

MASTER IN PUBLIC HEALTH

**Internship Report at the EMCDDA 's Public
Health Unit – Insights into the Medical Use of
Psychedelic Substances in the EU: regulatory
frameworks, public health challenges and
future directions**

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LIST OF ABBREVIATIONS AND ACRONYMS

AEs - adverse events

AUD - Alcohol Use Disorders

COM - Communication Unit

DG SANTE - Directorate-General for Health and Food Safety

DMT - Dimethyltryptamine

ECDC - European Centre for Disease Prevention and Control

ECHA - European Chemicals Agency

EDAS - European Drug Alert System

EFSA - European Food Safety Authority

EHU - European Health Union

EMA - European Medicines Agency

EMCDDA - European Monitoring Centre for Drugs and Drug Addiction

EU - European Union

EUDA – European Union Drug Agency

EWS - Early Warning System

EXO - Executive office unit

FDA - Food and Drug administration

HEA - Public health unit

HERA - Health Emergency Preparedness and Response Authority

ICT - Information and communication technology unit

LSD - Lysergic Acid Diethylamide

MDD - Major Depressive Disorder

MDMA - 3,4-Methylenedioxymethamphetamine

PTSD - Post-Traumatic Stress Disorder

SAP - Health Canada's Special Access Program

SAS - Risks to public safety and security unit

SCS - Supervised Consumption Site

SDI - Scientific coordination unit

TGA - Therapeutic Goods Administration

TRD - Treatment-Resistant Depression

UNODC - Nations Office on Drugs and Crime

WHO - World Health Organization

5-HT_{2A} - serotonin 2A receptor

ABSTRACT

Recent advancements in the medical application of psychedelic substances for a range of mental health disorders and palliative care have ignited substantial interest globally. This heightened interest is rooted in the recognition of the therapeutic potential of specific psychedelic substances and is fueled by the necessity for effective treatment options for complex mental disorders. As a result, diverse and evolving regulatory frameworks have emerged worldwide, raising important public health challenges.

A fundamental concern revolves around the establishment of robust regulatory frameworks and the adaptation of policies to ensure the safe and equitable utilization of psychedelic substances in medical settings, thereby minimizing potential risks. This endeavor entails navigating intricate ethical and legal landscapes. Additionally, regulatory supervision is indispensable to curb the proliferation of unlicensed or illicit psychedelic practices, which could endanger individuals seeking treatment.

To address these evolving landscapes, the European Monitoring Centre for Drugs and Drug Addiction (EMCDDA) has initiated several projects aimed, first, at enhancing understanding of the medical use of these substances, including research on effectiveness, potential harms, regulatory frameworks, and policy responses, as well as at exploring unlicensed or illegal settings where psychedelics are purportedly provided for therapeutic purposes. As such, throughout my internship at EMCDDA, we focused on several objectives. The first objective aimed to comprehend the current regulatory and complex frameworks governing the medical use of psychedelic substances in the EU, mapping policies regarding the recreational and therapeutic use of psychedelics and identifying areas where policy reform is needed. A second objective delved into exploring unlicensed psychedelic practices across Europe, aiming to understand the range and characteristics of these practices, highlighting the importance of regulating these practices to protect public health.

As the discourse surrounding psychedelics continues to evolve, it is imperative to maintain vigilance and adapt regulatory frameworks and policies accordingly. This ensures the safe and effective integration of psychedelics into therapeutic contexts and societal frameworks, ultimately promoting their responsible use and maximizing their potential benefits for public health.

INTRODUCTION

1. Public health system in the European Union

The public health system in Europe is a complex and multifaceted structure, integrating diverse national systems with overarching coordination and support from the European Union (EU). Each European state is primarily responsible for its healthcare services, although the EU plays a significant role in complementing national policies and harmonizing public health efforts across its member states[1] [2]. This involves systematically integrating public health measures into EU governance, ensuring a collective commitment to health protection, promotion, and crisis management[3].

The EU's involvement in public health has evolved significantly over the years, with structures, processes, and mechanisms developed to ensure that health policies and actions are effectively coordinated across Europe. The Maastricht Treaty of 1992 first introduced public health as a shared competence between the EU and its member states, allowing the EU to support and complement national health policies. The Amsterdam Treaty of 1997 further strengthened EU competencies in public health, particularly in addressing cross-border health threats. The Lisbon Treaty of 2007 expanded the scope of EU public health policy even further, providing a stronger legal basis for health initiatives and enhancing cooperation among member states on a wide range of health issues[4]. In recent years, the EU has focused on addressing new public health challenges, such as the COVID-19 pandemic, which underscored the importance of coordinated health responses across Europe[3].

Core institutions and agencies play a key role in advancing public health across the EU. The European Commission, the European Parliament, the Council of the European Union, and various EU agencies collaborate closely to ensure a high standard of health protection. These bodies work together to develop, implement, and evaluate health policies, promoting research and innovation, and effectively responding to health threats, ensuring that public health remains a priority within the EU[5].

The European Commission is central to developing and implementing EU health policies, proposing legislation, setting priorities, and coordinating with member states through its Directorate-General for Health and Food Safety (DG SANTE). DG SANTE ensures the effective implementation of public health, food safety, and health systems policies, collaborates with member states on health strategies, and monitors public health trends[6].

The European Parliament, as well as the Council of the EU plays a key role in shaping and overseeing health legislation proposed by the European Commission. It monitors the EU

health budget and the implementation of health policies and programs, ensuring policies align with EU objectives.

The EU can enact health legislation under the Treaty on the Functioning of the European Union, specifically through Article 168 (protection of public health), Article 114 (single market), and Article 153 (social policy). Key areas of legislation include patients' rights in cross-border healthcare, regulation of pharmaceuticals and medical devices (such as pharmacovigilance, falsified medicines, and clinical trials), health security and infectious diseases, digital health and care, tobacco control, and the regulation of organs, blood, tissues, and cells. Additionally, the Council of the EU can issue public health recommendations to member states[7].

Specialized agencies like the European Centre for Disease Prevention and Control (ECDC), European Medicines Agency (EMA), European Monitoring Centre for Drugs and Drug Addiction (EMCDDA)/ European Union Drug Agency (EUDA), European Food Safety Authority (EFSA), and European Chemicals Agency (ECHA) are vital to the EU's public health framework, focusing on disease control, medicine safety, drugs monitoring, food safety, and chemical safety, respectively[8].

The European Commission, in collaboration with EU agencies, regularly evaluates health objectives to ensure that they meet their goals and adapt to emerging public health challenges. This evaluation process includes analyzing health data, conducting impact assessments, and consulting with stakeholders to gather feedback on policy implementation. Central to this process are the ECDC and Eurostat, responsible for the collection and analysis of health data, thus providing evidence-based insights for policy-making across the EU[4].

Several EU programs offer critical funding and support for health initiatives, enabling member states to address current and future health challenges effectively. The actual EU4Health Programme represents the largest health program in the EU's history in terms of financial commitment. This program plays a crucial role in enhancing health systems, improving crisis preparedness, and promoting overall health across Europe, ensuring that health services are both accessible and of high quality[9].

Health challenges often span multiple sectors, so EU4Health collaborates with other EU programs, policies, instruments, and initiatives. For instance, the European Social Fund Plus aids vulnerable groups in accessing healthcare, while the European Regional and Development Fund focuses on enhancing regional health infrastructure. Horizon Europe supports health research, and the Union Civil Protection Mechanism establishes emergency medical supply

stockpiles. Additionally, Digital Europe and the Connecting Europe Facility contribute to building the digital infrastructure necessary for digital health. Other collaborative programs include InvestEU, the Single Market Programme, the Recovery and Resilience Facility, Erasmus+, and the Emergency Support Instrument[9].

In addition to these funding programs, the EU Health Security Framework, particularly strengthened by Decision 1082/2013/EU, significantly enhances the EU's ability to manage serious cross-border health threats[10]. This framework facilitates better coordination and information sharing among member states, setting up protocols for early warning and rapid response to prevent the spread of infectious diseases and other health crises.

Complementing this framework is the Health Emergency Preparedness and Response Authority (HERA), which plays a critical role in the EU's health security. HERA is tasked with managing the acquisition and distribution of essential medical countermeasures, such as vaccines and medications, ensuring their effective deployment during crises.

In response to the COVID-19 pandemic, the EU has made significant advancement in managing health emergencies and improving overall health security through the establishment of the European Health Union (EHU)[11]. Proposed by the European Commission on 11 November 2020, the EHU aims to enhance protection, prevention, preparedness, and response to health threats at the EU level. This initiative seeks to update key health security legislation to establish a more robust legal framework for managing cross-border health threats, enhancing governance through revised mandates for the ECDC and the EMA, and introducing a new EU Health Task Force to improve crisis management and address shortages of medical supplies[12].

Complementing these legislative and institutional updates, Country Health Profiles, produced in collaboration with the The Organisation for Economic Co-operation and Development and the European Observatory on Health Systems and Policies, provide a detailed assessment of health systems and outcomes in individual member states. These profiles identify strengths and areas for improvement, provide tailored recommendations, and enable the EU to promote best practices and foster collaboration, ensuring that the European Health Union's frameworks are informed by real-world data and address specific national needs[13].

Together, these programs and frameworks reflect a comprehensive approach to public health in the EU, one that emphasizes preparedness, innovation, and cooperation. By providing

funding, fostering research, and ensuring effective response mechanisms, the EU is building a robust health system capable of addressing both current and emerging health challenges[6].

1.1 European' s Agency: the past, present and future of EMCDDA/EUDA

EU agencies supported the EU's health policy making by providing expert analysis, data, and recommendations. In this view, the agency EMCDDA, substituted by the EUDA in July 2024, offers invaluable insights into drug use and addiction, which are critical for formulating effective public health policies[14].

The EMCDDA, established in 1993 and based in Lisbon, serves as the central hub for information and data on drugs and drug addiction in Europe. Its mission encompasses gathering, analyzing, and disseminating data on drug use patterns, prevalence, and trends, while also addressing the health and social consequences of drug use, such as infectious diseases, mental health disorders and social exclusion.

By collaborating with national monitoring centers, healthcare professionals, and law enforcement, and using tools like the Early Warning System (EWS), the EMCDDA provides a comprehensive evidence base for developing and evaluating drug policies across the EU.

Through its annual European Drug Report and other publications, the EMCDDA provided detailed insights into the state of the drug problem in Europe, highlighting key trends and emerging threats.

In addition to its monitoring and reporting functions, the EMCDDA conducted and supports research on various drug-related topics, including prevention, treatment, and harm reduction. It evaluates the effectiveness of different drug policies and interventions, offering evidence-based recommendations to policymakers. It plays a proactive role in shaping drug policy by organizing conferences, workshops, and training sessions aimed at enhancing the knowledge and skills of professionals in the field.

The agency also engaged in public awareness campaigns to educate the public about the risks associated with drug use and to promote healthy lifestyles.

Furthermore, the EMCDDA collaborated with international organizations, such as the United Nations Office on Drugs and Crime (UNODC) and the World Health Organization (WHO), to contribute to global efforts in addressing drug-related issues. This international cooperation

helps to share best practices and to align strategies across different regions, enhancing the overall effectiveness of drug policies worldwide.

In July 2024, the EMCDDA was officially succeeded by the EUDA under new legislation [15]. This transition follows an external evaluation of the EMCDDA, which highlighted the need for a more proactive and comprehensive approach to the evolving drug landscape. The proposal for the EUDA's expanded mandate stemmed from a thorough evaluation by the European Commission, conducted from 2018 to 2019, which included public consultations and was presented to the European Parliament, the Council, and the EMCDDA Management Board, with findings published in May 2019[14].

The transformation to the EUDA was further reinforced by the EU Drugs Strategy 2021-2025[16], approved by the Council on December 18, 2020, which called for a broader mandate. In response, the European Commission proposed this expanded remit in January 2022 to better handle emerging substances and illicit drug challenges. The legislative process concluded in June 2023, setting the EMCDDA on a one-year transition path to becoming the EUDA.

