NSW GOVERNMENT

NSWNMA Medicinal Cannabis Forum

Understanding the NSW & Australian Regulatory Framework & Approach

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Centre for Medicinal Cannabis Research and Innovation

- Established June 2015
- Director - Professor Mary O'Kane, NSW Chief Scientist & Engineer
- Advisory Council
- NSW Government commitment to evidence-based approach for safe and effective use of cannabis medicines
- Further understanding of cannabis and cannabis medicines and support evidence-based innovation:
  - support the NSW Government funded clinical trials ($9 million)
    - Children with severe treatment-resistant epilepsy
    - Adults with advanced cancer (palliative care), particularly appetite-related symptoms
    - Chemotherapy patients suffering from nausea and vomiting
  - information and education – general public, health professionals, researchers on the NSW regulatory framework and access pathways as well as emerging research
  - funds other research, including a cultivation and production research project at the NSW Department of Primary Industries
  - advises the NSW Government on policy issues relating to medicinal cannabis and domestic and international developments in cannabis research and policy
  - collaborate with Commonwealth and state/territory regulators

Policy & Regulatory Timeline – NSW & Commonwealth

Initiation phase *

Nov 13 NSW Legislative Council Inquiry

Nov 14: NSW Chief Health Officer chairs Expert Panel - advice on clinical trials

Dec 14: Premier announces $9 million commitment for at least three clinical trials
Terminal Illness Cannabis Scheme (TICS) established

Regulatory framework

Jun 15: Scheduling of cannabidiol as Schedule 4 drug

Oct 15: Special Access Scheme & Authorised Prescriber Scheme clarified pathways

Feb 16: *Narcotic Drugs Act 1967* amended to enable domestic cultivation

Aug 16: NSW amends regulations - allow lawful prescribing & supply of a greater range of unregistered cannabis medicines (THC, nabiximols, dronabinol (as 'single' ingredients) could already be prescribed prior to this)

Nov 16: TGA creates new Schedule 8 entries for cannabis and THC

Feb 17: Companies can apply for a license to import and store products on-shore

Jun17: CW Disallowance motion to allow use of Special Access Scheme A passed

Jul 17: ODC consultation on allowing Australian exports & ensuring domestic supply

Research & policy

Sep16: TGA commissions national clinical guidance with states and territories

Feb 17: Australian Advisory Council on the Medicinal Use of Cannabis established

Mar 17: International Forum on Medicinal Cannabis (regulators) hosted by Centre

May 17: CS&E review of the Medicinal Cannabis Compassionate Use Scheme released

Aug 17: NSW Minister for Health and Minister for Medical Research requests work on driving

* Preclinical work and clinical trials pre-dates this period

Access & Prescribing Challenges

- **NSW Government commitment**
  - Promote safety, evidence-based approach
  - QUM/Good Medical Practice
  - $21M over four years

- **Highly complex plant**
  - leaves and flowering tops contain > 480 distinct compounds
  - > 100 cannabinoids – with own pharmacological actions, potential (therapeutic / adverse), toxicity
  - terpenes – preclinical data indicate these organic compounds may modify the effects of cannabinoids, and have psychoactive and behavioural effects

- **Long history of use – anecdote, limited high quality evidence**, weak/mixed design (changing)
  - **Variable effects**

    e.g. epilepsy early trial results 1:10 seizure free, 3:10 benefit; known to be pro- and anti-convulsant; NEJM (May 2017) 43% receiving product >50% reduction in seizures but so did 27% placebo
  - **Understanding reports**

    product? placebo? potentiates other drugs? biology? course of disease? mix of factors?
  - **Less heard** – no effect, side-effects

- **Information**
  - Public less familiar with unregistered products and implications
    e.g. barriers to making comparisons; therapeutic hierarchy rationale

Challenges *continued …*

- **International regulatory forum March 2017 hosted by Centre**
  - Israel, The Netherlands, Germany, Canada, New Zealand
  - Different models
  - Common issues and challenges: evidence, data collection, information & education, access to quality consistent product, costs

