Response to a *Bill for an Act to establish the Regulator of Medicinal Cannabis, and for related purposes* (the Bill)

Submission from the Clinical Oncology Society of Australia and Cancer Council Australia

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The **Clinical Oncology Society of Australia** (COSA) is the peak national body representing health professionals from all disciplines whose work involves the care of cancer patients.

Cancer Council Australia is Australia's peak national non-government cancer control organisation and advises the Australian Government and other bodies on evidence-based practices and policies to help prevent, detect and treat cancer.

Contact: Paul Grogan

Recommendations:

- Any product for medicinal purposes must be evaluated against objective criteria to ensure a high standard of safety, efficacy and quality for a particular use or uses. If approving access to a product, or issuing a license for cultivation, production and distribution of medicinal cannabis, the product in question must be assessed against this criteria.

- By not requiring registration by the TGA, a product cannot apply to the Pharmaceutical Benefits Advisory Committee for reimbursement. Therefore a product cannot be available to a patient at a reduced price. Pricing of products on the register for regulated medicinal cannabis products must be public and transparent with an aim to provide products at a reasonable price.

- A patient requires sustainable access of a product. When granting access to cannabis products via the register, or a license for a producer to distribute a product, consideration must be given to the sustainable access of a product, including price affordability, for the duration of required use. This is another consideration in the evaluation of issuing a medicinal license.

- Specific application processes, conditions of a license and the obligations of a license holder for each area of approval (e.g. distribution, cultivation etc.) must be clear and transparent to the applicant and general public. It is essential that post license monitoring and reporting be enforced especially the licensee's responsibility to report any adverse events.

- The Bill must promote research integrity and ethical compliance within the conditions of granting an experimental medicinal cannabis license. This must include: the *Australian Code for the Responsible Conduct of Research* and the *National Statement on Ethical Conduct in Human Research*, including approval from a Human Research Ethics Committee to undertake the proposed research.

Background

Overview of the proposed Bill:

The objectives of this Bill are stated under Part 1, (3) *'The objects of this Act are to:*

(a) establish a Regulator of Medicinal Cannabis to perform the functions of the agency referred to in Article 23 of the Single Convention on Narcotic Drugs, 1961, as it applies in relation to cannabis because Article 28 of the Convention ; and

(b) provide for a national system, to apply in participating States and Territories, for regulating the production and use of medicinal cannabis products, and related activities such as research, in accordance with the Convention.'

Part 1, (4) Simplified outline of this Act:

This Act sets up the Regulator of Medicinal Cannabis to perform the functions of the agency referred to in Article 23 of the Single Convention on Narcotic Drugs, 1961, in relation to cannabis.

The regulator may approve medicinal cannabis products for inclusion in the register for regulated medicinal cannabis products. Products included in the register are regulated under this Act, rather than under the Therapeutic Goods Act 1989.

The regulator may make rules for licensing the production, use, experimental use and import and export of medicinal cannabis. The regulator has powers to monitor compliance with this Act and the rules, investigate breaches.

The Act applies only in participating States and Territories. A State or Territory may enter into an arrangement with the Commonwealth to become a participating State or Territory.

Cancer Council and COSA welcome the opportunity to review the Bill.

Overview of cannabis and cannabis products:

Cannabis and cannabinoids are derived from the Cannabis sativa plant. Cannabis, also known as marijuana (and colloquially as "grass", "pot", "weed", "hash" etc.), is made from the dried flowers and leaves of the Cannabis sativa plant. Cannabinoids are chemicals which act upon cannabinoid receptors, CB1 and CB2 in the body. Tetrahydrocannabinol (THC) and cannabidiol (CBD) are the most abundant and researched cannabinoids.

THC is the primary psychoactive component of cannabis and the most effective cannabinoid for alleviating nausea and vomiting, and for stimulating appetite[iii]. However, the therapeutic use of THC is limited by its psychoactive side effects. In recent years, there has been increased interest in non-psychoactive cannabinoid compounds such as CBD for therapeutic use to alleviate chemotherapy induced illness[iii].

A number of natural and synthetic cannabinoid products have been developed for use in a medical setting and act in the same way in the body as the plant product. Currently there are three main products:

- dronabinol, a synthetic form of THC[iv];
- nabilone, a synthetic form of THC[v]; and
- nabiximols, a chemically pure 50:50 mixture of THC and CBD[vivii].