The EUDA's enhanced tools and expanded competencies aim to improve the EU's response to health and security challenges related to illicit drugs. Key improvements include better monitoring of supply-side dynamics, addressing polydrug use, increasing the agency's visibility, strengthening international collaboration, support to member states, improve coordination across borders, and ensure a robust response to the multifaceted threats posed by illicit drugs[17]. This transformation reflects the EU's commitment to adapting its strategies and structures to better manage the complex and evolving nature of drug-related issues.

Under its new mandate, the EUDA's work focuses on three core areas: monitoring, preparedness, and competence development[18]. The EUDA will continue its vital role in collecting, analyzing, and disseminating data. Additionally, the EUDA aims to enhance the European Union's preparedness for drug-related challenges through a comprehensive approach organized into four interconnected service categories (reported below). This includes developing threat assessment capabilities in both health and security to anticipate and address new and emerging drug threats effectively investing in the creation of a *European Threat Assessment System*. The agency will establish a network of forensic and toxicological laboratories by the creation of *European Network of Forensic and Toxicological Laboratories* to support the monitoring of drug trends and provide training for national experts, thereby improving the EU's capacity to handle complex drug-related issues. A significant addition to its

toolkit is the European Drug Alert System, which will issue real-time alerts when high-risk substances appear on the market. This system will complement existing national alert systems and the EU Early Warning System on new psychoactive substances.

In addition to these new functions, the EUDA will invest in competence development focusing on enhancing the skills and knowledge of professionals working in the field. This includes providing training and facilitating knowledge exchange among member states to ensure that drug policies and interventions are grounded in solid scientific research.

The agency's comprehensive approach, organized into the service categories of Anticipate, Alert, Respond, and Learn, aims to improve the EU's overall response to drug-related challenges[18]. The **Anticipate** service helps the EU foresee and prepare for future drug-related issues and their potential impacts. The **Alert** service provides real-time warnings about new and emerging drug risks, supported by the European Drug Alert System, which complements existing national alert systems and the EU Early Warning System on new psychoactive substances. The **Respond** service enhances the EU's and member states' abilities to address drug-related challenges effectively, including by developing threat assessment capabilities in health and security and establishing a network of forensic and toxicological laboratories. Finally, the **Learn** service promotes knowledge exchange and supports the development of evidence-based drug policies and interventions.

Furthermore, the EUDA will play a stronger international role, supporting the EU in drug policy at a multilateral level. This includes reinforcing the role of national focal points to ensure that member states can provide relevant and timely drug-related data to the agency. Additionally, the EUDA will monitor developments related to the trafficking and diversion of drug precursors and contribute to the implementation of European drug precursors legislation.

The agency's new structure and functions are designed to provide a more comprehensive and coordinated approach to drug-related challenges, ensuring that the EU is better prepared to anticipate, alert, respond, and learn from these issues.

Objective	Action
Develop threat assessment capabilities in health and security	Increase the EU's preparedness to identify and respond to new threats.
Implement a new alert system	Establish the European Drug Alert System to issue warnings about high-risk substances, complementing existing systems.
Monitor and address poly-substance use	Create a network of forensic and toxicological laboratories to exchange information and train national experts.
Develop and promote evidence-based interventions and best practices	Provide research and support on health issues and drug markets, and support the evaluation and development of policies.
Strengthen international role	Support multilateral drug policy efforts and reinforce national focal points for data sharing.
Monitor drug precursor trafficking	Track developments related to drug precursor trafficking and support European drug precursors legislation.

Table 1. Overview of EUDA's objectives and the corresponding actions to address drug-related challenges [15].

1.1.1 EMCDDA, EUDA and their constituent sectors: organizational chart

The transition from the EMCDDA to the EUDA not only involves changes in scope and mandate but also significant alterations in the organizational structure. Indeed, the EUDA's expanded responsibilities and enhanced capabilities necessitate a more complex and integrated organizational chart.

EMCDDA's organizational structure

The EMCDDA's organizational structure was relatively straightforward, composed by (Fig.1):

1. **Director:** Head of the agency responsible for overall management and strategic direction.
2. **Management Board:** Composed of representatives from EU member states, the European Commission, and the European Parliament, overseeing the agency's activities and approving the work program.
3. **Scientific coordination unit (SDI):** Providing scientific guidance and ensuring the quality of the agency's work.
4. **Executive office unit (EXO):** supports the Director to achieve strategic plans and setting of priorities.

5. Operational Units:

- **Public health unit (HEA):** to support the development and implementation of evidence-based public health policies and responses, through the collection, analysis and dissemination of state-of-the-art information on drug use and its health and social consequences.
- **Risks to public safety and security unit (SAS):** to enhance EU and national preparedness for drug-related threats by providing high-quality data, analysis, and early warning on drug markets, crime, and harms.
- **Communication Unit (COM):** to provide high-quality and highly valued information service on the drugs phenomenon in Europe.
- **Reitox Network:** to coordinate national focal points across member states for data gathering and reporting.
- **Information and communication technology unit (ICT):** to study, implement and operate the information systems and electronic services that are required to support the scientific and administrative work processes.
- **Administrative Unit:** to strengthen the EMCDDA's role as a leading, knowledge-driven, and service-focused public administration.

Among the Operational Units, the HEA Unit is responsible for collecting, analyzing, and disseminating information on the health and social consequences of drug use in Europe. This unit is structured into several sectors, each focusing on specific aspects of drug-related health issues. The *Epidemiology Sector* gathers data on the prevalence and patterns of drug use across Member States. The sector also studies the demographic characteristics of drug users and the factors contributing to drug use. The *Health Consequences Sector* focuses on the health outcomes of drug use, such as drug-related infectious diseases (e.g., HIV/AIDS, hepatitis), mental health disorders, and drug overdoses. It works closely with national health authorities and international organizations to track and analyze these health consequences, providing a comprehensive picture of the public health burden of drug use. The *Policy and Interventions Sector* evaluates and improves drug policies and interventions by assessing harm reduction strategies, treatment programs, and prevention initiatives, identifying best practices, and recommending enhancements to public health efforts. The *Research and Innovation Sector* supports and conducts research on emerging drug issues, exploring innovative prevention, treatment, and harm reduction

methods, while fostering collaboration with academic and research institutions to stay ahead of evolving drug trends.

The HEA Unit's work is critical for informing the EMCDDA's reports and publications, which in turn support the EU's health policy making. The unit's efforts also contribute to the continuous evaluation and improvement of health objectives, ensuring that EU health policies remain effective and responsive to new challenges.

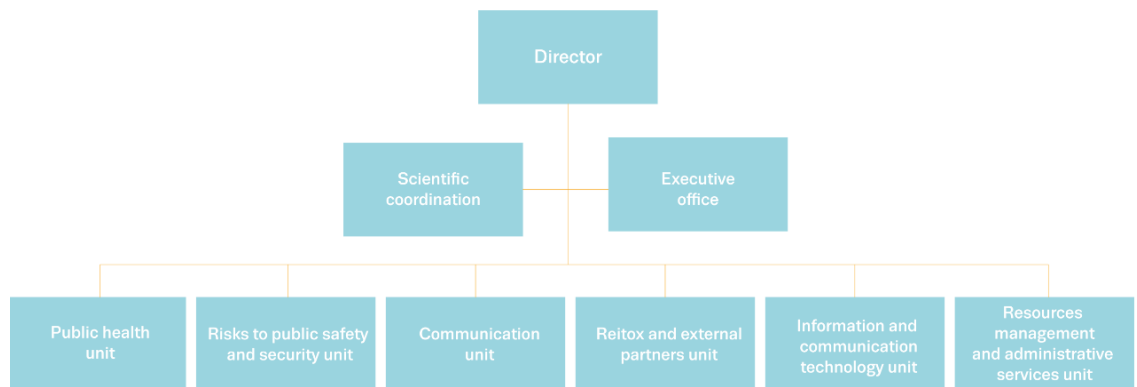


Figure 1. Organizational chart of EMCDDA [19]

EUDA's organizational structure

The EUDA's organizational chart reflects its broader mandate and more proactive role in addressing drug-related issues. Key components include:

1. **Executive Director:** Similar to the Director in the EMCDDA, but with a broader remit to oversee the expanded functions of the agency.
2. **Management Board:** Retained from the EMCDDA but with possibly expanded representation to reflect the agency's new responsibilities.
3. **Scientific Committee:** Continuing to provide scientific oversight, with an expanded role to cover new areas of responsibility.
4. **Strategic and Operational Units:**
 - **Data and Analytics Unit:** Enhancing the collection, analysis, and dissemination of data with a focus on new and emerging drug threats.

- **Threat Assessment Division:** A new division dedicated to assessing health and security threats related to drugs, including poly-substance use.
- **European Drug Alert System (EDAS):** Responsible for issuing real-time alerts on high-risk substances, complementing national alert systems and the EU Early Warning System.
- **Preparedness and Response Unit:** Focused on enhancing EU preparedness and response capabilities, including the European Threat Assessment System.
- **Forensic and Toxicological Laboratories Network:** Coordinating a network to exchange information on new trends and training national forensic experts.
- **Research and Policy Support Unit:** Developing and promoting evidence-based interventions and best practices, supporting policy development.
- **International Relations and Multilateral Cooperation Unit:** Strengthening the EU's role in international drug policy and ensuring coordination with global partners.
- **National Focal Points Coordination Unit:** Reinforcing the role of national focal points to ensure effective data collection and reporting from member states.
- **Drug Precursors Monitoring Unit:** Monitoring trafficking and diversion of drug precursors and supporting the implementation of related legislation.

External parties

External parties are a variety of stakeholders and collaborators, that interact with the agency to support its mission of monitoring and addressing drug-related issues in Europe. These external parties encompass EU Institutions and Agencies, National Focal Points, International Organizations, Contractors and Research Institutions, Non-Governmental Organizations and Civil Society, Professional Networks and Academic Institutions, Private Sector (Pharmaceutical companies, technology firms, and other private entities), General Public and Media.

By collaborating with external partners, the agency enhances its research capabilities, remains at the forefront of drug monitoring and addiction treatment developments, and provides accurate, up-to-date information to address emerging challenges effectively

Meetings with contractors are essential to the agency's collaborative approach, ensuring regular communication, coordination, and alignment on project goals. These meetings allow for reviewing progress, resolving issues, and maintaining a seamless partnership focused on advancing public health and safety in Europe. This ongoing dialogue enhances the agency's

ability to deliver robust data and comprehensive analysis, ultimately supporting EU policymakers in developing informed and effective drug policies. Through these collaborations, the agency can more effectively fulfill its mandate and respond to emerging challenges.

1.1.2 Key focus areas of EMCDDA/EUDA in addressing drug-related issues in Europe

The EMCDDA/EUDA investigates and monitors a comprehensive range of topics and substances to understand the dynamics of drug use, its health and social consequences, and to develop informed policy responses[20]. Their work encompasses several key areas:

- 1) **Drug Prevalence and Trends:** Monitoring the usage patterns and trends of various drugs across Europe, including new psychoactive substances (NPS).
- 2) **Health and Social Responses:** Evaluating and promoting effective health and social responses to drug-related issues, including harm reduction, treatment programs and best practice.
- 3) **Drug-Related Health Consequences:** Studying the health effects of drug use, such as overdoses, infectious diseases (e.g., HIV, hepatitis), and mental health disorders.
- 4) **Drug Markets and Crime:** Analyzing the dynamics of drug markets, including production, trafficking, and related criminal activities.
- 5) **Drug Policy and Legislation:** Providing evidence-based insights to inform drug policies and legislative frameworks within the EU.
- 6) **Prevention and Education:** Promoting preventive measures and educational programs aimed at reducing drug use and its negative consequences.
- 7) **Drug Use in Specific Populations:** Focusing on vulnerable groups, such as youth, prisoners, and marginalized communities, to understand and address their specific drug-related challenges.
- 8) **Research and Data Collection:** Supporting and conducting research to enhance understanding of drug-related issues and improve data collection methodologies.
- 9) **International Cooperation:** Collaborating with international organizations and countries outside the EU.
- 10) **Emerging Threats:** Identifying and responding to new and emerging drug-related threats through mechanisms like the European Drug Alert System.

