT FOR** INSTITUTIONAL REVIEW BOARDS/INDEPENDENT ETHICS COMMITTEES •

UNIFIED OPINION PREPARATION

SUGGESTIONS FOR STANDARDIZATION

VERSION 1

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LIST OF ABBREVIATIONS AND ACRONYMOUS

CAAE	Ethics Approval Submission Certificate
IRB/IEC	Institutional Review Board/Independent Ethics Committee
CNS	Brazilian National Board of Health
CONEP	Brazilian National Research Ethics Committee
WG	Work Group
PB	Plataforma Brasil
OP	Original Protocol
OM	Ordinary Meeting

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1. ACCREDITATION OF ETHICS COMMITTEES AND CONEP ACREDITA PROJECT

In the 1990s, the need to create an Ethical Analysis National System with the ability to operate in a network to monitor research with human beings carried out in the country was identified. Thus, the Institutional Review Boards/Independent Ethics Committees – IRB/IEC and the national instance called the Brazilian National Research Ethics Committee – CONEP linked to the Brazilian National Board of Health – CNS were established. The research and functioning regulation of this System was then guided by Resolution No. 196, published by the CNS on October 10th, 1996. Over the years, the System rules were expanded and updated, as was the System itself, in number of IRB/IEC and in the volume of research processed.

This System uses its own mechanisms, tools, and instruments of interrelation, in a cooperative work that aims, especially, to protect subjects in Brazil, in a coordinated and decentralized manner. However, CNS Resolution No. 466, of December 12th, 2012, which replaced the aforementioned rule, kept the ethical analysis of research protocols in thematic areas under the responsibility of CONEP. In these cases, CONEP is responsible for a second analysis since these protocols have already been analyzed by the local IRBs/IECs.

This specialized analysis is important to ensure the rights of subjects, and even though the National System of Ethics in Research with Human Beings in Brazil is currently properly structured and integrated, there is a need to promote advances in the ethical evaluation process, as well as the possibility of making the country more attractive to new research protocols and, also, promoting greater speed in the ethical analysis of such investigation protocols.

In this sense, the decentralization of the evaluation of research protocols in human beings, which is the responsibility of CONEP, is a necessity and provides greater effectiveness in the management of the ethical analysis chain by the IRB/IEC/CONEP System. For this purpose, CONEP Acredita Project was established, regulated by CNS Resolution No. 506, of February 3, 2016, which deals with the accreditation process for Institutional Review Boards/Independent Ethics Committees. This process aims to reinforce the decentralization of the IRB/IEC/CONEP System, maintaining the uniformity of the analysis criteria established by the CNS, in line with its current regulations (BRASIL, 2016), that is, it provides for greater agility in the processing of protocols at high risk, without diminishing the guarantees of the subjects' rights.

For the development of activities related to IRB/IEC Accreditation, CONEP Acredita Project was created, designed, and performed by CONEP technical advisors and reporting members.

The IRBs/IECs volunteering to participate in the accreditation process and meeting the criteria for submitting a proposal register for the Public Call Notice and, if approved, participate in pre-accreditation activities. Pre-accreditation is a step set forth in CNS Resolution No. 506 of 2016 and corresponds to monitoring and training activities, so that the IRB/IEC can harmonize the analyses of research protocols with what has already been carried out by CONEP.

It should also be noted that in addition to the design, coordination, and performance, CONEP Acredita Project team is responsible for creating the necessary teaching materials throughout the process.

The IRB/IEC that has the criteria for harmonizing the analysis of protocols and adaptations to the activities met (according to the vacancies provided for in the public notice to which it applied) will receive the certification of "Accredited". This certificate, granted by CONEP, delegates to this IRB/IEC the function of analyzing and monitoring protocols that are now the responsibility of this Committee (BRASIL, 2016).

Thus, this document aims to present elements that allow the understanding and standardization of the preparation of a Unified Opinion of the IRB/IEC/CONEP System, in order to guide the harmonization between the opinions issued by the IRBs/IECs in the accreditation process and CONEP.

Although developed within the context of IRB/IEC accreditation, this document can guide all IRBs/IECs in the System in the preparation of their opinions, as it deals with elements necessary for the preparation of all opinions, regardless of thematic area or degree of risk.

2. ETHICAL ANALYSIS AND ISSUE OF OPINIONS

The ethical analysis of the IRB/IEC and CONEP should lead in the issuance of a duly motivated Unified Opinion, which will present, in a clear, objective, and detailed manner, the decision of the collegiate (Brasil, 2012).

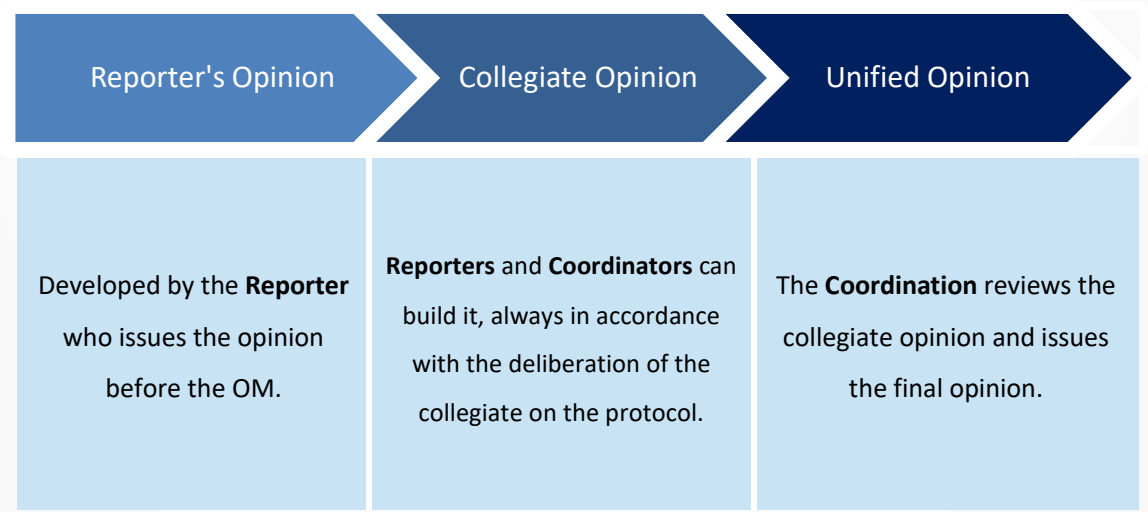
According to CNS Resolution No. 466, of 2012 (items VIII and IX), it is the responsibility of ethical regulatory entities to analyze research protocols involving human beings, with the issuance of a duly justified opinion, always guided, but not limited to, by the principles of impersonality, transparency, reasonableness, proportionality, and efficiency, within the deadlines established in the operational standard, avoiding redundancies that result in delays in the analysis.

According to CNS Operational Standard No. 001, of 2013 (item 2.1.E), the reporter opinion, issued at Platforma Brasil, must be prepared in a clear, objective, and detailed manner, to support the decision of the collegiate, with emphasis on the following points: ethical analysis of the protocol; risk-benefit of research and its social relevance; process of recruitment, inclusion and exclusion of subjects; process of obtaining the Informed Consent Form (ICF); rationale for the waiver of the ICF; procedures capable of ensuring secrecy and confidentiality; protection of subjects who are in a situation of vulnerability, when relevant; budget for carrying out research and performance schedule. It is important to emphasize the need to issue the reporter opinion before the meeting of the collegiate, because due to the maintenance of the existing secrecy in the System, the collegiate will only have access to the documents of a protocol after the issuance of the reporter opinion.

It is understood that the collegiate opinion, both the IRB/IEC and CONEP, is the result of discussions and convergence of collegiate opinions of these instances. In order to avoid exposing the names of the IRB/IEC members, who participated in this decision, the IRB/IEC coordination then issues the Unified Opinion. This last opinion is the official communication instrument between the IRB/IEC/CONEP System and the researcher, on the ethical evaluation of their project.

The sequence of opinions and those responsible for each step are shown in the figure below:

Figure 1 - Issuance of opinions during the process of a research protocol at Plataforma Brazil



Source: Ribeiro; Cantarutti; Sertorio; Rodrigues; Sfalsini, 2021.

One of the practices adopted by CONEP over the years was to establish a standard in the preparation of its Unified Opinions, since they are official documents and must be prepared clearly, following a logical and structured order.

In relation to the standardization and harmonization of Unified Opinions between the IRB/IEC and CONEP, it has to have:

- Standardization consists of defining a manner of organizing the information within the document, that is, the information will be arranged and grouped, allowing the full IRB/IEC and the researcher to have an efficient understanding of the information and pending issues listed in the opinion.;

- Standardization is also used to avoid personalization of the opinion, that is, to identify, in some manner, the study reporter. This practice contributes to maintaining the anonymity of IRB/IEC members, in accordance with the principle of impersonality;
- As it is a coordinated System subordinated to the same guidelines, opinions prepared by different IRBs/IECs must be similar in terms of structuring and language style adopted by the Committee (national entity), in order to provide the necessary harmonization in the application of the standards and document structuring.

