

RDC 39, June 05, 2008

Approves the RULES FOR THE CONDUCT OF CLINICAL RESEARCH among other provisions

The Collegiate Directors of National Health Surveillance Agency (ANVISA), in the use of the award on him by item IV of art. 11 of the Regulation approved by Decree No. 3029 of April 16, 1999, and in view of the provisions of section II and in paragraphs 1 and 3 of art. 54 of the Rules of Procedure adopted in accordance with Annex I of the Ordinance No 354 of ANVISA, from August 11, 2006, republished in DOU of August 21, 2006, at a meeting held on June 3, 2008, and

considering the need to update the documentation required for carrying out clinical research in Brazil;

considering the need to refine the list of documents required for the licensing of imports of medicines and products for exclusive use in clinical research;

considering Article 24 of Law 6360 of September 23, 1976 and Article 30 of Decree 79,094 of 05 January 1977;

considering Article 40 of Ordinance No. 354, August 11, 2006, which lists the functions and powers of the General Management of Drugs (GGMED), especially in your item IX

considering the Resolution RDC No .222, from December 28, 2006, and considering the resolutions of the National Health Council No. 196, October 10, 1996, no. 251, August 7, 1997, No. 292, July 8, 1999, and No. 346, January 13, 2005;

considering the guidelines of Good Clinical Practice in accordance with the Document of the Americas, document resulting from work of the Pan American Health Organization / World Health Organization

adopts the following resolution of Collegiate Directors and I, Director-President, determines its publication:

Article 1: It is the resolution adopted by this: "RULES FOR THE OBTAINING OF CE (Approval Document) FOR THE CONDUCT OF CLINICAL RESEARCH on national territory" and its annexes.

Article 2: The sponsor is defined as individual or company, public or private, which financially supports the research.

Article 3: In addition to the provision of financial resources necessary for the conduct of clinical research in the centers located in national territory, are tasks of the sponsor:

- (a) implementation and monitoring of clinical research;

- (b) ensuring the proper conduct of the protocol approved in advance by the relevant regulatory authorities;
- (c) the accuracy of the collected data and other tasks involving the security of "Good Clinical Practices";
- (d) the reporting of serious adverse events to ANVISA (NOTIVISA - SYSTEM INFORMATIZED WHICH RECEIVE REPORTS OF ADVERSE EVENTS).

§ 1º - In clinical studies regulated by this rule and are sponsored by national or international agencies to promote the research, philanthropic entities, non-governmental organizations (NGOs) or other non-profit organizations, it is assumed that investigator is responsible for coordinating the search for ANVISA assumes the role of representative of the sponsor, if there is a ORPC responsible for the conduct of it, should meet as a representative of the same for all the obligations contained in the main body of this article.

§ 2º - In the case of independent studies, for which the investigator has no financial assistance from a specific sponsor, including cases in receiving the medicines of research in the form of donation where the donor does not want to be characterized as a sponsor of the study, the researcher additionally assume the responsibilities set out in the main body of this article.

§ 3º - For the cases referred to in the preceding paragraph, the researcher is now called "investigator-sponsor."

§ 4º - In the cases above, all centers of the same protocol of clinical research should be subject to notification or inclusion of research center.

Article 4: It is understood Contract Research Organization (CRO) like every company regularly installed in national territory hired by the sponsor or the investigator-sponsor, which takes partially or completely, the role of the sponsor of clinical research.

§ 1º - All powers delegated to CRO`s employed by the sponsor or the investigator-sponsor must appear in an agreement and / or detailed contract, dated and signed by both parties.

§ 2º - The veracity of the information contained in the agreement are the responsibility of both parties.

§ 3º - The CRO`s must comply with all health standards relating to the conduct of clinical trials, as well as other rules, under Brazilian law.

§ 4º - For sponsors not legally established on national territory, the CRO hired will be responsible for all the tasks of the sponsor of clinical research.

§ 5º - ANVISA is responsible for the registration and regulation of the activities of CRO`s, regarding the conduct and monitoring of clinical trials regulated by this rule.

Article 5: This rule applies to all clinical research with drugs and medical devices (research involving therapeutic interventions or diagnostic not registered in Brazil) phases I, II and III and it may subsidize, in ANVISA, the record or any change post-

marketing, considering the current health standards and for which it requires the analysis of ANVISA and subsequent issuance of CE (Approval Document).

§ 1º - The post-marketing studies (Phase IV) are not primary object of this rule and are subject to the "Notification on clinical research – Class 1". It is established that the initiation of these studies should occur only after obtaining approval from the ethics in accordance with the law.

I - Except from the above provisions, the search for phase IV involving vaccines and research that aimed to evaluate effectiveness and safety for drugs wich have authorization for marketing or revalidation of it, being regarded as the phase III.

