



Australian Government  
Department of Health  
Therapeutic Goods Administration

# Changes to codeine product access: background to the decision to change from over-the-counter to prescription only

**Adjunct Professor John Skerritt**

Deputy Secretary for Health Products Regulation

Commonwealth Department of Health

November 2017

**TGA** Health Safety  
Regulation

# This presentation

- Evidence of codeine harm, misuse and abuse in Australia
- Codeine rescheduling process
- Implementation of the decision to up-schedule codeine-containing compounds
- Stakeholder engagement - NCCIWG
- Impacts on Rural and Regional Australia

# Public health safety concerns with codeine

- Codeine effects depend on an individual's ability to **metabolise it to morphine**
- Cases of **respiratory depression and death due to ultra-rapid metabolism** of codeine
- Many consumers inappropriately use **OTC codeine on a chronic basis**
- Substantial evidence of **harm from the misuse / abuse of OTC codeine**
- Mortality and morbidity (intestinal, renal and hepatotoxicity) sometimes due to massive paracetamol and ibuprofen consumption but **overdose usually the result of codeine-seeking behaviour**



# Codeine related deaths

## **Roxburgh et al (*Medical Journal of Australia 2015*)**

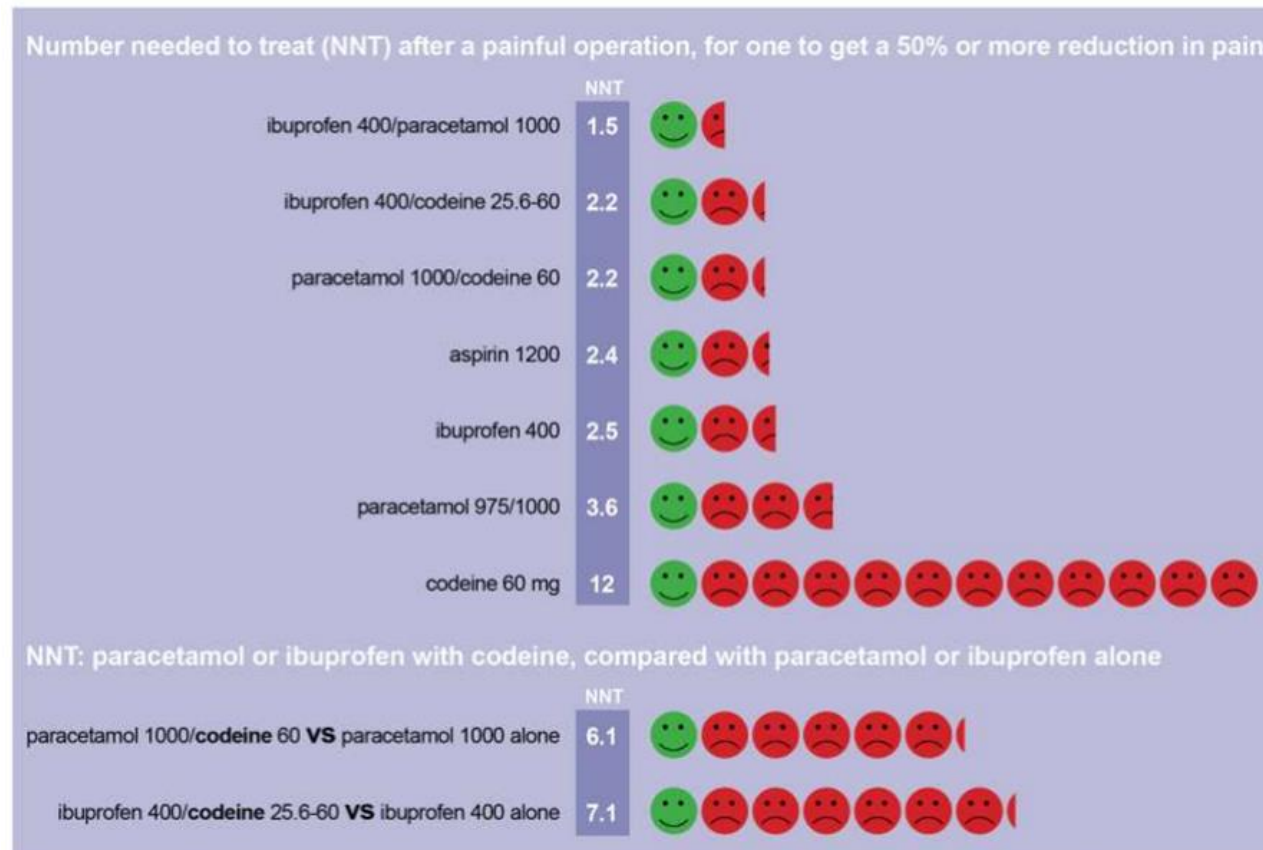
- 1437 codeine related deaths between 2000 and 2013
- Numbers more than doubled from 2000 to 2009
- Accidental overdose accounted for most of the increase in death
- 84 % due to multiple drug toxicity, 8 % specifically to codeine toxicity
- For every two S8 opioid deaths in 2009, there was one codeine-related death
- Where type of codeine was reported 40 % was OTC codeine

