Review of the Medicinal Cannabis Compassionate Use Scheme

NSW Chief Scientist & Engineer

April 2017
Dear Premier,

**Review of the Medicinal Cannabis Compassionate Use Scheme**

In May 2016 the former Premier of NSW, Mr Mike Baird, announced that I would oversee a broad review of the Medicinal Cannabis Compassionate Use Scheme (formerly known as the Terminal Illness Cannabis Scheme). This was to be in addition to a review of operational matters that was already underway, led by the Department of Premier and Cabinet.

This report provides the findings and conclusions related to both the operational issues and the broader review which focuses particularly on whether eligibility for the Scheme should be expanded to patients with particular non-terminal conditions.

I would like to acknowledge the time and support provided by the Department of Premier and Cabinet in leading much of the research and consultation for this review and the other government departments, medical experts and community leaders who provided their views to inform the review.

I would also like particularly to acknowledge the contribution of Emeritus Professor Laurence E. Mather.

Yours sincerely,

[Signature]

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Mary O’Kane
Chief Scientist & Engineer
EXECUTIVE SUMMARY

The Medicinal Cannabis Compassionate Use Scheme (formerly the Terminal Illness Cannabis Scheme) was established in December 2014 to extend compassion to adults with a terminal illness who use cannabis to relieve symptoms. The Scheme provides guidance to NSW Police Force Officers about using their discretion not to charge adults with a terminal illness for possession of a prohibited drug if they are registered with the Scheme, as well as up to three registered carers.

When established, it was agreed that the Scheme would be subject to a review of its operation against its objectives after 12 months. The review was undertaken by the Department of Premier and Cabinet and the findings are included in this report.

In May 2016, the Premier asked the Chief Scientist & Engineer to review the Scheme more broadly and, in particular, to consider whether it should be extended to include patients with specified non-terminal conditions. This followed growing community interest in the potential therapeutic benefits of cannabis for a wide range of medical conditions. This report also documents the findings and recommendations of this broader review.

There have been significant policy and regulatory developments since the introduction of the Scheme in 2014.

At a national level, the Therapeutic Goods Administration has clarified the legal pathways for access to unregistered cannabis-based medicines via the Authorised Prescriber and Special Access Schemes, as well as through clinical trials. Legislation is also in place to allow legal cultivation of cannabis under licence for medical and related scientific purposes. This makes the future supply of domestically produced cannabis-based medicines possible, in addition to what can be imported currently.

In NSW cannabis-based medicines meeting appropriate standards can now be lawfully prescribed. Specifically, NSW has amended its regulations applying to the prescription of certain unregistered therapeutic goods, including most cannabis-based products manufactured to appropriate quality standards for pharmaceuticals. This enables doctors to apply to prescribe unregistered cannabis-medicines in appropriate circumstances.

In addition to considering the implications of the recent regulatory reforms, the review considered the current level of scientific evidence for medicinal cannabis use and revisited the question of the potential harm arising from the use of untested or illicit product.

Research involving clinical trials and observational studies suggests that specific cannabis formulations may be useful for some patients with conditions such as refractory epilepsy, chemotherapy-induced nausea and vomiting, spasticity associated with multiple sclerosis, pain and appetite symptoms associated with advanced cancer, neuropathic pain, post-traumatic stress disorder, ulcerative colitis and several other conditions. Overseas, Ministries of Health in Israel, the Netherlands and Canada have produced guidelines for the use of cannabinoid products in specific circumstances.

None of the current evidence points to cannabis or cannabis derivatives working for all patients all of the time. However, cannabinoids are likely to be an appropriate therapy in a percentage of cases in some conditions. For example, early trial results for cannabidiol use in certain paediatric epilepsy syndromes show that approximately one in 10 children with treatment-resistant epilepsy may become seizure free and three in 10 may have some
reduction in seizures. The appropriate place of cannabis and cannabis-derived medicines in the treatment pathways is yet to be defined in many conditions.

The cannabis-based products covered in many of the studies in the scientific literature and overseas government guidelines are potentially available for prescription in Australia.

This means that for the medical conditions for which expanding eligibility for the Medicinal Cannabis Compassionate Use Scheme was considered, there is now a legal access pathway available, albeit one that is relatively untested and not yet well understood by the Australian medical community. This is likely to be because we are dealing with unregistered therapeutic goods that have to be imported (for now) and that do not have the conventional product information available that summarises the evidence and guides prescribing.

What has not changed since the Scheme’s introduction in 2014 are the problems of black market supply such as the unknown composition of products, lack of knowledge and information about dosage, potential contamination (with particular risks for immunosuppressed patients) and the potential for unpredictable drug-drug interactions. There are also potential public safety risks from exposure to illicit suppliers and organised crime.

If the legal pathway for access to cannabis products regulated as medicines was better bedded down, it would be straightforward to recommend that the Scheme be closed down and that all patients wishing to access cannabis or cannabis-derived products do so through the legal route.

Yet, while the legal routes have been clarified, at the moment there are a number of steps that can be complex and time consuming, such as the absence of product in Australia and the need to import. The announcement by the Commonwealth Government in February 2017 enabling companies capable of producing appropriately manufactured cannabis-based medicines to apply for a license to import and store products on-shore should go some way towards addressing this issue. However, it is still early days. Accordingly, it probably would be imprudent to wind up the Scheme at this time and the Review recommends it be retained with the current eligibility criteria, but made easier to use for those who are terminally ill.

