PharmOut

Report	
Project title	Response to the Inquiry into Cannabis and Hemp

1. Background

This report has been prepared as submission to the WA *Inquiry into Cannabis and Hemp*[59]. The scope of the report focusses on the main topics of the Inquiry – namely the potential to amend the current legislation and regulations which apply to cannabis and hemp in Western Australia, with particular reference to:

(a) the current barriers to pharmaceutical and nutraceutical use of cannabinoid products;

(b) medicinal cannabis, its prescription, availability, and affordability; and

(c) the potential benefits and risks of permitting industrial hemp for human consumption.

2. Executive Summary

Barriers to pharmaceutical use of medicinal cannabis mostly lie in high set up costs and licence fees, and businesses are hampered by the regulator's long processing times. This makes it difficult to quickly set up new contracts, adjust allowed quantities in permits, and supply new entities.

There are some regulatory barriers which would be addressed by select changes to the *Standard for the Uniform Scheduling of Medicines and Poisons* (SUSMP) (which directly impacts the WA *Medicines and Poisons Act 2014* and associated regulations). There is currently no framework that supports the presence of cannabis compounds in nutraceuticals (complementary medicines).

Most medical cannabis is prescribed via Special Access Category B and Authorised Prescriber Schemes. Clinical guidelines are available for health practitioners, but accessing product information and the products themselves has proven challenging due to advertising and wholesaler restrictions. Affordability is impacted by operational costs incurred by medicinal cannabis businesses (due to regulatory fees) however there are subsidies available to patients through private health cover (pharmaceutical extras).

Industrial hemp is already permitted for human consumption, however due to the common confusion between industrial hemp (for fibre, hurd, and pressed seed oil) and CBD that can be extracted from industrial hemp (under a medicinal cannabis licence) additional sections have been added to this report to discuss risk/benefit of CBD and other unexplored options.

3. Scope

The following is in scope for this response:

- Relevant Western Australian regulations
- Relevant Australian federal regulations
- Relevant examples of cannabis management from international bodies, and other Australian state and territories, as appropriate.

The following is out of scope: *The United Nations Single Convention on Narcotic Drugs of 1961.*

4. Definitions

In different sectors of the cannabis industry there is some interchange between cannabis terminology, thus some clarification for the terms used in the response is provided below:

Term	Definition
Low-THC strain	Cannabis strains that are compliant with industrial hemp limitations. These limits can vary in different state and territories but usually round off to <1% tetrahydrocannabinol (THC) in the plant material. Despite being low in THC, these strains are often high in cannabidiol (CBD), another commercially desirable cannabinoid. Low-THC strains can be used either for industrial hemp purposes or medicinal cannabis depending on licences obtained by the company.
Hemp	Cannabis grown under the *Industrial Hemp Act 2004* [1] and only used to create industrial hemp products.
Medicinal cannabis	Any cannabis strain that is cultivated or produced under the *Narcotic Drugs Act 1967* [2] (inclusive of low-THC and high-THC strains).

5. Clarifying the differences between industrial hemp and medicinal cannabis

Given the frequency of confusion between the industrial hemp and medicinal cannabis industries, it is important to clarify the differences before proceeding any further in this response.

In America the *2018 Farm Bill* removed hemp (which included low-THC derivatives of cannabis, such as CBD products) from the definition of marijuana in the Controlled Substances Act. This caused concern in the FDA[21] but was received with much enthusiasm by the American people. A curious parallel now exists in America where many states have gone on to develop "grey zone" hemp legislation where they allow CBD to be added to food or labelled as a dietary supplement, however this is illegal under the FDA federal law.

Some of this hemp "grey zone" thinking has also seeped[42,43] into Australia by opportunists thinking the American and Australian frameworks are transferrable. It is paramount that this confusion is minimised to ensure that local businesses understand the limitations of the industrial hemp and medicinal cannabis industry and their licences, as well as ensure therapeutic products are being manufactured to the required quality standards.

While the FDA regulates both food and drugs, Australia regulates these goods under different regulatory bodies and there is clear delineation between the TGA and the Food Standards Australia New Zealand (FSANZ) as well as the reach of their administration.

There are two very distinct purposes for low-THC cannabis crops in Australia. In the *Guideline: Security of Medicinal Cannabis*[5], the ODC specify between crops that contain the two main cannabinoids of interest:

- "Cannabis, with greater than 1% THC, is a narcotic drug with a high illicit value."
- "Cannabis containing less than 1% THC is usually referred to as hemp when cultivated for fibre and seed."

This essentially translates to strains that have "high-THC" and "low-THC."

High-THC may only be cultivated for medicinal cannabis purposes, however low-THC (i.e. hemp strains) may be cultivated for both industrial hemp and medicinal cannabis provided the licenced entity holds both their state's industrial hemp licence, and the ODC medicinal cannabis licence(s).

However, the activities that the two licences allow are very different, as summarised by the table below:

Licence	Industrial Hemp	Medicinal Cannabis
Regulatory Body/ Legislative Acts	The Department of Primary Industries and Regional Development (Industrial Hemp Act 2004[1])	• Office of Drug Control (OCD). *Narcotic Drugs Act 1967* [2] • Health Department of Western Australia. *Medicines and Poisons Act 2014* [3] • Therapeutic Goods Administration (TGA) - if manufacturing finished products. *Therapeutic Goods Act 1989* [23]
Starting materials	Low-THC cannabis strains (<1% THC)	Any cannabis strain with any combination of cannabinoids
Permission	Cultivate, harvest, and supply industrial hemp products to appropriately licenced third parties.	Depending on licences obtained; cultivate, produce, harvest, extract and manufacture medicinal cannabis products.
Products	Fibre and hurd from the stem, hemp seeds (both viable and non-viable), various hemp seed products, hemp seed oil (cold-pressing of seeds, NOT "full extract" or any extraction of cannabinoids).	Harvested cannabis flowers, resins or extracts of whole flowers, variety of intermediate and finished product forms.
Uses	Non-therapeutic purposes (e.g. clothes, cosmetics, food, etc.)	Therapeutic purposes (i.e. medicines).

