Australian Government Narcotic Drug Amendment Bill 2016
Background on Cannabis and its medicinal use
10 February 2016

Cannabis

Cannabis is derived from the plant *Cannabis sativa.* Cannabis is a complex drug comprised of approximately 60 unique cannabinoids, along with many other compounds. The main active ingredient responsible for the 'high' produced by cannabis is delta-9-tetrahydrocannabinol (THC). Other closely related substances that occur in cannabis include cannabidiol (CBD) and, in aged samples, cannabinol (CBN), both of which have quite different pharmacological effects to THC. Other compounds include the cannabivarins and cannabichromenes; they are all collectively known as cannabinoids.

Different strains of cannabis produce a different spectrum of chemical constituents. Some constituents may be only produced by very specific strains, or the same constituents may be present, but in different relative amounts. As a result, the medicinal properties of cannabis strains may vary widely.

Illicit use of cannabis

Australia has one of the highest per capita rates of illicit cannabis use in the world[1]. Cannabis is also the most the most used illicit drug in Australia. According to the 2013 National Drug Strategy Household Survey, 35 per cent of the Australian population reported using cannabis at some time in their lives, with 10.2 per cent having used it in the last 12 months. 3.5 per cent of Australians used cannabis in the week prior to the data collection.

The proportion of secondary school students reporting cannabis use has decreased in recent years. However, the 2011 Secondary School Survey still found that cannabis was the most commonly used illicit substance by this group, with 14 per cent of all secondary school students aged between 12 and 17 years reporting using the drug at some time in their life.

Chronic cannabis use can be associated with a number of negative health and social effects, including increased risk of respiratory diseases associated with smoking, cancer, decreased memory and learning abilities and decreased motivation in areas such as study, work or concentration.

There is a large body of research and evidence on the harms associated with cannabis use, in particular the 2010 report *The epidemiology of cannabis use and cannabis-related harm in Australia 1993-2007*. This report, published by the National Drug and Alcohol Research Centre at the University of New South Wales, found that the number of older users presenting to hospital with dependence and other cannabis related problems increased markedly between 2002 and 2007 and nearly doubled among users aged 30-39. Hospital presentations for cannabis-induced psychosis were highest among users aged 20-29.[2]

[1] Swift, W., Wong, A., Li, K.M., Arnold, J.C. & McGregor, I.S. (2013). Analysis of cannabis Seizures in NSW, Australia: Cannabis Potency and Cannabinoid Profile. *Plos One, 8(7)*.

[2] Roxburgh A, Hall WD, Degenhardt L, McLaren J, Black E, Copeland J, Mattick RP. The epidemiology of cannabis use and cannabis-related harm in Australia 1993-2007.

Evidence for medicinal cannabis

The use of any medication should be based on the evidence of safety and efficacy. Research into the effects of cannabinoids (and some other active compounds from cannabis) extends across a range of medical conditions including cancer-related nausea and pain, cancer-related wasting, acquired immunodeficiency syndrome (AIDS), neurological disorders and pain associated with muscle spasticity.

The majority of controlled studies investigate pharmaceutical preparations that contain cannabinoids rather than raw cannabis plant material ('crude cannabis'). This is primarily because it is particularly challenging to conduct robust clinical trials using raw plant material/crude cannabis. Among other things, it is difficult to ensure the consistency of the product and the dose; and with more than 400 compounds in the leaves and flowering tops, it is difficult to determine which compounds produce specific effects. This lack of consistency is also likely when an individual prepares his or her own cannabis products for medical use, noting the considerable variation that can occur from in terms of product strength or titration of dose.

Consequently, the use of cannabis/cannabis products for medicinal purposes remains contentious. In a recent edition of the British Medical Journal (BMJ) (April 2014), Professors Michael Farrell, Rachelle Buchbinder and Wayne Hall argue that there is no clear evidence for the effectiveness of cannabinoids in treating neuropathic pain arising from multiple sclerosis, or from other causes. Further, any benefits are likely to be modest and there is no clear evidence that purported benefits outweigh the possible harms[3].

By comparison, in the same journal, Professors Laurie Mather, Alex Wodak and William Notcutt cite evidence that the benefits of medicinal cannabis far exceed the harms when in the context of palliating distressing symptoms of a number of chronic conditions. These authors claim that Professor Farrell et al. do not discern between the harms reported from recreational use and supervised medical use. They advise that these authors have not cited papers which have reported longer term safety[4]. However, in considering these particular claims, it should be noted that the usual approach in terms of evaluating clinical evidence is to review the quality of the trials per se rather than the quantity of them.