- **Most products not regulated to medicines standards internationally**
  - **Batch to batch inconsistencies –** issue for multi-morbidity, fragile health, drug-drug interaction
  - **Not all 'no/low THC' are in practice**
    e.g. ICCI EU tested 29 CBD oils - 60% had THC but no labelling; 34% discrepancies in actual CBD content; 2/3 had unsatisfactory levels of polyaromatic hydrocarbons (classified as carcinogens and genotoxic mutagens)
  - **No active ingredient at all -** exploitative
    e.g. 2015 FDA warning letters, 6/18 cannabidiol products had no cannabinoids detected
  - **Contaminants** - pesticides, microbial/fungal contamination
    e.g. Feb 2017 – news report Ca USA fungal contamination implicated in patient death); solvents, adulteration

- **Few registered medicines** (one in Australia)
  - Lack pharmacopoeia, 'MIMS' (product information/consumer medicine information)
  - Must meet minimum quality standard (Therapeutic Goods Order No. 93) BUT
  - **Australian 'wholesale' imports** - **most lack basic safety & efficacy data** i.e. pharmacokinetic & pharmacodynamics to inform product choice & formulation; dosing regimen; route of administration; implications for drug-drug interactions, effects on conditions, toxicity

- **Experience using unregistered therapeutic goods –** mainly hospital-based specialists

- **Entrepreneurial driven medical and prescribing practice**

Established medicines pathways

Product Registration

- Generally illegal to supply if not registered with the Therapeutic Goods Administration (ARTG) - assessed for safety, quality, efficacy
- Currently only one cannabis product registered but not marketed (to change from November 2017) therefore must be imported as an unregistered medicine
- Regulatory reforms allow prescribing & supply of cannabis products if requirements met, requirements reflect that products are unregistered medicines (CW) & S8 controlled substances (NSW)

Context

"All medicines carry a risk of producing adverse reactions in some patients. Products carrying a higher risk, including all prescription medicines and over-the-counter medicines , receive a higher degree of pre-market assessment and, where the benefits of taking the medicine outweigh the risk of adverse reactions, are registered on the Australian Register of Therapeutic Goods (ARTG). An example might be the approval of a new cancer medicine for a target population where it is known the medicine is likely to result in relatively severe side effects"

TGA, Product regulation according to risk https://www.tga.gov.au/product-regulation-according-risk

Registered medicines

TGA conduct detailed evaluations of higher risk (registered) medicines before they can be approved for use in Australia in order to fully evaluate the balance between the benefits and the risk. The data in support of a new registered medicine should establish the quality, safety and effectiveness of the proposed product for the proposed usage (indication).

Medicines pathways *continued*

Listed medicines

Products such as vitamins, minerals, sunscreens and herbal complementary medicines carry a lower risk, and receive a lesser degree of initial assessment, than higher risk medicines. These products are listed on the ARTG provided certain conditions are met. The applicant must certifying that the claims made about the effectiveness of their product are accurate, that the relevant quality and labelling and packaging standards have been followed, that the medicine contains only approved ingredients and that the manufacturing facilities and processes have been assessed for compliance with standards of Good Manufacturing Practice.