For other, non-terminal conditions, the review recommends that the legal access route be pursued and that the Government provide specific help to accelerate access via this route to patients likely to benefit from cannabis-based drugs.
RECOMMENDATIONS

Recommendation 1
That the following administrative changes be made to the Scheme to improve its operation:
• registrants have the option to apply electronically
• the registration period is extended from 12 to 24 months
• a renewed communications strategy is implemented to improve awareness of the Scheme and how it operates among eligible people with a terminal illness, their carers, medical practitioners and other relevant professionals
• communication materials are revised to emphasise:
  o the confidential nature of the Scheme
  o that the Scheme does not provide supply and cannabis use remains illegal in general (unless authorised and prescribed by a medical practitioner)
  o that the NSW Government and medical practitioners are not prescribing or endorsing cannabis use under the Scheme
  o that the Scheme may not cover use or possession at hospitals, residential aged care facilities, hospices and other health facilities.

Recommendation 2
That the eligibility criteria and quantities of cannabis allowed under the Scheme remain unchanged.

Recommendation 3
That Government help medical practitioners to use available routes for accessing high quality and lawfully produced cannabinoid medicines in appropriate circumstances by:
• supporting medical practitioners with information about current evidence for indications and the legal pathways for prescribing and sourcing an appropriate medicinal cannabis product for patients
• continuing to support inter-jurisdictional work to expedite development of national clinical guidance for indications for use; dose; mode of administration; potential drug-drug interactions; and monitoring the use of unregistered cannabis-based medicines
• pursuing international collaboration on research, education and data collection to advance understanding and evidence for the use of medicinal cannabis products.
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1 INTRODUCTION

1.1 BACKGROUND TO THE SCHEME
The NSW Government developed the Medicinal Cannabis Compassionate Use Scheme (the Scheme) to extend compassion to adults who use cannabis to alleviate the symptoms of their terminal illness. The Scheme was formerly called the Terminal Illness Cannabis Scheme.

The Scheme aims to provide greater peace of mind for both terminally ill cannabis users and their carers. It provides guidelines to help NSW Police Force Officers determine when to use their discretion not to charge terminally ill cannabis users with possession of a prohibited drug. The guidelines also extend to carers who assist those people to administer cannabis.

NSW residents aged 18 years and over who have a terminal illness as defined by the Scheme are eligible to register, along with up to three carers. The terminal illness must be certified by a medical practitioner who is registered in Australia and involved in the ongoing care of the terminally ill patient.

The Scheme relies on registered people or their carers sourcing their own cannabis. In practice, this generally means that illicit cannabis products must be sourced.

The Scheme received Cabinet approval in September 2014 and became operational in December 2014. The first registrations were processed in January 2015.

1.2 PURPOSE OF THE REVIEW
The review of the Scheme was completed in two phases:
1. a review of operational matters was conducted by the Department of Premier and Cabinet. As part of the Cabinet decision to approve the Scheme, it was agreed that the Government would conduct a review of the Scheme after it had been in operation for 12 months
2. a review considering extension of the Scheme was overseen by the Chief Scientist & Engineer. In May 2016, the Premier announced that the Scheme would be renamed the Medicinal Cannabis Compassionate Use Scheme and that a review would be conducted to consider issues including whether the Scheme's eligibility criteria should be expanded.

This report covers the findings and recommendations from both of these review phases. The terms of reference for the review are at Appendix 1.

1.3 METHOD
Data was generated from a combination of methods, including: demographic data extracted from the Department of Justice Community Relations Unit (CRU) registration database; a survey sent to currently certifying medical practitioners; consultation with key stakeholders who have previously been consulted with throughout the development and implementation of the Scheme; and consultation with government, community and medical organisations. Advice was received from government agencies with responsibilities in health, justice, police and community services; medical specialists in the fields of oncology, palliative care, epilepsy, movement disorders, addiction, clinical pharmacology and toxicology; and community organisations including the Cancer Council, Cancer Voices and United in Compassion.
A survey was sent to 62 doctors who had recently certified a patient for the Scheme. Seventeen responses were received (27 per cent response rate).

Due to the absence of accurate estimates for the number of people in NSW that have a terminal illness, the review did not measure the impact of the Scheme in relation to the potential cohort of eligible participants.
2 CONSIDERATION OF OPERATIONAL MATTERS

2.1 PURPOSE AND SCOPE
The review of operational issues investigated the impact of the Scheme for participants and their carers, medical practitioners and Government departments that are involved in its administration and operation. In particular, the operational review examined:

- to what extent the Scheme is being utilised by people with a terminal illness and their views on the Scheme
- the impact the operation of the Scheme has had on Government agencies
- whether the Scheme is achieving its objective to alleviate the burden of stress experienced by people with a terminal illness who use cannabis and provides them with greater peace of mind
- whether improvements or efficiencies in the administration of the Scheme should be considered.

2.2 FINDINGS

2.2.1 The Scheme is being used by the intended cohort of people
Summarised data from the registry up to mid-December 2016 covering the demographics of participants, what conditions they have and the types of certifying practitioners involved is included at Appendix 3.

Analysis of the registered participant data indicated that the Scheme is being utilised by an appropriate cohort of people. Participants are typically older, cancer patients who are located across the State. The cumulative number of registrations has been steadily increasing.

Most certifying medical practitioners are general practitioners (GP), oncologists or palliative care specialists.

Participants nominate an average of two carers. There are some indications of illicit cannabis suppliers becoming registered as carers on the Scheme.

2.2.2 The Scheme has had some success in providing peace of mind to participants
Information from the consultation process indicates that the Scheme is achieving its objective of providing greater peace of mind to registered participants. In the survey of certifying practitioners, the majority of respondents indicated that the Scheme had moderately (47 per cent) or somewhat (41 per cent) provided peace of mind to the patient they certified for the Scheme, with the remaining 12 per cent indicating that it had fully provided peace of mind to their patients.