Medical use of cannabis and cancer:
Managing illness induced by chemotherapy, especially in patients with advanced cancer who have responded poorly to conventional relief options, is a significant problem for cancer patients and their doctors.

The potential benefits of cannabis and cannabinoids for symptom relief have been subject to a number of government reviews and public debate in recent years. This includes the establishment in September 2014 of a New South Wales (NSW) Government working group that will report to the Premier on its recommendations. NSW has also recently established the Terminal Illness Cannabis Scheme. Other jurisdictions, including the Commonwealth, have expressed an interest in evaluating the potential benefits of cannabis and cannabinoid use as a symptom-relief agent.

Neither cannabis and cannabinoids, nor its synthetic forms are currently approved for cancer-related therapeutic use in Australia.

The majority of evidence for the therapeutic benefit of cannabis and cannabinoids addresses their use in relieving the symptoms of cancer and cancer treatments such as chemotherapy. There is evidence that cannabis and cannabinoids in controlled delivery may have a benefit to cancer patients where conventional treatments are unsuccessful in providing relief in the following areas:

- for relieving nausea and vomiting in patients undergoing chemotherapy;
- as an adjunctive analgesic in patients with moderate to severe pain; and/or
- as an appetite stimulant for patients experiencing weight loss and muscle wasting

There is no current evidence that cannabinoids are effective at inhibiting tumour growth or treat or cure cancer in humans. In addition, there is no current evidence that cannabis or cannabinoids reduce risk or prevent cancer occurrence or promote good health.

The effects of cannabis and cannabinoids can differ significantly with different doses and between individuals.

Side effects from cannabis:
The short term effects of natural cannabis include loss of inhibition, anxiety or paranoia, difficulty concentrating, elevated heart rate, dry mouth and throat, vomiting, and hallucinations[viii]. Some people experience temporary psychosis (loss of contact with reality) as a result of taking certain cannabinoids[ix]. A systematic review found that potentially serious adverse effects, even when taken short term orally or intramuscularly, are likely to limit widespread use of cannabinoids as anti-emetic drugs for controlling chemotherapy related sickness[x].

Based on multiple studies, researchers found that smoking the cannabis plant delivers harmful substances and may be an important risk factor in the development of respiratory diseases and cancer of the lungs, mouth, and tongue, and an increased risk of bronchitis[xixii]. Marijuana smoke contains known carcinogens, however epidemiological studies exploring the link between marijuana and cancer risk have been inconsistent, and most recent epidemiologic studies have not found a substantial effect on cancer risk[xiiixiv].

Additional adverse health effects associated with chronic cannabis use include cannabis dependence (addiction), depression and decreased concentration, memory and impaired cognitive function[xv].

A systematic review of the adverse effects associated with the use of synthetic cannabis products found that there was no increased risk of serious adverse events, such as vomiting and urinary tract infections[xvi]. Non-serious adverse events such as dizziness, dry mouth, confusion, anxiety and nausea have been associated with the use of synthetic cannabis products[xviixviiixixxx].

When marijuana smoke is inhaled, cannabinoids enter the bloodstream quickly which can create a high, uncontrolled dose of cannabis. The secondary psychoactive compound is produced in smaller amounts than when marijuana is taken orally[xxi]. Smoking cannabis is not recommended, as the smoke form contains at least 50 of the same carcinogens as tobacco[xxii]. When taken orally, the THC is processed by the liver, which produces another secondary psychoactive compound.

Although currently used in some countries and in various forms, evidence to support the medicinal use of cannabis remains limited. Cancer Council does support the conduct of clinical trials into the benefits of its use to relieve the side effects of traditional chemotherapy where conventional methods have been unsuccessful. Cancer Council would expect that such research would be compliant with Australian law and research policy. There are significant risks associated with using cannabis in its natural plant form, synthetic and THC based products however, controlled research to identify any appropriate therapeutic benefits and methods should be supported.

In this response to the Bill, Cancer Council will address the interaction of current legislation; interaction of Australia research and ethical policy for conducting research on humans; licensing and ongoing conditions and; general impact on access for cancer related indications.

Cancer Council supports research into the potential benefits of cannabis and cannabinoids for cancer patients.

Addressing components of the Act:

Evaluation of cannabis and cannabis products included on the register.