3. CHANGE IN PROCEDURE: PROTOCOLS IN SPECIAL COLLEGE

CNS Resolution No. 196, 1996, updated in CNS Resolution No. 466, 2012, classifies the highest risk protocols in thematic areas, for analysis by CONEP. Further details on the division of special thematic areas are presented in Annex I of this document.

However, the System is undergoing a transition that will bring about changes in relation to the classification of protocols, especially considering the risks of the studies.

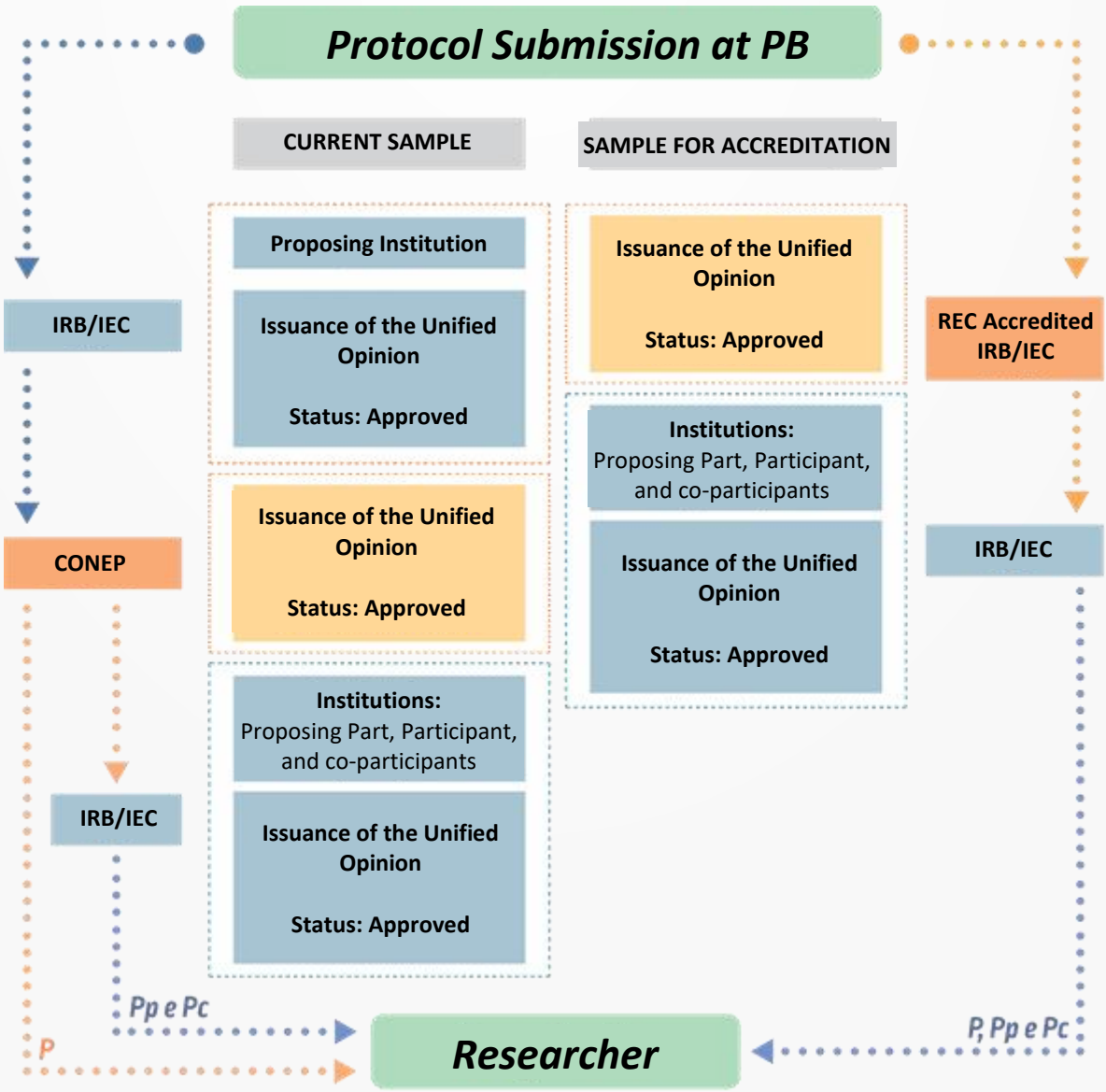
In 2020, CONEP sent a draft of the Resolution for public consultation, proposing a change in the flow of analysis of research protocols with human beings at Platforma Brasil (CNS, 2020). Due to the new scenario of changes in the flow of research protocols processing at Platforma Brasil, and after approval in all applicable instances, it was found that there will be significant operational changes that will directly impact the activities of the Accredited IRBs/IECs, as:

- The protocol will be referred directly to the Accredited IRB/IEC (or CONEP), after submission at Plataforma Brasil.
- During the evaluation of the Accredited IRB/IEC, all related documentation will be available for verification (without the possibility of editing) of the other IRB/IEC (proponent, participant(s) and co-participant(s), if any).
- After approval of the protocol by the Accredited IRB/IEC (or CONEP), this protocol will be evaluated, simultaneously, by the other IRB/IEC involved (including the IRB/IEC of the proposing institution).
- Once the operational capacity of the Accredited IRBs/IECs is exceeded, CONEP will be responsible for analyzing the surplus protocols, of a special collegiate;
- Accredited IRB/IEC (or CONEP) will carry out the general ethical analysis of the research protocol.

- The IRBs/IECs of the participating sites (proponent and others, if any) will carry out the ethical analysis regarding local issues.
- The new Platforma Brasil provides for a new form to be completed, in which information regarding the ICF will be inserted, arranged as follows:
    - closed fields (non-editable), with no ethical evaluation of the IRBs/IECs of the other participating sites;
    - open fields (editable: researcher, institution, and IRB/IEC data);
    - fields previously completed by Plataforma Brasil, with the rights of subjects (aiming to reduce the number of pending issues in the ICF).
- The IRBs/IECs of the participating sites retain the prerogative of approving or not the protocol in their linked institution, even if the study has been approved by the Accredited IRB/IEC or by CONEP;
- The first appeal instance will be the IRB/IEC where there is no approval, however the second (and last) appeal instance will be CONEP;
- Protocols falling into the areas provided for in item IX.4 of CNS Resolution No. 466, of 2012, will be considered “Protocols in special collegiate” until the publication of the rule related to the classification and processing of research;
- CONEP will implement and monitor the IRB/IEC accreditation process and propose a continuing education program.

In order to better visualize the proposed changes in the processing flows of the research protocols under CONEP's responsibility for the Accredited IRBs/IECs, the flowchart diagram is below. In items 3.1, 3.2 and 3.3, schematic representations of the procedures for processing the protocols of research at Plataforma Brasil and change of procedure due to the Accreditation Process.