Respondents commented that a key factor that contributed to a greater peace of mind for their registered patients was removing the fear of legal consequences of cannabis use.

2.2.3 Certifying medical practitioners have limited concerns about the Scheme
Approximately 76 per cent of certifying medical practitioners that responded to the survey reported that they did not have any concerns about certifying their patient/s for the Scheme.

The remaining respondents raised concerns that related to:
- legal implications
- the definition of terminal illness
• patient eligibility
• the ongoing responsibility of the certifying doctor.

Almost 90 per cent of respondents indicated that they would consider certifying patients for the Scheme in the future.

### 2.2.4 The registration and certification process is simple and effective

The majority of practitioners that responded (94 per cent) reported that the certification process took under 30 minutes. However, some respondents indicated that the process could be further improved and streamlined by the implementation of an online form.

Advocacy groups also indicated that the certification and registration process was relatively straightforward.

### 2.2.5 Some aspects of the Scheme were a cause of concern

#### The former name of the Scheme could be confronting for people with a terminal illness

Advocacy groups indicated that including the phrase “terminal illness” in the name of the Scheme could be confronting for potential and existing participants. For example;

> "This name is very confronting for patients and families alike. It labels the patient in the worst possible way and causes unnecessary psychological trauma, particularly for the young."

(United in Compassion - submission)

In recognition of this, the then Premier announced in May 2016 that the name of the Scheme would be changed to the Medicinal Cannabis Compassionate Use Scheme.

#### The 12 month registration period was a cause of concern

Once registered, participants remain on the Scheme for 12 months. Participants are eligible to re-register for the Scheme after 12 months.

As of December 2016, six participants had re-registered for the Scheme.

The low level of engagement with the re-registration process can partly be explained by the fact that about half of participants whose registrations had expired by December 2016 had died.

However, the consultation process identified that the absence of a follow-up reminder process for people whose registrations were soon to expire likely contributed to the low level of re-registrations.

In order to remedy this, a new process has been implemented whereby the Scheme’s register is linked with Births, Deaths and Marriages data. This allows the Department of Justice CRU to be notified of registered people who have died. The CRU can then contact the certifying medical practitioners of participants that have not died to remind them that their patients can re-register.

Stakeholders also proposed that the 12 month registration period could be extended.

Certifying practitioners that responded to the survey had differing views about the length of the registration period; 59 per cent of respondents felt that the registration should be ongoing whereas 24 per cent indicated that the registration period should remain as 12 months.

Advocacy groups indicated that the 12 month registration period was confronting for potential and current registered participants, as it may serve as an unnecessary reminder of the terminal nature of their illness. It was also viewed that the limited registration period could be an additional burden to participants that are already in ill health.
The NSW Australian Medical Association (AMA, 2016) noted that a 24 month registration period was its preferred option, “noting the emotional and practical sensitivities associated [with] certifying a terminal illness”.

The absence of a legal source of medicinal cannabis was a cause of concern
Under the current Scheme, sourcing cannabis is a matter for registered participants and their carers. Advocacy groups, medical practitioners and NSW Health indicated that sourcing cannabis was a cause of concern for people with a terminal illness. For example, a certifying medical practitioner responding to the survey indicated that: ‘While [the Scheme] condones the use of [cannabis] by patients, it does not deal with the problem of supply [or] purchase of the product, which my patient has found very challenging.’

Also, some stakeholders indicated that part of the concern about supply resulted from the mistaken belief that participation on the Scheme enabled participants to be provided cannabis, leading to disappointment and frustration when a product was not made available.

The quantities of products permitted by the Scheme were seen as inadequate
Some stakeholders felt that the specified quantities of cannabis products for the Scheme were too low.

Advocacy groups stated that the quantities are inappropriate, being based on criminal justice approaches for recreational cannabis use rather than the medical needs of participants.

This is discussed further in section 3.7.

2.2.6 Awareness of the Scheme and how it operates could be improved

Promotion of the Scheme to potential participants and their advocates could be improved
The Government has worked with relevant advocacy groups to raise awareness of the Scheme to people with a terminal illness who may use cannabis to alleviate their symptoms. For example, Cancer Voices NSW advised members and stakeholders about the Scheme through their newsletter and the Cancer Council NSW provided information to operators of their helpline that they could share with callers.

Despite such activities, there was broad agreement among stakeholders that there is a low level of awareness of the Scheme among people with a terminal illness.

This indicates a need for clear and targeted information about the Scheme to be available through health facilities and advocacy groups, in order to communicate the Scheme to people with a terminal illness that use cannabis to alleviate their symptoms better.

The Scheme has previously been promoted to medical practitioners through the NSW AMA and through the development of targeted communications materials. However, there was general agreement that the Scheme could be better promoted to medical practitioners. Less than half of certifying medical practitioner respondents had heard of the Scheme before discussing it with their patient. Currently, information about the Scheme is primarily shared among medical practitioners by word of mouth.

For people that are aware of the Scheme, some aspects of its operation are misunderstood
Overall, the stakeholders consulted largely agreed that the communication resources explaining the operation of the Scheme have been generally effective.

However, there are aspects of the Scheme which were seen to be unclear from the materials. In particular, NSW Health indicated that some registered participants were under the impression that the Scheme provided a source of legal cannabis. These misunderstandings had led to participants calling on pharmacists, doctors and other health care professionals to assist them in sourcing cannabis.
There was confusion as to whether the Scheme extended to registered participants admitted to hospitals or living in residential care. This is problematic for healthcare facilities, as staff are restricted in their ability to assist Scheme participants to administer or store illicit substances.

