INFOCARD ELANBiz
Clinical Trials in Costa Rica [1]

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This Infocard provides an overview of the opportunities in Costa Rica to perform clinical trials for any European SMEs dedicated to biotechnological, chemical and pharmaceutical research in order to have regulatory compliance in product development and obtain market access.

Sector description

Clinical studies can be performed competitively in Costa Rica. The country has recently filed a Human Research Law, which is pioneer for Latin America, and has the advantage of reducing time for approval of the research protocol, being the fastest in the region. The public and private institutional structure is clearly regulated and there are quick accessible procedures, as well as certified hospitals and researchers with clinical experience. European companies especially interested in entering the North American market will benefit from conducting clinical studies in Costa Rica since the system follows the FDA (Food & Drug Administration) modality.

The pharmaceutical industry is highly regulated, which requires that all research and development of new drugs comply with clinical trials: pre-clinical phases for the study of pharmacokinetics and pharmacodynamics in cellular or animal models at the laboratory level and clinical studies (Phases I, II, III and IV) in humans to determine safety, dosage, efficacy, adverse reactions in order to validate and approve a drug in the market, nationally or internationally.

Costa Rica carries out 20% of the clinical trials in the Central American and Caribbean region, excluding Puerto Rico, therefore ranked third in the region, after Guatemala and Panama. About 150 clinical trials have been carried out in Costa Rica for more than three decades with sponsors

[1] *"Content information provided in this document, is of general nature only. For more detailed information, events and commercial trade offers as well as commercial business contacts, please contact the Commercial Offices on the member States, the European trade organizations and bilateral chambers of commerce."*

from European multinational companies such as Roche, Novartis, and GlaxoSmithKline, as well as US-origin, such as Pfizer, among others.

The country has the complete chain of institutional and legal structure with international trajectory, including public and private contract management organizations (SMOs: Site Management Organization), contract research organizations (CROs: Contract Research Organization). At the regulatory level, the institutional structure is established through the National Health Research Council (CONIS) of the Ministry of Health, the scientific ethics committees (CECs) and hospitals with international accreditation. The research companies follow the Good Practices of Clinical Trials according to ICH. The National Insurance Institute, in turn, grants a liability insurance policy for sponsors to protect the institutions and patients involved. See section "Institutional Structure".

At the legal level, Costa Rica has consolidated a solid legal framework since it enacted the Human Research Law (No. 9234 of 2014) and its corresponding Regulation (No. 39061-S of 2015), being the 1st country in Latin America that has a human research law. See section "Law & Regulation for Clinical Trials".

Among the **success factors of Costa Rica** for conducting biomedical research, the speed in the approval of the clinical trial research protocol by the CEC stands out (on an average of 2 months). In addition, other success factors are:

a. An educated population that understands their voluntary involvement in a research project
b. A varied ethnicity
c. The public and private health system of international recognition
d. Comparable health indices with developed countries, and
e. Qualified staff

Due to the characteristics of the population, the opportunity niche for European companies to perform clinical trials in Costa Rica is in the area of diagnostic investigations and therapies in cancer.

While in Latin America two thirds of the region carries out mainly clinical trials in Phase III (see publication in Section Links of Interest: "Clinical Trials in Latin America"), in Costa Rica the clinical trials that are carried out regularly are Phases I, II and III[2].

[2] Phases I, II, III consist of different stages of validation of tests carried out in humans:
- Phase I: Evaluates the safety, tolerance and safe dosage range of the medication in experimental groups of 20 and 50 volunteers (usually healthy patients)

Law & Regulation for Clinical Trials

Biomedical research in Costa Rica is regulated by Law 9234 "Biomedical Research Regulatory Law" and its corresponding regulation (link in Spanish only):

- **Law 9234 (April 2014)**

http://www.pgrweb.go.cr/scij/Busqueda/Normativa/Normas/nrm_texto_completo.aspx?param1=NRTC&nValor1=1&nValor2=77070&nValor3=96424&strTipM=TC