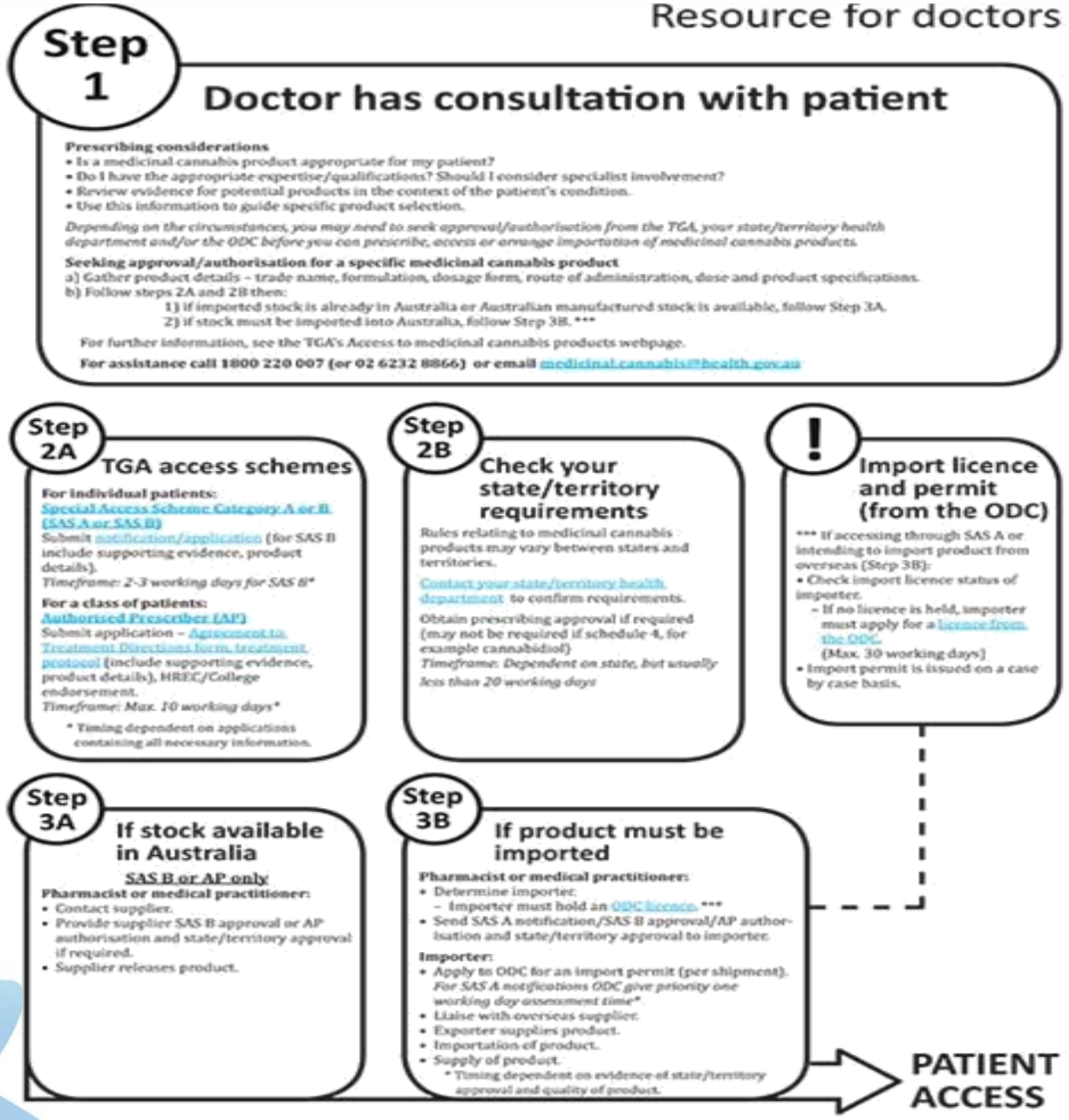
Access to unregistered medicines

- Commonwealth Law allows for access to unregistered medicines in some circumstances
- Established TGA pathways
  - **Clinical trial schemes**
  - **Authorised Prescriber** – protocol for an identified cohort of patients, specified circumstances, specific product & dose, written consent; requires Ethics Cttee/Specialist College endorsement
  - **Special Access Scheme** (Cat A or B) – prescribed for each individual patient

    SAS A - notification, requires import/export permits (less timely)

    "*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 for authority (only SAS B can use on-shore products)



Source: TGA https://www.tga.gov.au/access-medicinal-cannabis-products-steps-using-access-schemes

