

NATIONAL ETHICS BODY FOR RESEARCH TECHNICAL REPORT

(version 1.1, dated 09/30/2026)

LAW No. 14,874/2024, DECREE No. 12,651/2025 AND INAEP ORDINANCE No. 3/2026 Single Ethical Analysis in Multicenter Research

This page brings together guidelines for researchers, Research Ethics Committees (RECs), institutions, sponsors, and participants regarding the single ethical review of multicenter research.

The answers clarify the application of Law No. 14,874/2024, Decree No. 12,651/2025, and Inaep Dispatch No. 3/2026. They do not replace these regulations nor create obligations or exemptions not provided for in the applicable provisions.

1. Nature, purpose and principles

This Technical Report constitutes a regulatory guidance instrument, of a non-normative nature. Its purpose is to clarify the practical application of Law No. 14,874/2024, Decree No. 12,651/2025, Inaep Dispatch No. 3/2026, and other current regulations related to the ethical analysis of multicenter research.

This document does not create obligations, documentary requirements, competencies, or restrictions not foreseen in the applicable regulations. It also does not replace current regulations, the opinion issued by the Research Ethics Committee (CEP), the competent ethical review body, nor the evaluation of the particularities of each research protocol involving human subjects. In case of divergence, the applicable legislation and regulations prevail.

The guidelines aim to promote predictability, harmonization, and transparency in the operation of the National System of Ethics in Research with Human Beings (Sinep), through the...

Clarification of the understandings applicable to recurring questions from Ethics Committees, researchers, sponsors, and institutions involved in conducting multicenter research.

1.1 Guidance and non-binding nature

The responses reflect Inaep's institutional understanding of the application of current regulations, without introducing any innovation to the legal order. Alternative operational solutions may be adopted when they are compatible with the legislation and preserve the unique ethical analysis.

to provide equivalent protection for the rights, safety, and well-being of the participants.

The advisory nature of this does not preclude compliance with obligations stipulated by law, decree, The responses distinguish, as appropriate, between obligations arising from existing regulations, interpretations intended to clarify those obligations, and recommendations for best practices.

1.2 Regulatory security and predictability

Consolidating recurring questions into a public document promotes the uniform application of rules and reduces divergent interpretations within the National System for Research and Development (SINEP). It also allows researchers, sponsors, and institutions to know in advance the expected procedures, the limits of action for different actors, and the documents that are actually required. necessary.

Predictability does not authorize the creation of requirements through extensive interpretation. Documentary requirements remain subject to articles 13 and 14, § 8, of Law 14.874/2024.

1.3 Dialogue and continuous updating

The questions and answers may be updated based on queries submitted by Ethics Committees, researchers, institutions, sponsors, research participants, and other interested parties. This updating allows for clarification of application difficulties and improvement of operational flows without having to amend existing regulations for each question.

This document does not replace the regulatory process when the solution requires the creation of an obligation, the expansion of competence, the restriction of a right, or the definition of a requirement not established in the legislation.

1.4 Administrative efficiency and reduction of duplication

Disseminating common guidelines reduces repeated individual consultations, conflicting requirements, and rework in the processing of protocols. In a single ethical review system, this function is relevant to avoid local analyses, opinions, or records that do not add protection to participants.

Optimizing procedures should preserve the traceability of decisions, the channels for reporting risks and complaints, and the immediate adoption of protective measures when necessary.

2. Single ethical review regime

2.1 What characterizes a multicenter study?

Answer — It is research conducted in different study centers, by more than one researcher, and under a single protocol, as per article 2, item XXXV, of Law No. 14.874/2024.

2.2 Who performs the ethical review of multicenter research?

Answer — The analysis of research involving more than one center in the country is carried out by a single Ethics Committee (CEP), preferably the one linked to the coordinating center. This CEP issues the ethical opinion and communicates its decision to the CEPs of the other participating centers.

The rules of competence related to risk classification, accreditation, and certification of Ethics Committees (ECs) must be observed. Preference for the ECC linked to the coordinating center is not absolute: the designation of a different ECC must be formally justified and substantiated.

2.3 Which expression should identify the postal code that issues the single opinion?

Answer — The correct term is “CEP responsible for the sole ethical review.” The expression “CEP linked to the coordinating center” should be used when the text specifically refers to the institutional link, since the responsibility for analyzing the protocol is preferential, not... necessarily assigned to the CEP of the coordinating center.

2.4 Does the single ethical opinion cover all participating centers?

Answer — Yes. The opinion has ethical validity for the participating centers in the country covered by the approved protocol. This validity does not, in isolation, authorize the start of activities in each location, which remains conditional on institutional authorization and applicable health or sectoral requirements. The same research should not receive autonomous ethical decisions in each institution.

2.5 Can the Ethics Committee linked to the participating center, on its own initiative or at the institution's request, conduct a new ethical review or issue a second approval?

Answer — No. In multicenter research, a single Ethics Committee (CEP) is responsible for conducting the ethical analysis, issuing the opinion, and communicating its decision to the CEPs of the other participating centers.

This limitation stems from Law [14.874/2024](#) and Decree [12.651/2025](#).

The Ethics Committee of the participating center cannot reassess the scientific, methodological, or ethical merit already evaluated, formulate new pending issues, or demand changes to the protocol or approved documents. This prohibition does not prevent the participating Ethics Committee from exercising the protection and local monitoring responsibilities foreseen in Inaep Dispatch No. 3/2026.

2.6 What are the responsibilities of the participating center's Ethics Committee after single ethical approval?

Answer — Although it does not have the authority to conduct a new analysis of the protocol or issue another ethical decision regarding the research, the Ethics Committee of the participating center retains the responsibility of being the local reference body. The Ethics Committee of the participating center remains an instance of ethical protection within the institution where the research is conducted.

This means that, upon becoming aware of a situation occurring at the center that may affect the rights, safety, or well-being of participants, it is the responsibility of the participating Ethics Committee to:

- Welcome participants and receive questions, complaints, or reports; • Communicate risks, violations, deviations, and other relevant occurrences at the center; • to support the adoption, by the institution and those responsible for the research, of the measures necessary protective locations;
- recommend that the institution adopt immediate measures in the face of serious risk or imminent; and
- Forward to the appropriate authority situations that require a decision on the protocol, its suspension, or the alteration of approved documents.

