

Clinical research: a view from the north of Brazil

Pesquisa clínica: Uma visão do norte do Brasil

Investigación clínica: una vista desde el norte de Brasil

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Abstract

Clinical research is important for understanding pathologies and discovering therapeutic innovations. In Brazil, although it is expanding and has aroused interest in researchers and institutions, especially in this period of the COVID-19 pandemic, it is still characterized as a new area, and in many regions of the country there is a lack of research that prioritizes the demand for diseases of national importance. Thus, the aim of this study was to map clinical research centers in addition to studies on this topic, focusing on the northern region of Brazil. The study was carried out by searching the database of the CNPQ Directory of Research Groups, Brazil Platform, National Health Surveillance Agency, National Network of Clinical Research, Brazilian Registry of Clinical Trials and ClinicalTrials.gov. The North region, although having relevant centers, these in number are inferior to other regions of Brazil. Likewise, in the state of Tocantins, clinical studies are still a modest reality. In this sense, the need for an equal distribution of research centers in the country and investments in clinical studies, especially in Tocantins is highlighted, as there are several demands in the national territory due to regional differences in the population and potential of each location.

Keywords: Clinical protocols; Clinical trial; Regional development; Neglected diseases.

Resumo

A pesquisa clínica é importante para compreensão de patologias e descobertas de inovações terapêuticas. No Brasil, embora esteja em expansão e tenha despertado interesse em pesquisadores e instituições, principalmente nesse período da pandemia de COVID-19, ainda é caracterizada como uma área nova sendo que em muitas regiões do país há uma carência de pesquisas que priorizem a demanda de enfermidades de importância nacional. Dessa forma, o objetivo deste estudo foi mapear os centros de pesquisa clínica além de pesquisas nesta temática, com foco na região norte do Brasil. A pesquisa foi realizada por buscas na base de dados do Diretório de grupos de pesquisa do CNPQ, Plataforma Brasil, Agência Nacional de Vigilância Sanitária, Rede Nacional de Pesquisa Clínica, Registros Brasileiros de Ensaios Clínicos e ClinicalTrials.gov. A região Norte embora possua centros de relevância, esses em número são inferiores a outras regiões do Brasil. Da mesma forma, no estado do Tocantins os estudos clínicos ainda são uma realidade modesta. Nesse sentido, destaca-se a necessidade de uma distribuição igualitária de centros de pesquisa no país, e investimentos em estudos clínicos, especialmente no estado do Tocantins já que existem diversas demandas no território nacional devido às diferenças regionais da população e potencialidades de cada local.

Palavras-chave: Protocolos clínicos; Ensaios clínicos; Desenvolvimento regional; Doenças negligenciadas.

Resumen

La investigación clínica es importante para comprender las patologías y descubrir innovaciones terapéuticas. En Brasil, si bien se está expandiendo y ha despertado interés en investigadores e instituciones, especialmente en este período de la pandemia COVID-19, todavía se caracteriza como un área nueva, y en muchas regiones del país hay una falta de investigación que prioriza la demanda de enfermedades de importancia nacional. Así, el objetivo de este estudio fue mapear los centros de investigación clínica además de la investigación sobre este tema, con un enfoque en

la región norte de Brasil. La investigación se llevó a cabo mediante la búsqueda en la base de datos del Directorio de Grupos de Investigación del CNPQ, Plataforma Brasil, Agencia Nacional de Vigilancia Sanitaria, Red Nacional de Investigación Clínica, Registro Brasileño de Ensayos Clínicos y ClinicalTrials.gov. La región Norte, aunque tiene centros relevantes, estos en número son inferiores a otras regiones de Brasil. Asimismo, en el estado de Tocantins, los estudios clínicos siguen siendo una modesta realidad. En este sentido, existe la necesidad de una distribución equitativa de los centros de investigación en el país, e inversiones en estudios clínicos, especialmente en el estado de Tocantins, ya que existen varias demandas en el territorio nacional por diferencias regionales en la población y potencial de cada ubicación.