2. Commonly used illicit drugs

The agency aims to provide to the EU and its Member States with a comprehensive and accurate overview of drug-related issues across Europe, providing a solid evidence base to inform drug policy. The agency plays a key role in overseeing and monitoring a wide range of illicit drugs, including but not limited to, substances such as:

1. **Cannabis:** As the most widely used illicit drug in Europe, the EMCDDA/EUDA closely monitors consumption trends, health effects, and policy developments related to cannabis. This includes both recreational and medicinal use, with the agency analyzing data on prevalence and potential health risks.
2. **Cocaine:** The second most prevalent illicit drug in Europe, particularly in urban settings. The agency examines patterns of use, the social and health consequences, and market dynamics.
3. **Synthetic Stimulants:** This group includes substances such as amphetamines, methamphetamines, and synthetic cathinones. The agency tracks their use, associated health risks, and trends in production and distribution across Europe.
4. **MDMA:** Known as ecstasy, MDMA is frequently used in nightlife and recreational settings. The EMCDDA/EUDA examines consumption trends, associated risks, and the effectiveness of harm reduction strategies related to MDMA use.
5. **Opioids:** Opioids, including heroin, remain a critical focus due to their high potential for addiction and overdose. The agency monitors trends in opioid use, demand for treatment, and the health impacts, including overdose-related deaths.
6. **New Psychoactive Substances (NPS):** These are newly emerging drugs that are not yet subject to international control. The EMCDDA/EUDA operates an early warning system to rapidly detect, assess, and respond to these substances

2.1 Psychedelics drugs

Alongside the more well-known substances available on illicit drug markets, several other substances with hallucinogenic, anaesthetic, dissociative or depressant properties are also monitored. Indeed, psychedelic substances have recently garnered substantial interest both within the EU and internationally for treating mental health disorders and palliative care[21]. In response, the EMCDDA has launched a project aimed at deepening the understanding on the medical use of such substances, their regulatory frameworks, and the current state of research in the EU and worldwide.

2.1.1 What are psychedelics?

Psychedelics, a subclass of drugs known for inducing altered states of consciousness—often referred to as "trips" or an "expansion of consciousness"—include both classic serotonergic hallucinogens like mescaline, Lysergic Acid Diethylamide (LSD), psilocybin, and dimethyltryptamine (DMT), as well as atypical hallucinogens such as salvia and 3,4-Methylenedioxymethamphetamine (MDMA) [22]. These substances can be categorized into different classes based on their pharmacological effects (typical or atypical) and chemical structure (Fig.2), although there is no definitive classification system for them. Most psychedelic drugs fall into one of three chemical families: tryptamines, phenethylamines, or lysergamides, with LSD being classified as both a tryptamine and a lysergamide and called as “classical/typical psychedelics”[23]. The primary mechanism of action for these typical substances is through serotonin 2A receptor agonism (5-HT_{2A}). By binding to these receptors, psychedelics modulate brain circuits crucial for sensory perception and cognition. However, the exact ways in which psychedelics alter perception and cognition producing their hallucinogenic effects through the 5-HT_{2A} receptor, remain largely unclear[24]. In addition, the psychedelic experience is often likened to non-ordinary forms of consciousness similar to those experienced during meditation and near-death experiences, which may also involve altered activity in the brain's default mode network. Ego death is often regarded as a central aspect of the psychedelic experience.

Most psychedelics are classified as illegal under international conventions, the 1971 UN Convention on Psychotropic Substances, with some exceptions made for religious practices or scientific research. Nevertheless, recreational use of psychedelics remains widespread.

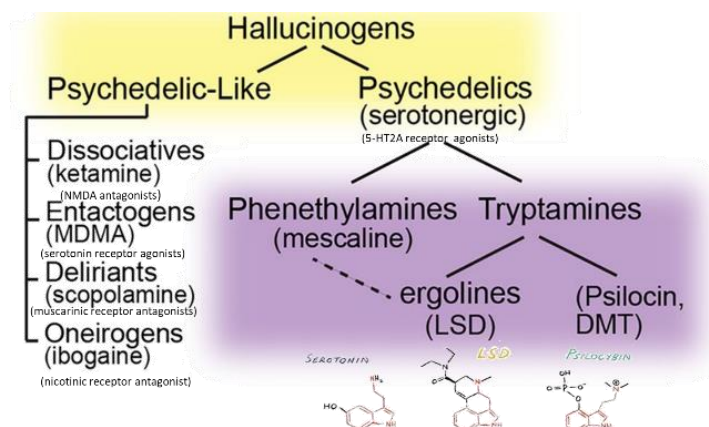


Figure 2. Hallucinogens classification based on the pharmacological effects. Adapted from [25].

2.1.2 Psychedelic medical use

Mental disorders have emerged as a significant global public health issue, impacting individuals, societies, and economies on a large scale. In 2019, almost a billion people, including 14% of the world's adolescents, were affected by a mental disorder[26]. Traditional pharmacotherapy often fails due to slow onset, undesirable side effects and drug resistance over time, and the concomitant development of new psychopharmacological treatments has not evolved so far. This underscores the urgent demand for innovative therapies in neuropsychiatry. Recently, psychedelics have re-emerged in the psychopharmaceutical field, showing considerable promise as potential treatments for various mental health disorders particularly for treatment-resistant conditions like depression, Post-Traumatic Stress Disorder (PTSD), anxiety, pain associated with life-threatening illnesses, and neurodegenerative disorders[27].

Psychedelic substances have a long history of use in traditional and indigenous medicine, as well as in ritualistic or ceremonial practices. The modern era of psychedelic research began with Albert Hofmann's synthesis of LSD in 1938. By 1943, Hofmann had become the first person to experience the effects of LSD, an event that marked the beginning of significant scientific and cultural exploration of psychedelics in the 1950s and 60s. In that time, extensive research explored the therapeutic potential of psychedelics for treating various mental health conditions[28]. However, this research was abruptly halted in the early 1970s when psychedelics were classified as Schedule I drugs under the United Nations Convention on Psychotropic Substances. This classification, that is reserved for substances deemed to have no accepted medical use and significant potential for harm and dependence, created substantial barriers to conduct further research into psychedelic therapeutic potential, resulting in a long gap in the development of psychedelic medicines[28].

In recent years, several psychedelic substances have attracted renewed interest. Extensive preclinical and clinical research has advanced our understanding of the pharmacodynamics and pharmacokinetics of these substances and how they might affect brain[29][25]. Among the most studied substances there are the psilocybin, MDMA and LSD. Psilocybin has shown efficacy in reducing symptoms of depression and anxiety related to cancer[30], Major Depressive Disorder (MDD)[31][32], Treatment-Resistant Depression (TRD)[33][34], obsessive and compulsive behaviors[35], eating disorders[36] and nicotine and Alcohol Use Disorders (AUD)[37][38]. MDMA is another well-studied compound, with research supporting its efficacy in treating PTSD [39], AUD [40] as well as anxiety and depression[41]. LSD has shown

clinical potential in reducing end-of-life anxiety [42], anxiety [43] and in treating PTSD [44] and MDD[45].

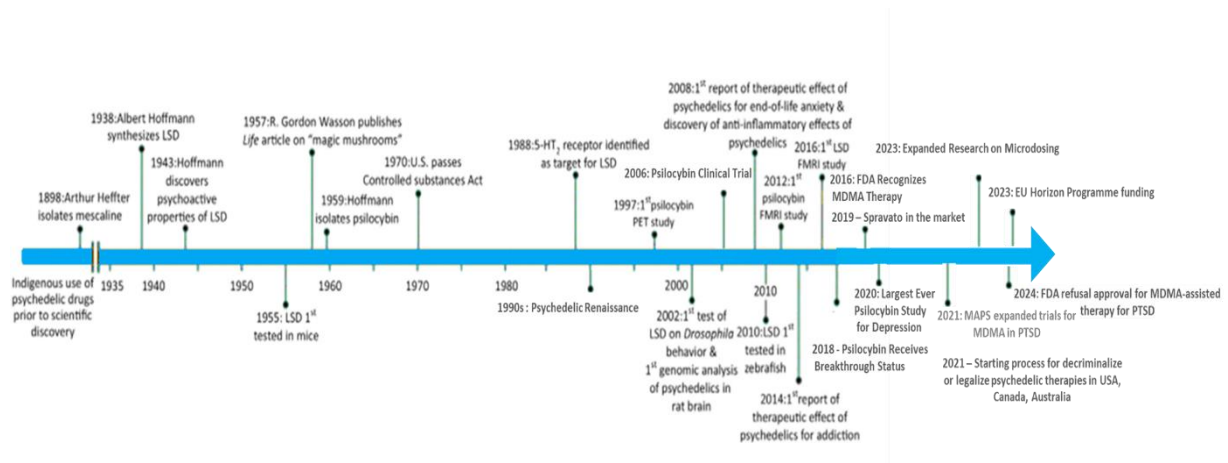


Figure 3. Brief history of psychedelics research and developments. Adapted from [46]

2.1.3 Psychedelics in clinical trials

Currently, numerous clinical trials are exploring the therapeutic potential of psychedelics, including studies on psilocybin for TRD, MDMA for PTSD, LSD for anxiety, Ayahuasca for depression and addiction [47], ketamine for various disorders [48], and ibogaine for opioid addiction [27]. These trials are conducted under strict regulatory oversight to ensure participant safety and ethical compliance. Many of these studies combine the administration of psychedelics with counseling, such as MDMA-assisted therapy, while others focus solely on the pharmacological properties of the substances [49] [50].

Despite the promise shown in some trials, psychedelic clinical research faces significant challenges [51]. These challenges stem from the unique nature of psychedelics, their effects on consciousness, the set and setting, the regulatory and ethical frameworks surrounding their use in research.

A major issue is the difficulty of maintaining blinding control, which is essential for preventing bias in clinical trials. Indeed, the pronounced effects of psychedelics often make it clear to participants and researchers who is receiving the active substance versus a placebo. This "functional unblinding" can distort trial outcomes as expectations influence results. Strategies like using active placebos or varying doses have been proposed to mitigate this problem, but

fully addressing it remains complex[52][53]. This issue was one of the reasons for the recent rejection authorization of MDMA to treat PTSD from FDA. In a recent workshop about psychedelics medicine held in April 2024, “Multi-stakeholder workshop on psychedelics – Towards an EU regulatory framework” [54], the EMA proposed several strategies to address the challenges of functional unblinding in psychedelic clinical trials. One approach is to use remote, blinded independent raters, who assess outcomes separately from those administering the treatment. Another strategy involves implementing a blinding questionnaire, where participants in both the treatment and control groups are asked to guess their group allocation and explain their reasoning, helping to measure the extent of unblinding. The EMA also suggested conducting controlled trials with varying dose levels to manage unblinding, which can help determine dose-response relationships, identify the minimum effective dose, and compare the effects of the active substance against a placebo. Additionally, the workshop highlighted that both, expectancy and the nocebo effect, can influence treatment outcomes in psychedelic trials, emphasizing the importance of comprehensive informed consent and trained facilitators to mitigate this risk.

Another challenge on therapeutic outcomes is the influence of "set" and "setting", the mindset of the participant and the environment in which the drug is administered [55]. These factors introduce variability that is hard to control and standardize, making it difficult to draw consistent conclusions across different trials[56][57]. The altered states of consciousness induced by psychedelics also raise ethical and safety concerns, requiring strict protocols to protect participants from adverse reactions or exacerbated mental health conditions[57]. According to the recommendations of the workshop[54], protocols for psychedelic treatments should include standardized frameworks for psychological support or psychotherapy, consisting of preparatory sessions, administration sessions, and integration sessions. Moreover, another control group is needed to understand whether the therapeutic effects are more dependent on psychotherapy or patient safety support.

In this way, the integration of psychotherapy with psychedelic treatment in clinical trial introduces additional challenges. Many psychedelic therapies are conducted in conjunction with psychotherapy, which makes it difficult to isolate the effects of the drug from the therapeutic context. While this integration is essential for ensuring the safety and efficacy of the treatments, it also introduces additional variables that can affect trial outcomes and complicate the assessment of the drug's efficacy[59][44][49].

