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Barriers to researching psilocybin and other controlled drugs: what are our options?

Overview

1. Research into psilocybin and other high research value drugs is being seriously hindered by the stringent controls placed on them by their status as Schedule 1 substances under the Misuse of Drugs Regulations 2001. This paper discusses the historical legislative context to then inform four regulatory solutions that could resolve this issue to increasing degrees of success and consistency with the evidence.

2. UN legislation underpins the controls on psilocybin in the UK but does not obstruct the freedom of the UK to modernise its domestic classification and scheduling systems. The Government has not commissioned or published any recent analysis of the harms of psilocybin.

3. The Misuse of Drugs Act 1971 is calibrated to enable access to controlled drugs for medical use but fails to account for scientific research. For clarity, scientific research is different to medical research in that psilocybin for scientific research purposes would never achieve market authorisation as product or formulation.

4. While a *de Minimis* quota would go some way to removing barriers and facilitating research, its possible implementation or the removal of Schedule 1 licences to bring controls in line with Schedule 2 could be insufficient solutions.

5. The most expedient and evidential way to facilitate medical *and* scientific research into psilocybin is to reschedule the compound to Schedule 2 with restrictions on prescribing.

6. The most comprehensive solution to the problem of barriers to research to controlled drugs more generally is an amendment to the Misuse of Drugs Regulations 2001 which could allow for the manufacture, distribution, supply, possession and administration of controlled drugs for the specific and limited purpose of scientific research only.

7. A one time evidence review and reshuffle of the contents of Schedule 1 would once and for all solve the problem of barriers to researching all controlled drugs in the UK and communicate a commitment to life sciences research and evidence based policy. This change would allow the UK to seize opportunities as they present themselves and to consolidate its position as a world

leader in the field.

8. Acknowledging the political complexity in regulatory reform, this paper discusses the pros and cons of four regulatory ways to resolve the issue.

Contents

1. The Problem

1.1 There is a substantial body of evidence suggesting a causal relationship between psilocybin's Schedule 1 status and barriers to research. These barriers to research have been recognised by HMG as significant enough to warrant revision since 2017.

Numerous researchers, organisations and institutions have expressed concern that science is being hindered, and opportunities are being squandered due to these barriers to research on Schedule 1 substances (compared to restrictions on researching Schedule 2 controlled substances). These barriers take the form of increased duration, increased costs and increased stigma. Details can be found in our 2020 report *Medicinal Use of Psilocybin: Reducing Barriers to Research and Treatment*, as well as *Schedule 1 barriers to research in the UK: An in-depth qualitative analysis*, *Restrictions on drugs with medical value: Moving beyond stalemate* and *Adverse effects of psychedelics: From anecdotes and misinformation to systematic science*.

We are currently waiting for the ACMD's publication of Part 2 of their Review of Barriers to Research on Controlled Drugs, a report which itself is the latest of several attempts by HMG, dating back to 2017, to solve the issues posed to research by the stringent controls on Schedule 1 drugs. But while psilocybin remains in Schedule 1 of the MDR 2001, life sciences research and the public continue to suffer and in short, opportunities are lost. Whilst some research is possible as noted by HMG, current regulations effectively prevent research for all but a very small group of organisations with enough resources to endure the significant bureaucratic obstacles. In practice, this stunts innovation and free market competition in the life sciences sector. It also reduces the ability of non-corporate research institutions to carry out equally vital pre-clinical and experimental work. **There is clear consensus that these barriers to research *exist and are substantial* enough that a solution must be found.**

2. The Context

2.1 Historic UN legislation underpins the controls on psilocybin in the UK.

As a result of the UK's close adherence to international guidance, that is the 1961 Single UN Convention on Narcotic Drugs (CND 61) and the following 1971 UN Convention on Psychotropic Substances (CPS 71), which was introduced to account for a variety of novel stimulants and other drugs such as LSD, psilocybin has been stringently controlled under UK law for 51 years. Under the Misuse of Drugs Act 1971 (MDA 71) psilocybin is in Class A, meaning it carries the most severe penalties for its possession and supply, more so than heroin for example. Under the associated Misuse of Drugs Regulations 2001 (MDR 01) it is Schedule 1, meaning that its use in research is so tightly controlled that it is only possible with a Home Office licence, while its prescription by a medical professional is not permitted without express permission from the secretary of state. It is often quoted that drugs belonging to this schedule are thought to have no medicinal value. There is no mention of this definition in the law itself and it is increasingly challenged by the emerging global evidence on the medical applications of psychedelics.

2.2 The international laws were implemented without due consideration of the evidence.

The controls on psilocybin under the CND 61 and CPS 71, and thus the MDA 71 and MDR 01, were not guided by scientific evidence on relative harms and benefits, but rather by social and political factors. From the late 1940s onwards, psychedelic drugs (such as LSD and later psilocybin) were being studied by research scientists and higher education institutions as adjuncts to psychotherapy, but it was their association with the 'counter-cultural' and 'revolutionary' movements of 1960s that caught the attention of lawmakers. Social unease, amplified by media sensationalism, was seized upon by the Nixon administration to implement laws that would allow for the dispersion and disruption of groups organising within these movements[1]. The US criminalised the possession of LSD in 1968, the same year that the UN began developing the international control framework for these substances. Psilocybin was controlled in the UK in 1971. This has led to a near total scientific and medical blackout on their use lasting close to 40 years.

2.3 The rationale for the Schedule 1 status of psilocybin in the UK has not been reviewed for fifty years despite major scientific advances.

In the half century since psilocybin was first controlled in the UK, the Government has never commissioned a scientific review on its status. The Home Office recently confirmed once again that there had been no recent review of the evidence of the harms of psilocybin in response to WPQ #2168 on the 20th May 2021. This is interesting when considered in the context of the 'clarification of the law' by which fresh psilocybin containing mushrooms were criminalised in 2005. This was heavily criticised both at the time, for example by Minister Paul Goggins who noted that "the Home Office received no submissions in favour of the clarification of the law in respect of magic mushrooms prior to the Drugs Act 2005 being granted Royal Assent on 7th April and four submissions against" and subsequently by the House of Commons Science and Technology Committee in their 2006 report *Making a Hash of It* in which the Home Office is charged with actively avoiding a review of the evidence of the harms of psilocybin mushrooms:

> The Government's use of a clarification of the law to put fresh magic mushrooms in Class A contravened the spirit of the Misuse of Drugs Act and meant that the ACMD was not given the chance to consider the evidence properly before responding. [...] The Chairman of the ACMD's attitude towards the decision to place magic mushrooms in Class A indicates a degree of complacency that can only serve to damage the reputation of the Council. [...] The ACMD should have spoken out against the Government's proposal to place magic mushrooms in Class A. Its failure to do so has undermined its credibility and made it look as though it fully endorsed the Home Office's decision, despite the striking lack of evidence to suggest that the Class A status of magic mushrooms was merited on the basis of the harm associated with their misuse.

(the relevant section is reproduced in full in Annex 1 of this document).

[1] *John Erlichman quoted in 'Legalize It All', Harper's Magazine, 2016*

2.4 The UN drug control treaties do not obstruct the freedom of the UK to modernise its domestic classification and scheduling systems.