§ 2º - Clinical research involving medical devices that fall in classes I and II (RDC/ ANVISA No. 185/2001) are subject to the Notification in Clinical Research - Class 2. For products framed in class III and IV of medical devices, are subject to the assessment in Clinical Research.

§ 3º - Clinical Research involving dietary interventions wich don't have authorization for marketing as a food product, be subject to "Notification in Clinical Research - Class 3".

§ 4º - Clinical Research framed in any of the conditions described in previous paragraphs, but involving procedures for import and / or export, will be subject to "Notification in Clinical Research - Special Class" and issue, within 30 working days from the date of receipt of notification by the competent field of ANVISA, a Special Approval Document (CEE).

§ 5º - The Researches evaluated by other regulatory bodies, like the National Biosafety Technical Commission (CTNBio), the Management Board of Genetic Heritage (CGEN), and others, involving procedures for import and / or export shall be subject to "Notification in Clinical Research - Class 4 ". Fall is here the observational and epidemiological surveys involving procedures for import and / or export.

§ 6º - The research supported under the same conditions mentioned in the preceding paragraph, but not involving import procedures and / or export, shall not be subject to this rule.

Article 6: This rule does not apply to studies of Bioavailability and Bioequivalence.

Article 7: Repealing the resolution RDC No 219 of September 20, 2004.

Article 8: Concepts

a) Investigator's Brochure - compilation of clinical and non-clinical data about the investigational products, relevant to their study in human beings.

b) National Independent Ethics Committee (CONEP) - affiliated authority, of consultative, deliberative, regulatory, educational, and independent nature, connected to the National Health Council, created in accordance with Resolution CNS 196/96;

c) Independent Ethics Committee (IEC) - Interdisciplinary and independent affiliate, with “public function”, of consultative, deliberative, and educational character, registered with the National Independent Ethics Committee (CONEP) in accordance with Resolution CNS 196/96, created to defend the interests of research subjects regarding their integrity and dignity and to contribute to the development of researches within ethical standards.

d) Special Communication (SC) - Authorizing document, issued by the New Drugs, Research and Clinical Trial Management - GEPEC, that allows the execution of the research protocol, in a certain Research Site and, whenever the case, the import of the product(s) involved in the protocol;

e) Request Form for Consent in Clinical Trial - Document standardized by ANVISA on which the interested party requests consent for the execution of a clinical trial and presents information on the product(s) to be used.

f) Research Institution - public or private organization, legally organized and qualified, where the clinical researches are performed. For the purposes hereof, the term “Research Site” is used as a synonym of “Research Institution”.

g) Import license (IL) – it is the act required to the goods subject to non-automatic licensing and electronically requested by the importer or its legal representative, through SISCOMEX;

h) Clinical Trial - Any investigation in human beings, with registered products or products to be registered, with the purpose of finding or verifying the pharmacodynamics, pharmacokinetics, pharmacological, clinic and/or other effects of the product(s) investigated, and/or identifying the adverse events to the investigational product(s), assessing its safety and/or efficacy.

i) Researcher in charge - person in charge of the coordination and performance of the research in a certain center, and for the integrity and well-being of the research subjects, after the signature of the Informed Consent Form, with respect to the maintenance of the ethical criteria for all procedures during the course of the study. For the purposes hereof the terms “Responsible Researcher” and “Responsible Investigator” are synonyms;

j) Research protocol - Document covering the description of the research in its essential aspects, information related to the research subjects, to the qualification of the researchers and all responsible authorities;

k) SISCOMEX - Integrated Foreign Trade System;

Article 9: This resolution enters into force on the date of its publication.

ANNEX I

REGULATION FOR PREPARE DOSSIERS AND OBTAINING APPROVAL DOCUMENT (CE) FOR THE CONDUCTION OF CLINICAL RESEARCH WITH DRUGS IN NATIONAL TERRITORY

Article 1: The dossier of submission for ASSESSMENT IN CLINICAL RESEARCH should be composed of the following documents:

I - Document 01: Application forms, FPP1 and FPP2, duly completed, originals, for all investigated products and qualitative information of comparator that will be used in research, as the models in Annexes IV and V of this resolution.

II - Document 02: Letter forwarding the Protocol of Clinical Research, signed by the legal representative of the sponsor or investigator-sponsor, together with the Application Form in Clinical Research (FPPC), Annex VI, stating:

- a) Title of Research and the code of protocol (if any), showing the date and its version;
- b) Name and number of the Register of Individual (CPF) of the Principal Investigator responsible for conducting the study in each sought center;
- c) Research center(s) in which a clinical trial will be conducted, accompanied by the status of approval or not by their ethics committee and the number of National Register of Establishment of Health (CNES); research centers related to another institution (hospital or clinic), can use the CNES number of their entity;
- d) Number of subjects expected in the research, overall, in Brazil, and in each center in the national territory;
- e) Ethics committee responsible for ethical approval of the protocol joined to CONEP (1st Center), as model in Annex VI of this resolution.