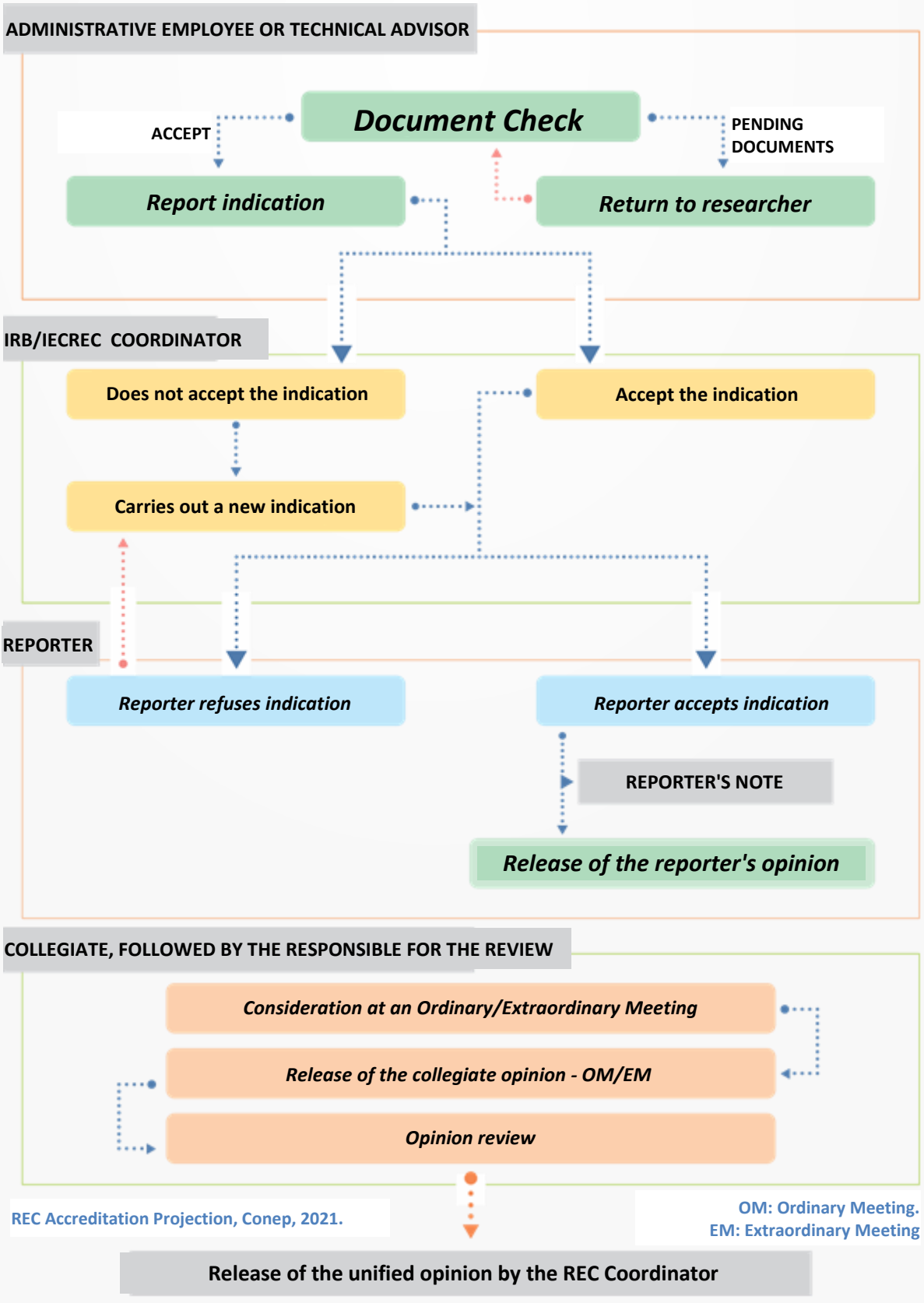
3.1 The flowchart below exemplifies the main changes in the procedures in the Institutions: Proposer, Participant(s) and Co-Participant(s).



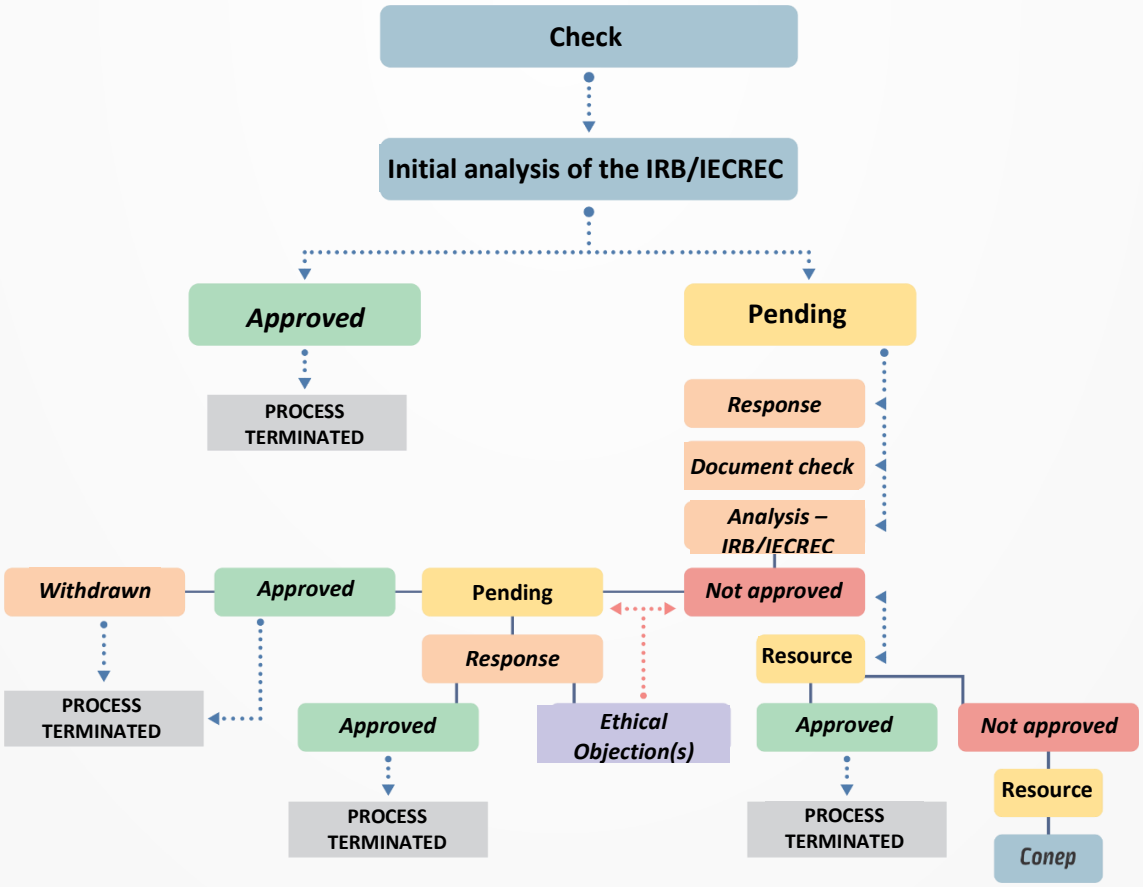
P: Coordinating Site Project (proposing institution)
Pp: Participating Site Project. PC: Co-Participant Site Project

IRB/IECREC Accreditation Project, Conep, 2021

3.2 Processing flow of research protocols at Plataforma Brasil.



3.3 Study analysis flowchart - original, response, appeal, and amendment



COMPLEMENTARY MATERIAL:

IRB/IEC Manual - version 3.2.39.

http://plataformaBrasil.saude.gov.br/login.jsf;jsessionid=6788FC02357A673602F59987387C4FB6.server er-plataformaBrasil-srvjpdf132.

4. OPINION PREPARATION

The Unified Opinion is a document presented to the researcher, in written form, in which the IRB/IEC presents its response regarding the analysis of the research protocol, in accordance with current ethical standards. In general, it is structured with information from the research protocol and the considerations of the ethical analysis carried out by the IRB/IEC/CONEP System.

4.1 Initial Analysis - Original Research Protocol (OP)

This is the first ethical assessment of documents submitted to the IRB/IEC.

4.1.1. Drafting the Opinion:

The IRB/IEC's opinion must be prepared according to the standard established by the Committee. This document must be developed taking into account the following characteristics:

- Formality
- Impersonality
- Transparency
- Reasonableness
- Proportionality
- Efficiency
- Clarity, objectivity, and sufficient detail
- Be self-explanatory (contain basic project information)

Based on the aspects reported, the opinion must always consider:

- Relevance and scientific and social value of the proposed study;
- Adequacy of the methodology to the objectives pursued, with emphasis on potential risks to participants;
- Degree of vulnerability of subjects and protective measures.

In Annex II of this document, there is a suggestion of standardization for this type of opinion. Below are suggestions for completing the structured fields of the opinion.

COMPLEMENTARY MATERIAL:

Editorial Manual of the Presidency of the Republic/Casa Civil.

3rd Edition, Revised, current. and amp. – Brasília: Presidency of the Republic, 2018.

Available at: http://www4.planalto.gov.br/centrodeestudos/assuntos/manual-de-redacao-da-presidencia-da-republica/manual-de-redacao.pdf.