It is sometimes claimed that the UK's obligations under international drug law limit its sovereign freedoms to make changes to domestic controls. However, the UN conventions do not have a direct effect on the UK. In practice, the intensity of legal control concerning the production, distribution and use of drugs is a matter for each contracting state. The UN legislation (CPS 71 and CND 61) is advisory and with no direct binding legal influence on signatories. This was recognised in the House of Commons Science and Technology Committee's 2006 report, Making a Hash of It:

> "**The UN drug control treaties do not pose a major barrier to reform of the UK system of drug classification.** This is in accordance with the observation made in the Runciman report *Drugs and the Law* that "although they rule out the legalisation of any prohibited drug other than for medical, scientific or limited industrial purposes, the conventions allow more room for manoeuvre than is generally understood""
>
> (p11. *Making a Hash of It* report by House of Commons Science and Technology Committee 18 july 2016 - emphasis in the original).

2.5 The MDA 71 is calibrated to enable access to controlled drugs for medical use, but fails to account for purely scientific research.

The preamble to the 1971 UN drug convention recognised "*that the use of psychotropic substances for medical and scientific purposes is indispensable and that their availability for such purposes should not be unduly restricted.*" UK drug law, however, diverges from the spirit of the conventions by not explicitly requiring regulations to allow for scientific use.

Clinical trials are methods of ascertaining whether a drug could be used as a safe and effective medicine - called here 'medical investigation' - and lead towards market authorisation. Whereas how these drugs work and what the implications are of how they work in the brain - what we call 'scientific investigation' - and the novel insights that are produced from such research, does not lead towards the market authorisation of these drugs. And yet both of these lines of investigation (medical and scientific) are hindered by the barriers imposed on Schedule 1 drugs.

The MDR 01 allows controlled drugs to be used for medicinal purposes, as required by Section 7(3) of the MDA 71, but these regulations are not designed—and do not function in practice—to deliver appropriate regulatory pathways for purely scientific activity with controlled drugs.

Controlled drugs with recognised medicinal uses (i.e. market authorisation) are regulated under Schedules 2-5 of the MDR 01 with the level of regulatory control (i.e. the Schedule) typically depending on expert advice from the ACMD following review of the evidence. This evidence-based process ensures that the regulation of medicinal use is commensurate with potential harms and benefits. However, there is no equivalent evidence-based process to regulate scientific research with drugs that have *not* been granted market authorisation as medicines. These are regulated, by default, under Part 1 of the Misuse of Drugs

(Designation) Order 2001 and Schedule 1 of the MDR 01. All such drugs are thereby placed in the same regulatory category irrespective of the balance of potential harms and potential scientific value.

This one-size-fits-all approach has been a profound regulatory failure, giving rise to the over-regulation of substances with high research value that are not—or not yet—authorised as medicines. Policymakers have been unwilling to reschedule Schedule 1 drugs (e.g. psilocybin) before market authorisation, but few other options exist to reduce the regulatory burden for researchers, a Catch 22 situation. Historically, the regulatory burden has deterred research. In the current context of increasing commercial and research interest in Schedule 1 drugs such as psilocybin, the regulatory burden effectively limits R&D to a small group of established companies with sufficient resources to endure the high costs and long delays, thereby limiting competition and innovation.

The reality of drug research is that significant scientific advances in the understanding of human physiology (and many other fields of value) can result irrespective of the use of those drugs in clinical practice, or lack thereof. This is illustrated by the significant contributions to the understanding of the physiology of the human brain that have resulted from neuroimaging research with psychedelic drugs—achieved separately to their ongoing development as medicinal products. For a regulatory framework to effectively permit the availability of controlled drugs for both medicinal *and* scientific uses—as the parties to the UN conventions intended—the latter have to be understood as distinct from MHRA authorisation and no less deserving of evidence-based regulatory process. For as long as there are no regulatory categories in UK law to differentiate non-medicinal controlled drugs on the basis of use and potential harm, there will be no evidence-based regulation of drug science.

2.6 Scientific research is undervalued leading to a degree of inertia affecting UK life sciences.

Scientific investigation can and does lead to the discovery of potential treatments, pharmaceutical or otherwise, which sometimes reach market authorisation, but its value is not dependent on and wholly determined by that possibility. The policy that drugs are not rescheduled until they reach market authorisation ignores and devalues this vital type of research, leading to a situation in which barriers to research are perpetuated and UK science suffers. Only once a drug has recieved market authorisation is there any application of evidence-based policy. Until then, all research is equally hindered because Schedule 1 doesn't discriminate between drugs of different harm and scientific value.

3. Possible Solutions

There is a range of possible solutions which could be implemented to address current barriers to research with psilocybin. What follows is a consideration of four options which would, to differing degrees, solve the issues faced by researchers looking to study high research value drugs, including the psychedelics, and psilocybin in particular, in the UK. These options are:

1. *De minimis* quotas
2. Scrapping S1 licences
3. Rescheduling with restrictions

4. Expanding the MDR

3.1. A *De Minimis* quota

The concept and effects of a research organisation carve out and *de minimis* quota as a solution in the case of psilocybin and the other psychedelics were discussed in our paper '*De minimis' Research Organisation Quotas are an Inappropriate and Inadequate Response to the Barriers to Research Imposed by Schedule 1 in the Case of Psilocybin* (reproduced in full in Annex 2, attached alongside this document). The following summary is adapted from that report.

The ACMD are investigating barriers to researching substances controlled under Schedule 1 of the Misuse of Drugs Regulations 2001 with their findings due to be released in a two part report. The first of these focuses on the barriers to researching synthetic cannabinoid receptor agonists (SCRAs), the second on other controlled drugs.

In the first part of the report a *de minimis* quota for 'research organisations' was recommended to mitigate the barriers to research identified in the call for evidence. While the level of this quota may be appropriate to mitigate some of the barriers faced by those looking to study SCRAs, the same approach could not be appropriately applied to all substances controlled under Schedule 1. For example, it would be complicated to determine the relevant levels for a wide range of different drugs, and it could increase bureaucracy at all stages of the process. It has also been noted that in order to allow for human research with good sample sizes and allow for the cost saving enabled by bulk buying for human clinical research, the limit would have to be quite high or it will be burdensome and/or require a Schedule 1 licence nonetheless. As such, in the case of psilocybin, and many other high research value substances in Schedule 1, a *de minimis* quota of this sort could be inappropriate and inadequate in resolving the issues faced by researchers and may in fact increase bureaucratic barriers, and perpetuate or even exacerbate the very issue it sets out to resolve.

Interestingly if a low *de minimis* quota were introduced in the case of psilocybin 'scientific' research would be facilitated whilst 'medical' research, as in extensive, large cohort, clinical trials would not.

3.2 Scrapping of Schedule 1 licences

According to Home Office guidance most higher education and research institutions do not have to apply for Home Office licences in order to possess and study Schedule 2 controlled substances, meaning that beyond the usual institutional precautions and record keeping requirements, research of any amount of a Schedule 2 controlled substance can continue uninhibited.

Bringing licensing of Schedule 1 substances, entirely or just for high research value drugs, into line with the rules for Schedule 2 would facilitate research. Without the need to apply for a licence, researchers could more easily obtain, transport, store and use these substances. The scrapping of Schedule 1 licences would remove the bureaucracy and the fees for the licence, allowing these studies to be conducted with the limited resources of time and money afforded by research grants and funds available to students and researchers via their institutions.

That said, researchers report that in attempting to study Schedule 1 substances they are affected by the stigma associated with them, saying that it negatively impacts funding applications, ethical approval, and the possibility of inter-departmental, inter-collegiate and inter-institutional collaboration, all of which are vital to a healthy and forward moving contemporary research atmosphere.[2] When studying Schedule 2 controlled substances in a similar manner, these issues simply do not exist.