## **Deaths for 2007 to 2011 (*National Coronial Information System Aug 2014*)**

- Codeine without morphine detected – 573
- Morphine plus codeine – 515
- Use of codeine combination product potentially implicated – 769

# Little evidence that OTC codeine is more effective than alternatives without codeine

Summary of Cochrane systematic reviews of the medical literature



- Summarised by NPS Medicineswise [www.nps.org.au/medical-info/clinical-topics/news/paracetamol-ibuprofen-combinations-for-acute-pain](http://www.nps.org.au/medical-info/clinical-topics/news/paracetamol-ibuprofen-combinations-for-acute-pain)
- Very recent RCT evidence in post-operative pain *AK Chang et al. JAMA 318:1661 Nov 2017*
- Codeine also associated with constipation, neuro-inflammation/hyperalgesia

# 6 MISUSE OF PHARMACEUTICALS



**1 in 20** (4.8%) people misused a pharmaceutical in the last 12 months

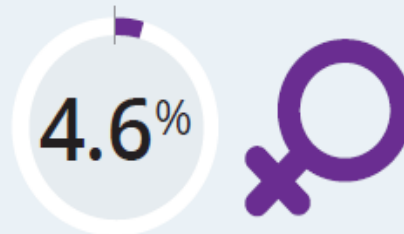
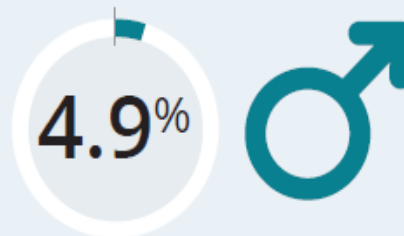


