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https://doi.org/10.22239/2317-269x.02043

Policy analysis on the regulation of the medicinal use of products derived from *Cannabis* spp. in Brazil (2014-2021)

Análise política sobre a regulamentação do uso medicinal dos produtos derivados da *Cannabis* spp. no Brasil (2014-2021)

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Received: 14 fev 2022
Approved: 07 nov 2022

How to cite: Araújo PS, Costa EA, Sandes CFB, Cruz ECD, Rocha JS, Soares LCC, Pereira MT. Policy analysis on the regulation of the medicinal use of products derived from *Cannabis* spp. in Brazil (2014-2021). Vigil Sanit Debate, Rio de Janeiro. 10(4):71-80, November 2022. https://doi.org/10.22239/2317-269X.02043

ABSTRACT

Introduction: The medicinal use of *Cannabis* derivatives divides opinions in civil society. However, for many patients who need treatment, the regulation of the importation and use of these products represents hope and quality of life. **Objective:** To identify the main facts and positions related to the regulation of medicinal products based on *Cannabis* from 2014 to 2021 by Anvisa, the Ministry of Health, the Chamber of Deputies and the Federal Councils of Pharmacy and Medicine. **Method:** This is a case study resulting from the analysis of the facts and positions identified by different actors, selected considering a time frame from 2014 to 2021. The production of data included sources from the Thematic Axis database Medicines, Blood, Pharmaceutical Assistance and Health Surveillance Policies, developed in partnership with researchers from the State University of Bahia, which is part of the Observatory of Policy Analysis in Health of the Collective Health Institute of the Federal University of Bahia. **Results:** Several countries, such as Argentina, Mexico, Thailand, Canada, Israel, and several states in the USA, have changed their legislation so that it is possible to expand the use of *Cannabis*-based drugs. In Brazil, however, this is a long process, which involves several divergences and positions of different political actors. **Conclusions:** The topic is relevant; discussions and debates allow society to be informed about how the government is conducting the regulation to allow the production of *Cannabis*-based medicines as a therapeutic alternative for conditions that do not yet have drug therapies.

KEYWORDS: Medical Marijuana; Government Regulation; Health Surveillance

RESUMO

Introdução: O uso medicinal dos derivados da *Cannabis* divide opiniões na sociedade civil. Entretanto, para muitos pacientes que necessitam do tratamento, a regulamentação da importação e o uso desses produtos representam esperança e qualidade de vida. **Objetivo:** Identificar os principais fatos e posicionamentos relacionados à regulamentação dos produtos medicinais à base de *Cannabis* no período de 2014 a 2021 por parte da Anvisa, do Ministério da Saúde, da Câmara dos Deputados e Conselhos Federais de Farmácia e de Medicina. **Método:** Trata-se de uma pesquisa qualitativa do tipo estudo de caso, resultado das análises dos fatos e posicionamentos identificados pelos distintos atores selecionados, considerando o recorte temporal de 2014 a 2021. A produção de dados incluiu fontes do banco de dados do eixo temático Políticas de Medicamentos, Sangue, Assistência Farmacêutica e Vigilância Sanitária, desenvolvido em parceria com pesquisadores da Universidade do Estado da Bahia. O eixo integra o Observatório de Análise Política em Saúde do Instituto de Saúde Coletiva da Universidade Federal da Bahia. **Resultados:** Vários países como Argentina, México, Tailândia, Canadá, Israel e diversos estados dos EUA têm alterado sua legislação para que seja possível ampliar o uso de medicamentos à base de *Cannabis*. No Brasil, no entanto, este é um

processo longo, que envolve várias divergências e posicionamentos de diferentes atores políticos. **Conclusões:** O tema se mostra relevante, discussões e debates permitem que a sociedade seja informada sobre como o governo está conduzindo a regulamentação para permitir a produção de medicamentos à base de *Cannabis* como uma alternativa terapêutica para condições que ainda não contam com terapêuticas medicamentosas.

PALAVRAS-CHAVE: Maconha Medicinal; Regulação Governamental; Vigilância Sanitária

INTRODUCTION

Cannabis sativa L., popularly known as marijuana, is a plant of the *Moraceae* family that has therapeutic properties, with records of its use since antiquity for medicinal and recreational purposes. Stand out in the *C. sativa L.* two phytocannabinoids: Δ9 - Tetrahydrocannabinol (Δ9 - THC), main psychoactive constituent, and cannabidiol (CBD), a non-psychoactive substance described in the scientific literature as possessing anticonvulsant, antipsychotic, anti-inflammatory, antiepileptic, and anxiolytic properties[1,2,3].