In summary: whoever analyzes and approves is responsible for the analysis and the opinion; whoever executes is responsible for conducting the research; and the local Ethics Committee acts as an institutional point of protection, support, and communication, without conducting a second analysis.

Figure 1. Role of the local ethics committee in the single ethical review in multicenter research.



Source: Inaep. Image generated by Artificial Intelligence.

2.7 How should the records required by the platform be handled?

Answer — Records, replications, or statements required solely to facilitate processing will be operational in nature. They should not produce a merit-based opinion, validation, or additional ethical approval.

When Plataforma Brasil requires a statement from the participating postal code, item VII of Decree No. 3/2026 must be observed, which recommends specific text to identify this.

Operational purpose. The statement may not open a new period for ethical analysis, raise pending issues regarding the merits, or condition the effectiveness of the single opinion.

2.8 Does the single ethical review regime apply to amendments made to research approved before Inaep Dispatch No. 3/2026?

Answer — Yes. The single ethical review regime applies to amendments submitted from June 8, 2026, the date of entry into force of Inaep Order No. 3/2026, even if the research has received ethical approvals previously.

In these cases, the analysis of the amendment will be the responsibility of the Ethics Committee (CEP) linked to the coordinating center originally registered in the research. It will not be necessary to subsequently define another CEP among those that issued the previous approvals. This rule preserves the continuity and traceability of the process and considers the operational limitations of the current platform for changing the coordinating center and its respective CEP.

Opinions issued prior to the entry into force of this Order remain fully valid. The transition to the single ethical review regime does not require ratification of previous approvals, nor does it authorize a complete re-analysis of the protocol, nor does it require the opinion of the Ethics Committees of the other participating centers. The responsible Ethics Committee must analyze the amendment and its effects on the approved protocol, including any repercussions on the risk-benefit ratio, consent, and protection of participants. This evaluation should be limited to the proposed changes and the aspects of the protocol directly affected by them, without reopening matters already duly analyzed and not modified.

Following the decision, the opinion on the amendment must be communicated to the participating centers and, where applicable, to the respective Ethics Committees, producing effects for all centers covered by the single protocol.

Exceptionally, if the Ethics Committee of the originally registered coordinating center is unable to operate, has ceased its activities, or does not possess accreditation or certification compatible with the research risk, the definition of the responsible Ethics Committee must observe the guidelines of Inaep, without this implying a complete re-analysis of the protocol.

2.9 When does the single ethical opinion begin to have effects for the participating centers?

Answer — After approval by the Ethics Committee responsible for the single review, the Brazil Platform replicates the protocol for the researchers responsible for the participating centers. It is the responsibility of the researcher responsible for the respective center to submit it to the Ethics Committee of their institution for registration, information, and local monitoring purposes. Therefore, once the submission is made, the single ethical approval formally covers the participating center, without the need for a new opinion.

It is important to note that the only valid protocol for the study is the one approved by the Ethics Committee responsible for the single ethical review.

2.10 How should the inclusion or regularization of a participating center on the Brazil Platform be carried out?

Answer — The inclusion of a new participating center must be done through an amendment submitted to the Ethics Committee responsible for the single ethical review. The coordinating researcher must include the center in the research registration on the Brazil Platform, insert the relevant documentation, and submit the amendment for analysis.

The evaluation by the responsible Ethics Committee should focus on the inclusion of the center and its potential ethical impacts, especially regarding:

- to the identification of the institution and the responsible local researcher; • to the adequacy of the local information in the Informed Consent Form or Assent Form, when applicable;
- to specific conditions that may affect the protection of participants; and • to changes to the protocol or other documents resulting from the inclusion.

After the amendment is approved, the local principal investigator must submit the amendment for research registration with the Ethics Committee (CEP) of their institution, following the procedure described in item 2.8. This registration is exclusively for scientific purposes, traceability, and local monitoring, and does not constitute a new submission for analysis.

Administrative, contractual, or regulatory package documents required by the sponsor or institution must be handled by the appropriate authorities. Even if they are uploaded to the platform, their submission does not authorize the local Ethics Committee to re-examine the protocol or issue a new ethical approval.

2.11. Does the single ethical review apply to all multicenter research or only to clinical research?

Answer — The single ethical review is not limited to clinical research. It applies to research involving human beings that is multicenter, that is, carried out in different research centers, by more than one researcher and under a single protocol. The rule stems from Article 14, § 7, of [Law No. 14.874/2024](#), and article 27 of [Decree No. 12,651/2025](#), encompassing research with human subjects from all areas of knowledge, taking into account their specific characteristics.

3. Institutional authorization and consent

3.1 Does ethical approval replace authorization from the participating institution?

Answer — No. They are different and complementary evaluations. The Ethics Committee evaluates the ethical aspects of the protocol. The institution verifies the administrative, healthcare, and operational conditions and decides on whether the research can be conducted within its scope.

The activity may only begin after ethical approval by the competent Ethics Committee and the applicable institutional authorizations. The administrative evaluation cannot replicate the ethical judgment already made.

3.2 Is a letter of consent an ethical endorsement?

Answer — No. The letter of consent, or equivalent institutional document, formalizes the institution's administrative agreement to the research being conducted. It does not replace the opinion of the Ethics Committee (CEP) and does not authorize the CEP linked to the participating center to reassess the merits of the protocol. Its function is to demonstrate that the competent authority is aware of the activities to be carried out and agrees with their development within the institutional scope. The document

It does not transfer to the manager the authority to approve the research protocol from an ethical standpoint.

3.3 Should the consent of the coordinating center institution be included in the initial dossier?

Answer — The letter of consent formalizes administrative authorization and, as a rule, can be obtained concurrently with the ethical review. Its absence will not prevent the protocol from being considered, except when the document contains information necessary for the ethical evaluation or when its presentation is expressly provided for in applicable regulations. The research may only begin after authorization from the competent institution. However, it is good practice to include the consent of the Coordinating Center.

3.4 Is a letter of consent from all centers required before ethical submission?

Answer — No, as a general requirement. The consent of the other participating centers is not mandatory in the initial dossier, except when its presentation is foreseen in a normative act or is relevant to the matter analyzed, according to article 14, § 8, of Law No. 14.874/2024. The single analysis focuses on the protocol and its safeguards, and not on the prior conclusion of all local administrative processes. This does not exempt each institution from authorizing the research before the start of its activities.