III - Document 03: Declaration of Responsibility and Commitment signed by the legal representative of the sponsor or the investigator-sponsor, as form available in Annex II of this resolution.

- a) In case of sponsors not placed in Brazil, it is also requested the Declaration of Responsibilities and Commitment of the CRO responsible for conducting the study in Brazil.
- b) Dossiers send to ANVISA by CROs should submit certified copy of the agreement (contract or statement), writing, dated and signed by the CRO and sponsor of the research, which should contain the delegations and distribution of tasks and obligations of each party.

IV - Document 04: Budget for research, presenting in detail the resources allocated for its implementation, detailing spending on medical visits and other health professionals, hospital materials, examinations subsidiary (among other things, radiological and laboratory), various equipments and payment for research centers.

V - Document 05: Proof of Deposit Health Surveillance Rate (TFVS) in accordance with the law. Will be allowed through collection of the same TFVS, the notification of new centers of research and / or alteration of centers already reported, within a period of

up to 06 (six) months from the date of submission of the primary application. Exceeded this period, is necessary to petition the subject: "Inclusion of Research Center", with the necessity of a new collection of TFVS. For the "Assessment in Clinical Research", it is requested the original proof of payment of TFVS. And, when applicable, the proof of exemption from payment of TFVS - GRU.

VI - Document 06: Consolidated written opinions of the latest version of the Clinical Protocol and of the Informed Consent by the Ethics Committee responsible for the coordinator center of the study. The remaining consolidated written opinions entered by the others Ethics Committees, which centers were listed in the ASSESSMENT IN CLINICAL RESEARCH dossier, should be send to ANVISA as they are issued.

a) The analysis, the study authorization and issuance of the CE (Approval Document) by ANVISA is linked only to the ethical approval for the coordinator center. Thus, the issue of the CE is not linked to the presentation of the letters of approval by other ethical committees. However, the beginning of the research in the others centers should occur only after the receipt of ethics approval in accordance with the law.

b) The Ethics Committee(s) responsible for assessment the protocol must be duly registered in CONEP. The evidential document should be available for inspection at the research renter, as well as the list of members of the Ethic Committee in the time of approval of the protocol.

c) The update of the list of centers on the Approval Document (CE) does not depend on presentation of the document 06 in cases of "notification" or "inclusion" of research centers. It is established that the beginning of the study in these centers should occur only after obtaining ethical approval, in accordance with the law.

VII-Document 07 – Letter of approval of the Protocol by CONEP, to be send to ANVISA when available, when applicable. The issuance of the Approval Document (CE) by ANVISA is not linked to the presentation of this document, but the beginning of the research can only happen after the receipt of all relevant ethical approvals.

VIII - Document 08: Protocol of Clinical Research in Portuguese.

IX - Document 09: Letter of Commitment of the Investigator (for each research center) - declaration signed and dated by the investigator responsible for conducting research in the center, in which he undertakes to follow the proposed protocol, comply with applicable regulatory requirements, Good Clinical Practices and Good Laboratory Practices, ensuring, at all times, the rights, safety and welfare of subjects under his responsibility (Annex VIII).

X - Document 10: Declaration of infrastructure of the center(s) necessary for the development of the research, with the concordance of responsible of the institution.

XI - Document 11: Informing the state of registry of drug and / or product in ANVISA and in other countries

XII - Document 12: Summary information about the conduction of the research in Brazil and in other countries, listing all the countries participating in the study,

estimated date for start and end of the research and an estimative for inclusion of subjects in each country in the research.

For studies conducted only in Brazil, the document will provide the above information on local centers, including the number of centers and subjected estimated, expected date for starting and finishing the search.

XIII - Document 13: *Curriculum vitae* of the principal investigator available on the “Lattes Platform” and list of clinical research team, with their expertise and roles to play in the clinical trial

XIV - Document 14: Brochure of Investigator, for clinical trials of phases I, II and III, and / or the directions of use of the product, in the case of clinical trials in phase IV (where applicable), containing information about the product and having its suitability the stage of development according to current Good Manufacturing Practices (chemical name, chemical formulas and / or structural, pharmaceutical and physical properties of the molecule-chemical or molecular entity, including description of the (s) formulation (s) of the strength of Specific conditions for storage and handling, tables with data from studies of stability (achieved by then), and observance of Good Manufacturing Practices) by providing light through scientific results obtained in previous phases, including pre-clinical, placing the emphasis on safety Toxicity, adverse events and efficacy / effectiveness of the product.

a) Because of the inherent characteristics of biological medicines due to their way of obtaining, must be submitted compared with controls in specific cases between hands produced in different scales, including stability, production and controls

XV - Document 15: When applicable, to present the estimative of the quantity of drugs and all other products that are imported to all participating centers, justifying its quantitative, considering the information provided in the protocol, as the steps of the research, the number of subjects provided, the duration of each stage, and daily dosage, as form set out in Annex VII of this resolution.