Palabras clave: Protocolos clínicos; Ensayo clínico; Desarrollo regional; Enfermedades desatendidas.

1. Introduction

Clinical research is a very important area within Brazilian science, since we had the development and discoveries of important vaccines, drugs and medicines. However, these surveys are often restricted to large centers. With the advent of generics and the construction of a pharmaceutical industrial pole in the country, there was an expansion and interest of researchers and institutions in this theme, mainly during the pandemic period when science, and mainly clinical research, was challenged to investigate and produce new drugs to fight the COVID-19 virus.

In Brazil, clinical trials are evaluated by regional Research Ethics Committees (Comitês de Ética em Pesquisa - CEPs) and in some cases, there is a need for a second authorization that is made by the National Research Ethics Commission (Comissão Nacional de Ética em Pesquisa - CONEP). The approval by the National Health Surveillance Agency (Agência Nacional de Vigilância Sanitária - ANVISA) through the Management of New Medicines, Research and Clinical Trials is equally essential for research aimed at registering new drugs, in addition to adhering to the principles of Good Clinical Practice (GCP), which is an indisputable requirement for quality in the development of clinical studies involving human beings (Zucchetti & Morrone, 2012).

Clinical studies are grouped into 4 phases: Phase I, aims to determine the safety associated with different doses, possible occurrences of toxic effects, as well as studies of the mechanism of action of the drugs, all carried out in healthy volunteers. Phase II occurs after the dose is determined in phase I, where the objective is to evaluate the efficacy in individuals with a certain disease, and different doses can also be studied. Phase III expands safety and efficacy studies to a larger number of participants to define the risk-benefit ratio of using the therapy. The last one, Phase IV, called Pharmacovigilance, occurs after commercialization, in which the medicine remains under observation and surveillance for possible side effects (Brasil, 2018; Cardoso & Rabelo, 2019).

As an initial aspect for the realization and generation of reliable data in clinical studies, as well as its storage, it is necessary to create specific centers called the Clinical Research Center. These in Brazil are consolidated for the most part by the relation and development of services for foreign industries, with a lack of research that prioritizes the demand for diseases of national importance, often neglected by foreign interests (Silveira et al. 2016).

In addition, an unprecedented initiative to encourage the development of clinical research and make Brazil more competitive on the international stage was the Clinical Research Action Plan published in March 2018. The action attempts to expand the country's capacity to develop and attract clinical research that contributes to the quality of life of the Brazilian population. This plan provides for short, medium and long-term actions, structured in six axes: ethical regulation, health regulation, training in clinical research, scientific and technological development, National Clinical Research Network (Rede Nacional de Pesquisa Clínica - RNPC) and knowledge management (Brasil, 2018).

Such actions allow the development of clinical research in the Brazilian scenario, whose benefits are not limited only to the scientific and technological ones, but also brings significant improvements to the population. Among these benefits are the attraction of investments and the consequent economic movement, substantial increase in scientific production, expansion

of the access and strengthening of the country's health system (Cardoso & Rabelo, 2019). Clinical research also contributes to answering fundamental questions about well-being promotion, diagnosis and treatment of diseases, aiming at the development of new technologies to contribute to the improvement of the population's quality of life (Brasil, 2020). Therefore, the aim of this study was to map clinical research centers in addition to research on this topic, focusing on the northern region of Brazil.

2. Methodology

The inquiry for the research groups was carried out in the database of the CNPQ research group directory, using filters for the states of the North region and in the large area of health sciences. The search was carried out in consultation with the current base of research groups, whose records were up to date. All groups retrieved in the search were investigated regarding the description of its lines of research and if it was noted that the group conduct clinical research for the development of new drugs it was included in the results. In case of doubt, an e-mail was sent to the group leader for confirmation. From the groups recovered in this investigation, data related to the year of formation, allocation institution, predominant area, repercussions of the group, lines of research and human resources were recorded.

