

ACMD

Advisory Council on the Misuse of Drugs

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Rt. Hon. Sajid Javid MP
Home Secretary
2 Marsham Street
London, SW1P 4DF

19 July 2018

Dear Home Secretary,

RE: Scheduling of *Cannabis*-derived medicinal products

Thank you for your commission of 3 July 2018, which the Advisory Council on the Misuse of Drugs (ACMD) has accepted. This report presents our short-term advice on the scheduling of *Cannabis*-derived medicinal products.

1. *Cannabis*-derived medicinal products

The ACMD agrees with the Chief Medical Officer for England (CMO) that there is now evidence of medicinal benefit for some *Cannabis*-derived products in certain medical conditions for some patients.^{1,2,3,4,5,6,7}

The ACMD advises that clinicians in the UK should have the option to prescribe *Cannabis*-derived medicinal products that meet the requirements for medicinal standards to patients with certain medical conditions. It is therefore appropriate for

¹ Thiele EA, Marsh ED, French JA et al. Cannabidiol in patients with seizures associated with Lennox Gastaut syndrome (GWPCARE4): a randomised, double blind, placebo-controlled phase 3 trial. *Lancet* 2018;Jan 25. pii: S0140-6736(18)30136-3.

² Devinsky O, Cross JH, Laux L et al. Trial of cannabidiol for drug resistant seizures in the Dravet syndrome. *New Eng J Med* 2017;376:2011-20.

³ Devinsky O, Patel A, Cross JH et al. Effect of cannabidiol on drop seizures in the Lennox Gastaut Syndrome. *New Eng J Med* 2018;378:1888-97.

⁴ Rice J, Cameron M. (2018) Cannabinoids for Treatment of MS Symptoms: State of the Evidence. *Curr Neurol Neurosci Rep.* 18(8):50.

⁵ Tzadok M, Ulriel-Siboni S, Linder I, Kramer U, Epstein O, Menascu S, Nissenkorn A, Yosef OB, Hyman E, Granot D, Dor M, Lerman-Sagie T, Ben-Zeev B.(2016). CBD-enriched medical *Cannabis* for intractable pediatric epilepsy: The current Israeli experience. *Seizure.* 35:41-4.

⁶ Mücke M, Phillips T, Radbruch L, Petzke F, Häuser W. (2018) *Cannabis*-based medicines for chronic neuropathic pain in adults. *Cochrane Database of Systematic Reviews* 2018, Issue 3. Art. No.: CD012182.

⁷ Whiting PF, Wolff RF, Deshpande S, et al. (2015). Cannabinoids for Medical Use. A Systematic Review and Meta-analysis. *JAMA.* 313(24):2456–2473.

these medications to not be subjected to the requirements of Schedule 1 of the Misuse of Drugs Regulations 2001, as amended (MDR).

Conclusion 1: *Cannabis*-derived medicinal products [*Cannabis* (excluding Sativex), *Cannabis* resin, cannabidiol and cannabidiol derivatives (not being Dronabinol or its stereoisomers)] of the appropriate medicinal standard should not be subjected to Schedule 1 requirements.

2. Defining *Cannabis*-derived medicinal products

The CMO's report states that "*using other forms, such as grown or street Cannabis, as a medicine for therapeutic benefit is potentially dangerous*".⁸ The ACMD agrees that raw *Cannabis* (including *Cannabis*-based preparations) of unknown composition should not be given the status of medication.

Prescribers, patients, regulators and policy-makers must have confidence in the effectiveness, composition and consistency of *Cannabis*-derived medicinal products to ensure patient safety. *Cannabis*-derived medicinal products should meet defined safety and quality assurance standards to ensure that they do not put patients at risk of harm. Risks to patients may arise from impurities and adulterants, and variability in the composition of active constituents.

One of the complexities of this area is the lack of clarity of what *Cannabis*-derived medicinal products are. The ACMD has identified this as a problem that needs addressing with clear definitions. The Department of Health and Social Care (DHSC) and the Medicines and Healthcare products Regulatory Agency (MHRA) should agree on appropriate definitions and medicinal standards following appropriate consultation. The ACMD requests the development of appropriate definitions to be completed in a timely manner, so that it does not introduce unnecessary delays to the ACMD's 'longer term' review, or prevents doctors prescribing *Cannabis*-derived medicinal products to patients where there is an identified need and likelihood of benefit.

Recommendation 1: The DHSC and MHRA to promptly develop a clear definition of a *Cannabis*-derived medicinal product.

In this short term review, the ACMD acknowledged that evidence of the benefits and harms associated with using *Cannabis*-derived medicinal products is still emerging. In light of this, the ACMD initially recommends the most stringent controls for prescription of *Cannabis*-derived medicinal products. The longer term review will consider the appropriate scheduling in more detail.