In response to this, in September 2016, NSW Health published advice for public health facilities which explains the effect of the Scheme for possession of cannabis in hospitals.

Certifying practitioner survey respondents indicated that they felt that patients generally understood that the Scheme only applied to people with a terminal illness and that the medical certification must be completed by a doctor involved in the patient’s ongoing care.

Three applications were made from interstate, which suggests that there may have been some confusion that this Scheme is only open to residents of NSW and the guidelines only apply within NSW.

Another unexpected issue described by an advocacy group was that members of the public who may be eligible for the Scheme believed that police would be informed of their cannabis use once registered, which is not the case.

Doctors that have certified patients and responded to the survey generally understand how the Scheme works but some aspects remain misunderstood. For example, only approximately 50 per cent of survey respondents indicated that they were fully aware of their role in the certification process, and, similar to their patients, the sourcing of cannabis remains an area of misunderstanding.

**Patients continue to engage with their doctor about the Scheme after certification**

Almost two thirds of certifying doctors who responded to the survey indicated that they had discussed the Scheme with their patient after certification. The most common reasons medical practitioners gave for these ongoing conversations were coordinating with other care or medication and discussing cannabis use and its benefits and/or side effects.

### 2.2.7 Estimated impact on Government resources

The CRU noted that it has been able to manage the registration process within existing resources. It estimates that, since the Scheme became operational, between five and seven hours a week have been spent processing applications although, due to the nature of the work, this has required oversight from a senior manager.

The Office of the Chief Health Officer within NSW Health indicated that the Scheme has had a significant impact on Ministry of Health resources within the Office, due to fielding calls and responding to correspondence about the Scheme. After an initial large volume of calls and correspondence, approximately once a month the Office will receive an inquiry from a health care professional requesting advice about how to manage a Scheme participant in a health care facility. An information bulletin has been developed to assist NSW Health employees to understand their responsibilities regarding this issue.

**Law enforcement**

NSW Police indicated that they felt police officers were aware of the Scheme and their role in its operation, with low records of incidents and communications by police about the Scheme.

However, there are some recent indications of illicit cannabis suppliers being registered as carers in the Scheme.
2.3 SUMMARY

The findings of this part of the review indicate that the Scheme is largely operating as intended, is generally being used appropriately, and contributes to the peace of mind of registered participants.

However, some concerns were raised which can be addressed.

First, the phrase ‘terminal illness’ in the original name of the Scheme (Terminal Illness Cannabis Scheme) and the 12 month registration period were seen as confronting. To remedy the first issue, in May 2016, the then Premier announced that the name of the Scheme would be changed to the Medicinal Cannabis Compassionate Use Scheme. This change has already taken effect.

DPC and Department of Justice have already taken steps to improve the re-registration process by linking Births, Deaths and Marriages data to the Scheme’s register, and the registration period should be extended to 24 months, to be applied retrospectively to current participants.

To improve the registration process, registrants should have the option to send through their applications electronically by e-mail.

There appears to be a low level of awareness about the Scheme among people with a terminal illness and medical practitioners and some aspects of the Scheme’s operation are also misunderstood. The recent guidance material about cannabinoid-containing products in public health facilities and revised communications materials should help address these issues.

In particular, messaging should re- emphasise that:

• the Scheme does not provide supply, and cannabis use remains illegal (unless a suitable lawfully produced product has been appropriately prescribed under state and Commonwealth regulatory arrangements)
• the NSW Government and certifying medical practitioners do not prescribe or endorse the use of cannabis under the Scheme
• health care professionals in hospitals and residential facilities cannot help participants administer or store cannabis
• participant personal and health information will not be shared other than in the review, administration and enforcement\(^1\) of the Scheme.

\(^1\) As provided for in the registration forms.
3 CONSIDERATION OF EXTENSION OF THE SCHEME

3.1 PURPOSE AND SCOPE
In May 2016, the then Premier announced that the Scheme would be reviewed to determine whether the objectives, scope, terms and conditions of the Scheme remain appropriate. Specifically, the review considered:

• whether the eligibility criteria for the Scheme should be expanded to include:
  o adults with non-terminal health conditions, including:
    ▪ conditions that are the subject of the NSW Government’s medicinal cannabis trials; and
    ▪ other conditions for which medicinal cannabis has allegedly provided relief, such as refractory epilepsy and auto-immune disorders
  o children with relevant health conditions
• whether the quantity and form of cannabis currently covered by the Scheme could be amended
• how the Scheme aligns with the Government’s broader approach to medicinal cannabis and current national developments
• other ways the Scheme could be improved to better meet the needs of the NSW community.

3.2 CALLS TO EXPAND ELIGIBILITY
Many people write to the NSW Government about medicinal cannabis issues, in the order of about 25 per month. Many are distressed and desperate for relief from the symptoms of particular terminal and non-terminal conditions, for example, neuropathic pain, when they have exhausted other treatment options or find those options unacceptable. In some cases, these patients are using illicit cannabis and report that it provides some relief or improvement in symptoms. In others they have read reports online or heard from their peers that cannabis may be helpful for them and they want the opportunity to try it.

This has led to some calls for the eligibility for the Scheme to expand to adult patients with non-terminal conditions and child patients with particular conditions. In some cases the calls are accompanied by requests for decriminalisation of cannabis. Others suggest this could be considered a temporary measure until such time as a legal and fully medical model of prescribing cannabis-based medicines was bedded down.

3.3 REGULATORY CHANGES SINCE THE SCHEME COMMENCED
In considering whether the Scheme should be extended, the review took into account the implications of the significant regulatory changes since the Scheme commenced in December 2014.