Some studies have also identified the potential of THC in treating cancer-related nausea and sickness. The 2013 NSW Legislative Council Report on the use of cannabis for medicinal purposes noted the evidence, however, that the antiemetic properties of THC are not as effective as other available anti-nausea drugs and would not likely be used as a first line treatment. As THC's antiemetic effects are achieved through different pathways than other available drugs, its possible use could only extend as far as providing an alternative to patients who are not responding to, or who cannot tolerate, standard treatments, or in addition to standard treatments[5].

On 24 October 2014, Medscape Medical News reported that 'initial data from an open-label study in treatment-resistant epilepsy of pharmaceutical-grade cannabidiol – the nonpsychoactive ingredient in marijuana that is believed to be responsible for its antiepileptic action – suggest that it reduces seizure rate by about 30 per cent.' The new 'product, said to

[3] Farrell, M, Buchbinder, R & Hall, W, Should doctors prescribe cannabinoids? British Medical Journal (BMJ) April 2014
[4] Mather, L, Wodak, A & Notcutt, W, New plea for cannabis scripts British Medical Journal (BMJ) April 2013
[5] New South Wales. Parliament. Legislative Council. General Purpose Standing Committee No. 4 The use of cannabis for medical purposes / General Purpose Standing Committee No. 4. [Sydney, N.S.W.] : the Committee, 2013 (Report ; no 27)

be 98 per cent pure cannabidiol, in development under the brand name Epidiolex by GW Pharmaceuticals, which funded this study, was associated with a greater than 50 per cent reduction in seizures in 39 per cent of patients.' Meanwhile, 'a second study of patients using many different types of medical marijuana has found not dissimilar results, with one third of patients reporting a seizure reduction of 50 per cent or more.'

Commonwealth laws

Cannabis is a narcotic drug that is tightly controlled in Australia. The cultivation, production, manufacture, import, export, distribution, trade, possession, use and supply of cannabis and cannabis derived products, along with all other narcotic drugs, are regulated by a number of Commonwealth laws.

These laws include the:

- *Criminal Code 1995,* which makes it illegal to traffic, import, export, manufacture, cultivate or possess cannabis in any form;
- *Narcotic Drugs Act 1967*, which addresses the manufacture of narcotic substances (including cannabis);
- *Customs Act 1901*, which addresses the import and export of narcotic substances, including a regime under the *Customs (Prohibited Imports) Regulations 1956* that allows for the importation of cannabis for medical and scientific purposes;
- *Therapeutic Goods Act 1989*, which addresses the regulation and supply of authorised medicines and medical products; and
- *Quarantine Act 1908*, which provides the legislative basis for human, plant and animal quarantine activities in Australia.

In addition, various Commonwealth, state and territory laws provide penalties for possessing, using, making, selling, or driving under the influence of, cannabis. There are also laws that prevent the sale and possession of bongs and other smoking equipment in some States and Territories.

International obligations

Australia is a party to international agreements that aim to restrict production, manufacture, export, import, distribution, trade, and possession of narcotic drugs (including cannabis) exclusively to medical and scientific purposes.

The Commonwealth has responsibility for ensuring that any Commonwealth, state or territory scheme for the cultivation of cannabis for medicinal purposes is consistent with Australia's international obligations under the following three international drug control conventions:

- the *Single Convention on Narcotic Drugs 1961*, which specifies the obligations of signatory states in relation to narcotic drugs listed in schedules annexed to the Convention;
- the *Convention on Psychotropic Substances 1971,* which aims to limit the use of psychotropic substances to medical and scientific purposes and also to ensure their availability for those purposes; and
- the *United Nations Convention Against Illicit Traffic in Narcotic Drugs and Psychotropic Substances 1988*, which aims to promote cooperation between parties to address various aspects of illicit traffic in narcotic drugs and psychotropic substances.

Under the Single Convention, Australia, through the Commonwealth Government, has an obligation to carefully control, supervise and report on various stages of cannabis cultivation, production and manufacture. The purpose of the Single Convention is to establish a framework to both prevent abuse and diversion of controlled narcotics and to facilitate the availability of such drugs for medical purposes. The enabling legislation for these obligations is the *Narcotic Drugs Act 1967,* which is administered by the Health Portfolio, in concert with the Attorney-General's Department.

