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Psychedelic Medicines 2024

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Brazil: Law and Practice & Trends and Developments

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BRAZIL

Law and Practice

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Contents

Dannemann Siemsen comprises a team of experts dedicated to defending IP since 1900. Recognised as leaders in Latin America, the firm operates throughout the world and offers first-rate IP services and litigation, covering all industry segments as well as attending to IP firms from all different regions. Dannemann Siemsen's patent team – the largest in Brazil – combines experts with a different technical background that allows it to develop the most comprehensive strategies to protect clients' innovations. The firm's trade mark department uses advanced technology to handle clients' cases from searches to appeals, with strategic thinking for trade mark portfolio management and supervision structures, including with regard to digital media. It has more than 120 years of experience built in human knowledge, respect, ethical values, diversity, and a continuous pursuit of staying one step ahead of future changes.

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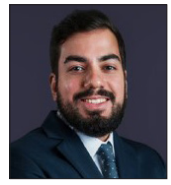

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1. Regulatory Overview

1.1 Primary Laws and Regulations

The main laws and regulations relating to psychedelic medicines in Brazil are:

- Law No 6,360/1976 – provides regulation for health surveillance of medicines, drugs, pharmaceutical ingredients, cosmetics, sanitisers and other products;
- Law No 9,279/1999 – established the National System of Health Surveillance (*Sistema Nacional de Vigilância Sanitária*, or SNVS) and created the Brazilian Health Regulatory Agency (*Agência Nacional de Vigilância Sanitária*, or ANVISA);
- Law No 9,961/2000 – created the National Regulatory Agency for Private Health Insurance and Plans (*Agência Nacional de Saúde Suplementar*, or ANS);
- Law No 10,742/2003 – provides regulatory standards for the pharmaceutical sector and created the Drugs Market Regulation Chamber (*Câmara de Regulação do Mercado de Medicamentos*, or CMED);
- Law No 11,343/2006 (the "Anti-Drugs Law") – established the National System of Public Policies on Drugs (*Sistema Nacional de Políticas Públicas sobre Drogas*, orSisnad), provides measures for the prevention of misuse, care and social reintegration of drug users and addicts, establishes rules for the repression of unauthorised production and illicit trafficking of drugs, defines crimes, and makes other provisions;
- Ministry of Health (MoH) Ordinance No 344/1998 – technical regulation concerning substances and drugs subject to special control; and
- ANVISA Ordinance No 898/2015 – established a Working Group between ANVISA and the Ministry of Justice to optimise the classification and control of narcotic, psychotropic, precursor and proscribed substances (as well as other substances and plants subject to special control).

ANVISA Resolution of the Collegiate Board (*Resolução da Diretoria Colegiada*, or RDC) No 38/2013 regulates expanded access, compassionate use and post-study drug supply programmes. In summary, ANVISA RDC No 38/2013 establishes the following definitions.

- Expanded access programme – a programme to make available a promising new drug (not yet registered with ANVISA or commercially available in Brazil) that is undergoing or has completed a phase III trial and is aimed at a group of patients who have serious debilitating and/or life-threatening diseases and no satisfactory therapeutic alternative with registered products.
- Compassionate use programme – a programme to allow the supply for personal use by a patient, who is not a participant in an expanded access or clinical research programme, of a promising new drug (not yet registered with ANVISA) that is in the process of clinical development and intended for patients who have serious debilitating and/or life-threatening diseases and no satisfactory therapeutic alternative with products registered in Brazil. The allowance granted by ANVISA for compassionate use is personal and not transferrable.
- Post-study drug supply programme – a programme to allow the continued supply of medicines to research subjects at no cost, applicable in cases of termination of the study or when their participation ends.

ANVISA's approval process for expanded access, compassionate use and post-study

drug supply programmes begins with a request from the sponsor of a clinical trial or the sponsor's representative organisation. Requests for approval of expanded access and compassionate use programmes are analysed by ANVISA according to the following criteria:

- severity and stage of the disease;
- absence of a satisfactory therapeutic alternative in Brazil for the clinical condition and its stages;
- severity of the clinical condition and presence of co-morbidities; and
- assessment of the risk-benefit ratio of using the requested medication.

With ANVISA's permission, the supply of the medicine authorised in the expanded access and compassionate use programmes should be guaranteed as long as there is benefit to the patient, at the doctor's discretion.