3.3 Rescheduling to Schedule 2 with restrictions

Rescheduling psilocybin to Schedule 2 would solve all of the issues brought to the attention of the Home Office by researchers and stakeholders as pertains to this substance. This particular option, *rescheduling with restrictions*, is even more conservative than a full rescheduling as was the case with the 2018-created category of cannabis-based products for medicinal use (CBPM). By including simple restrictions, the substance to which it applies, in this case psilocybin, would not be prescribable outside of research until it has reached market authorisation through the usual routes. Facilitating research would shorten the time needed to bring a new medicine to market, if it proves effective, rescuing the UK from this vicious Catch-22. Such a legislative change, which has been confirmed as already having received approval from the Prime Minister[3], could be easily implemented in the case of psilocybin. We include an example of a **Statutory Instrument for this that can be found in Appendix 1 of this document.**

When CBPMs were moved from Schedule 1 to Schedule 2 (without marketing authorisation) in November 2018, the Home Office wrote:

- **"The rescheduling may lead to increased UK research [...] as these products can be tested more easily."**
- **"This may lead to economic benefits for UK businesses and health benefits to patients if this research leads to new and improved [medicinal products]."**
- **"In principle, research is ongoing and could lead to more effective treatment, lower costs, better understanding and management of risks, and improved health and wellbeing, over the medium term."[4]**
- The current Chief Medical Adviser to the UK Government, Prof Chris Whitty, later stated that moving CBPM to Schedule 2 was **"the single most important thing that could be done by Government" to support the development of an evidence base[5].**

The major source of diverted medicinal drugs is by prescription prior to diversion. Moving psilocybin to Schedule 2 for research purposes is unlikely to increase the risk of diversion because the drug is

[2] *Schedule 1 barriers to research in the UK: An in-depth qualitative analysis*
[3] *Warning UK faces 'worst research blackout in history' as Home Office falters on drug law*
[4] Home Office, 2018. Impact Assessment. The Misuse of Drugs (Amendments) (Cannabis and Licence Fees) (England, Wales and Scotland) Regulations 2018.
[5] Professor Chris Whitty, Chief Medical Adviser (2019). Health and Social Care Committee, Oral Evidence: Drugs Policy: medicinal cannabis, HC 1821, 26 March 2019 Q222.

administered to participants under clinical supervision, rather than being prescribed for use in the community. **This is in line with ACMD advice that "the risk of diversion and misuse in a research setting is likely to be minimal."**[6]

The proposed research-only model of rescheduling would support legitimate scientific and commercial development while maintaining stricter controls on psilocybin than on other controlled drugs associated with greater potential for harm, including diamorphine, methamphetamine, and cocaine. It would not affect existing legal controls on criminal use or supply. This model may also serve as a basis for future scheduling decisions; there are other Schedule 1 drugs under investigation as treatments for mental health conditions for which there are similar clinical arguments to support rescheduling, albeit with less immediate urgency.

(Section adapted from our 2020 report *Medicinal Use of Psilocybin: Reducing Barriers to Research and Treatment*)

3.4. Expanding the scope of the MDR 2001

As described above in Section 2.5, the UK has different levels of regulation for the medicinal use of controlled drugs, designed to reflect the balance of potential harms and benefits, as well as regulatory and advisory processes for evidence-based review and rescheduling. However, there is only a single level of regulation for the scientific use of 'non-medicinal' controlled drugs (i.e. Schedule 1 of the MDA 01 and Part 1 of the Misuse of Drugs (Designation) Order 2001). As this single level of regulation does not discriminate between more harmful and less harmful drugs, the regulatory requirements must be substantial in order to prevent unintended consequences.

In the case of psilocybin, the Government has conceded that it has never conducted a review of potential harmfulness. A previous report by the CDPRG concluded that psilocybin has significant research value, carries relatively low potential harms, and is accordingly among an unknown number of Schedule 1 drugs on which scientific research is overregulated. To achieve parity between medicinal and scientific use of controlled drugs (in the spirit of the UN conventions), regulations concerning the latter must involve the same standardised evidence-based procedures that currently exist to categorise drugs according to relative harms and benefits. The current regulatory framework fails to achieve this and, in that regard, cannot be considered evidence-based policy.

One possible solution could see the Schedules of the MDR 01 expanded to regulate both scientific and medicinal use under respective pathways. Under such a model, evidence-based rescheduling of 'non-medicinal' controlled drugs would avoid over-regulation of research while continuing to protect against unintended consequences of diversion and inappropriate prescribing. Whether under a new provision, or by amending the effect of the Designation Order 2001, medicinal use would continue to be

[6] Bowden-Jones, O., on behalf of the Advisory Council for the Misuse of Drugs. (2017). RE: Legitimate use of controlled drugs: research and healthcare. Letter to Victoria Atkins MP, Parliamentary Under Secretary of State for Crime, Safeguarding and Vulnerability.

permissible only in the context of market authorisation or special Home Office approval.Schedule-specific controls on research-only use would otherwise apply.

In effect, this model is equivalent to the previous possible solution (III), except that it examines the overall scope and function of the MDR 01 rather than providing for drug-specific exceptions. Such an option would be a greater regulatory reform challenge, but would more directly address the underlying problem and set the scene for a single, comprehensive evidence-based review of Schedule 1.

In summary, the expansion of the scope and function of the MDR 01 to provide a new regulatory pathway for the scientific use of controlled drugs, parallel to the current regulation of medicinal use, under a flexible evidence-based scheduling system. This would allow the Home Office to consider research value alongside medicinal use in scheduling decisions, thereby permitting a regulatory framework in which the controls on drug research are commensurate with the specific uses and harms of controlled drugs. A double-pathway approach would prevent the medicinal use of controlled drug products until market authorisation.

Conclusion

Barriers to research into controlled drugs in the UK, and their consequences, have been brought to the attention of the Government for many years, with active steps being taken to resolve these issues being initiated in 2017. Five years later the issues still remain, much to the disappointment of those UK pioneers who spotted opportunities in drug development and research early and expected greater investment and progress–many feel that these opportunities are now being missed. Calls for solutions have been increasing alongside the growth of interest in psychedelic substances and the growing evidence of their potential as breakthrough treatments. As billions of research dollars pour into the field revived after a near 40 year blackout, the emerging field of psychedelic medicine is increasingly dominated by and capitalised upon by the USA and Canada. The frustration of the research community who wish to study controlled drugs in the UK is a direct result of the MDR 01 controlling prescription of drugs which have not yet reached market authorisation while over regulating their use in legitimate research without reason. There has been a vital flaw present in the UK legislation since its inception, with serious consequences that must be resolved.

The options laid out above amount to four separate solutions to the current impasse. It is our firm view that the Government should act quickly to resolve the issue of barriers to researching psilocybin. This could be easily and rapidly achieved by rescheduling with restrictions to mitigate inappropriate prescribing. Whilst reform can be carried out on a case by case basis, it is our recommendation that the Government make a small adjustment to the MDR 01 which would align it more closely with the intention of international law and thereby permit research to be conducted into controlled drugs without unnecessary hindrances both now and in the future. Such an amendment as the one we suggest would bring regulations on scientific use of controlled substances to the forefront of the legislation, and alongside an evidence based review and reshuffle of the contents of Schedule 1, communicate a direct commitment to life sciences research in the UK. This change would allow the UK to seize opportunities as they present themselves and to consolidate its position as a world leader in the field.

Annex 1.

