



**Australian Government**

**Department of Health**

Therapeutic Goods Administration

# CLINICAL EVIDENCE AND ACCESS FOR MEDICINAL CANNABIS PRODUCTS

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**TGA** Health Safety  
Regulation

# The government's intent

- Treat medicinal cannabis products as medicines
- Provide **patient access to medicinal cannabis** largely outside the standard registered medicines route
- **Provision of a quality medicine** through doctors prescription
- **Encourage clinical trials** to support potential future TGA registration
- The **Health Products Regulation Group has oversight**
  - Import, cultivation and manufacture (Office of Drug Control)
  - Product GMP, product scheduling and patient access through the Therapeutic Goods Administration (TGA)
- **States and Territories** also have a role in regulation

# Community hope and belief



“ Please can someone recommend the best oil  
And how I can get it. I have stage 4 aggressive bowel cancer. ”

“ Could someone please PM me and let me know how I can get cannabis oil  
for my son who has brain cancer, we have gotten him cannabis but have  
had no luck at all getting the oil, we are desperate at this stage. ”

“ Hi, how can I get some oil to try. I have terminal lung cancer and didn't  
think you could get it in oz. Please pm me if possible. Thanks heaps. ”

“ Ordered my oil today. Can't handle the side effects of the drug I have to  
take for my brain tumour. Fingers crossed it helps! ”

“ Has anyone here cured Esophagus Cancer  
with Cannabis oil? ”

“ If anyone could point me in the right direction for CBD and THC for my  
mum's lung cancer, please pm me. Based in Melbourne ”

“ I have several autoimmune diseases including Hashimoto's thyroiditis. I've  
heard cannabis can work in healing my thyroid. I'm clueless about cannabis.  
Any info would be great. ”

“ My cousin has Aspergers and autism. He self harms, screams and makes  
so much noise the neighbours and nursing home want to evict him. We  
are desperate for some CBD oil  
How do I get access to it... Thank you ”

“ Hi folks. I have a very rare disease that causes severe pain all over my body.  
I have the flowers, I would like to know of a recipe to produce pain capsules  
or oil that I can ingest, because I just found out I have emphysema and  
need to stop smoking. Cheers. ”

# Evidence

## Whiting et al 2015

- There was moderate quality evidence to support the use of cannabinoids for the treatment of:
  - chronic pain and
  - spasticity.
- There was low quality evidence suggesting that cannabinoids were associated with:
  - improvements in nausea and vomiting due to chemotherapy,
  - weight gain in HIV infection,
  - sleep disorders, and
  - Tourette syndrome.
- Cannabinoids were associated with an increased risk of short-term AEs.

# Evidence

## National Academies of Science 2017 report

- The National Academies of Sciences, Engineering and Medicine conducted a rapid turn-around comprehensive review of recent medical literature on **The Health Effects of *Cannabis* and Cannabinoids** which was released in 2017. The 16-member committee adopted the key features of a systematic review process, conducting an extensive search of relevant databases and considered 10,000 recent abstracts to determine their relevance



# Evidence

## National Academy of Science 2017 Report

- In adults with chemotherapy induced nausea and vomiting, oral cannabinoids are effective anti-emetics.
- In adults with chronic pain, patients who were treated with cannabis or cannabinoids are more likely to experience a clinically significant reduction in pain symptoms
- In adults with multiple sclerosis (MS) related spasticity, short-term use of oral cannabinoids improves patient-reported spasticity symptoms.
- For these conditions the effects of cannabinoids are modest; for all other conditions evaluated there is inadequate information to assess their effects.

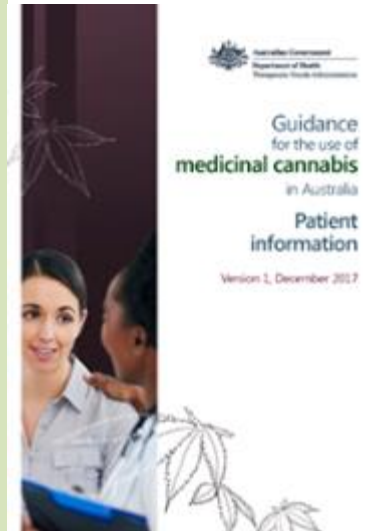
# Evidence

## National Academies of Science 2018 Update on 2017 report

- Conclusive or substantial evidence for the treatment of chronic pain in adults; chemotherapy-induced nausea and vomiting and spasticity associated with multiple sclerosis.
- Moderate evidence was found for secondary sleep disturbances
- Limited, insufficient or absent evidence supporting improvement in appetite, Tourette syndrome, anxiety, posttraumatic stress disorder, cancer, irritable bowel syndrome, epilepsy and a variety of neurodegenerative disorders