- **Regulation 39061-S (July 2015)**

http://www.pgrweb.go.cr/scij/Busqueda/Normativa/Normas/nrm_texto_completo.aspx?param1=NRTC&nValor1=1&nValor2=81213&nValor3=103450&strTipM=TC

The new law describes biomedical research as a way to develop knowledge on human health. It can be observational, epidemiological, or non-interventional (experimental), clinical or interventional. The law states that health research in which human beings participate must be governed by the principles of respect for the dignity of the people, providing benefit, non-maleficence, autonomy and distributive justice. Likewise, participation in biomedical research should always be voluntary, thus participants are not be remunerated.

The participation of an individual in a clinical research will require the expressed, specific, written and signed consent or fingerprinting of the patient or its legal representative. In addition, clinical research involving a person with legal incapacity or a minor may only be carried out when the results are expected to produce real and direct benefits for their health.

A notable factor of the new law is the creation of means for the support of the National Council for Health Research (CONIS) as an organ of the Ministry of Health in charge of ensuring the quality of research and its strict adherence to human rights. All approved clinical research must pay a 3% CONIS canon fee to initiate trials. It should be noted that European companies that wish to carry out research in collaboration with a state university in Costa Rica can take advantage of the exemption of the canon when the principal investigator is contracted by a state

-Phase II: Evaluates efficacy and safety of the new medicine. Group of voluntary patients of 100 and 300 people.
-Phase III: Confirms the efficacy of the new drug by comparison with placebo or existing marketed treatments and determines long-term safety. Group of hundreds to thousands of patient volunteers.

university centre. This is not valid for public health centres such as the Costa Rican Social Security Fund or the surveillance and research centres for diseases such as INCIENSA.

Other remarkable elements of the Law are:

- Allows the transfer of biological samples when the study is multi-center.
  Must comply with the UN3373 Standard that certifies the laboratory for the transport of biological material (IATA)
- Trials with children are allowed only when a real and direct health benefit can be anticipated
- Patient registration for the clinical trial voluntarily, without remuneration
- Ensures that the sponsor provides free medication to the participant during the investigation and, sometimes, also after the conclusion of the investigation
- Prior approval of the CEC it is required as a prerequisite for initiation; there must guarantee that the contract research organization does not have conflict of interest with the sponsor and does not receive any gratuities
- Public or private CECs can approve the investigation in a single instance, unlike before in which there were two instances
- Requires the joint guarantee of sponsor with the contract research organization to comply with the provisions of the law
- Allows for exchange of biological samples when research is multi-centered. Must comply with the Norm UN3373 that certifies the laboratory for transport of biological material (IATA)

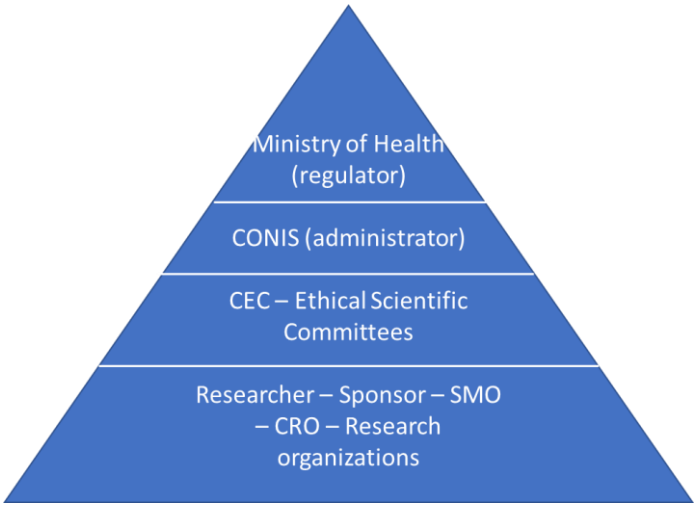
The regulation for this Law establishes the accreditation of the CECs and of the contract research organizations. Likewise, it indicates the approval process of investigations according to the following scheme:

Source: Presentation by Soley, Saborio & Associates at the 1st Simposium on Biomedicine at TEC

Costa Rica distinguishes itself from other Latin American countries in the speed of the process for research protocol approval, which can be approved in just 2 months, providing a unique competitive advantage throughout the region.