An Extract from pages 26, 27 & 28 of the *Making a Hash of It* report

by House of Commons Science and Technology Committee

18 July 2016

(emphasis in the original)

Magic mushrooms

54. Magic mushrooms contain psilocin and psilocybin, naturally-occurring compounds with hallucinogenic properties. Psilocin and psilocybin were designated Class A drugs under the Misuse of Drugs Act 1971, apparently on account of their hallucinogenic properties. Psilocin is also listed under Schedule I, the highest level of prohibition, under the UN's Convention on Psychotropic Substances 1971. Sir Michael Rawlins, Chairman of the ACMD, told us: "I have no idea what was going through the minds of the group who put it in Class A in 1970 and 1971 […]It is there because it is there". The Home Office has admitted that it has never conducted any research into psilocin use and that there is "no clear evidence of a link between psilocin use and acquisitive or other crime"

55. In the past a legal loophole meant that fresh magic mushrooms were not treated as controlled drugs, providing that they had not been 'prepared' (i.e. dried, packaged, cooked etc.). Section 21 of the Drugs Act 2005, which came into force on 18 July 2005, makes it an offence to import, export, produce, supply and possess with intent to supply magic mushrooms in any form. Because the decision to place magic mushrooms in Class A was a clarification of the law rather than a reclassification decision, the Government was not obliged to seek the advice of the ACMD in the usual manner. Nevertheless, the Government told us that it "did write to the ACMD, and ask for its views on [its] proposals before the Drugs Bill was introduced". The ACMD endorsed the move, telling us: "in March 2004 the Technical Committee heard that, over recent years, there had been a substantial increase in the number of retail outlets selling 'fresh' magic mushrooms. In fact HM Customs and Excise estimated the importation of 8,000–16,000 kgs during 2004". However, the ACMD did not conduct a full review of the evidence in arriving at its decision. **The Government's use of a clarification of the law to put fresh magic mushrooms in Class A contravened the spirit of the Misuse of Drugs Act and meant that the ACMD was not given the chance to consider the evidence properly before responding.** We also note the admission by the Home Office Minister Paul Goggins that "the Home Office received no submissions in favour of the clarification of the law in respect of magic mushrooms prior to the Drugs Act 2005 being granted Royal Assent on seven April and four submissions against".

56. In fact, we encountered a widespread view that the Class A status of magic mushrooms does not reflect the harms associated with their misuse. The RAND report concluded that the Government's

decision "was not based on scientific evidence", noting that "the positioning of them in Class A does not seem to reflect any scientific evidence that they are of equivalent harm to other Class A drugs". The RAND report pointed out that "National Statistics show that for deaths in which drug poisoning (listed on the death certificate) was the underlying cause of death, between 1993 and 2000 there was one death from magic mushrooms and 5,737 from heroin" and that "The lethal dose for humans is about one's own body weight in mushrooms".102 Professor Blakemore was also of the view that "if one could look at all the evidence for harm available now, including social harms, one would say [the classification of magic mushrooms] is wrong". The Government's own 'Talk to Frank' drug information website states that "Magic Mushrooms are not addictive in any way". The drugs charity Release told us that "There was little transparency as to the reasoning behind this policy", describing it as "an unacceptable situation". Paul Flynn MP was also of the view that "The policy appears to have been driven by something other than evidence" and warned that "other more dangerous mushrooms, not covered by the current law, could be substituted for those that are prohibited". Recent press reports, and data from the European Monitoring Centre on Drugs and Drug Addiction (EMCDDA), suggest that substitution with legal hallucinogens – including potentially lethal mushrooms of the Amanita family – is already happening.

57. We were, therefore, surprised and disappointed to hear Sir Michael Rawlins, Chairman of the ACMD, tell us that "it was not a big issue" whether magic mushrooms were in the right Class. In Sir Michael's view: "there are bigger, more important issues to worry about than whether fresh mushrooms join the rest of the other things in Class A". **The Chairman of the ACMD's attitude towards the decision to place magic mushrooms in Class A indicates a degree of complacency that can only serve to damage the reputation of the Council.** Martin Barnes, Chief Executive of DrugScope and a member of the ACMD, did not share Sir Michael's nonchalance. He told us that he was "not aware that the full council were asked to deliberate on this" and that "it was wrong for the Home Secretary to seek to enact [the change] in primary legislation without properly consulting the ACMD and giving it time to deliberate on it". Mr Barnes was also of the view that "the evidence has indicated that [magic mushrooms are] in the wrong classification". **The ACMD should have spoken out against the Government's proposal to place magic mushrooms in Class A. Its failure to do so has undermined its credibility and made it look as though it fully endorsed the Home Office's decision, despite the striking lack of evidence to suggest that the Class A status of magic mushrooms was merited on the basis of the harm associated with their misuse.**

Annex 2.

Statutory Instrument for the Rescheduling of Psilocybin with Restrictions

We propose that Schedule 1 drugs with high research value are rescheduled to Schedule 2, with statutory safeguards to prevent inappropriate prescribing. This would allow for UK-based research to be facilitated without increasing the possibility of harm caused to the public. The following text represents a draft provision intended to restrict the use of a controlled drug, in this case psilocin or esters of psilocin, to legitimate scientific research, except where the drug is an authorised medicinal product:

"1) A person shall not order or supply (whether by issuing a prescription or otherwise) a product containing psilocin or esters of psilocin, unless that product is—

a) for use in the course of, or in connection with, approved scientific research; or

b) a medicinal product with a marketing authorisation.

2) A person shall not supply psilocin or esters of psilocin to be administered or self-administered in premises other than premises that have been named and approved by a relevant ethics review body, unless the supply is pursuant to an order that complies with paragraph 1(b).

Interpretation—

"marketing authorisation" has the same meaning as in the Human Medicines Regulations 2012;

"approved scientific research" means scientific research carried out by a person who has approval from a relevant ethics review body to carry out that research;

"relevant ethics review body" means—

a) a research ethics committee recognised or established by the Health Research Authority under Chapter 2 of Part 3 of the Care Act 2014, or

b) a body appointed by any of the following for the purpose of assessing the ethics of research involving individuals—

i. the Secretary of State, the Scottish Ministers, the Welsh Ministers, or a Northern Ireland department;

ii. a relevant NHS body;

iii. a body that is a Research Council for the purposes of the Science and Technology Act 1965;

iv. an institution that is a research institution for the purposes of Chapter 4A of Part 7 of the Income Tax (Earnings and Pensions) Act 2003 (see section 457 of that Act);

v. a charity which has as its charitable purpose (or one of its charitable purposes) the advancement of health or the saving of lives;

"charity" means—

a) a charity as defined by section 1(1) of the Charities Act 2011,

b) a body entered in the Scottish Charity Register, or

c) a charity as defined by section 1(1) of the Charities Act (Northern Ireland) 2008;

"relevant NHS body" means—

a) an NHS trust or NHS foundation trust in England,

b) an NHS trust or Local Health Board in Wales,

c) a Health Board or Special Health Board constituted under section 2 of the National Health Service (Scotland) Act 1978,

d) the Common Services Agency for the Scottish Health Service, or

e) any of the health and social care bodies in Northern Ireland falling within paragraphs (a) to (d) of section 1(5) of the Health and Social Care (Reform) Act (Northern Ireland) 2009.

""clinical trial" has the same meaning as in the Medicines for Human Use (Clinical Trials) Regulations 2004."

Annex 3.