1.2 Regulatory Bodies

In Brazil, medicines are governed by a comprehensive and complex regime of legislation and regulations spanning many different areas of law. The legislative and regulatory landscapes are also very dynamic, as government authorities constantly update regulatory processes and policies.

In the Brazilian health regulatory system introduced by Law No 6,360/76, a drug may be marketed only if:

- it has been previously registered with ANVISA, according to Law No 9,782/99; and
- its price has been established by the CMED, as per Law No 10,742/03.

As regards access to drugs, given that the healthcare system is primarily public in Brazil, patients do not have out-of-pocket expenses in most cases, inasmuch as drugs considered to be essential to public health are provided by the Brazilian government. In the private healthcare system, health insurance companies must at least supply patients with drugs included in the List of Procedures issued by ANS.

Accordingly, the main regulatory bodies charged with enforcing the laws and regulations governing the medical psychedelics industry are:

- ANVISA – the Brazilian regulatory body (created in 1999 within the MoH) entitled to enforce public health protections, oversee drug approvals and sanitary standards, regulate the import of drugs, and issue regulatory approval for clinical trials;
- ANS – the regulatory body (created in 2000 within the MoH) responsible for the regulation, standardisation, control and inspection of activities that guarantee private healthcare;
- National Committee for Technology Incorporation (*Comissão Nacional de Incorporação de Tecnologias no Sistema Único de Saúde*, or CONITEC) – the body responsible for advising the MoH in the incorporation or disinvestment of health technologies into the Unified Healthcare System (*Sistema Único de Saúde*, or SUS); and
- National Research Ethics Commission (*Comissão Nacional de Ética em Pesquisa*, or CONEP) – provides ethical review and approval for clinical trials.

1.3 Self-Regulatory Authorities

There are no self-regulatory authorities that govern the psychedelic medicine industry or psychedelic trials in Brazil.

1.4 Existing Market

The Brazilian market of psychedelic drugs is incipient, even though it seems to be gradually evolving by acknowledging the therapeutic potential of psychedelic substances following the development of clinical data and new regulatory approaches on the matter in other jurisdictions.

In a notable regulatory development, ANVISA approved esketamine (S-isomer of ketamine) hydrochloride in 2020 for treating treatment-resistant depression. Ketamine, although not a classic psychedelic, shares some pharmacological properties with this class of substances. The substance had already been used in the past as an anaesthetic in diagnostic and surgical interventions; however, until 2020, it did not have regulatory approval for psychiatric treatment. For further details, please see "Esketamine and ketamine as regulatory precedents" in the Brazilian Trends and Developments chapter of this guide.

In addition, during the past few decades, Brazil has made limited exceptions for traditional and cultural uses of psychedelics. Ayahuasca, a traditional Amazonian brew containing dimethyltryptamine (DMT), has been legally permitted for use within certain religious practices since the 1980s. For more on the case of ayahuasca, please see "Ayahuasca: balancing freedom of religion and drug prohibition" in the Brazilian Trends and Developments chapter of this guide.

However, other psychedelics remain firmly restricted, with minimal legal permissions for research purposes.

1.5 Challenges Facing Market Participants

Brazil is at a critical point in its approach to psychedelic substances as potential treatments for mental health disorders. The historical and regulatory landscape has shaped public perception and legal frameworks, often hindering research and clinical applications. Even though the therapeutic potential of substances such as psilocybin, 3,4-Methylenedioxymethamphetamine (MDMA), and DMT is increasingly recognised, regulatory bodies require compliance with strict rules to ensure patient safety and evidence quality assurance.

Difficulties faced by applicants in obtaining approval to conduct clinical trials with psychedelic substances reinforces the need for regulatory reforms that facilitate research while maintaining safety standards.

2. Cross-Jurisdictional Matters

2.1 Common Cross-Jurisdictional Issues

There are no common or specific cross-jurisdictional issues concerning psychedelic substances in Brazil.

2.2 How Access Is Affected by Foreign Law and Regulation

Even though foreign law and regulation are not applicable in Brazil, the Brazilian regulatory approach to psychedelics has historically mirrored global trends, with strict prohibitions influenced by international drug control conventions. Substances such as lysergic acid diethylamide (LSD), MDMA, psilocybin and DMT were widely classified as illegal amid global drug control efforts, without differentiation between their recreational and potential therapeutic uses. This policy approach placed psychedelics in the

same category as addictive narcotics, imposing restrictions that have hindered research and clinical applications for many years.