CBD and THC are among the cannabinoids of scientific and therapeutic interest. However, although the *C. sativa* L. plant appears on the list of prohibited plants that can originate narcotic and/or psychotropic substances from the Ordinance of the Health Surveillance Secretariat of the Ministry of Health (SVS/MS) No. 344, of May 12, 1998, and that until 2015 THC and CBD were included in the list of proscribed substances in this resolution, international treaties signed by Brazil granted as an exception their use "for medical and scientific purposes, under the control and direct supervision of the member country" and "for scientific and very limited medical purposes"[4,5].

Patients with difficult-to-control epilepsy, Alzheimer's disease, Parkinson's disease, autism, undergoing oncology treatment, among other conditions, from 2014 began to request judicial authorization to guarantee access to imported products derived from *Cannabis* as a last therapeutic alternative, running into legal and economic restrictions for access. However, due to the high cost of the imported product, cases of lawsuits that requested authorization for the cultivation of the plant and oil extraction began to appear throughout Brazil[6].

A preliminary study observed that, between 2016 and 2019, 17 sentences were handed down by the Federal Court in Brazil authorizing the cultivation of *Cannabis* for medicinal purposes, relating to 16 individual lawsuits for 17 patients and a collective lawsuit that benefited 140 patients linked to a social organization in the state of Paraíba. In the individual actions, the patients had a diagnosis of cerebral pituitary adenoma, Silver Russell syndrome, autism, epilepsy, disc herniation, depression, Parkinson's, West syndrome, Dravet syndrome, retinitis pigmentosa, and neuropathic pain. The beneficiaries of the actions were nine patients aged between 4 and 16 years, five aged between 32 and 60 years and three with undetermined age. The patients in the class action lawsuit mostly had epilepsy, but also Parkinson's, Alzheimer's, and cancer. The sentences were handed down by the Federal Courts of the states of Acre, Bahia, Ceará, Paraíba, Rio de Janeiro, Rio Grande do Norte, Rio Grande do Sul, São Paulo, and the Federal District[7].

The increase in demand for the medicinal use of *Cannabis* derivatives is mainly due to the scientific findings observed from the 1990s onwards on the so-called cannabinoid system in the human organism, consisting of cannabinoid receptors, endocannabinoids, and the enzymes that catalyze their synthesis and degradation, opening new paradigms in the treatment of various pathologies. The requests that are being demanded are for products consisting exclusively of CBD and CBD+THC, in different concentrations, pharmaceutical forms (oral oily solution, oral gel, oral spray, etc.), of various brands/manufacturers, without registration with the Brazilian National Health Surveillance Agency (Anvisa), of foreign origin, and not available in the domestic market[8].

The process of regulating the medicinal use of products derived from *Cannabis* spp. in Brazil is complex and the consequences of these facts involve political actors and civil society, which makes it important to understand the context in which these decisions were taken and how they had repercussions. The objective of this article was to identify the main facts and positions related to the regulation of medicinal products based on *Cannabis* in the period from 2014 to 2021 by Anvisa, Ministry of Health, Chamber of Deputies, and Federal Councils of Pharmacy (CFF) and Medicine (CFM).

METHOD

This is qualitative research of the case study type, resulting from the analysis of the facts and positions identified by the different actors selected considering the time frame from 2014 to 2021.

Data production included sources from the database of the thematic axis Medication Policies, Blood, Pharmaceutical Assistance and Health Surveillance, developed in partnership with researchers from the State University of Bahia. This thematic axis integrates the Observatory of Political Analysis in Health of the Institute of Collective Health of the Federal University of Bahia (OAPS ISC/UFBA).

According to the dynamics of the axis, data are collected monthly, and the researchers monitor and discuss the news published on institutional sites defined to classify and select

those with a view to the potential of constituting political facts and whose contents constitute an OAPS database. In order to identify the facts and the positioning of the actors, the production of data for this study was based on the selection of information obtained, primarily in the link news related to the theme, available on the websites of selected institutions, understood as actors in the regulation process of *Cannabis* derivatives with therapeutic purposes, namely: Anvisa, Ministry of Health, CFF, CFM, and the normative production of the Chamber of Deputies. Additionally, news produced by websites of representatives of civil society, specialized and interested in the subject, were included.