Clinical Trials with Psilocybin - Completed and Ongoing

What follows is a list of the 11 completed clinical trials of psilocybin since 2006. Prior to this date no research had been undertaken on the molecule since 1971 due to the imposition of draconian international law in 1961, before which hundreds of studies were published, albeit at a standard now considered to be sub-optimal. Following this is a list of the 52 ongoing clinical trials involving psilocybin (if this list was to include studies of LSD, DMT, MDMA and other psychedelics it would run over 20 pages long). The list shows psilocybin's consistent safety profile in controlled conditions and an impressive range of disorders being investigated, indicative of the psilocybin's transdiagnostic potential. The effect sizes in the completed trials, often after a single dose, are extremely impressive even in conditions which are not amenable to the standard treatments available. The current evidence has been considered enough for the FDA to fast track psilocybin as a treatment for depression by granting it 'breakthrough therapy' status and NIDA have awarded $4 Million USD to researchers at Johns Hopkins for studies in smoking cessation. In Australia the TGA has awarded $15 Million AUD in grants to study psilocybin-assisted therapy as a mental health treatment. Meanwhile, the slice of a pie set to grow in value to $10 Billion USD by 2027, deserved by the UK for initiating the resurgence of psychiatric treatment research known globally as the psychedelic renaissance, is being abdicated to those jurisdictions taking active steps to facilitate this research.

Completed Clinical Trials Involving Psilocybin Listed by Date

Table 1. Completed Contemporary Clinical Trials Involving Psilocybin (post 2006)

Study	Indication and sample size (n)	Design	Main efficacy outcome
Moreno et al (2006)	Obsessive compulsive disorder, n=9	Single-arm, within subjects, variable doses. Up to four doses of psilocybin	All patients showed improvements within 24 h of a treatment but no effect of dose.
Grob et al (2011)	Anxiety and depression in end-stage cancer, *n*=12	DB-RCT, crossover, inert placebo. Single dose of psilocybin.	Significant reductions in trait anxiety at 3 months and depression at 6 months.
Johnson et al (2014)	Long-term chronic tobacco smoking, *n*=15	Open-label. Up to three doses of psilocybin after four CBT sessions.	80% of sample abstinent at 6 month follow-up.

Bogenschutz et al (2015)	Alcohol dependence, *n*=10	Open-label. Up to two doses after seven motivational therapy sessions.	Significant decrease in drinking behaviors for up to 9 months.
Carhart-Harris et al (2016)	Treatment-resistant MDD, *n*=12+study extension to *n*=20	Open-label. Two doses of psilocybin.	Significant decreases in depressive symptoms for up to 6 months.
Ross et al (2016)	Anxiety and depression related to life-threatening cancer, *n*=29	DB-RCT, crossover, niacin=active placebo. Single dose of psilocybin.	Significant decreases in anxiety and depression *vs* niacin at 7 weeks (pre crossover) and sustained for 6.5 months.
Griffiths et al (2016)	Anxiety and depression related to life-threatening cancer, *n*=51	DB-RCT, crossover, VLD psilocybin=control. Single dose of psilocybin.	Significant decreases in anxiety and depression *vs* VLD at 5 weeks (pre crossover). Effects sustained for 6 months.
Davis et al (2020)	Major Depressive Disorder, *n*=27	DB-RCT, waiting list controlled (8 weeks), Two psilocybin sessions (session 1: 20mg/70 kg; session 2: 30mg/70 kg), 11 hours psychotherapy.	Clinically significant antidepressant response to psilocybin therapy persisted for at least 4weeks, with 71% of the participants continuing to show a clinically significant response (≥50% reduction in GRID-HAMD score) at week 4 of follow-up.
Anderson et al (2020)	Demoralized older long-term AIDS survivor men *n*=18	Open-label, group therapy comprising 8–10 group therapy visits and one psilocybin administration visit (0·3–0·36 mg/kg po)	Clinically meaningful change in demoralization from baseline to 3-month follow-up.

Carhart-Harris et al (2021)	Major Depressive Disorder, *n*=59	Phase 2, DB-RCT, 2 doses of 25 mg of psilocybin 3 weeks apart plus 6 weeks of daily placebo vs two separate doses of 1 mg of psilocybin 3 weeks apart plus 6 weeks of daily oral escitalopram; all the patients received psychological support.	Change in depression scores on the QIDS-SR-16 at week 6 (the primary outcome) did not differ significantly between the trial groups.
Schindler et al (2021)	Migraine, *n*=10	DB-RCT, cross-over , adults with migraine received oral placebo and psilocybin (0.143 mg/kg) in 2 test sessions spaced 2 weeks apart. Headache Diaries.	Reduction in weekly migraine days from baseline was significantly greater after psilocybin than after placebo.

Abbreviations: DB-RCT, double-blind randomised controlled trial; VLD, very low dose.

Ongoing Clinical Trials Involving Psilocybin Listed by Database

The EU Clinical Trials Register lists the following clinical trials of psilocybin as ongoing as of 20/10/21:

Table 2. Ongoing Clinical Trials Involving Psilocybin within the UK and EU

EudraCT no.	**Study title**	**Medical condition**	**Results**
2018-003382-34	Prophylactic effects of psilocybin on chronic cluster headache: an open-label clinical trial and neuroimaging study.	Chronic cluster headache.	Not yet available.
2017-003288-36	The Safety and Efficacy of Psilocybin in Participants with Treatment Resistant Depression (P-TRD)	Treatment Resistant Depression (P-TRD)	Not yet available.
2020-001348	A multicentre study to assess safety and efficacy of	Treatment-Resistant	Not yet

-25	psilocybin in patients with treatment-resistant depression following completion of COMP 001 and COMP 003 trials (P-TRD LTFU)	Depression (P-TRD)	available.
2017-000219-18	Psilocybin vs. escitalopram for major depressive disorder: comparative mechanisms	Major Depressive Disorder	Not yet available.
2018-003573-97	A randomised, placebo controlled trial of psilocybin in treatment resistant depression: A feasibility study	Major depressive disorder	Not yet available.
2019-004054-28	Psilocybin as a Treatment for Anorexia Nervosa: A Pilot Study	Anorexia Nervosa	Not yet available.
2018-002577-22	The safety and efficacy of psilocybin as an adjunctive therapy in participants with treatment-resistant depression	Treatment-Resistant Depression (P-TRD)	Not yet available.
2019-003984-24	A phase II randomized, double-blind, active placebo-controlled parallel group trial to examine the efficacy and safety of psilocybin in treatment-resistant major depression	Treatment-Resistant Depressive Episode or Treatment-Resistant Recurrent Depressive Disorder of moderate to severe degree without psychotic features	Not yet available.
2020-002790-94	The Effect of Psilocybin on MDD Symptom Severity and Synaptic Density – A Single Dose Randomized, Double Blind, Placebo-Controlled Phase 2 Positron Emission Tomography Study	Major Depressive Disorder	Not yet available
2020-000829-55	Can a one-off administration of psilocybin reduce alcohol intake in patients with alcohol use disorder? A randomized, double-blinded, placebo-controlled clinical trial.	Alcohol dependence syndrome	Not yet available

The N.I.H U..S National Library of Medicine Clinical Trials Register (clinicaltrials.gov) lists the following clinical trials of psilocybin as ongoing in the North American region as of 20/10/21:

Table 3. Ongoing Clinical Trials Involving Psilocybin in North America

NCT number	Study title	Medical condition	Results
NCT04932434	Psilocybin Therapy for Depression and Anxiety in Parkinson's Disease	Parkinson Disease Depression Anxiety	Not yet available.
NCT05065294	Psilocybin Therapy for Depression in Bipolar II Disorder	Bipolar II Disorder	Not yet available.
NCT03866174	A Study of Psilocybin for Major Depressive Disorder (MDD)	Major Depressive Disorder	Not yet available.
NCT04593563	The Safety and Efficacy of Psilocybin in Cancer Patients With Major Depressive Disorder	Major Depressive Disorder	Not yet available.
NCT04739865	The Safety and Efficacy Of Psilocybin as an Adjunctive Therapy in Participants With Treatment Resistant Depression	Treatment Resistant Depression	Not yet available.
NCT04982796	Psilocybin-Enhanced Psychotherapy for Methamphetamine Use Disorder	Amphetamine-Related Disorders	Not yet available.
NCT05029466	Psilocybin for Treatment-Resistant Depression	Treatment Resistant Depression	Not yet available.
NCT03356483	Efficacy of Psilocybin in OCD: a Double-Blind, Placebo-Controlled Study.	Obsessive-Compulsive Disorder	Not yet available.
NCT04656301	Safety and Efficacy of Psilocybin for Body Dysmorphic Disorder	Body Dysmorphic Disorders	Not yet available.
NCT04052568	Effects of Psilocybin in Anorexia Nervosa	Anorexia Nervosa	Not yet available.
NCT04123314	Psilocybin for Depression in People With Mild Cognitive Impairment or Early Alzheimer's Disease	Depressive Symptoms Depression Alzheimer Disease Mild Cognitive Impairment	Not yet available.