Single paragraph: Quantitative changes resulting from changes in logistics in a clinical trial should be sent to ANVISA. The amendments require approval of the Ethics Committee or the National Commission on Ethics in Research must be submitted with necessary approvals held by these entities

XVI - Document 16: Provide documentation concerning the control of transmission of Transmissible Spongiform Encephalopathies (TSEs), according to the existing health standards or justify the exemption of this document.

a) If the lot to be imported is the same as the petitioner, after release of the Approval Document (CE) simply submitting a statement confirming this fact when seeking permission for import licenses, since such certificates TSE were evaluated and considered valid for this batch manufactured with such ingredients.

b) In cases of new batches, it is necessary to submit certificates of safety with respect to the TSE.

XVII - Document 17: Request Form of Import Licensing. Fill the Request Form of import licensing as model in Annex III of this resolution. Submit this document along with the process of Approval in Clinical Trial or separately after the issuance of the Approval Document (CE), is at the discretion of the Sponsor. If this form will be submitted to the process of Clinical Trial, this will be considered along with the process, and due authorization of the board SISCOMEX will be granted with the permission of Clinical Trial.

XVIII - Document 19: For confirmation of therapy studies (Phase III) present proof of the clinical trial is listed in the database for registration of clinical trials International Clinical Trials Registration Platform / World Health Organization (ICTRP / WHO) or other recognized by International Commit of Medical Journals Editors (ICMJE).

Article 2: The dossier for obtaining the Approval Document (CE) must be accompanied by a copy on CD-ROM (PDF file, Word or "open documents").

§ 1º: ANVISA is responsible for security and maintenance of confidentiality of any information contained on the CD-ROM.

§ 2º: The electronic documents should allow textual search.

§ 3º: The sending of the copies of documents on CD-ROM applies to the adoption, by ANVISA, the tools of information technology enabling the electronic submission of documents requested.

Article 3: For the "Notification of Clinical Trial Center" and "Inclusion of Clinical Trial Center" present the documents I, V, IX, X, XIII, and the title page to certify the submission to the Ethics Committee of the center.

§ 1º: The letter of approval of the Protocol by the Ethics Committee for center(s) to be included and / or notice should be sent when issued by competent authority ethics. The update of the Approval Document (CE) independent of submission of this document. It is conditioning the beginning of the study at the center after due approval of ethical bodies.

§ 2º: In the cases provided in Art 3, Paragraph 1, for the inclusions and notifications center of clinical trial is requested all documents for ASSESSMENT IN CLINICAL RESEARCH, except the documents VI, VII, VIII, XI, XII, XIV, XVIII. The procedure for importing may done centrally by the coordinator center or subsequently by individual centers.

Article 4: For "Notification in Clinical Research" is required to produce documents I, II, III, VI, IX, X, XI, XIII, XV, XVI, XVII, a summary of the protocol of clinical research, including population, rationale, objectives, design, number of subjects, parameters for evaluating efficacy and safety, and statistical considerations, and the title page of the Ethics Committee responsible for examining the submission of the center.

§ 1º: If the study in question do not receive the ethic approval, the manager of the study will resubmit the products and medicines to the country of origin or destroy them on national territory and sending document to certify that such action to ANVISA

Article 5: Amendments to the protocol of Clinical Research subject to approval by the Ethics Committee should be sent to ANVISA by the sponsor or his legal representative with a copy of the document certifying its approval by the ethics entity, if applicable. Such amendments must be accompanied by a copy on CD-ROM (PDF file, Word or Open Documents).

Article 6: The initial request of the Import Licensing (LI) should be send to ANVISA and must comply with all other existing health determinations by completing a form, as model in Annex III of this resolution.

§ 1º: For subsequent boarding permissions, the approval of the LI will occur at the site of the resourcefulness of the products by presenting the Approval Document (CE), if there is no change in batch and / or quantity;

§ 2º: The LI's number, quantity and date of authorization for each shipment will be informed in the progress reports, as provided in Article 7 of Annex I of this resolution.

§ 3º: the Import Licensing (LI) can be requested by presenting a list of all products from the same batch necessary for the conduct of research centers across the petitioner, according to estimates reviewed and approved by the competent field of ANVISA. The quantity could be imported at once, in this case should be noted the "single LI" in Annex III or by means of various commitments of shipment until the agreed amount is reached.