3. Legal and Regulatory Developments

3.1 Access to Psychedelic Medicines Today

Brazil's current legislative and regulatory landscapes concerning psychedelic drugs is restrictive. Even though Brazil's regulatory stance on psychedelics reflects a gradual shift shaped by international research developments and the increasing interest in alternative mental health treatments, most psychedelic substances such as LSD, psilocybin, MDMA, mescaline and DMT are categorised as proscribed substances, pursuant to MoH Ordinance No 344/1998 – marking them as prohibited drugs with no authorised therapeutic use.

Applicants for clinical trials are also facing difficulties in obtaining regulatory approval and, ultimately, this jeopardises patients' access to potential treatments. In Brazil, clinical trials are strictly regulated to ensure the safety and efficacy of – and ethical standards for – investigational drugs. For further details, please see "Regulatory barriers to psychedelic research" in the Brazilian Trends and Developments chapter of this guide.

Although access to medical psychedelics does not seem to be a top priority in the regulators' agenda, recent developments (eg, the approval of esketamine for treating treatment-resistent depression mentioned in **1.4 Existing Market**) have set a positive precedent. Such developments suggest that medicines based on psychedelic substances can be approved by ANVISA and made available safely to the population when GCP requirements and the conditions of safety, quality and efficacy are met.

3.2 Legislative Routes to Wider Access

Initial legislative routes should acknowledge the therapeutical potential of psychedelic substances and create mechanisms to allow and foster the conduction of clinical trials and the review of marketing authorisation applications related to psychedelic drugs in an efficient manner while ensuring patient's safety and deterring abusive practices.

Brazil has a robust legislative and regulatory structure in respect of pharmaceutical drugs. However, the challenges involved in the therapeutic use of psychedelic drugs are not addressed in a specific, objective manner.

One example of how the lack of specific, formal regulation focused on the therapeutic use of psychedelic drugs may jeopardise patients' access to potential treatments is the *Instituto Phaneros* case. Owing to the absence of clear provisions on the current regulation, a research organisation called the Phaneros Institute (*Instituto Phaneros*) – focused on the evaluation, research and development of Psychedelic-Assisted Psychotherapy (PAP) in Brazil – struggled to obtain proper authorisations from ANVISA to conduct clinical trials with MDMA and psilocybin for treatment of post-traumatic stress disorder and major depression, respectively.

Instituto Phaneros was only able to compel ANVISA to review the merits of the authorisation applications for the referred clinical trials upon a court order. However, ANVISA eventually denied the applications by concluding that:

- as the research involved the administration of a psychedelic substance to human beings and therefore a high health risk would be involved in the intended activities, the focus of the assessment should be on the prevention of product deviation and on the safety conditions for conducting clinical studies, including the safe administration of the product to patients; and
- *Instituto Phaneros* would have not complied with all regulatory requirements to demonstrate safety in the administration to patients, as well as in the handling, safe-keeping and disposal of the psilocybin substance.

For further details and analysis of the *Instituto Phaneros* case, please see "Instituto Phaneros case: strict requirements for psychedelic research" in the Brazilian Trends and Developments chapter of this guide.

3.3 Adult-Use Markets

Currently, the chances of a regulated "adult-use market" for psychedelic substances in Brazil seem to be low. There has been some deliberation in the sense of decriminalising possession of prohibited substances for personal use – for example, June 2024, the Supreme Court decided to decriminalise marijuana possession for personal use and set the amount at up to 40 grams or six female plants to differentiate the user from the trafficker. Nonetheless, the Brazilian Congress is reviewing Constitutional Bill No 43/23, which aims at including a provision in the Federal Constitution stating that it is a crime to possess or carry any quantity of drugs or narcotics "without authorisation or in disagreement with a legal or regulatory determination".

Given that Brazil's regulatory approach to psychedelics has historically mirrored global trends, it seems the development of regulated markets for the recreational use of psychedelic drugs might encourage increased debate in Brazilian society and, as a consequence, legislative initiatives addressing the matter in the country. However, the absence of legislative initiatives to regulate and foster the therapeutic use of psychedelic substances indicates that it will take a long time for Brazilian authorities – including members of the executive, legislative and judiciary branches – to embark on thoughtful discussions concerning the recreational use of psychedelic substances.

