

Legislative Council Government Administration Committee A

An Inquiry into and report on the use of natural botanical medicinal cannabis flower and extracted cannabinoids for medical purposes

TASMANIAN GOVERNMENT SUBMISSION



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Introduction

The Tasmanian Government is compassionate to the suffering of patients who seek relief from symptoms such as pain, nausea and vomiting induced by cancer treatments and those suffering chronic conditions such as epilepsy and multiple sclerosis.

We are open to the trial and potential use of medicinal cannabis in Tasmania, subject to a proper evidence-based approach, a robust and strong local regulatory framework, and appropriate approvals from national regulators.

Australia has a long standing requirement that potent medicines supplied to its citizens have demonstrable, high standard evidence of quality, safety and efficacy. The application of Australia's Therapeutic Goods Framework, which requires that medicinal cannabis products with high level therapeutic claims be assessed against these standards, is supported.

Cannabis is an illegal drug under both Commonwealth and state laws, and is the most widely misused substance in Tasmania and Australia. Australia's long standing approach to the regulation of medicines supplied to its citizens should be the primary consideration when examining the use of cannabis for medicinal purposes. The legalisation of cannabis is a separate issue entirely.

The assessment of whether or not cannabis or cannabinoids is accepted as a legitimate medical therapy should remain subject to the usual drug approval process, managed by the Therapeutic Goods Administration (TGA).

At present, there is limited clinical evidence on the clinical efficacy of cannabis and cannabinoids. It is also noted that very few if any of the clinical trials identified within this submission have evaluated newer medications or formulations for those conditions, or compared the clinical efficacy of cannabis or cannabinoids to those newer formulations.

Further, there are already a number of safe and effective medications available for the symptoms and conditions that medicinal cannabis is purported to be effective in treating.

Notwithstanding this, medical science is continually evolving and appropriately conducted clinical trials facilitate the ongoing development of more effective treatments across a range of indications.

The Tasmanian Government is committed to evidence–based medicine and a scientific approach to health care, and supports clinical trials where they are properly conducted through the existing national medicines regulatory framework.



It is difficult to reconcile attitudes and perceptions around the illegal use and harms of a drug, with the potential to harness its therapeutic benefits. It is becoming apparent that the purported benefits of cannabis use should be weighed against its well described risks and harms. It is considered that significantly more scientific clinical trials are needed before consideration can be given to the use of either botanical medicinal cannabis (crude cannabis) or extracted cannabinoids for medical purposes.

It should be noted that the Tasmanian Government has a limited role in the regulation of therapeutic goods. The assessment of the quality, safety and efficacy of medicines is primarily a function of the Australian Government.

In summary, the Tasmanian Government notes that there is limited unequivocal evidence on the clinical efficacy of medicinal cannabis and the Government is supportive of properly conducted trials taking place. The existing national medicines regulatory framework provides the mechanism for the conduct of such trials.

The Tasmanian Government will properly consider any proposal put to it regarding medicinal cannabis on a case by case basis by assessing the merits consistent with current relevant standards and State and Commonwealth legislation.

Cannabis Use

Australia is one of the highest prevalence countries for illicit cannabis use. The 2010 National Drug Strategy Household Survey Reportⁱ found that 10.3 per cent of Australians aged 14 and over self-reported having used it in the previous 12 months and 35.4 per cent having ever used it. Self-reported cannabis use in the previous 12 months in Tasmania was the lowest of all states and territories at 8.3 per cent.

The first results from the 2013 National Drug Strategy Household Surveyⁱⁱ report similar findings, with 10.2 per cent self-reported having used in the previous 12 months; and 34.8 per cent self-reported as having ever used. No state or territory specific data is available as yet.

Although the self-reported rate of cannabis use has been periodically declining in Tasmania since 1998, cannabis is still the most readily available and easily obtained illicit drug in the State. Cannabis is the second principal drug of concern for the majority of the people seeking treatment from Tasmania's alcohol and drug services, both State services and those in the community sector, accounting for 35 per cent of closed episodes of treatment in 2011-12ⁱⁱⁱ (the most recent year for which published data is available). This was the highest of all states or territories and compares to the national rate of 22 per cent.

In terms of law enforcement activities in 2012-13^{iv}, cannabis accounted for:



- around 70 per cent of all illicit drug arrests in Tasmania;
- over 90 per cent of the number of illicit drug seizures in Tasmania; and
- over 90 per cent of the weight of illicit drugs seized in Tasmania.

The short term adverse effects of crude plant-based cannabis include:

- loss of inhibition;
- anxiety or paranoia;
- difficulty concentrating;
- faster heart rate;
- dry mouth and throat;
- vomiting; and
- hallucinations.