The material was organized in Excel® spreadsheets standardized and individualized for each consultation site, selecting the news that presented the possibility of constituting a political fact[9]. In addition, for the purpose of identifying and analyzing the political position of actors and institutions of the State and civil society, the reflections that have been developed within the scope of OAPS[10] which were organized in some publications. The political analysis in health in OAPS takes power as a central category, having the health sector as a reference and, therefore, how power is appropriated, accumulated, distributed and used in this sector and in society. Based on this reference and according to the objective of the study, we sought to group the political facts, the actors and their positions related to the regulation of medicinal products based on *Cannabis* with medicinal purposes in a timeline.

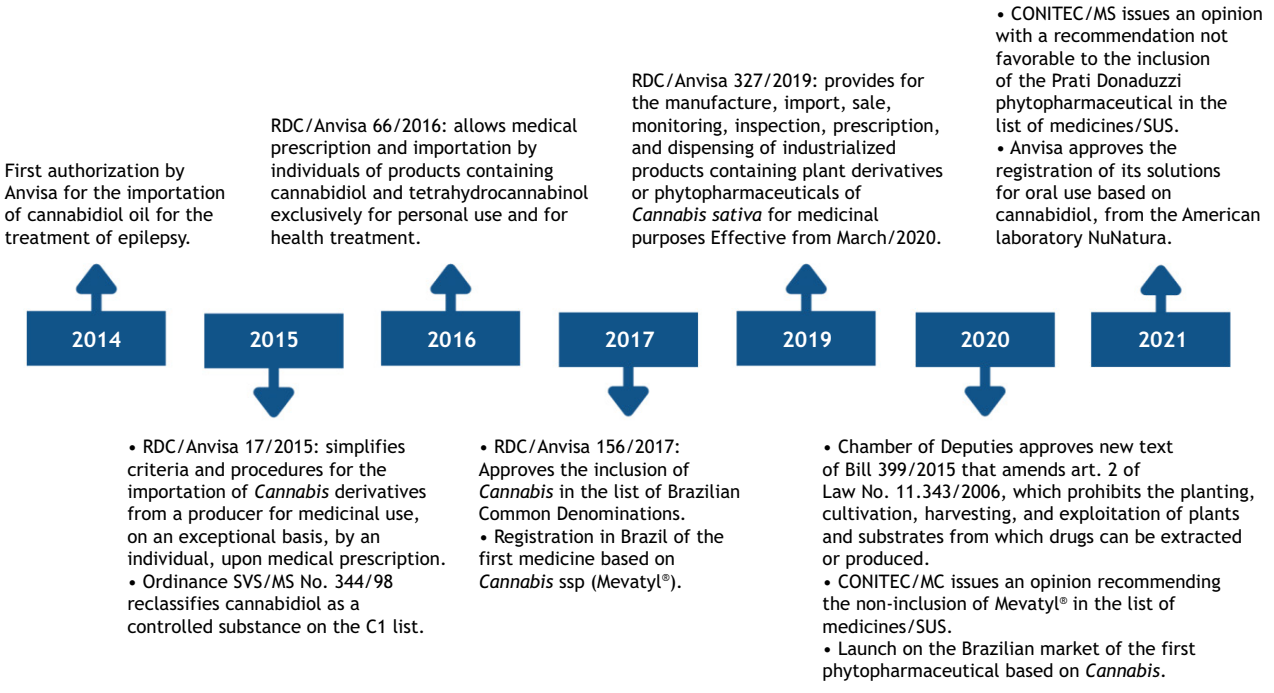
To complement the study, a literature review was carried out to identify articles in the Scientific Electronic Library Online (SciELO) and Periodicals Portal of the Coordination for the Improvement of Higher Education Personnel of the Ministry of Education (Capes/MEC), with the descriptors "Cannabis medicinal" (medicinal Cannabis), "canabinoides" (cannabinoids), "canabidiol" (cannabidiol), "THC", "regulamentação" (regulation), and "políticas de saúde" (health policies).