Trends and Developments

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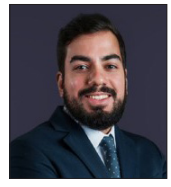

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Regulation of Psychedelic Drugs in Brazil

As mental health challenges continue to rise worldwide, researchers and healthcare providers are exploring alternative treatments beyond traditional drugs. Psychedelics – once dismissed and stigmatised – are undergoing a renaissance within the field of psychiatric treatment. Substances such as psilocybin, lysergic acid diethylamide (LSD) and 3,4-Methylenedioxymethamphetamine (MDMA) are believed to have therapeutic benefits in treating conditions such as depression, anxiety, addiction and post-traumatic stress disorder (PTSD), often where conventional therapies fail.

Brazil, known for its rich biodiversity and unique cultural heritage, has a complex relationship with psychedelics. Indigenous groups have used substances such as ayahuasca ceremonially for centuries, yet regulatory bodies currently impose restrictions on many psychedelic substances, limiting their therapeutic and research potential. With other countries moving towards the regulated use of psychedelics, Brazil faces an opportune moment to reassess its policies and get in touch with the traditional knowledge of its original communities.

The Brazilian Constitution establishes health as a universal right and a state duty, fulfilled through policies that ensure equitable access to healthcare. The Unified Health System (*Sistema Único de Saúde*, or SUS) operates a nationwide network to provide health services, manage public health needs, and incorporate essential medical supplies.

The Brazilian Health Regulatory Agency (*Agência Nacional de Vigilância Sanitária*, or ANVISA) was created under the Ministry of Health (MoH) to enforce public health protections and oversees drug approvals, sanitary standards, and regulating imports. When a drug is identified as strategic for public health, the National Committee for Technology Incorporation (*Comissão Nacional de Incorporação de Tecnologias no Sistema Único de Saúde*, or CONITEC) – a commission within the MoH – evaluates its incorporation into the SUS after ANVISA's approval. This enables federal, state and municipal healthcare providers to acquire drugs under public bidding regulations, ensuring the drugs' availability to Brazilian citizens.

This article explores the Brazilian situation in terms of psychedelic drug regulation, drawing lessons from international models and considering the future of psychedelic research and therapeutic application in Brazil. For the purposes of this article, the category of psychedelics encompasses both classic (eg, psilocybin, dimethyltryptamine (DMT), mescaline, LSD) and non-classic psychedelic substances (eg, ketamine, MDMA).

Historical context and present challenges

Brazil's regulatory stance on psychedelics reflects a gradual shift, shaped by international research developments and the increasing interest in alternative mental health treatments. This section examines the historical and regulatory journey of psychedelics in Brazil, focusing on existing classifications, current ANVISA policies, and the barriers that researchers face when conducting clinical studies.

Brazil's regulatory approach to psychedelics has historically mirrored global trends, with strict prohibitions influenced by international drug control conventions. Substances such as LSD, MDMA, psilocybin and DMT were widely classified as illegal amid global drug control efforts, without differentiation between their recreational and potential therapeutic uses. This policy approach

placed psychedelics in the same category as addictive narcotics, imposing restrictions that have hindered research and clinical applications.

Ayahuasca: balancing freedom of religion and drug prohibition

During the past few decades, Brazil has made limited exceptions for traditional and cultural uses of psychedelics. Ayahuasca, a traditional Amazonian brew containing DMT, has been legally permitted for use within certain religious practices since the 1980s.

The regulation of ayahuasca for religious purposes in Brazil represents a complex interplay between cultural rights and health governance. In 1985, Brazil's Federal Narcotics Council (*Conselho Federal de Entorpecentes*, or CONFEN) began investigating the religious use of ayahuasca, leading to the eventual permission of its sacramental use by organised religious groups in 1992. This allowance was further protected under the 1988 Brazilian Constitution, which ensures freedom of religion.

CONFEN conducted studies that recognised the cultural and social significance of ayahuasca in religious practices, particularly in the *União do Vegetal* and *Santo Daime* religions. This has contributed to its ongoing legal acceptance.

However, the regulation of ayahuasca maintains strict parameters – including prohibiting commercialisation and exportation – to prevent potential abuse and diversion from spiritual contexts. Also, any diversion from the sacramental and religious use of ayahuasca could potentially lead to the agents involved being charged with crimes under the Anti-Drugs Law (Law No 11,343 of 23 August 2006).

The case of ayahuasca represents a nuanced approach within Brazilian regulation, acknowledging the significance of psychedelics in traditional ceremonies. Nonetheless, other psychedelics remain firmly restricted, with minimal legal allowances for research purposes.