Table edited from the *Cultivation of Medicinal Cannabis vs Hemp* [24].

In summation, there are differences between industrial hemp and medicinal cannabis, namely in the parts of the plants that are allowed to be processed and their intended products. There is some flexibility provided for low-THC strains so long as the appropriate licences are held by the licenced entity.

Report	
Project title	Response to the Inquiry into Cannabis and Hemp

6. The current barriers to pharmaceutical and nutraceutical use of cannabinoid products

6.1. Pharmaceutical

Barriers to pharmaceutical use from a patient perspective is covered in section 7. In order to minimise repeating content, this section will focus on the regulatory barriers that impact medicinal cannabis licencees, and make recommendations for improving those regulations that would benefit businesses in terms of operational processes and costs.

6.1.1. Pharmaceutical barrier 1 - Poisons Scheduling

It is hard to discuss purely local barriers to the pharmaceutical use of medicinal cannabis as the WA *Medicines and Poisons Act 2014* [3] is impacted directly by the TGA's SUSMP[4] as well as the *Australian code of good wholesaling practice for medicines in schedules 2, 3, 4 & 8* [45]. The SUSMP classifies different substances depending on their level of risk and their abuse potential, with S2 being the lowest risk and available from pharmacies, to S9 as the highest risk and prohibited by law unless required by medical/scientific research.

Due to the complexity of compounds present, cannabis has multiple entries in SUSMP, however the overarching one is S8 Controlled Drugs, which covers the cannabis plant starting materials as well as extracted THC. However, this category only applies when those materials are prepared or packed for therapeutic use - cannabis plant research materials are still, impractically, in the S9 category despite other categories for cannabis (S8 and S4) being available.

Low-THC plant material also falls within the S8 category despite not having commercially extractable quantities of THC. This contrasts with its main extractable cannabinoid of interest, CBD, which is classified under S4 Prescription Drugs.

As the classification of a substance goes up, so too does the cost of security and businesses may be expected to install climb proof fencing, CCTV, safes or strongrooms, access control measures, etc. Waste disposal also becomes complicated as it also falls under S8 by default - when produced on an industrial level, S8 poisons require controlled destruction by waste contractors. All of this adds to operational costs.

All of this is just a brief summary of some of the impracticalities with scheduling - the table below provides a much more detailed breakdown of main categories of cannabis in SUSMP, and also recommends improvements on the current status quo:

Category	Description	Improvements
Schedule 9 (S9) Prohibited Drug	It covers cannabis that is either: • produced in the unlicenced black market, and • any cannabis plant material that is to be used for scientific research and analysis purposes.	No other poisons schedule (S8, S4) includes scientific research for cannabis **plant** material in that schedule, only extracts of certain cannabinoids – for more detail see comments for the other categories.

PharmOut

Report	
Project title	Response to the Inquiry into Cannabis and Hemp

Category	Description	Improvements
Schedule 8 (S8) Controlled Drug	This covers: • viable cannabis seeds, extracts, resins, the cannabis plant, and any part of the cannabis plant) when prepared or packed for human therapeutic use under the *Narcotic Drugs Act 1967*, and/or *Therapeutic Goods Act 1989* • tetrahydrocannabidiols (THC) extracts in products manufactured in accordance with the *Narcotic Drugs Act 1967* This also covers by default: • any other cannabinoids that are found in the cannabis plant regardless of whether they are psychoactive (such as cannabinol, cannabigerol, cannabichromene, etc. See SUSMP entry for Nabiximols as an example) • non-psychoactive and non-therapeutic accessory plant compounds that can be extracted from the plant (e.g. flavonoids, terpenes, etc.) • cannabis waste materials ("any part of the cannabis plant" also includes cannabis stalks, etc. that contain extremely low levels of extractable cannabinoids[50, 51]).	**a) Main change required:** • Leave S8 exclusively for high-THC strains and recategorise low-THC cannabis plant materials (for therapeutic use) into S4 alongside CBD. Discussion: The inclusion of "cannabis seeds, extracts, resins and the plant" as an umbrella statement for ALL cannabis strains regardless of cannabinoid content contradicts the lower security requirements for low-THC strains as outlined by the ODC *Guideline: Security Of Medicinal Cannabis*[5] (i.e. businesses are only required to match what is suitable for industrial hemp). Note that the ODC has only recently changed the security requirements for low-THC in 2020[5] but the industry has had to conform with S8 requirements since 2016. S8 cannabis also has stricter storage requirements than S4 cannabis, oftentimes requiring storage "in a strongroom with a detection device" (*Medicines and Poisons Regulations 2016, section 98, 2c/Schedule 3, section 2*[46]) as opposed to storage "in an area or in a manner that prevents physical access to the medicine" (*Medicines and Poisons Regulations 2016, section 90, 1b*[46]). Having to meet the storage and security requirements for S8 when growing low-THC crops adds unnecessary start up and running costs for medicinal cannabis businesses. **b) Other changes required:** • Include allowance for scientific research and analysis of cannabis plant material (currently S9). Note that there is currently an ongoing TGA consultation into proposed amendments to the Poisons standard that seeks to recategorize cannabis plant material for research into S7 (Dangerous Poison)[47]. However, the proposal is not practical given there are already other categories for cannabis that can be utilised (and subsequently edited to include this extra permission for research).