3.5 Does the absence of consent from a participating center preclude ethical review?

Answer — No, not in isolation. The center may be identified in the protocol before the submission of its approval. The institution must, however, authorize the research before the start of any activity at that location. This solution allows the Ethics Committee to evaluate the complete multicenter design while preserving the administrative competence of the participating institutions. If the subsequent inclusion modifies the approved protocol or documentation, it must follow the amendment procedure.

3.6 Can a contract, agreement, or adhesion document replace a letter of consent?

Answer — Yes. The capacity of the centers to carry out the research is ethically relevant, as inadequate staffing, infrastructure, assistance, or security conditions may compromise the rights and well-being of the participants. It is recommended that the protocol include, at least for the coordinating center, an institutional document or statement demonstrating its agreement with the research and the availability of conditions compatible with the planned activities.

3.7 Can the institution refuse to proceed after ethical approval?

Answer — Yes. The institution retains its administrative competence and may refuse to authorize or interrupt activities within its scope when the necessary conditions are absent or in the face of immediate risk. This decision does not, in itself, alter the merit of the ethical opinion, but it must be communicated when it impacts the execution of the protocol. The refusal may result from insufficient infrastructure, human resources, care capacity, data protection, contractual conditions, or other justified institutional limitations. It produces effects only in the respective center and does not equate to the revocation of the ethical opinion for other locations.

3.8 What is the procedure for recording an unforeseen interruption of a study at a research center?

Answer — The principal investigator must submit to the Ethics Committee responsible for the single review, via amendment, the change to the list of participating centers, accompanied by a report containing the reason for the early termination, the status of the participants in relation to the phases foreseen in the protocol, and the destination of the data and biological samples collected. The document must also establish, if applicable, the referral plan for those who did not complete the procedures, the need for any eventual breaking of blinding, the guarantee of continuity of care and full support to those who need it, and the conditions for access to the benefits of the study, such as post-study examinations and medication, in addition to other information relevant to the case.

3.9 Can the institution request a technical opinion from its Ethics Committee before deciding to participate?

Answer — Yes. Before formalizing its adherence, the institution may consult the local Ethics Committee (CEP) to obtain technical support related to the ethical aspects of the protocol and the institutional conditions for its execution. According to Opinion No. 00392/2026/CONJUR-MS/CGU/AGU, this opinion is exclusively internal and consultative in nature. It does not constitute a new ethical analysis or approval, does not affect the validity of the single opinion, and does not assign a decision-making function to the local Ethics Committee in the National System for Ethics in Public Health (Sinep). As the Opinion clarifies:

"Such action should not be confused with ethical re-analysis, insofar as it does not result in a judgment on the validity of the protocol and the research, but only supports the institutional decision to adhere to or not adhere to the research."

Since this is an internal consultation, without the nature of an ethical analysis or a decision-making act by Sinep, the request and advisory opinion of the local CEP should not be processed through the Plataforma Brasil, and should be formalized within the institution's internal administrative workflow.

After formal acceptance, the institution and the local Ethics Committee may not require a new ethical review, revise the approved protocol, or establish additional ethical conditions for the commencement of the research. According to the Opinion:

"Once participation in the research is formalized, the institution – nor its Ethics Committee – is not given any further authorization."

"To condition the commencement of the study on the completion of a new ethical review or the revision of the initially approved protocol, under penalty of contravening the single ethical review regime provided for in Law No. 14,874/2024."

4 Roles and responsibilities

4.1 What are the responsibilities of the main actors?

Answer — Responsibilities must be interpreted in conjunction with Law No. 14,874/2024, Decree No. 12,651/2025, and Inaep Dispatch No. 3/2026, as per the table below.

Actor	Main responsibilities	Limits
Ethics Committee responsible for the single ethical review.	Analyzes protocols and amendments; issues a single opinion; evaluates reports, complaints, and events; and determines protection, suspension, or termination measures, when applicable. Articles 12, 14, § 7, 16, and 55 of Law No. 14,874/2024.	It does not replace administrative, health, and care competencies or contractual.
ZIP code linked to Center/Institution the participant	It welcomes participants; receives complaints; monitors local conditions; communicates relevant facts; and recommends protective measures, in accordance with Decree No. 3/2026.	It does not re-analyze the protocol, does not issue a second approval, and does not alter the single opinion.
Participating institution or executor	It verifies institutional conditions and, after receiving a favorable opinion, authorizes the start of operations locally. It is jointly responsible for the management and assistance related to complications and injuries. Articles 18, § 3, item II, 26, § 3, and 51 of the Law.	Performs merit analysis in the administrative field. It does not conduct ethical analyses or issue opinions on the subject.

Actor	Main responsibilities	Limits
Coordinating Researcher	Coordinates the centers; submits amendments; consolidates information; forwards the annual report; and complies with articles 16, 22, 34 and 53 of the Law.	Coordination does not absolve the other actors of their responsibilities.
Principal investigator at Center/ Institution	Submits the protocol for the knowledge of the local Ethics Committee when replicated by the Brazil Platform; Conducts the protocol in its respective center; protects participants; maintains records; allows monitoring and inspection; and reports serious or unexpected events. Art. 27 of the Law.	Do not submit the protocol for further local approval. being the submission solely for registration and communication purposes with the CEP by PB, without prejudice to direct risk communication and complaints.
Sponsor	Selects qualified institutions; secures resources; maintains data integrity; monitors; reports security findings; and is responsible for assistance and compensation. Articles 23, sole paragraph, and 26 of the Law.	Delegation does not absolve the entity of its ultimate responsibility. Article 26, § 1, of the Law.

5 Consent and assent

5.1 Who reviews the Informed Consent Forms and Assent Forms to be used in the participating centers?

Answer — The Ethics Committee responsible for the single ethical review examines the Informed Consent Forms, Assent Forms, and other materials from the consent or assent process. Ethics Committees linked to participating centers may collaborate with local information, but will not issue new approvals. The analysis should focus on common elements and ethically relevant differences, without requiring the repetition of versions that only change registration data. Local contributions should be presented in an organized manner, allowing the Ethics Committee to distinguish administrative adaptations from changes that influence the participant's decision.