The longer term adverse health effects associated with chronic cannabis use include:

- increased risk of bronchitis;
- lung cancer and other diseases of the respiratory system;
- cannabis dependence (addiction);
- depression; and
- decreased concentration, memory and ability to learn new things.

Cannabis is considered to be a drug of addiction for approximately 8 to 10 per cent of those who use it^{v} .

The enormous variation of the level of delta-9-Tetrahydrocannabinol (THC) and possible contamination occurring from pesticides and other contaminants, as well as the delivery system (smoking with or without tobacco or vaporisation), all contribute to the possible adverse effects and harms.

Cannabinoids and THC/CBD

Cannabinoids are the major active components of cannabis, the most recognised of which are THC and cannabidiol (CBD). THC is responsible for producing the psychoactive effects of cannabis. It is claimed it can also be used to produce therapeutic effects that help to reduce pain, nausea and vomiting, and to stimulate appetite. CBD is non-psychoactive and may reduce the unwanted psychoactive effects of THC.

The level of THC, and thus its potency, is not consistent across different types of cannabis plants. The ways in which the plants are grown, cross-bred and genetically modified have been refined over the years to maximise the THC content. Recent research in New South Wales has indicated high levels of THC at around 15 per cent with minimal CBD content.



This is an important point, as any pharmaceutical preparations for research or clinical trials needs to consider the THC/CBD content ratios and the effects of those for the purported therapeutic intervention, and the possible side effects or short or long term adverse health effects.

The industrial hemp industry

It is important to note that the Tasmanian Government supports the continuance and further development of the industrial hemp industry for the production of seed and fibre. The plant varieties used generate very low levels of THC and other cannabinoids. Statements in this submission are made in respect of the proposition for the medical use of cannabis plant (mostly containing high levels of cannabinoids) and cannabinoids, and are not intended in any way to reflect on the industrial hemp industry.



I. The efficacy and safety of natural botanical medicinal cannabis flower and extracted cannabinoids for medical purposes

The use of cannabis for medicinal purposes should be based on the standard current criteria for regulation of all medicines – especially effectiveness and safety.

It is noted that there is limited unequivocal evidence on the clinical efficacy of the use of either natural botanical cannabis, or extracted cannabinoids for a range of medical conditions or symptoms for which it is purported to be effective in treating. It should be noted that the evidence for efficacy and safety is based primarily on relatively few short-term studies with small sample sizes of selected, mostly neuropathic pain conditions. Most studies conclude that more research is needed ^{vi vii}.

Properly conducted, ethical and robust human clinical trials are required. It is appropriate that unproven and experimental treatments only proceed in humans where there are proper protections for patients including clinical oversight. Such considerations should not be compromised by a short term commercialisation agenda.

Defining the issues

It is also important to note that there is a clear and important distinction between the use of regulated pharmaceutical products and the use of cannabis (an illegal drug) for the notional relief of symptoms associated with a range of medical conditions, including pain relief.

There is also an important distinction between the regulation of cannabis or cannabinoid products for medicinal use, or its use for purely (illegal) recreational use.

It is equally important to note that the use of natural botanical medicinal cannabis flower and extracted cannabinoids for medical purposes are two very separate issues. The first refers to the use of crude plant material; whilst the second refers to the extraction of one or more active components of that crude plant material and (it is presumed) making that into something that can be used for medical purposes.

There is risk in combining the two.

Based on current research and evidence, cannabis and cannabinoids are primarily intended to be used as either an adjunctive treatment (that is, in combination with other treatments) or as a second line treatment (that is, as a treatment reserved for use in patients in whom standard treatment has proven ineffective or been poorly tolerated because of side effects). This is because of limited evidence of efficacy.



There are claims that medical cannabis is beneficial in the treatment of a variety of conditions including chronic pain, cancer, epilepsy (including Dravet's Syndrome), in aged care, glaucoma, HIV/AIDS, post-traumatic stress disorder, multiple sclerosis, and certain forms of arthritis.

Literature Search - Major reviews in the last 10 years

A review of the current literature was conducted. Given the extent of the published literature on cannabis, the search was focused on major reviews since 2005 on the subject of the efficacy and safety of natural botanical medicinal cannabis flower and extracted cannabinoids for medical purposes. The search was conducted of the Cochrane Library, Pubmed, EMBASE and TRIP databases and the RHH Medicines Information files.

A report on the literature review with references is attached (Attachment I).

1.1 The efficacy and safety of <u>natural botanical medicinal cannabis flower</u> for medical purposes

Most of what is known about the adverse effects of smoked cannabis comes from studies of long-term recreational users; and most regular cannabis smokers in these studies have also smoked tobacco^{viii}.