Project title	Response to the Inquiry into Cannabis and Hemp

Category	Description	Improvements
		• Recategorise other non-psychoactive cannabinoids (e.g. cannabinol, cannabigerol, etc.) into S4. (Therapeutic potential of other cannabinoids are not fully characterised, however they do not merit the S8 category.) • Specify that other non-psychoactive and non-therapeutic ancillary cannabis extracts are excluded from the standard (e.g. flavonoids, terpenes, etc.). There is a potential resale value for these compounds in other non-therapeutic goods (i.e. scents in oils, cleaning products, etc.). • Exclude cannabis plant waste from S8 category (by perhaps redefining as "agricultural waste"). Currently all cannabis waste requires controlled destruction under supervision by an authorised person or qualified waste management contractor[48] (despite having essentially negligible levels of extractable cannabinoids[50, 51]). This would also help reduce operating costs for businesses as they would be able to compost on site (as with industrial hemp). **c) SUSMP Recommendations** Modify initial SUSMP entry for S8 CANNABIS in the following way: "# CANNABIS (including seeds, extracts, resins and the plant, and any part of the plant) when prepared or packed for human therapeutic use*, or analytical and scientific research…"'* **except** iii) when captured by the CANNABIDIOL entry in Schedule 4 or Schedule 3; or *iv) when captured by the CANNABIS entry in Schedule 4* v)…..hemp seed oil containing 75 mg/kg or less of cannabidiol and 10 mg/kg or less of tetrahydrocannabinols." *vi) ….when plant material meets the definition of "agricultural waste"* *vii) ….when extracts do not fall into the psychoactive or therapeutic category (i.e. accessory plant compounds like flavonoids, terpenes, etc.)*

Project title	Response to the Inquiry into Cannabis and Hemp

Category	Description	Improvements
Schedule 4 Prescription Drugs	CBD extracts in preparations for therapeutic use or analytical and scientific research, containing 98% or more of CBD. **Note:** this excludes cannabis strains/plant matter that has low-THC content, complies with industrial hemp strain requirements, and can only be extracted for CBD or other non-psychoactive cannabinoids.	See comment for CBD and other non-psychoactive cannabinoids in S8. **SUSMP Recommendations:** Add new entry for low-THC cannabis materials (that can encompass other undefined cannabinoid extracts like cannabinol, cannabigerol, etc., as well as allow low-THC cannabis strains to be analysed and researched outside the S9 controls): *CANNABIS (including seeds, extracts, resins and the plant, and any part of the plant), when prepared or packed for human therapeutic use, or analytical and scientific research, when:* *a) plant material meets the standard for industrial hemp in the relevant state or territory* *b) cultivated or produced, or in products manufactured, in accordance with the Narcotic Drugs Act 1967; and/or* *c) for use in products manufactured in accordance with the Narcotic Drugs Act 1967; and/or* *d) imported as therapeutic goods, or for use in therapeutic goods, for supply, in accordance with the Therapeutic Goods Act 1989; and/or* *e) in therapeutic goods supplied in accordance with the Therapeutic Goods Act 1989,* *except:* *i) when it is in a product to which item 4, 8, 10, 11 or 12 of Schedule 5A to the Therapeutic Goods Regulations 1990 applies; or* *ii) when separately specified in the NABIXIMOLS entry in this Schedule; or* *iii) when captured by the CANNABIDIOL entry in Schedule 4 or Schedule 3; or* *iv) hemp seed oil containing 75 mg/kg or less of cannabidiol and 10 mg/kg or less of tetrahydrocannabinols.* *vi) when plant material meets the definition of "agricultural waste"* *vii) when extracts do not fall into the psychoactive or therapeutic category (i.e. accessory plant compounds like flavonoids, terpenes, etc.)* **Additional comment** In an interesting loophole, veterinarians are allowed to import and prescribe CBD products to animals directly under their care, however they are not allowed to use locally manufactured CBD products as the *Narcotic Drugs Act 1967* does not allow manufacture for **animals,** only humans[41]. This is a missed market opportunity, and the *Narcotic Drugs Act 1967* could be updated to incorporate this permission.

PharmOut

Project title	Response to the Inquiry into Cannabis and Hemp

Category	**Description**	**Improvements**
Schedule 3 Pharmacist Only	For preparations of CBD where the maximum recommended daily dose is 150 mg or less.	**Comment:** Originally the maximum recommended daily dose during the TGA's initial safety review was 60mg or less a day[6]. The cannabis industry expressed concern, protesting the "*proposed dose [was] potentially sub-therapeutic and may present a barrier for sponsors to register a Schedule 3 preparation on the ARTG*".[7] (S3 drugs require an Over the Counter registration to be listed on the Australian Register of Therapeutic Goods (ARTG)[8]. Application for product registration would include a full submission to support its intended use, including data relating to the efficacy for any indications for the product.) Even though the maximum dose of CBD has been increased to 150mg orally, the same complaint regarding sub-therapeutic dose could arguably be made for the new concentration given the considerable variation in dosage schemes and route of administration employed across studies thus far.[49] (It should be noted in the review by Larsen and Shahinas, that the majority of 150mg oral doses did not produce any observable clinical effect compared to placebo.)