To consult the clinical studies carried out in Brazil, the database of the National Health Surveillance Agency [ANVISA] (2020) was consulted in order to recover the researches authorized in the last 5 years (from January 1, 2015 to July 20, 2020). The studies that were being carried out in the northern region were included in the results. This search was conducted manually, looking for the places where the recovered clinical trials were performed. Also, in the ANVISA environment, a consultation was held on the base of Bioequivalence and Bioavailability centers (2020), and if it contained any one from the northern region, this would also be included in the results. In addition, the same procedure was done in order to recover northern groups participating in the National Clinical Research Network (Rede Nacional de Pesquisa Clínica - RNPC) (Brasil, 2010).

On the Brazilian Clinical Trials Records (Registros Brasileiros de Ensaios Clínicos - REBEC) (2020) platform, a search was performed containing the terms; Tocantins, Palmas, Araguaína, Porto Nacional and Gurupi (used in independent searches) that included interventional studies in all recruitment situations and with institutions of all types, without age limits. This search was carried out on June 27, 2020.

On the same date, the ClinicalTrials.gov database was also consulted, applying the filters for the country Brazil and in the city field the cities Palmas, Araguaína, Porto Nacional and Gurupi were researched as they are the most populous centers in the state.

Finally, on July 28, 2020, a search was carried out on the Plataforma Brasil website, in order to consult among the works approved by each Ethics Committee in the state of Tocantins, those that fit the objectives established in the present study. The research was carried out by municipality, for example: Palmas, Araguaína, Porto Nacional and Gurupi. The essays were consulted within the time frame from January 1, 2019 to July 28, 2020.

3. Results

The search on the platform of the Research Groups Directory, found 90 records of groups in the large area of Health Sciences. Out of these, 4 pointed out in their descriptions that they conduct clinical research. The state of Pará has a greater participation in relation to the number of groups, followed by the state, Amazonas and Tocantins. No groups were found in the states of Roraima, Rondônia, Amapá and Acre. The state of Amazonas has a very representative center, which is the Carlos Borborema Clinical Research Institute (Instituto de Pesquisa Clínica Carlos Borborema - IPCCB). This is an interdisciplinary, multiprofessional and interinstitutional research group dedicated to the study of the main infectious diseases in the Brazilian

Amazon. It is maintained and sponsored by the Dr. Heitor Vieira Dourado Foundation of Tropical Medicine (Fundação de Medicina Tropical Dr. Heitor Vieira Dourado- FMT-HVD). This group works as a consortium signed by FMT-HVD with the State University of Amazonas (Universidade do Estado do Amazonas - UEA) and the Leônidas & Maria Deane Institute (Fiocruz Amazônia). The main lines of research are: malaria, arboviruses, sexually transmitted infections, hepatitis, tuberculosis, accidents by venomous animals, among other relevant diseases for the population of the Amazon (Instituto de Pesquisa Clínica Carlos Borborema Amazonas, 2020).

The groups representing the state of Pará recovered were the Prospecting and Analysis of Amazonian Nature Resources (Prospecção e Análise de Recursos da Natureza Amazônica - PARDANAM), it was formed in 2020, is linked to the Federal University of Western Pará (Universidade Federal do Oeste do Pará - UFOPA), whose description points to technological innovation in the area as a guideline plant protection. The group conducts a research aimed at the development of herbal medicines, nutraceuticals and other pharmaceutical bioproducts from raw materials extracted from Amazonian biodiversity, and it operates throughout the entire Research, Development & Innovation process, from the ethnopharmacological investigation of the raw materials together to traditional local communities, up to the analytical steps related to bioactivity and toxicity.