Institutional Structure

The following chart describes the hierarchical order of the public and private institutional entities involved and regulated under the law and regulation of clinical trials in Costa Rica:



Source: Presentation by Soley, Saborio & Associates at the 1st Simposium on Biomedicine at TEC

The activities and responsibilities of each entity is described below, as well how they are related to each other for carrying out clinical trials:

- **Ministry of Health of Costa Rica**

  The Ministry of Health of Costa Rica is the governing body of health responsible for ensuring and generating policies that promote the best quality of health for the population, while having the power to retain goods at customs or in the market if they represent a risk to health. Link to Ministry of Health website:

  https://www.ministeriodesalud.go.cr/index.php/estructura-organizacional

- **CONIS**

  CONIS is the National Health Research Council (CONIS) which was created under the Law 9234 for Biomedical Research. According to Article 34 "*The National Health*

Research Council, hereinafter CONIS, is created as an independent, multidisciplinary body, of ethical, technical and scientific nature, responding to the Ministry of Health with a degree of maximum deconcentration and with instrumental legal personality". The purposes of the CONIS are established in Article 35 of the same Law that says "*CONIS must guarantee the quality of the investigations and its strict adherence to human rights. Its members must act with absolute independence of criteria, avoiding in their decisions the influence of political and commercial interests*."

CONIS is the national regulatory authority that oversees the quality, safety, efficacy and safety of products of sanitary interest, in order to contribute to the protection and improvement of the health of the population.

Link to CONIS: https://www.ministeriodesalud.go.cr/index.php/consejos/conis
https://www.ministeriodesalud.go.cr/index.php/regulacion-de-la-salud/autoridad-reguladora-de-medicamentos

- **CEC**

  A scientific ethics committee (CEC) is in charge of reviewing, supervising and approving clinical trials. It can be public or private; composed of an independent committee of doctors, statesmen and members of the community. CEC's responsibilities are to ensure that the studies are ethical, protect the rights and welfare of the participants and ensure that the risks are reasonable compared to the potential benefits.

The country has many CECs, one of which is the Comité Ético Científico de la Universidad de Costa Rica, (CEC of the public University of Costa Rica), for example, created on June, 22nd, 2000. It serves as a research tool for the research carried out at that University as well as the following list of activities:

- Evaluate ethically and scientifically the clinical studies, in an independent, competent and timely manner, free of political, institutional, scientific and market influence
- Establish ethical guidelines for research involving human beings
- Follow up on approved research trials
- Recommend to the Vice-Rector of Research in the event of suspension if any investigation fails to comply with ethical principles, violates legal provisions or causes serious harm to the participants

- Dissemination and training of researchers on bioethics and research ethics

Contract research organizations and Site Management Organizations (CRO, SMO)

In Costa Rica there are several public and private site management organizations (SMOs) and contract research organizations (CROs) established with a trajectory of several decades, among which some are listed below. For more information, the following link provides a list of all the investigations carried out by types of diseases: www.ensayosclinicoscostarica.com

- **ICIC Instituto Costarricense de Investigaciones Clínicas.**

The National Institute of Clinical Research (ICI) is a private institution founded in 1991 dedicated to the full cycle of clinical trials research (SMO, CRO, the only private CEC). This organization promotes clinical research in Latin America, having completed more than 150 Phases II to IV studies in both adults and children in various areas of medicine. ICIC has developed a solid teaching program for the training of physicians, members of ethical scientific committees, and health personnel on topics of Bioethics, Good Clinical Practices since the beginning of this program in 1998. This organization seeks to promote the creation of more clinical research centers through a network program called LARENET.
Link: http://cec-icic.com/el_instituto.php