Determining the appropriate dosage is another significant issue. The dose-response relationship for psychedelics varies widely among individuals, necessitating careful studies to find the right balance between therapeutic effects and adverse reactions[58]. This variability complicates trial design and execution, as individualized dosing strategies and long-term assessments are needed to differentiate between therapeutic benefits and subjective experiences.

Regulatory hurdles add another layer of complexity. Many psychedelics are classified as Schedule I drugs, signifying a high potential for abuse and no recognized medical use. This classification imposes stringent controls, making it difficult for researchers to obtain the necessary permissions to conduct studies, often delaying or obstructing research[60].

In addition, psychedelic trials present unique challenges for informed consent due to heightened suggestibility and unpredictable subjective effects[61]. The informed consent process must thoroughly prepare patients for these experiences, allowing them to feel empowered and well-informed about the potential mindset changes induced by treatment. In the EU, the responsibility for approving informed consent forms and processes lies with national ethics committees, and requirements vary by country. Therefore, EMA does not enforce these obligations, as they fall under national regulations or professional codes.

Addressing these challenges requires careful trial design, robust regulatory frameworks, and ongoing research. Establishing a pan-European multidisciplinary advisory body could help create a unified framework, including standards for training, licensing, ethics, and safety[54]. Furthermore, securing adequate research funding, particularly for large-scale clinical trials, is critical to advancing the understanding of psychedelic medicines.

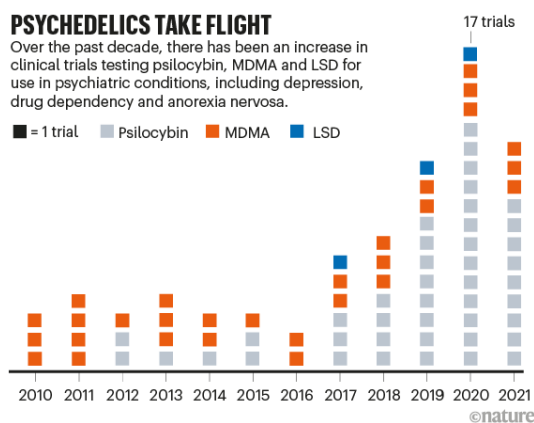


Figure 4. Clinical trials with psychedelics overtime [62]

2.1.4 Adverse effects and risks of the psychedelic substances

Psychedelic substances are typically regarded as physiologically safe and have a low potential for abuse [63]. However, the risks associated with psychedelic use vary based on several factors, including the type of substance, dosage, purity, usage patterns and the set and setting of consumption. In addition, limited data on long-term or intensive use risks are available.

The main safety concerns are lasting psychological adverse reactions such as persisting anxiety, dissociation, or flashbacks[64]. Nonetheless, there is a significant gap in the reporting and study of adverse events (AEs) in many psychedelic trials.

AEs in clinical trials are unintended medical occurrences that may or may not be related to the treatment. They are classified as “Acute” if they occur during dosing sessions or “Late” if they arise at least 24 hours after dosing and may continue throughout the trial. Cardiovascular effects are common (31.1%)[63], as well as neuropsychiatric side effects[64][65] such as anxiety and depressive mood[66]. AEs are documented in a Case Report Form, detailing their severity, seriousness, and relation to the product. The Principal Investigator must report all AEs to regulatory bodies and ethics committees, following specific safety reporting guidelines.

In psychedelic-assisted psychotherapy, concerns include patient vulnerability during altered states of consciousness, risks of harm or abuse[67], particularly in unlicensed settings like 'psychedelic retreats'[68]. Such incidents emphasize the critical need for stringent ethical guidelines to prevent misconduct and ensure participant safety.

The risks of using psychedelics for unregulated therapeutic purposes are not well investigated, although there are documented risks related to recreational patterns of MDMA use, including acute poisonings and deaths or neurological and cardiovascular toxicity, and of ketamine consumption, associated to mental health problems and urological complications [69].

The distinctive psychopharmacological effects of psychedelics require heightened vigilance and stringent ethical oversight to manage potential risks and maintain the integrity of clinical trials.

2.1.5 Set and setting for psychedelic harm reduction

The concept of "set and setting" is pivotal in psychedelic studies, emphasizing that the quality and outcomes of psychedelic experiences are significantly influenced by both an individual's

internal state ("set") and the external environment ("setting")[70]. "Set" includes their mood, psychological preparedness, and underlying mental health conditions. On the other hand, "setting" encompasses the physical and social environment in which the psychedelic experience occurs, such as the location, people, and atmosphere. Both components are crucial in shaping the psychedelic experience, influencing not only the nature of the experience itself but also its potential benefits and risks[71]. By examining how these elements interact, it becomes clear that both psychological and environmental factors must be carefully managed to optimize safety and therapeutic outcomes[58]. There are different modalities of set and setting. In therapeutic settings, psychedelics are used under the guidance of trained professionals, often within a controlled environment designed to facilitate healing experience[72][73]. The therapeutic settings are carefully curated to maximize positive outcomes and minimize risks, with a strong emphasis on creating a safe and supportive atmosphere, often carried out in a comfortable living room with calming music and an aesthetically pleasing ambience[74].

Clinical "setting" involves a research context where psychedelics are studied for their efficacy and safety. Here, setting is controlled and standardized to ensure consistency and reliability in the research findings. The clinical environment is designed to minimize variables that could affect the outcomes [75].

In ritualistic or ceremonial contexts, psychedelics are used as part of traditional or spiritual practices. The setting in these cases often involve culturally specific practices and rituals that influence the experience[73] [76].

Recreational use of psychedelics often occurs in informal settings, such as social gatherings or parties. The set and setting in these instances are less controlled, which can introduce variability and risks[76].

Incorporating set and setting principles into public health policies can significantly enhance the effectiveness of harm reduction programs [77]. Moreover, educate the public and professionals about the importance of set and setting can lead to more informed and safer use of psychedelics.

2.1.6 Overview of the regulatory framework for psychedelic substances

Psychedelic substances are governed by a complex regulatory framework that includes both international treaties and national laws[78]. Primarily, these substances fall under the 1971 UN Convention on Psychotropic Substances, which categorizes them based on their potential for abuse and medical value, aiming to control their use while permitting legitimate medical and scientific applications. Within the EU, this framework is further guided by the EU Drug Strategy 2021-2025 and Council Regulation (EC) No 111/2005, which ensures a coordinated approach to drug control across member states, including psychedelics.

In European countries, psychedelics are typically classified into four schedules, with Schedule I indicating the highest potential for abuse and Schedule IV the lowest[79]. Most psychedelics are classified as Schedule I substances, subjecting them to stringent legal and regulatory controls. Recently, the WHO Expert Committee on Drug Dependence (WHO-ECDD) has begun discussions on possibly rescheduling these substances, and this, potentially opens new avenues for research[80].

There has been a growing trend among European countries to reform drug laws, particularly concerning psychedelics, alongside an increase in clinical research into their therapeutic potential. While most countries maintain strict controls over psychedelics as controlled substances, some are beginning to explore their therapeutic applications through research projects. In Czechia, for example, the Drug Action Plan 2023-2025 has earmarked funding for research with psychedelics in addiction treatment (Office of the Government of the Czech Republic, 2023). At EU level, in early 2024, the Horizon Europe program awarded EUR 6.5 million in funding for psychedelic therapy research for treatment-resistant mental disorders in palliative care[69]. These developments suggest potential shifts in regulatory frameworks to accommodate emerging evidence of the medical benefits of psychedelics[81]. In April 2024, the EMA held a multi-stakeholder workshop to establish regulatory guidelines for the development and therapeutic use of psychedelic substances in Europe [54].

Currently, no classical psychedelics have been approved by regulatory authorities at the EU or Member State level for treating neuropsychiatric disorders. However, the atypical psychedelic esketamine, marketed as Spravato[82], has received marketing authorization for use in adults with MTRD. Beyond this, the EMA has not evaluated or approved any other psychedelic medicines for patient use within the EU.

Notable regulatory changes in Europe include the decriminalization of possession and personal use of all illicit drugs, including psychedelics. Several European countries, such as Austria, Belgium, Croatia, Czechia, Estonia, Portugal, Slovenia, and Spain, have decriminalized drug use and possession, although the sale and distribution of scheduled substances remain illegal[83][69]. For instance, Portugal supports research into the medical benefits of psychedelics, focusing on harm reduction and therapeutic applications. The United Kingdom classifies psychedelics as Class A substances under the Misuse of Drugs Act 1971, imposing the highest level of control and penalties. However, there are ongoing discussions about rescheduling or decriminalizing certain psychedelics for therapeutic use, with some approved trials exploring their potential for treating mental health conditions. Research into the medical use of psychedelics is funded by the National Health Service (NHS), with recent political advocacy for policy reform regarding psilocybin. In the United Kingdom, therapies involving N,N-dimethyltryptamine (DMT), psilocybin, and MDMA received the 'Innovation Passport Designation' (IPD) by the Medicines and Healthcare products Regulatory Agency in 2021. The IPD status offers a toolkit to support all stages of the research and approval process as part of the broader 'Innovative Licensing and Access Pathway', which is designed to accelerate patient access and encourage early engagement from commercial and non-commercial developers. Germany regulates psychedelics under the Controlled Substances Act (BtMG), classifying substances like psilocybin and MDMA under strict controls. However, interest in their medical use is growing, with recent pilot projects and research initiatives exploring their therapeutic potential for conditions like depression. Denmark also faces ambiguity regarding the potential therapeutic use of psilocybin for treating substance use disorders, despite its illegal status. Finland has similar uncertainties, particularly concerning Ayahuasca's plant ingredients, which are not specifically scheduled as controlled substances, although DMT is classified as illegal. The Netherlands is often seen as the most liberal European country regarding drug regulation. Although psilocybin mushrooms are classified as illegal, the use and possession of small amounts of certain psychedelic substances, such as psilocybin truffles and liquid peyote, are decriminalized. Additionally, the use of Ayahuasca in religious or spiritual contexts is permitted under Article 9 of the European Convention on Human Rights, although the manufacture and sale of illicit drugs remain illegal. The Netherlands also allows some research into the therapeutic uses of psychedelics under regulated conditions. Spain regulates psychedelics under strict controls but is actively involved in research studies examining their potential therapeutic uses. Switzerland stands out as a pioneer, decriminalizing the consumption of small quantities of certain controlled substances and allowing medical

doctors to apply for special clinical permission to administer psychedelics like MDMA or psilocybin and conduct research with LSD under limited circumstances[44]. Additionally, Switzerland allows the religious use of Ayahuasca by groups such as the União do Vegetal Church without requiring a permit for its sale.

Countries outside of Europe, including Canada, Australia, and several U.S. states, have adopted various strategies to facilitate access to psychedelics for medicinal purposes[81]. This reflects a global shift towards reevaluating and potentially expanding the medical use of these substances. The surge in research and clinical trials, coupled with growing interest from commercial entities and the public, is prompting policymakers to respond. Consequently, some states have legalized psychedelic-assisted therapies under different regulatory frameworks; some under medical frameworks, which focus on integrating psychedelics into clinical settings under strict medical supervision, others under guidance-based approaches, which emphasize the importance of set and setting, psychological support, and integration practices [84]. However, no state has yet fully implemented a comprehensive and regulated treatment model for psychedelics This raises important questions about the challenges of administering these substances in a controlled setting.

In the U.S., interest in the therapeutic potential of psychedelics is growing, as evidenced by legislative actions and an increase in psychedelic research. The National Defense Authorization Act mandates the Department of Defense to study psychedelics for PTSD and traumatic brain injury. Moreover, the FDA has granted breakthrough therapy status to MDMA-assisted therapies for PTSD (2017), psilocybin for TRD (2018), and MDD (2019), and recently provided draft guidance on conducting clinical trials of psychedelics[85]. Various states have enacted laws to legalize, decriminalize, or study psychedelics[60]. Policymakers in Oregon and Colorado are facing the challenging task of developing regulatory frameworks for psychedelics within their states. Indeed, recent policy developments include Colorado's passage of the Natural Medicine Act (Proposition 122) in November 2022, which established the Natural Medicine Advisory Board to guide the creation of state-sanctioned "healing centers". These centers will initially offer psilocybin and psilocin, with plans to expand to DMT, ibogaine, and mescaline by June 2026. Proposition 122 also decriminalized activities such as growing, possessing, or using these "natural medicines." Similarly, Oregon became the first U.S. state to legalize psilocybin-assisted therapy in November 2020[86].