Industrial hemp products are excluded from SUSMP as there is no therapeutic application, however they still have cannabinoid limits:

- Hemp seed oil (obtained by cold expression from seeds) - not allowed to contain more than 75 mg/kg of CBD and 10 mg/kg of THC[4].
- Hemp fibre products – must containing 0.1% or less of THC[4] (note that this is different in Western Australia - in the *Industrial Hemp Act 2004*, processed industrial hemp must not contain more than 0.35% of THC[1]).

6.1.2. Pharmaceutical barrier 2 - Fees and start-up costs

The operational viability of medicinal cannabis businesses is not just impacted by poisons scheduling security requirements, but also hugely impacted by fees from theODC. When compared to other regulators, ODC fees are considerably more expensive. Select examples of fees (based on new applications) are provided in the table below:

Licences	Types of fees	Approximate cost*
ODC[52]	• Licence applications can vary from $8,030-$9,320 • Permit application are $3440 per permit, (generally need one per licence) • Licence variations vary from $1,100 - $5,500 depending on complexity (per licence). • Permit variations vary from $120-$2,900 depending on complexity (per permit) • Planned inspection $3670 • Annual licence charge $12,010 • Annual site charge $19,230	(1 licence, 1 permit): ~$46,370
WA Poisons[53]	• Wholesale/manufacture licence is $562 • Renewal $255 • Amendments $82. • Inspection fee – unable to locate data.	~ $562 + inspection fee
WA Industrial Hemp[54]	• New licence $328 • Renewal $131 • Inspection cost (if a full day) $1,263.00	~$1,841
TGA[55]	• Annual manufacturing - $820 • Variation $820 • Inspection fees of $1020/hour/inspector) (Total costs have been calculated including inspection by 1 inspector for 7hrs/day and 3 days on site).	~$22,240

* "Best case" scenario in first year of operation with no amendments.

To meet licencing and permit costs, cultivators have to achieve a minimum harvest output to produce enough medical cannabis materials to break even.

Initially, higher costs for ODC licences were aimed at only attracting serious applicants, however this has resulted in:

- smaller businesses being unable to afford starting up in the new industry, and
- high pricing of cannabis products.

6.2. Pharmaceutical barrier 3 - ODC processing times

At the commencement of the medicinal cannabis industry, the ODC were bombarded with applications which impacted their processing times. Despite the number of applications dropping in recent years, the processing times are still long. According to their most recent cost recovery statement, the ODC indicated that their processing times were as follows:

- cannabis licence application - approximately 210 days
- application to vary a cannabis licence: Simple – approximately 70 days
- application to vary cannabis licence: Complex – approximately 210 days.[61]

This will hopefully improve after the reforms to the single licence scheme, but a case study has been provided below that demonstrates the impracticality of operating under such time constraints.

6.2.1. Client Case study

PharmOut has assisted multiple cannabis businesses through the ODC processes over the past four years, and this case is notable as an example of how quickly costs can add up and how cannabis businesses can be significantly hindered by bureaucracy and processing times:

Client A has spent close to $200k with the ODC over a 14-month period. This has included annual fees for licences and sites, as well as inspection fees, and complex licence and permit variations.

Business environments tend to be very dynamic by nature, with new customers or suppliers identified, and contracts drawn up quickly. However, the ODC require a new licence/permit variation to be submitted whenever there is a change to supply chain (even to providers they have approved before, e.g. a security company or testing lab), and any changes to approved Standard Operating Procedures (which not even the TGA require).

Complex variations to permits cost $5,500, and for Client A, one of the permit variations captured the acquisition of another medicinal cannabis company. Paperwork for the variation was submitted in May 2021, however, as of Jan 2022, this paperwork has not yet been approved (245 days later) and exceeds the ODC's stated 210 working day timeline.

Another complex permit variation was submitted a month before planting as a new order had come in and another strain of cannabis needed to be included in the cultivation plan. However, the regulator's processing time (70 days) exceeded the planting schedule.

The compliance burden and processing timelines by the regulator are restrictive, costly, and ultimately unsustainable.

6.3. Barriers preventing nutraceutical use of medicinal cannabis

The use of cannabis in nutraceuticals is prevented by the TGA's definition of complementary medicines (which includes nutraceuticals):

"In Australia, medicinal products containing such ingredients as herbs, vitamins, minerals, nutritional supplements, homoeopathic and certain aromatherapy preparations are referred to as 'complementary medicines' and are regulated as medicines under the Therapeutic Goods Act 1989." [9]

The standard that controls which compounds can be included in complementary medicines is the *Therapeutic Goods (Permissible Ingredients) Determination (No. 3) 2021.* [10] This standard does not include any cannabinoid compounds, therefore THC, CBD, nor any other cannabinoids are permitted to be used as ingredients in complementary medicines.

Further discussion about nutraceuticals is conducted in section 8.

7. Medicinal cannabis, its prescription, availability, and affordability

This section will be brief as there are organisations that provide specific target market data analysis regarding the uptake of medicinal cannabis in Australia, e.g. FreshLeaf Analytics[11] and Cannabis Access Clinics[12]. There was also a detailed senate inquiry conducted in January 2020 into *Current Barriers to Patient Access to Medicinal Cannabis in Australia*[13].

7.1. Prescription of medicinal cannabis

As most cannabis products are considered unapproved medicines, prescription occurs through the Special Access Scheme B (SASB) and Authorised Prescriber (AP) scheme. There have been some recent reforms that make it easier to access cannabis by reducing administrative burden and increasing flexibility of product choice[56].