# Clinical evidence reviews

- **Conducted by team** from UNSW, USyd, UQ and collaborators
- Focus on epilepsy, MS, pain types, nausea and vomiting and palliative care
- Systematic reviews of **published reviews** and **findings of individual studies** using Medline, Embase, PsycINFO, and EBM Reviews
- **Studies published** from 1980 to early 2017
- **Priority was given to RCTs but also included observational studies,** e.g. case reports, retrospective chart reviews, self-report surveys
- These reviews were **published in December 2017**





# Epilepsy

- In patients with paediatric-onset drug-resistant epilepsy, cannabidiol products **reduced seizure frequency by 50 per cent or more in up to half of the patients** and achieved seizure freedom in a small number of patients.
- This is when cannabidiol products are used as an **add-on to current treatments** in drug-resistant epilepsy in children and young adults.
- There are few studies of whether cannabidiol is effective in treating adult epilepsy.



# Epilepsy

- Five RCTs and 17 observational studies were identified - **all examined CBD as adjuvant treatment** (in addition to standard antiepileptic drugs)
- **Randomised controlled studies**
  - In patients with paediatric-onset drug-resistant epilepsy CBD products reduced seizure frequency and achieved seizure freedom compared with placebo
  - 14% of patients withdrew because of treatment-related adverse events
  - Doses of cannabidiol required were reasonably high (20mg/kg/day) and some uncertainty around contribution of the effect of CBD on clobazam metabolism
- **Observational studies:**
  - In 14 of 17 studies, 56% of patients reported reductions in seizures of 50% or more.
  - In 7 paediatric studies 13% were estimated to be seizure-free
  - 10 studies reported improved quality of life in paediatric and adult groups

# Cancer and HIV induced nausea and vomiting

- 11 met inclusion criteria, but were mainly against old medicines
- In **managing CINV in adults**, THC/ analogues were more effective than placebo, and as effective prochlorperazine at completely controlling nausea and vomiting, and controlling /reducing nausea
- Comparison of cannabinoids against **newer anti-emetics** is required
- Research on cannabinoids for **CINV in children** is more limited
- Evidence of efficacy of cannabinoids in treating **nausea and vomiting in late stage AIDS and terminal cancer** was equivocal

# Cancer and HIV induced nausea and vomiting

- High-THC medicinal cannabis products were as effective as many of the prescription medicines they were compared with when most of the studies were carried out (1980s/90s).
- In recent years, much more effective prescription medicines for nausea and vomiting have become available but there have been very few comparisons of medicinal cannabis products with these medicines.
- Therefore, medicinal cannabis products should only be prescribed after newer standard approved treatments have failed.



# Palliative care

- 9 double blind or open label RCTs studies with a total of 1561 participants were included, but evidence was low quality
- **In cancer patients**, there were **no significant differences** between cannabinoids and placebo for improving caloric intake, appetite, nausea/vomiting, pain, dizziness, mental health or sleep problems
- **In HIV patients**, cannabinoids were superior to placebo for weight gain and appetite **but not for nausea/vomiting**
- **No convincing evidence** suggesting that cannabinoids are of value for anorexia or cachexia (weakness and wasting) in cancer or HIV

# Palliative care

- There was little evidence of benefit to advanced cancer patients with chronic pain. The published studies also showed little effect on appetite, nausea/vomiting, pain, dizziness, mental health or sleep problems.
- There is no evidence that medicinal cannabis has any anti-cancer activity in human studies or that it can slow the progression of these conditions.



# Multiple sclerosis

- **Nabiximols are TGA approved** for the use in MS for muscle spasticity.
- 11 systematic reviews with data from 32 studies with 3146 patients.
- These included 10 moderate/high-quality RCTs, that examined if cannabinoids reduced pain and spasticity.
- Five reviews concluded that there was **evidence that cannabinoids** may be effective for symptoms of **pain and/or spasticity** and positive effects on **sleep and bladder symptoms**
- **Mixed findings** were reported on quality of life, ataxia/tremor and disability/disease progression
- **A lack of studies** with non-cannabinoid comparators is a major evidence gap

# Multiple sclerosis

- There is some evidence to suggest that medicinal cannabis products may be effective for treating the pain symptoms of MS although this is inconsistent.
- Studies differ as to whether medicinal cannabis products can help improve bladder function, sleep, quality of life, ataxia/tremor and disability/disease progression.
- There are currently no studies that compare medicinal cannabis products with commonly-used medications for MS pain and spasticity, so medical cannabis products are more suitable for those who have not responded adequately to other anti-spasticity medication.