Regulatory frameworks for psychedelic services in other countries are explicitly medicalized. In Australia, the Therapeutic Goods Administration (TGA) announced in February 2023 that

psychiatrists could begin prescribing MDMA for PTSD and psilocybin for TRD starting in July 2023[87]. These substances were reclassified from Schedule 9 (prohibited substances) to Schedule 8 (controlled drugs in a medical setting), allowing authorized psychiatrists to prescribe them under specific conditions before full regulatory approval[88].

In Canada, Health Canada issued guidelines in December 2022 for managing risks in clinical trials involving psychedelic-assisted psychotherapy, focusing on therapist qualifications, clinical settings, informed consent, and good manufacturing practices. In January 2022, Health Canada expanded its Special Access Program to include psilocybin and MDMA, allowing healthcare professionals to access these substances for patients with serious conditions when other treatments have failed[89][90]. Since then, approximately 200 patients have received psilocybin and 40 patients have received MDMA under the SAP, primarily for conditions like MDD, end-of-life psychological distress, and PTSD[91]. Additionally, Health Canada is forming a scientific committee to further explore the clinical treatment of mental health disorders using psychedelics[89].

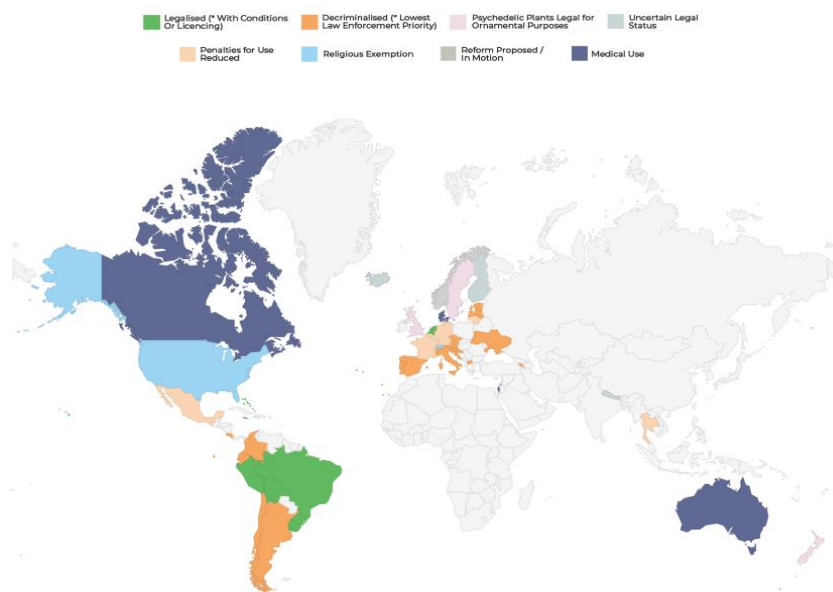


Figure 5. Status of psychedelics policy reform efforts across the globe. From [94]

Overall, policy developments in this area have been driven by significant advocacy from industry interests and the general public. Numerous psychedelic advocacy groups and

pharmaceutical companies are actively pushing for policy changes and the approval of psychedelic substances for various medical indications. In contrast, many researchers are cautioning policymakers against making hasty decisions, emphasizing the importance of allowing ongoing trials to be completed within the existing regulatory frameworks for novel medicines[92][93].

Compassionate Use Programs

In the EU, the 'compassionate use' program provides access to unauthorized medicines under developments' in strict conditions for patients with life-threatening or severely disabling conditions that do not respond to existing therapies. This program permits the use of experimental substances, offering personalized treatment. Eligibility for compassionate use is determined on a case-by-case basis [95]. This program differs from 'named-patient basis access,' where physicians independently request unauthorized or foreign-authorized medicines for specific patients, without involvement from the EMA.

The EMA provides recommendations for compassionate use programs, although each EU member state coordinates these programs according to its own rules. In some countries, unproven treatments are regulated in line with the 37th paragraph of the Declaration of Helsinki. These ethical principles, established in 1964, permit the use of unproven interventions when no effective alternatives are available, provided expert advice is sought. The intervention should then be studied, with new findings documented and made publicly accessible. In the EU, discussions are growing about including psychedelics in compassionate use programs[96], as to be authorized, the medicine must be under investigation in ongoing clinical trials or have started the marketing authorization process, as the case of MDMA or psilocybin. Certain countries currently allow compassionate use of LSD, MDMA, and psilocybin [97].

In Switzerland, the 'Swiss Federal Act on Narcotics' permits the use of psilocybin, LSD, and MDMA for resistant disorders. The Swiss Medical Society for Psycholytic Therapy (SPÄT), received special authorization to conduct psycholytic therapies with MDMA and LSD, treating around 170 patients in over a thousand sessions[98].

Off-labels

Off-label use means prescribing an approved medication for purposes not specifically sanctioned by regulatory authorities, such as treating an unapproved medical condition, age group, dosage, or method of administration [99]. This approach is typically considered when no authorized treatments are available for a particular disease or condition, or when existing approved treatments have proven ineffective or intolerable for the patient. In these cases, doctors must inform patients that the safety and effectiveness of the medication for its off-label use have not been officially established.

Unlike most psychedelic substances, ketamine is an exception. Initially approved for anesthesia, is now widely used off-label for conditions like depression and PTSD, often without proper patient screening or trained professionals on staff. Despite the approval of esketamine (SPRAVATO®) for mood disorders, access remains limited, and many clinics operate in an unregulated space as the regulatory requirements for off-label medication use are generally minimal[100].

2.1.7 Unlicensed use of psychedelics in non- medical setting

Recent global advancements in the medical application of serotonergic psychedelics have generated increased interest in the EU and worldwide. Although none of these substances, aside from esketamine (SPRAVATO®), have been granted marketing authorization in Europe, there is a growing trend of unregulated use for therapeutic purposes. This is evident in the increasing number of unlicensed psychedelics “practice “or “retreats” that claim to provide healing treatments. These establishments, often operating outside legal or regulatory oversight, range from shamanistic settings tied to indigenous rituals to environments resembling medical clinics where psychedelics are administered[69]. These unlicensed venues often attract clients by referencing ongoing research studies to make assertions about the effectiveness and safety of psychedelic therapies. However, medical applications should involve treating specific conditions using established protocols in licensed facilities, coupled with psychotherapy or counseling provided by certified professionals.

Furthermore, there is growing concern about the circulation of “training manuals” across Europe, instructing individuals on administering psychedelics in unregulated environments[69]. The risks associated with these practices are significant, particularly because psychedelics can induce altered states of consciousness that heighten suggestibility,

vulnerability, and the potential for abuse, as well as issues like false memories and retraumatization, especially in the absence of licensed and trained professionals, in addition to all the ADs previously reported[101].

Moreover, there is a rising popularity of the "microdose" which typically involves regularly consuming sub-perceptual doses of psychedelics. This further highlights the spread of unregulated psychedelic use. Manuals for microdosing are becoming increasingly prevalent across Europe, yet there remains a lack of definitive evidence demonstrating that microdosing is either effective or safe[69].

2.2 Psychedelics and their impact in public health

The potential regulation of psychedelics holds significant implications for public health, offering a mix of opportunities and challenges[51]. Primarily linked to counterculture, psychedelics are now being reevaluated for their therapeutic potential as research on psilocybin and MDMA suggests they may effectively treat some psychiatric conditions such as depression and PTSD[102]. These findings point to the possibility of improved patient outcomes, including symptom relief and enhanced quality of life for those who have not benefited from conventional treatments[21]. In this way, the use of psychedelics could lead to substantial healthcare savings in long term by offering effective treatments for conditions that are otherwise difficult to manage[103]. Beyond these promises, psychedelics may have broader positive effects on public health. Successful integration of these substances into treatment could help reduce the stigma associated with mental health disorders, promoting a more open dialogue about treatment options. This shift could encourage individuals to seek help earlier and more frequently, potentially improving overall mental health outcomes[104][105].

Thus, if integrated effectively, psychedelics could provide new solutions for complex mental health issues and offer alternatives for those who have not responded to traditional therapies [106]. However, public health concerns associated with integrating psychedelics into clinical settings highlight the need for careful consideration of cost, regulation, safety, and equity[107][108]. One of the main concerns regards *safety* due to the unpredictable nature of psychedelic experiences and the correct use of psychedelics. While some individuals may benefit from these substances, others may encounter distressing or unpredictable reactions. The lack of standardized protocols and adequate training for healthcare providers could further complicate their use, potentially putting patient safety at risk[109]. Additionally,

regulatory challenges present a significant barrier to the broader adoption of psychedelics. Currently, the scheduling of these substances as illegal or highly restricted limits the development of comprehensive treatment protocols and inhibits the expansion of psychedelic therapies into mainstream healthcare settings.

In addition to this gap regulation, the integration of psychedelics into clinical settings faces substantial obstacles[110]. One major challenge is the *high cost* associated with their administration and the comprehensive support required for effective therapy. Psychedelic treatments often involve complex protocols that include extensive preparatory and integration sessions, specialized training for therapists, and continuous monitoring of patient progress[109]. These elements contribute to a significant financial burden for the healthcare systems[111]. Moreover, the current healthcare infrastructure may not be equipped to support the widespread adoption of psychedelic therapies with high demand and limited resources, and the integration of psychedelics would require a shift in practice and the development of new guidelines.

Other concerns are about *accessibility and equity*[112]. Psychedelic therapies could be expensive and may not be covered by insurance, limiting access for many patients[111]. This raises questions about how to ensure that these potentially treatments are available to all individuals who could benefit from them, not just those who can afford out-of-pocket expenses[108]. Thus, the potential for disparities in access and regulatory inconsistencies remains a concern[101]. Variability in state-level regulations could result in uneven access to psychedelic therapies and potentially exacerbate existing inequalities in healthcare[111]. These disparities could impact marginalized communities disproportionately, highlighting the need for a more coordinated and equitable approach to the regulation[108]. In this view, the main challenge in public health is to ensure they become equitably accessible and optimally practiced by mitigate risk and reduce harm [108].

In addition, the *ethical implications* of psychedelic use in therapeutic settings must also be addressed. Issues such as informed consent, participant vulnerability, and the potential for misuse in unsupervised environments require robust ethical guidelines and oversight[101][111].

Public interest in psychedelics has surged, driven by significant media attention and grassroots advocacy movements that frames access to psychedelics for the decriminalization of personal use[113]. Consequently, the use of psychedelics has increased notably, with a significant rise

in use among adults aged 19 to 30 over the past decade[114]. At the same time, there is also emerging evidence of an increase in emergency department visits and hospitalizations associated with psychedelic use[115].

The rapid growth of public interest in psychedelics has been accompanied by a surge in private investment, driven in part by the FDA's 2019 designation of psilocybin as a "breakthrough therapy." This designation has led to significant venture capital inflows into the psychedelic industry, projected to be worth nearly \$12 billion USD by 2029, outpacing the cannabis market[116] [117] and prompting pharmaceutical companies to fund clinical trials. Further, some companies are seeking exclusive rights to psychedelic access in medical contexts and there is a rapid increase in the number of patents. For example, synthetic formulations of psilocybin are emerging, such as COMP360 owned by Compass Pathways[30]. Combination drugs and even the context in which they are being administered have been patented[118]. This surge in public interest and private investment has amplified pressure on governments to liberalize or decriminalize access to psychedelics[119]. In response, there have been increasing openness to explore and implement psychedelic regulation, including the approval of esketamine for treatment-resistant depression in various states[111].