Cannabis products may be registered on the Australian Register of Therapeutic Goods but requires the support of clinical evidence, which is expensive and time-consuming to secure. The cost of registering novel products is high[55] and so most of the supply within the medicinal cannabis industry is proceeding down SAS B and AP schemes.

7.2. Availability and affordability of medicinal cannabis

The TGA restricts the advertising of medicinal cannabis products[14] (i.e. advertising is not permitted for unapproved products; controlled drugs and prescription drugs may only be advertised to health professionals). This has made it difficult for prescribers to become educated about the applications and availability of medicinal cannabis products in the market, though clinical guidelines for medicinal cannabis are available[60]. However, the industry has launched several platforms to assist prescribers, suppliers, and patients (e.g. Althea Concierge[15], Honahlee[16]).

Cannabis products are not currently included on the Pharmaceutical Benefits Scheme (other than Epidiolex[57]), however patients are able to use private health insurance (pharmaceutical "extras" cover) towards their prescriptions[17].

There are some misunderstandings in the industry about cannabis product supply chain permissions, i.e. no "middle man" or wholesaler is allowed, and suppliers must

maintain direct control over products through to pharmacy and patients. (This is specified in the TGA guidance for the *Supply and wholesaling of medicinal cannabis products*[18]).

This requirement impacts supply chains as medicinal cannabis businesses are not allowed to release products for supply until they have sighted the prescription (and pharmacies are not allowed to stockpile and wholesale cannabis products in excess of prescription repeats).

Long cultivation times can also cause logistical challenges when fulfilling orders, however reports received from PharmOut clients around the time of the flower finished product shortages[19] indicate that this was more due to the issues discussed in section 6.2 regarding the approval of supply as opposed to actual limitations in stock.

8. The potential benefits and risks of permitting industrial hemp for human consumption.

Given the consumption of industrial hemp was authorised by the Food Standards Australia New Zealand (FSANZ) in 2017, this query is slightly redundant.

FSANZ recognised that hulled and non-viable low-THC hemp seed foods "may provide a useful alternative dietary source of nutrients and polyunsaturated fatty acids, particularly omega-3 fatty acids." A detailed assessment of risk is provided in their *Approval Report - Proposal P1042* [20].

In addition, the Department of Primary Industries and Regional Development states that feeding hemp fibre or hemp products to animals is not prohibited[21] however all producers are responsible for ensuring that any animals or animal products they produce do not contain substances that would contaminate food.

Thus, any further assessment of the human consumption of industrial hemp products, namely pressed seed oil, is not required on the part of the WA state government.

However, given the common confusion between industrial hemp and CBD extracted from industrial hemp (as covered in section 5) and the question about nutraceuticals in 6.2, it is suspected that the question may instead be asking about the benefits and the risks of permitting CBD for human consumption (in a nutraceutical form). Thus, the remainder of this section will be focussed on CBD as a stand in for the "industrial hemp" initially posed in the question.

8.1. Benefits of CBD for human consumption

In terms of benefits, there are already known and approved uses of CBD medicinally [59 and 60], however the low doses remain a bone of contention. CBD has proven clinical effects when administered as a therapeutic good but less so in low doses. This then begs the question: is there any point in dedicating effort to reform regulations to allow CBD into the complementary medicines category when the doses would result in a negligible measurable outcome? It would seem the current categorisations (S4, S3) are the most suitable ones (pending more convincing data). This ties back to the discussion in section 6.1.

8.2. Risk of CBD for human consumption

Safety studies have already been performed by the TGA[6] and others[49 and 58], however as an additional thought experiment, this section uses Epidiolex as a case study.

Produced by GQ Pharmaceuticals, Epidiolex is a liquid formulation of non-synthetic CBD, designed to be administered orally. It is the only CBD drug to have been fully approved by regulators in the US[25], Australia[26], and Europe[27]. Used to treat two rare and severe forms of treatment-resistant epilepsy (Dravet and Lennox-Gastaut syndromes), doses for Epidiolex are recommended to start at 5 mg/kg/day and increase to a maximum of 20mg/kg/day[20]. (Note that this is 20 times higher than the proposed low dose identified in the TGA safety review[6].)

US regulators have raised concerns over potential liver injury, interaction with concomitant medication and drugs, and unknown effects on sensitive populations (e.g. adolescents elderly, children, pregnant women, etc.)[29]. An additional concern regarding the unknown effects of long-term cumulative exposure was also raised by Canadian regulators back in 2013 [30].

The Epidiolex product leaflet indicates observed side effects of somnolence, diarrhea, vomiting, sleep disorders, fatigue, and others[28]. While side effects and potential liver injury due to drug-drug interactions can be alleviated by clinical guidance and supported by instructions for use, there are remaining questions regarding the use of CBD by men and by pregnant women. These questions trickle over into the argument against the compound's widespread use.

In animal studies, there is some evidence to indicate that CBD may interfere with embryo implantation and the development of the placenta. Chick embryo exposure to CBD was shown to decrease the embryo viability by 50-80% and cause a delay in the embryonic maturity. Similar findings have been reported in zebrafish studies. In mice, prenatal exposure to CBD also led to an increase in defects observed for face and eye formation[31].

CBD interference in human pregnancy is also confirmed in an earlier review conducted by the National Academies of Sciences, Engineering, and Medicine (NASEM). One of the major findings identified a strong relationship between marijuana use during pregnancy and lower birth weight. NASEM has stressed the need for further research to fully determine the effects pre, peri, and postnatally [32].