The Australian National Council on Drugs is the principal advisory body to the Australian Government on alcohol, tobacco and other drugs use. It has recently released a paper *Medical use of cannabis: Background and Information Paper*^{ix} (Attachment IA). The paper notes that the evidence base for medical uses of cannabis is very much incomplete, and the majority of currently available evidence is about pharmaceutical preparations rather than crude cannabis. It also notes that whilst there have been some studies on the reported use of medicinal cannabis for a range of conditions including one Australian study, those studies have reported use and self-reported patient perceptions and provide no evidence of efficacy.

The enormous variation of the level of THC (and other active components) and possible contamination occurring from pesticides and other contaminants, as well as the delivery system, ie smoking with or without tobacco or vaporisation, all contribute to the possible adverse effects and harms.



1.2 The efficacy and safety of extracted cannabinoids for medical purposes

The three currently available pharmaceutical cannabinoids, available as registered products or as unregistered products under the TGA's Special Access Scheme (SAS) are:

- Nabiximols, containing a 1:1 ratio of THC and CBD extracted from cannabis plants and available in Australia under prescription as a spray for oro-mucosal administration, has been registered by Novartis in Australia for the treatment of spasticity associated with multiple sclerosis unresponsive to other treatments and is known under the trade name of Sativex;
- Dronabinol, a synthetic form of THC, has been approved for treating chemotherapy induced nausea and vomiting and AIDS related weight loss. It is also marketed with a trade name of Marinol; and
- Nabilone, another synthetic form of THC, is a licensed medicine used to treat chemotherapy related nausea and vomiting.

It should be noted that while these products are available for restricted indications, the costs to patients, funding schemes or hospitals are substantial. For instance, on United States web sites, two weeks supply of nabilone Img is indicated as \$US210 and supply of dronabinol costs between \$US 293 and \$US 2,018 for the same treatment period.

In an article recently published in the British Medical Journal (BMJ)[×], Should doctors prescribe cannabinoids? researchers from the National Drug and Alcohol Research Centre, University of New South Wales; Monash Department of Clinical Epidemiology, Cabrini Hospital; Department of Epidemiology and Preventive Medicine, School of Public Health and Preventive Medicine, Monash University, Melbourne; and University of Queensland Centre for Clinical Research, Herston, Queensland examined the effectiveness and safety of medicinal cannabis from literature searches of the Cochrane Central Register of Controlled Trials; Medline and Embase.

The review considered indications for which cannabinoids have received regulatory approval in one or more countries, as well as use in chronic pain, being the common most reported medical reason for use. A copy of the BMJ article is attached (Attachment 2).

It concluded that many of the examined trials and literature do not compare the use of cannabis or cannabinoids with the other regulated medications for the particular medical condition or symptom. It also concluded there is no clear evidence for effectiveness of using cannabis for treating pain; that any benefits are likely to be modest; and that there is no clear evidence that alleged benefits outweigh possible harms, but also acknowledged that more research is needed.



A review of the evidence that cannabis or cannabinoids may be useful as a medicine, and published in The Open Neurology Journal in 2012^{xi} Medical Marijuana: Clearing Away the Smoke came to a number of conclusions:

- there were mixed results dependent upon percentage of THC for analgesic effects for chronic pain short term in the use of smoked cannabis;
- significant reduction of pain in the use of dronabinol (up to 25 mg daily) compared to placebo, and mixed effects on spasticity associated with multiple sclerosis;
- meta-analyses indicates the cannabinoids, dronabinol and nabilone are equivalent to or more effective than metoclopramide and neuroleptics for the acute and delayed nausea and emesis due to cancer chemotherapy, although with less favourable side effects;
- dronabinol (5 mg daily) significantly outperformed placebo in terms of short term appetite enhancement in AIDS patients with clinically significant weight loss; and
- three trials with nabiximols in over 600 patients noted mean intensity of patientrated spasticity in multiple sclerosis was significantly reduced compared to placebo, however observer-rated spasticity was not reduced. Another study found significant reduction in observed spasticity among those administered active smoked cannabis vs placebo (THC levels unknown).

However, that review also noted that in reviewing the possible acute and long term adverse effects of cannabinoids, other agents commonly prescribed for chronic pain and/or spasticity including opioids; tricyclic antidepressants and antiepileptic drugs; baclofen and similar; and benzodiazepines also have adverse effects, and are also subject to abuse and dependence and withdrawal symptoms. A copy of the article is attached (Attachment 3).