Despite the financial enthusiasm surrounding psychedelics, the safety and therapeutic efficacy of these substances in humans have not been thoroughly investigated[120]. Much of the existing research faces methodological challenges that undermine its validity. This is exemplified by the recent FDA rejection of MDMA for PTSD treatment from Lykos Therapeutics [121].

As governments consider review psychedelic policies of legalization /decriminalization, key issues must be addressed to ensure safe and effective implementation[81][93][122]. Lessons from cannabis legalization highlight the risks of inconsistent regulations, industry influence, and inadequate oversight, leading to public confusion, overconsumption, and drug diversion[123]. The promotion of medical cannabis occurred with limited evidence of efficacy and safety, largely influenced by for-profit entities and lacking sufficient regulatory oversight[124]. The psychedelic industry is making strong claims based on limited evidence, which could lead to similar problems. To avoid these pitfalls, it is crucial to minimize the influence of industry in shaping psychedelic policies. Careful consideration of the benefits and risks, ethical guidelines, and robust public health education are essential to prevent misuse and ensure informed decisions. The legal status of psychedelics will significantly impact how

these substances are regulated, prescribed, and monitored, further influencing their integration into public health systems.

In conclusion, while the potential benefits of psychedelics in treating mental health conditions are significant, careful consideration of their public health implications is essential. Addressing disparities in access and regulation, ensuring robust safety protocols, and providing accurate public education are critical steps in maximizing the positive impact of psychedelics while mitigating potential risks.

2.3 Why is the EMCDDA/EUDA involved in the medical use of psychedelic substances?

The EMCDDA/EUDA provides to the EU and its Member States a factual understanding of European drug problems and a solid evidence base to support the European debate on drug issues. Every year the agency publishes an overview of drug-related issues across Europe, providing a solid evidence-based to promote drug policy discussions[125]. The agency is significantly involved in monitoring all the psychoactive substances in which there are still limited information about effects and patterns of use. In this view, the medical use of psychedelic substances is under the critical view of the agency for different reasons. The first reason is because for psychedelics, compared to other substance monitoring by the agency, much less is known about the prevalence, harms and risks associated with their use. All these substances are listed in Schedule I of the 1971 Convention limiting scientific and medical purposes. Monitoring these studies allows the agency to develop a deeper understanding of the potential medical properties and the associated risks and harms of these substances.

In addition, psychedelics are being investigated for treating SUD, a rapidly evolving area with several ongoing studies and clinical trials[37]. This is directly relevant to the EMCDDA's mandate. Although conclusive results are pending for some substances, there is moderate evidence for the controlled use of psilocybin and ketamine[126]. In addition, there is an increased unlicensed "medical" use of psychedelics from people seeking to treat drug addiction in Europe. This could have a potential implication for harm reduction and drug treatment services[127].

Due to the public interest in psychedelics substances, the agency wants to keep abreast of developments in the medical use under international control, in the same way of cannabis [128] and heroin [79]. For instance, the EMCDDA has been involved in examining the evidence

base and regulatory frameworks for the medical use of cannabis and cannabinoids in response to growing interest and policy development in European countries. Many of the questions explored for cannabis could similarly apply to psychedelics, such as the effectiveness and health risks associated with their medical use and the relevant regulatory frameworks. Staying informed on these developments prepares the EMCDDA/EUDA to respond to rapidly changing policies and requests for information from EU decision-makers, national policymakers, and professionals in the drug field.

Indeed, regulation of psychedelics market is an evolving field. A possible change in licensed medical uses of psychedelics may boost unlicensed use and illicit markets. Claims about treatment efficacy, based on ongoing studies, are being used by unlicensed providers offering psychedelic therapies. It is unlikely that psychedelic-assisted therapies will be comprehensively covered by national or private health insurance systems in the immediate term, even if these substances receive marketing authorization in the EU. This might lead people to seek treatment in unlicensed settings or through self-medication to reduce costs. There is also a risk that medical use could be co-opted for non-medical purposes, similar to developments observed in the medical cannabis field. The substantial commercial interest in psychedelics adds to the complexity of policy and regulatory challenges.

Moreover, existing structures in mental health field, may not be equipped to handle the unique challenges of administering psychedelics, including patient supervision and safeguarding during altered states of consciousness. This adds complexity for national policymakers, who may look to the EMCDDA/EUDA for guidance. Developing a comprehensive understanding of the issues related to the medical use of psychedelics will benefit the EMCDDA/EUDA in supporting national policymakers effectively.

In this direction, the EMCDDA Single Programming Document 2023–2025 includes a commitment to improve understanding of the therapeutic use of psychedelics, including scaling up expertise around the current state of research (evidence of effectiveness), potential harms, regulatory frameworks and policy responses. Due to the limited information that currently exists in this area, the EUDA, former EMCDDA, has launched two projects to increase understanding of key developments and respond to concerns raised by policymakers, that are objectives of this internship.

INTERNSHIP DESCRIPTION AND OBJECTIVES

3. Internship description

The internship was conducted at the EMCDDA, focusing primarily on supporting research projects related to the medical use of psychedelic substances.

The internship lasted four months, from October 2023 to January 2024, within the Public Health Unit (HEA) and consisted of 556 hours of in-person work. Staff members of the HEA were required to work on-site at the institute from 8:30 AM to 6:30 PM for two days per week, generally on Tuesday and Wednesday, with the remainder of the week allocated for remote work.

The internship was carried out under the direct supervision of Dr. Alexander Soderholm, project manager for the project on medicinal use of psychedelic substances, and Dr. Liesbeth Vandam, head of the support to policy sector within the EMCDDA. Supervision included weekly meetings on Tuesday mornings from 10am to 12pm to provide guidance, prepare for meetings with external partners and contractors, ensure that the internship objectives were met, monitor progresses, and share information from various sources. Extra meetings were planned at convenience and generally they were on Wednesday afternoon.

In addition, we held weekly on-line meetings with contractors, who were external experts and research organizations collaborating with the EMCDDA on specific projects related to psychedelics. These on-line meetings were held overall on Monday morning and additional meetings were planned at convenience during the rest of the week. These meetings were crucial for reviewing progress, discussing deliverables, and ensuring that the project objectives were met effectively and efficiently.

Throughout the duration of the internship, I was involved in different projects and activities, as reported in the table 2, and described more in details below.

The workload varied each week, with regular meetings scheduled on Tuesday mornings, Wednesday afternoons, and Friday afternoons.

During the first two weeks of my internship, my focus was primarily on understanding the safety and security protocols of the EMCDDA. This included special training sessions on the agency's secure platforms and familiarizing myself with building regulations. These initial weeks also provided an opportunity to gain an overview of the EMCDDA's work, allowing me to connect with individuals from different units and understand overall the work of HEA Unit at the EMCDDA and its various sectors. With this, I had the opportunity also to gaining a

comprehensive understanding of agency’s crucial role within the European Union, the roles and functions of the European Commission, and other relevant EU agencies as well, in order to expand my knowledge of health policy-making, particularly in the evaluation of health objectives in EU.

After this introductory phase, we transitioned to the specific activities outlined in the work plan.

Activities	Oct 2023	Nov 2023	Dec 2023	Jan 2024
Project 1 Medical Use of Psychedelic: Research and practice	Active	Active	Completed	Completed
Project 2 Medical Use of Psychedelic: a scoping study to map and describe practices in the EU	Completed	Completed	Active	Active
Development of Informational Materials FAQs, Reports, Presentations	Active	Active	Active	Active
Writing of the editorial manuscript	Completed	Completed	Active	Active

Table 2. Chronogram of activities at EMCDDA during the internship

In addition to the scheduled activities outlined in the chronogram, extra activities took place on a weekly or monthly basis.

Every first week of the month, we held a general meeting with all HEA members. These meetings were designed to integrate information, discuss progress, address challenges, and coordinate efforts across various projects of the HEA Unit. This ensured alignment with strategic objectives and enhanced overall collaboration within the team.

Weekly journal clubs were also instituted, providing a platform for team members to present and discuss recent research findings, stay updated on the latest developments in the field, and foster a culture of continuous learning and scientific inquiry. These journal clubs held every Friday afternoon, featured presentations by different EMCDDA staff members, as well as external visitors and students.

During the four months, we also participated in several meetings with the Reitox network of national focal points. Reitox serves as a bridge between national drug information systems, and it is the primary channel through which the EMCDDA exchanges data and methodological

information on drugs and drug addiction across Europe. Moreover, the agency hosted informative sessions and congresses. Significant meetings in December 2023 with the participation of all the EMCDDA members, were held by the general director to discuss the EMCDDA's new mandate and the transition to the new agency EUDA.

A particularly formative experience was the visit to the mobile methadone bus and the consumption rooms at "Ares do Pinhal Association for Social Inclusion" in Lisbon organized by the EMCDDA for all the visitors making part of the EMCDDA staff members, to have a close and in-situ view about the drug situation in Portugal. This visit provided a unique, hands-on opportunity to observe Portugal's harm reduction approach to drug use. Ares do Pinhal is a Portuguese NGO established in 1986, focusing on social inclusion and support for people who use drugs. It is well-known in the community for its numerous methadone vans scattered across Lisbon. The methadone program is part of a significant shift in drug policy that Portugal underwent 15 years ago under the left-leaning government of Jorge Sampaio. This shift was in response to a severe heroin problem and the high accessibility of drugs in Lisbon's Casal Ventoso neighborhood. The mobile methadone bus offers opioid substitution therapy to individuals with drug addiction, ensuring they receive treatment in a safe and accessible way. Recently, Ares do Pinhal launched its first fixed-site Supervised Consumption Site (SCS), offering both inhaling and injecting rooms for the community, along with a drop-in center featuring a café and clothes room. In addition, it also provides a wide range of services: blood testing (TB, HIV, syphilis, etc.), syringe exchange, condoms, other medications (e.g. antibiotics) and education. The consumption rooms provide a supervised environment where individuals can use drugs under medical supervision, reducing the risks of overdose and disease transmission. We had the opportunity to meet Dr. Hugo Faria, a psychologist that coordinates one of two Low Threshold Mobile Units for methadone program, together with Dr. Lucas Wiessing, principal scientist of EMCDDA in the HEA. This visit offered an invaluable, on-the-ground perspective of how Portugal's progressive drug policies are implemented, allowing us to better understand the challenges and solutions involved in addressing drug addiction at the community level.



FIGURE 6. Pictures of the visit at Ares do Pinhal Association in Lisbon with Dr. Hugo Faria and Dr. Lucas Wiessing.

3.2 Internship objectives

At the beginning of the internship, the first concern was to understand the role of the EMCDDA and the EU in health policy making. This included gaining knowledge about how health policies are created, implemented, and evaluated, as well as developing a comprehensive understanding of the functioning of the EMCDDA and other relevant EU agencies.

Upon my arrival, two different projects were underway in the HEA in the psychedelics field. Concrete objectives were to contribute to two research projects on psychedelic substances that EMCDDA started in collaboration with different contractors. This involved actively participating in project meetings and review processes, conducting research and analysis, performing literature reviews, and developing informational materials.

Specific Objectives:

1. Support Phases 1 of the project on the medical use of psychedelic substances:

○ Project 1: “Medical Use of Psychedelic Substances: Research and Practice”

The objective of this project was to create a scientific report about the development of the medical use of psychedelics. This report was redacted in collaboration with contractors, neuroscientists working at the Champalimaud Foundation in Lisbon. In this part, I was involved in conducting a peer review of the systematic literature in order to ensure accuracy, relevance, and rigor of the technical report. This process involves critically evaluating the

methodology, findings, and conclusions of the report to ensure they meet high standards of scientific validity.

- **Project 2: “Medical Use of Psychedelic Substances: a scoping study to map and describe practices in the EU”**

The objective of this project was to write a report exploring the different settings—legitimate, unlicensed, and illegal—where psychedelics are purportedly provided for therapeutic purposes. This was made in collaboration with the drug agency of Cech Republic. Here, I was involved in participating in weekly meetings with contractors to discuss progress and helping them in the search of the different setting and in reviewing project deliverables. This last, involved assessing the content, methodology, and applicability of the deliverables.