5.2 All centers must submit their own versions of the Informed Consent Form or the Term of Agreement?

Answer — No. A base model is recommended, accompanied, when necessary, by delimited local fields or modules. Submitting different versions is not necessary when the differences are limited to registration data and do not alter the approved ethical core. A single ethical review does not require that all participants receive a document.

Materially identical: requires that common elements and ethically relevant local adaptations be examined by a single CEP (Code of Ethics for Ethics).

5.3 When should specific versions be submitted?

Answer — When there are relevant differences in population scope, procedures, risks, language, responsibilities, or safeguards, the applicable version should reflect the activities actually performed, and the differences should be described in the protocol and highlighted to the responsible Ethics Committee. In these cases, the specific version does not represent bureaucratic duplication, but a requirement for fidelity to the consent process. The participant must receive information corresponding to the activities, risks, and assistance channels actually available at the location where they participate.

5.4 Should the content of the terms be identical across all centers?

Answer — Not necessarily. Common ethical elements should remain harmonized, but terms may be adapted to the characteristics of the participants and the activities carried out in each location. Absolute identity of terms may be inappropriate when centers recruit different audiences or carry out different stages. Harmonization should focus on the common ethical core, while local adaptations should be proportionate, justified, and clearly identified.

5.5 What contact information should be included in the Informed Consent Form?

Answer — In accordance with item V of Inaep Dispatch No. 3/2026, the address, telephone number, and email of the Ethics Committee responsible for the single ethical analysis must be clearly stated. The contact information for the Ethics Committee linked to the participating center may be included as a supplementary support channel, without creating doubt about the decision-making authority.

5.6 Is it mandatory to include Inaep's contact information in the Informed Consent Form?

Answer — No. Law No. 14,874/2024, Decree No. 12,651/2025 and Order No. 3/2026

They do not establish this general requirement.

Inaep's contact information may be provided as supplementary information, but it does not replace the contact information for the responsible Ethics Committee and the research team.

5.7 Are 24/7 telephone support and a backup hospital always mandatory?

Answer — No, as a uniform requirement for all research. The need for these The allocation of resources should take into account the nature of the research, the procedures, the foreseeable risks, the participants' conditions, and the possibility of unforeseen events occurring outside the research center's usual operating hours.

The absence of these resources will only be acceptable when compatible with the research risk and when the protocol demonstrates that the proposed assistance channels and measures are sufficient to protect the participants. In any research that may

In cases where clinical complications may occur, the protocol should present a care plan proportionate to the identified risks, indicating, as applicable:

- The signs, symptoms, or situations that require contact with the research team;
- The available channels and hours of service;
- The professional or team responsible for clinical guidance and decisions;
- Procedures for urgent and emergency care;
- The referral health service or available care structure;
- The referral and transport flow, when necessary;
- Measures for continuity of care;
- The method for recording, evaluating, and communicating incidents and events.

adverse; and

- the responsibilities of the researcher, the sponsor, and the institution for research-related assistance.

A 24/7 helpline is necessary when research risks may arise at any time and require immediate guidance from the team, a clinical decision related to the protocol, or rapid coordination with healthcare services. The line must be effectively available, staffed by a trained professional, or connected to a workflow that ensures a timely response. Providing a number that operates only during administrative hours does not fulfill the purpose of protection when there is a possibility of an incident outside of those hours.

A backup hospital, or equivalent care service, is necessary when the procedures or products under investigation could produce acute complications that exceed the center's capacity to provide care. Backup care may be provided by the institution's own structure or by a formally defined referral service, provided there is capacity compatible with the risks, a viable referral flow, and conditions for timely care. The requirement should not be reduced to the generic indication of a hospital, nor does it presuppose, in all cases, the signing of a specific agreement; the arrangement presented must be sufficient and verifiable.

In research studies without clinical intervention or those where the risks do not require emergency research-related assistance, channels and schedules compatible with the foreseeable needs of the participants may be adopted. Even so, the means of contacting the researcher and the Ethics Committee (CEP) must be clearly communicated, as well as guidance on how to proceed in case of doubt, harm, or unforeseen events.

When applicable, the Informed Consent Form and materials provided to the participant should clearly state:

- Who should be contacted in case of any incident related to the research;
- Telephone number and other contact channels, with their respective hours;
- Where and how the service will be provided;
- How to proceed outside the center's operating hours; and
- That, in the event of an urgent or emergency situation, the participant should immediately seek the appropriate health service, without necessarily waiting for prior contact with the research team.

Ethical evaluation must verify not only whether the telephone number or hospital was specifically indicated, but also whether the care plan is proportionate to the risks, feasible in the local context, and capable of guaranteeing timely assistance. It is unacceptable to transfer to the participant the costs or responsibility for organizing necessary care due to research-related harm.

This guidance stems from the obligation to ensure healthcare assistance in cases involving intervention, based on Article 3, VIII, of Law No. 14,874/2024, as well as the sponsor's responsibility for compensation and necessary healthcare assistance related to any damages suffered as a result of participation in the research, in light of Article 23, caput and sole paragraph, in conjunction with Article 26, XV; the sponsor's responsibility to guarantee adequate resources, including for the resolution of adverse events, under the terms of Article 26, item VI; the co-responsibility of institutions for comprehensive assistance, provided for in Article 26, § 3; and the researcher's responsibilities for clinical monitoring and for protecting the safety and well-being of participants, provided for in Article 27, items V and XII, all of Law No. 14,874/2024.

5.8 Can the Informed Consent Form or Assent Form be submitted with open administrative fields?

Answer — Yes. The base model may contain delimited fields for later completion of the identification and contact information of the local researcher, the institution, and the Ethics Committee, as well as the address and location of service. These fields may not include elements essential to the participant's decision. The coordinating researcher, the sponsor, and the institutions must maintain a documented mechanism for controlling the versions used in each center, without modifying the approved ethics committee.

5.9 Administrative or graphic changes to the Informed Consent Form and the Assent Form must Can they be processed via amendment?

Answer — No, when the changes are limited to telephone number, address, institutional contact, header, footer, pagination, logo, or formatting and do not modify or conceal the approved content, they may be processed via notification (notification classification option: "other"). Processing may occur simultaneously at the Ethics Committee responsible for the single analysis (for information purposes) and at the local Ethics Committee (in the latter only for registration purposes). If they affect comprehension, risk presentation, rights, procedures, or assistance channels, they must be submitted to the Ethics Committee responsible for the single ethical analysis via amendment.