'The regulator may approve medicinal cannabis products for inclusion in the register of regulated medicinal cannabis products.' Division 1 (4)

'Products included in the register are regulated under this Act, rather than under the Therapeutic Goods Act 1989.' Division 1 (4)

Cancer Council Australia/COSA discussion:

As stated in the Explanatory Memorandum, the Bill *'provides a system of regulating medicinal cannabis that is entirely separate from the Therapeutic Goods Act 1989*[xxiii]. This does not restrict sponsors who develop cannabis based pharmaceutical products from applying to the Therapeutic Goods Administration (TGA) to sell their product instead of using the licensing scheme within the Bill.

The objectives of the *Therapeutic Goods Act 1989* are:

1. The objects of this Act are to do the following, so far as the Constitution permits:

   (a) provide for the establishment and maintenance of a national system of controls relating to the quality, safety, efficacy and timely availability of therapeutic goods that are:
      (i) used in Australia, whether produced in Australia or elsewhere;

      or

      (ii) exported from Australia;

   (b) to provide a framework for the States and Territories to adopt a uniform approach to control the availability and accessibility, and ensure the safe handling, of poisons in Australia[xxiv]

Under the *Therapeutic Goods Act 1989*, the TGA must evaluate a therapeutic good as demonstrating a high standard of safety, quality and efficacy or performance before they can be lawfully imported, manufactured, supplied or exported in Australia.[xxv] Australian health care consumers and the broader community expect that medicines accessed with a prescription from their medical practitioner are of a high quality, safe and efficacious for the intended use.

In addition, the contents of the *Poisons Standard 2015* sits within paragraph 52D(2)(b) of the *Therapeutic Goods Act 1989*.The *Poisons Standard 2015* contains the *Standard for the Union Scheduling of Medicines and Poisons (SUSMP).* It serves the following two purposes:

1. The SUSMP contains the decisions of the Department of Health's recommendations to Australian States and Territories regarding the classification of poisons onto Schedules which sets the level of control on the availability of poisons.

2. The SUSMP includes model provisions for labelling, containers, storage and possession of poisons in general, which are intended to be adopted for use in each jurisdiction of Australia, according to local requirements and local law.

As per the SUSMP cannabis is a Schedule 9 substance (except when separately specified in the schedule). A Schedule 9 substance is classified as a *'substance 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 or Territory Health Authorities.'*

Other forms of cannabis are listed under Schedule 8. A Schedule 8 substance is classified as a *'substance, which should be available for use but require restriction of manufacture, supply, distribution, possession and use to reduce abuse, misuse and physical or psychological dependence.'* Additional provisions are attributed to nabiximols and dronabinol.[xxvi]

The *Therapeutic Goods Act 1989*, including the *Poisons Standard*, forms a crucial part of the evaluation of the quality, safety and efficacy of a therapeutic product prior to being available to the patient.

> *'the regulator is satisfied that the cannabis product is suitable for medicinal use.'*
> Division 2 (13) 2b

The Bill allows the regulator to register a cannabis product based on the regulators satisfaction that the product is 'suitable for medicinal use'. This subjective assessment does not acknowledge any process undertaken by an applicant in seeking a product to be registered, including responding to specific criteria such as clinical outcomes and patient safety. The absence of a structure to objectively evaluate the application should also be noted. A rigorous review process is critical, for example, the review of therapeutic products prior to registration on the Australian Register of Therapeutic Goods. In the context of the Bill this is essential as people will be exposed to the product either through access (medicinal license) or research (experimental license). Assessment determines whether any risks associated with the product outweigh the benefit to the patient.

The Explanatory Memorandum acknowledges that the *'register is modeled on the Australian Register of Therapeutic Goods'*. The Australian Register of Therapeutic Goods is a list of all products authorised by the TGA to be lawfully supplied in Australia.[xxvii] The Australian Register of Therapeutic Goods lists the details of each product including; a products name, formulation details, sponsor name and manufacturer. A complete list of products and their details is publicly available. Also, the Australian Public Assessment Reports (AusPAR) for prescription medicines provides information about the TGA evaluation of a prescription medicine and the considerations that led to the TGA to approve or not approve an application.[xxviiixxix]This is also available publicly.

Although *'modeled on the Australian Register of Therapeutic Goods'* the register of regulated medicinal cannabis '*must not be made available to the public'* (Division 3 (18) 2. This does not provide transparency of a product's details or the assessment that was undertaken by the regulator. Full disclosure is important for prescribers to access the complete details of a

product, information for a patient, and the public availability of product details encourages market competition to promote the ongoing development of quality products.