RESULTS AND DISCUSSION

The results presented in the timeline (Figure) summarize the main political facts identified in the period from 2014 to 2021. It should be noted that no relevant facts were identified in 2018, according to the data analyzed.

Discussions about the medicinal use of cannabinoid derivatives in Brazil became more frequent in 2014 due to the authorization to import CBD oil for a patient with severe epilepsy unresponsive to other treatments[11]. *Cannabis* and its derivatives were still considered banned substances in the country at the time. This fact gives rise to several requests for import authorization to justice by patients.

As a result of these facts, the medical category, through the CFM, published Resolution No. 2,113, of December 16, 2014, which approved the compassionate use of CBD exclusively for neurology, neurosurgery, psychiatry specialties and only for the treatment of epilepsy in children and adolescents refractory to conventional treatments. The CFM Resolution established that both prescribers and patients had registration in the Regional Council of Medicine (CRM)/CFM system for monitoring safety and adverse events[12].



Source: Elaborated by the authors, 2022.

Figure. Timeline on the regulation of the medicinal use of products derived from *Cannabis* sp. in Brazil.

In 2015, Anvisa published regulations simplifying criteria and procedures for importing products derived from *Cannabis* for medicinal use, on an exceptional basis, by individuals and upon medical prescription. This regulation of CBD-based products in association with other cannabinoids was a relevant fact, since, although these products were prohibited in Brazil at the time, the growing tension of patients with serious clinical conditions refractory to other treatments for some diseases contributed to the adequacy of the regulations. Resolution of the Collegiate Board (RDC) No. 17, of May 6, allowed greater agility to the import process with specific rules related to the product for patients who needed treatment, registered with Anvisa[13].

In that same year of 2015, CBD was reclassified as a controlled substance, and became part of the C1 list of Ordinance SVS/MS No. 344/1998, thus ceasing to be a proscribed substance, facilitating imports and enabling research on the effects of CBD and therapeutic use in the country[14]. With another measure, in August 2015, Anvisa started to authorize the exceptional purchase of the product not only for patients with epilepsy, but for several pathologies, such as chronic pain and Parkinson's disease. Additionally, in 2016, an update of the lists of Ordinance SVS/MS No. 344/1998 opened the possibility for the medicinal use of THC[15].

As a result of the work of society organizations interested in the therapeutic use of these products, in 2016, Anvisa, in compliance with a court decision, published RDC No. 66, of May 6, 2016, allowing the medical prescription and importation, by individuals, of products containing CBD and THC substances in their formulation, exclusively for personal use and for health treatment. Anvisa adopted measures to overturn the judicial decision, given the problems that this decision could entail, since such substances, not having registrations in Brazil, would not have proven safety and efficacy[16].

Also in 2016, Anvisa updated Annex I of Ordinance SVS/MS No. 344/1998 and included, in the A3 list, drugs derived from *C. sativa*, in a maximum concentration of 30 mg of THC per milliliter and 30 mg of CBD per milliliter. This update is related to the registration process of the drug Mevatyl®. In addition to this measure, the update of the list of products with CBD with simplified authorization for import was published, through RDC No. 128, of December 2, 2016[17].

As a result of a movement of interested social segments, in 2017, *C. sativa L.* was included in the list of Brazilian Common Denominations (DCB)[18]. All these changes in health regulations allowed the drug Mevatyl® to obtain health registration in 2017. Mevatyl® was the first drug derived from *Cannabis* registered in the country, but it was already approved in 28 countries, indicated in the package insert for the symptomatic treatment of moderate to severe spasticity related to multiple sclerosis[8].

In that same year, the National Committee Technology Incorporation (Conitec) of the Ministry of Health carried out a synthesis of evidence and concluded that no studies with active comparators had been found, thus not guaranteeing the robustness of the evidence so far available on this drug. In addition, they highlighted that an international evaluation did not demonstrate cost-effectiveness in the Mevatyl treatment for moderate to severe spasticity related to multiple sclerosis[8].