5.10 Should the specific terms of studies approved before Inaep Order No. 3/2026 be replaced by a single base model?

Answer — Not necessarily. Regularly approved terms remain valid, provided they are adequate to the legislation and current research conditions. Harmonization may occur when there is an amendment that modifies the consent process, a need to update information for participants, or a concrete advantage for your research.

Understanding and protection. The mere existence of previous local versions does not require a new submission or the obtaining of new consent.

6 Amendments and alterations

6.1 What changes should be submitted as an amendment?

Answer — After the start of the research, any change that interferes with the risk-benefit ratio or the approved documentation must be submitted in writing and with justification by the coordinating researcher to the responsible Ethics Committee, in accordance with Article 16 of Law No. 14.874/2024. The criterion is substantive, not merely formal. Changes capable of affecting the participant's decision, risk assessment, procedures, responsibilities, or safeguards require ethical review. Purely registration-related changes may follow a simplified flow, provided they do not modify the documentation in its ethical content.

6.2 Can an amendment be implemented before approval?

Answer — Only when the participant's safety depends on immediate implementation. In other cases, the change must await approval from the Ethics Committee, as per article 16, § 1.

6.3 How to process a specific change for a center?

Answer — Amendments to the protocol, even those relating to a participating center, must be submitted exclusively by the coordinating researcher to the Ethics Committee responsible for the project. Unique analysis. The amendment should identify:

- the center to which the change applies; • the justification for the change; • the documents affected; • its possible effects on the participants; and • whether or not the change has repercussions on the other centers.

It is the responsibility of the Ethics Committee (CEP) responsible for the single ethical review to evaluate the change and issue the respective opinion. When the change is exclusively local, the decision will only have effects for the identified center. Similar changes relating to several centers may be consolidated into a single amendment.

In the current configuration of the Brazil Platform, after the amendment is approved by the Ethics Committee responsible for the single ethical review, the process can be replicated for the researchers responsible for the participating centers. When the system requires submission to the respective Ethics Committees to allow subsequent processing, these actions must be carried out exclusively for registration, information, and operational continuity on the platform, in the same manner as the single review of the original project.

6.4 Does the inclusion of a new center require an amendment?

Answer — Yes, the inclusion of a research center that is not yet part of the approved protocol. The amendment must be submitted and reviewed by the Ethics Committee responsible for the single ethical analysis. After approval, due to procedural issues on the current Brazil Platform (PB), the researcher from the new center will submit it to their Ethics Committee, which will issue an opinion solely for registration purposes, i.e., without further ethical analysis. Regarding the start of the new center's activities, it will be up to the institution to determine when it can begin, as this is an administrative matter.

6.5 What to do when the change invalidates the approved research?

Answer — There is no current normative definition of when a change "disqualifies" the research. The use of this expression, without objective criteria, can result in divergent decisions and the undue requirement to submit a new protocol.

The topic should be addressed in specific guidelines from Inaep.

The modifications should be evaluated according to their effects on the objectives, design, methodology, population, interventions, risk-benefit ratio, and approved documents. The submission of a new protocol should only be required when there are criteria expressly defined in a standard or guideline from INAEP (National Institute for Research and Educational Studies and Research), and a generic statement that the alteration "mischaracterizes" the research is not sufficient.

6.6 Do purely registration-related changes require a new analysis?

Answer — No. Merely registration-related changes do not require a new ethical review when they do not modify the protocol, the participants' rights, the essential information of the consent, the procedures, the risks, the benefits, the responsibilities, or the protection measures foreseen.

Examples of situations that may be treated as registration changes, as applicable:

- Correction of material or typographical errors; •
 - Updating of telephone number, email address, or administrative contact information; •
 - Updating of the institutional name, without changing the institution or the conditions under which the research is conducted; •
 - Correction or updating of identification data that does not alter responsibilities; and •
 - Other updates without ethical, scientific, healthcare, or operational repercussions on the subject.
- the research.

In the current configuration of the Brazil Platform, it is recommended that the change be submitted by the coordinating researcher as a notification, using the classification "Other," accompanied by a brief description of the updated information and, when necessary, the corresponding document.

The notification serves the purpose of registration, awareness, and preservation of traceability. Therefore, it should not be treated as an amendment nor submitted to a new deliberation by the Ethics Committee. The responsible Ethics Committee may only verify whether the modification is effectively cadastral. If it identifies a possible ethical repercussion, it must indicate, in a reasoned manner, the need for an amendment.

When the update pertains exclusively to one participating center, the local principal investigator must communicate it to the coordinating researcher, who will then be responsible for notifying the Ethics Committee responsible for the single ethical review.

Changes involving, for example: are not classified as merely registration-related.

- Replacement of the principal investigator or change of responsibilities;
- Inclusion, exclusion, or replacement of a participating center;
- Change of the location where the procedures are performed;
- Alteration of infrastructure or assistance conditions;
- Modification of the recruitment or consent process; or
- Any change capable of affecting the safety, rights, or well-being of the participants.

These situations should be presented as an amendment and analyzed by the Ethics Committee responsible for the single ethical review.

6.7 Who reviews amendments to multicenter studies?

Answer — Amendments are submitted by the coordinating researcher to the Ethics Committee responsible for the single ethical review. The opinion on the amendment covers the centers to which the change applies. The Ethics Committee linked to the participating center does not conduct a new analysis; its role is to receive the information necessary for local monitoring, communicate specific details or risks, and monitor the implementation of the approved change. When the amendment applies only to a specific center, the opinion must delimit the centers covered.

7. Communications, security and monitoring

7.1 Does the term "notification" define the ethical treatment of the document?

Answer — No. The content takes precedence over the name assigned by the system. If the document alters the protocol, the risk-benefit ratio, the consent, or any other safeguard, it must follow the amendment flow.

7.2 Does the notification need to be approved?

Answer — Communication intended for scientific or monitoring purposes does not require approval. When the content requires an ethical decision, it should be submitted through the corresponding procedure, with a reasoned decision from the responsible Ethics Committee. The expression "notification approval" should be avoided when there is no decision-making content. (Page 16 of 26)

The document merely reports a fact; it is sufficient to record and acknowledge it. If it contains an ethical alteration, it should be treated as an amendment or through the specific applicable procedure.