Reports on male reproductive toxicity in mouse models indicate that CBD exposure results in lower levels of testosterone and testicular weight. These findings are also in line with observations made in studies of rats and rhesus monkeys[31].

However, Epidiolex appears to have taken all of this into account. In the product technical document, the company indicates that they have conducted tests on female fertility using doses up to 250mg/kg/day (60 times greater than the maximum recommended human dose for the product). A dose of 125 mg/kg/day was observed to have an impact on foetal body weights and also impacted the face structure of rat pups. Embryo mortality was observed at a 250mg/kg/day dose. At doses 150mg/kg/day and higher, slower growth, sexual maturation (small testes), and decreased activity were observed. In juvenile rats, developmental toxicity was noted at 100mg/kg/day (approximately 20 times that advised for paediatric subjects)[28].

From this, Epidiolex appears to have addressed the main concerns regarding CBD, however, treatment populations still warrant further professional monitoring to best capture the effects of long-term administration. It is also not clear if these observations in animal studies are fully transferrable to humans, or relevant to CBD being used to treat other health conditions in other dosage forms. Indeed, the study by Larsen and Shahinas indicate that CBD is even more effective in a nasal spray at much lower doses[49].

9. Additional discussion

There are other areas in the legislative framework that could be further investigated if more widespread use of CBD is desired. Three facts are known for sure:

- High concentrations of CBD are considered S4.
- A 150mg/day dose of CBD is considered S3.
- The TGA concluded in their safety review that known adverse events of CBD at low doses were not serious, and that they considered 60mg a safe daily dose[6].

Based on the TGA's own classifications (and safety review), it indicates that different concentrations of CBD can be regulated differently. In addition, if the TGA considers 60mg or 150mg a safe daily dose under S3, then arguably any dose lower than those could be taken off the SUSMP entirely.

There are also international precedents for treating CBD differently. For example:

- In 2020, the EU ruled that CBD "should not be considered as drug within the meaning of the United Nations Single Convention on Narcotic Drugs of 1961 in so far as it does not have psychotropic effect. As a consequence, cannabidiol can be qualified as food, provided that also the other conditions…are met." [33] Indeed, CBD is considered a "Novel Food," [34] and a quick search on the EU website reveals a number of applications that support values ranging from 4mg/day,[36] 50mg/day,[35] and 150mg/day[37].
- The EU also recently updated their cosmetics guidelines to add CBD as an approved ingredient[38].
- South African legislation allows CBD as a supplement when in pack sizes containing 600mg or less of CBD and limited to maximum dose of 20mg/day. Otherwise, it is considered a prescription only medication (Schedule 4) [39].
- During the WHO's critical review of cannabis, they recommended removing cannabis from Schedule IV of the 1961 Single Convention on Narcotics Drugs and clarified that cannabidiol (CBD) should not be under international control. (This has generated some controversy as there are still some details that require further clarification.)[40]

Currently there are some local legislative blocks that do not allow CBD into cosmetics or complementary medicines in Australia. This is due to where CBD is listed the Poisons Schedule (S4 and S3). To open up the market there are at a minimum, 3 pieces of legislation that need to be changed (using the original minimum safety CBD limit identified by the TGA as an initial reference):

- SUSMP[4] – e.g. to exclude 60mg CBD from being listed in the Poisons Standard, or to be listed under S5 or S6 (which would allow it to be used in cosmetics).
- Therapeutics Goods (Excluded Goods Determination 2018)[44] – e.g. to allow the 60mg/day dose as an allowable ingredient in cosmetics (right now the legislation does not allow any substance that is included in S2,3,4 or 8 of SUSMP).
- Therapeutic Goods (Permissible Ingredients) Determination (No. 3) 2021 [10]– e.g. to allow <60mg/day dose as an allowable ingredient in listed complementary medicines/supplements.

As a complete alternative, WA could also look into introducing its own decriminalisation bill, as was done in ACT via the *Drugs Of Dependence (Personal Cannabis Use) Amendment Bill 2018*. This allowed private home grows and possession of cannabis provided there is no commercial supply, or production beyond stated limits.[62]

