1. Objective

Provide the administrators with guidelines for the Clinical Trial Authorization Request process as well as a description of the requirements in order to standardize the documentation to be submitted.

2. Range:

Applicable to the clinical trial authorization request process, which is submitted to the OGITT through the INS Documentary Processing Area.

The performance of CE in Peru requires prior authorization through Directorial Resolution granted by OGITT of the INS, under the conditions and under the requirements established by the Clinical Trials Regulation. To do this, consider the definition of clinical trial and investigational product to which the regulation extends:

Clinical Trial (Art. 2 numeral 11 of the REC)
All research carried out in humans to determine or confirm clinical, pharmacological, and/or other pharmacodynamic effects; detect adverse reactions; study the absorption, distribution, metabolism and elimination of one or more products under investigation, in order to determine their efficacy and/or their safety. Research subjects are pre-assigned to the investigational product and assignment is determined by the research protocol.
Product under investigation (Art. 2 numeral 36 of the REC)
It is a pharmaceutical product or medical device that is investigated or used as a comparator in a clinical trial, including products with health registration when they are used or combined, in the formulation or in the packaging, in a different way than authorized, or when used to treat an unauthorized indication, or to obtain more information about its authorized use. For the purposes of this Regulation, the terms "pharmaceutical product" and "medical device" refer to what is stated in Law No. 29459, Law of Pharmaceutical Products. Pharmaceuticals, Medical Devices and Health Products.

3. Abbreviations

- ANM: National Authority for Pharmaceutical Products, Medical Devices and Products Health (ANM), previously known as DIGEMID.
- ATD: Documentary Processing Area of the INS
- CIEI: Institutional Research Ethics Committee
- CT: clinical trial
- FOR: Form
- ICRTP: Acronym in English corresponding to the International Clinical Trials Registry Platform of the WHO: *International Clinical Trials Registry Platform.*

INS : National Institute of Health

- IP: Principal Investigator
- MINSA: Ministry of Health
- OGITT: General Office for Research and Technology Transfer
- ICO: Contract Research Organization

WHO : World Health Organization

- REC: Regulation of Clinical Trials
- REPEC: Peruvian Registry of Clinical Trials
- SIGANET: Integrated Administrative Management System
- TUO: Unique Ordered Text

4. Steps and requirements prior to the process:

4.1. Access to REPEC and registration of the sponsor and its legal representative in the country.

- The Sponsor and the institution that legally represents it in the country (in case of delegation of tasks and functions related to the EC) must be registered with REPEC. The requirements for the Sponsor Registration and Contract Research Organization (OIC) registration procedures are available on the REPEC website: http://www.ensayosclinicos-repec.ins.gob.pe

• Once registered, the sponsor and/or the OIC can request that the user account be generated from the REPEC website.

4.2. Approval by the Research Institution and by an Institutional Research Ethics Committee (CIEI) accredited by the INS.

- Prior to requesting the authorization of the CB, the following must be obtained: 1) The approval of the execution of the clinical trial by the Research Institution that houses the research center where the study is planned to be carried out and 2) the approval by the CIEI with valid accreditation.
- The approval documents of both entities must follow the guidelines established by the INS (See section 6 of this guide, literals c and d).