- **INCIENSA – Investigación Observacional Epidemiológica**

The Costa Rican Institute for Research and Education in Nutrition and Health (INCIENSA) is a public institution belongs to the Office of the Minister of Health and has the following responsibilities:

- Prevent and control priority public health problems, through the development of specialized epidemiological surveillance systems
- Carry out public health research to generate knowledge that supports decision-making
- Transfer the knowledge generated through teaching and communication processes

Link: http://www.inciensa.sa.cr/

- **ICIMED – Investigación en Ciencias Médicas**

The Medical Sciences Research Institute is a Site Management Organization (SMO) that subscribes a private contract with the sponsor, the contract research organization and / or the researchers for carrying out any of the in the execution of the clinical trial. Enlace: http://www.icimed.cr/

Research Institutions

Research contract management organizations are responsible for managing all resources, patients, information management, etc. These coordinate the clinical trials agreement with the doctors and patients of the hospitals in the administration of the medication and the data collection. In Costa Rica there are two private hospitals that have international accreditation according to the Joint Commission International (http://www.jointcommissioninternational.org):

- Hospital Clinica Biblica
- CIMA Hospital

Legal Infrastructure

The following are some of the law firms that have experience in participating in the legal aspects of the practice of clinical trials in Costa Rica, among others:

- Bufete Soley, Saborío & Asociados
  http://www.soley-saborio.com

- Bufete Zurcher, Odio & Raven
  http://www.zurcherodioraven.com

- Bufete Facio y Cañas
  http://www.fayca.com/

- Bufete AriasLaw
  http://www.ariaslaw.co.cr

Examples of clinical trials that have concluded:

Clinical trials carried out in Costa Rica have been performed with sponsors of large pharmaceutical companies such as ROCHE, GlaxoSmithKline, Astra Zeneca, Pfizer, Merck, Johnson & Johnson, Novartis, Amgen, Janssen Cilag, Elli Lilly, Abbott, among others. Most of the research is listed in https://www.ensayosclinicoscostarica.com/

Some 150 clinical trials conducted in Costa Rica are listed in international publications, such as: https://clinicaltrials.gov/ct2/search/map?map=CA

Costa Rica carries out 20% of the clinical trials in the Central American and Caribbean region, excluding Puerto Rico, therefore ranked third in the region, after Guatemala and Panama.

Costa Rica has also participated in international studies with world reference organizations in collaboration with local institutions such as, the National Institute of Health (NIH of the USA) with ICIC and the World Health Organization (WHO) with INCIENSA of Costa Rica and ROCHE. In this way clinical trials in Costa Rica have helped to reveal information about pandemic diseases, such as AIDS, cervical cancer, stomach cancer, asthma, diabetes, hypertension, among others. Some contributions of Costa Rican research to world health is listed in the Annex.

Examples of European or American companies that trusted their clinical trials in Costa Rica:

Links of Interest

- **CINDE** – investment promotion agency of Costa Rica: http://www.cinde.org/es/sectores/ciencias-de-la-vida
- **Biomedical and Equipment and Materials Registration Manual – CINDE:** http://cdn.cinde.org.s3.amazonaws.com/content/resources/10.pdf?1433882143
- **Presentation of CEC-INCIENSA at the Council of Doctors and Surgeons: "**Expectativas de los CECs ante la Ley Reguladora de Investigación Biomédica (Ley 9234)**"**
- **Clinical Trials in Latin America: A region of diversity, a world of opportunity** https://www.pharm-olam.com/sites/default/files/poi-clinical-trials_whitepaper-latin-america.pdf
- **International observatory for clinical trials worldwide:** https://www.centerwatch.com/clinical-trials/listings/locations.aspx

This Infocard has been prepared by the expert in Costa Rica.

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