Anvisa opened two Public Consultations (PC No. 654 and PC No. 655) in 2019, to find out the public opinion regarding the medical use of *Cannabis* and research authorization on its use in Brazil and discuss technical and administrative requirements for the cultivation of *Cannabis* spp. plant for medicinal and scientific purposes, with emphasis on the broad participation of institutions, the pharmaceutical industry, and users of these products. At the end of 2019, Anvisa, through the publication of RDC No. 327, of December 9, 2019, regulated the manufacture, import, commercialization, monitoring, inspection, prescription and dispensing of industrialized products containing vegetable or phytopharmaceuticals derivatives from *C. sativa* for medicinal uses[19]. However, the proposal dealing with planting was shelved, a decision considered restrictive and insufficient by specialists, associations and patients who need *Cannabis*[20] products.

Anvisa considered that the scientific evidence available regarding CBD in clinical therapy was still weak and, for this reason, products derived from *Cannabis* were not classified as drugs. Anvisa has created a new category, that of products derived from *Cannabis* for medicinal purposes, which are granted a health license instead of registration, following the trend of other regulatory agencies. Regulatory agencies in several countries have highlighted the need for more evidence regarding the effectiveness and safety of these products, considering the evidence-based medicine (EBM) approach in decision-making. There is a shortage of studies such as systematic reviews and randomized clinical trials, important evidence to support decisions in regulatory systems in countries[21,22].

In March 2020, RDC No. 327/2019 came into force, allowing companies interested in marketing products derived from *Cannabis* in Brazil to request registration from Anvisa. The norm did not authorize the planting and determined that *Cannabis* products should be prescribed in the condition of refractory response to other therapeutic options available on the Brazilian market, and that the formulations should contain as actives exclusively plant derivatives or phytopharmaceuticals from *C. sativa*, predominantly, CBD, and no more than 0.2% THC, except for products intended for palliative care exclusively for patients with no other therapeutic alternatives and in irreversible or terminal clinical situations. The products were restricted to oral or nasal use and could not be used by children under 2 years of age[23].

Therapeutic indication and guidelines regarding the dose and form of use of products derived from *Cannabis* are the responsibility of physicians and must be dispensed exclusively by pharmacists in drugstores. The prescription must be accompanied by the Prescription Notification "B" and the Free and Informed Consent Form (TCLE) signed by the patient or their legal representative,

pursuant to Ordinance SVS/MS No. 344/1998 and its updates[23]. The non-medical use of *Cannabis* spp. remains criminalized in the country, as well as medicinal use for conditions without recognized clinical evidence[20].

In 2019, no official position from the Ministry of Health or news related to the regulation of the medicinal use of products derived from *Cannabis* spp. Only the position of the Minister of Health, Luiz Henrique Mandetta, was verified, who declared to the press that CBD could be included in the Unified Health System (SUS)[24].

According to Radis magazine, Anvisa's approval was just the first step in accepting the use of *Cannabis* as a medicine in Brazil, considering that there is still a ban on growing the species in Brazil. Thus, the use of the substance is only possible by importing derived products. In the opinion of non-governmental organizations (NGOs) that produce *Cannabis* derivatives with judicial authorization, the regulation prevents access to these products, which arrive at very high prices in Brazil[25].

In 2019, the CFF followed the discussions in PC on the regulation of the use of products based on *Canna-bis* and demonstrated an institutional position favorable to medicinal use. In the debate, the CFM highlighted technical and ethical issues regarding the therapeutic use of this and other products derived from *Cannabis*[26,27].

There were movements in the federal legislature on the subject. Among the productions of the Federal Chamber of Deputies on *Cannabis,* requests for a public hearing were identified to discuss the subject of cultivation, production, and registration of medicines based on *Cannabis* spp. in Brazil. It was noted that some of these requests were from deputies from various political parties of the center and right wings. Few requests for a public hearing on *Cannabis* were identified that sought to include in the debate invited representatives of *Cannabis* cultivation associations, researchers and users of *Cannabis* for medicinal purposes[28].

The discussion on the regulation of the cultivation of *Cannabis* spp. resurfaced in the National Congress through the resumption of Bill No. 399 of 2015 authored by Federal Deputy Fábio Mitidieri (PSD/SE). The Bill intended to amend art. 2 of Law No. 11,343, of August 23, 2006, which prohibits in the national territory the planting, cultivation, harvesting, and exploitation of plants and substrates from which drugs can be extracted or produced. According to the justification presented in the Bill, the objective would be to facilitate the commercialization of medicines that contain extracts, substrates, or parts of the *C. sativa* plant in its formulation. A substitute text to the original project was delivered in August 2020 to the presidency of the Chamber of Deputies[28,29].