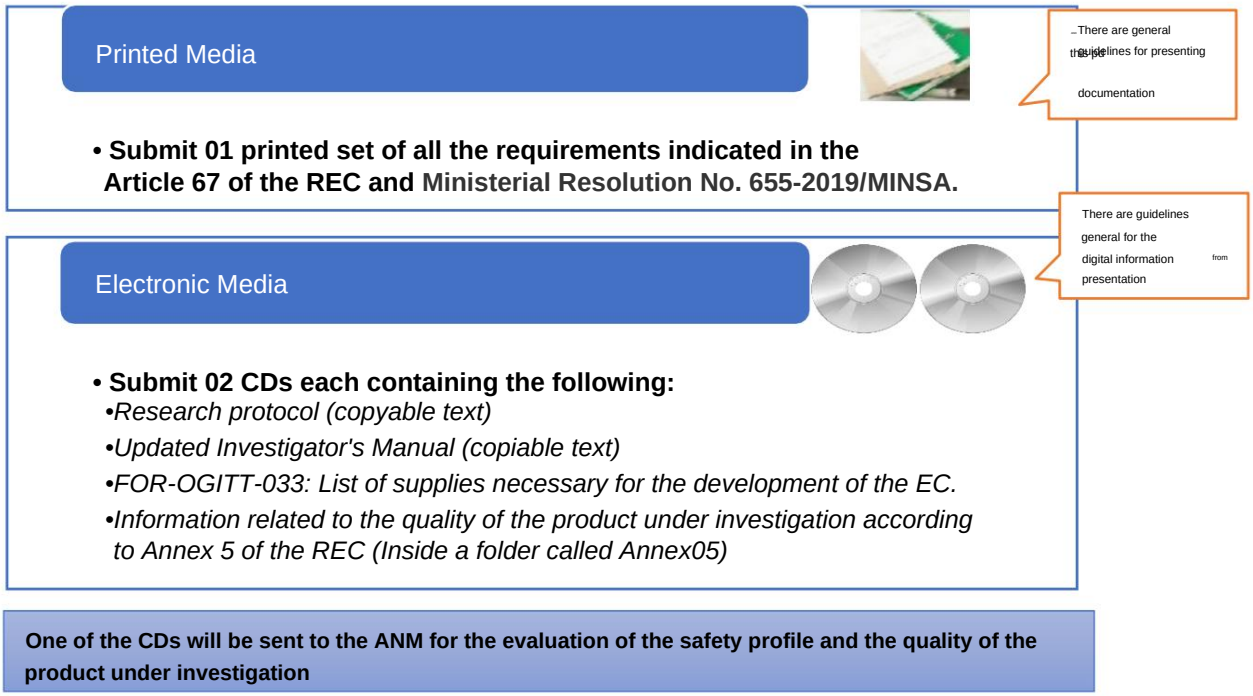
4.3. In the case of investigational products that are manufactured in the country.

- These products, for their use in the scope of a clinical trial, must have a manufacturing authorization issued by the ANM. (Article 90 of the REC)

5. Presentation of the file:

ÿ The provisions of the ***General Guidelines Guide for the presentation of procedures related to the regulation of clinical trials*** **VERY IMPORTANT**

ÿ There is documentation that must be submitted in printed and electronic version, as follows:



6. Description of the requirements for this procedure.

ORDER a)	REQUIREMENT	REQUIREMENT DESCRIPTION
	Request for authorization of the clinical trial, according to the registration form established in the REPEC (Peruvian Registry of Clinical Trials) that includes information on the proof of payment.	- Corresponds to **FOR-OGITT-028:** Clinical trial authorization request, which is available through REPEC and must be completed electronically. - The name or company name of the sponsor and its legal representative in the country, registered in the REPEC, must coincide with the company name indicated in all the documentation of the file presented. - Once the process is completed, the information provided in this form will be visible internationally through the WHO International Clinical Trials Registry Platform (ICRTP), of which REPEC is a member. Therefore, proper entry of information is required. - Failure to complete the information requested in the FOR or place: *"See in the protocol"* or other similar text will be subject to observation. The payment for the processing fee includes the evaluation of 01 research center. If additional research centers are proposed, a payment must be made for each of them.
b)	Copy of the approval document issued by the legal representative of the research institution(s) where the clinical trial will be carried out according to the model established in the Clinical Trial Procedures Manual.	This document must comply with the guidelines established in the **Manual of Clinical Trial Procedures:** Guide for the presentation of the approval document issued by the Research Institution where the clinical trial will be carried out.
c)	Sworn statement according to the model established in the Manual of Procedures for clinical trials, signed by the sponsor and principal investigator, which establishes that there is no financial conflict of interest in the execution of the clinical trial.	- Corresponds to **FOR-OGITT-063:** Sworn statement by the Sponsor and Principal Investigator Send original document, duly signed, having to record the surnames and names according to how they appear on the respective DNI. - A form must be completed for each proposed research center. Verify that the data entered regarding the RCI, name of the institution and research center, title of the EC, as well as the establishment's categorization resolution number and its RENIPRESS number are correct.
d)	Sworn statement signed by the sponsor and principal investigator on the conditioning of the research center where the clinical trial will be carried out according to the model established in the Manual of Clinical Trial Procedures.	- Corresponds to **FOR-OGITT-064:** Affidavit on conditioning of the research center Send original document, duly signed, having to record the surnames and names according to how they appear on the respective DNI. - A form must be completed for each proposed research center. Verify that the data entered regarding the RCI, name of the institution and research center, title of the EC, as well as the establishment's categorization resolution number and its RENIPRESS number are correct. - Regarding the Conditioning section of the research center, in the case of research centers located in health establishments