§ 4º: In cases where there is a quantitative change in or modification of lot, the notification of change in quantitative or notification of a change of lot must be sought from the competent field of ANVISA responsible for the research protocol, along with the documentation provided to control the TSE, according to existing law, prior to submission of a new LI.

§ 5º: Repeals are items 1, 1.1, 1.2 and 2, 2.1, 2.2 and 2.3 of Annex XXXII of the DRC / ANVISA No. 350, 2005.

Article 7 : The sponsor, or investigator-sponsor, or ORPC should petition the ANVISA reports on the search (referring to the protocol in question and not by individual research center), on an annual basis and a final report, which may be made up to 90 days after the closure of the research in Brazil;

§ 1º: The “not protocolization” of the annual reports causes the immediate cancellation of the Approval Document(CE) and LI's petitioner.

§ 2º: For purposes of counting of time dealing with the main body of this article, it is considered as a starting date, which was issued in the first Approval Document(CE) of the study.

Article 8: For the adoption of a clinical research concerning the technical and scientific aspects and the issue of the Approval Document(CE), the technical area of ANVISA shall review the matter, except for the cases of Notifications is in Clinical Research set out in paragraphs 1, 2, 3, 4 and 5 of Article 5 of this standard and may, at any time, even for the notifications above, ask the search for more information, including data on the safety and efficacy of the product under test, or, clarification of controversial information or who manage technical questions.

§ 1º: In the case of multicenter studies, the ANVISA had a single Approval Document(CE), covering all approved centers, provided they complied with all determinations specified in the existing loads. The EC will be updated when the "Notification of Research Center" and / or "Inclusion of Research Center."

§ 2º: The ANVISA may, during the passing of a clinical research, request more information on those responsible for its implementation or monitoring, and conduct inspections at the centers petitioner, noting the degree of adherence to current Brazilian legislation and the Practice Clinics (Document of the Americas in Good Clinical Practice).

Article 9: The approval of research involving new drugs and / or innovative, not registered in Brazil, developed and manufactured in Brazil, will take on submission of the notification of manufacturing lots of special intended exclusively for clinical research.

Article 10: If a sponsor or a particular ORPC, during the search, delegate or transfer to another ORPC the execution of specific tasks, must be protocolized in ANVISA, in the form of an addition, the agreement reached between the shares involved, or the declaration of delegation of responsibilities, which must be clearly the duties of each part involved.

Single paragraph. For cases where transfer of responsibility occurs, the initial process should be canceled and a new dossier should be protocolized on behalf of the new responsibility.

Article 11: In cases of merger, acquisition and / or divisions of companies it is requested copies of all documents related to corporate operations, provided that all interference with the pre-existing legal structure of the new company and the presentation of a new statement of responsibility signed by the parties involved.

Single paragraph: This request has no ties to the subject of petition "Transfer of Ownership," and is not subject to deliberation by the area competent in matters of clinical research if approved by the Board on Economic Defense (CADE).

Article 12: The notification of adverse events in clinical trials under this rule must be conducted via NOTIVISA.

§ 1º: should be reported serious adverse events, possible, probable or definitely related to the product (s) (s) in trial, the investigator-sponsor and / or the sponsor occurred in national territory;

§ 2º: The controller by the research in ANVISA must notify, from knowledge of fact, this events within 15 business days, except for cases involving death is the subject of the research, where the notification must occur in seven days,

Article 13: Omission cases will be resolved in light of other national and international guidelines (Document of the Americas for Good Clinical Practice) and will be addressed by the industry for research and clinical trials of ANVISA.

Article 14 Penalties: Failure to comply with the provisions of this resolution leads to health violation, the violator shall be subject to penalties stipulated in Law 6.437/77.

§ 1º: Depending on the report of its inspection, the analysis of adverse events reported, or that information will become available, the ANVISA can determine the temporary suspension of research, suspension of research activities of the clinical investigator involved in inappropriate conduct of a protocol Search, or even the eventual cancellation of a clinical research at the center in question or at all centers in Brazil. Based on these data, the ANVISA can also notify other relevant organs (such as the Federal Council of Medicine and the National Health Council) and maintain a list of centers not recommended.

§ 2 º:It is characterized as very serious infraction health, the research whose activities have occurred before the due approvals health and / or ethical, with the investigator and the sponsor of suspended its activities along the ANVISA and subject to penalties stipulated in Law 6.437/77.