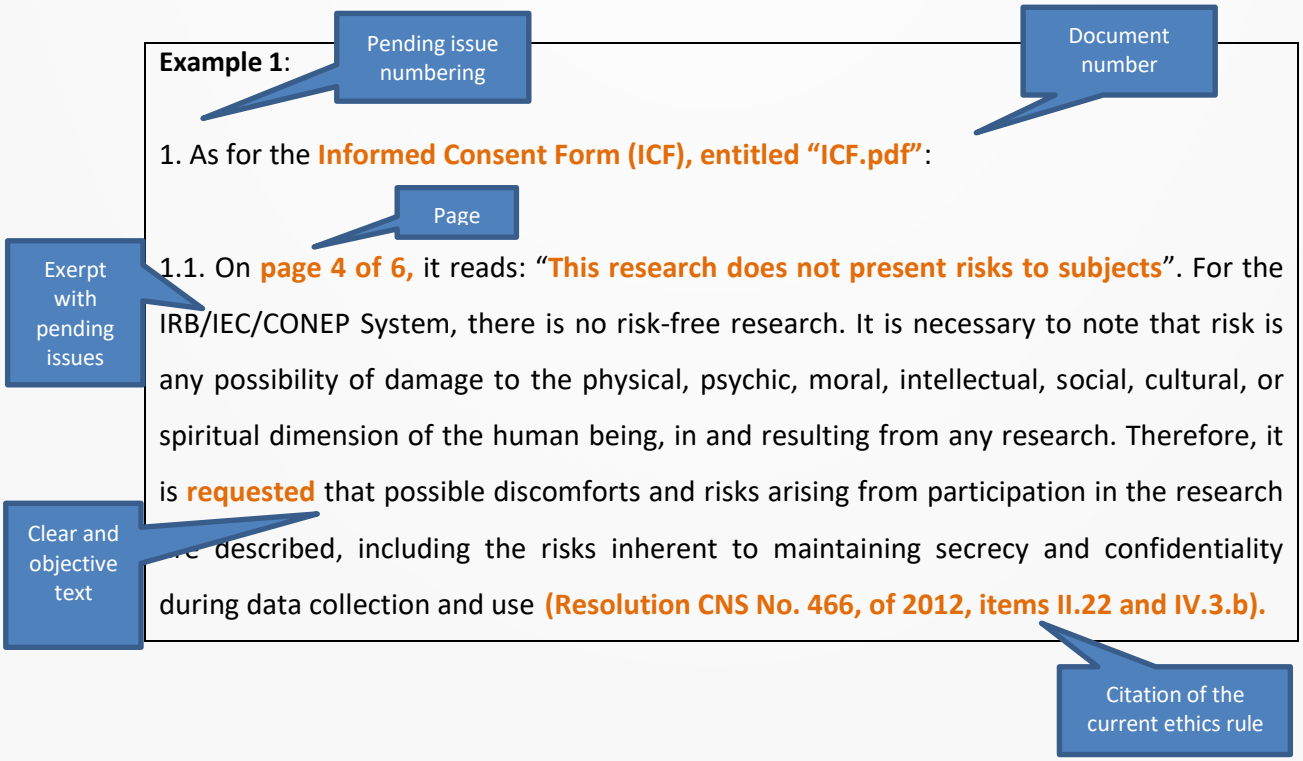
REPORTER OPINION	
*Opinion Number :	534
Report Date:	30/Nov/2011
*Project presentation:	Complete with general information about the study, for example, introduction, hypothesis, methodology, and inclusion and exclusion criteria.
*Research objective:	Complete general information about the study objectives, for example, primary objectives, secondary objectives, and other objectives.
*Assessment of risks and benefits:	Complete with general information, according to the researcher, about the potential risks and benefits of the study.
*Comments and Considerations on the research:	When relevant, enter data relevant to the protocol (for example, study design, biological samples, use of placebo, etc.)
*Considerations on the mandatory submission forms:	When necessary, insert information about the documents forwarded for analysis. It is not necessary to repeat the names of the documents here.
Recommendations:	Insert only when there is a need to indicate recommendations to the researcher, without obligation. (Do not include issues in this field).
*Conclusions or Pending issues and List of Inadequacies:	Insert the pending items prepared by the reporter or the RECIRB/IEC in the other opinions.

The IRB/IEC is advised, if it deems it appropriate, to use the information provided in the Project Basic Information and Detailed Project documents, to prepare the Unified Opinion.

The pending issues prepared by the IRB/IEC must necessarily be based on the ethical standards in force.

It is advised that the preparation of pending issues follows a pattern pre-established by the IRB/IEC, paying special attention to the following characteristics:

- Being in the 3rd person;
- Citing the document and the page where the ethical pending issue was found;
- Citing the part of the document that is not adequate, when applicable;
- Explaining, clearly and objectively, the inadequacy;
- Indicating the resolution (or other guideline of the IRB/IEC/CONEP System) in force that supported the pending issue.



In certain situations, the ethical pending issue refers to the absence of some information or ethical guarantee and, in these cases, the citation of the inappropriate passage in the preparation of the pending issue will not be applicable.

Example 2:

Numbering of pendency

Document name

1. As for the **Informed Consent Form (ICF) - (file entitled "ICF.doc"**, version 1, posted on 3/19/2015:

Ethical pending issue

1.1. The ICF **does not ensure the subject the right to reimbursement** as a result of participating in the research, if necessary. Therefore, it is **requested** that the excerpt is rewritten, ensuring in a clear and affirmative manner, the reimbursement of expenses incurred by the subject and their companion as a result of their participation in the research, being able to cite as an example the transport and food, but not being restricted to them **(CNS Resolution No. 466, of 2012, items II.21 and IV.3.g).**

Clear and objective text

Citation of the standard current ethics.

Closing example for opinions can be viewed in Annex III of this document.

4.2 Reply and Appeal

The IRB/IEC Response Opinion aims to analyze the answers to the questions (pending issues) contained in the Unified Opinion previously issued by the Committee, upon receipt of a response letter, reformulated (corrected) documents and others that the researcher deems necessary (or whose inclusion has been requested by the IRB/IEC).

The appeal opinion prepared by the IRB/IEC evaluates the possibility of reversing the previous analysis by the IRB/IEC, of not approving the protocol, by sending an appeal letter and/or documents that the researcher deems necessary to present new elements.

4.2.1 Preparation of the opinion: To prepare the opinion, the following must be observed:

- During the preparation of the response or appeal opinion, it is important to present the information from the previous opinion, to make clear what has already been analyzed;
- It is suggested that the fields "Project Presentation", "Research Objective", "Risk and Benefit Assessment", "Research Comments and Considerations", and "Considerations on mandatory submission forms" of the response/appeal present the same information as in the original opinion; if there is any change to these elements, it must be included in the corresponding field;
- In the field “Conclusions or Pending issues, and List of Inadequacies”, it is suggested that the pending items be copied from the previous Unified Opinion; then insert the response (copy the researcher's answer) and, at the end, insert the reporter's analysis. In Annexes III and IV of this document there are the standardization suggestions for the response and appeal opinions.

Example:

1. Regarding the Informed Consent Form (ICF), entitled “ICF.pdf”:

1.1. On page 4 of 6, it reads: “This research does not present risks to participants of research". For the CEP/Conep System, there is no risk-free research. It is necessary to observe that risk is any **possibility** of damage to the physical, psychic, moral, intellectual, social, cultural or spiritual dimension of the human being, in and resulting from any research. Therefore, it is requested that the possible discomforts and risks arising from participation in the research be described, including the risks inherent in maintaining secrecy and confidentiality during data collection and use (CNS Resolution No. 466, of 2012, items II.22 and IV.3.b).

ANSWER: We make the requested change. The new text is on page 4 of the new version of the ICF (ICF_v2.pdf).

ANALISIS: Pending issue met.

Note:

Answer letter: must be sent in an orderly manner, presenting the answers to all pending issues listed in the opinion.

Appeal Letter: must be sent in an orderly manner, presenting the answers to the pending issues that were not fully met and that led to the non-approval of the study.

Example:

1. Regarding the Informed Consent Form (ICF), entitled “ICF.pdf”:

1.1. On page 4 of 6, it reads: “This research does not present risks to subjects”. For the IRB/IEC/CONEP System, there is no risk-free research. It is necessary to note that risk is any possibility of damage to the physical, psychic, moral, intellectual, social, cultural, or spiritual dimension of the human being, in and resulting from any research. Therefore, it is requested that the possible discomforts and risks arising from participation in the research be described, including the risks inherent in maintaining secrecy and confidentiality during data collection and use (CNS Resolution No. 466, of 2012, items II.22 and IV.3.b).

RESPONSE: The requested change was performed. The new text is on page 4 of the new version of the ICF (ICF_v2.pdf).

ANALYSIS: Pending issue was not met. The researcher informed in the ICF that the study presents risks, however they did not describe them in the document.

RESOURCE: The requested change was performed. Find attached the new version of the ICF (ICF_v3.pdf).

ANALYSIS: Pending issue met.

4.3. Amendment (E)

Amendment is any proposed modification to the original project, presented with the rationale that motivated it. Amendments must be presented to the IRB/IEC in a clear and succinct manner, identifying the part of the protocol to be modified and its rationales. The amendment will be analyzed by the bodies that carried out the final approval (IRB/IEC and/or CONEP).

4.3.1. Preparing the Opinion:

The IRB/IEC amendment opinion must be prepared according to the standard established by the Committee. This document must be developed considering the characteristics listed in section "4.1.1 Preparation of the opinion".

Based on the reported aspects, when preparing the opinion, the following aspects must be verified:

- The presentation of the rationale that motivated the presentation of the amendment, duly supported;
- The identification of changes made to the amendment documents;
- The relevance of the modifications;
- Maintaining the objectives and methodologies of the original project, as the amendment cannot change them;
    - If there are important changes in objectives and methods, the responsible researcher must submit a new research protocol to the IRB/IEC/CONEP System.
- The degree of vulnerability of subjects and the proposed protective measures.

In Annex V of this document, there is a suggestion of standardization for this type of opinion. Below are suggestions for completing the structured fields of the opinion.