10. References

1. Department of Primary Industries and Regional Development. *Industrial Hemp Act 2004*. https://www.legislation.wa.gov.au/legislation/statutes.nsf/main_mrtitle_449_homepage.html (2018).
2. Federal Register of Legislation. *Narcotic Drugs Act 1967*. https://www.legislation.gov.au/Details/C2021C00483 (2021).
3. Health Department of Western Australia. *Medicines and Poisons Act 2014*. https://www.legislation.wa.gov.au/legislation/statutes.nsf/law_a147008.html (2021).
4. Therapeutic Goods Administration. *The Standard for the Uniform Scheduling of Medicines and Poisons (SUSMP).* https://www.tga.gov.au/publication/poisons-standard-susmp#electronic (2021).
5. Office of Drug Control. *Guideine: Security Of Medicinal Cannabis.* https://www.odc.gov.au/publications/guideline-security-medicinal-cannabis (2020).
6. Therapeutic Goods Administration. *Review on the safety of low dose cannabidiol*, https://www.tga.gov.au/alert/review-safety-low-dose-cannabidiol (2020).
7. Therapeutic Goods Administration. *Notice of final decision to amend (or not amend) the current Poisons Standard – cannabidiol,* https://www.tga.gov.au/scheduling-decision-final/notice-final-decision-amend-or-not-amend-current-poisons-standard-cannabidiol (2020).
8. Therapeutic Goods Administration. *OTC new medicines registration process*. https://www.tga.gov.au/publication/otc-new-medicines-registration-process (2020).
9. Therapeutic Goods Administration. *An overview of the regulation of complementary medicines in Australia*. https://www.tga.gov.au/overview-regulation-complementary-medicines-australia (2013).
10. Federal Register of Legislation. *Therapeutic Goods (Permissible Ingredients) Determination (No. 3) 2021*. https://www.legislation.gov.au/Details/F2021L01449 (2021).
11. FreshLeaf Analytics Reports. https://freshleafanalytics.com.au/reports/ (2021).
12. Cannabis Access Clinics. *Australian Medicinal Cannabis Pricing Analysis*. https://caclinics.com.au/wp-content/uploads/2019/06/CAC_MedicinalCannabisPricingAnalysis_Online.pdf (2018)
13. Parliament of Australia. *Current barriers to patient access to medicinal cannabis in Australia*. https://www.aph.gov.au/Parliamentary_Business/Committees/Senate/Community_Affairs/Medicinalcannabis/Report (2020).
14. Therapeutic Goods Administration. *Advertising guidance for businesses involved with medicinal cannabis products*. https://www.tga.gov.au/publication/advertising-guidance-businesses-involved-medicinal-cannabis-products (2019).
15. Althea Concierge. https://althea.life/concierge/ (date unknown).
16. Honahlee. https://honahlee.com.au/ (date unknown).
17. Honahlee. *PBS & Private Health Cover For Legal Medical Cannabis*. https://honahlee.com.au/articles/health-insurance-cover-cbd-cannabis/, (2021).
18. Therapeutic Goods Administration. *Supply and wholesaling of medicinal cannabis products (MCP)*. https://www.tga.gov.au/sites/default/files/supply-and-wholesaling-medicinal-cannabis-products-mcp.pdf (2021).
19. Cohen, R. *Flower shortage hits Australian patients*. https://www.cannabiz.com.au/flower-shortage-hits-australian-patients/ (Cannabiz 2021)
20. Food Standards Australia New Zealand. *Approval report – Proposal P1042 Low THC Hemp Seeds as Food*.

https://www.foodstandards.gov.au/code/proposals/Documents/P1042%20Low%20THC%20hemp%20as%20a%20food%20AppR.pdf (2017)

21. Department of Primary Industries and Regional Development. *Industrial hemp in Western Australia*. https://www.agric.wa.gov.au/hemp/industrial-hemp-western-australia-0 (2021)
22. Food and Drugs Administration. *Hemp Production and the 2018 Farm Bill*. https://www.fda.gov/news-events/congressional-testimony/hemp-production-and-2018-farm-bill-07252019 (2019)
23. Therapeutic Goods Administration. Therapeutic Goods Act 1989. https://www.legislation.gov.au/Details/C2021C00376 (2021
24. Lean, A. *Cultivation of Medicinal Cannabis vs Hemp*. https://www.pharmout.net/cultivation-of-medicinal-cannabis-vs-hemp/ (2019)
25. Food and Drugs Administration. *What You Need to Know (And What We're Working to Find Out) About Products Containing Cannabis or Cannabis-derived Compounds, Including CBD*. https://www.fda.gov/consumers/consumer-updates/what-you-need-know-and-what-were-working-find-out-about-products-containing-cannabis-or-cannabis (2020)
26. Therapeutic Goods Administration. *Guidance for the use of medicinal cannabis in Australia: Patient information*. https://www.tga.gov.au/publication/guidance-use-medicinal-cannabis-australia-patient-information (2017)
27. European Medicines Agency. *Epidyolex*. https://www.ema.europa.eu/en/medicines/human/EPAR/epidyolex (2021)
28. Greenwich Biosciences. *EPIDIOLEX® (cannabidiol) offers flexible dosing for tolerability and response optimization*. https://www.epidiolexhcp.com/dosing-and-calculator (2021)
29. Throckmorton, D. *Cannabis Policies For the New Decade*, Cannabis Policies For the New Decade - 01/15/2020 | FDA (2020).
30. Health Canada. Information for Health Care Professionals. https://www.hc-sc.gc.ca/dhp-mps/alt_formats/pdf/marihuana/med/infoprof-eng.pdf (2013)
31. Argueta, D.A.; Ventura, C.M.; Kiven, S.; Sagi, V.; Gupta, K. *A Balanced Approach for Cannabidiol Use in Chronic Pain*. Frontiers in Pharmacology, page 561 (2020).
32. National Academies of Sciences, Engineering, and Medicine. *The health effects of cannabis and cannabinoids: The current state of evidence and recommendations for research.* The National Academies Press. (2017)
33. EU Parliament. *EU Parliamentary Questions 19 March 2020*. https://www.europarl.europa.eu/doceo/document/E-9-2021-001517_EN.html#def1 (2020)
34. Varallo, C. *EU Commission – CBDs has to be considered novel food*. https://foodlawlatest.com/2021/05/24/eu-commission-cbds-has-to-be-considered-novel-food/ (2021)
35. CBDepot. *Public summary of the dossier: Synthetic trans-Cannabidiol.* https://ec.europa.eu/food/system/files/2019-11/novel-food_sum_ongoing-app_2019-1371.pdf (2019)
36. Farmabios S.p.A. Via Pavia. *Public summary of the dossier: Synthetic Cannabidiol (CBD)*. https://ec.europa.eu/food/system/files/2021-04/novel-food_sum_ongoing-app_2020-2174.pdf (2020)
37. Cibdol AG. *Summary of the application (-)-Cannabidiol derived from chemical synthesis*. novel-food_sum_ongoing-app_2019-0935.pdf (europa.eu) (2019)
38. Hemp Industry Daily. *EU market regulator updates cosmetics guidelines to add CBD as legal ingredient*. https://hempindustrydaily.com/eu-market-regulator-updates-cosmetics-guidelines-to-add-cbd-as-legal-