In the state of Pará, the Chemical-Pharmaceutical Technology & Therapeutic Innovation group, created in 2005 and linked to the Federal University of Pará, was also recovered. This one develops research in the planning, utilization, development and application of natural and synthetic bioactive products such as antioxidants, anti-inflammatory drugs, analgesics, vasodilators, neuro-protectors and neglected diseases through the identification, characterization and selection of chemical and biological properties of bioactive or inert natural constituents, which can be used in pharmaceutical and medical practice, as well as in the search for routes aimed at the applicability of products extracted from the Amazon region. It is proposed to study new candidates for drugs derived from heterocyclics and phenolic compounds, using techniques and methods of rational, synthetic and biotechnological planning.

In Tocantins, there is the representation of the Basic and Health Sciences Laboratory. The group was created in 2012 and is linked to the Federal University of Tocantins (Universidade Federal do Tocantins - UFT). In its lines of research, it develops pre-clinical and clinical studies of products of natural origin.

At the base of the RNPC, the representatives of the Northern Region are the Foundation of Tropical Medicine of Amazonas and the João de Barros Barreto University Hospital of the Federal University of Pará (figure 1) (Brasil, 2010).

The Hospital of the Tropical Medicine Foundation of Amazonas (FMT-AM) is the largest in Brazil in the area and seeks to invest in research that can fill the treatment gap in tropical and infectious diseases. In order to strengthen regional research, FMT-AM establishes partnerships with state and federal universities, research institutes; and international, private laboratories, the Global Fund to Fight AIDS, Tuberculosis and Malaria, the Centers for Disease Control and Prevention in the United States and the University of Barcelona (Brasil, 2010).

The other representative of the North Region in the RNPC is the Clinical Research Center of the João de Barros Barreto University Hospital (*Hospital Universitário João de Barros Barreto* - HUIBB). Acting in several lines of research, HUIBB maintains a partnership with the Research Institute Evandro Chagas and with the Nucleus of Tropical Medicine at UFPA to carry out clinical research in several areas (Brasil, 2010).

In the ANVISA database on Bioequivalence and Bioavailability (2020) centers, no national certified centers were found in the North. The base has records of centers in Ceará, Goiás, Minas Gerais, Paraná, Pernambuco, Rio de Janeiro and São Paulo.

The Fiocruz Clinical Research Network (RFPC) is an initiative that brings together research groups from Fiocruz in order to strengthen the strategic role of this activity in the institution and promotes interaction between more than 60 clinical

research groups from Fiocruz, in addition to representing them with the National Clinical Research Network (RNPC). A research group in the North region participates in this network, whose title is called Fiocruz Clinical Research Group on Endemic Infectious Diseases in the Amazon (RFPC, 2020).

Figure 1. Research Centers in the RNPC.



Source: *Rede Nacional de Pesquisa Clínica – RNPC* (2018).

The search for clinical trials authorized by ANVISA (2020) in the last 5 years recovered 508 special reports, out of them 42 had the participation of health establishments and research centers in the North Region (Table 1). It can be observed that there is no participation of centers in the state of Tocantins in clinical studies authorized by ANVISA in the last 5 years.

Table 1. Health establishments in the North Region registered in ANVISA's special communications in the last 5 years.

Health establishments	Nº of CE	State
Center for Research in Tropical Medicine of Rondônia	2	RO
North Brazilian Association for Prevention and Health Care	1	AM
Foundation of Tropical Medicine of Amazonas	9	AM
State University of Pará	18	PA
Nativida - Neonatal Screening Service Center LTDA	1	RO
State Public Foundation Hospital de Clínicas Gaspar Viana	5	PA
Alfredo da Mata Foundation of Tropical Dermatology and Venereology	1	AM
Hemotherapy and Hematology Center of Pará	2	PA
Amazon Telehealth Pole	1	AM
Oncológica Brasil S/S LDTA.	3	PA
28 de Agosto Emergency Hospital	1	AM
Municipal Health Department of Belém	1	PA

Source: ANVISA (2020).