REPORTER OPINION	
*Opinion Number :	534
Report Date:	30/Nov/2011
*Project presentation:	Present general information about the study, for example, introduction, hypothesis, methodology, and inclusion and exclusion criteria.
*Research objective:	Present general information about the objectives of the study, for example, primary objectives, secondary objectives, and other objectives.
*Assessment of risks and benefits:	Present general information about the potential risks and benefits of the study.
*Comments and Considerations on the research:	Present the rationale(s) for the amendment and inform the changes made to the amended documents.
*Considerations on the mandatory submission forms:	When necessary, insert information about the documents referred to analysis. It is not necessary to repeat the names of the documents here.
Recommendations:	Insert only when there is a need to indicate recommendations to the researcher, without mandatory compliance.
*Conclusions or Pending issues and List of Inadequacies:	List the pending items prepared by the reporter or IRB/IEC.

If deemed appropriate, the IRB/IEC is advised to use the information provided in the Basic Information of the Project and Detailed Project documents, to prepare its opinions of the reporter, the collegiate, and Unified opinion.

Pending issues prepared by the IRB/IEC must necessarily be based on the current ethical standard.

It is suggested that the preparation of pending issues follows a pattern pre-established by the IRB/IEC, with special attention to the following characteristics (example in item 4.1.1):

- Being in the 3rd person;
- Citing the document and the page where the ethical pending issue was found;
- Citing the part of the document that is not appropriate;

- Explaining, clearly and objectively, the inadequacy;
- Indicating the resolution (or other guideline of the IRB/IEC/CONEP System) in force that supported the pending issue.

Closing example for opinions can be viewed in Annex III of this document.

4.4. Notification (N)

Notification is a functionality that must be used when there is a need to forward documents to the IRB/IEC, for example, Project Start Communication, Institution Authorization Letter, Partial and Final Report, but not limited to.

Note that the notification should not propose changes in the study. Proposals to modify the study must be processed as an amendment. In the event that the notification proposes modifications to the study, the IRB/IEC must reject this notification and request that the documents be submitted at Plataforma Brasil via amendment.

4.4.1. Preparing the Opinion:

The IRB/IEC Amendment Opinion must be prepared according to the standard established by the Committee. This document must be developed taking into account the characteristics listed in section “4.1.1 Preparation of the opinion”.

It is important to emphasize that, for notification, it is possible to release the Unified opinion only with the status of “Approved”, “Not Approved” and “Withdrawn”. In this sense, it will not be possible to issue an opinion with a status of “Pending issue”, as described (see Manual IRB/IEC – Version 3.2.39).

In Annex VI of this document, there is a suggestion of standardization for this type of opinion, and the suggestions for completing the fields follow below:

REPORTER OPINION	
*Opinion Number :	534
Report Date:	30/Nov/2011
*Project presentation:	Present notification information.
*Research objective:	Present the objectives of the notification, for example: sending a partial study report and canceling the study.
*Assessment of risks and benefits:	Present general information about the potential risks and benefits of the study.
*Comments and Considerations on the research:	Where relevant, you may provide more information about the notification.
*Considerations on the mandatory submission forms:	When necessary, enter information about the documents referred to analysis. It is not necessary to repeat the names of the documents here.
Recommendations:	Insert only when there is a need to indicate recommendations to the researcher, without mandatory compliance.
*Conclusions or Pending issues and List of Inadequacies:	Present the conclusion of the analysis - Approved, Not Approved, or Withdrawn, and the motivation for each of the options.

Examples of completing notification opinion fields:

Presentation of the Notification:
This Notice refers to the request to cancel the study in Brazil.

Purpose of Notification:
Submission of Study Cancellation Letter.

Comments and Considerations on the Notice:
The Responsible Researcher presents the following rationale for canceling the study (document "Cancellation.pdf", dated 8/12/2020): "The group responsible for the interim analysis of the study verified that the test drug did not show efficacy when tested on the subjects, for this reason, we are canceling the study in Brazil and in the world. We will discontinue all subjects from the experimental arm".

Closing example for opinions can be viewed in Annex III of this document.

4.5. Withdrawn

It involves the preparation of an opinion that will exclude the original protocol or an amendment from Platforma Brasil. Such procedure may be performed at the request of the researcher or when the IRB/IEC/CONEP System deems it necessary (e.g., studies that were started before ethical approval).

In Annex VII of this document, there is a suggestion of standardization for this type of opinion, and the suggestions for completing the fields follow below:

REPORTER OPINION	
*Opinion Number :	534
Report Date:	30/Nov/2011
*Project presentation:	Present general information about the study, for example, introduction, hypothesis, methodology and inclusion criteria.
*Research objective:	Present general information about the objectives of the study, for example, primary objectives, secondary objectives, and other objectives.
*Assessment of risks and benefits:	Present general information about the potential risks and benefits of the study.
*Comments and Considerations on the research:	Present a summary of the events and the reasons that led the IRB/IEC to withdraw the study from Plataforma Brazil.
*Considerations on the mandatory submission forms:	When necessary, enter information about the documents referred to analysis. It is not necessary to repeat the names of the documents here.
Recommendations:	Insert only when there is a need to indicate recommendations to the researcher, without mandatory compliance.
*Conclusions or Pending issues and List of Inadequacies:	Inform that the study is being withdrawn from Plataforma Brazil.

Examples of completing the fields of the Opinion of Withdrawal:

Comments and Considerations on the Notice:

The responsible researcher informed that during the initial analysis of the research protocol, in the IRB/IEC/Conep System, the worldwide recruitment of the study was terminated, and the Brazilian sites will not be able to participate in the research. In this sense, it is requested the withdrawal of the Brazil Platform research protocol.

Closing example for opinions can be viewed in Annex III of this document.

Annex I - Thematic Area of CONEP responsibility

According to item IX.4 of CNS Resolution No. 466, of 2012, CONEP thematic areas of competence (in the table below) are:

1. Human genetics, when the project involves:
1.1. sending abroad genetic material or any human biological material to obtain genetic material, except in cases where there is cooperation with the Brazilian Government;
1.2. storage of biological material or human genetic data abroad and in the country, when in agreement with foreign institutions or in commercial institutions;
1.3. changes to the genetic structure of human cells for *in vivo* use;
1.4. research in the area of human reproduction genetics (reprogenetics);
1.5. behavioral genetics research; and
1.6. research in which the irreversible dissociation of data from subjects is set forth;

2. Human reproduction: research dealing with the functioning of the reproductive system, procreation, and factors that affect the reproductive health of humans, and in this research all those who are affected by its procedures will be considered "subjects". CONEP will be responsible for analysis when the project involves:
2.1. assisted reproduction;
2.2. handling of gametes, pre-embryos, embryos, and fetus; and
2.3. fetal medicine, when it involves invasive procedures;

3. Therapeutic equipment and devices, new or not registered in the country;

4. New invasive therapeutic procedures;

5. Studies with indigenous populations;

6. Research projects involving genetically modified organisms (GMOs), embryonic stem cells and organisms that represent high collective risk, including organisms related to them, in the areas of: experimentation, preparation, cultivation, manipulation, transport, transfer, import, export, storage, release into the environment and disposal;
7. Protocols for establishing and operating biobanks for research purposes;
8. Research with coordination and/or sponsorship originating outside Brazil, except for those co-sponsored by the Brazilian Government; and

Regarding the thematic areas described in the aforementioned Resolution, CONEP published, in 2017, Circular Letter No. 172 CONEP/CNS/MS, which provides clarifications regarding the selection of the Thematic Area at Platforma Brasil. This document informs the main characteristics that must be observed in order to select one of CONEP thematic areas of competence, with the purpose of speeding up the proceedings at Platforma Brasil. Such guidelines are described in the following table.

Thematic Area	Subarea	Clarifications
Human genetics	Sending genetic material or any human biological material to the abroad, for carrying out genetic tests.	This area should be selected only in cases **where there is a forecast** of sending some human genetic material (DNA/RNA etc.) or human biological sample abroad, specifically in cases where the objective is to carry out a genetic test. ***Note: when the study predicts that such steps will be carried out only in Brazil, and there is no submission of data and information collected for aggregation in the research results (CNS Resolution No. 292, of 1999 (items I.c), the study should not be framed in this thematic area.***
	Storage of biological material or human genetic data in Brazil and abroad.	This area should be selected **only** in cases where the study foresees: a. storage of genetic material or data abroad; b. storage of genetic material or data in Brazil, when: I. stored in commercial institutions; II. agreements with commercial institutions; III. agreements with foreign institutions.
	Changes in the genetic structure of human cells for *in vivo* use.	This area should be selected only for studies involving the editing of genetic material in human somatic cells *in vivo* (*in vivo* gene therapy) and in human somatic cells *in vitro*, with subsequent transfer of these cells to the organism (*ex vivo* gene therapy), and in genetically modified human stem cell research intended for *in vivo* use in humans.
	Research in the field of human reproduction genetics (reprogenetics).	This area should only be selected for studies involving reproductive technologies (assisted reproduction) and genetic engineering. **Note: the researcher should not select this subject area if the study does not involve both areas.**

Thematic Area	Subarea	Clarifications
Human genetics	Behavioral genetics research.	This area should be selected only for studies whose objective is to establish possible relationships between the participant's genetic characteristics and their influences **on human behavior**.
	Research in which the irreversible dissociation of data from subjects is set forth.	This area should be selected only for genetic studies that involve the collection of biological samples or data that initially have the participant's personal identifiers and that, throughout the study, will be irreversibly dissociated, making it impossible to definitively link the biological samples to the participants and making it impossible to return the results to the participants, even if they request them.