Current classification: MoH Ordinance No 344/1998

ANVISA oversees the regulation of controlled substances in Brazil, including psychedelics. ANVISA's primary framework for these substances is outlined in MoH Ordinance No 344/1998, which classifies controlled substances based on their therapeutic potential and risk profile.

The classification defines substances as narcotic (Lists A1 and A2), psychotropic (Lists A3, B1, B2), other substances subject to special control (List C1), retinoic (List C2), immunosuppressive (List C3), anabolic (List C5), substances that are precursors to narcotics and/or psychotropic substances (List D1), chemical inputs used for the manufacture and synthesis of narcotics and/or psychotropic substances (List D2 – Subject to Control by the Ministry of Justice and Public Security), proscribed plants and fungi that can produce narcotic and/or psychotropic substances (List E), and prohibited substances in Brazil (List F).

The list of prohibited substances in Brazil encompasses narcotic substances (List F1), psychotropic substances (List F2), precursor substances (List F3), and other substances (List F4). Currently, psychedelics such as LSD, psilocybin, MDMA, mescaline and DMT are categorised as F2 substances, marking them as prohibited drugs with no authorised therapeutic use.

i) Challenges in updating MoH Ordinance No 344/1998: New Psychoactive Substances (NPS)

New Psychoactive Substances (NPS), as defined by the United Nations Office on Drugs and Crime (UNODC), are synthetic compounds designed to mimic the effects of controlled drugs such as cannabis, LSD, and methamphetamine. These substances evade current drug regulations, emerging rapidly in global markets and complicating enforcement efforts. Between 2009 and 2021, more than 1,124 NPS were identified, highlighting the challenge of keeping MoH Ordinance 344/1998 up to date.

To address these challenges, Brazil's Ordinance No 898/2015 established a Working Group – comprising experts from ANVISA, the Ministry of Justice and federal law enforcement agencies – to enhance the regulatory model for classifying controlled substances. This group aims to expedite the detection and classification of NPS, utilise collaboration with forensic labs through notification forms, and streamline NPS' inclusion in controlled substances lists.

Regulatory barriers to psychedelic research

In Brazil, clinical trials are strictly regulated to ensure the safety and efficacy of – and ethical standards for – investigational drugs. ANVISA requires all clinical trial protocols for drugs to follow rigorous guidelines aligned with international Good Clinical Practice (GCP) and the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH). ANVISA Resolution of the Collegiate Board (*Resolução da Diretoria Colegiada*, or RDC) No 09/2015 harmonises local regulation with global standards, streamlining the approval process and setting fixed review times for Clinical Development Dossiers.

The National Research Ethics Commission (*Comissão Nacional de Ética em Pesquisa*, or CONEP) collaborates closely with ANVISA by providing ethical review and approval of clinical trials. Whereas ANVISA evaluates the scientific and methodological integrity of studies, CONEP ensures ethical compliance by safeguarding participant rights and overseeing informed consent protocols. All clinical trials must receive joint approval from both ANVISA and CONEP before commencement, demonstrating a dual regulatory framework that enhances study oversight and participant protection.

For researchers to conduct clinical trials involving controlled substances (including psychedelics), they must obtain special permissions from ANVISA and other regulatory bodies. Each will require detailed safety protocols and justification for the study's potential benefits.

By way of example, in order to carry out activities involving substances subject to special control (listed in MoH Ordinance No 344/1998), a private company must obtain a Special Authorisation (*Autorização Especial*, or AE) from ANVISA by proving specific technical and administrative requirements, as set out in ANVISA RDC No 16/2014. In the case of proscribed substances – which includes psychedelic substances – and the plants from which they originate, as well as the proscribed plants (according to Annex I of MoH Ordinance No 344/1998), study and research activities will only be allowed when duly authorised by ANVISA by means of a Special Simplified Authorization for Teaching and Research Establishments (*Autorização para Ensino e Pesquisa*, or AEP) (ANVISA RDC 16/2024, Article 4, paragraph 3).

i) Instituto Phaneros case: strict requirements for psychedelic research

In 2022, ANVISA restricted the requirements for obtaining an AEP by limiting the definition of "teaching and research establishments" to cover only "higher education or technical institutions (including their support foundations) that operate in the strictly academic sphere" (ANVISA RDC 659/2022, Article 4, Item VI), which would basically allow only universities and higher education institutes to engage in research involving proscribed substances. Consequently, research organisations that did not operate in the strictly academic sphere lost the prerogative to conduct study and research activities with proscribed substances.