NSW process and requirements

- An authority issued by Secretary NSW Health**,** to prescribe and supply a product for a particular patient (or patients in a clinical trial) http://www.health.nsw.gov.au/pharmaceutical/Pages/cannabis-products.aspx
    - Cannabidiol-only medicines (<2% of other cannabinoids) - TGA approval only
    - Approval under NSW *Children and Young Person's Act 1998* may be required
    - Application may be referred to the Cannabis Products Sub-committee to advise delegate-clinicians expert in use of medicines including unapproved medicines, consult specialist disciplines as needed
- An approval from Commonwealth Department of Health to import and/or supply product under Special Access, Authorised Prescriber or Clinical Trial schemes https://www.tga.gov.au/access-medicinal-cannabis-products-steps-using-access-schemes
- Can make applications to TGA and NSW Health at the same time
- Product must meet the standards for cultivation and manufacture developed by the TGA, consistent with any other medicine (for cannabis - Therapeutic Goods Order 93) https://www.tga.gov.au/therapeutic-goods-orders)

Prescriber

- Must be a medical practitioner
- Expected to be specialist in the management of the disease or condition being treated
- No limits on conditions
- Application is consistent with how other unregistered products are assessed *

* NSW: authority required from NSW Health to prescribe certain psychostimulant medications, some schedule 8 opioid medications, some benzodiazepines, and all unregistered or pharmacy extemporaneously-compounded schedule 8 products.

* Unregistered products obtained by a Queensland Hospital under Special Access Scheme Category B e.g. Midodrine (orthostatic hypotension); Rufinamide (seizures related to Lennox-Gastaut syndrome); Benzbromarone (gout); Mexiltine (chronic neuropathic pain) Donovan P. (2017) *Access to unregistered drugs in Australia*; Australian Prescriber https://www.nps.org.au/australian-prescriber/articles/access-to-unregistered-drugs-in-australia#article

Application consistent with how other unregistered products are assessed

Individual Patient Use form

Section F: Patient ....▶ *If applying for the purpose of conducting a clinical trial under the CTN or CTX scheme, go to Section H*		
Patient Name:		
	(first names)	*(family name)*
Also known as *(if applicable)*:		
	(first names)	*(family name)*
Patient Residential Address:		
Suburb/Town:		Postcode:

Provide the following details for the product	
Trade Name	
Active ingredient(s)	
Manufacturer Name	
Manufacturer Address	
Dose form and strength	

Section G: Clinical indication and use *(Attach any additional information that may be of assistance in assessing your application)*
Diagnosis relevant to treatment with cannabis:
Clinical indication for use of cannabis product:
Describe previous pharmacotherapy and/or non-pharmacotherapy to treat the patient's condition
Explain why you are prescribing this product for this patient, addressing potential benefits and harms
Provide a summary of the scientific evidence relied upon to support the treatment: *(Attach or cite scientific evidence relied upon e.g. journal articles; for nabiximols in multiple sclerosis, ARTG listing is the evidence)*

Application to prescribe & supply cannabis product

**For drugs dosed on a mg/kg basis or mg/m²*

A. Patient details

Patient name: _____ MRN: _____

Date of Birth: _____ _____ Weight/ BSA* _____

Home Address: _____

B. Planned treatment date: _____

C. Product Profile

Active ingredient(s) (Australian Approved Name)	
Trade Name	
Dosage Form(s) – provide full details	
Manufacturer/Supplier	
Pharmacological class and action (summary)	

F. Reasons for request

Explain your reasons for wanting to use this drug.

Treatment details: Dosage, administration details, duration of treatment, concomitant therapy, etc	
Treatment history: Describe previous therapy and outcomes.	
Alternative therapy: Describe therapy currently available for this indication (if not already described in treatment history).	
Monitoring requirements: Describe the objective criteria that will be used to monitor effectiveness.	