7.3 To whom should serious adverse events be reported?

Answer — Serious adverse events from any center involved in the study must be reported to the Ethics Committee that approved the research, in accordance with article 55 of Law No. 14,874/2024, without waiting for prior notification from another Ethics Committee.

Furthermore, Article 27, item X, mandates that the researcher promptly report all serious or unexpected adverse events to the sponsor and the health authority. These reports cannot be conditional upon or await the completion of a consolidated report.

The Ethics Committee (CEP) linked to the participating center may gather local information, monitor the actions taken, and forward its evaluation or recommendation to the responsible Ethics Committee. This statement is informative and protective in nature and does not constitute an ethical opinion.
competitor.

When an event occurs at a participating center, the institution and its associated Ethics Committee (CEP) must be informed simultaneously whenever such information is necessary for assistance, investigation of the event, or the adoption of immediate protective measures. Communication cannot depend on sequential processing between the Ethics Committees.

It is the sole responsibility of the Ethics Committee (CEP) responsible for the single ethical review to assess the repercussions of the event on the protocol and issue an ethical decision with effects for one, some, or all centers, including regarding the need for:

- Request additional information; • Modify the protocol
- or approved documents; • Temporarily interrupt recruitment; • Suspend
- procedures or interventions; • Notify participants; or • Suspend
- the research.

If there is a discrepancy between the opinion of the local Ethics Committee (CEP) and the assessment of the responsible Ethics Committee (CEP), the decision of the CEP that approved the research will prevail in the ethical analysis. The discrepancy must be recorded and forwarded to that CEP with the respective justifications and evidence. If a controversy relevant to the safety of the participants persists, the matter must be submitted to INAEPEP (National Institute for Ethics in Research), without prejudice to urgent protection measures.

The competence of the Ethics Committee responsible for the single opinion does not prevent the researcher, the institution, or the sponsor from immediately suspending recruitment at the affected center.

Intervention or other procedures in the face of serious or imminent risk. These measures do not require prior ethical authorization, but must be promptly communicated to the responsible Ethics Committee, accompanied by justifications and the measures taken.

7.4 Does the adoption of urgent measures depend on prior analysis by the Ethics Committee?

Answer — No. Immediate measures necessary for the participant's safety must be taken and promptly communicated to the appropriate authorities.

7.5 Do all deviations and violations require individual analysis?

Answer — No. The form of communication and evaluation may be proportional to the nature, severity, frequency, and possible consequences of the occurrence. However, a distinction must be made between deviation from protocol and violation of protocol.

Under the terms of Law No. 14.874/2024, a protocol violation is a deviation that may compromise the quality of the data, the integrity of the research, or the safety or rights of the participants.

Similar or recurring occurrences may be assessed jointly or in a consolidated manner, when applicable, provided that this does not hinder the identification of risks or delay the adoption of measures necessary to protect participants.

Deviations without significant ethical repercussions may be recorded and consolidated according to the monitoring plan. Violations, in turn, remain subject to the obligations of prompt reporting stipulated by law, even though their assessment may occur jointly with similar occurrences.

7.6 How should notifications regarding deviations and violations of protocol be handled?

Response — Notifications regarding deviations and violations of protocol, regardless of the center where they occurred, must be submitted, on the Brazil Platform, to the Ethics Committee responsible for the single ethical review, observing the communication obligations foreseen in the legislation and applicable norms. In the Brazil Platform workflow, it is the responsibility of the coordinating researcher to make this submission and clearly identify the centers involved.

When the event occurs at a participating center, the Ethics Committee (CEP) linked to the respective institution may be informed in parallel, through a notification sent by the researcher responsible for the center, for local awareness and monitoring. This communication does not replace submission to the CEP responsible for the single ethical review.

The ethics committee linked to the participating center does not require a statement, opinion, or deliberation on the occurrence and does not authorize a new analysis of the merits or a concurrent ethical decision on the protocol. Any necessary statements from the participating ethics committee Page **18 of 26**

The actions exclusively related to processing on the Brazil Platform will be operational in nature and will not constitute a new ethical analysis or approval.

If the participating Ethics Committee becomes aware of a situation that requires local protection measures, it must exercise the powers provided for in Inaep Dispatch No. 3/2026 and make the appropriate communications to the Ethics Committee responsible for the single ethical analysis and to Inaep.

7.7 How can we ensure that the Ethics Committees of participating centers have access to the information necessary for local monitoring?

Answer — The document is analyzed only once; sharing with local Ethics Committees (ECIs) occurs for informational purposes, protection, and monitoring, without requiring further ethical approval. Notifications, reports, serious adverse events, violations, and other documents that may affect the protocol should be submitted to the ECI responsible for the single ethical review. This ECI is responsible for conducting the ethical evaluation and issuing decisions applicable to the research.

The Ethics Committee linked to the participating center should receive the following information for its records, registration, and local monitoring purposes:

- Serious adverse events that occurred at your center; • Deviations or violations verified locally; • Complaints, grievances, or risks related to participants at your center; • Protective measures adopted by the institution; • Suspensions or interruptions that affect the center; and • Decisions of the responsible Ethics Committee that have an effect on local activities.

General reports, aggregated notifications, and documents without specific implications for a particular center do not need to be resubmitted to the respective local Ethics Committee, except when their disclosure is necessary for the protection of participants or the fulfillment of institutional responsibility.

Until the Brazil Platform automatically shares this information, the local principal investigator may submit it to their institution's Ethics Committee (CEP) solely for informational and record-keeping purposes. This process does not constitute a new ethical review.

The local Ethics Committee (CEP) should not issue an opinion of approval, disapproval, ratification, or validation. If the Brazil Platform formally requires the issuance of an opinion to conclude the processing, the use of a standardized statement is recommended, with the following content:

Statement for registration and information: The Ethics Committee acknowledges receipt of the document and the decision issued by the Ethics Committee responsible for the single ethical review. No new merit review was conducted, and this statement does not constitute approval, ratification, or ethical validation.

The local statement cannot raise pending issues, modify the central decision, or impede its effects. If the local Ethics Committee identifies a risk, violation, or relevant new information, it must communicate it to the Ethics Committee responsible for the single ethical review, which will decide on its repercussions for the protocol.

7.8 How should a new version of the Investigator's Brochure be classified?

Answer — The classification depends on the content of the update and its effects on the approved research and documentation.