ANNEX II

STATEMENT OF RESPONSIBILITY AND COMMITMENT TO SPONSOR FORM

STATEMENT FORM National Health Surveillance Agency Researches, Clinical Trials, New Drugs and Biologics Management - GPBEN Coordination of Research and Clinical Trials - CEPEC Sponsor Declaration					RDC 39/2008 Note: The search can be initiated only after the approval and issuance of ethics CE.
1. Sponsor's name:					
2. Sponsor's address:				Telephone:	
3. Name of Product or Product Study:					
4. Indications:					
5. Multicentre Trial <input type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> International <input type="checkbox"/> National Top of the planned survey in Brazil : _____ (month / year) Termination of the planned survey in Brazil : _____ (month / year) Planned start of the search in the World : _____ (month / year) Termination of the research provided in the World : _____ (month / year) Duration of Study : _____ Duration of Treatment : _____ Drug approved in Brazil: <input type="checkbox"/> Yes <input type="checkbox"/> No: °. _____ Registry number: Medicines approved in the World: <input type="checkbox"/> Yes <input type="checkbox"/> No Countries where the drug is approved : _____ Date of first approval : ____/____/____ (month / year) Trade Names in places of Approval : _____					
6. Information on all trial sites:					
Institution	CNES	Status CEP	Subjects in the site	Investigator	CPF
7. Title and code of the Research (include date and version):					
8. Research with the participation of ORPC (Contract Research Organization): <input type="checkbox"/> Yes <input type="checkbox"/> No (If yes, attach contract and letter of delegation) Name, Address and Telephone of ORPC: Responsible person:					
9. Responsibilities The sponsor, through its legal representative below-signed, declares to be responsible in Brazil for the conduct of clinical trial on medicines, entitled: (insert the title of the study) We assume before the National Health Surveillance Agency - ANVISA, the responsibilities below: <ul style="list-style-type: none"> to provide full and free assistance to trial subjects regarding the occurrence of adverse events arising from the use of medicines investigated or procedures used in accordance with the approved Clinical Protocol; to distribute the drugs in research only to research institutions authorized to participate in this clinical research; at the end of the study, account the products imported and not used, giving its proper destination, whether its destruction in the national territory either returned to the origin, keeping the regular records of the procedures adopted; to disseminate the results of clinical trial, after the conclusion of that with proper analysis of the data, including statistical analysis when appropriate, even if the results are favorable or not; to ensure that the drug under investigation is produced according to Good Manufacturing Practices. 					
10. Signature of Sponsor or Responsible Authorized _____ <div style="text-align: right;">Date ____/____/____</div>					

ANNEX III

Request Form for Authorization of IMPORTATION LICENSING



**National Health Surveillance Agency
Researches, Clinical Trials, New Drugs and Biologics Management
Request Form for Authorization of Importation Licensing (L.I.)**

version 1.5

Trial Data

Datavisa exp file number: Nº of the file (Process #):

Clinical Protocol Code: Title of the trial:

Approval Document Number:

Data from Interested

Company Name:

CNPJ:

Email address:

Telephone number:

Fax number:

☐ Responsible for importation

Prosecutor Name*:

CPF*:

Number of the L.I.

Request:

Date:

Permits for single import? ☐ Yes ☐ No

Warning: It is forbidden to use the L.I. for more than a study

Licensing of import replacement?

☐ Yes ☐ NO

Data from L.I. to replace

Nº LI:

DATAVISA nº: date

Planned number of subjects to the trial

In theWorld:

In Brazil:

Calculation of Rational, qualitative and quantitative of products to use in the study in Brazil:

Importation for

Clinical Trial



Information on the imported products

List of pharmaceutical used:

Abstract:

Product to import data		Comment/Additional Consideration								
<input type="checkbox"/> Active principle or placebo Trade name Presentation Route of administration Daily Dose Unit / Day										
Total amount needed for the study as the document specified in existing legislation Amount requested in this L.I.										
Batch number (required): Proform INVOICE (optional): <input type="text"/>										
Batches authorized by Cepec: <input type="text"/>										
total amount to import for the trial:		Quant. Unit (tablets,...)								
Batches	<table border="1"><thead><tr><th>L.I. Number</th><th>doc. Number</th><th>quantity unembarrassed</th><th>balance</th></tr></thead><tbody><tr><td></td><td></td><td></td><td>0</td></tr></tbody></table>	L.I. Number	doc. Number	quantity unembarrassed	balance				0	
L.I. Number	doc. Number	quantity unembarrassed	balance							
			0							
Quantity needed until the end of the study (Balance)										

Há equipamento ou produto para a saúde ? ☐ Sim ☐ Não

Dados do produto a importar	Comentário/Observação
<input type="checkbox"/> Product data to be imported	
Description Trade name Model Manufacturer	
Total quantity for the study document as specified in the legislation. Amount requested in this L.I.	
Batch number (required): INVOICE Proform (optional):	
Comment / Note Amount requested in this L.I.	
Batch number (required):	

INVOICE Proform (optional):					
Batches authorized by					
Cepec:					
	total amount to import for the trial:				
Batches	L.I. Number	doc. Number	quantity unembarrassed	balance	
				0	
Amount needed until the end of the study (Balance)					