2. Development of informational materials

For this objective I was involved in differs tasks:

- Develop a presentation and background document on psychedelic policy developments.

This task involves researching and synthesizing information on global policy developments related to psychedelics focusing on key countries. The focus on key countries will provide a comparative perspective on different regulatory approaches and their outcomes. After the research steps, we developed a comprehensive presentation and background document that will aid in disseminating findings to stakeholders, informing policy debates, and guiding future research and policy initiatives. This task underscores the importance of staying informed about international trends and their implications for domestic policy and practice.

- Writing of the editorial to be published in a scientific journal.
- Assist in drafting and reviewing Frequently Asked Questions (FAQs) related to the project. This task involved distilling technical details

into clear, accessible language and ensuring that the information addresses common queries and concerns. Creating and refining these FAQs was important for effectively communicating complex information to a broad audience.

3.3 Projects description and implementation

The EMCDDA's Single Programming Document 2023–2025 emphasizes the need to enhance understanding of the therapeutic use of psychedelics by expanding knowledge on current research, potential harms, regulatory frameworks, and policy responses. In this view, two projects were implemented.

Project 1: “Medical Use of Psychedelic Substances: Research and Practice”

This first project was relating in understanding the medical use of psychedelic substances, the current state of research, practice and developments. The ultimate goal was to better comprehend the medical use of these substances within the EU and globally, focusing on their regulatory frameworks and the current state of research. This comprehensive approach ensures that the EMCDDA remains well-informed about the evolving landscape of medical psychedelic use, supporting informed policymaking and public health strategies in the EU.

For this project, a contract was issued for 12 months with a group of researchers of Champalimaud Foundation to develop a technical report covering:

- a) Current regulatory frameworks for the medical use of psychedelic substances in the EU, including 'special access' and 'compassionate use' programmes.
- b) The current state of research and clinical trials in the EU and globally, as well as frameworks for conducting research and clinical trials.
- c) The outcomes of these trials, including evidence on the effectiveness and health risks associated with the medical use of psychedelic substances.

In addition to these points, the report was the base for developing the 'Frequently Asked Questions' in collaboration with the EMCDDA members.

To ensure the quality of this technical report, a group of international scientific peer reviewers was identified to provide critical comments. These reviewers, selected for their expertise, help ensure the report's robustness.

Upon my arrival, the report was already completed, and I joined and participated in the peer review process that took almost two months.

Thus, for Monday to Friday I was involved in a comprehensive review of the technical reports entailing a thorough analysis of the literature, evaluating the content, methodology, and significance of the research presented. The main task was to identify the most recent and relevant studies for the report in case something was not updated, ensure that all presented information was accurate and matched the data in the literature review. The review also involved evaluating the presentation and interpretation of the research findings, ensuring that the results were clearly presented and accurately interpreted. Finally, all references were verified to be accurate, up-to-date, and relevant to the paper's content. Constructive feedback was provided on areas where the paper could be improved, such as suggesting additional analyses, identifying gaps in the argument, or recommending further research papers.

Every Tuesday, I had a meeting with the supervisor as well as with the scientific unit of EMCDDA, in order to discuss the advancement in the review process and the gaps that were found during the revision.

After the internal review process, the report was reviewed by experts, followed by another round of review by the agency's members to assess the implementation of the feedback. The whole report was completed only at the beginning of January 2024.

Simultaneously, I was involved in discussing and developing the outline of the technical report and the 'Frequently Asked Questions' section based on the information wrote in this report.

Being involved in these processes provided a highly formative experience, giving me a quick and comprehensive overview of the key topics related to psychedelics and their current regulatory landscape. This served as a valuable foundation of knowledge, acting as a springboard for deeper exploration of psychedelics throughout the entire internship period.

Project 2: "Medical Use of Psychedelic Substances: a scoping study to map and describe practices in the EU"

With the recent panorama in the regulation of psychedelic substances worldwide, there is an increase patterns of their use in non-regular setting in Europe. In particular, it appears that the use of psychedelics for therapeutic or spiritually oriented reasons is increasing overall during psychedelic 'retreats' and other similar practices, claiming to provide therapeutic benefits. These unlicensed or illegal settings range from 'shamanistic' environments with

roots indigenous traditions ritualistic and religious uses of, to entities that appear to mimic clinical settings where psychedelics are administered. Furthermore, health claims also appear to be influencing changes in consumption habits, for example related to “microdosing”. A recent EMCDDA meeting highlighted the need to improve data collection on the various uses of psychedelic substances and the settings in which they are consumed. The spread and impact of psychedelic retreats across Europe remain unclear, but these settings may pose significant health risks to users associated with the altered states of consciousness such as suggestibility, vulnerability, abuse, false memories, and retraumatization, particularly in the absence of licensed and trained professionals.

To better understand these evolving issues, the EUDA has an ongoing project on mapping the existence of psychedelic-related practices and interventions in Europe.

The study examines the range of existing setting - legitimate, unlicensed, and illegal-, practices, the services offered, associated costs, and the characteristics and motivations of people attending these settings.

The project's objectives will be achieved by collecting and analyzing data from various sources, including the Reitox network of national focal points (NFPs), an in-depth questionnaire directed at key experts, and comprehensive desk-based research. This approach is designed to provide the EMCDDA with a robust technical report on the topic.

At the moment of my arrival, the project was recently started. The project comprised different tasks that will guide the creation of this report. I was mainly involved in the following activities:

1. Analysis of Relevant Reitox NFP Workbooks:

The aim of this analysis was to collect data about markets, policies and patterns of psychedelic consume across Europe. This analysis was important to collect information for the creation of the short online survey and the follow-up questionnaire.

2. Creation of the Short Online Survey:

The aim of this point was to create a short survey targeting Reitox NFPs and other key networks to map existing practices in the EU.

3. Creation of Follow-up Questionnaire: This questionnaire will be administered to key experts in the field to gather detailed information on current national situations regarding settings offering psychedelic substance therapies. The topics that this questionnaire covered was to understand the current national situations, responses of

national competent authorities, applicable regulatory frameworks, services offered, costs, and characteristics and motivations of users.

4. **Desk-Based Research/Literature Review:** In this point I was implicated in helping and collecting supportive research that complements the information gathered from activities 1, 2, and 3. This research was collect through different sites and forums. In order to do it and maintained reproducibility, several strategies were used, such as the “Multi-lingual Search Strategy” based on the search of standard “key words” previously discussed to be use in this desk-based research. These strategies were decided and agreed upon in consultation with the project team to ensure comprehensive coverage.

During my stay, the work schedule was agreed upon between the tenderer and the EMCDDA, following the timeline indicated below

Activity 1. Prepare and agree a work plan, that was mainly accorded in November. The workplan was decided to start with the examination of the data of Reitox NFP Workbooks and the desk-based research/literature review.

Activity 2. - Discuss and develop outline of technical report in close collaboration with EMCDDA and contractors.

-Agree search terms for desk-based research with the EMCDDA project team.

These activities were decided in December to start to give a shape to the technical report.

Activity 3. Complete a review of the relevant Reitox NFP workbooks (e.g. treatment, legal and markets), focusing on information provided by NFPs on unlicensed settings of psychedelics for therapeutic purposes. In conjunction, we begun desk-based research. This activity was made in between December and January. At the beginning of December, we held regular weekly meetings to discuss the most appropriate keywords for the desk-based research and the NFP workbooks review, and those that should be avoided. We also reviewed the research findings and strategized how to proceed to the next phase.

Activity 4. Creation and administration of short survey to Reitox NFPs and other key networks based on results from Activity 1 - 4. The created a short survey that was ready to be sent to the key network in the field only the last week of my internship after passing the approval of the scientific committee of the EMCDDA.

The rest of activities, currently undergoing, but that I did not take place, are the development of the follow-up questionnaire to key experts based on results from Activity 4, analyze the

results of survey and questionnaire data and draft a technical report on the medical use of psychedelic substances, based on the results of preceding activities.

This was a formative experience for me, as I was involved in the entire process from the very beginning—helping shape the report to the creation of the survey. Developing the survey was particularly important, as it gave me valuable insights into how desk-based research informs policy-making. I thoroughly enjoyed the process of designing the survey and understanding its broader impact.

Description of the other activities and outcomes

These tasks collectively aim to develop and disseminate comprehensive, accurate, and accessible informational materials helping to support decision-making and public engagement in the field of psychedelic research and policy.

To develop a presentation and background document on Psychedelic Policy Developments:

This task entails an extensive review and analysis of global policy developments related to psychedelics. The focus was identifying key countries that have pioneered or significantly altered their regulatory frameworks concerning psychedelic substances. By concentrating on key countries, the aim is to highlight different regulatory approaches, their implementation strategies, and their outcomes. This comparative analysis will offer valuable insights into the effectiveness and challenges of various policy models.

In this line, I developed at the end of November a thorough presentation at EMCDDA to facilitate the dissemination of findings. These materials will be designed to support policy debates about the use of psychedelics in medical setting.

From this experience, I gained valuable skills in translating research findings into practical tools for policy discussions. By developing a comprehensive presentation at the EMCDDA, I learned how to effectively communicate complex information to diverse audiences, furthering my understanding of how research can inform real-world decision-making in healthcare.

To write an Editorial for a Scientific Journal Publication:

I was involved in the writing of an editorial paper to be published in a scientific journal in collaboration with EMCDDA. The editorial summarizes key findings from the projects, discuss their implications, and highlight the importance of continued research and policy development in the field of psychedelics.

Being involved in writing an editorial paper for publication in a scientific journal allowed me to refine my writing and research skills in a different context in which I use to work, while gaining insight into the academic publishing process with international organizations. Crafting the editorial taught me how to effectively summarize key project findings, analyze their broader implications, and emphasize the importance of ongoing research and policy development in the field of psychedelics. This experience strengthened my ability to contribute to meaningful discussions in public health and policy.

To assist in the Drafting and Reviewing of Frequently Asked Questions (FAQs) Related to the Projects

I was involved in the development and review of the FAQs and the new psychedelics page on the EMCDDA website during the first two months of my internship. This involved frequently meeting with the Scientific Unit as well as the Information and Communication Units. A training session on the EMCDDA webpage tools, including how to update information, was conducted by the Communication Unit. The session included a practical example using FAQs related to other drug substances.

The FAQs were designed to address common queries and concerns about the medical use of psychedelic substances, including the therapeutic applications and clinical research, the prevalence and patterns of their use in Europe, and the presence of unlicensed and illegal practices. Thus, we set questions that effectively communicate the project's findings from recent reports, research and related information to the public and other stakeholders. In doing it, technical and scientific information were translated into clear, accessible language. This is critical for making complex concepts understandable to a non-specialist audience and highlights the importance in bridging the gap between research findings and public understanding.

On the 30th of July the EUDA has recently published a FAQ document on the therapeutic use of psychedelic substances https://www.euda.europa.eu/publications/frequently-asked-questions-faq/faq-therapeutic-use-psychedelic-substances_en.

This resource aims to enhance understanding of key developments, address policymakers' concerns, and provide insights into ongoing research. This experience enhanced my ability to anticipate common concerns or misunderstandings and address them in a way that is accessible to a broader audience. It was valuable in improving my attention to detail and sharpening my skills in writing for clarity and public engagement, which are essential for both scientific communication and policy development.

3.4 Personal aims and outcomes

Through this internship, I aimed to blend and merge my academic background in the neurobiological mechanisms of addiction and in public health, respectively from my PhD in Neuroscience and the current master's in public health, with practical policy analysis, thereby contributing to the EMCDDA's efforts to address drug-related challenges in Europe.

During this internship, I first strength my understanding of the EMCDDA's role in shaping and evaluating health policies within the European Union for drug use. I was, then, engaged directly with the processes of data collection, review, and dissemination of the medical use of psychedelics, contributing to the agency's mission of providing comparable information on drugs and drug addiction.