**1 in 8** (12.8%) had misused a pharmaceutical in their lifetime

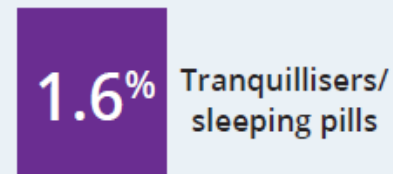


## Pharmaceutical misuse

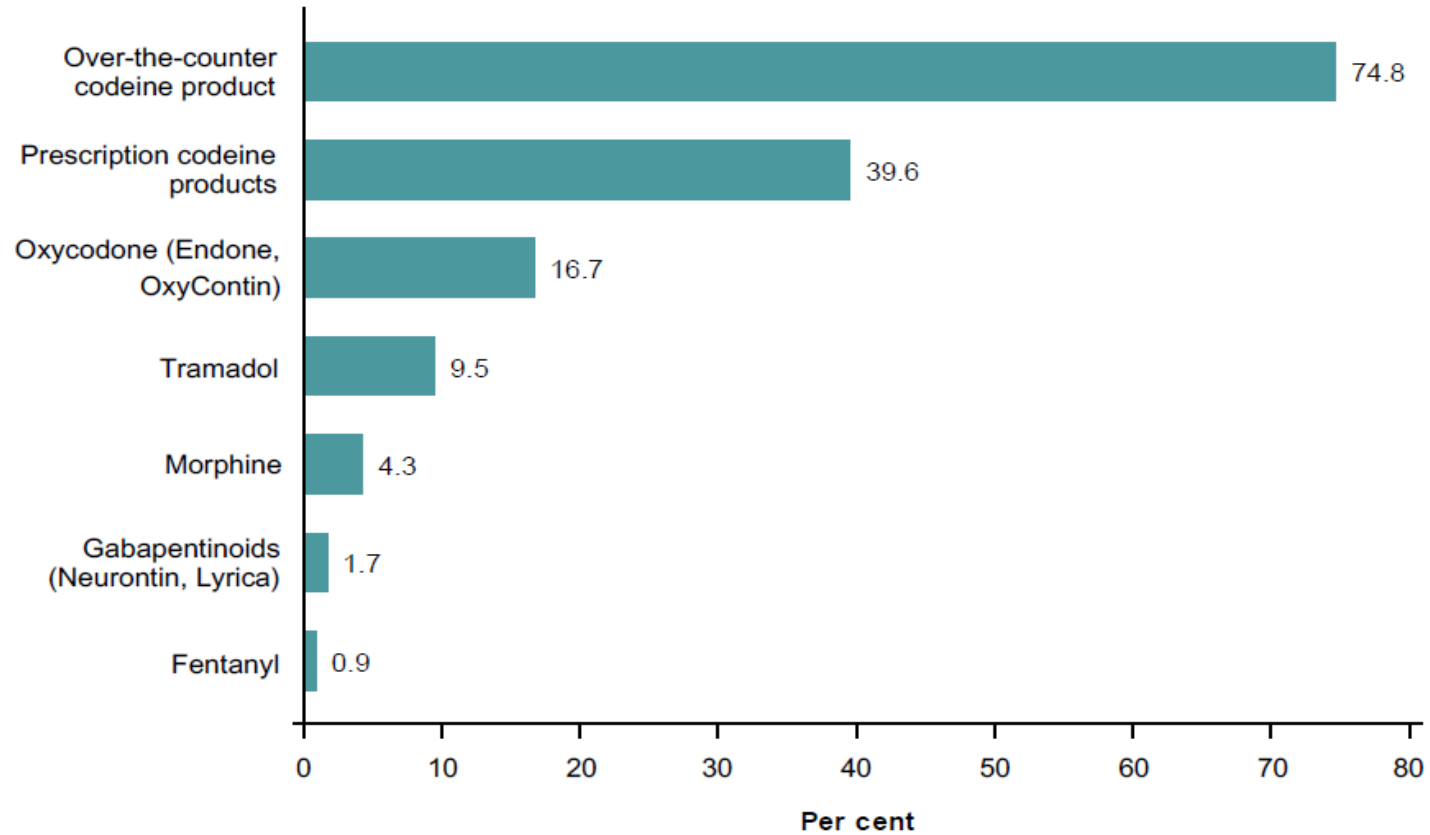
Males and females misused pharmaceuticals at similar rates



Pain-killers/opioids most commonly misused pharmaceutical, followed by Tranquillisers/sleeping pills







(a) Used in the past 12 months.

Note: Base is recent users of pain-killers and opiates.

Source: Table 6.7.

**Figure 6.3: Types of pain-killers/opiates misused, recent(a) users of pain-killers/opiates aged 14 and over, 2016 (%)**

# What is Scheduling ?

- A national classification system that controls how medicines and poisons are made available to the public
- Substances classified by level of **regulatory control over their availability**
- The Poisons Standard consists of decisions regarding the classification of substances into **Schedules**

<b>Schedule 1</b>	Not currently in use
<b>Schedule 2</b>	Pharmacy Medicine
<b>Schedule 3</b>	Pharmacist Only Medicine
<b>Schedule 4</b>	Prescription Only Medicine OR Prescription Animal Remedy
<b>Schedule 5</b>	Caution
<b>Schedule 6</b>	Poison
<b>Schedule 7</b>	Dangerous Poison
<b>Schedule 8</b>	Controlled Drug
<b>Schedule 9</b>	Prohibited Substance
<b>Schedule 10</b>	Substances of such danger to health as to warrant prohibition of sale, supply and use



# *All scheduling decisions include consideration of a set of “factors” under the Scheduling Policy Framework*

## **Scheduling Policy Factors for Pharmacist-Only Medicines (Schedule 3)**

- The medicine is **substantially safe with pharmacist intervention** to ensure the quality use of the medicine. There may be potential for harm if used inappropriately
- The **use of the medicine at established therapeutic dosages is not expected to produce dependence**
- Where there is a risk of misuse, abuse or illicit use identified, **the risk can be minimised through monitoring by a pharmacist**