In summary, the Bill does not outline a review process for the approval of a medicinal license issued under the medicinal cannabis licensing scheme. The register must allow patients to access information about the product they are taking and for medical practitioners, knowledge of what is the most suitable product for the individual.

'medical practitioners, or classes of medical practitioners, to prescribe regulated medicinal cannabis products.' Division 3 (19) 1d

'The Narcotic Drugs Act 1967 and the Therapeutic Goods Act 1989 do not apply in relation to an activity engaged in, or a thing dealt with, in accordance with authorization under the authorized patients and carers scheme.' Division 4 (4)

Under the *Therapeutic Goods Act 1989*, before a prescription medicine is available on the therapeutic market, the sponsor must first have it evaluated as safe, of high quality and efficacious by the TGA. All submissions to the TGA are assessed by scientific and clinical experts to ensure the benefits of a product outweigh any risk, including potential toxic side effects of prolonged use. This risk assessment approach is intended to assure consumers that products they take are safe for their intended use, while still providing access to products that are essential to their health needs[xxx] Not only does this provide assurance for patients, it also supports medical practitioners to be confident that a product they prescribe has met the above requirements to provide a therapeutic benefit.

Medicines with a high risk, classed as category Aust R, can still be made available if considerable benefits are demonstrated and are obtained only through prescription after consultation with a health practitioner[xxxi] A higher level of the evaluation of data relating to safety, manufacturing and efficacy is applied to Aust R category medicines. Given the degree of risk cannabis products would be Aust R medicine and require a prescription for access. As the Bill does not require the involvement of the *Therapeutic Goods Act 1989* this risk benefit assessment by the TGA and classification of higher risk medicines is absent.

'The Narcotic Drugs Act 1967 and the Therapeutic Goods Act 1989 do not apply in relation to an activity engaged in, or a thing dealt with, in accordance with a medicinal license.' Division 3 (4)

'Subsection (4)/(5) does not prevent the Therapeutic Goods Act 1989 applying in relation to: a. the manufacture of therapeutic goods (within the meaning of the Act) from cannabis produced, transported or stored in accordance with a medinical license' Division 3 (16) 5a. & (20) 6.

As noted earlier, the *Therapeutic Goods Act 1989* encompasses the *Poisons Standard,* therefore, it could be assumed that the Bill has not recognised the classification of cannabis and cannabis products under the *Poisons Standard*. It is important to note that there are currently restrictions placed on access to these products based on the degree of risk associated with their use. The Explanatory Memorandum defines a cannabis product as either:

a. cannabis, or a product derived from cannabis that is intended for medical use; or
b. a synthetic version, that is intended for medicinal use, or a product derived from cannabis[xxxii]

Cannabis, except for products separately specified in the schedule, is classified as a Schedule 9 substance - *a substance 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 or Territory Health Authorities.* [xxxiii] Cannabis based products, nabixmols, dronabinol and nabilone are Schedule 8 substances – *a substance which should be available for use but require restriction of manufacture, supply, distribution, possession and use to reduce abuse, misuse and physical or psychological dependence*[xxxiv]*.* Additional provisions are attributed to nabiximols and dronabinol which are outlined in Appendix D of the SUSMP.

Therefore, access to the natural cannabis plant for medical or scientific research, or for analytical teaching or training purposes can be granted by the regulator under this Bill if the regulator is considered a Commonwealth and/or State or Territory Health Authority. This would satisfy access approval for experimental license and would make Schedule 8 substances available for purposes of a medicinal license. This would introduce the need to comply with the *Therapeutic Goods Act 1989* as it encompasses the *Poisons Schedule*.

Cancer Council Australia/COSA summary recommendation:

The Australian population must be assured that any therapeutic product for the purpose of addressing a health condition is safe and effective for the given indication.

- Any product for medicinal purposes must be evaluated against objective criteria to ensure a high standard of safety, efficacy and quality for a particular use or uses. If approving access to a product, or issuing a license for cultivation, production and distribution of medicinal cannabis, the product in question must be assessed against this criteria.

- By not requiring registration by the TGA, a product cannot apply to the Pharmaceutical Benefits Advisory Committee for reimbursement. Therefore a product cannot be available to a patient at a reduced price. Pricing of products on the register for regulated medicinal cannabis products must be public and transparent with an aim to provide products at a reasonable price.