Transmissible Spongiform Encephalopathies

Is there any raw material that may be obtained from animal tissues or fluids? Yes () No ()

TABLE Q1

Filling:

If importation of medicines fill one table Q1 per pharmaceutical form:

Identification of the product:

Batch number:

Manufacturer Name:

Address:

City: Country:

Category:

☐ Food

☐ Cosmetic

☐ Medicines

☐ Medical devices

☐ Finished product ☐ semi-prepared ☐ Bulk ☐ Raw material

Purpose of Importation

☐ Marketing / Manufacture

☐ Research

☐ Studies to register in MS

☐ Free Sample of Medical Device

☐ Donations

☐ Other

Quantity (specify the international metric unit):

Physical state / pharmaceutical form:

Conservation conditions:

Manufacture Date:

Shelf life:

TABLE Q1

Filling:

In the case of medicines should fill one per pharmaceutical form:

Fill in the spaces below for each substance or ingredient:

Repeat as many fields as are the substances / ingredients:

1. Substance (DCB, DCI, CAS, INCI):

2. Trade name:

3. Synonyms:

4. Function in the formulation:

☐ Active principle

- ☐ Excipient / co-formulant
☐ Other:

5. family classification:

- ☐ bovine
☐ Goat
☐ Pig
☐ Sheep ☐ Other: Plant

6. Tissue / fluids and category as Annex of the RDC No 305/02:

7. Name of supplier:

8. Country (supplier):

9. Country (origin of the tissue / cell):

Yes (☐) No (☐)

Is there table Q 1 and documentation provided in the table Q3 of the RDC 68/03?

☐ Yes ☐ No

. "Article 3 should be presented to each importation the information of the tables Q1 and Q2 and the copy of the matching documents referring to the table Q3."

Click the Yes option also when there is change in manufacturer or supplier of raw material

Controlled drug?

☐ Yes ☐ No

Portaria. 344/98,
List

Conditions for storage and transport

Statement of responsibility

I assume, civil and criminally, full responsibility for the accuracy of the information presented here (including to the excesses imported), the destruction of goods not used in the study, or to ensure the return to the source and distribute the goods in question only to centers that have the appropriate regulatory approvals.

Company/Institution:

Date

Signature

CNPJ:

Responsible Name:

CPF:

This field is for exclusive use of the health authority

ANNEX IV

CLINICAL TRIAL APPLICATION FORM 1 (FPP1)



National Health Surveillance Agency
Clinical Research
Clinical Trial Application Form 1 (FPP1)

Document Identification

(For use of the government body)

1	Number of file (Process #)		2	Request (Day / Month / Year) / /	
Company Data					
3	Applicant Company		4	Number of Authorization /Register	
5	Manufacturer		6	Number of Authorization / Register	
Data Product					
7	Therapeutic class / category		7b	<input type="checkbox"/> synthetic or semi-synthetic <input type="checkbox"/> Physiotherapies <input type="checkbox"/> Biological	
8	Characteristics of the study		8b	Controlled Studies	
<input type="checkbox"/> Open <input type="checkbox"/> Randomized <input type="checkbox"/> Double Blind <input type="checkbox"/> Single Blind <input type="checkbox"/> Parallel groups <input type="checkbox"/> Crossed Groups <input type="checkbox"/> Other: Please specify _____			<input type="checkbox"/> Placebo <input type="checkbox"/> Active Comparator <input type="checkbox"/> Other: Please specify _____		
9a	CID-10		9b	CID-10	
9c	CID-10		9d	CID-10	
9e	CID-10		9f	CID-10	
10	Population under study: <input type="checkbox"/> Age of 12 <input type="checkbox"/> More than 65 years <input type="checkbox"/> Indians <input type="checkbox"/> Women of childbearing age (only) <input type="checkbox"/> Patients with special needs <input type="checkbox"/> Not applicable				
11	The study is: <input type="checkbox"/> Strictly National <input type="checkbox"/> Foreign Cooperation				
12	Is there exclusive use of placebo in the study? <input type="checkbox"/> Yes <input type="checkbox"/> No				
13	Clinical indication to research				
14	Name of Substance		14b	Active Brand / Supplement	
			14c	Product Description	

[illegible]

ANNEX V
CLINICAL TRIAL APPLICATION FORM 2 (FPP2)



National Health Surveillance Agency
Clinical Research
Clinical Trial Application Form 2 (FPP2)

Document Identification
(For use of the government body)