After intense mobilization of several parliamentarians from different parties who requested hearings with specialists in the area in Brazil and other countries, representatives of medical and pharmaceutical categories, non-governmental institutions, jurists, representatives of public security institutions, and regulatory bodies, Bill No. 399/2015 received a favorable opinion from the rapporteur Deputy Luciano Ducci (PSB-PR) in April 2021 and was finally approved by the special commission created to discuss the matter on June 8, 2021[28].

The vote on the replacement for rapporteur Luciano Ducci (PSB-PR) was tied and approval was given by the rapporteur's casting vote. The approved text allows carrying out the activities of cultivation, processing, research, transport, production, industrialization, manipulation, commercialization, import, and export of products based on *Cannabis* for medicinal, cosmetic, and textile purposes. This proposal extends the original text authored by Fábio Mitidieri, which proposed permission for the cultivation of *Cannabis* only by legal entities, such as: companies, patient associations, and NGOs[28].

After the approval of the Bill, different positions of the parliamentarians were observed. The project's rapporteur emphasized that the focus of the project is only related to the medical use of *Cannabis* and denied that the opinion he prepared does not have any issue that deals with the release of the recreational use of marijuana. There were also controversial highlights by parliamentarians opposing the proposal, such as the highlight made to art. 3 of the approved text. The article deals with the articulation and coordination of activities that prevent misuse and repression of unauthorized production, among others, to the National System of Public Policies on Drugs. Deputies emphasized surprise as a highlight made by considering that the suppression of this measure allows the cultivation to be carried out unrestrictedly without the requirements that were placed by the rapporteur[30].

In April 2020, the laboratory that registered the drug Mevatyl® requested an assessment for incorporation into the SUS, however, Conitec did not recommend the incorporation of the drug in the symptomatic treatment of moderate to severe spasticity related to multiple sclerosis. The drug was considered safe, however, the level of evidence of efficacy outcomes was considered of low quality[31]. Thus, the only drug consisting of cannabinoid derivatives registered in the country remains unincorporated into the SUS and its acquisition is only possible through direct disbursement. The high cost of purchasing this medication is one of the factors that lead patients or their representatives to request access through the courts.

In May 2020, after granting a sanitary license by Anvisa, a national pharmaceutical laboratory (Prati Donaduzzi) launched on the market a phytopharmaceutical derived from *Cannabis* consisting of 200 mg/mL of CBD. Unlike the drug Mevatyl®, which has a specific indication for the treatment of spasticity, the Brazilian product was registered as a phytopharmaceutical (drug of plant origin), with no pre-defined clinical indication. This means that it can be prescribed for any condition where CBD is considered potentially beneficial for the patient[32].

Conitec released a technical report in February 2021, with the objective of evaluating the efficacy, safety, cost-effectiveness,

and budgetary impact of CBD, in view of the request for the incorporation of CBD 200 mg/mL by the pharmaceutical company Prati Donaduzzi for the treatment of children and adolescents with epilepsy refractory to antiepileptic drugs to the SUS, by the Ministry of Health[33].

Conitec's report supported a PC, opened and closed in March 2021, with the unfavorable preliminary recommendation for the inclusion of the phytopharmaceutical in the list of SUS drugs, understanding that the clinical evidence available regarding the risk and benefit of the drug is questionable and presented high cost-effectiveness and budget impact results[33]. In May 2021, a new report was published by Conitec, which once again decided, unanimously, to recommend the non-incorporation of CBD for children and adolescents with epilepsy refractory to antiepileptic drugs in the SUS, for the same reasons previously manifested[34].

Despite yet another rejection of the proposal to incorporate medicines based on *Cannabis* derivatives into the SUS, the development of new products still seems to be of interest to the productive sector. In April 2021, products were registered, at concentrations of 17.18 and 34.36 mg/mL, with up to 0.2% THC through Resolution RE No. 1,525, of April 14, 2021[35,36].

The publication of Anvisa's RDC No. 327/2019, in 2019, was an important historical and sanitary fact to enable the manufacture and importation of products derived from *Cannabis* in Brazil, leaving, however, a gap in access to drugs when the cultivation of *Cannabis* for medicinal and research purposes was not authorized. Given the high cost of importing inputs and drugs already registered, patients and NGOs find in judicialization the way to legal access to these products[20].