Another recent study: Effect of dronabinol on progression in progressive multiple sclerosis (CUPID): a randomised, placebo-controlled trial published in The Lancet Neurology^{xii} in 2013 investigated whether the main active constituent of cannabis (THC) is effective in slowing the course of progressive multiple sclerosis (MS). This was a randomised placebo-controlled three year trial of nearly 500 people with MS. The study authors concluded there is little evidence to suggest that THC has a long term impact on the slowing of progressive MS; although benefits were noted for those at the lower end of the disability scale.



A 2010 randomised placebo-controlled double-blind clinical trial of the cannabis-based medicinal product Sativex, in painful diabetic neuropathy, was undertaken to assess the efficacy of Sativex as adjuvant treatment in painful diabetic neuropathy in 30 subjects. The primary outcome measure was change in mean daily pain scores, and secondary outcome measures included quality of life assessment. The study^{xiii} found there was significant improvement in pain scores in both groups, and no significant differences in secondary outcome measures. However, patients with depression had significantly greater baseline pain scores that improved regardless of intervention, suggesting that depression is a major confounder and may have important implications for future trials.

Additional Cochrane database reviews have found no evidence that cannabinoids are effective in the improvement of disturbed behaviour in dementia or in the treatment of other symptoms of dementia ^{xiv}; that cannabinoids may be useful for controlling chemotherapy-induced nausea and vomiting, noting that harmful side effects may limit their widespread use ^{xv}; improvements in tic frequency and severity for use of cannabinoids for Tourette's Syndrome were small although reviewed trials reported a positive effect ^{xvi}; and insufficient evidence was found to support or refute the use of cannabis or cannabinoid compounds for people suffering schizophrenia ^{xvii}.



2. If, and how, natural botanical medicinal cannabis flower and extracted cannabinoids could and/or should be supplied for medical use

This term of reference is addressed in two parts.

2.1 If, and how, natural botanical cannabis flower and extracted cannabinoids <u>could</u> be supplied for medical use

Information on the legislative framework applying in Australia generally and in Tasmania is provided below.

The national scheduling model

In the national Standard for the Uniform Scheduling of Medicines and Poisons (SUSMP) cannabis and tetrahydrocannabinols and their alkyl homologues and derivatives (including cannabidiol) are included in Schedule 9 (Prohibited Substances). Schedule 9 substances are those "which may be abused or misused, the manufacture, possession, sale or use of which should be prohibited by law except when required for medical or scientific research, or for analytical, teaching or training purposes with approval of Commonwealth and/or State and Territory Health Authorities."

The entries in the SUSMP are:

- (a) CANNABIS except:
 - a) when separately specified in these Schedules; or
 - b) processed hemp fibre containing 0.1 per cent or less of tetrahydrocannabinol and products manufactured from such fibre.
- (b) TETRAHYDROCANNABINOLS and their alkyl homologues except:
 - (a) when separately specified in this Schedule;
 - (b) when included in Schedule 8;
 - (c) in hemp seed oil, containing 50 mg/kg or less of tetrahydrocannabinols when labelled with a warning statement:

Not for internal use; or

Not to be taken; or

(d) in products for purposes other than internal human use containing 50 mg/kg or less of tetrahydrocannabinols.



The Tasmanian Poisons Act 1971

In the Tasmanian *Poisons Act 1971* Indian Hemp is specifically defined as a prohibited plant. Other prohibited plants include the opium poppy and coca leaves. Indian hemp is defined as:

- (a) Any plant or part of a plant of the genus cannabis;
- (b) The resin, whether crude or purified, obtained from any plant or part of the plant of the genus cannabis; or
- (c) Any preparation containing any such resin-

by whatever name that plant, part, resin, or preparation may be called, and includes the achene or seed of any such plant but does not include any fibre of any such plant from which the resin has been extracted.

The Tasmanian Poisons Act 1971 adopts the SUSMP entry for tetrahydrocannabinols.

Section 49(1) and 47(3) Prohibition of possession and supply of prohibited plants except under licence

Section 49 of the Tasmanian *Poisons Act 1971* states that a person shall not have in his possession a prohibited plant (whether in its original form or not) or any part of a prohibited plant. Exceptions are made for holders of licences to grow under Section 52, those transporting such plants for legitimate processing and employees of licensed manufacturing chemists.

Further to this, Section 47(3) states that a person shall not sell or supply a prohibited plant or prohibited substance to another person or traffic in such a plant or substance. Section 47(4) makes exceptions consistent with those under Section 49.

No provision is made in the *Poisons Act 1971* for supply of prohibited plants to persons for personal use.

Section 55- Provision for the use of prohibited substances in Tasmania

Section 55(1) of the Tasmanian *Poisons Act 1971* creates offences for the importation, making, refining, preparation, possession, use, sale or supply of a prohibited substance. Section 55(2) states, however, that Section 55(1) does not apply to the importation, making, refining, preparation, possession or use of a prohibited substance in an exempted public institution for educational, experimental or research purposes.