NCT03300947	Psilocybin for Treatment of Obsessive Compulsive Disorder	Obsessive-compulsive Disorder (OCD)	Not yet available.
NCT04661514	Evaluation of Psilocybin in Anorexia Nervosa: Safety and Efficacy	Anorexia Nervosa	Not yet available.
NCT05068791	Psilocybin-facilitated Treatment for Chronic Pain	Fibromyalgia, Primary	Not yet available.
NCT03554174	Psilocybin - Induced Neuroplasticity in the Treatment of Major Depressive Disorder	Major Depressive Disorder	Not yet available.
NCT03341689	Psilocybin for the Treatment of Migraine Headache	Migraine Headache	Not yet available.
NCT04433845	The Safety and Efficacy of Psilocybin in Participants With Type 2 Bipolar Disorder (BP-II) Depression.	Treatment Resistant Depression	Not yet available.
NCT04218539	Repeat Dosing of Psilocybin in Migraine Headache	Migraine Headache	Not yet available.
NCT04433858	An Open Label Study of the Safety and Efficacy of Psilocybin in Participants With Treatment-Resistant Depression (P-TRD)	Treatment Resistant Depression	Not yet available.
NCT04950608	Pilot Study of Psilocybin-Assisted Therapy for Demoralization in Patients Receiving Hospice Care	Demoralization Cancer-related Problem/Condition	Not yet available.
NCT04522804	Study of Psilocybin Enhanced Group Psychotherapy in Patients With Cancer	Cancer related distress	Not yet available.
NCT04620759	Psilocybin Treatment of Major Depressive Disorder With Co-occurring Alcohol Use Disorder	Major Depressive Disorder Alcohol Use Disorder	Not yet available.
NCT03806985	Effects of Psilocybin in Concussion Headache	Post-Traumatic Headache	Not yet available.

NCT02037126	Psilocybin-facilitated Treatment for Cocaine Use	Cocaine-Related Disorders	Not yet available.
NCT05035927	Evaluation of Psilocybin (TRP-8802) to Decrease Hyperphagia	Hyperphagia	Not yet available.
NCT04410913	Pilot Trial of Visual Healing® in Psilocybin-assisted Therapy for Alcohol Use Disorder	Alcohol Use Disorder	Not yet available.
NCT04882839	Evaluating the Feasibility, Safety and Efficacy of Psychotherapy Assisted Psilocybin for Treatment of Severe OCD	Obsessive-compulsive Disorder	Not yet available.
NCT02421263	The Effects of Psilocybin-Facilitated Experience on the Psychology and Effectiveness of Religious Professionals	Religious or Spiritual Problem	Not yet available.
NCT01943994	Psilocybin-facilitated Smoking Cessation Treatment: A Pilot Study	Nicotine Dependence	Not yet available.
NCT02243813	Effects of Psilocybin-facilitated Experience on the Psychology and Effectiveness of Professional Leaders in Religion	Religious or spiritual problem	Not yet available.
NCT04161066	Adjunctive Effects of Psilocybin and Buprenorphine	Opioid Use Disorder	Not yet available.
NCT05042466	Northwest Therapies Trauma Psilocybin Study Compassionate Use Study	Trauma, Nervous System	Not yet available.
NCT04630964	The Effect of Psilocybin on MDD Symptom Severity and Synaptic Density	Major Depressive Disorder	Not yet available.
NCT04959253	Psilocybin in Depression Resistant to Standard Treatments	Treatment Resistant Depression	Not yet available.
NCT03775200	The Safety and Efficacy of Psilocybin in Participants With Treatment Resistant Depression	Treatment Resistant Depression	Not yet available.
NCT02981173	Psilocybin for the Treatment of Cluster Headache	Cluster Headache	Not yet available.
NCT02061293	A Double-Blind Trial of Psilocybin-Assisted Treatment of Alcohol Dependence	Alcohol Dependence	Not yet available.

The N.I.H U..S National Library of Medicine Clinical Trials Register (clinicaltrials.gov) lists the

following clinical trials of psilocybin as ongoing outside of the North American region as of 20/10/21:

Table 4. Ongoing Clinical Trials Involving Psilocybin outside of North America

NCT number	Study title	Medical condition	Results
NCT04989972	Assessing the Efficacy of Micro-dosed Psilocybin on Reducing Anxiety & Depression Levels in Adults	Anxiety and Depression	Not yet available.
NCT04905121	Phase 1b Study in Patients With Short-Lasting Unilateral Neuralgiform Headache Attacks	Short Lasting Unilateral Neuralgiform Headache Attacks	Not yet available.
NCT04718792	Psilocybin for Treatment of Alcohol Use Disorder: a Feasibility Study	Alcohol Use Disorder (AUD)	Not yet available.
NCT04141501	Clinical and Mechanistic Effects of Psilocybin in Alcohol Addicted Patients	Alcohol Use Disorder	Not yet available.
NCT03715127	Clinical, Neurocognitive, and Emotional Effects of Psilocybin in Depressed Patients - Proof of Concept	Major Depressive Disorder	Not yet available.

The Australia Clinical Trials Register (australianclinicaltrials.gov.au) lists the following clinical trials of psilocybin as ongoing outside of the North American region as of 20/10/21:

Table 5. Ongoing Clinical Trials Involving Psilocybin in Australia

Trial ID	Study title	Medical condition	Results

ACTRN12619001225101	Psilocybin-assisted psychotherapy for the treatment of depression and anxiety associated with life-threatening illness	Depression in terminal illness Anxiety in terminal illness	Not yet available.

Annex 4.

De minimis Research Organisation Quotas are an Inappropriate and Inadequate Response to the Barriers to Research Imposed by Schedule 1 in the Case of Psilocybin.

Overview

1) **The ACMD are investigating barriers to researching substances controlled under Schedule 1 of the Misuse of Drugs Regulations 2001 with their findings released in a two part report.** The first of which focuses on the barriers to researching synthetic cannabinoid receptor agonists (SCRA), the second on other controlled drugs.

2) **In the first part of the report a *de minimis* quota for 'research organisations' was recommended to mitigate the barriers to research identified in the call for evidence.** While the level of this quota may be appropriate to mitigate some of the barriers faced by those looking to study SCRA's, the same level could not be appropriately applied to all substances controlled under Schedule 1.

3) **In the case of psilocybin, and many other high research value substances in Schedule 1, a *de minimis* quota of this sort would be inappropriate and inadequate** in resolving the issues faced by researchers and may in fact increase bureaucratic barriers, and perpetuate the very issue it sets out to resolve.

4) **The implementation of a *de minimis* quota for psilocybin would leave the evidence for its current status as a S1 controlled substance unreviewed and it's evidence lacking position unaddressed and perpetuated.** This is important because psilocybin's current status is based on no body of evidence whatsoever and the evidential basis for its scheduling has not recently been reviewed as confirmed by the Home Secretary.