ingredient/?utm_medium=email&utm_source=newsletter&utm_campaign=INTL_20210205_NEWS_Weekly (2021)
39. Verhoef, A. *South Africa reschedules CBD & THC, but opens a narrow window*. https://hemptoday.net/south-africa-reschedules/ (2020)
40. Walsh, J., Jelsma, M., Blickman, T., Bewley-Taylor, D. The WHO's First-Ever Critical Review of Cannabis. https://www.tni.org/en/publication/the-whos-first-ever-critical-review-of-cannabis (2019)
41. Lean, A. *S4 CBD for pets and livestock*. https://www.pharmout.net/s4-cbd-for-pets-and-livestock/ (2021)
42. Therapeutic Goods Administration. *Claims about hemp and CBD oils misleading consumers.* https://www.tga.gov.au/behind-news/claims-about-hemp-and-cbd-oils-misleading-consumers (2018)
43. Therapeutic Goods Administration. *Rick's Hemp Oil Full Spectrum Hemp Supplement 500 mg*. https://www.tga.gov.au/alert/ricks-hemp-oil-full-spectrum-hemp-supplement-500-mg. (2021)
44. Federal Register of Legislation. *Therapeutics Goods (Excluded Goods Determination 2018)*. https://www.legislation.gov.au/Details/F2021C00847 (2021).
45. Therapeutic Goods Administration. *Australian code of good wholesaling practice for medicines in schedules 2, 3, 4 & 8.* https://www.tga.gov.au/publication/australian-code-good-wholesaling-practice-medicines-schedules-2-3-4-8 (2010)
46. Health Department of Western Australia. *Medicines and Poisons Regulations 2016*. https://www.legislation.wa.gov.au/legislation/prod/filestore.nsf/FileURL/mrdoc_43423.pdf/$FILE/Medicines%20and%20Poisons%20Regulations%202016%20-%20%5B00-h0-00%5D.pdf?OpenElement (2020)
47. Therapeutic Goods Administration. *Consultation: Proposed amendments to the Poisons Standard – ACCS, ACMS and joint ACCS/ACMS meetings, March 2022* https://www.tga.gov.au/sites/default/files/consultation-proposed-amendments-poisons-standard-accs-acms-and-joint-accsacms-meetings-march-2022.pdf (2021)
48. Health Department of Western Australia. *Disposal of medicines.* https://ww2.health.wa.gov.au/Articles/A_E/Disposal-of-medicines (unknown when page was posted)
49. Larsen, C., Shahinas, J. *Dosage, Efficacy and Safety of Cannabidiol Administration in Adults: A Systematic Review of Human Trials.* https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7092763/ (2020).
50. Wilks, D. *Testing for truth part 8: are there cannabinoids in stems and stalks?* https://www.orangephotonics.com/testing-for-truth-part-8/ (2020)
51. Kleinhenx, D.M., et al. *Nutrient concentrations, digestibility, and cannabinoid concentrations of industrial hemp plant components.* https://www.sciencedirect.com/science/article/pii/S2590286520300859 (2020)
52. Office of Drug Control. *Guidance: Fees and Charges.* https://www.odc.gov.au/publications/fees-and-charges (2021)
53. Department of Health. *Application forms for Licences and Permits.* https://ww2.health.wa.gov.au/Articles/A_E/Application-forms-for-Licences-and-Permits (unknown date)
54. Department of Primary Industries and Regional Development. *Licensing industrial hemp activities in Western Australia.* https://www.agric.wa.gov.au/plant-biosecurity/licensing-industrial-hemp-activities-western-australia (2020)
55. Therapeutic Goods Administration. *Fees and charges: summary From 1 December 2021*. https://www.tga.gov.au/sites/default/files/fees-and-charges-summary-1-december-2021.pdf (2021)

56. Lean, A. *TGA Updates for Medicinal Cannabis*. https://www.pharmout.net/tga-updates-for-medicinal-cannabis/ (2021)
57. Department of Health. *Cannabidiol.* https://www.pbs.gov.au/medicinestatus/document/445.html. (2022)
58. Santos, R.G., et al. *Serious adverse effects of cannabidiol (CBD): a review of randomized controlled trials*. https://www.tandfonline.com/doi/full/10.1080/17425255.2020.1754793 (2020)
59. Parliament of Western Australia. *Inquiry into Cannabis and Hemp*. https://www.parliament.wa.gov.au/parliament/commit.nsf/0/78055DF4E73607E74825876F001F67DD?opendocument&type=sub (2021)
60. Therapeutic Goods Administration. *Medicinal cannabis - guidance documents.* https://www.tga.gov.au/medicinal-cannabis-guidance-documents (2020)
61. Office of Drug Control. Cost Recovery Implementation Statement (CRIS). https://www.odc.gov.au/sites/default/files/cris-regulation-of-medicinal-cannabis-2021-22.pdf (2021)
62. Australian Capital Territory Legislation Register. *Drugs of Dependence (Personal Cannabis Use) Amendment Bill 2018*. https://www.legislation.act.gov.au/b/db_59295/ (2018)