An "exempted public institution" means a public institution that is declared by the Minister, by order. The main exempted public institution undertaking research in Tasmania is the



University of Tasmania. These activities may only be undertaken in compliance with conditions determined by the Minister for Health.

The supply of nabiximols (Sativex), dronabinol and nabilone

It should be noted that the cannabinols, nabiximols (Sativex®), dronabinol and nabilone are included in Schedule 8 of SUSMP and are not subject to the prohibitions applying to Schedule 9 substances. A prescriber must seek approval from the Secretary for the Department of Health and Human Services before prescribing or supplying nabiximols. Approval must be sought from the Secretary of the Commonwealth Department of Health under Section 19 of the *Therapeutic Goods Act 1989* to prescribe dronabinol or nabilone.

The Tasmanian Misuse of Drugs Act 2001

The Tasmanian Misuse of Drugs Act 2001 creates offences for the cultivating, possessing, using and selling or supplying a controlled plant.

The following are listed in Schedule 1 Part 3 - Controlled plants:

- cannabis;
- cannabis oil; and
- cannabis resin.

Tetrahydrocannabinols are listed as Controlled Drugs, consistent with the SUSMP entry.

The growing of industrial hemp in Tasmania

The status of industrial hemp should be differentiated from that of high THC varieties.

Industrial hemp is grown under licence from seed that will reliably produce plants of low THC content. The plant remains prohibited until its THC content is established as being below the permitted limit, currently 0.35% THC.

The listing of "industrial hemp seed" in Schedule 8 of the Poisons List allows for the trading of this commodity under licence. High THC varieties remain classified as Prohibited.

Conclusion

The national poisons scheduling model recommends prohibitions on cannabis, tetahydrocannabinols and cannabinoids. Due to the recognised harms in the community these recommendations are adopted by all states and territories.



Cannabis and cannabinoids cannot currently be supplied in Tasmania for medicinal use due to the prohibitions in the *Poisons Act 1971* and *Misuse of Drugs Act 2001*. The only exceptions to this are supply of nabiximols (Sativex®), dronabinol and nabilone when in Schedule 8 of the SUSMP and the importation, making, refining, preparation, possession or use of a prohibited substance in an exempted public institution for educational, experimental or research purposes.

2.2 If, and how, natural botanical cannabis flower and extracted cannabinoids <u>should</u> be supplied for medical use?

A primary concern from a public health perspective is that, given the evidence of the short and long term adverse physical and mental health effects of the use of cannabis or cannabinoids as noted earlier in this submission, and given the lack of the evidence of their efficacy or safety, the community should expect no less than a robust scientific approach to the use of any cannabis or cannabinoid product for medical or therapeutic uses.

The various local and national media reports of parents and other people providing children and others with an untested product containing a cannabis extract the quality or THC levels of which is completely unknown, raises significant issues and concerns of the short and long term harms to those immature and developing brains and the short and potentially longer term legal liabilities. These products are being sourced by illegal means and as such there is no legal recourse for users.

The secondary but equally important concern from a public health perspective when considering if, and how natural botanical cannabis flower or extracted cannabinoids should be supplied for medical use, is the obvious potential for diversion for illicit use.

It is considered that significantly more scientific clinical trials are needed before consideration could be given to the use of either botanical medicinal cannabis (crude cannabis) or extracted cannabinoids for medical purposes.

The National Drug Strategy 2010-2015

The National Drug Strategy 2010-2015 (NDS), to which all governments have committed, is Australia's overarching strategic framework for action on alcohol, tobacco and other drugs. The NDS and the Tasmanian Drug Strategy 2013-2015 (TDS) are underpinned by the goal to reduce the harms caused by drug abuse. This approach focuses on reducing the supply, or availability, of alcohol, tobacco and other drugs; reducing demand through prevention, early intervention and treatment; and reducing the harms associated with the use of alcohol, tobacco and other drugs.



The NDS notes the increasing harms from cannabis as a continuing challenge. Likewise, the TDS notes increasing use of cannabis as a matter of concern.

Approvals framework

No form of cannabis can be approved for medicinal use unless an application is made to the TGA with supporting data to assess its quality, safety and efficacy. Until medicinal cannabis is proven to provide more relief than the options currently available, the Australian Government cannot override these safety controls and legalise the use of cannabis as a medicine.