5) **It is reasserted that the best possible alternative recommendation is that psilocybin be rescheduled to Schedule 2 of the MDR 2001 with restrictions to facilitate research whilst mitigating any possibility of inappropriate prescribing and diversion,** requiring as it does an appropriate review of the evidence to be conducted by the ACMD**.**

In order to combat the barriers to researching synthetic cannabinoids found to be imposed by their Schedule 1 (S1) status under the Misuse of Drugs Regulations 2001 (MDR 2001), the Advisory Council on the Misuse of Drugs (ACMD) has proposed a 'research organisation' carve-out and permissible *de minimis* quota per organisation.[7]

This briefing paper cautions that a similar recommendation in the case of psilocybin would inadequately address the research issues and barriers for this drug as identified in the July 2020 CDPRG report *Medical Use of Psilocybin: Reducing barriers on research and treatment*:[8]

- Such a *de minimis* quota for research organisations looking to study psilocybin not only leaves many issues unresolved;
- It could actually increases bureaucratic burdens;
- And furthermore fails to recognise that in the case of psilocybin its S1 status is entirely unjustified, as it is based on no body of evidence whatsoever and the evidential basis for its scheduling having never been reviewed.

Thus we suggest that it would be preferable to swiftly reschedule psilocybin to Schedule 2 with restrictions, as previously and continually recommended by both the CDPRG and many other organisations and researchers cognisant of the evidence.

Overview of the Issue of Psilocybin's Scheduling Under the Misuse of Drugs Regulations 2001

The current landscape of treatment options to mitigate the worsening mental health crisis is barren. Over 5 million British citizens are suffering from depression, 1.2 million of whom are treatment-resistant. With the exception of Esketamine there have been no new pharmacological treatments for depression in over 30 years. Evidence from early clinical trials is indicating that psilocybin may be a revolutionary psychiatric intervention for treatment resistant depression and other hard to treat conditions[9].

Current scheduling of psilocybin actively and unnecessarily obstructs the research required to realise its potential as a treatment. The current S1 designation of psilocybin, and other promising substances such as MDMA, poses serious barriers to research in the UK in the form of increased time, costs and stigma, deterring many researchers from engaging in this promising line of research at all. This blocks patient access and hinders the growth of promising research into these substances coming out of the UK, stifling the development of the Life Sciences sector. Fundamentally, the status of many substances in S1 is inconsistent with the evidence of their harm and potential utility. While the UK stalls on removing the barriers to research faced by those looking to work with psilocybin in research settings millions of patients go untreated and competitive advantage in a sector set to grow to over £10 billion by 2027 is acceded to jurisdictions overseas[10].

[7] Considerations of barriers to research Part 1: Synthetic cannabinoid receptor agonists (SCRA), ACMD, 2021.
[8] Medical Use of Psilocybin: Reducing barriers on research and treatment, Rucker et al., 2020.
[9] ibid.
[10] Psychedelic Drugs Market Size Is Projected To Reach $10.75 Billion By 2027

The History of ACMD Barriers to Research Reviews

The Home Office has a history not just in relation to psilocybin of unnecessarily maintaining a climate of inertia in relation to rescheduling S1 substances. Four years ago, in July 2017 Amber Rudd, then Home Secretary, commissioned a review of the barriers to research caused by drugs designated as S1 under the MDR 2001. In December 2017 the ACMD submitted their short and long term recommendations, but it took over a year, until January 2019, for the so-called 'short-term' recommendations to be acted upon, whereas the long term recommendations were rejected entirely as unfeasible. It would seem that the inertia within the Home Office (HO) when it comes to decisions pertaining to the medical application of controlled drugs has a history older than the contemporary issue of the rescheduling of psilocybin (as addressed within the CDPRG report *Misinterpretation of the Misuse of Drugs Act 1971 and the Misuse of Drugs Regulations 2001 in the case of the call for the rescheduling of psilocybin*).[11]

Recommendations from the ACMD on "barriers to legitimate research with controlled drugs," are currently awaited. The self commissioned work streams of the ACMD for 2020, published in December 2019, included the creation of a working group to establish scheduling decision making including Standard Operating Procedure (SOP) for their scheduling recommendations under the MDR 2001 with the goal of establishing "a systematic process for ensuring consistency in scheduling decisions", itself published in May 2021. In February 2020, the ACMD put out a call for evidence regarding barriers to legitimate research with controlled drugs, specific to synthetic cannabinoid receptor agonists (SCRA). While the report *Considerations of barriers to research Part 1: Synthetic cannabinoid receptor agonists (SCRA)* was published on 30th July 2021, the call for evidence was extended to controlled drugs beyond synthetic cannabinoids in March 2021. The deadline for this further evidence was the end of May 2021. As of October 2021, no publication date for 'Part 2' has yet been announced.

The recommendations within the ACMD's Report *Considerations of barriers to research Part 1: Synthetic cannabinoid receptor agonists (SCRA)*

The detrimental effect of an S1 designation on research has been recognised by the ACMD in relation to cannabis. 'Part 1' of the ACMD's report recognised that in the case of third generation SCRA S1 does erect barriers to research; academic research into SCRA suffers from the barriers of increased time, cost and bureaucracy due to researchers having to apply for multiple licences, as well as the requirements of safe storage and record keeping, leading to lost opportunities for research and collaboration, and making it "harder for the UK to participate in a global research community". Pharmaceutical companies, similarly, suffer from increased time, cost and lost opportunities leading them to "consider moving operations to countries with fewer restrictions". Contract Research Organisations (CRO) are equally affected "causing a loss of opportunity as companies look to countries where it is easier to carry out this research." In short, 'Part 1' of the report recognised a significant cost to the UK life sciences industry due to the restrictions imposed on researching S1 substances.

[11] Misinterpretation of the Misuse of Drugs Act 1971 and the Misuse of Drugs Regulations 2001 in the case of the call for the rescheduling of psilocybin, CDPRG, 2021.

The ACMD writes that "the objective of this report is to facilitate high quality research in the UK" and that it "tries to balance removing barriers to research with minimising the risk of diversion and to control substances that have been found to be harmful." Out of four main options considered to mitigate the barriers to research, the ACMD deemed it most appropriate and effective in the case SCRA's for the HO to amend the MDR 2001 to define bodies known as 'research organisations' who would be allowed a *de minimis* limit for all third generation SCRA and would not require import/export licences for most third generation SCRAs. As such, the report puts forward 3 recommendations:

> **Recommendation 1** - To ensure that proposed changes only apply to legitimate research, the ACMD recommends that the Home Office defines the term 'research organisation'.
>
> **Recommendation 2** - The ACMD recommends that the MDR should be amended to permit such 'research organisations' to produce/possess/supply/offer to supply a 100mg de minimis limit for compounds described under the synthetic cannabinoid generic definition of the Misuse of Drugs Act 1971 (MDA) and the MDR.
>
> **Recommendation 3** - The ACMD recommends that the MDR should also be amended to permit 'research organisations' defined in recommendation 1 to import/export up to 100mg of synthetic cannabinoids, except those that come under international control.[12]

The Inadequacy of a *De Minimis* Limit for 'Research Organisations' in the Case of Psilocybin

While it is recognised that these are SCRA specific recommendations that respond to the evidence received via submission to the ACMD, we strongly caution against the ACMD making similar recommendations in relation to psilocybin. Given that many of the barriers identified in the ACMD's 'Part 1' report will equally affect psilocybin and other Schedule 1 controlled substances it is not illogical to assume that similar options will be explored to mitigate these same barriers.