According to Portal Sechat[37], there are 51 patients in Brazil authorized to cultivate *Cannabis* at home, in addition to an association that serves more than 2,000 people in Paraíba, the *Associação Brasileira de Apoio Cannabis Esperança* (Abrace). Abrace filed a lawsuit in 2017 (No. 0800333-82.2017.4.05.8200/PB) in which it obtained authorization to cultivate *Cannabis* for medicinal purposes and, consequently, to produce and distribute therapeutic oils derived from the plant to its associates[38].

In February 2021, Abrace published that Anvisa filed a request for the suspension of Abrace's rights to plant, harvest, handle, and produce CBD-based products at the Federal Regional Court of the 5th Region (TRF-5), initiating a large social mobilization in support of the continuity of its activities[39].

Anvisa issued a public note denying having filed any lawsuit to suspend decisions favorable to Abrace, however, it states that the authorization given to the association was conditional on compliance with certain health requirements, which, according to Anvisa, are not being observed, which forced the Agency to report the situation to the TRF-5[40]. Some of the requirements demanded by Anvisa refer to the sanitary adequacy of the laboratory and delivery of documentation to receive the Company Operating Authorization (AFE) and the Good Manufacturing Practices Certificate (CBPF), for example.

In March of the same year, after an inspection at the headquarters of Abrace together with representatives of Anvisa, the federal judge Cid Marconi decided to revoke his decision and maintained the operation of Abrace, however he imposed deadlines for Abrace to comply with judicial and health determinations[41]. For many defenders of the cultivation of *Cannabis*, Anvisa's decision does not just reflect a sanitary regulation but a political position that goes against the position of exemption that belongs to the regulatory agencies[42]. Meanwhile, Abrace continues to try to comply with the determinations in the established time to continue to serve patients associated with the supply of CBD oil.

Anvisa had already gone to court in other situations to suspend the activities of associations that produce medicinal oil with CBD. Also in 2020, the Support Association for Medicinal *Cannabis* Research and Patients (Apepi) obtained provisional authorization from Anvisa to research, cultivate, manipulate, transport, extract oil, package, pack, and distribute to current members, according to nominal list, reports, requisitions, and medical prescriptions, after legal action moved by the association in the same year. Anvisa appealed against the decision and the injunction was suspended by the Federal Regional Court of the 2nd Region (TRF-2), losing Apepi the right to plant, handle, and distribute oil with a derivative of *Cannabis*[43,44].

The definition of regulatory frameworks in Brazil that ensure patient access to *Cannabis* products and medicines, as well as in other countries, is related to cultural and historical aspects. An integrative review[45] evaluated regulations on the medical use of *Cannabis* in the United Kingdom, Germany, Italy, the Netherlands, Canada, Israel, and Australia. The study concludes that globally, countries adopt regulations with different approaches as a result of historical and cultural factors.

However, despite differences in their regulatory approaches, all countries agree on the need for continuing education for physicians and other health professionals. Another aspect identified in the analysis highlights the need to simplify policy formulation and establish effective communication between physicians, patients, and policy makers. The construction of collaborative networks with an interest in expanding access to *Cannabis* for medicinal purposes can mobilize international institutions capable of evaluating and regulating the use of medicinal *Cannabis*, overcoming the difficulties faced.

Looking at experiences elsewhere, the study found that the best performing regulations were developed in a timely and efficient manner. Neglecting these opportunities to advance the creation and establishment of regulations can create regulatory vacuums that are often filled by other interest groups, such as industry and lobby groups.

In the USA, despite the fact that about nine out of 10 adults across the country support the legalization of *Cannabis* for therapeutic purposes and about two thirds of the population live in areas where the use of medical *Cannabis* is legal, contradictorily, what is observed is that *Cannabis* remains classified as a Class I drug according to the Federal Controlled Substances Act, that is,

the cultivation, distribution, and use of *Cannabis* remains prohibited and each US state sets its own rules[46].

The lack of a regulatory system, together with the aggressive marketing of the industry in the USA, conveyed to the population the idea of a type of scenario in which *Cannabis* would be accessible to everyone, this perception does not contribute to the development of scientific evidence and the development of uniform regulations, much less so that those who need *Cannabis* as a therapeutic resource feel comfortable with the use of products[45].