Specifically, I was aimed to:

1. **Enhance understanding of health policy making:** I gained practical experience in the intricacies of health policy evaluation within the EU framework, with a particular focus on how scientific evidence is translated into policy decisions and recommendations.
2. **Contribute to ongoing research on psychedelic substances:** I supported the EMCDDA's projects on the medical use of psychedelic substances, leveraging my scientific expertise to review literature, draft FAQs, write an editorial and contribute to policy discussions on these emerging therapies.
3. **Develop communication skills:** I improved my ability to communicate complex scientific concepts to policymakers and the general public, thereby enhancing the impact of research findings on public health outcomes.

4. **Build professional networks:** I established connections with professionals and experts in the field of public health and drug policy, fostering collaborations that could enhance future research and policy initiatives.

This experience will not only enhance my skills as a future public health professional but also provide valuable insights that hopefully will inform my future research and career in public health and drug policy.

3.5 Connection between the internship and the study program

Drug addiction is a significant public health concern worldwide. Addressing the topic of substance use and abuse from both, preventive and treatment perspectives, is crucial for public health to resolve the consequences resulting from drug trafficking, misuse, and related harm. Interning at EMCDDA give me a unique opportunity to gain specialized knowledge to the field of drug addiction and its implications for public health by providing with insights into the latest research, trends, and policies. This enables me to understand the intersection between these factors and public health practice.

The internship at the EMCDDA provided a unique platform to bridge the theoretical knowledge from the master's program in Public Health with hands-on experience in a real-world setting. This connection is evident in several key areas. First, it enhanced my understanding of health policy, particularly those related to drug addiction and the medical use of psychedelics. Engaging with health policies provided insights into regulatory frameworks, underscoring the complexity and importance of effective regulation in health outcomes. This also helped me in understand how international health policies are formulated and harmonized across different states, offering a broader understanding of global health challenges and solutions.

In addition, the internship allows to get general knowledges related to epidemiology of psychedelics and risks assessment aiming to evaluated health and social risks associated with the use of these substances and establishing interventions and policies related to the medical use of psychedelics.

The internship also emphasized the importance of research and evidence-based practice. Supporting systematic literature reviews at the EMCDDA honed my skills in critically appraising scientific literature, a key component of evidence-based for public health decision-making.

Moreover, developing evidence-based FAQs and supporting dissemination aligned with public health goals of education and health promotion, emphasizing the role of accurate information in improving health outcomes.

Interdisciplinary collaboration was another critical aspect of the internship. Working alongside policymakers, scientists, and public health experts at the EMCDDA reflected the interdisciplinary nature of public health work. This collaboration not only enhanced my understanding of different perspectives and expertise but also broadened my professional network.

Lastly, the focus on emerging health issues, such as drug addiction and innovative therapies like psychedelic substances for medical use, highlighted the importance of understanding the complexities involved in addressing evolving health challenges.

DISCUSSION

Recent advancements in the medical use of psychedelics have garnered significant global interest from researchers, doctors, spiritual leaders, and general public. These substances show promise in addressing conditions like treatment-resistant depression, addictive disorders, PTSD, and psychological distress at the end of life[21]. However, the diverse range of psychedelics and the variety of conditions under study, combined with the lack of standardized research protocols and technical challenges related to the placebo and nocebo effects, present substantial obstacles to validating their therapeutic potential in clinical settings[51][75].

Currently, most psychedelics are classified as Schedule I drugs under international conventions, which severely restricts research and the safe use of these substances. Consequently, there is an urgent need to develop robust regulatory frameworks and adaptive policies that ensure patient safety, facilitate ongoing research, standardize clinical practices, and promote equitable access to these therapies[129], limiting the harm [24].

The regulatory frameworks for psychedelic services are inherently complex, especially when multiple stakeholders are involved[127]. Developing guidelines and policies requires addressing critical ethical considerations, such as defining appropriate uses of psychedelics, balancing competing interests to ensure equitable access, and determining the appropriate involvement of various stakeholders[83]. To navigate these challenges, several potential frameworks are under consideration.

Medicalization of psychedelics refers to their use for therapeutic purposes under the supervision of healthcare professionals, necessitating the reclassification of these substances from Schedule I to Schedule II[71]. This shift would permit the use of psychedelics in controlled clinical settings and allow pharmaceutical companies to patent psychedelic medications. However, it also risks limiting access to those with private insurance or the financial means to afford costly treatments[24].

Exclusively medicalizing psychedelics poses significant public health challenges[51]. While medicalization can ensure controlled use and therapeutic benefits, it alone does not address broader societal issues. For psychedelics to be reintegrated into society in a safe and equitable manner, it is crucial that medicalization be paired with decriminalization and/or legalization[90].

Legalization would remove restrictions on the production, sale, and use of psychedelics, enabling regulated commercial access and helping to prevent unsafe, unregulated use. Decriminalization would eliminate criminal penalties for possession, reducing legal risks and encouraging individuals to seek help without fear of legal repercussions[122]. Without these complementary measures, those who cannot afford medically supervised treatments might turn to underground sources, exposing themselves to unregulated substances and legal consequences[113]. In a context where self-medication with psychedelics is increasing, overmedicalization without decriminalization or legalization undermines harm reduction efforts and perpetuates existing inequalities, while ignoring the potential benefits of a more inclusive and regulated approach to psychedelic use[122].

The experience with cannabis underscores the importance of openly debating the legalization of nonmedical use rather than framing it solely as a medical issue [123]. Lessons from cannabis policy also highlight the need to counteract the exaggeration of psychedelic research findings, promote rigorous clinical research on dosing and potency, limit the influence of for-profit industries in shaping policies, and ensure coordination among states in regulating the production, sale, and distribution of psychedelics, whether for medical or recreational use[124]. Effective regulation of psychedelics will require more robust enforcement and national oversight compared to the current approach to cannabis regulation. The delegation of regulatory responsibilities to local states has led to inconsistent regulations and a fragmented regulatory environment, with variations in doses and patterns of use, contributing to a chaotic regulation[123].

If governments choose to legalize psychedelics for medical use, establish stringent licensure criteria for prescribers, therapists, and hospitals will be essential. There is significant uncertainty about how psychedelics should fit into current treatment models, including their use alongside other therapies, the appropriate clinical setting, and the patient populations that would benefit most[111]. These uncertainties complicate cost-effectiveness assessments considering also regional differences in healthcare systems[106].

Additionally, the medicalization of psychedelics alone will present challenges for religious communities, particularly Indigenous and shamanic practitioners, who may view this process as a form of cultural appropriation that undermines the spiritual significance of these substances and exposing themselves to legal consequences for the use of psychedelics outside the medical setting[127]. Historically, Indigenous peoples have been excluded from decision-making processes related to psychedelic research and policy. To avoid repeating these

exclusionary practices, a new approach grounded in partnership and trust is essential, prioritizing Indigenous principles such as community participation, capacity building, respect, responsibility, and reciprocity[130].

Globally, there is growing momentum to regulate the use of psychedelics for medical and therapeutic purposes, with notable developments in countries like Australia, the United States, and Canada. This includes the TGA in Australia's Authorized Prescriber pathway for psychiatrists[87], legislative adaptations in the US, initiatives by the US FDA such as the release of draft guidance[93], and Health Canada's Special Access Program (SAP)[91]. Although this panorama, the recent rejection for authorizing MDMA in the treatment of PTSD from FDA may will have important implication in the near future[131].

In Europe, changing patterns in psychedelic use are emerging, with different regulations across countries. So far, no psychedelics have been approved at the Member State or EU level for the medical treatment of neuropsychiatric disorders. However, only one psychedelic has been approved, esketamine, or Spravato, for the treatment of resistant depression [69][83].

The EUDA/EMCDDA has launched several initiatives to deepen understanding of the medical use of psychedelics, including comprehensive research into their effectiveness and potential harms, as well as the regulatory frameworks and policy responses surrounding their use. One objective of my internship at EMCDDA involved analyzing these issues by mapping current policies related to both recreational and therapeutic use of psychedelics and identifying areas where policy reform might be necessary. This understanding is crucial for creating a regulatory environment that supports therapeutic innovation while ensuring patient safety.

In Europe, small steps are being taken in this field, with the EMA addressing the unique challenges associated with conducting clinical trials on psychedelics. These challenges include issues related to placebo selection, expectancy effects, dosing, and maintaining blinding in trials. The EMA has included provisional guidance on psychedelics in the updated draft guideline for the clinical investigation of depression, emphasizing the importance of randomized, double-blind placebo-controlled trials to determine the efficacy and safety of these substances[132]. This was highlighted in the recent workshop of psychedelic substances held by EMA in April[54]. Despite these developments, robust regulatory guidance is still missing. This is essential for ensuring patient safety by establishing strict protocols for patient screening, dosing, administration, follow-up care and continuously monitoring the safety and efficacy of psychedelic treatments through post-marketing surveillance and adverse event reports[132].

In addition to the guidelines, adaptive policies should be implemented for addressing the challenges faced by clinical models, including provider shortages, high costs, and the representation of marginalized communities that may be excluded due to cost, stigma, or lack of access to specialized care[111]. These policies should include provisions for subsidized treatments, community-based care models, and outreach programs targeting marginalized populations[111]. Additionally, policies that recognize and respect cultural contexts, ensuring that traditional knowledge is not exploited and that Indigenous practitioners are integrated into the broader therapeutic landscape are needed[127]. As the field of psychedelic medicine grows, there is a risk of commercialization overshadowing ethical considerations. Policies must strike a balance between encouraging innovation and preventing the commodification of psychedelic therapies in ways that could lead to unethical practices or exacerbate health inequalities[108].

In addition to their therapeutic uses, psychedelics might contribute to health promotion and prevention, potentially impacting social determinants such as race, community dynamics, and health equity[133]. Psychedelics may also play a role in addressing broader public health issues, particularly by reducing health disparities and promoting wellness, spirituality, and creativity[101]. Initial research is investigating their role in addressing societal issues like racial trauma, domestic violence, recidivism, suicidality[134].

However, if the focus on psychedelics remains primarily biomedical without investment in equity, in both, research and policy, it may fail to produce widespread, equitable health outcomes and positive social effects.

Public health involvement in the field of psychedelics is crucial. Ensuring they are accessible and used effectively is essential. Additionally, if their broad use poses safety risks or could lead to exploitation, public health must work to mitigate these risks and minimize harm. Despite this, current public health involvement with psychedelics remains limited.

Psychedelics have increasingly moved beyond research settings, with a notable rise in recreational and underground use worldwide, despite varying policies[56]. Tens of millions of individuals report having used psychedelics at some point in their lives. This expanding use includes unregulated and often illegal practices, where psychedelics are integrated into wellness, therapeutic, or spiritually oriented interventions[76]. Many of these practices reference recent medical research to market their services. However, these unauthorized settings pose significant risks, as individuals seeking treatment may be exposed to unsafe practices and unverified therapeutic claims[56]. To effectively address the therapeutic and

community contexts of psychedelic use, a multi-faceted approach is essential for preparing the field.

The EMCDDA is investigating these unlicensed or illegal settings, where psychedelics are purportedly provided for therapeutic purposes. This investigation was addressed in the second objective of my internship. This exploration revealed the diverse nature of these settings, from shamanistic retreats to pseudo-clinical environments, each with varying levels of risk and legitimacy[69]. A dual focus on both legitimate therapeutic practices and the risks of unauthorized settings is crucial for developing informed and balanced policies that can safeguard public health while fostering legitimate therapeutic practices.

In conclusion, the rapidly evolving scenario around psychedelic research and development has led to an increase in clinical trials and growing recognition of their therapeutic potential. Despite this, developing safe and effective psychedelic medicines is complex, with unique challenges in clinical study design and regulatory requirements. The regulation of psychedelics requires a comprehensive approach that balances patient safety, equitable access, cultural sensitivity, and ethical considerations. This includes not only the reclassification and medicalization of psychedelics but also their decriminalization and the development of policies that promote harm reduction and social justice. Only through such a multifaceted approach can psychedelics be safely and effectively reintegrated into society. Through comprehensive research and informed policy-making, it is possible to harness the benefits of psychedelics while safeguarding public health. The work conducted during my internship at EMCDDA contributes to this ongoing effort, providing valuable insights into the current landscape and paving the way for future advancements in the field.

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