Australian Government
Department of Health
Therapeutic Goods Administration

Interim decision and reasons for decision by delegate of the Secretary to the Department of Health

5 April 2016

(ACMS meeting – March 2016)

Notice under subsections 42ZCZP of the Therapeutic Goods Regulations 1990 (the Regulations)

A delegate of the Secretary to the Department of Health hereby gives notice of delegate's interim decisions for amending the Poisons Standard (commonly referred to as the *Standard for the Uniform Scheduling of Medicines and Poisons* - SUSMP) under subsections 42ZCZP the Therapeutic Goods Regulations 1990 (the Regulations). This notice also provides the reasons for each decision and the date of effect (the implementation date) of the decision.

The delegate's interim decisions and reasons relate to:

- A scheduling proposal initially referred to the March 2016 meeting of the Advisory Committee on Medicines Scheduling (ACMS#17).

Scheduling proposals referred to the expert advisory committees

Pre-meeting public notice

A 'pre-meeting' public notice inviting submissions on the scheduling proposals referred to the expert advisory committees was published on 20 January 2016 on the TGA website at: Public notice about scheduling.

Redacted versions of public submissions received in response to the public notice will be published on or after the date of this notice at: Public submissions on scheduling matters.

Interim decisions

This notice provides the interim decisions of the delegates, the reasons for those decisions and invites further submissions from the applicant and parties who made valid submissions in response to the original invitations for submissions (published on 20 January 2016 at https://www.tga.gov.au/consultation-invitation/consultation-proposed-amendments-poisons-standard-acms-and-accs-meeting-march-2016).

Further submissions must be relevant to the proposed amendment, must address a matter mentioned in section 52E of the *Therapeutic Goods Act 1989* and be received by the closing date **19 April 2016**.

Further submissions from parties other than those who made a valid submission in response to the original invitation or the applicant, or those received after the closing date, need not be considered by the delegate.

Please note that all valid submissions received on or before the closing date will be published following removal of confidential information. It is up to the person making the submissions to highlight any information which they wish to be considered as confidential. Material claimed to be commercial-in-confidence will be considered against the guidelines for the use and release of confidential information set out in Chapter 6 of the *Scheduling Policy Framework for Medicines and Chemicals* (SPF, 2015), issued by the Australian Health Ministers' Advisory Council (AHMAC). The SPF is accessible at: AHMAC - Scheduling policy framework for medicines and chemicals.

Persons making submissions are strongly encouraged to lodge submissions in electronic format (word or unsecured PDF preferred) via the email address provided below. Submissions, preferably in electronic format, should be made to:

> Medicines.Scheduling@tga.gov.au for items referred to the Advisory Committee on Medicines Scheduling.

The closing date for further submissions is **19 April 2016**.

Privacy and your personal information

Your personal information is protected by law, including the *Privacy Act 1988*. It is collected by the Australian Government Department of Health for the purposes of identifying the person making a submission as part of the public invitation process, and contacting that person about their submission, for example to seek clarification of issues raised in the submissions.

The consequences of not providing your personal information may result in the Department being unable to communicate with you about your submission.

The Department is unlikely to disclose your personal information it has collected as part of the public comment process to any other Department, body or person or to overseas recipients.

More information about the Department's management of personal information is contained in the Department's privacy policy. The Department's privacy policy contains information such as how you may access the personal information the Department holds about you, how you can seek correction of it, and how you may complain about a breach of the Australian Privacy Principles.

The Department's privacy policy is available on the Department of Health website.

Alternatively, you may contact the Department by telephone on 02 6289 1555 or freecall 1800 020 103, or by using the online enquiries form.