Rationale: controlled substance - promote patient safety, avoid misuse and diversion

Application requirements	Why?
1. Evidence standard treatments known to be effective have been tried	• Approved treatments with better evidence or safety information should be tried before experimental products
2. Reasons for wanting to prescribe the product	• Prescribers must understand why an experimental product is appropriate
3. Evidence of the suitability of the medicine to treat the patient's particular condition, symptoms	• Limited evidence for safety and efficacy • Prescribers must understand the product information (or lack thereof) to select the most appropriate product
4. Assessment of potential benefits and harms	• Good prescribing practice - evidence-based treatment, benefits and risks of a specific product
5. Evidence of the quality, safety and efficacy of the proposed product, including active ingredients, dose and strength, mode of administration	• Many products have little or no information about their composition, PK data or efficacy • Mode of administration can impact metabolism of a product (e.g. ethanol based oral-mucosal spray vs oil via PEG)
6. How the patient will be monitored and assessed to evaluate efficacy, whether treatment should continue	• To promote patient safety during treatment • To reduce the risk of prescriber-patient conflicts
7. How known or potential side-effects or harms will be monitored	• Prescribers must monitor patient receiving unapproved experimental products more closely than for standard approved treatments

Schedule 8 Medicinal Cannabis Products

Jurisdictional snapshot

Source: Therapeutic Goods Administration (adapted)

State / Territory	Specialists	GPs	Process
ACT	Yes	Yes with specialist support	Specific process
QLD – patient class (CINV, palliative care, MS, resistant paediatric epilepsy)*	Yes - certain specialists	No	Must follow QLD clinical guidance; no application needed
QLD – single patient	Yes	Yes – with longitudinal treating relationship with the patient	Application to DG of QLD Health
NSW	Yes	Yes with specialist support	Specific process
VIC – General S8 (imported or non VIC manufacture) **	Yes	Yes	Standard S8 process
TAS	Yes	No	Specific process
SA standard	Yes	Yes with specialist support	Standard S8 process
WA – notification (like TGAs AP)	Yes	Initial application made by specialist then GP ongoing	Specific process
WA - authorisation (like TGA SASB)	Yes	Yes with specialist support	Specific process
NT	Yes	Initial application made by specialist then GP ongoing	Standard S8 process

* Patient class prescribers must notify Department within 7 days of commencing treatment

** *Access to Medicinal Cannabis Act 2016* (Vic) will provide an eligible patient pathway (currently children with intractable epilepsy) but Act not yet commenced and will only apply to locally produced product. When commences, initial application made by specialist and then GP ongoing prescribing; specific process

S8 Schedule 4 Medicinal Cannabis Products

Jurisdictional snapshot

Source: Therapeutic Goods Administration (adapted)

Most jurisdictions do not have specific requirements for S4 medicinal cannabis products except the following (e.g. NSW – cannabidiol requires TGA approval only)

State / Territory	Specialists	GPs	Process
QLD – patient class (CINV, palliative care, MS, resistant paediatric epilepsy)	Yes (certain specialists)	No	Must follow QLD clinical guidance; no application needed
QLD – single patient	Yes	Yes – with longitudinal treating relationship with the patient	Application to DG of QLD Health
TAS	Yes	Not eligible to prescribe	Specific process

For further information – jurisdictions outside NSW			
ACT	http://health.act.gov.au/public-information/businesses/pharmaceutical-services/medicinal-cannabis	**SA**	http://www.sahealth.sa.gov.au/medicinalcannabis
VIC	https://www2.health.vic.gov.au/public-health/drugs-and-poisons/medicinal-cannabis	**WA**	http://ww2.health.wa.gov.au/Articles/A_E/Cannabis-based-products
QLD	https://www.health.qld.gov.au/public-health/topics/medicinal-cannabis/overview	**NT**	https://health.nt.gov.au/professionals/environmental-health/therapeutic-medicines-containing-cannabinoids-medicinal-cannabis
TAS	http://www.dhhs.tas.gov.au/psbtas/publications		

NSW Medicinal Cannabis Compassionate Use Scheme

- Established December 2014 – to extend compassion to adults with a terminal illness (formerly Terminal Illness Cannabis Scheme)
- **Not supply** - guidelines for NSW Police to exercise discretion; registrants with small quantity cannabis/products not lawfully prescribed + up to 3 registered carers
- Maximum quantities: Cannabis leaf 15 g, Cannabis oil 1g, cannabis resin 2.5 g
- Certification by a registered medical practitioner involved in ongoing care that person has a terminal illness as defined by the Scheme (not endorsing use):

  'an illness which, in reasonable medical judgement will, in the normal course, without the application of extraordinary measures or of treatment unacceptable to the patient, result in the death of the patient.'