It will be submitted as an amendment when it introduces changes that affect the protocol, consent, security measures, risk-benefit ratio, or other safeguards.

It will be submitted as a notification if these elements are not changed.

The coordinating researcher must present a summary of the changes and justify the classification adopted. Simply changing the version number or date does not, in itself, determine the applicable workflow.

7.9 How should security letters, explanatory letters, and other sponsor communications be handled?

Answer — The content and effects of the document determine the flow, not the title assigned by the sponsor or platform. *Safety Letters*, *Protocol Clarification Letters*, *Dear Investigator Letters*, and equivalent communications will be registered as notifications when they only inform or clarify facts. They will be submitted as amendments when they modify procedures, responsibilities, consent, security measures, or the risk-benefit ratio. Information that reveals immediate risk requires the adoption of necessary protective measures, followed by prompt communication.

7.10 How should reports and other documents be submitted?

follow-up?

Answer — Partial, annual, or general reports must be submitted to the Ethics Committee responsible for the single analysis annually and whenever requested, as per article 27, item IX, of Law 14.874/2024. The coordinating researcher must submit these reports.

Annual or general reports, ethically relevant deviations, and documents that may have repercussions on the protocol should be forwarded to the Ethics Committee responsible for the single ethical review. Exclusively local occurrences must be recorded and reported by the coordinating researcher and the Ethics Committee responsible for the single analysis. If the occurrence has specific relevance to the center, the local researcher must also submit it to the local Ethics Committee for scientific purposes. Administrative deviations without ethical repercussions may be consolidated periodically. As a rule, there is no requirement for duplicate submission to all participating Ethics Committees, except for the needs of local monitoring or technical requirements of the system.

7.11 How does the CEP linked to the participating center conduct local follow-up?

Answer — Monitoring may include welcoming participants and receiving complaints; communicating local events, risks, violations, and difficulties; verifying facts that indicate non-compliance with the approved protocol; and coordinating with the principal investigator, the institution, and the Ethics Committee responsible for the single ethical review. It will be proportional to the risk and may not replicate the ethical review, institute local periodic approval, or create documentary requirements without normative basis.

7.12 How is the flow of serious adverse events compatible with Circular Letter No. 13/2020?

Response — A serious adverse event must be promptly reported to the Ethics Committee responsible for the single ethical review, pursuant to Article 55 of Law No. 14,874/2024. The Ethics Committee linked to the center and the institution where the event occurred must be informed simultaneously, via notification, when necessary for assistance, investigation, local monitoring, or the adoption of protective measures, exclusively for registration purposes, in order to preserve the unity of the ethical assessment. However, in situations that pose an immediate risk to participants, the center has a duty to act promptly to safeguard the safety and well-being of those involved. The coordinating researcher and the sponsor must consolidate the safety information from all centers. Circular Letter No. 13/2020 remains applicable only insofar as it is compatible with the legislation and subsequent acts, without multiple analyses of the same event.

7.13 Does the statement from the Ethics Committee linked to the participating center, required by Plataforma Brasil after the single ethical approval, need to be deliberated in a collegiate meeting?

Answer — No. When the statement is required exclusively for registration and completion of the processing on the Brazil Platform, and the protocol already has a duly issued opinion from the Ethics Committee responsible for the single ethical analysis, a new collegial deliberation by the participating Ethics Committee on the protocol is not required.

In this situation, the statement is exclusively operational in nature and does not constitute a new ethical analysis, ratification, validation, or second approval. It is recommended to use the standard text proposed by Inaep in Dispatch No. 3, of May 29, 2026, item VII, subparagraph "a".

The participating Ethics Committee (CEP) must observe the necessary procedures for registration and notification within the Committee itself, without reopening the analysis of the scientific, methodological, or ethical merit already assessed by the responsible CEP.

7.14 Should the specific materials from a center be forwarded to the Ethics Committee responsible for the single ethical review?

Answer — It depends on the nature of the material. Specific materials from the center that contain ethically relevant content should be sent to the Ethics Committee responsible for a single ethical review before use, especially:

- recruitment materials;
- Information directed to participants;
- Local adaptations of the Informed Consent Form or Assent Form;
- Research-related care guidelines;
- Procedural modifications;
- Additional protective measures; or
- Changes that could affect rights, safety, well-being, or decision-making participation.

These materials should be submitted as amendments when they modify previously approved content.

Documents that are exclusively administrative, institutional, or registration-related do not need to be mandatorily notified, except when there is a specific regulatory or operational requirement. Their communication to the CEP (Ethics Committee) will be optional when intended only to facilitate registration, traceability, or local monitoring.

Standardized participant cards, forms, and materials may be approved as base models. The subsequent addition of local information, such as the institution's name, address, phone number, and team contact, will not require further review, provided that:

- the approved content is fully preserved;
- no new guidelines or statements are included;
- there are no changes to the protection measures; and
- the information entered is exclusively for registration purposes.

When there is doubt about the nature of the modification, the researcher may submit the material as a notification for information and registration. This notification, when made, will not imply a new merit analysis.

8. Dialogue between the Postal Codes

8.1 When can the responsible CEP consult the participating CEPs?

Answer — Communication between the responsible Ethics Committee and the participating Ethics Committees constitutes a good practice of cooperation and protection of participants and should be encouraged throughout the research.

Before the final decision, consultation is especially useful when there are relevant local particularities, such as the sociocultural characteristics of the participants, vulnerabilities, care conditions, recruitment strategies, or risks related to implementation at that center.

The consultation is collaborative in nature. It does not transfer responsibility for the analysis, does not require local approval, and does not authorize competing decisions.

After approval, communication must continue whenever information or decisions arise that could affect the centers and the protection of participants.

8.2 Should a fixed period of five working days be granted for a response?

Response — It is recommended, in accordance with Inaep Dispatch No. 3/2026, that the Ethics Committee linked to the coordinating center ensure that the Ethics Committees of the participating centers have a minimum of five working days to submit considerations regarding specific vulnerabilities of the populations involved, regional particularities, sociocultural aspects, or local institutional arrangements, before issuing the final opinion.

This timeframe constitutes a best practice recommendation aimed at making the dialogue between Ethics Committees effective and allowing knowledge of the local context to contribute to the protection of participants. It is not an independent legal deadline, an additional stage of ethical analysis, or a condition for the validity of the single opinion.