- A patient requires sustainable access of a product. When granting access to cannabis products via the register, or a license for a producer to distribute a product, consideration must be given to the sustainable access of a product, including price affordability, for the duration of required use. This is another consideration in the evaluation of issuing a medicinal license.

Conditions of licensing and licensing for experimental use

'*The rules may provide for an entry in the register of regulated medicinal cannabis to be removed or varied on application by the person in relation to whom the entry is registered, or on the regulator's own initiative.*' Division 2 (14)

'A person may apply to the regulator for a cannabis product to be included in the register of regulated medicinal cannabis products in relation to a person' Division 2 (13) 1.

Medicinal cannabis licensing scheme:

Division 3 (16) 1. *'the rules may prescribe a scheme (the medicinal cannabis licensing scheme) for the regulator to issue licenses (medicinal licenses) authorising persons (medicinal license holders) to engage in one or more of the following activities:*

(a) producing cannabis for medicinal or experimental use;
(b) Transporting or storing cannabis for medicinal or experimental use;
(c) Manufacturing or storing cannabis products;
(d) transporting or storing regulated medicinal cannabis products;
(e) providing regulated medicinal cannabis products to authorised patients and authorised carers;
(f) other activities incidental to the activities referred to in paragraphs (a) and (e)'

Experimental cannabis licensing scheme:

Division 5 (20) 4. *'the experimental cannabis licensing scheme must provide for an experimental license to be subject to such conditions as are appropriate for ensuring:*

(a) that any cannabis produced or dealt with in accordance with the scheme is accounted for; and
(b) that any cannabis products manufactured or dealt with in accordance with the scheme are accounted for; and
(c) that the scheme operates in accordance with the Convention.'

Cancer Council Australia/COSA discussion:

The Bill is not clear about how a license application is made and assessed, including against what selection criteria a license application is evaluated. In addition, a medicinal license can be granted for different purposes and therefore conditions of the license would vary depending on the purpose granted. All purposes that a medicinal license can be approved for are listed under Division 3 (16) 1. Conditions of the license are crucial to ongoing compliance.

'An experimental license may authorise individuals to use, possess, supply or administer cannabis products to the extent necessary for the experimental purpose.' Division 5 (20) 3.

The Bill does not acknowledge any requirement to comply with Australian standard guidelines or policy for proposing or conducting research on humans. The regulator *'issues licenses (experimental licenses) to authorising persons (experimental license holders)'* Division 5 (20) 1, however the Bill does not mention the need to fulfill a formal assessment

process or authorisation from a Human Research Ethics Committee to commence cannabis product research on humans.

The purpose of the *Australian Code for the Responsible Conduct of Research (2007)* is to guide institutions and researchers in responsible research practices. The Code promotes research integrity and explains what is expected of researchers by the community[xxxv]. Institutions develop their own codes of conduct and procedures for investigating misconduct based on this guide.

The *National Statement on Ethical Conduct in Human Research (2007)* consists of a series of guidelines on ethical conduct in human research and is intended for use by[xxxvi]:

- any researcher conducting research with human participants;
- any member of an ethical review body reviewing that research;
- those involved in research governance; and
- potential research participants.

Both the *Australian Code for the Responsible Conduct of Research* and the *National Statement on Ethical Conduct in Human Research* were developed jointly by the Australian Research Council, the National Health and Medical Research Council and Universities Australia. Fulfilling the requirements of both documents is standard practice.

A Human Research Ethics Committee reviews research proposals against the principles within the *National Statement on Ethical Conduct in Human Research* for research involving humans. In Australia, this Committee ensures that research is ethically appropriate and conducted in accordance with relevant standards and guidelines[xxxvii]

Cancer Council Australia/COSA summary recommendation:

- Specific application processes, conditions of a license and the obligations of a license holder for each area of approval (e.g. distribution, cultivation etc.) must be clear and transparent to the applicant and general public. It is essential that post license monitoring and reporting be enforced especially the licensee's responsibility to report any adverse events.

- The Bill must promote research integrity and ethical compliance within the conditions of granting an experimental medicinal cannabis license. This must include: the *Australian Code for the Responsible Conduct of Research* and the *National Statement on Ethical Conduct in Human Research*, including approval from a Human Research Ethics Committee to undertake the proposed research.

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