The search in the ANVISA database allowed the retrieval of a group from the state of Rondônia, the Center for Research in Tropical Medicine (*Centro de Pesquisa em Medicina Tropical - CEPEM*), which is an agency responsible for research on tropical diseases in the Amazon region, linked to the State Health Secretariat of Rondônia, non-profit. It was founded in Costa Marques - Rondônia, in 1986 and currently it has employees and researchers trained to meet the needs and expectations of society in various areas of public health, such as virology, microbiology, biochemistry, technical platform, molecular biology, hepatitis, epidemiology, entomology and genetics. The unit works in partnership with several national and international research entities, such as the Pasteur Institute (France), the Oswaldo Cruz Foundation, Pan American Health Organization, collaborations with the University of São Paulo, Federal University of Rio de Janeiro, in addition to from international institutions, such as the Universities of Massachusetts and Virginia (USA), which collaborate with research in the areas of immunology and entomology. CEPEM also works in conjunction with the Tropical Pathology Research Institute (*Instituto de Pesquisas em Patologias Tropicais - IPEPATRO*).

The REBEC search related to clinical research in Tocantins retrieved 2 study records. One of them was registered on June 4, 2012, with a last update in June 2013. This study has reported as the scientific title The Use of Topiramate in Crack Addiction and as sponsors the Federal University of Tocantins and the Municipal Health Secretariat of Palmas. On the REBEC website, the study is currently being recruited (REBEC, 2020).

The second study related to clinical research in Tocantins has the scientific title: the use of an emulsion formula of the type Paracetamol Therapeutic Ice Cream in the Postoperative of Children: A randomized clinical trial. This study was registered on February 23, 2020 and it is sponsored by the Lutheran University Center of Palmas (*Centro Universitário Luterano de Palmas - CEULP/ULBRA*) and the Lutheran University of Brazil (*Universidade Luterana do Brasil - ULBRA*); it is not in the recruitment phase (REBEC, 2020) yet. This study was also found in the Plataforma Brasil database, being the only clinical research in the state of Tocantins recorded in this database among the 280 studies found during the research for the established period. Among the essays found on the site, 167 are from the city of Palmas, 60 from Araguaína, and in a less amount, Porto Nacional presented 53 results.

The search in the ClinicalTrials.gov database retrieved a record aimed at clinical studies with drugs, the latter being in phase IV with a real completion date of July 2010. This study aimed to determine whether amphotericin B is effective against *visceral leishmaniasis* in Brazilian children. Amphotericin B was compared to *meglumine antimoniate*. This study had the

participation of the Hospital for Tropical Diseases of Araguaína and the Hospital Dona Regina de Palmas, with collaboration and sponsorship from the University of Brasília and the Ministry of Health.

4. Discussion

An important focus of clinical research is the patient, who often does not have access to better treatment options. Adequate research protocols allow more modern treatments or procedures (Dainesi & Goldbaum, 2012) to these patients. However, clinical research developed in Brazil is still not very competitive at the international level due to several obstacles, among which we highlight the lack of infrastructure, qualification of research centers and human resources, and the little knowledge of health professionals and the population regarding clinical trials conducted in the country (Brasil, 2020). This statement is reinforced by what was found in the present research, which shows an uneven representation of clinical research centers in Brazil, because although the North region has some of quality with good infrastructure, they lose in number in relation to the representation of other regions. In addition, with regard to the state of Tocantins, its population remains unrepresented in the national clinical research scenario.

This fact meets the needs raised in the diagnosis of Clinical Research in Brazil held at the Forum “Clinical Research in Brazil: International Competitiveness and Challenges”, and in the Clinical Research Action Plan in Brazil, scientific and technological promotion is foreseen in order to improve the scientific capacity installed in clinical research (Brasil, 2020).

According to RNPC objectives, it is opportune to encourage and to ensure the participation of Brazilian researchers in the development of clinical studies for the evaluation of genuinely national and priority medicines, products or inputs for SUS. Clinical research centers trained with sufficient infrastructure and human resources may make Brazil capable of facing global competition, in addition to developing health products and supplies that are a priority to the health needs of the Brazilian population (Brasil, 2010). However, about the institutions regulated in the program, only two institutions are from the North region. Thus, the lack of financial and scientific incentives in the northern region of Brazil is noticeable, since without the basic structure for the development of research, there is a consequent limitation of technological training, autonomy and self-sufficiency of clinical studies conducted in the region (Brasil, 2010).