The time period should begin to run from the moment the participating CEP (Ethics Committee) is provided with the information necessary to understand the issues on which a statement is requested.

The consultation should objectively indicate the local aspects on which contributions are expected, avoiding the generic referral of the protocol for further comprehensive analysis.

During this period, the participating postal code may, for example:

- Submit a written statement;
- indicate specific vulnerabilities or risks of the local context;
- To present information about institutional or care conditions;
- suggest safeguards related to the population or the center; and
- To participate, by invitation, in the meeting of the Ethics Committee responsible for the single ethical analysis, in order to discuss with the rapporteur and share experiences regarding local particularities.

The opinion of the participating Ethics Committee (CEP) is advisory in nature. It does not constitute an approval opinion, does not transfer decision-making authority, does not authorize the direct formulation of pending issues to the researcher, and does not reopen the ethical review at the participating center. The Ethics Committee responsible for the single ethical review is responsible for evaluating the contributions received and deciding on their incorporation into the opinion.

The five-business-day deadline must be met within the maximum 30-business-day period for ethical review, as stipulated in Article 14 of Law No. 14.874/2024. Consultation with participating Ethics Committees does not suspend or interrupt this legal deadline.

In more complex situations or when there is a justified need to delve deeper into relevant local issues, the responsible Ethics Committee may grant a longer period, provided that this is compatible with the legal timeframe for the analysis and does not compromise the protection of the participants.

Failure to respond within the given timeframe:

- This does not equate to the consent or approval of the participating Ethics Committee;
- It does not allow us to presume the absence of local particularities;
- does not prevent the continuation of the single ethical analysis; and
- This does not preclude the possibility of subsequent communication of risk, complaint or local event. relevant.

If the feedback is received after the deadline but before the final decision, it is recommended that it be considered whenever feasible. Information regarding relevant risk, violation of rights, or need for protection should be received and evaluated at any time, including after the research has been approved.

8.3 Does the silence of the participating CEP (Ethics Committee) mean agreement?

Answer — No. The absence of a response does not prevent the continuation of the single analysis, but it does not equate to agreement nor does it allow us to presume the absence of risks or particularities. local.

8.4 How to proceed in the event of a serious or imminent risk in a center?

Response — Upon becoming aware of the situation, the Ethics Committee (CEP) linked to the participating center may recommend to the institution's management the immediate interruption of activities at that location and must communicate this fact to the responsible Ethics Committee and to INAEPP, as per Dispatch No. 3/2026. The local administrative interruption should not be confused with the ethical suspension of the protocol. This measure stems from the institution's duty of protection and management power. Its effects are limited to the center until the responsible Ethics Committee assesses any potential repercussions on the protocol and other locations.

8.5 How to report to Inaep a possible breach of the single ethical review procedure?

Response — Researchers, participants, sponsors, institutions, Ethics Committees (CEPs), and other interested parties may use the official channels disclosed by INAEPP to report repeated ethical reviews, requirements for second approvals, unfounded documentary requirements, unjustified refusal to receive communications, or other non-compliance. The communication should identify, when possible, the protocol number, the Ethics Committees and institutions involved, describe the facts, and present the available documents. INAEPP may request clarifications and adopt appropriate guidance, supervision, or investigation measures. Communication channels: Email: inaep.fiscalizacao@saude.gov.br and General Ombudsman.

from the SUS – OuvSUS, available at the following link: <https://www.gov.br/saude/pt-br/canais-de-atendimento/ouvSUS>.

9 Transitional provisions and regulatory compatibility

9.1 Are previous resolutions, operational standards, circular letters, and guidelines still applicable?

Answer — Not automatically or entirely. The rules of the National Health Council remain applicable only insofar as they do not contradict Law No. 14,874/2024, Decree No. 12,651/2025, and subsequent rules of INAEP. The absence of express repeal does not maintain the applicability of a provision incompatible with the new regime. The superseded acts and provisions may be subject to express repeal in a process of review or consolidation of regulations.

The provisions that mandate multiple analyses of the same protocol, grant the participating Ethics Committee the authority to issue a second approval, or create steps and requirements incompatible with the single ethical review regime do not apply to multicenter research workflows. The formal revocation of previous acts must occur through a specific instrument, while preserving acts that have already been validly performed.

10 References

BRAZIL. Law No. 14,874, of May 28, 2024. Provides for research with human beings and establishes the National System of Ethics in Research with Human Beings.

BRAZIL. Decree No. 12,651, of October 7, 2025. Regulates Law No. 14,874, of 28 of May 2024.

BRAZIL. Ministry of Health. National Ethics Committee for Research. Order No. 3, of May 29, 2026. Establishes guidelines for the centralized ethical review of multicenter research within the scope of SINEP (National System for Research Ethics).

BRAZIL. Attorney General's Office. General Counsel of the Union. Legal Counsel to the Ministry of Health. General Coordination of Health Affairs. Opinion No. 00392/2026/CONJUR-MS/CGU/AGU, dated April 23, 2026. Guidelines regarding the workflow for ethical review of research protocols in Ethics Committees, in compliance with Law No. 14,874/2024 and Decree No. 12,651/2025.

*What changed in this version (1.1, 06/30/2026):

1. Correction of identification and source.

On page 4 of 25, the figure presented was not correctly identified and referenced; the following were included, respectively:

Figure 1. Role of the local ethics committee in the single ethical review in multicenter research.

Source: Inaep. Image generated by Artificial Intelligence.

2. Punctuation correction

On page 14, in the question "How to process a specific change for a center?"

Where it

reads: "Amendments to the protocol, even those relating to a participating center, must be submitted exclusively by the coordinating researcher..."

It should read:

"Amendments to the protocol, even those relating to a participating center, must be submitted exclusively by the coordinating researcher..."

On page 15, in the question "Do purely registration changes require a new analysis?"

Where it

reads: "No, purely registration changes do not require a new ethical review..."

It should

read: "No. Purely registration-related changes do not require a new ethical review..."

3. Formatting Correction On

page 13 of 25, the question " 5.8 **Can the Informed Consent Form or Assent Form be submitted with open administrative fields?**" was not properly highlighted.

4. Numbering

On page 20 of 25, the item numbering has been changed to the correct sequence from 7.8 onwards.

National Ethics Committee for Research (Inaep)

Technical Report - Single Ethical Review in Multicenter Research Version: 1.1,

February 19, 2026