A potential *de minimis* quota of 100mg as regards psilocybin is inadequate for a number of reasons.

1) In the first instance, the quota itself is far too low for psilocybin and of course if the ACMD were to make a similar recommendation they would consult with research organisations for an appropriate level, but that said, 'Part 2' is not solely concerned with psilocybin.

2) There are many controlled substances in Schedule 1 into which research could be conducted, as such a separate *de minimis* quota would have to be set for a number controlled drugs - for example LSD has an active threshold in the ug, while for psilocybin it is 100s of times higher - with numerous changes to legislation having to be made to accommodate these limits.

[12] Considerations of barriers to research Part 1: Synthetic cannabinoid receptor agonists (SCRA), ACMD, 2021.

3) A *de minimis* quota, is in practice unwieldy in that it adds another step and another level of bureaucracy, both at the border and at every step of the process of producing or obtaining and transporting and studying the controlled substance - that is not *the* controlled substance, but rather *every* controlled substance for which a *de minimis* quota is set. The level of bureaucracy involved would be analogous to, and possibly even exceed the rejected 'Research Schedule' recommendation given by the ACMD to the HO in 2017.

4) A question is also raised as to whether the quota refers to the active compound. How, for example, is one to test the levels of psilocybin within raw or dried plant material of psilocybin containing mushrooms to verify that a license for them is not required without first having a license which would allow the researchers to be able to test this?

5) It is inconsistent with the evidence for harm and sends the signal that the ACMD is complicit in the perpetuation of its evidence-lacking scheduling.

A *de minimis* quota is an unnecessary and negligible prophylactic against diversion.
The risk of diversion is another factor considered by the ACMD in forming this recommendation. A low limit is thought to limit the risk of diversion, which indeed it would as it is already as low as it can be, that is, there is no evidence of increased diversion from drugs in Schedule 2 than in Schedule 1, even though many drugs in Schedule 2 have both higher demand and street value than those within Schedule 1 (compare for example the street price of cocaine to psilocybin containing mushrooms £100 per gram compared to £10 per gram respectively). Not only that but it is the case that the majority of diversion occurs from prescription, rather than from research settings, in the case of psilocybin it is given within a clinical setting and never taken home, reducing the risk even further.[13] This view is consistent with ACMD advice that "the risk of diversion and misuse [of controlled drugs] in a research setting is likely to be minimal".[14]

A key aim of rescheduling psilocybin which is not served by a *de minimis* quota is to reduce stigma currently associated with research and a *de minimis* quota would not remove the necessity of obtaining licenses for most researchers.
One researcher consulted on the *de minimis* quota noted that it does not does not remove stigma, one of the major barriers to research with Schedule 1 controlled substances in academic settings and that a *de minimis* quota may actually increase costs for researchers and lead them to go through the same process and payment for licenses regardless of the new quota:

> "When we use PCP (Schedule 2) we buy in bulk as it's much cheaper, this new rule would still preclude us doing this for psilocybin [without first obtaining numerous expensive S1 licenses]."

[13] Medical Use of Psilocybin: Reducing barriers on research and treatment, Rucker et al., 2020.
[14] RE: Legitimate use of controlled drugs: research and healthcare. Letter to Victoria Atkins MP, Parliamentary Under Secretary of State for Crime, Safeguarding and Vulnerability. Bowden-Jones, O., on behalf of the Advisory Council for the Misuse of Drugs. 2017.

The 'Part 1' report states that the new *de minimis* limit "would facilitate drug discovery by removing the need for a licence in most cases" - unfortunately 'in most cases' is not good enough. The same researcher said:

> "I think the main issue with being allowed small amounts is there's a huge potential for breaking the rules by going over the limit, and the limit is far too low for clinical work, even for pretty basic animal studies it's too low."

The ACMD does recognise that the "proposed de minimis limit does not provide sufficient amounts for later stage drug development or clinical trials" - psilocybin is already in late stage 2 clinical trials and the licenses needed for Schedule 1 research in the UK are creating an environment in which many of the necessary sites utilised in the 'multi-site' phase 3 trials will take place abroad.

With a *de minimis* quota sufficiently high, experimental and clinical research would be somewhat facilitated but it would miss the point entirely - that there is no evidential basis for the S1 status of psilocybin. Psilocybin's status is nothing more than convention based on the MDA 1971 which itself is based upon the Convention on Psychotropic Substances 1971, which we know has no substantial evidential basis itself. The convention is meant to act as guide rather than rule, in fact much of our Scheduling isn't consistent with it, for example the promising psychedelic medicine 2C-B is S1 in the UK and Schedule 2 at the UN level, this is but one of many inconsistencies.

The Alternative - Rescheduling Psilocybin with Restrictions on Prescribing

The definition of a research organisation is not in itself a bad recommendation, but the equivalent definition within our recommendation, that of allowing for the use of psilocybin (and others) in studies overseen and approved by ethics committees, achieves the same ends without having to adjust the MDA 1971 as well as the MDR 2001.

With a statutory instrument (see draft in annex 1) only the MDR 2001 would need to be amended via the negative procedure to be commensurate with the evidence of psilocybin's harm and medicinal potential profile. Not only that but the issues raised above, those exacerbated or left unchanged by a *de minimis* research organisation quota, are all solved by rescheduling - and send the message that the UK Government is responsive to emerging evidence and up to date with the most modern scientific research.

The implementation of a *de minimis* quota for psilocybin would not only fail to address the barriers to research adequately, but would, most importantly, not require the ACMD to review the evidence for the appropriateness of psilocybin's current designation as controlled under S1, leaving it unreviewed and it's evidence lacking position unaddressed.

Conclusion

While the report *Considerations of barriers to research Part 1: Synthetic cannabinoid receptor agonists (SCRA)* was published on 30th July 2021, the call for evidence was extended to controlled drugs beyond synthetic cannabinoids in March 2021. The deadline of the call for further evidence was the end of May 2021 - 5 months later we are still waiting for the publication of this report and it has now been 14 months since July 2020 when the CDPRG report *Medical Use of Psilocybin: Reducing barriers on research and treatment* was presented to the Minister Kit Malthouse. While the UK fails to act on this proposal, now approved by both the public and the Prime Minister, other jurisdictions pull ahead capitalising on UK based science.

In the 13 months that passed between the ACMD submitting their short and long-term recommendations aimed at facilitating research into Schedule 1 controlled substances, and their respective actioning and rejection, in 2018 the now Health Secretary Sajid Javid requested that the Chief Medical Officer review the evidence concerning the Scheduling of Cannabis Based Products for Medicinal Use, this review took a period of two weeks. This then prompted the Home Secretary to commission a review from the ACMD on the matter. The whole process of rescheduling medical cannabis took approximately four months, a drastically reduced timeline. This is stated here to reiterate the fact that there is precedent for rescheduling prior to market authorisation, and even though actioned prior to the ACMD's SOP for scheduling procedures was established, is still not precluded from taking place, as detailed in the CDPRG report *Misinterpretation of the Misuse of Drugs Act 1971 and the Misuse of Drugs Regulations 2001 in the case of the call for the rescheduling of psilocybin*. It is also worth noting here that at the time and still to this day there is considerably more evidence of the safety and efficacy of psilocybin than there was for cannabis.

We propose that rather than the implementation of *de minimis* quotas for each and every one of the Schedule 1 controlled drugs according to their psychoactivity, instead, drugs with high research value, such as psilocybin, should be rescheduled to Schedule 2 of the MDR 2001, with statutory safeguards to prevent inappropriate prescribing. This would allow for UK-based research to be facilitated without increasing the possibility of harm caused to the public.