Part A - Interim decision on a matter referred to an expert advisory committee

1. Scheduling proposals referred to the March 2016 meeting of the Advisory Committee on Medicines Scheduling (ACMS#17)

1.1 Cannabis

Scheduling proposal

The medicines scheduling delegate (the delegate) has referred the following scheduling proposal for consideration by the Advisory Committee on Medicines Scheduling (ACMS):

- To enable appropriate access to medicinal cannabis products by creating new Schedule 8 entries for the following substances for internal human therapeutic use:
  - Cannabis (plant and flowering tops),
  - Botanically derived extracts (or derivatives) of cannabis, and
  - Tetrahydrocannabinols (THC) where they are botanically derived from cannabis,

  including when prepared or packed for therapeutic use, and where the substances have been:
  - produced or manufactured in accordance with the *Narcotic Drugs Act 1967*; or
  - imported in accordance with the Customs (Prohibited Imports) Regulations 1956.

  except when included elsewhere in Schedule 8 or Schedule 4.
- Cannabis and Tetrahydrocannabinols would remain Schedule 9 substances:
  - for human therapeutic use when it does not fit the above criteria, or
  - when not for human therapeutic use, or
  - does not fit any other current exceptions.

Options for additional controls on these substances through an entry in Appendix D of the SUSMP could include one of the following:

- Restriction of access to state/territory authorised medical practitioners (current Item 1 - Poisons available only from or on the prescription or order of an authorised medical practitioner); or
- restricting access to:
  - clinical trials conducted under the TG Act when unapproved products including these substances are used I.e. Clinical Trial Notification (CTN) or Clinical Trial Exemption (CTX); and
  - supply as an unapproved product through the TGA Special Access Scheme Category B or the Authorised Prescriber scheme similar to the current Item 3 (Poisons available only from or on the prescription or order of a medical practitioner authorised or approved by the Secretary of the Commonwealth Department of Health under section 19 of the *Therapeutic Goods Act 1989*); or
  - restricting access by creating an entry such as "Poisons available only from or on the order of a specialist physician".

Substance summary

Cannabis is a term used to describe a range of varieties of the Cannabis genus, however *Cannabis sativa* is the botanically accepted name. The Cannabis plant produces a resin containing compounds called cannabinoids. Some cannabinoids possess psychoactive properties.

Cannabis sativa contains about 60 cannabinoids of which the main active constituent is delta-9-tetrahydrocannabinol. Delta-9- tetrahydrocannabinol has anti-emetic properties and is used for the control of nausea and vomiting associated with cancer chemotherapy in patients who have failed to respond adequately to conventional anti-emetics. Another active cannabinoid present in *Cannabis sativa* is cannabidiol (CBD) that is reputed to have analgesic, anticonvulsant, muscle relaxant, anxiolytic, neuroprotective, anti-oxidant and anti-psychotic activity.

Nabiximols is a specific extract of *Cannabis sativa* which contains a range of cannabinoids, of which tetrahydrocannabinols and CDB in approximately equal proportions comprise not less than 90% of the total cannabinoid content. Nabiximols are registered for use in Australia as a buccal spray preparation (Sativex®) as an adjunctive treatment for the symptomatic relief of neuropathic pain in multiple sclerosis in adults.

Nabilone is a synthetic cannabinoid used as an anti-emetic in the treatment of nausea and vomiting caused by chemotherapy and also for patients who are not responsive to conventional anti-emetic treatments.

Scheduling status

Cannabis and cannabinoids are currently listed in Schedules 4, 8 and 9, as well as being listed in Appendix D and Appendix K, as follows:

Schedule 9 Entries

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.

TETRAHYDROCANNABINOLS and their alkyl homologues **except**:

a) when separately specified in this Schedule;

b) when included in Schedule 4 or Schedule 8;

c) in hemp seed oil, containing 50 mg/kg or less of tetrahydrocannabinols when labelled with a warning statement:

   i. Not for internal use; or

   ii. Not to be taken; or

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

SYNTHETIC CANNABINOMIMETICS except when separately specified in these Schedules.

2-[(1R,3S)-3-HYDROXYCYCLOHEXYL]-5-(2-METHYLNONAN-2-YL)PHENOL
*(Cannabicyclohexanol or CP 47,497 C8 homologue).