As a signatory to the Single Convention, Australia is obliged to regularly provide information to the International Narcotics Control Board to allow it to carry out these functions. Failure to meet those international obligations contains certain risks, including potential damage to Australia's international reputation for its progressive, balanced and comprehensive approach to dealing with the problems posed by the use and misuse of drugs in the community.

The International Narcotics Control Board also requires annual estimates of the areas harvested, amounts produced, amount of raw material and refined products in stock, amounts required for importation in the current and next calendar year, estimates for cultivating in the next calendar year, relevant trends in use for medical purposes, estimates of the areas to be used for cultivation in the next year and quantities obtained by the manufacturers.

In relation to cannabis, Australia, as a Member State of the Commission on Narcotic Drugs, would be required to report these estimates to the International Narcotics Control Board annually or more frequently. In order to meet these requirements, the Australian Government Department of Health would require manufacturers to regularly report these estimates to the Department.

The Commonwealth currently has laws to regulate the import, export and manufacture of cannabinoids and cannabis raw material, but these do not allow the lawful cultivation in Australia of cannabis plants for medicinal purposes.

Cultivation of cannabis

Presently, the Commonwealth is unable to grant licences for the production of locally cultivated and produced cannabis for medical use and remain compliant with the obligations in the Single Convention or the *Narcotic Drugs Act 1967*.

Under the Single Convention, there is a general exception for the cultivation of the cannabis plant exclusively for industrial purposes (fibre and seed) or horticultural purposes and this currently occurs in several states and territories in Australia. Extraction of any form of cannabis (which may be commonly referred to as industrial hemp) for non-industrial/horticultural purposes, such as extraction of hemp for cannabidiol for human consumption, is subject to the Single Convention.

Article 23 of the Single Convention requires that an agency oversee any cultivation of cannabis plants (other than for industrial/horticultural use) permitted by a Party to that Convention. The agency is required to designate cropping areas, licence cultivators, and purchase and take physical possession of the harvested cannabis (including industrial hemp if not cultivated for industrial/horticultural purposes) and to exercise exclusive rights in relation to importing, exporting, and wholesale trading and maintaining stocks of cannabis other than those held by manufacturers of medicinal cannabis and cannabis preparations.

There have historically been small amounts of cannabis legally cultivated in Australia by universities for experimental and forensic purposes, but this has not invoked Australia's obligations under the Single Convention as the cultivation has not been for medicinal purposes.

However, cultivation for medicinal purposes would enliven the Commonwealth's obligations under Article 23 of the Single Convention and require the Commonwealth to establish an authority to regulate the cultivation of cannabis for medicinal and scientific purposes.

There are already mechanisms in place to enable supply to medicinal cannabis products through the *Therapeutic Goods Act 1989,* where they are not included on the Australian Register of Therapeutic Goods. These include supply through clinical trials and for individual patients, supply under the Special Access and Authorised Prescriber Schemes. The difficulty and cost of obtaining medicinal cannabis products from international suppliers, however, creates an access barrier for the conduct of clinical trials and for people who may benefit from using cannabis for medicinal purposes in consultation with their doctor. Enabling the option to cultivate cannabis for medicinal purposes in Australia will mean that there is potentially a level of supply that meets the demands for clinical trials or other supply options. The inability to readily access products also creates an environment where black markets for medicinal purposes are forming, thus posing potential dangers to the consumer as products are not tested or monitored for quality or safety.

The cultivation of cannabis for medicinal purposes is not currently allowed for under the *Narcotic Drugs Act 1967*. There are already provisions in the *Narcotic Drugs Act 1967* through which manufacturing of a narcotic drug can be licensed (as have been used for the processing of poppy straw for many years). Refining, extraction or other processes (e.g. making extracts, tinctures, cannabis oil) from cannabis (including industrial hemp) is subject to the manufacturing controls set out in the *Narcotic Drugs Act 1967*.

Current Access Schemes

The Special Access Scheme outlined in the *Therapeutic Goods Act 1989* refers to arrangements = provides for the TGA to pre-approve the import and/or supply of an unapproved therapeutic good for a single patient where prescribed by a doctor, case by case. In recent years, the TGA has received Special Access Scheme applications for approval to supply medicinal cannabis products for individual patients.

Medical practitioners can supply unapproved therapeutic goods with few limitations to 'Category A' patients (a person who is seriously ill with a condition from which death is reasonably likely to occur within a matter of months, or from which premature death is reasonably likely to occur in the absence of early treatment) but the TGA must be notified within a month of the decision being made by way of a certification by the medical practitioner. However, current scheduling provisions for most forms of cannabis do not allow for this provision to be used.