01	Number of file (Processs #)	02	Request (Day / Month / Year)
03	Subject of Petition (codes and description)	04	Fact Generator (datavisa)
05	Title of Clinical Protocol	06	No. of the Protocol (version and date)
		07	Stage Research I () II () III () IV ()
Company Data			
08	Name / Official name	09	CNPJ
10	City / Town	11	State/District
		12	Country
Manufacturer Data			
13	Manufacturer	14	Number of Authorization /Register
15	City / Town	16	State/District
		17	Country
Applicant Data			
18	Name	19	CNPJ / CPF
20	City / Town	21	State/District
		22	Country
			BRAZIL
Data of Presentation			
23	Registration number (if any)	24	shelf life (in months)
25	Presentation of the Product	26	Number of the formula

27	Route of Administration	28	Physical state / Pharmaceutical form
29	Restriction of Use	30	Conservation Conditions
30	Controlled Drug		

Statement of Responsibility

We assume civil and criminally, full responsibility of the information provided here (including a description of the components of the formula and Presentations attached), as well as the quality of the product (s) (s) to be used in the research being presented, including the appropriate cases, their sterility and / or pyrogen-free.

Legal Responsible Responsible

Pharmacist (Signature and Stamp) (Signature and Stamp)

ANNEX VI

PRESENTATION OF STUDY FORM

PRESENTATION OF STUDY FORM

Trial Information		
COMPANY		FAX:
TITLE OF THE TRIAL		
PROTOCOL CODE ou Number		VERSION/DATE:
NUMBER OF SUBJECTS TO THE TRIAL	WORLD:	BRAZIL:
CEP (FIRST SITE)		

Informations about the Research Sites					
INSTITUTION				PRINCIPAL INVESTIGATOR	
Name	CNES*	Status of approval by the CEP	Planned number of subjects per site	Name	Insurance Registration Number (CPF)

* Establishment of National Register of Health – CNES: available in http://cnes.datasus.gov.br/Listar_Est_Nome.asp?VTipo=0

Name of Legal Responsible

Signature of Legal Responsible

ANNEX VII

PLANNED AMOUNT OF PRODUCTS TO IMPORT

PLANNED AMOUNT OF PRODUCTS TO IMPORT

Trial Information	
COMPANY	
TITLE OF THE TRIAL	
PROTOCOL Number or Code	VERSION/DATE:
DURATION OF THE STUDY	
DURATION OF THE TREATMENT *	
NUMBER OF SITES IN BRAZIL	
NUMBER OF SUBJECTS TO THE TRIAL IN BRAZIL	
SITE COMPETITIVE INCLUSION?	() YES () NO
NUMBER OF PLANNED IMPORTATION	

* Period in which the subject of trial receive the treatment. In the case of studies involving periods without treatment, specify the number of cycles / steps / doses planned

Information on drugs to be imported			
Other products to be imported			

Description of the object	Presentation	Volume administered to subject of search	Amount to be imported (units and kits)

Remarks

Rational Calculation to justify the amount to be imported

"Any change concerning the above estimate should be reported to ANVISA in an application for importation license (LI) and notified to the study approved."

Name of Legal Responsible

Signature Legal Responsible

STATEMENT OF RESPONSIBILITY AND COMMITMENT OF THE INVESTIGATOR

<p>National Health Surveillance Agency Researches, Clinical Trials, New Drugs and Biologics Management - GPBEN Coordination of Research and Clinical Trials - CEPEC</p>	<p>RDC 39/2008 Note: The search can be initiated only after the approval and issuance of ethics CE.</p>
<p>1. Investigator's Name and address:</p> <p>CPF: _____</p>	
<p>2. Name and address of the institution where the research will be developed:</p> <p>Number of National Register of Establishment of Health (CNES): _____</p>	
<p>3. Name and Address Services (Laboratory of Clinical Chemistry, radiological, etc.). Which will be used in the trial:</p>	
<p>4. Name and Address of Institutional Review Board responsible for the assessment of trial</p>	
<p>5. Name of Sub Investigators who will participate in the trial:</p>	
<p>6. Title and Code of the trial that will be conducted by the Investigator (include date and version):</p>	

FORM

<p>7. Responsibilities:</p> <ul style="list-style-type: none"> I agree to conduct the trial according to the clinical protocol, with the Good Clinical Practices, with the Good Laboratory Practices and with Resolution 196/96. Only implement changes in the protocol after notifying the sponsor and the Research Ethics Committee, except changes necessary to protect the safety, rights and welfare of trial subject. I agree to conduct and supervise the clinical trial personally. I agree to inform the sponsor of the study and the Institutional Review Board (CEP) about the serious adverse events that will occur during the development of the research. I have read and understood the information contained in the investigator's brochure, including the potential risks and side effects of drugs under study. I agree to start the clinical trial only after obtaining the necessary ethical approvals (CEP / CONEP) and regulatory approval (ANVISA) <p>I assume, civil and criminally, the veracity of the information presented here</p>
<p>8. Investigator's Signature</p> <p>Date: ____/____/____</p> <p>_____</p>