Schedule 4 Entries

CANNABIDIOL in preparations for therapeutic use containing 2 per cent or less of other cannabinoids found in cannabis.

Schedule 8 Entries

DRONABINOL (delta-9-tetrahydrocannabinol) when prepared and packed for therapeutic use.

NABILONE

NABIXIMOLS (botanical extract of *Cannabis sativa* which includes the following cannabinoids: tetrahydrocannabinol, cannabidiol, cannabinol, cannabigerol, cannabichromene, cannabidiolic acid, tetrahydrocannabinolic acid, tetrahydrocannabivarol, and cannabidivarol, where tetrahydrocannabinol and cannabidiol (in approximately equal proportions) comprise not less than 90 per cent of the total cannabinoid content) in a buccal spray for human therapeutic use.

Appendix Entries

Appendix D, Part 3 – *Poisons available only from or on the prescription or order of a medical practitioner authorised or approved by the Secretary of the Commonwealth Department of Health and Ageing under section 19 of the Therapeutic Goods Act 1989.*

DRONABINOL (delta-9-tetrahydrocannabinol).

Appendix D, Part 1 – *Poisons available only from or on the prescription or order of an authorised medical practitioner.*

NABIXIMOLS

Appendix K

DRONABINOL (delta-9-TETRAHYDROCANNABINOL)

NABIXIMOLS

PART 1 - INTERPRETATION

"**Hemp seed oil**" means the oil obtained by cold expression from the ripened fruits (seeds) of *Cannabis sativa*.

Scheduling history

The scheduling of cannabis and its extracts has been considered by the National Drugs and Poisons Scheduling Committee (NDPSC) on a number of occasions. Currently, cannabis is a Schedule 9 substance, i.e., a prohibited substance which may be abused or misused and the manufacture, possession, sale or use of which is prohibited by law. An exemption exists for cannabinoid substances listed in lower schedules, and for processed hemp fibre and its products containing 0.1 percent or less of tetrahydrocannabinol.

Dronabinol (delta-9-tetrahydrocanabinol) was considered by the NDPSC in 1994 following a recommendation that it be included in Schedule 8 of the Standard for the Uniform Scheduling of Drugs and Poisons (SUSDP), for use in patients with advanced HIV disease with irreversible weight loss. At the time the NDSPC agreed to include dronabinol in Schedule 8 for therapeutic use.

Nabilone was considered at the July 1984 NDPSC meeting and included in Schedule 8 following that meeting. It is used as an anti-emetic in the treatment of nausea and vomiting caused by chemotherapy, primarily for patients who are not responsive to conventional anti-emetic treatments.

In 2009 the NDPSC considered scheduling requirements for the product Sativex®, which contained CBD and small amounts of other cannabinoids, and its access under jurisdictional laws and the Special Access Scheme (SAS). Members agreed that it was appropriate to allow access to Sativex® and suggested that a pragmatic approach would be to create a Schedule 8 entry for this specific formulation, in conjunction with an Appendix D, paragraph 3 listing to facilitate its use within the various jurisdictions.

Nabiximols was considered by the committee in October 2009 for inclusion as a specific entry after an issue was raised that some jurisdictions were unable to allow SAS access to the substance as it was captured under Schedule 9. The Committee agreed on the Schedule 8 listing with specific reference to buccal sprays.

In May 2010, Nabiximols was included in Schedule 8 and Appendices D and K. The Appendix D, Part 3 entry was made to limit access through the SAS. The Appendix K entry was agreed due to its sedating effects.

In March 2013, the committee advised that a change in the Appendix D entry for Nabiximols from Paragraph 3 to Paragraph 1would be appropriate noting the requirement for specialist oversight for safe prescribing of the drug.

Pre-meeting public submissions

35 submissions were received. 27 submissions supported the proposal, 4 submissions opposed, 3 submissions did not state a position, and 1 submission was for information only.

The public submissions will be made available following publication of this notice at https://www.tga.gov.au/scheduling-delegates-decisions-public-submissions.