Recommendation 2: Once the definition of a *Cannabis*-derived medicinal product has been developed, the ACMD advises that only products meeting this definition be moved into Schedule 2 of the MDR pending our further advice.

There are currently a number of internationally available products which may meet these medicinal standards.

⁸ Davies, S.C. "Cannabis Scheduling Review Part 1, The therapeutic and medicinal benefits of Cannabis based products – a review of recent evidence" London: Department of Health and Social Care (2018)

3. Mitigating harms associated with inappropriate prescribing and diversion

The ACMD identified potential risks relating to inappropriate prescribing and diversion of *Cannabis*-derived medicinal products. These risks need to be carefully considered and appropriate ‘checks and balances’ applied to avoid harms to patients and others.

Recommendation 3: In addition to the provisions of Schedule 2 of the MDR, the ACMD recommends that the DHSC, MHRA and Home Office should develop additional frameworks and clinical guidance for ‘checks and balances’ to maintain safe prescribing of *Cannabis*-derived medicinal products.

The ACMD looks forward to working with the DHSC, MHRA and Home Office on these proposals as part of the longer term review and anticipates that wider consultation will be required.

4. Future research of *Cannabis*-derived products

Understanding of the potential therapeutic uses of *Cannabis*-derived products is still developing.⁹ Carefully conducted clinical trials are needed to establish the effectiveness of these products and to understand the short and long term safety of using them.

Conclusion 2: Clinical trials to establish the effectiveness and safety of *Cannabis*-derived medicinal products are urgently required.

The research community has expressed concern that Schedule 1 acts as a ‘barrier to research’. This is important to understand and is an issue with implications not just for *Cannabis*, but also for other Schedule 1 drugs where a potential therapeutic benefit has been proposed.

Conclusion 3: The ACMD considers that it is important that *Cannabis* is not seen in isolation but as an example of a wider issue of potential ‘barriers to research’ associated with other drugs in Schedule 1.

We await the Government’s full response to the ACMD’s interim advice on legitimate use of controlled drugs: research and healthcare (December 2017) and we are firmly committed to further work in this area.¹⁰

5. Synthetic cannabinoids

Synthetic cannabinoids are available in illicit street products such as ‘Spice’ and ‘Mamba’. There is clear evidence of significant harms and a number of deaths

⁹ Nugent SM, Morasco BJ, O’Neil ME, Freeman M, Low A, Kondo K, et al. (2017). The Effects of *Cannabis* Among Adults With Chronic Pain and an Overview of General Harms: A Systematic Review. *Ann Intern Med.* 167:319–331.

¹⁰ Advisory Council on the Misuse of Drugs (December 2017) Legitimate use of controlled drugs: research and healthcare. https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/670663/ACMD_Letter_-_Legitimate_use_of_controlled_drugs_research_and_healthcare_22_Dec_17.pdf

caused by the use of synthetic cannabinoids in certain groups, including vulnerable populations (e.g. street homeless and prison populations).^{11,12,13,14}

While the ACMD accepts that further research into this complex group of diverse substances is important, given the associated potency and harms, the ACMD needs further time to consider and consult on the unintended consequences of potential rescheduling.

Recommendation 4: At present, synthetic cannabinoids should remain in Schedule 1 of the MDR pending the 'longer term' review by the ACMD.

6. Compounds unintentionally captured by generic definitions of synthetic cannabinoids

Current generic definitions intended to control synthetic cannabinoids have unintentionally captured a large number of compounds. Some of these compounds may have potential therapeutic benefits. The ACMD strongly supports further research to gain a better understanding of these compounds and to support the development of new medicines.

The ACMD's ongoing work on legitimate use of controlled drugs: research and healthcare will address this issue.

Yours sincerely,



Dr Owen Bowden-Jones
Chair of the ACMD

¹¹ Paul ABM, Simms L, Amini S, Paul AE. (2018). Teens and Spice: A Review of Adolescent Fatalities Associated with Synthetic Cannabinoid Use. J Forensic Sci. 63: 1321-1324.

¹² Tait RJ, Caldicott D, Mountain D, Hill SL, Lenton S. (2016) A systematic review of adverse events arising from the use of synthetic cannabinoids and their associated treatment, Clinical Toxicology, 54:1, 1-13,

¹³ Castaneto MS, Gorelick DA, Desrosiers NA, Hartman RL, Pirard S, Huestis MA. (2014). Synthetic cannabinoids: Epidemiology, pharmacodynamics, and clinical implications, Drug Alcohol Depend. 144, 12-41

¹⁴ Cohen K and Weinstein AM. (2018). Synthetic and Non-synthetic Cannabinoid Drugs and Their Adverse Effects-A Review From Public Health Prospective. Front. Public Health 6:162.