One of those research organisations was the Phaneros Institute (*Instituto Phaneros*), an institute focused on the evaluation, research and development of Psychedelic-Assisted Psychotherapy (PAP) in Brazil. Prior to the new restriction imposed by ANVISA on which institutions could be allowed to engage in research activities with proscribed substances, ANVISA granted two AEPs to *Instituto Phaneros*:

- AEP No 012/2016 concerning authorisation for research entitled "Psychotherapy assisted with 3,4 Methylenedioxymethamphetamine (MDMA) in the treatment of post-traumatic stress disorder"; and
- AEP No 004/2019 concerning authorisation for research entitled "Psilocybin in the treatment of major depression: Phase 2 pilot clinical trial".

In view of the new restriction imposed by ANVISA RDC No 659/2022, ANVISA began to deny AEP applications submitted by *Instituto Phaneros*, which – as a result – would make all the research projects unfeasible. In parallel, ANVISA suggested that the institute should request an AE, which would be the course of action if the activities were being conducted by a private company.

In response, *Instituto Phaneros* filed a lawsuit against ANVISA seeking to invalidate the new restriction that required the institute to be a "higher education or technical institution" to obtain the AEP in order to move forwards with its PAP trial related to psilocybin. The trial judge granted the request to order ANVISA to review the merits of the AEP application, prohibiting the summary rejection that was based solely on the grounds that *Instituto Phaneros* was not a "higher education or technical institution" and therefore could not request the referred authorisation.

In response, ANVISA submitted a Technical Opinion with its considerations on the merits of the administrative request – in which the regulatory entity maintained its decision to deny the AEP application. ANVISA performed a strict analysis of the documentation submitted by *Instituto Phaneros* and concluded that – seeing as the research involved the administration of a psychedelic substance to human beings and therefore a high health risk would be involved in the intended activities – the focus of the assessment should be on the prevention of product deviation and on the safety conditions for conducting clinical studies, including the safe administration of the product to patients.

After reviewing the technical conditions of the study, ANVISA denied the AEP application, owing to:

- the lack of crucial information to ensure the control of substances subject to special control, as there was no information on the locations where the studies would be conducted;

- the lack of knowledge of the manufacturer of the substance – which would only be defined at the time of the importation – preventing the qualification of the supplier/exporter of the product and jeopardising the feasibility of complying with the international trade in controlled substances;
- the lack of presentation of the contracts between the companies that would perform the customs procedures for the release of the imported products at the customs terminals and perform the transportation of the investigational product;
- the lack of a standard procedure for qualifying companies (including the lack of contract with transportation and cleaning services companies);
- the lack of validation of the electronic spreadsheet for controlling product distribution, demonstrating a failure to comply with all the necessary steps to guarantee product traceability;
- non-conformity in identification of the cupboard used to store the products;
- stock of substances – corresponding to two years of consumption – exceeding the quantities foreseen to meet the needs of six months of consumption, in non-compliance with MoH Ordinance No 344/1998;
- the lack of preventive action that periodically assesses the robustness of security systems; and
- the lack of a standard procedure for hiring employees, such as a judicial background check.

In addition, ANVISA highlighted that the projects presented in the AEP request involved other institutions that (like *Instituto Phaneros*) would have to comply with all regulatory requirements to demonstrate safety in the administration to patients, as well as in the handling, safe-keeping and disposal of the psilocybin substance. Therefore, all 14 clinics where the substance was intended to be administered should have had authorisation from ANVISA to engage in activities involving controlled substances – which they did not have.

ANVISA's response in the *Instituto Phaneros* case demonstrates the caution with which studies involving psychedelics have been treated by the agency, especially in view of the high risk associated with both patient safety and the fear of products being misused.

The *Instituto Phaneros* case also presents another level of complexity that ANVISA must learn to navigate – namely, the association of a drug treatment with psychotherapy. In the Food and Drug Administration (FDA)'s Guidance for Industry entitled "Psychedelic Drugs: Considerations for Clinical Investigations", the American regulatory agency states: "Many of the psychedelic drug development program[me]s involve administering the investigational drug and then engaging in psychological support or psychotherapy either while the subject is experiencing the acute effects of the drug or in a subsequent session. This additional variable both complicates the assessment of effectiveness and presents a challenge for any future product labeling."