There is also an approval route where a medical practitioner applies to the TGA to supply unapproved therapeutic goods to 'Category B' patients (persons not considered to be in Category A but could include Category A patients). The applicant must be able to provide clinical justification for the use of the product for the particular patient. The majority of these requests for approval are able to be dealt with efficiently (2-7 days) but there is a small subset

which may require more extensive discussion with the requesting doctor as to the safety and clinical justification.

A second pathway for access to unapproved medicines is through the Authorised Prescriber Scheme. Individual medical practitioners meeting certain criteria including approval of a Human Research Ethics Committee or the endorsement of a relevant specialist college can apply to the TGA to be approved as an 'Authorised Prescriber'. Applicants are required to provide treatment protocols for TGA agreement. The treatment protocols outline the parameters under which a product will be used.

An Authorised Prescriber can prescribe specified unapproved therapeutic goods or a class of unapproved therapeutic goods to individual patients, in their immediate care, without further TGA approval. The Authorised Prescriber is required to report to the TGA the number of patients treated every six months and there is a requirement that any adverse events associated with use of the medicine are reported to the TGA.

Clinical Trials

There are two avenues through which a clinical trial involving an unapproved medicine can be conducted in Australia. These are the Clinical Trial Notification (CTN) and the Clinical Trial Exemption (CTX) Schemes. Like all prospective medicines, supply of crude, herbal cannabis or cannabis-derived products such as oils or tinctures could be pursued through this route.

The CTN Scheme is a notification scheme only and does not involve a formal TGA approval process. Nonetheless, CTN trials cannot commence until the trial has been notified to the TGA and the appropriate notification fee paid. Under the CTX Scheme, a trial sponsor submits an application to conduct clinical trials to the Therapeutic Goods Administration for evaluation, comment and approval. Under both schemes the sponsor of the clinical trial must obtain approval from both a Human Research Ethics Committee and from the institution at which the trial is to be conducted before the trial can commence. For the vast majority of clinical trials, sponsors use the CTN route, given the rigorous approval processes they go through in institutions such as universities.

Pharmaceutical grade products

There are currently a small number of pharmaceutical grade products that are either derived from cannabis or contain synthetic cannabinoids. There are no pharmaceutical cannabinoids approved for treatment of epilepsy in Australia; however, *Epidiolex*® (cannabidiol) is being made available as an unapproved drug in the USA and there are clinical trials involving children and young adults with Dravet and Lennox-Gastaut syndromes underway. There is also another substance, Cannabidivarin, which is a homolog of cannabidiol, which is understood to be in the very early stages of a clinical trial.

General supply of these products in Australia requires TGA approval for inclusion on the Australian Registrar of Therapeutic Goods. Supply of unapproved products can occur as outlined above.

Due to the current scheduling of these products, an importer would also require a permit under the *Customs (Prohibited Imports) Regulations* from the Office of Drug Control in the Department of Health

International models

Cannabis and cannabis products for medicinal purposes have been available overseas for over a decade. This includes a number of overseas jurisdictions such as Canada, 21 states of the United States, Israel, the Netherlands and a number of other European countries.

It is important to note however that no current international model features market authorisation of raw, herbal cannabis from any national medicines regulator. In many of these jurisdictions people are able to access raw herbal cannabis for smoking, either grown by themselves or grown commercially on compassionate grounds, usually through a permission scheme on recommendation by a medical clinician. This approach is concerning as raw herbal cannabis can be of varying strength and composition making dosing inaccurate and there are respiratory risks associated with inhaling smoke from raw dried plant matter.

The Dutch official cannabis grower, Bedrocan, is developing chemically distinct cannabis varieties with a different profile of cannabinoids and terpenes, another pharmacologically interesting compound found in cannabis. At this moment, four different cannabis varieties are available through Dutch pharmacies. New varieties are being developed as part of Bedrocan's research and development program. Any new variety needs to be fully standardised to guarantee a reproducible and reliable chemical composition. The Dutch system is currently regulated by the Netherlands Government.

Other companies, such as GW Pharmaceuticals, have opted for a more regulated pharmaceutical approach including listing of products within each relevant country's pharmaceutical registration systems. For example, Nabiximols (Sativex) is a Schedule 8 drug in Australia and may be obtained from from the manufacturer with a valid prescription.