- Current status: 521 registered patients (384 active registrations), 663 registered carers
- **Review of scheme released May 2017**
  - Continue to be available to people with terminal illness in recognition system still being bedded down
  - Administrative changes to improve operations
  - Not extend to others- recognise risks; encourage lawful pathways available

Progress

Clinical trials in NSW

- 11 currently registered (government and industry $); ~1,000 people in NSW will participate
- Building network of clinicians (learning) as well as evidence

Government funded paediatric Compassionate Access Scheme (CAS) & trials

- 21 paediatric neurologists are Authorised Prescribers
- Children with severe treatment-resistant epilepsy access Epidiolex® under CAS from July 2016
- To date 50 treated
- Additional 26 doses – takes to 66 children at any one time able to be treated (from Sept 2017)
- Government funded RCT using novel therapeutic (Cannabidivarin) commencing Q1 2018
- NSW children accessing two industry funded Phase 3 international RCTs of Epidiolex® for seizures in:
    - Tuberous Sclerosis Complex
    - Dravet syndrome

Progress *continued*

Chemotherapy induced nausea and vomiting (CINV)

- Cannabinoid product for nausea where other non-cannabinoid anti-emetics have been ineffective
- Status
  - Stage 1 [on track]: ten sites across NSW, 80 patients
  - Stage 2 [scheduled Q1 2018]: additional 250 patients
- **Post-treatment continued access for those receiving benefit** – standardised protocol established to facilitate access
- Patients are also accessing similar products outside this trial through the TGA Special Access Scheme Category B

Palliative care

- Focusing on quality of life, particularly appetite and appetite-related symptoms
- Status
  - Stage 1 [on track]: pharmacokinetics to understand drug and dosing, 2 hospital sites, 30 patients,
  - Stage 2 [scheduled Q1 2018]: additional 250 patients, multiple regional, metropolitan sites,
- **Centre convened meeting with palliative care specialists, research leaders and NSW Health August 2017**
  - Access pathways for people with terminal illness where potential benefits > risks
  - Outcome: develop protocols to assist, build on models of paediatric epilepsy CAS Authorised Prescriber network with protocol; CINV post-treatment standard protocol

Progress *continued*

Applications by NSW practitioners - authorisation to prescribe & supply to individuals

- Gradually increasing; excluding clinical trials and Authorised prescriber:
  - Applications to NSW Health: 43 (end July 2017); excludes cannabidiol-only applications
  - Applications to TGA under Special Access Scheme B: cannabidiol only12 (end July); plus 43 THC/CBD formulations
- NSW Health application form revised to make information requirements clearer; criteria published; following up with individual practitioners approved/not approved so process and rationale understood

National guidance

- Commissioned by TGA, NSW supporting ($50,000)
- Conditions: epilepsy (children & adults), palliative care, pain (cancer or AIDS related; neuropathic; chronic non-cancer), nausea and vomiting (cancer or AIDS related), Multiple Sclerosis (spasticity)
- Progressing: several meetings over 2017; next on 13 September in Sydney
- TGA released list of clinical trials and studies used to inform guidance being developed (August 2017)
- Guidance to be released for different indications from end 2017

Driving

- Minister requested work be undertaken on driving related issues
- Offence of driving with presence of cannabis (THC) – laws predate lawful prescribing
- High level interagency steering committee to review issues, consult and provide advice to Government

How can we help?

- **Questions and information needs**
  - We can inform FAQs and other resources for your membership
  - We can provide content for your communications
  - We are updating the Centre website to address common questions and topic areas
  - We can provide general advice as questions arise
- **Contact us by email at CMCRI@moh.health.nsw.gov.au**