ACMS advice to the delegate

The ACMS advised that both cannabis and tetrahydrocannabinols, including their extracts, be down-scheduled from Schedule 9 to Schedule 8 for human therapeutic use of cannabis products where the cannabis has been obtained in accordance with the *Narcotic Drugs Act 1967* and, where relevant, the Customs (Prohibited Imports) Regulation 1956.

The committee agreed to recommend a new Appendix D, Part 1 entry to provide for substances to be available only from or on the prescription or order of a medical practitioner authorised under State or Territory legislation.

The matters under subsection 52E (1) of the *Therapeutic Goods Act 1989* considered relevant by the Committee included: 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 the public health.

The advice comprised of the following:

- There is growing clinical trial use of cannabis-based products for an increasing range of therapeutic conditions. Schedule 8 is appropriate for safety profile providing a suitable level of oversight (for low risk of dependence when compared to opioids) and safety for these medicines.

- In clinical trials there is moderate-quality evidence to support use of cannabinoids in the treatment of chronic pain and spasticity as well as low-quality evidence of benefit in chemotherapy-related nausea, vomiting, weight gain in HIV, sleep disorders and Tourette syndrome. These conditions require diagnosis, management and monitoring under an appropriate medical practitioner. Many cannabis-based products are being developed as therapeutic products and tested in clinical trials to enhance the evidence base for efficacy.

- In some individuals high doses can cause psychoactive effects (euphoria, hallucinations etc) however cannabinoids pose a lower risk of toxicity or abuse than other existing Schedule 8 drugs such as opioids and amphetamines.

- Dosage, formulations and presentation of medicinal products are unknown at this time. However, products will have to be labelled in accordance with Schedule 8 requirements. Formulations will be dependent upon the clinical need.

- There is potential for misuse and/or abuse as with all other Schedule 8 controlled drugs. However cannabis has low risk of physical dependence but it may be a pathway to more addictive drugs. Abuse of the substance may have long term effects particularly in young people. Moving to Schedule 8 will allow some improved access under jurisdictional laws for patients who have been prescribed medicinal cannabis products. It will also provide greater ability to undertake research and clinical trials to gather further evidence of therapeutic efficacy.

Delegate's considerations

The delegate considered the following in regards to this proposal:

- Scheduling proposal;
- Public submissions received;
- ACMS advice;
- Section 52E of the *Therapeutic Goods Act 1989*;
- Scheduling factors[1];
- Other relevant information.

Delegate's interim decision

The delegate's interim decision is to create:

- new Schedule 8 entries for Cannabis and Tetrahydrocannabinols (being extracts, or derivatives of extracts, of cannabis) for human therapeutic use, and
- new Appendix D Item 1 entries for Cannabis and Tetrahydrocannabinols, and
- new Appendix K entries for Cannabis and Tetrahydrocannabinols.

For both Cannabis and Tetrahydrocannabinols the Schedule 8 entries are further restricted to substances:

- where the cultivation, production and manufacture of the substances in Australia is only under the *Narcotic Drugs Act 1967*, and
- where the substances are imported into Australia under the Customs (Prohibited Imports) Regulations 1956 with any further production or manufacture of the substances in Australia being under the *Narcotic Drugs Act 1967*, if required.

The new Appendix D Item 1 entries for Cannabis and Tetrahydrocannabinols place an additional control on the substances such that the substances will only be "available from or on the prescription or order of an authorised medical practitioner" where the medical practitioner has been authorised by the "appropriate authority" as defined in Part 1 paragraph 1(1) of the SUSMP which are generally senior health executives of the states and territories.

The new Appendix K entries for Cannabis and Tetrahydrocannabinols are because of the potential sedation effect of these substances and place a requirement for products including these substances to be labelled with a warning regarding their sedation potential.

The proposed implementation date is 1 June 2016.

