CONSERVATIVE
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A briefing paper by the Conservative Drug Policy Reform Group

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.[1]

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*:[2]

- 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[3].

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[4].

[1] Considerations of barriers to research Part 1: Synthetic cannabinoid receptor agonists (SCRA), ACMD, 2021.
[2] Medical Use of Psilocybin: Reducing barriers on research and treatment, Rucker et al., 2020.
[3] ibid.
[4] 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*).[5]

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.

[5] 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.[6]

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.

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

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

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.[7] 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".[8]

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]."

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:

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[7] Medical Use of Psilocybin: Reducing barriers on research and treatment, Rucker et al., 2020.
[8] 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.

> "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.

Annex 1

Statutory Instrument for the Rescheduling of Psilocybin with Restrictions

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."