# Relevant SPF Factors for Prescription Only Medicines (Schedule 4)

- The **ailments or symptoms that the substance is used for** require medical, veterinary or dental intervention
- The use of the substance requires **adjunctive therapy or evaluation**
- The use of the substance at **established therapeutic dosage levels may produce dependency** but has a moderate propensity for misuse, abuse or illicit use
- The **seriousness, severity and frequency of adverse effects** are such that monitoring or intervention by a medical practitioner is required to minimise risk
- The **margin of safety between the therapeutic and toxic dose** of the substance is such that it requires medical, intervention to minimise risk
- The **use of the substance has/ is likely to contribute to communal harm**

# Current availability of codeine products

## Schedule 2 – Pharmacy only - CODEINE preparations for coughs and colds when:

- compounded with phenylephrine and not more than one analgesic substance
- 10 mg or less of codeine per tablet or liquids with 0.25 % or less of codeine
- Recommended daily dose not exceeding 60 mg and in packs containing not more than 6 days' supply
- e.g. **cough relief products** such as **Codral** and **Demazin**, as well as pharmacy generic cough medicines that contain codeine

## Schedule 3 – Pharmacist only - CODEINE when:

- compounded with one or more other active substances, of which not more than one is an analgesic
- 12 mg or less of codeine per tablet or liquids with 0.25 % or less of codeine
- Recommended daily dose not exceeding 100 mg and in packs containing not more than 5 days' supply
- e.g. **combination pain relief medicines** such as **Panadeine**, **Nurofen Plus** and **Mersyndol**, as well as pharmacy generic products that contain codeine

## Amendments to the Poisons Standard (rescheduling process)

- Any individual or organisation can apply to have a substance rescheduled
- The decision is made by the Secretary (not the Minister) of Health, but in practice a senior medical doctor at TGA makes the decision as a "delegate"
- The delegate examines must determine the scope of the current entry and whether other schedule(s) are more appropriate
- SPF Factors and considerations under S52e of the Therapeutic Goods Act
- The decision making process includes advice from a Ministerial Advisory Committee (ACMS) and extensive public consultation periods

# “Matters to be considered in making a scheduling decision”

*Defined in section 52E of the Therapeutic Goods Act 1989*

- a) the risks and benefits of the use of a substance
- b) the purposes for which a substance is to be used and the extent of use of a substance
- c) the toxicity of a substance
- d) the dosage, formulation, labelling, packaging and presentation of a substance
- e) the potential for abuse of a substance
- f) any other matters that the Secretary considers necessary to protect public health



## **Therapeutic Goods Act 1989**

No. 21, 1990

### **Compilation No. 68**

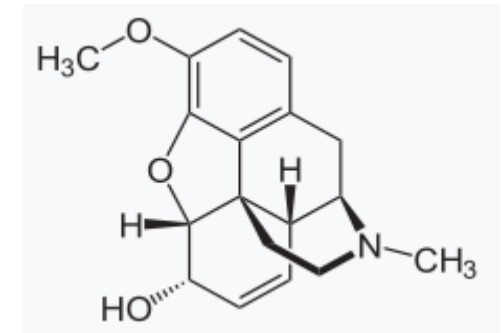
<b>Compilation date:</b>	1 July 2017
<b>Includes amendments up to:</b>	Act No. 47, 2017
<b>Registered:</b>	13 July 2017

# Consideration of the evidence

## TGA Safety Reviews (in-house & commissioned)

- **2012:** Lack of evidence to support the efficacy of OTC codeine cough and cold medicines in children under 12 years of age
- **2015:** Contra-indicated the use of codeine in children younger under 12 years of age for any reason, and in children 12-18 years post adenotonsillectomy
- **2016:** Limited evidence to support the efficacy of OTC codeine as an analgesic

*“The combination of lack of efficacy, risk of acute toxicity and dependence suggests that the use of OTC codeine is not warranted”  
(O’Reilly D et al. BMJ Case Reports 2015)*