The control of the use of medicinal *Cannabis* was another aspect observed in the countries analyzed in the study. The supervision of the activities of the pharmacies responsible for dispensing these drugs is relevant but the findings drew attention to very conservative regulations on supervision and the authors drew attention to the risk of fueling the illicit market. It is important to ensure regulatory mechanisms that are developed and improved in line with political and scientific developments. It is necessary to reconcile the need to develop guidelines and regulations on the use of medicinal *Cannabis* that ensure a control that is neither too rigid nor too broad[45].

It appears that, in the experience observed in the United Kingdom, Canada, Australia, Germany, Italy, Holland, Canada, and Israel[45], the political context and research related to medicinal *Cannabis* has developed rapidly and in line with changes in the attitude of the population. However, the regulatory frameworks on the subject face challenges that focus on issues involving the scarcity and uncertainties in the scientific evidence necessary for decision-making on medicinal *Cannabis*. Furthermore, the existence of regulatory frameworks in a country is no guarantee that procedures will be followed or even that this will result in access to medical marijuana for patients in need, expanding clinical research and thus generating scientific evidence that allows regulatory agencies to make safer decisions.

Recently, there was news about the *habeas corpus* judgment of two cases by the Superior Court of Justice, which unanimously decided to authorize the planting of *Cannabis* for medicinal purposes. This decision was celebrated by the social movement in favor of the medicinal use of the plant[47].

It should be noted the recent decision handed down by the CFM through Resolution No. 2,324, of October 11, 2022, which restricted the prescription of *Cannabis* derivatives to CBD only and for two conditions of severe and refractory epilepsy. The decision provoked several demonstrations by the pharmaceutical industry, patient associations, and medical professionals. Criticisms included allegations of restrictions on medical autonomy, prejudice to conducting studies and concerns about restrictions on patient access to treatment, in addition to accusations of political use of the theme. The measure was controversial, and, after great repercussions, the CFM submitted the aforementioned resolution to a new public consultation and the Federal Public Prosecutor's Office instituted a procedure to assess whether the resolution violates the right to health, provided for in the Federal Constitution[48].

CONCLUSIONS

Several countries, in Latin America and around the world, regardless of their positions on repression of drugs, have changed their legislation and internal regulations to allow – and even encourage – the production of drugs based on *Cannabis*; that is the case of Peru, Chile, Colombia, Argentina, Mexico, Thailand, Canada, Israel, in addition to the European Union, and several US states.

The medicinal use of *Cannabis* derivatives divides opinions in civil society; the fact that *Cannabis* is associated with the illicit use of marijuana encourages opposition to the use of medicinal products derived from it. However, for many patients who need treatment, the regulation of the importation and use of these products represents hope and quality of life.

The theme is relevant, discussions and debates allow society to be informed about how the government is conducting regulations to allow the production of drugs based on *Cannabis* as a therapeutic alternative for certain conditions that do not yet have drug therapies.

A Resolution edited by Anvisa (RDC No. 327/2019) allows companies and research institutions to import the raw material for studies and drug development, but the cost is high and is reflected in the final product, in addition to the existence of barriers to the incorporation of these new products, which directly impacts the population's access. The possibility of authorizing the cultivation can make the raw material less expensive and Brazil less dependent on importing these inputs. The new text of Bill No. 399/2015 brings back this debate.

Meanwhile, NGOs and patient associations continue to sue the courts for the right to plant, produce CBD-based oil, distribute it among registered patients but they also encounter some obstacles related to authorization and sanitary adaptations.

By understanding learnings from other countries and implementing them in policy formulation, it is hoped that the introduction of medicinal *Cannabis* in Brazil can finally proceed in a way that maximizes clinical research and patient benefit in order to expand access to these products to people in need.

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Author's Contributions

Araújo PS, Costa EA, Sandes CFB - Conception, planning (study design), acquisition, analysis, data interpretation, and writing of the work. Cruz ECD, Rocha JS, Soares LCC - Data acquisition, analysis, and interpretation. Pereira MT - Acquisition, analysis, data interpretation, and writing of the work. All authors approved the final version of the work.

Conflict of Interests

The authors inform that there is no potential conflict of interest with peers and institutions, politicians, or financial in this study.