# Chronic non-cancer pain

- 102 trials of all types of study designs considered
- Most studies with nabiximols, THC/ analogues, THC-rich preparations
- Most evidence on cannabinoids was from studies where **cannabinoids were adjuvant interventions and not first line treatments for pain**
- Patients who had cannabinoids for **MS-related neuropathic pain** were more likely to experience a 30% reduction in pain (low confidence) and decrease in pain scores (moderate confidence)
- patients who had cannabinoids for **non-MS related neuropathic pain** were more likely to experience a 50% reduction in pain and a reduction in pain scores
- **Insufficient information** to make a conclusion about cannabinoids for the treatment of pain associated with **arthritis and fibromyalgia**

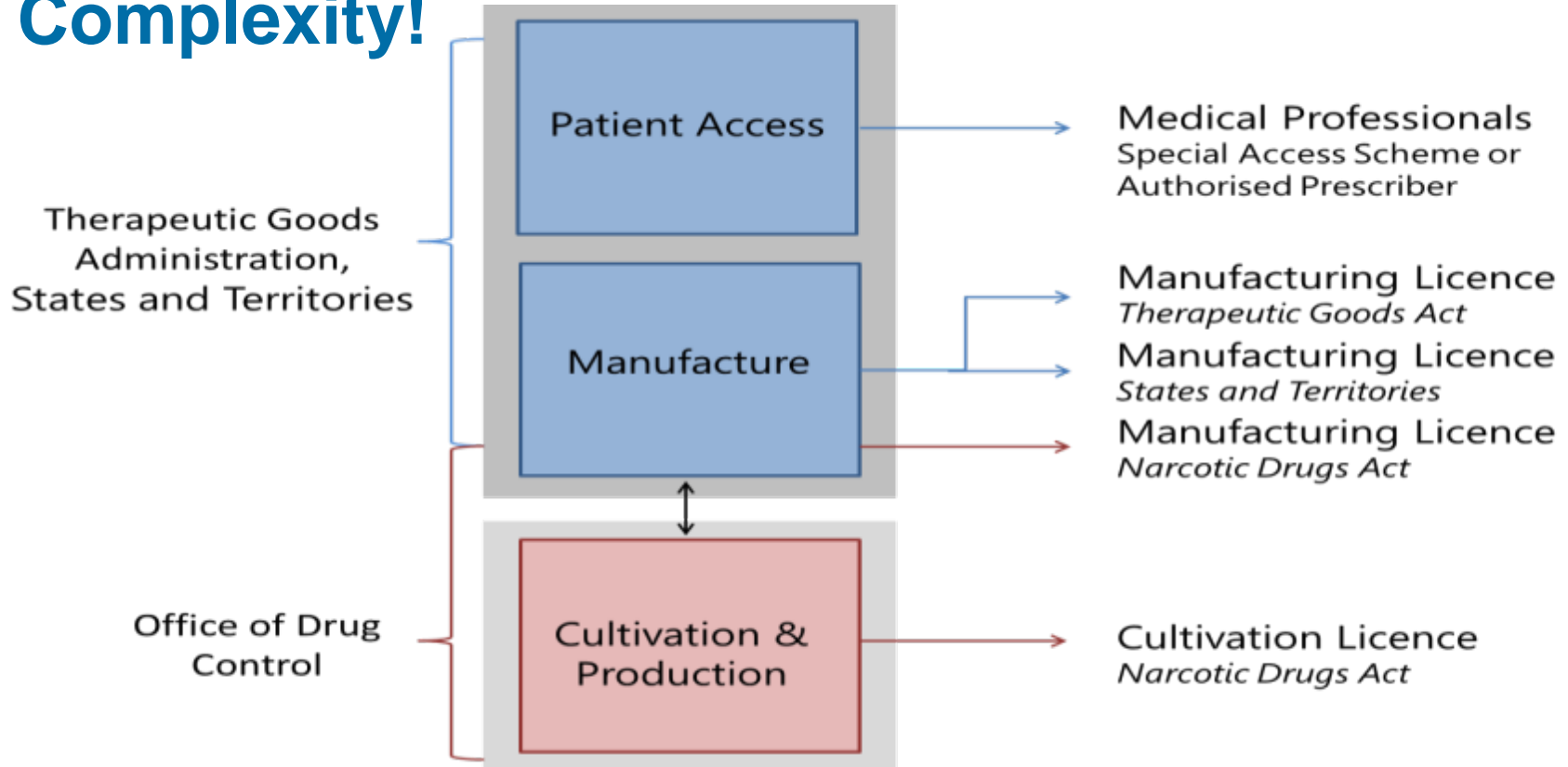
# Chronic non-cancer pain

- There is some evidence that the delta-9 tetrahydrocannabinol (THC) extract of cannabis can reduce pain in both MS-related neuropathic pain and other forms of neuropathic pain, but for many people the reduction in pain may be modest.
- There is insufficient information to make a conclusion about cannabinoids for the treatment of pain associated with arthritis and fibromyalgia.
- While some individuals with pain have reported that their use of opioids has been reduced when they also use medicinal cannabis, clinical studies in this area are still ongoing.