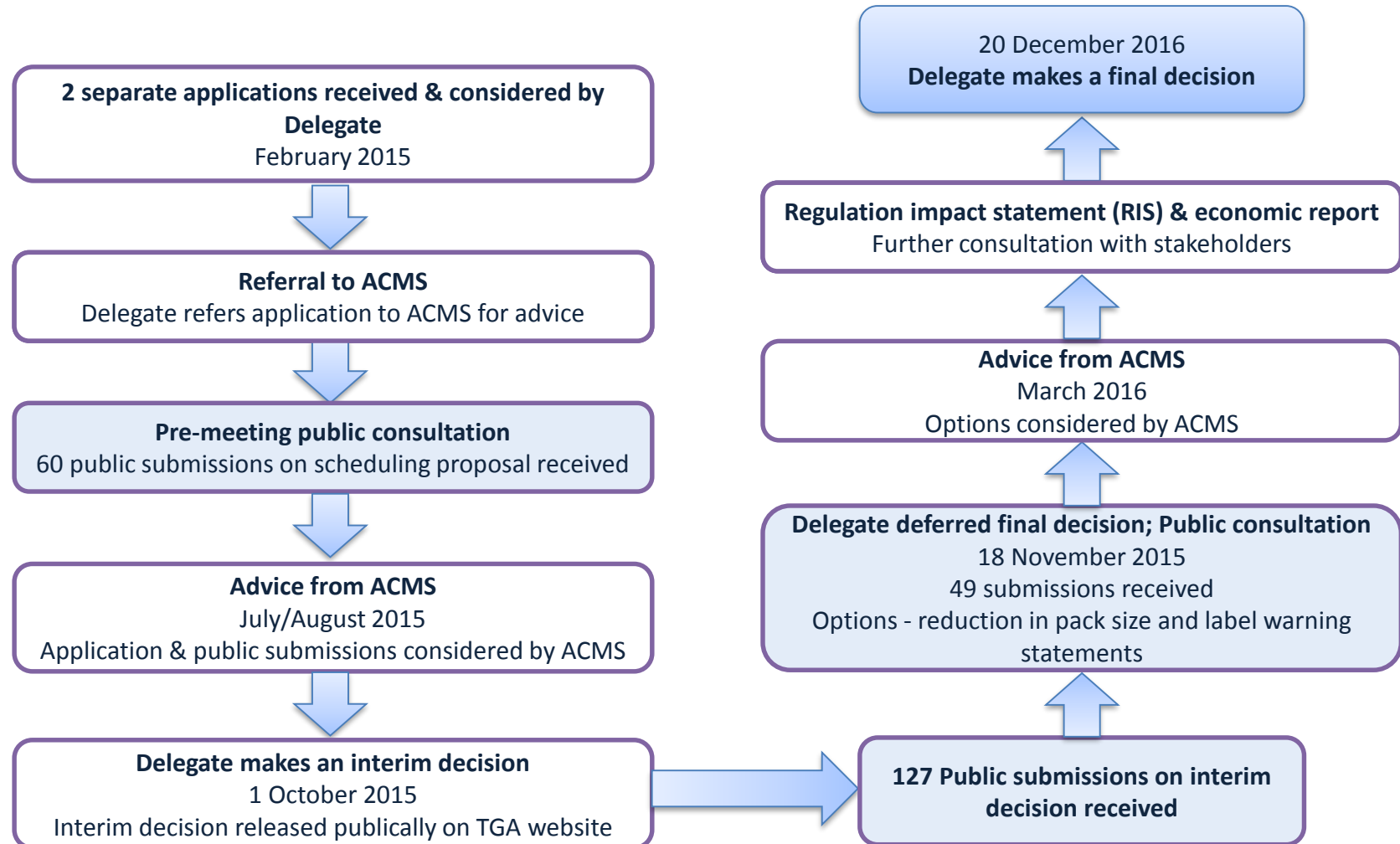


# Stakeholder Engagement



- 3 public consultation periods with over 230 submissions
- Targeted consultation with:
  - Peak bodies (PGA, AMA, ASMI, PSA, RACGP, ANZCA.....)
  - Sponsors/manufacturers of low-dose codeine containing medicines
  - Broader Department of Health (MBS & PBS)
  - State and territory health departments through the ACMS in July 2015 and March 2016