The matters under subsection 52E (1) of the *Therapeutic Goods Act 1989* considered relevant by the delegate included: a) the risks and benefits of the use of the substance; b) the purposes for which a

[1] Scheduling Policy Framework for Medicines and Chemicals (SPF, 2015)

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

The reasons for the decision are:

- There is an increasing use of cannabis and cannabis extracts (including Tetrahydrocannabinols) in clinical trials in Australia and overseas. The current Schedule 9 status of the substances produces barriers to clinical trials being undertaken across Australia and by creating Schedule 8 entries for these substances their availability for clinical trials is improved, within the restrictions of Schedule 8 substances.

- There is some evidence to support the use of cannabinoids in the treatment of some conditions when these conditions are not adequately treated by other medications.

- In these cases the current Schedule 9 entries preclude individuals being able to access appropriate cannabinoid products for appropriate clinical justified conditions except through clinical trials where they can be conducted. By creating the Schedule 8 entries and the Appendix D Item 1 entries individuals will be able to have appropriate cannabinoid products including these substances prescribed where the medical practitioner is appropriately authorised to prescribe them.

- The proposed Schedule 8 entry for Cannabis includes the plant, its seeds, its extracts and derivatives of the extracts.

- The proposed Schedule 8 entry for Tetrahydrocannabinols is for Tetrahydrocannabinols extracted from, or derived from the extracts, of cannabis and does not include synthetic Tetrahydrocannabinols.

- The restrictions on the Schedule 8 entries to substances cultivated, produced and manufactured under the *Narcotic Drugs Act 1967* ensures that the substances are being legally cultivated, produced and manufactured in Australia within the controls of the Act.

- The restrictions do allow products containing these substances to be Schedule 8 when imported under the Customs (Prohibited Imports) Regulations 1956 and when any further production or manufacture occurs under the *Narcotic Drugs Act 1967,* if required.

- It should be noted that any supply and import of products containing these substances is still required to comply with the *Therapeutic Goods Act 1989* and the Therapeutic Goods Regulations 1990. Therefore any product containing these substances not on the Australian Register of Therapeutic Goods will need an exemption or approval to be legally supplied under the *Therapeutic Goods Act 1989*.

- It should be noted that for these substances any use outside of the specific schedule entries will make the substances Schedule 9.

Schedule entries

Schedule 9

Retain existing entry:

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.

Amend entry

TETRAHYDROCANNABINOLS and their alkyl homologues **except**:

a) when included in Schedule 4 or Schedule 8;

b) processed hemp fibre containing 0.1 per cent or less of tetrahydrocannabinol and products manufactured from such fibre.

c) in hemp seed oil, containing 50 mg/kg or less of tetrahydrocannabinols when labelled with a warning statement:

i) Not for internal use; or

ii) Not to be taken; or

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

Schedule 8 – New Entries

CANNABIS (including seeds, extracts and derivatives of extracts) for human therapeutic use, including that plant or any part of the plant when prepared or packed for that use, when:

a) cultivated, produced or manufactured in accordance with the *Narcotic Drugs Act 1967*; and

b) if relevant, imported in accordance with the Customs (Prohibited Imports) Regulations 1956,

except when:

c) separately specified in Schedule 4; or

d) separately specified in the NABIXIMOL entry in this Schedule

TETRAHYDROCANNABINOLS being extracts, or derivatives of extracts, of cannabis, for human therapeutic use, when:

a) produced or manufactured in accordance with the *Narcotic Drugs Act 1967*; and

b) if relevant, imported in accordance with the Customs (Prohibited Imports) Regulations 1956

except when:

c) in hemp seed oil, containing 50 mg/kg or less of tetrahydrocannabinols when labelled with a warning statement:

i) Not for internal use; or

ii) Not to be taken; or

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

e) separately specified in the NABIXIMOL entry in this Schedule.

Appendix D – New item 1 entries

CANNABIS

TETRAHYDROCANNABINOLS

Appendix K - New entries

CANNABIS

TETRAHYDROCANNABINOLS