In NSW and most other states and territories, there is now a legal basis for a full supply chain and the lawful prescribing of a broader range of cannabis-based products than was previously possible.

When the Scheme commenced in December 2014 this was not the case. NSW legislation allowed for research in humans using cannabis, but prescribing outside of clinical trials was limited to a small number of medicines, including nabiximols (Sativex®) which is registered on the Australian Register of Therapeutic Goods for management of spasticity associated with multiple sclerosis. However, Sativex® is not routinely marketed in Australia.
At the Commonwealth level unregistered cannabis products could theoretically have been accessed through the Authorised Prescriber and Special Access Schemes, although these pathways had not been widely used for cannabis products. Also, the Commonwealth Narcotic Drugs Act 1967 allowed for the manufacturing of cannabis products, but not cultivation of the raw material in Australia.

Since then, there have been several key developments:

- the Therapeutic Goods Administration (TGA) has clarified the legal pathways for access to unregistered cannabis-based medicines via the existing Special Access and Authorised Prescriber schemes
- in consultation with states and territories, cannabidiol (where containing 2 per cent or less of other cannabinoids) was scheduled as a prescription-only medicine (Schedule 4) to enable clinical trials and use as an unapproved medicine (1 June 2015)
- also in consultation with states and territories, the TGA created new Schedule 8 entries for cannabis when lawfully produced or imported for human therapeutic use (1 November 2016). These new Schedule 8 entries were automatically adopted in the NSW Poisons List under the NSW Poisons and Therapeutic Goods Act 1966
- NSW has amended its regulations applying to certain unregistered therapeutic goods. From 1 August 2016, regulations and processes have been in place to enable doctors to apply for approval to prescribe unregistered cannabis-based medicines in appropriate circumstances. A subcommittee to the NSW Medical Committee has been established to review applications from prescribers and provide advice to the Secretary of NSW Health regarding issuance of authorities
- the Commonwealth Government has amended legislation to allow cannabis to be cultivated in Australia for medical and related scientific purposes, ensuring Australia maintains its compliance with the United Nations Single Convention on Narcotic Drugs
- in 2016 the NSW Department of Primary Industries received an authority from the Commonwealth Department of Health to undertake cultivation research that will fill knowledge gaps about growing cannabis for potential therapeutic purposes in Australia. Since then, the Commonwealth Office of Drug Control has granted two commercial licences.

There is also a much better understanding of the types and quality of cannabis-based products that are being used under lawful regimes overseas and that have been studied to some extent. Typically, most cannabis products contain mixtures of tetrahydrocannabinol (THC) and cannabidiol as active ingredients in different ratios, or they can be in the form of plant material containing a vast array of cannabinoids. There are some international manufacturers producing cannabis-based products to Good Manufacturing Practice standards, for example, in Canada, Israel and the Netherlands.

These developments have, relatively quickly, created the legal basis for a full supply chain in Australia.

However, it must be acknowledged that Australia is still in the early stages of the use of cannabis-based products as medicines. It is expected that medical practitioners may be cautious about prescribing unregistered medicines where high-quality evidence is limited and assurance of the quality of the product is not equivalent to a registered medicine. As there are currently no cannabis products legally manufactured as medicines in Australia, doctors have needed to look at importing overseas supplies in the short to medium term themselves.

In February 2017, the Commonwealth Government announced that companies capable of producing appropriately manufactured cannabis-based medicines would be able to apply for a license to import and store products on-shore until authorised for supply to a patient.

If approved companies choose to use this pathway to import a supply of a suitable product, it is expected that doctors will find that the prescription of pharmaceutical-grade cannabis-
based products less complex and faster. It is also expected to reduce the costs considerably.

In due course, the Commonwealth Government’s amended legislation to allow local cannabis cultivation for medical and related scientific purposes should lead to domestically produced products being available.

3.4 POTENTIAL RISKS ASSOCIATED WITH USE OF UNREGULATED CANNABIS

Contamination
The lack of easy access to regulated cannabis-based medicines is a fundamental limitation of the current Scheme. There are potential health and safety risks for patients from consuming illicit cannabis, in particular, contamination (heavy metals, pesticides and herbicides and pathogens), unknown dosage levels (including method of administration), and risks associated with illegal dealings, such as exploitation.

As an input to this review, Emeritus Professor Laurence E. Mather prepared a paper that describes some of the main risks associated with consumption of illicitly produced cannabis, particularly for very ill people. This paper is included at Appendix 4 (Mather, 2016). Mather highlights studies indicating that fungal and bacterial contamination is of particular concern as is the potential toxicity from heavy metal and agrochemical contamination.

Microorganisms such as fungi and bacteria are to be expected in unprocessed botanicals (Mather, 2016), which when inhaled can lead to infections which can be of particular concern to patients who have compromised immune systems. A Dutch study on cannabis available in Dutch coffee shops found that products were often contaminated with pathogens and fungi, including types which are capable of producing hazardous mycotoxins, such as carcinogenic aflatoxins (Hazekamp, 2006).

Mather (2016) notes that, despite many user expectations or supplier reassurances, there can be no assurance that an unregulated cannabis product has a reasonable standard of purity or is free from contamination. Residual extracting solvents in oils and other preparations are an additional risk.

Unknown composition
The composition and active cannabinoid content of illicit or unregulated cannabis products is often unknown, which is a major concern should unregulated cannabis material be used to attempt to treat serious medical conditions (Mather, 2016).