# Codeine rescheduling process



## Release of the decision - 20 December 2016



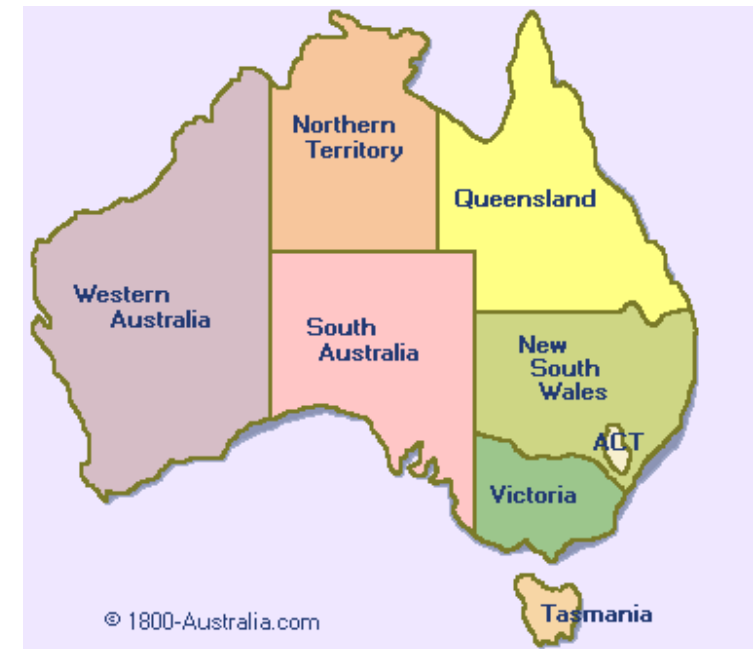
- **Regulation Impact Statement (RIS) for Codeine**
  - Outlined the economic, social and regulatory impacts of changing the way codeine is made available to the public
- **KPMG economic modelling report**
  - Regulatory and economic impacts of scheduling options modelled
  - Net benefit only achievable when low-dose codeine was up-scheduled to prescription only
- **FAQs** for healthcare professionals, pharmacists and consumers
- Links to 3 **scientific reports**
- **Company sponsors** of low-dose codeine products notified
  - Some will convert products to S4, others will withdraw them

# KPMG: Economic effects of codeine up-scheduling

- **Some increase** in the numbers of GP consultations
- **Unlikely that consumers will attend GP solely for a prescription for codeine**, but consultations likely to be for chronic pain or other medical conditions
- **Additional costs to the MBS** of \$204 m over 10 years
  - 83 % of these increased costs identified relate to costs of improved treatment options rather than costs of additional GP visits to obtain prescriptions
- The **overall positive net benefit to society** ~\$5.2 bn over 10 years, due to:
  - accidental death prevention
  - improved quality of life, due to more effective treatment options
  - prevention of adverse events related to unintentional overdose of paracetamol or ibuprofen
  - reduced dependence and reduced risk of dependence

# Implementation of scheduling recommendations

- **States and territories adopt by reference** scheduling recommendations in the Poisons Standard and give effect to them through their drugs and poisons legislation
- Each jurisdiction reserves the **right to implement a different scheduling decision** to that included in the Poisons Standard
- AHMAC (Heads of state and territory health departments) committed to **national uniformity**
- **So exceptions are rare** e.g. additional labelling requirements of S3 OTC medicines in QLD, separate framework for Victorian-produced medicinal cannabis



# Widespread support from professional and consumer groups for up-scheduling of codeine-containing products

- AMA
- RACGP
- Rural Doctors Association of Australia
- RACP
- Faculty of Pain Medicine, ANZCA
- Chapter of Addiction Medicine
- Pain Australia
- Consumer Health Forum



# Nationally Coordinated Codeine Implementation Working Group (NCCIWG)

## Objectives

- Assist with implementation
- Assist with the identification of education, information gaps in the various sectors
- Find innovative ways to disseminate information
- Assist in determining appropriate, consistent key messages for each sector
- Assist in assessing expected impacts on chronic pain patients (including in regional and remote Australia)

# Nationally Coordinated Codeine Implementation Working Group (NCCIWG)

## Representation

- Consumer groups
- States and Territories
- Health practitioners (medical, nursing, allied health – physiotherapy, pharmacy etc.)
- Clinical colleges/ societies (Pain/Addiction Medicine/AMA/ACRRM/PGA/PSA etc.)
- NPS MedicineWise, ScriptWise



# Rural and remote Australia

- Representation on NCCIWG
- Department of Health Roadshows
- NPS MedicineWise “regional field force” targeting rural communities
- Engagement of PHNs
- Specific communications strategies (e.g. Pain Australia etc.) with a regional focus
- Aged care facilities
- Aboriginal Health Organisations
- Codeine hub (specific link for rural and remote communities)



## Codeine hub: [www.tga.gov.au/codeine](http://www.tga.gov.au/codeine)

- Changes to patient access for codeine-containing compounds explained
- Specific information for rural and remote communities provided
- Links to information on chronic pain management, support services etc.
- Alternatives to physical access to GPs (prescribing by registered nurses, phone advice etc.)
- Links to community health centres and remote health services