Challenges

In their submission to the New South Wales Legislative Assembly General Purpose Standing Committee No. 4 Inquiry into Medical use of cannabis, Professors Wayne Hall and Michael Farrell (Attachment 4) discuss both the challenges of making medicinal cannabis available, and potential models for providing medical cannabis. Their submission notes findings that:

- 'suggest at the very least a blurring of boundaries between recreational and medical cannabis use among patrons of the California medical marijuana program.' (page 16);
- 'The medical marihuana (sic) scheme provides an unapproved drug of uncertain safety and efficacy for many indications, at substantial cost, to a small number of patients, when other pharmaceutical drugs with better evidence of efficacy that have been through the regulatory process may not be provided by the Canadian government.' (page 18);

As noted in the National Cannabis Prevention and Information Centre (NCPIC) submission to the New South Wales Legislative Assembly General Purpose Standing Committee No. 4 Inquiry into Medical use of cannabis (Attachment 5):

'Cannabis had been made available for medicinal purposes in eighteen US states and Washington DC, however, without controlling for the quality or safety of the product. The problems that have arisen with this approach are manifold. Firstly because the cannabis that has been legalised is the same plant substance that is taken by recreational users and the mode of delivery of the drug has remained the same (i.e. it is predominantly smoked). This means that all of the risk factors of smoking (cardiovascular and respiratory, addiction to tobacco when mixed with the cannabis) are present. The Journal of Global Drug Policy and Practice reported that in 2011 over 85% of the 40,000 people enrolled in the medical marijuana program in Oregon USA were using it for purported chronic pain. In addition, there is some evidence to suggest that children and adolescents are gaining easier access to the drug on the basis of some medical condition and this places these young people in the



position of risks to physical and mental health in the longer term that have been documented above. In the USA, cannabis use is higher in states where cannabis has been legalised for medical purposes.'

Grant et al ^{vii} note when assessing the potential of cannabinoids for therapeutic purposes there are risks to be considered, and the potential for misuse, abuse or addiction must be assessed, and in the context that the potential longer-term harms of the use of cannabinoids nor which cannabinoids or which combinations may achieve the best results are fully understood. It also recommends additional trials which should include consideration of delivery systems, i.e. smoking, vaporization, and oral mucosal spray because cannabinoids are variably and sometimes incompletely absorbed from the gut, and bioavailability is reduced by extensive first pass metabolism.

A press report has pointed to concern in Colorado at 29 hospital admissions of children after cannabis exposure over the period 2012 to April 2014 with two admissions to an intensive care unit for treatment of severe adverse effects ^{VA}.

Farrell et al ^{vi} noted there is no clear evidence for effectiveness of cannabis or cannabinoids for treating pain; that any benefits are likely to be modest; and there is no clear evidence that the reputed benefits outweigh possible harms. It is also unknown due to lack of robust clinical trials of the longer term harms of the use of cannabis or cannabinoids for a variety of conditions.

Alternative pathways

This submission, due to the current lack of sound clinical evidence of the safety or efficacy of the use of either, contends that many more evidence-based clinical trials, from a mainstream medical research perspective, are needed before the use of cannabis or cannabinoids for medical uses can be seriously considered.



3. The legal implications and barriers to the <u>medicinal use</u> of natural botanical medicinal cannabis flower and extracted cannabinoids in Tasmania

Australia has a long standing requirement that potent medicines supplied to its citizens have demonstrable, high standard evidence of quality, safety and efficacy. The Tasmanian Government supports the application of Australia's Therapeutic Goods framework which requires that medicinal cannabis products with high level therapeutic claims be assessed against these standards. These standards are necessary to the protection and advancement of public health.

No therapeutic good is risk free – all medicines carry a risk of producing adverse reactions in some patients. It is appropriate that any cannabis based medicines receive proper pre-market assessment with both benefits and risks considered.

The Commonwealth *Therapeutic Goods Act 1989* requires that any product for which therapeutic claims are made must be included in the Australian Register of Therapeutic Goods before it can be supplied in, imported to or exported from Australia.

Pharmaceutical cannabis products should only be approved based on robust peer reviewed scientific evidence. Evidence can be generated through properly conducted clinical trials.

The Commonwealth *Therapeutic Goods Act1989* requires the registration of medicines where high level claims are made. The Tasmanian *Therapeutic Goods Act 2001* adopts the Commonwealth legislation and ensures application of the legislation to all manufacturers and traders of medicines in Tasmania. The Tasmanian legislation makes no provision for exemption.

The TGA has statutory expert committees it may call upon to obtain independent advice on scientific and technical matters. Manufacturers of all medicines must have a Licence to Manufacture Therapeutic Goods issued by the TGA. The production of medicines must be compliant with the Code of Good Manufacturing Practice to ensure that all medicines produced are at a high standard.

There are many products available on the Australian Government's Pharmaceutical Benefits Scheme (PBS) or through the State hospital system that have already been assessed by the TGA for the treatment of chronic and acute pain, epilepsy, nausea and vomiting associated with chemotherapy, HIV/AIDS and the symptoms of multiple sclerosis.