This and many of the other risks associated with use of unregulated cannabis products are illustrated in a recent finding from the Health Care Complaints Commission regarding a deregistered medical practitioner injecting two women with a cannabis preparation with the intention of treating their ovarian cancer, resulting in serious adverse events and prolonged hospitalisation (HCCC, 2016).

In Australia, evidence suggests that illicit cannabis is often high in tetrahydrocannabinol (THC), the cannabinoid that causes psychoactive effects, and low in other cannabinoids, particularly cannabidiol, the compound that may have some therapeutic or beneficial effects in patient groups such as those with refractory epilepsy (Swift, Wong, Li, Arnold, & McGregor, 2013).

Potential drug-drug interactions
In addition to these risks raised by Mather (2016), the use of illicit cannabis without medical oversight also raises concerns of unpredictable drug-drug interactions.
There was consensus among consulted medical experts that not enough was known about the potential for cannabis to interact with other treatments, such as cancer chemotherapy or immune suppressant medication.

Some experts noted that there were risks that cannabis use could affect how other drugs are metabolised. Ware and Tawfik (2005) explain that THC and other cannabinoids are metabolised by the same enzymes that metabolise other commonly prescribed medications, which may potentially lead to significant drug-drug interactions. A recent paper (Gaston, Liu, Cutter, Bebin, & Szafierlarski, 2016) explains that several antiepileptic drugs have significant drug-drug interactions with cannabidiol, highlighting the importance of monitoring levels of other antiepileptic drugs in patients receiving cannabidiol.

Others discussed concerns about cannabis use in people undertaking chemotherapy treatment. One oncology expert noted that cannabis may make chemotherapy more toxic, and other experts raised concerns that cannabis use could cause particular problems for people with weakened immune systems (including those undertaking chemotherapy treatments).

**Exposure to illicit suppliers**
A further issue, given that potential registrants have to seek supply from the illicit market, is concern of exposure to illicit suppliers and organised crime, and the potential exploitation of desperate people. Those selling cannabis may promote the potential beneficial of their products for a wide variety of health conditions but are not able to supply supporting evidence.

Unknown substances may be used to increase the weight of cannabis or make it appear more potent. In the United Kingdom, there were incidents of tiny glass beads added to cannabis to add weight and mimic THC-containing resin glands (McLaren, Swift, Dillon, & Allsop, 2008).

**Increased potential for long-term illicit cannabis use**
Expanding the Scheme to non-terminal conditions would open up the possibility of indefinite or long-term participation in the Scheme, and correspondingly long-term use of illicit cannabis. Evidence suggests that regular exposure to cannabis can be associated with alterations in the brain (Lorenzetti, Solowij, & Yucel, 2016). Also, evidence suggests that around 9 per cent of cannabis users can develop cannabis dependence. This increases to 17 per cent among those who start using cannabis in adolescence (Volkow, Baler, Compton, & Weiss 2014).

There is also research indicating an association between regular and prolonged cannabis use and poor mental health in some users. Hall (2015) reports that regular cannabis users have double the risk of experiencing psychotic symptoms and disorders, particularly where there is personal or family history of such disorders and when use starts in adolescence. There is also evidence of an association between use of cannabis and earlier onset of psychotic illness (Large, Sharma, Compton, Slade, & Nielsen, 2011).

There is also the general issue that people might use an unproven and/or ineffective therapy long term.

### 3.5 DOCTORS HAVE RESERVATIONS ABOUT AN EXPANDED SCHEME

The certification from a doctor involved in a patient’s ongoing care is central to the current Scheme. Feedback from medical experts across the fields consulted (oncology, neurology, palliative care, addiction medicine) was that the use of regulatory pathways and standardised products of known composition was preferred to an expansion of the Scheme.
Doctors raised particular concerns associated with the risk that patients may avoid or defer conventional treatment, and the limited quality evidence of the efficacy of cannabis for different conditions. Opposition to or lack of support for an expanded Scheme is more likely given that the Scheme requires participants to source illicit cannabis. Medical experts emphasised that clinical models of care require practitioners to be aware of the potential risks and benefits of a particular therapeutic product and weigh up these risks, which is not possible in an illicit, variable product.

**Deferred of conventional treatments**
There was significant concern from medical experts that there is currently considerable misinformation and confusion about the potential efficacy of cannabis among some patient groups. Some medical experts indicated that, despite the absence of scientific evidence in well-controlled human studies, some patients believe that cannabis use could cure a range of conditions.

As a result, medical experts indicated that there is a strong risk that expansion of the Scheme may cause their patients to defer or refuse conventional treatments in favour of using cannabis, or that cannabis use may make people unsuitable for standard medical treatments. Medical experts report the experience of patients choosing to use cannabis products in an attempt to ‘cure’ their cancer, only to return for care when their disease has advanced and is now incurable by standard therapies.

The American Cancer Society has recognised this risk and has advised that using cannabis as treatment while avoiding or delaying conventional medical care for cancer may have serious health consequences (ACS, 2015).

Expanding the Scheme and suggesting that a wider range of people should access illicit cannabis could increase the risk that people would defer or avoid conventional treatment in favour of unproven cannabis treatments.

**Limited high-quality evidence of the efficacy of medicinal cannabis**
When discussing the potential expansion of the Scheme, medical experts highlighted the lack of conclusive evidence about the benefits of medicinal cannabis, particularly with regards to the efficacy of cannabis in comparison to conventional treatments.

Medical experts also noted that much of the available evidence is anecdotal or results from animal trials or non-randomised controlled trial methods.