		of the first level of care (categories I-2, I-3 and I-4) must comply with the provisions of article 57 of the REC. To support what is stated in literal b), the following must be documented: • Have a professional trained in cardiopulmonary resuscitation • Current agreement with a higher level health facility within a nearby area for emergency care and hospitalization of research subjects, as well as the current agreement for the transfer of research subjects to said establishment. - The presentation of the indicated documentation does not presume the conformity of the research center by the OGITT. Depending on the nature of the study, other requirements may be requested (art. 53 of the REC). Likewise, the OGITT will evaluate all the considerations of the research study so that the benefit-risk balance is favorable for the research subject. (Article 57 of the REC).
and)	Copy of current insurance policy (Insurance contract) acquired by the sponsor.	Submit complete documentation of the contracted policy according to the definition indicated in number 34 of article 2 of the REC. Check, among other things, the validity, if the coverage includes the EC and that there are no exclusions that contravene what is indicated in the REC.
f)	Sworn statement from the sponsor that they have a financial fund that immediately guarantees free care and treatment under investigation, in the event of any adverse event of the clinical trial, as long as the insurance policy is activated and according to model established in the Manual of Clinical Trial Procedures.	Corresponds to **FOR-OGITT-029** Sponsor's sworn statement that it has a financial fund. The amount earmarked for the financial fund is different from the amount indicated in the contracted insurance policy coverage. The amount to be considered will be established by the sponsor based on the number of subjects to be included in the country and the possible risks of adverse events.
g)	Research protocol in the Spanish version and in the original language if it is different from Spanish, and Informed Consent Form(s), according to the respective Annex 1 and Annex 4, of the Clinical Trials Regulation, approved by the CIEI accredited by the INS, also attaching to each of them a copy of the approval document issued by the respective CIEI, according to the model established in the Manual of Clinical Trial Procedures. These documents are presented in electronic (PDF format to copyable text).	The protocol must include the information indicated in **Annex 1 of the REC:** Guide for the research protocol The Informed Consent Form (FCI) must contain the information indicated in **Annex 4 of the REC:** Guide for the informed consent form. The approval document must comply with the guidelines established in the **Manual of Clinical Trial Procedures:** Guide for the presentation of the research protocol approval document and the informed consent form(s) issued by the CIEI. The documents are presented electronically (PDF format to copyable text). The Informed Consent Forms must be approved and sealed by the CIEI (must contain the CIEI seal)