Thematic Area	Subarea	Clarification
Human Reproduction	Assisted reproduction.	This area should be selected for studies that are dedicated to researching technical procedures of assisted reproduction, a new approach or the change of one of the stages of assisted reproduction, but not limited to.
	Handling of gametes, pre-embryos, embryos, and fetuses.	This area should be selected for studies that aim to manipulate, on an experimental basis, gametes, pre-embryos, embryos, and fetuses.
	Fetal medicine, when it involves invasive procedures.	This area includes research with invasive procedures, in which there is a need to break the natural barriers to penetrate the uterine cavity during pregnancy, opening a door or access to the internal environment, as in research that needs access to amniotic fluid or the umbilical cord, perform a biopsy, but not limited to.

Thematic Area	Clarification
New or unregistered therapeutic equipment and devices in the country	This area should be selected only for studies that involve the development of new equipment and/or devices for the treatment of diseases. "New" means equipment and devices that: a. they still do not have a sanitary registration with Anvisa; b. have a different indication from the one registered with Anvisa. **Note: studies that involve the development of a new diagnostic test are not included in this area.**

Thematic Area	Clarification
New invasive therapeutic procedures	This area should only be selected for studies that involve the use of a NEW therapeutic procedure that can penetrate the body's natural barriers (for example, the skin), and may or may not open a door or access to the internal environment. In this sense, it can be mentioned as examples the development of a new surgical or radiotherapy technique. **Note: this area does not include research in which the focus is the development of a new drug, even if administered invasively (for example, injectable drugs).**

Thematic Area	Clarification
Studies with indigenous populations	Based on CNS Resolution No. 304/2000, indigenous populations are considered to be “people with their own organizations and identities, due to the awareness of their historical continuity as pre-Columbian societies”. **Note: this area is restricted to the population described above, not being selected for studies with other populations that do not fall into the definition, such as quilombolas.**

Thematic Area	Clarification
Research projects involving genetically modified organisms (GMOs), embryonic stem cells and organisms that represent high collective risk, including organisms related to them, in the areas of: experimentation, preparation, cultivation, handling, transport, transfer, import, export, storage, release into the environment and disposal.	This area must be selected for any study in human beings that involves: a. genetically modified organisms – GMO (organism whose genetic material – DNA/RNA – has been modified by any genetic engineering technique, in accordance with Law No. 11,105 of 3/24/2005, art. 3, item V); b. embryonic stem cells (embryo cells that have the ability to transform into cells of any tissue of an organism, in accordance with Law No. 11,105 of 3/24/2005, art. 3, item XI); c. organisms that represent high collective risk. Regarding these, it is clarified that this area should be selected only for studies that include biological agents with great power of transmissibility by the respiratory route or of unknown transmission, which cause human and animal diseases of high severity, and with a high capacity of dissemination in the community and the environment.

Thematic Area	Clarification
Protocols for establishing and operating biobanks for research purposes.	This area must be selected when authorization is requested from CONEP for the establishment and operation of an institutional biobank, that is, authorization for the creation of a structure intended to collect and store samples of biological materials that will be used in future research projects. Note: according to CNS Operational Standard No. 001/2013, Annex II, this type of submission is not yet implemented at Platforma Brasil, therefore, according to Circular Letter No. 003/2020, the documentation must be sent via email (conep.biobancos@saude.gov.br) to CONEP.

Thematic Area	Clarification
Research with coordination and/or sponsorship originating outside Brazil, except for those co-sponsored by the Brazilian government.	This area should be selected for studies that are coordinated by foreign institutions and/or that receive funding from foreign institutions. The cases below do not qualify for analysis by Conep: a. research in which Brazilian participation is restricted to the academic training of the foreign researcher linked to the national postgraduate program; and that do not involve Brazilian research participants in any of their stages; b. research whose stages are entirely carried out abroad, without receiving, in Brazil, data and information collected for aggregation in the research results; and that have been approved by a research ethics committee or equivalent body in the country of origin; c. researches whose foreign participation is restricted to the availability of a research grant abroad.

Thematic Area	Clarification
Projects that, at the discretion of the IRB/IEC and duly justified, are deemed worthy of analysis by CONEP.	This area can only be selected by the IRB/IEC, in cases where the Committees deem it necessary for Conep to also analyze the study, due to query, relevance, or other reasons. **Note: it should be noted that it is mandatory to send a rationale indicating the reason for analysis by Conep.**

Annex II - Standardization Recommendation for the Opinion of the Original Protocol (OP)

UNIFIED OPINION

Project Presentation:

The information listed in the fields "Project Presentation", "Research Objective" and "Risk and Benefits Assessment" was taken from the document Basic Research Information No. XX, dated in XX/XX/XXXX (and "Detailed Project" – when necessary).

INTRODUCTION Insert text from the Basic Research Information document.
HYPOTHESIS Insert text from the Basic Research Information document.
METHODOLOGY Insert text from the Basic Research Information document.
INCLUSION CRITERIA Insert text from the Basic Research Information document.
EXCLUSION CRITERIA Insert text from the document Basic Research Information.

Research Objective:

PRIMARY OBJECTIVE Insert text from the Basic Research Information document. SECONDARY OBJECTIVE Insert text from the Basic Research Information document.

Assessment of Risks and Benefits:

RISKS Insert text from the Basic Research Information document.
BENEFITS Insert document text Basic Research Information.

Comments and Considerations on the Research:

The IRB/IEC will be able to make a concise, explanatory summary, with considerations about the research.
The abstract may mention the type of study (e.g., whether randomized, double-blind, multicenter, etc.), information on the storage of biological material, the presence of a letter about carrying out the study in the country of origin, and other information important to the understanding of the protocol.

Considerations on mandatory submission forms:

If there is no consideration: "See field 'Conclusions or Pending Issues and List of Inadequacies'.
It is important to point out that, in this field, there should NOT be a request for adequacy or clarification.

Recommendations

This field can be completed with suggestions from the IRB/IEC to the responsible researcher, who will have the choice of accepting the recommendation or not.
If there is no recommendation, the text is indicated: See field "Conclusions or Pending Issues and List of Inadequacies".

Conclusions or Pending Issues and List of Inadequacies:

Field for pending issues found in the study.
If the IRB/IEC does not observe ethical pending issues in the protocol, it may inform: "There were no ethical pending issues seen in the study documents".

Annex III - Standardization Recommendation for the Response Opinion

UNIFIED OPINION

Project Presentation:
The information listed in the "Project Presentation", "Research Objective", and "Risk and Benefit Assessment" fields were taken from the Research Basic Information document (Insert text of the last pending opinion from the IRB/IEC).

INTRODUCTION Insert text of the last pending opinion from the IRB/IEC.
HYPOTHESIS Insert text of the last pending opinion from the IRB/IEC.
METHODOLOGY Insert text of the last pending opinion from the IRB/IEC.
INCLUSION CRITERIA Insert text of the last pending opinion from the IRB/IEC.
EXCLUSION CRITERIA Insert text of the last pending opinion from the IRB/IEC.

Research Objective:
PRIMARY OBJECTIVE Insert text of the last pending opinion from the IRB/IEC.
SECONDARY OBJECTIVE: Insert text of the last pending opinion from the IRB/IEC.

Assessment of Risks and Benefits:
RISKS Insert text of the last pending opinion from the IRB/IEC.
BENEFITS Insert text of the last pending opinion from the IRB/IEC.

Comments and Considerations on the Research:
If there are comments: insert Text of the last pending opinion from the IRB/IEC.
If there is no comment, the text is indicated: "See field 'Conclusions or Pending Issue and List of Inadequacies'.

Considerations on mandatory submission forms:
If there is consideration: insert text of the last pending opinion from the IRB/IEC.
If there is no consideration, the text is indicated: "See field 'Conclusions or Pending Issues and List of Inadequacies'.
It is important to emphasize that, in this field, there should be no request for adequacy or clarification.

Recommendations
This field can be completed with suggestions from the IRB/IEC to the responsible researcher, who will have the choice of accepting the recommendation or not.
If there is no recommendation, the text is indicated: "See Conclusions or Pending Issues and List of Inadequacies field".