Australian medical bodies have similarly discussed limits on evidence of cannabis efficacy. The Royal Australian College of General Practitioners has stated that:

> "The current evidence base for the medical use of cannabis is highly heterogeneous, comprising a relatively small number of randomised clinical trials when stratified by condition, symptom, or intervention type. The studies are also of variable quality i.e. high risk of bias such as incomplete outcome data, low statistical power, and short follow-up time." (RACGP, 2016)

The NSW Ministry of Health indicated that even less is known about the efficacy of cannabis for children than for adults. The research that does exist for children is often based on subjective methods such as parental reporting, rather than scientific evidence.

The Canadian Paediatric Society stated that:

> "There are insufficient data to support either the efficacy or safety of cannabis use for any indications in children, and an increasing body of data suggests possible harm, most importantly in specific conditions" (CPS, 2016).

In addition to limited quality evidence on the efficacy of cannabis, medical experts cautioned that children and young people may be particularly susceptible to the potential negative effects of cannabis use.
There are cases where children have been taken to hospital following the consumption of cannabis. One case in Italy involved cannabinoid poisoning in a preschool child who had been prescribed hemp seed oil by his paediatrician to strengthen his immune system (Chinello, Scommegna, Shardlow, Mazzoli, De Giovanni, Fucci, Borgiani, Ciccacci, Locasciulli, & Calvani, 2016). Other cases in Israel involve children being hospitalised with cannabis poisoning after consuming marijuana that was meant to be used by relatives (El-Chai & Elizera, 2016).

The potential risks of cannabis use for children have contributed to Health Canada advising that medicinal cannabis should not be used for people aged under 25 years (Health Canada, 2016b).

The limits of available evidence and the need to ensure future studies undertaken are robust were highlighted in major reviews and reports released recently, including by the Irish Health Products Regulatory Authority, which concluded that:

“The scientific evidence supporting the effectiveness of cannabis across a large range of medical conditions is in general poor, and often conflicting. Cannabis has potential therapeutic benefits but these need to be better defined through clinical research” (Health Products Regulatory Authority, 2017).

The US National Academies of Sciences, Engineering and Medicine review of health effects of cannabis and cannabinoids makes a number of recommendations for a research agenda. This includes identifying critical research questions that can be addressed in the short and longer term and steps to ensure that sufficient data are being gathered (National Academies of Sciences Engineering and Medicine, 2017).

Limitation of use in hospitals and other facilities
Because the cannabis sourced under the police discretion model underpinning this Scheme remains a prohibited substance, staff in hospitals and other facilities cannot store or administer cannabis used under the Scheme if a patient is admitted to hospital.

Expansion may be seen as government endorsement of illicit cannabis for therapeutic purposes
The NSW Government has emphasised its commitment to a medical approach to cannabis use that is based on the evidence-based use of safe, known and standardised products. However, any expansion of the Scheme to non-terminal conditions has the potential to undermine this approach.

The community may perceive expansion as Government endorsement or support of the safety or efficacy of illicit cannabis for non-terminal conditions.

This risk is supported by the findings from the operational review of the Scheme, which indicate that some people believed that the Scheme signified government endorsement of the therapeutic benefits of illicit cannabis use.

3.6 SPECIFIC ISSUES ASSOCIATED WITH CONSIDERING EXPANSION TO CHILDREN
Illicit substance use by children raises child protection issues
The Department of Family and Community Services (FACS) stated that parents or caregivers supporting cannabis use in children would fall within the current mandatory reporting framework, as this involves the administration of an illicit product to a child.

Caseworkers have encountered situations in which they had been called to assess the welfare of a child that had been given cannabis by a parent or caregiver, for therapeutic purposes. FACS reported that these situations create difficulties for caseworkers as they may be unsure whether to report the cannabis use if there are no other welfare concerns present and the parents are motivated by their desire to help their child.
FACS reported that it is likely that these issues would remain even if a child were a registered participant on an expanded Scheme, as participation would not affect the fundamental concern of a child having access to an illicit product.

Further, special medical treatment cannot be given to children unless in accordance with s175 of the *Children and Young Persons (Care and Protection) Act 1998*. It is an offence under that Act to administer a drug of addiction (Schedule 8 medication) to a child for a period of more than 10 days in any 30 day period, unless appropriately authorised. The Scheme also does not provide for human research ethics committee approval which is usually required for experimental treatment of children.

### 3.7 QUANTITIES OF CANNABIS PERMITTED

The review considered whether the permitted quantities of cannabis under the current Scheme are suitable. Currently, Scheme participants cannot possess more than 15 grams of cannabis leaf, one gram of cannabis oil or 2.5 grams of cannabis resin. These quantities are in line with the Cannabis Cautioning Scheme, which provides for formal police cautioning of adult offenders detected for minor cannabis offences.

Some stakeholders have argued that the allowable quantities are too low, and that frequent re-supplying of illicit cannabis could be stressful and difficult for people with a terminal illness and their carers.

Evidence on the quantity of cannabis consumed for medicinal purposes is limited. Some research suggests that the average use of cannabis leaf for medicinal purposes may be between one and three grams a day (Health Canada, 2016a). Research on medicinal cannabis use in the Netherlands indicates an average daily dose of 0.7 grams of dried cannabis (Hazekamp & Heerdink, 2013).

The review notes that the Scheme provides for the registered person with a terminal illness and each of their registered carers to possess the allowed quantities. As participants on the Scheme nominate an average of two registered carers, this in practice equates to potential access to 45 grams of leaf at any time. This would be up to 60 grams for participants with three registered carers.

NSW Police Force has indicated that it does not favour an increase in the quantities allowed for under the Scheme.
4 CONCLUSIONS AND RECOMMENDATIONS

This review suggests that administrative improvements to the existing Scheme be implemented, but eligibility criteria not be expanded and allowable quantities remain the same.