h)	In the case of a foreign sponsor: Copy of the proof of the delegation of functions to the representative of the sponsor, duly apostilled, otherwise legalized by the Ministry of Foreign Affairs of Peru.	- The document must be legible in order to display data of the foreign company (business name, trade name, registration number), record the names of the authorized legal representative who signs the document, and their position within the organization. - Data of the national company to whom the power of attorney will be granted (company name, commercial name, RUC number), data of the person to whom the power of attorney will be granted (names, surnames and DNI). Likewise, it must be indicated if this company is considered its subsidiary or branch and/or another. Specify whether it is empowered to channel all communications to the OGITT of the INS for the duration of the execution of the EC. - If activities or tasks related to a CE are legally transferred, they must be clearly defined in order to prevent others from being carried out that are not known to the sponsor, who is the one who assumes the responsibility of the CE (initiation, maintenance, conclusion and financing).), considering the validity of the document, the delegation must be within the framework of the Clinical Trials Regulation, the related standards and the respective international standards. - Consign express powers to register the sponsor, change the sponsor's name, withdraw the claims of the procedures related to the EC authorization and to file administrative appeals (reconsideration and appeal), if applicable. - The document is not older than 90 calendar days and it is mandatory to attach the translation into Spanish. - The delegation of functions indicated in this document must serve as input for the registration of information of numeral 3 of FOR-OGITT 028 (Responsibilities). - If the sponsor is local and legally transfers any or all of its tasks and functions related to the EC to another institution in the country, a copy of the proof of delegation of functions must also be submitted (the Hague Apostille does not apply in this case).).
i)	Updated Investigator's Manual, in Spanish version and original language if different from Spanish. This can be replaced according to the conditions	- Consider the provisions of **Annex 2 of the REC:** Investigator's Handbook - This document must be validated and updated regularly by the sponsor, at least once a year.

	indicated in Annex 2 of this Regulation. These documents are presented electronically (PDF format to copyable text).	year. - In the case of products under investigation that have a sanitary registration in Peru and are used under the conditions of use authorized by the ANM, the Investigator's Manual may be replaced by the authorized technical data sheet. - In the case of investigational products that have a sanitary registration in the country and when the investigational product is used in conditions other than those authorized by the ANM, the authorized insert will be provided, together with the **scientific information that justifies the use of the** product. **investigational product under test conditions.** - These documents are submitted electronically (PDF format to copyable text).
j)	Information related to the quality of the (electronic research product in accordance with Annex 5 of this Regulation.	Consider the provisions of **Annex 5 of the REC:** Information related to the quality of the research product to be submitted as part of the requirements for the authorization of a clinical trial
k)	Detailed national total budget of the clinical trial, according to the model established in the Manual of Clinical Trial Procedures.	- Corresponds to **FOR-OGITT-032:** Total Budget detailed national clinical trial. - Send original document, duly signed, and must include the full names and surnames, according to how they appear on the respective DNI.
l)	List of supplies necessary for the development of the trial according to the format established in the Manual of Clinical Trial Procedures.	- Corresponds to **FOR-OGITT-033:** List of products and supplies to be used in the clinical trial. - Send original document, updated, with date and corresponding signature. Consign the surnames and names according to how they appear on the respective DNI. - Take into account that this document will be sent to the ANM together with the information on the quality of the product under investigation for the purposes of the binding technical opinion. Therefore, the information consigned in this FOR must be consistent with the quality information sent. - If you consider the coding system, it is essential to attach the respective description, duly signed by the sponsor or its legal representative in the country. - Assess whether the quantity of the FOR-OGITT-033 investigational product (IP) (including comparators) is reasonable, considering the duration time, number of patients to enroll, number of investigation centers, number of doses per patient, stock reservation, expiration date of the products, among others.
m)	Documented life updated no curriculum of the entire research team of each research center, according to the model established in the Manual of Trial Procedures Clinicians, attaching a copy of the documents that prove training in Good Clinical Practices and Ethics in Research in human beings of the entire research team, with a validity not	- Corresponds to **FOR-OGITT-031:** Curriculum vitae of the research team - Send original document, updated and signed. - Regarding numeral 6: information regarding the availability of time to conduct the clinical trial: • The information to be included in this section can be presented in tables at the discretion of the professional. • If the PI does not have active studies (neither as principal investigator or sub-investigator), indicate:

	more than three (3) years old.	"The Researcher has no active studies" • It will be considered an "active clinical trial" until it has been submitted to the OGITT of the INS, the Closure of the Research Center or the Final Report of the Research Center for said study.