Conclusions or Pending Issues and List of Inadequacies:
This is a response to the opinion embodied in IRB/IEC n.° xxxx dated xx/xx/xxxx

1. Transcribe the pending issue.
RESPONSE:
ANALYSIS: In the event the pending issue is not met, the analysis must be unified/justified, indicating, at the end, "pending issue partially met" or "pending issue not met", when applicable.

Annex IV - Standardization Recommendation for the Opinion of Appeal

UNIFIED OPINION

Project Presentation:
The information listed in the "Project Presentation", "Research Objective", and "Risk and Benefit Assessment" fields were taken from the Research Basic Information document (Insert text of the last pending opinion from the IRB/IEC).

INTRODUCTION Insert text of the last Non-Approved IRB/IEC opinion.
HYPOTHESIS Insert text of the last Non-Approved IRB/IEC opinion.
METHODOLOGY Insert text of the last Non-Approved IRB/IEC opinion.
INCLUSION CRITERIA Insert text of the last Non-Approved IRB/IEC opinion.
EXCLUSION CRITERIA Insert text of the last Non-Approved IRB/IEC opinion.

Research Purpose:
PRIMARY OBJECTIVE Insert text of the last Non-Approved IRB/IEC opinion.
SECONDARY OBJECTIVE: Insert text of the last Non-Approved IRB/IEC opinion.

Assessment of Risks and Benefits:
RISKS Insert text of the last Non-Approved IRB/IEC opinion.
BENEFITS Insert text of the last Non-Approved IRB/IEC opinion.

Comments and Considerations on the Research:
If there is a comment: insert text of the last Non-Approved IRB/IEC opinion.
If there is no comment, the text is indicated: "See field 'Conclusions or Pending Issue and List of Inadequacies'.

Considerations on mandatory submission forms:
If there are considerations: insert text of the last Non-Approved IRB/IEC opinion.
If there is no consideration, the text is indicated: "See field 'Conclusions or Pending Issue and List of Inadequacies'.
It is important to note that this field should not include a request for adequacy or clarification.

Recommendations
This field can be completed with suggestions from the IRB/IEC to the responsible researcher, who will have the choice of accepting the recommendation or not.
If there is no recommendation, the text is indicated: "See field 'Conclusions or Pending Issue and List of Inadequacies'.

Conclusions or Pending Issue and List of Inadequacies:
This is an appeal to the IRB/IEC Unified Opinion n.° xxxx, dated xx/xx/xxxx

1. Transcribe the pending text, the researcher's response and the subsequent analysis of the IRB/IEC that ended in the non-Approval.
RESOURCE:
ANALYZE:

Annex V - Standardization Recommendation for the Amendment Opinion

UNIFIED OPINION

Project Presentation:
The information listed in the "Project Presentation", "Research Objective", and "Risk and Benefit Assessment" fields were taken from the Research Basic Information document (and "Detailed Design" – when necessary).

INTRODUCTION Insert text from the Basic Research Information document.
HYPOTHESIS Insert text from the Basic Research Information document.
METHODOLOGY Insert text from the Basic Research Information document.
INCLUSION CRITERIA Insert text from the Basic Research Information document.
EXCLUSION CRITERIA Insert text from the document Basic Research Information.

Research Objective:
PRIMARY OBJECTIVE Insert text from the Basic Research Information document.
SECONDARY OBJECTIVE Insert document text Basic Research Information.

Assessment of Risks and Benefits:
RISKS Insert text from the Basic Research Information document.
BENEFITS Insert text from the Basic Research Information document.

Comments and Considerations on the Research:
Present the rationale(s) for the amendment and prepare a brief summary of the changes proposed by the researcher, indicating the documents that were changed.

Considerations on mandatory submission forms:
If there is no consideration, the text is indicated: 'See field 'Conclusions or Pending Issue and List of Inadequacies'.
It is important to note that this field should not include a request for adequacy or clarification.

Recommendations
This field can be completed with suggestions from the IRB/IEC to the responsible researcher, who will have the choice of accepting the recommendation or not.
If there is no recommendation, the text is indicated: "See field 'Conclusions or Pending Issue and List of Inadequacies'.

Conclusions or Pending Issue and Lists of Inadequacies:
Preparation of pending issues regarding ethical pending issues observed by the IRB/IEC when analyzing the changes highlighted in the documents of the research protocol.
If the IRB/IEC does not note ethical pending issues in the protocol, it may inform: "There were no ethical pending issues noted in the amendment documents".

Annex VI - Standardization Recommendation for the Notification Opinion

UNIFIED OPINION

Project Presentation:
Insert a brief summary of the notification referred to review.

Research Purpose:
Insert a brief description of the notification objectives, for example: sending a partial study report and study cancellation.

Assessment of Risks and Benefits:
According to the researcher:
RISKS Insert text from the Basic Research Information document.
BENEFITS Insert text from the Basic Research Information document.

Comments and Considerations About the Research:
When necessary, enter more information about the documents referred to analysis.

Considerations on mandatory submission forms:
If the reporter deems necessary, he/she may provide further information on the notification. It will not be necessary to repeat the document names in this field.
If there is no consideration, the text is indicated: "See field 'Conclusions or Pending Issue and List of Inadequacies'.
Note that, in this field, there should be no request for adequacy or clarification.

Recommendations
This field can be completed with suggestions from the IRB/IEC to the responsible researcher, who will have the choice of accepting the recommendation or not.
If there is no recommendation, the text is indicated: "See field 'Conclusions or Pending Issue and List of Inadequacies'.

Conclusions or Pending Issue and Lists of Inadequacies:
Note the ethical pending issue observed by the IRB/IEC, when analyzing the notification documents, motivating the non-approval of the study.
If the IRB/IEC does not note ethical pending issue in the notification, it may inform: "There were no ethical pending issue noted in the notification documents".

Annex VII - Standardization Recommendation for the Withdrawal Opinion

UNIFIED OPINION

Project Presentation:
The information listed in the fields "Project Presentation", "Research Objective", and "Risk and Benefits Assessment" were taken from the Basic Research Information document (and "Detailed Project" - when necessary).

INTRODUCTION Text of the Basic Research Information document.
HYPOTHESIS insert text from the Basic Research Information document.
METHODOLOGY Insert text from the Basic Research Information document.
INCLUSION CRITERIA Insert text from the Basic Research Information document.
EXCLUSION CRITERIA Insert text from the Basic Research Information document.

Research Objective:
PRIMARY OBJECTIVE Insert text from the Basic Research Information document.
SECONDARY OBJECTIVE Insert text from the Basic Research Information document.

Assessment of Risks and Benefits:
RISKS Insert text from the Basic Research Information document.
BENEFITS Insert text from the Basic Research Information document.

Comments and Considerations on the Research:
It is suggested that detailed information be included in this field to support all requests for a withdrawal protocol/amendment from Plataforma Brasil.

Considerations on mandatory submission forms:
If there is no consideration, the text is indicated: "See field 'Conclusions or Pending Issue and List of Inadequacies'.
It is important to note that it should not be included in this field or clarification.

Recommendations
This field can be completed with suggestions from the IRB/IEC to the researcher, who will have a choice of accepting the recommendation or not.
If there is no recommendation, the text is indicated: "See field 'Conclusions or Pending Issue and List of Inadequacies'.

Conclusions or Pending Issue and Lists of Inadequacies:
Text suggestion:
In view of the above, the Institutional Review Board/Independent Ethics Committee (IRB/IEC) manifests itself by canceling the study or the amendment (use the form relevant to the situation). In this sense, the IRB/IEC will not proceed with the analysis of the research project. It should be noted that, later, if there is interest, the researcher must submit a new submission for ethical analysis of the IRB/IEC/CONEP System.

5. Annex VIII - Closures of Unified Opinion

After analyzing the reporter opinion by the collegiate, the following options will be available to the IRB/IEC Coordinator: approved, not approved, pending, and withdrawn.

In the option “Opinion Status”, it will be necessary to select the option that falls into the decision issued by the plenary of the IRB/IEC.

In the option “Final Considerations at the IRB/IEC's Criteria”, the Committee may insert standardized opinion closings, according to the situation of each of the options given in the “Opinion Status” field. In this sense, they follow standardized recommendations for closing opinions.