It is worth mentioning that the North region holds in its territory the Amazon, which is the largest tropical forest in the world and stands out for having the greatest diversity of animals and plants on the planet (Marcon et al. 2012). It is estimated that in the Amazon there are between 5 and 10 thousand plants with pharmacological potential, but there is still a small number of chemical studies aimed at their usefulness as an input for the pharmaceutical, cosmetic and food industries (Embrapa, 2016).

Diniz and Diniz point to a fragile Amazon Regional Innovation System that is unable to generate the “inputs” necessary for the exploitation of biodiversity resources from high-tech industries, as the pharmaceutical and medication industries are based (Diniz & Diniz, 2018). These authors emphasize that the development of science, technology and innovation in the Amazon is very important to its integration with the scientific and technological development of the current world. However, as observed in the present survey, there is an asymmetry in relation to the scientific and technological development of the Amazon in relation to the country and the rest of the world (Diniz & Diniz, 2018).

Another aspect identified in the Clinical Research Action Plan in Brazil is the lack of knowledge of managers, health professionals and the general population about clinical trials conducted in the country and their results. One of the causes of this little knowledge that could be confirmed in the present survey is the difficulty of access to the researches developed. In the databases consulted, there is a lack of filters, which make it easier to retrieve and access more precisely the studies developed and being carried out. In many databases, such as ANVISA's on authorized clinical trials, retrieval of studies had to be performed manually and individually, which makes it difficult to diagnose the research scenario in states and regions.

In the CNPQ Directory of Research Groups, there is an absence of data, and the descriptions of the groups are often inaccurate about the development of clinical studies. In this sense, Klein (2017) point out the invisibility of this type of research in funding agencies, by researchers, in the use of Lattes and groups directory when filling out their profiles due to an option for filling descriptive research activities, which it allows several omissions and divergences of information on the part of its users. Thus, there is a need to expand the notion of transparency for more information on how the results are constructed, so it is possible to know the production contexts and the collectives triggered in each enterprise (Klein, 2017).

The globalization of clinical research allows for a vast exchange of information, and Brazil, with its growing participation in this scenario, has been working to expand the ethical debate on clinical research in health, in order to improve and streamline new clinical studies in the country, maintaining its procedural rigor (Dainesi & Goldbaum, 2012). There is still a lot to be done, mainly with regard to the equal distribution of research centers in the country, since there are several demands in the national territory due to the regional differences of the population and the potential of each location. In this sense, a way of stimulating innovation must be based on interactivity between teaching-research institutions and health services, thus promoting an environment with higher quality, development and productivity (Brasil, 2010).

5. Conclusion

In this survey, it can be concluded that although the North region has quality clinical research centers, these are still asymmetric in relation to other regions in Brazil. The state of Tocantins remains underrepresented in this scenario, with a negligible participation in clinical studies carried out in the national territory. This highlights the need for investments in clinical research in this state.