In Tasmania patients with HIV/AIDS have access to the latest first line antiviral and supportive treatments through the PBS and the State hospital system. All these medicines are registered and have had their benefits and risks properly assessed.



There has already been a cannabis derived product registered in this country, being Sativex®. This product has completed the necessary assessments by the TGA and has been approved for the indication of treatment resistant spasticity in multiple sclerosis. Sativex has not been listed for subsidy under the PBS. The substances dronabinol and nabilone, as unregistered products, are available through the TGA's Special Access Scheme.

Development of new cannabinoid pharmaceuticals

The development of new cannabis derived pharmaceuticals is ongoing. GW Pharmaceuticals, a biopharmaceutical company and marketer of Sativex, announced on the 6 June 2014 that the United States Food and Drug Administration (FDA) has granted Fast Track designation to a cannabidiol product, Epidiolex®, in the treatment of Dravet Syndrome, a rare form of childhood epiliepsy. Cannabidiol is a cannabinoid with different properties to tetrahydrocannabinol and is thought to have potential for a wider medical application. Phase 2/3 clinical trials will commence this year; such research normally includes studies of effects on 100 to 200 people with the targeted disease. Phase 3 studies on the treatment of another epileptic condition, Lennox-Gastaut Syndrome, are expected to commence in 2015.

This research continues on cannabinoids within the quality, safety and efficacy framework supported by the FDA and the TGA. A drug development program with Fast Track designation is afforded greater access to the FDA for the purpose of expediting a drug's development, review and potential approval to get important new drugs to the patient earlier. Registration of Epidiolex by the FDA may facilitate its availability in Australia through the TGA's Special Access Scheme.

Report by NSW Upper House Committee

Further to the above there are two matters raised by the NSW Upper House Committee in respect of the use of therapeutic goods that are noteworthy:

- 1. The NSW Committee limited the scope of its recommendations and did not support long term use of cannabis in chronic debilitating pain patients. The Committee commented "... owing to the present absence of evidence on the long term effects of cannabis use, and the risks associated with smoking it, the Committee considers that at this stage, the target group for this provision should not include people with chronic conditions."
- 2. The NSW Committee noted that "... the supply of seeds, plants and equipment to a patient, whether by a carer or another third party, may contravene the Therapeutic Goods Act". (See pg xv of report)



Conclusion:

The medical use of cannabis and cannabis flower that fall outside existing regulatory and legal frameworks is not supported. In contrast to cannabis derived pharmaceutical products (registered and accessed through the Special Access Scheme), the quality and safety of available cannabis plant is, at this stage, variable and unregulated. The Australian community expects therapeutic goods in the marketplace to meet an acceptable standard of safety and quality.



4. The legal implications and barriers to the <u>growing and</u> <u>commercialisation of cannabis flower</u> and extracted cannabinoids in Tasmania

The current legislative position with cannabis and cannabinoids is detailed under 2.1.

There are legislative provisions for the commercial growing of Prohibited Plants in Tasmania, an example being the growing of poppies for the production of narcotic substances.

Growers are licensed under Section 52 of the *Poisons Act 1971*. Growers are only permitted to supply a licensed manufacturing chemist. Licences for manufacturing are issued at the discretion of the Minister for Health under Section 16 of the *Poisons Act 1971*. These licences may be granted unconditionally or subject to such conditions and restrictions as the Minister determines.

Matters such as quality control, research and development have normally been the domain of a manufacturer in the poppy industry. Processors apply strict quality control measures in their manufacturing and undertake research and development in both improved agricultural and manufacturing yields.

Australia is a signatory to two international agreements that are overseen by the United Nations and that restrict the production, export, import, distribution, trade, possession and use of cannabis and other narcotic drugs. They are the Single Convention on Narcotic Drugs (1961) and the Convention on Illicit Traffic in Narcotic Drugs and Psychotropic Substances (1988).

International security and supply models

The development of appropriate security and supply models will be essential should cannabis be grown on a commercial scale in Tasmania in the future, and should be informed by international experience.

In Europe (particularly in the Netherlands) and in Canada, the growing and supply of medicinal cannabis is well established and highly regulated. Licensees must comply with prescribed requirements in relation to: police checks for all individuals involved in growing, transporting and manufacturing; site location; building security, including electronic monitoring; ventilation of facilities; storage; transport, etc.

The manner in which medicinal cannabis is supplied and administered is also highly regulated. In the Netherlands, supply occurs through pharmacies, and in Canada through licensed producers. The issue of supply directly impacts on avenues for diversion, with access to dry leaf cannabis providing the highest risk.