7. Presentation of additional documentation during the process.

7.1. At the time of submitting the request, the administrator may attach to the file additional documentation to that required in article 67 if they consider that it may be useful in the administrative management of their procedure.

7.2. Regarding the incorporation of additional documentation requested by the OGITT and/or the ANM:

• Once the process has begun, the OGITT may request additional documentation based on the observations noted in the evaluation carried out by the OGITT and/or the ANM.

These observations will be communicated by the OGITT by official letter.

- The administrator must respond to said observations in a single opportunity, presenting the requested documentation within a maximum period of 30 business days from receipt of the official letter.

- In cases where there is a material impossibility duly justified by the company to fully comply with the request, the OGITT may extend the term, provided that the extension request is made before the expiration of the granted term.

7.3. Regarding the incorporation of additional documentation that has not been requested by the OGITT of the INS or the ANM, once the process has started:

- The evaluation of the file by the OGITT and the ANM is carried out based on the documentation presented by the company. It is presumed that this corresponds to current and complete information regarding each of the requirements contemplated.

• Once the process has started, new information about the product under investigation or the clinical trial protocol could be available (and that the administrator did not know at the time the process was started). Some examples of information that is considered

relevant are:

- New version of the clinical trial protocol
- New version of the investigator's manual
- New documentation corresponding to annex 05 of the REC
- New List of supplies necessary for the development of the clinical trial,

that modifies aspects linked to Annex 05 of the REC.

- Pursuant to the provisions of article 40, paragraphs d) and e) of the REC, it is the responsibility of the sponsor to communicate this information to the OGITT. A printed and electronic version (on CD) should be submitted as soon as possible. If this additional information corresponds to information on the safety and/or quality of the product under investigation, a copy in an additional electronic version (on CD) must be attached to be sent to the ANM.

- According to the information submitted, the term for the evaluation of said documentation may be extended for up to 30 business days for the OGITT of the INS and/or the ANM; as appropriate. However, the administration, taking into account the complexity of the additional information presented, will resolve the request in the shortest time possible.

8. Oral presentation of the investigational product

8.1. On a voluntary basis, the sponsor or its legal representative in the country may consider making an oral presentation of the investigational product within the authorization process of a clinical trial. These meetings will be expository and will be attended by representatives of the OGITT Evaluation Team and the ANM.

8.2. This meeting must be requested by means of a written document addressed to the General Directorate of the General Office of Research and Technology Transfer or by mail consultaensayos@ins.gob.pe

8.3. The OGITT will communicate through said mail, indicating the date and time of the scheduled meeting according to availability.

8.4. The duration of the presentation is 20 minutes and must contain at least the following aspects:

- Summary of the clinical trial protocol, how the investigational product will be administered and in which countries the clinical trial will be carried out.
- Description of the product under investigation (physical and chemical properties, formulation and dose, mechanism of action route of administration.
- Results of preclinical studies (results of pharmacological safety studies, clinical findings in single dose and repeated dose toxicity studies, reproductive and developmental toxicity, or others that are applicable).
- Pharmacokinetic parameters evidenced in clinical trials (life time mean, AUC, Cmax, metabolism and elimination.
- Efficacy and safety results (studies carried out, adverse events recorded according to age, sex, drug dose, with emphasis on those related to the investigational product).

9. Attention to queries and document reception hours

9.1. Inquiries can be sent to the email consultaensayos@ins.gob.pe, specifying the procedure: *"EC Authorization Request "*, the file registration number (according to SIGANET) and the EC number.

9.2. To request a meeting with the OGITT team write to the email: consultaensayos@ins.gob.pe indicating: a) meeting agenda and b) list of people who will attend. You can attach in the mail, any relevant information for purposes of the meeting. Your request will be evaluated by the OGITT and will be subject to availability. A response email will be sent to you. If you require the participation of the ANM team in the meeting, indicate it in your request.

9.3. Document reception hours at the ATD are from Monday to Friday from 8:00 am to 4:15 p.m.