Remove barriers to clinical research for schedule 1 drugs with therapeutic potential

Regulation of clinical research on schedule 1 drugs with therapeutic potential should be reviewed, argue Leslie King, David Nutt and David Nichols

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There is growing interest in the clinical use of drugs listed in schedule 1 of the UK Misuse of Drugs Regulations. 1 MDMA, for example, has some value in treating post-traumatic stress disorder (PTSD), 2 whereas psilocybin has use in treating resistant depression 3 and alcohol use disorder. 4 There are early indications that N,N-dimethyltryptamine (DMT) assisted therapy could be of huge benefit to those with poor mental health. 5

A decade ago, we reviewed the restrictions imposed by schedule 1 on neuroscience research and treatment innovation. 6 Problems included the need for a licence to produce, possess, or supply schedule 1 drugs in the UK and an import-export licence to take them across the border. Apart from the cost of these licences, which might be beyond the budget of small research groups, other limitations include long delays in obtaining licences (typically a year), the highly bureaucratic process of obtaining licences, and that licences restrict activities to a single site thereby inhibiting external collaboration. The situation is further complicated because pure substances are difficult or expensive to obtain because custom synthesis organisations also need licences.

There is a danger of the argument becoming circular: if a substance has no current medicinal value, then it goes into schedule 1. But if a substance is in schedule 1 then by definition it has no medicinal value. None of this is helped by a restrictive statement in the United Nations Convention on Psychotropic Substances of 1971: “In respect of substances in Schedule 1, the Parties shall: Prohibit all use except for scientific and very limited medical purposes by duly authorized persons, in medical or scientific establishments which are directly under the control of their Governments or specifically approved by them.”

Compounding this is the absence of any political appetite to review the (entirely domestic) classification of drugs controlled under the Misuse of Drugs Act (1971). 3, 7 The few reclassifications that have occurred are almost always to a higher, more restrictive, class. That is the so-called drug policy ratchet. 8 It is clear from studies in the UK and elsewhere that there is, at best, a weak association between the harm of substances and their classification in that act. 9, 10 Similar concerns have been highlighted in the US about the difficulty in pursuing studies on schedule 1 drugs. 11 The regulatory system in the US might be even worse than in the UK as researchers have to contend with the complex interaction between the Controlled Substances Act, the Food and Drug Administration, the Drug Enforcement Administration, and others.

The Australian government has recently announced rescheduling of the current poisons standard of psilocybin for treatment resistant depression and MDMA for treatment resistant PTSD. 12 In the light of that, we ask whether anything has changed in the UK. The Home Office Advisory Council on the Misuse of Drugs (ACMD) has belatedly recognised the issues raised, and it published a report on barriers to research with synthetic cannabinoid receptor agonists in 2021. 13 Its recommendations included that the Misuse of Drugs Regulations should be amended to allow domestic research using up to 100 mg of a schedule 1 drug without licence and allow a similar amount to be imported or exported except where the synthetic cannabinoid receptor agonists are controlled internationally. In his response, however, Chris Philp, the minister of state for crime, policing and fire, made no specific comment on that recommendation, preferring to wait for an ACMD review of schedule 1 drugs in general. 14 A call for evidence by the ACMD was issued two years ago, 15 but its report is yet to be published. Some limited clinical research with schedule 1 drugs does occur, but it has yet to explore their full potential.

The placement of “psychedelic” drugs such as psilocybin in schedule 1 over 50 years ago was based on scant scientific evidence. Numerous studies have shown that they cause far less harm to individuals and society than many other psychoactive drugs. It is therefore anomalous that they are more tightly controlled than drugs such as heroin, which is responsible for significant mortality and morbidity yet, in the UK, sits in schedule 2. The misuse of controlled drugs intended for clinical use is extremely rare. An unfortunate feature of UK legislative policy is that almost all new potentially psychoactive substances added to the Misuse of Drugs Regulations are automatically placed in schedule 1. Generic control of certain N-benzyl-substituted phenethylamines introduced into the Misuse of Drugs Act in 2014, for example, included the carbon-11 labelled version of 251-NBOHm, also known as [11C]Cimbi-5, a useful radiotracer in positron emission tomography.

Because the legal status of psychedelic drugs in national legislation derives largely from the UN Convention on Psychotropic Substances, 16 we think that progress in this area is best tackled internationally rather than on a piecemeal local basis. There might be eventual merit in reviewing the status
of all schedule 1 drugs in the UN Convention of 1971, as set out in the Green List,\(^7\) which is a list of substances under international control. The World Health Organization Expert Committee on Drug Dependence should now review the current status of a limited number of drugs. These include psilocybin, MDMA, other tryptamine derivatives such as DMT and other phenethylamine derivatives such as \(^{11}\)C]Cimbi-5. To do otherwise would be to deny the prospect of improving the lives of many.

Competing interests: Leslie A King and David E Nichols declare no conflict of interest. David J Nutt is advisor to the following companies that are working with psychedelic substances: Alagen Pharmaceuticals, Alvarius and Neurotherapeutics Ltd His research team at Imperial College, London, have received research support in the form of pure psilocybin for clinical research from Compasspathways, Small Pharma Ltd, Beckley Psytec and Usona Institute.

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