According to the FDA, this is because "psychotherapeutic interventions have the potential to increase expectancy and performance biases" and, as such, "sponsors should plan to justify the inclusion of a psychotherapy component and describe any trial design elements intended to reduce potential bias or to quantify the contribution of psychotherapy to the overall treatment effect".

Owing to the restricted status, the extensive documentation required for obtaining the necessary licences, the complexities of specific study designs, and the understandable difficulties in acquiring the necessary substances for research, these procedural challenges could potentially limit the number of clinical trials conducted domestically.

Considering the potential that psychedelics may have for the treatment of mental disorders and considering the increased interest of both the public and the industry in drugs based on psychedelic substances, it is expected that – in the coming years – ANVISA (like the FDA) will begin to issue communications, guides, decisions, and new regulations on the performance of research with psychedelics in Brazil.

Esketamine and ketamine as regulatory precedents

In a notable regulatory development, ANVISA approved esketamine (S-isomer of ketamine) hydrochloride in 2020 for treating treatment-resistant depression. Ketamine, although not a classic psychedelic, shares some pharmacological properties with this class of substances. The substance had already been used in the past as an anaesthetic in diagnostic and surgical interventions; however, until 2020, it did not have regulatory approval for psychiatric treatment.

Formerly classified as part of List C1 (other substances subject to special control), ketamine received its reclassification to List B1 (psychotropic substances with medical use) in 2022 – as did esketamine. Along with the modification of the regulatory status of the substances, ANVISA also included in MoH Ordinance 344/1998 two requirements for ketamine and esketamine-based drugs:

- that pharmaceutical drugs containing the substances ketamine and esketamine may only be dispensed and taken in healthcare establishments; and
- that pharmaceutical drugs containing the substance esketamine as a nasal spray must be administered in healthcare facilities under the observation of a healthcare professional and the patients must be monitored until they are considered clinically stable and ready to leave the facility.

The requirement of controlled settings and strict guidelines for prescription and administration, which is also in place in other countries, helps to prevent abuses and mitigate the risk of serious adverse outcomes resulting from sedation and dissociation.

The approval of esketamine in Brazil marked a significant step in the regulatory landscape for alternative treatments of mental health conditions.

Perspectives on IP rights and biodiversity

Brazil's Intellectual Property Law (Law No 9,279/96) allows novel compounds, formulations and processes to be patented if they meet the requirements of novelty, inventive step, and industrial applicability. The increasing interest in psychedelic substances for therapeutic applications – such as psilocybin for treating depression, MDMA for alleviating PTSD, and DMT for addressing various mental health issues – has fuelled research and development efforts in this field.

However, defining what qualifies as a "new" invention becomes intricate when it involves naturally occurring substances. Even though synthetic variations of psychedelics may be eligible for patent protection, naturally sourced

compounds are often included in the exceptions that prevent the patenting of biological materials found in nature. This situation poses significant challenges for Brazil's patent system as it seeks to balance the need to protect innovation while ensuring access to traditional knowledge, especially in relation to indigenous and traditional communities that have been using these substances for centuries.

In this context, Brazil's Biodiversity Law (Law No 13,123/2015) could play a relevant role. This legislation regulates access to genetic resources and the associated traditional knowledge, mandating that any use of biodiversity must be conducted with prior informed consent from indigenous communities and must ensure fair and equitable sharing of benefits derived from such resources. The Biodiversity Law adds another layer of complexity to the patenting process by requiring that patent applicants disclose the origin of the genetic material used in their inventions and comply with the rules surrounding access and benefit-sharing.

Conclusion

Brazil is at a critical point in its approach to psychedelic substances as potential treatments for mental health disorders. The historical and regulatory landscape has shaped public perception and legal frameworks, often hindering research and clinical applications. Although the therapeutic potential of substances such as psilocybin, MDMA and DMT is increasingly recognised, regulatory bodies require compliance with strict rules to ensure patient safety and evidence quality assurance.

The *Instituto Phaneros* case highlights the need for regulatory reforms that facilitate research while maintaining safety standards. The approval of esketamine sets a positive precedent, suggesting that – when GCP requirements and the conditions of safety, quality and efficacy are met – medicines based on psychedelic substances can be approved by ANVISA and made available safely to the population.

By reassessing current classifications and restrictions, Brazil can foster a regulatory environment that promotes innovation and expands access to effective mental health treatments. Ultimately, this will benefit its citizens and enhance overall public health.

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