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References

- Brasil. Departamento de Ciência e Tecnologia, Secretaria de Ciência, Tecnologia e Insumos Estratégicos, Ministério da Saúde. (2010). National clinical research network: Brazilian response and mitigation of international dependency. *Rev Saude Publica.*, 44, 575–578.
- Brasil. Ministério da Saúde. (2018). Brasil institui o Plano de Ação de Pesquisa Clínica para aumentar competitividade no país. Recovered from <https://www.saude.gov.br/noticias/sctie/42825-brasil-institui-o-plano-de-acao-de-pesquisa-clinica-para-aumentar-competitividade-no-pais>
- Brasil. Ministério da saúde. (2020). Plano de ação de pesquisa clínica no Brasil.
- Brasil. Ministério da saúde. Secretaria de Ciência, Tecnologia e Insumos Estratégicos. (2010). Rede Nacional de Pesquisa Clínica. Brasília: Ministério da Saúde.
- Brasil. Secretaria de Ciência T e IE. Rede Nacional de Pesquisa Clínica [Folder]. 2010. Recovered from <https://rute.rnp.br/web/sig-rede-nacional-de-pesquisa-clinica-mpc>
- Brasil. (2018). Consolidado de normas de registro e notificação de fitoterápicos. *Agencia Nac Vigilância Sanitária.*, 1–655.
- Cardoso, F., Rebelo, F. (2019). A importância da pesquisa clínica para o Brasil. *Assoc da Indústria Farm Pesqui.*, 1, 1–52.
- Centros de Bioequivalência e Biodisponibilidade - Anvisa. (2020). Recovered from <http://portal.anvisa.gov.br/centros-de-bioequivalencia-e-biodisponibilidade>
- CEPEM. (2020). Recovered from <https://sites.google.com/site/cepemipepatro/>
- Consulta de Ensaio Clínicos Autorizados pela Anvisa. (2020). http://www7.anvisa.gov.br/Datavisa/Consulta_Comunicados/Consulta_CE_Autorizados.asp
- Dainesi, S. M., & Goldbaum, M. (2012). Pesquisa clínica como estratégia de desenvolvimento em saúde. *Rev Assoc Med Bras.*, 58, 2–6.
- Diniz, M. B., & Diniz, M. J. T. (2018). Exploração dos recursos da biodiversidade da Amazônia Legal: uma avaliação com base na abordagem do Sistema Nacional/Regional de Inovação. *Redes.*, 23, 210.

Diretório de Grupos de Pesquisa - Plataforma Lattes - CNPq. (2020). <http://lattes.cnpq.br/web/dgp>

Empresa Brasileira de Pesquisa Agropecuária. (2016, novembro).

Santana, I. (2016). Potencial farmacológico de espécies da Amazônia é tema de palestra no IV CBRG. Recovered from <https://www.embrapa.br/busca-de-noticias/-/noticia/18162156/potencial-farmacologico-de-especies-da-amazonia-e-tema-de-palestra-no-iv-cbrg>

Home - ClinicalTrials.gov. (2020). Recovered from <https://clinicaltrials.gov/ct2/home>

Instituto de Pesquisa Clínica Carlos Borborema Amazonas. (2020). Recovered from <https://www.ipccb.org/>

Klein, V. P. (2017). Invisibilidade da Pesquisa Clínica no Brasil: considerações a partir de fontes de informação em Ciência & Tecnologia. *Rev Eletron Comum Inf Inov Saúde*, 11, 1–9.

Marcon, J. L., Menin, M., Araújo, M. G. P., & Hrbek, T. (2012). *Biodiversidade Amazônica: caracterização, ecologia e conservação*.

Rede Fiocruz de Pesquisa Clínica - Fundação Oswaldo Cruz (Fiocruz): Ciência e tecnologia em saúde para a população brasileira. (2020). Recovered from <https://portal.fiocruz.br/rede-fiocruz-de-pesquisa-clinica-rfpc>

Registro Brasileiro de Ensaio Clínicos. (2020). Recovered from <http://www.ensaiosclinicos.gov.br/>

Silveira, C., Barros, A., & Rau, C. (2016). Evolução Da Pesquisa Clínica Nacional E Das Medidas De Regulação Pelos Conselhos De Ética E Anvisa. Recovered from <http://www.cpgls.pucgoias.edu.br/7mostra/Artigos/SAUDE E BIOLOGICAS/EVOLUÇÃO DA PESQUISA CLÍNICA NACIONAL.pdf>

Zucchetti, C., & Morrone, F. B. (2012). Perfil da pesquisa clínica no Brasil. *Clin Biomed Res.*, 32, 340–347.