# Access to Medicinal Cannabis Products

# Complexity!



# Medicinal cannabis products are available through “unapproved products” pathways

- **One ARTG product available** - SATIVEX® indicated for refractory spasticity in Multiple Sclerosis
- **Clinical trials**
- **Authorised prescriber**
- **SAS A - notification pathway** for patients who are 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
- **SAS B - application pathway** for patients that do not fit SAS A (or for doctors who would like to use bulk imported stock)



# Individual importation of medicinal cannabis

- **Medical practitioners** can arrange patient by patient importation to fill prescriptions issued using TGA SAS A
  - Requires a licence under the *Customs (Prohibited Import) Regulations 1956*
- **Individual patients** can utilise travellers' exemption
  - to carry up to 3 months supply of medicines with them on a ship or aeroplane entering into Australia with a valid doctor's prescription
  - Prior State Health Department approval may also be required



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# Authorised Prescriber



An Authorised Prescriber is a medical practitioner who may supply a specified unapproved therapeutic good to patients with a specific indication

## **Authorised Prescribers must:**

- obtain approval from an HREC or endorsement from a specialist college
- have training and expertise appropriate for the condition and the proposed use of the product, and
- be able to best determine the needs of the patient and to monitor the outcome of therapy
- Submit a report every 6 months with the number of patients treated



# SASB

## Delegate considers the product, the patient and the prescriber

### Product

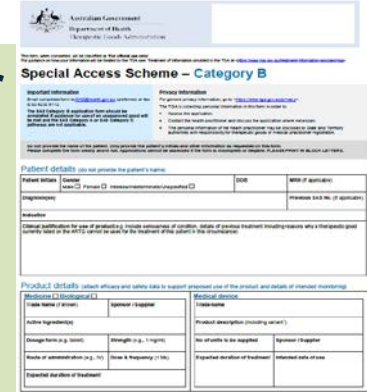
- TGO 93
- Appropriateness of formulation
- Dosage, Route of administration, Duration of treatment

### Patient

- Diagnosis, indication being treated and the seriousness of the condition
- details of past treatment and justification for use of an unapproved product
- Intended monitoring of efficacy/adverse effects

### Prescriber

- GP or specialist?
- Are they the patient's regular treating doctor?



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**Special Access Scheme – Category B**

**Important information:** This form is used to apply for a Special Access Scheme (SAS) for a medicine that is not registered in Australia. It is used to apply for a Special Access Scheme (SAS) for a medicine that is not registered in Australia.

**Product details (unless otherwise specified):**

Product name (as supplied)	Strength (e.g., 1 mg/ml)	Formulation (e.g., tablet)	Manufacturer
Product description (including serial)	How it will be supplied	Supplier (Supplier)	Intended date of use

**Patient details (you will provide the patient's name):**

First name	Last name	DOB	Sex of applicant
Address	Postcode	Telephone (incl. no. of applicant)	

**Product details (unless otherwise specified):**

Product name (as supplied)	Strength (e.g., 1 mg/ml)	Formulation (e.g., tablet)	Manufacturer
Product description (including serial)	How it will be supplied	Supplier (Supplier)	Intended date of use

# Streamlining of SASB application process



## Working with the states and territories

- Each state and territory has its own policy or legislation around access to medicinal cannabis products
- In January this year Minister Hunt wrote to each of the states and territory health Ministers encouraging them to remove duplication of assessment process for medicinal cannabis applications and agree to adopt a single online application portal for the submission of applications.
- A SAS online portal was already being developed as part of MMDR, it was decided to include state and territory cannabis requirements as part of this portal

# Streamlining of SASB application process

## NSW

- 2<sup>nd</sup> March 2018 Minister Hunt and NSW Health Minister Brad Hazzard announced that NSW and TGA would be working together to streamline patient access through the SAS.
- **NSW removing review committee** for medicinal cannabis applications and considering applications with a view to Schedule 8 requirements only
- developing **single NSW/TGA forms** for SAS
- **Single data input and decision emails** for the prescribers
- **A 48 hour decision timeframe for applications**
- On the 21st of March 2018 the NSW/TGA SAS forms were published

# Streamlining of SASB application process

## Council of Australian Governments meeting (COAG)

- On the 13<sup>th</sup> of April each of the state and territory health ministers met at COAG and agreed to “adopt the NSW/TGA medicinal cannabis trial”
- TGA is still working with the states and territories to find out to what extent they will be adopting the NSW/TGA approach.
- Some states may need to repeal legislation, for others it means significant policy change.
- Development of the SAS online portal is progressing rapidly despite the challenge of uncertainty regarding the state and territory requirements
- **The portal is due for release second half 2018**



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# QUESTIONS?