Closing of Unified Opinion - "Approved" status		
Original	Biomedical	In view of the above, the Institutional Review Board/Independent Ethics Committee - IRB/IEC, in accordance with the attributions defined in CNS Resolution No. 466, of 2012, and in Operational Standard No. 001, of 2013, of the CNS, approves the research protocol.
	CHS	In view of the above, the Institutional Review Board/Independent Ethics Committee - IRB/IEC, in accordance with the attributions defined in CNS Resolution No. 510, of 2016, in CNS Resolution No. 466, of 2012, and in Operational Standard No. 001, of 2013, of the CNS, approves the proposed research protocol.
Amendment	Biomedical	In view of the above, the Institutional Review Board/Independent Ethics Committee - IRB/IEC, in accordance with the attributions defined in CNS Resolution No. 466, of 2012, and in Operational Standard No. 001, of 2013, of the CNS, approves the proposed amendment to the research project.
	CHS	In view of the above, the Institutional Review Board/Independent Ethics Committee - IRB/IEC, in accordance with the attributions defined in CNS Resolution No. 510, of 2016, in CNS Resolution No. 466, of 2012, and in Operational Standard No. 001, of 2013, of the CNS, approves the proposed amendment to the research project.
Notification	Biomedical	In view of the above, the Institutional Review Board/Independent Ethics Committee - IRB/IEC, in accordance with the attributions defined in CNS Resolution No. 466, of 2012, and in Operational Standard No. 001, of 2013, of the CNS, approves the notification submitted for the research project.
	CHS	In view of the above, the Institutional Review Board/Independent Ethics Committee - IRB/IEC, in accordance with the attributions defined in CNS Resolution No. 510, of 2016, in CNS Resolution No. 466, of 2012, and in Operational Standard No. 001, of 2013, of the CNS, approves the notification presented for the research project.

Closing of Unified Opinion - "Pending Issue" situation		
Original	Biomedical	In view of the above, the Institutional Review Board/Independent Ethics Committee - IRB/IEC, in accordance with the attributions defined in CNS Resolution No. 466, of 2012, and in CNS Operational Standard No. 001, of 2013, will await the questions above to be responded to issue its final opinion. According to CNS Resolution No. 466, of 2012, and Operational Standard No. 001, of 2013, of the CNS, pending issues must be answered exclusively by the responsible researcher, within 30 days, from the date of sending the opinion by the IRB/IEC. After this deadline, the research protocol can be filed, and the process closed.
	CHS	In view of the above, the Institutional Review Board/Independent Ethics Committee - IRB/IEC, in accordance with the attributions defined in CNS Resolution No. 510, of 2016, in CNS Resolution No. 466, of 2012, and in Operational Standard No. 001, of 2013, of the CNS, will await the questions above to be responded, for the issuance of its final opinion. According to CNS Resolution No. 510, of 2016, CNS Resolution No. 466, of 2012, and CNS Operational Standard No. 001, of 2013, pending issues must be answered exclusively by the responsible researcher, within 30 days from the date of submission of the opinion by the IRB/IEC. After this period, the research protocol can be filed, and the process closed.
Amendment	Biomedical	In view of the above, the Institutional Review Board/Independent Ethics Committee - IRB/IEC, in accordance with the attributions defined in CNS Resolution No. 466, of 2012, and in CNS Operational Standard No. 001, of 2013, will await the questions above to be responded the questions above, for the issuance of its final opinion. According to CNS Resolution No. 466, of 2012, and Operational Standard No. 001, of 2013, of the CNS, pending issues must be answered exclusively by the responsible researcher, within 30 days, from the date of sending the opinion by the IRB/IEC. After this deadline, the Amendment may be filed, and the process terminated.
	CHS	In view of the above, the Institutional Review Board/Independent Ethics Committee - IRB/IEC, in accordance with the attributions defined in CNS Resolution No. 510, of 2016, in CNS Resolution No. 466, of 2012, and in Operational Standard No. 001, of 2013, of the CNS, manifests itself by waiting for the above questions to be answered, for the issuance of its final opinion. According to CNS Resolution No. 510, of 2016, CNS Resolution No. 466, of 2012, and CNS Operational Standard No. 001, of 2013, pending issues must be answered exclusively by the responsible researcher, within 30 days from the date of submission of the opinion by the IRB/IEC. After this deadline, the Amendment may be filed, and the process terminated.

Closing of Unified Opinion - "Non-Approved" situation”		
Original	Biomedical (1st time)	In view of the above, the Institutional Review Board/Independent Ethics Committee - IRB/IEC, in accordance with the attributions defined in CNS Resolution No. 466, of 2012, does not approve the research project, in the terms in which it is proposed. According to CNS Resolution No. 466, 2012, and CNS Operational Standard No. 001, of 2013, the researcher will have up to 30 days to file an appeal, presenting a new fact that justifies the reanalysis. After this period, the protocol will be filed.
	Biomedical (2nd time)	In view of the above, the Institutional Review Board/Independent Ethics Committee - IRB/IEC, in accordance with the attributions defined in CNS Resolution No. 466, of 2012, and in Operational Standard No. 001, of 2013, of the CNS, manifests itself to maintain the previous decision not to approve the research project, in the terms in which it is proposed. The protocol will be filed and, if it is in the interest of the researcher, they may submit a new amendment to the IRB/IEC/CONEP System, with the aforementioned changes/corrections that motivated the non-approving opinion or file an appeal with the Brazilian National Institutional Review Board/Independent Ethics Committee - CONEP.
	CHS (1st time)	In view of the above, the Institutional Review Board/Independent Ethics Committee - IRB/IEC, in accordance with the attributions defined in CNS Resolution No. 510, of 2016, and in CNS Resolution No. 466, of 2012, does not approve the project of research, in the terms in which it is proposed. According to CNS Resolution No. 510, of 2016, CNS Resolution No. 466, of 2012, and CNS Operational Standard No. 001, of 2013, the researcher will have up to 30 days to appeal, presenting a new fact that justifies the reanalysis. After this period, the protocol will be filed.
	CHS (2nd time)	In view of the above, the Institutional Review Board/Independent Ethics Committee - IRB/IEC, in accordance with the attributions defined in CNS Resolution No. 510, of 2016, in CNS Resolution No. 466, of 2012, and in Operational Standard No. 001 of 2013 of the CNS, maintain the previous decision of not approving the research project, in the terms in which it is proposed. The protocol will be filed and, if it is in the interest of the researcher, they may submit a new amendment to the IRB/IEC/CONEP System with the aforementioned changes/corrections that motivated the non-approving opinion or file an appeal with the Brazilian National Institutional Review Board/Independent Ethics Committee - CONEP.

Amendment	**Biomedical (1st time)**	In view of the above, the Institutional Review Board/Independent Ethics Committee - IRB/IEC, in accordance with the attributions defined in CNS Resolution No. 466, of 2012, does not approve the proposed amendment to the research project, in the terms in which it is introduced. According to CNS Resolution No. 466, of 2012, and CNS Operational Standard No. 001, 2013, the researcher will have up to 30 days to file an appeal, presenting a new fact that justifies the reanalysis. After this period, the protocol will be filed.
	Biomedical (2nd time)	In view of the above, the Institutional Review Board/Independent Ethics Committee - IRB/IEC, in accordance with the attributions defined in CNS Resolution No. 466, of 2012, and in Operational Standard No. 001, of 2013, of the CNS, maintains the previous decision of not to approve the proposed amendment to the research project, in the terms in which it is presented. The amendment will be filed and, if it is in the interest of the researcher, they may forward a new amendment to the IRB/IEC/CONEP System with the aforementioned changes/corrections that motivated the non-approving opinion or file an appeal with the Brazilian National Research Ethics Committee - CONEP.
	CHS (1st time)	In view of the above, the Brazilian National Research Ethics Committee - CONEP, in accordance with the attributions defined in CNS Resolution No. 510, of 2016, and in CNS Resolution No. 466, of 2012, does not approve the proposed amendment to the research project, in the terms in which it is presented. According to CNS Resolution No. 510, of 2016, CNS Resolution No. 466, of 2012, and CNS Operational Standard No. 001, of 2013, pending issues must be answered exclusively by the responsible researcher in the period of 30 days, from the date of submission of the opinion by the IRB/IEC. After this period, the protocol will be filed.
	CHS (2nd time)	In view of the above, the Institutional Review Board/Independent Ethics Committee - IRB/IEC, in accordance with the attributions defined in CNS Resolution No. 510, of 2016, in CNS Resolution No. 466, of 2012, and in Operational Standard No. 001, of 2013, of the CNS, maintain the previous decision of not approving the amendment to the research project in the terms in which it is proposed.
Notification	**Biomedical**	In view of the above, the Institutional Review Board/Independent Ethics Committee - CEP, according to the attributions defined in CNS Resolution No. 466, of 2012, does not approve the notification submitted to the research project.
	CHS	In view of the above, the Institutional Review Board/Independent Ethics Committee - IRB/IEC, in accordance with the attributions defined in CNS Resolution No. 510, of 2016, and in CNS Resolution No. 466, of 2012, does not approve the notification submitted to the research project.

Closing of Unified Opinion - situation of "Withdrawn
The Institutional Review Board/Independent Ethics Committee - IRB/IEC decides to close the project process, which is why it will not issue an ethical analysis opinion on this proposal.

6. REFERENCES

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