It is noted that commonly the responsibility for providing the required security across all aspects of the medicinal cannabis industry lies with the licensees and the regulatory authorities. The role of police is in processing individual police checks, conducting site checks as part of the application process, and in responding to reports of interference with crops and cannabis product.

Consumer Safety

Levels of protection will need to be considered for approved users of medicinal cannabis, and their carers, to limit them being the targets for diversion. Safe mechanisms for supply and administration will be paramount.

Public Safety

Current debate has focussed on the potential benefits of medicinal use of cannabis for the terminally ill, and persons seroconverting from HIV to AIDS. The social functioning of persons that fit within this cohort will vary considerably, and it will be important to more broadly consider public safety issues, such as driving under the influence of cannabis.



5. The potential impact on agricultural or other sectors within Tasmania

The Tasmanian Government welcomes the development of new agricultural opportunities in Tasmania.

Preliminary research into the overseas production of high THC cannabis cultivars for medical applications indicates that the crop is grown in high security intensive cropping greenhouses. Intensive indoor production also boosts yields significantly as the crop is environmentally controlled and therefore not subject to weather variables or the limitations of seasons, meaning it can be produced continuously. Because of the need for high level security to grow high THC crops and the benefits of intensive, climate controlled production, it is likely that a similar model would be required in Tasmania.

Outdoor production would require extensive and costly security fencing, would limit crops to seasonal production, and would require considerably higher input costs than intensive indoor production methods. Thus there appears to be minimal scope for large scale open field production, and limited opportunities for agricultural enterprises to include broad acre medical cannabis production on their farms.

The Tasmanian Government is also aware of the views of Poppy Growers Tasmania regarding the production of medical cannabis in the State and the need to be mindful of any potential impacts on the international reputation of the poppy industry in the State.



6. Any other matters incidental thereto.

Medicinal Cannabis trials in Tasmania

There is potential for research into medicinal cannabis in Tasmania. The conditions of any trials must be determined by the Minister for Health under Section 55(2) of the *Poisons Act* 1971. It is appropriate that unproven and experimental treatments only proceed in humans where there are proper protections for patients, including clinical oversight. These considerations should not be compromised by a short term commercialisation agenda.

There are normally three elements to proposals for the use of medicinal cannabis- the cultivation of the plant, its processing and the human trials. The human trials could potentially proceed with cannabis or cannabinoids grown and processed outside Tasmania.

The growing of the cannabis in this state will require security of a very high standard with endorsement of the arrangements by Tasmania Police. National police checks are required for the applicant and the company's directors.

Section 55 of the *Poisons Act 1971* only provides for the making, refining, preparation or use of a prohibited substance in an exempted public institution such as the University of Tasmania. A contract or agreement with the University for processing and human trials would need to be established.

Trials on the administration of substances to humans always create concern at the risk to participants. There are many specifications in respect of such activities. There would need to be advice of the name the chief medical investigator and confirmation of the clinical trial design, the participant and staff numbers and resources. There would need to be confirmation that the legal requirements such as indemnity and informed consent are met.

The legislative framework in Tasmania appears to be different from that in Victoria, in that it already provides for the Tasmanian Minister for Health to authorise trials at an exempted public institution (University of Tasmania), either by approving each individual for the trial or by giving a general approval to an investigator to enrol patients – this would depend on the Minister's Determination of Conditions.

Further to the above evidence must be provided of compliance with the National Health and Medical Research Council's:

- The National Statement on Ethical Conduct in Human Research; and
- The Australian Code for the Responsible Conduct of Research.



In addition there must be compliance with the TGA's Note for Guidance on good Clinical Practice (CMP/ICH/135/95) and evidence would be required of compliance with the TGA's Clinical Trial Notification or the Clinical Trial Exemption requirements. Information on the TGA's requirements is available at:

http://www.tga.gov.au/industry/clinical-trials.htm

Information on the requirements for Australian clinical trials is available at:

http://www.australianclinicaltrials.gov.au/home

Attached is a document detailing the requirements for trials for the growing, processing and use of cannabis or cannabinoids in human trials in Tasmania (Attachment 6). Also attached is the poster "QUM (Quality Use of Medicines) From the Start for Healthy Outcomes" by the Medicines Industry Liaison Group which details the development cycle for medicines in Australia. (Attachment 7).

Seeking further health advice

It is important that the Legislative Council Inquiry talk to a broad range of health professionals in relation to this matter. The following specialisations as listed as a suggestion:

- Palliative Care specialists;
- Oncologists;
- Pain Management specialists;
- Chapter of Addiction Medicine;
- Paediatricians;
- Neurologists; and
- Psychologists.



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