Because there are now clarified legal pathways for access to cannabinoid medicines and due to the considerable risks associated with unregulated cannabis products, this review advises that the eligibility for the Scheme not be extended to non-terminal patients or children at this time.

Medical experts consulted emphasised that access to a regulated medicine product was a preferred option. Under a regulated approach medical practitioners would know the composition of medicinal cannabis products, understand the potential benefits and possible side effects, and be able to supervise their patients engaged in this therapy better.

However, there is a need for Government to support doctors in using the regulated pathways for access to lawful cannabis-based medicines for patients who are not responding to conventional treatment options. This should include advancing the evidence base and supporting education, working to streamline regulatory and approval processes where appropriate, and pursuing options to make acquiring products easier for doctors who judge the use of a cannabis-based medicine to be an appropriate next step in an individual patient’s treatment.

An important initiative is the development of national clinical guidance being led by the Commonwealth Therapeutic Goods Administration with support from states and territories. This will assist clinicians to make informed decisions when determining whether to prescribe cannabis-based medicines. This work is expected to be completed in 2017. Also, the NSW Government is engaging international partners, including convening a forum with regulatory experts from Israel, The Netherlands, Germany, Canada and New Zealand and other Australian jurisdictions in March 2017.

Recommendation 1
That the following administrative changes be made to the Scheme to improve its operation:

- registrants have the option to apply electronically
- the registration period is extended from 12 to 24 months
- a renewed communications strategy is implemented to improve awareness of the Scheme and how it operates among eligible people with a terminal illness, their carers, medical practitioners and other relevant professionals
- communication materials are revised to emphasise:
  - the confidential nature of the Scheme
  - that the Scheme does not provide supply and cannabis use remains illegal in general (unless authorised and prescribed by a medical practitioner)
  - that the NSW Government and medical practitioners are not prescribing or endorsing cannabis use under the Scheme
  - that the Scheme may not cover use or possession at hospitals, residential aged care facilities, hospices and other health facilities.

Recommendation 2
That the eligibility criteria and quantities of cannabis allowed under the Medicinal Cannabis Compassionate Use Scheme remain unchanged.
Recommendation 3
That Government helps medical practitioners to use available routes for accessing high quality and lawfully produced cannabinoid medicines in appropriate circumstances by:

• supporting medical practitioners with information about current evidence for indications and the legal pathways for prescribing and sourcing an appropriate medicinal cannabis product for patients
• continuing to support inter-jurisdictional work to expedite development of national clinical guidance for indications for use; dose; mode of administration; potential drug-drug interactions; and monitoring the use of unregistered cannabis-based medicines
• pursuing international collaboration on research, education and data collection to advance understanding and evidence for the use of medicinal cannabis products.
5 REFERENCES


1. **Background**
   - The NSW Government developed the Terminal Illness Cannabis Scheme ('TICS') to extend compassion to adults with a terminal illness who use cannabis and/or cannabis products to alleviate their symptoms, and carers who assist them.
   - TICS commenced in December 2014 and provides guidelines for NSW police officers to help them determine the appropriate circumstances in which to use discretion not to charge a registered adult, as well as up to three registered carers for that person.
   - DPC has conducted a review of operational issues to assess how well TICS has achieved its original objectives.
   - In May 2016, the Premier announced that TICS would be renamed the Medicinal Cannabis Compassionate Use Scheme ('Scheme') and that a broader review of the Scheme would be conducted.

2. **Purpose of the Review**
   - The Review will assess whether the objectives, scope, terms and conditions of the Scheme remain appropriate, including evaluating:
     a. whether the eligibility criteria for the Scheme should be expanded to include:
        i. adults with non-terminal health conditions, including:
           i. conditions which are the subject of the NSW Government’s medicinal cannabis clinical trials; and
           ii. other conditions for which medicinal cannabis has allegedly provided relief, including refractory epilepsy and Stiff Person Syndrome; and
        ii. children with relevant health conditions;
     b. whether the quantity and form of cannabis covered by the Scheme remains appropriate;
     c. how the Scheme aligns with the Government’s broader approach to medicinal cannabis and current national developments; and
     d. how the Scheme could otherwise be improved to better meet the needs of the NSW community.

3. **Conduct of the Review**
   - The Review will include an assessment of the Scheme’s objectives, scope, terms and conditions and all other relevant matters, and the findings of the review of operational issues.

4. **Governance**
   - The Review will be undertaken by the Department of Premier and Cabinet, and will be oversighted by Professor Mary O’Kane, NSW Chief Scientist & Engineer and Director of the Centre for Medicinal Cannabis Research and Innovation.
   - Professor O’Kane will deliver the review report to the Premier, including findings and conclusions related to both the operational issues and broader review, and publish it on the Centre for Medicinal Cannabis Research and Innovation website.

5. **Consultation**
   - As necessary, additional consultation will be undertaken with:
     a. clinical and academic specialists;
     b. consumer groups and advocacy groups;
     c. medical practitioners and professional bodies; and
     d. NSW Government agencies.
APPENDIX 2 UTILISATION OF THE SCHEME

As of 16 December 2016, 310 individuals with a terminal illness had registered for the Scheme. This includes:

- 213 current registrations
- 45 lapsed registrations (status of the registered participant unknown)
- 52 cancelled registrations (communication to CRU indicated that the registered participant had died).

The highest number of registrations occurred in September 2016 and the cumulative number of registrations has been steadily increasing (Figure 1).

Recently, from August to October, a higher number of applications were processed than any other period.

Figure 1: Breakdown of new (bar) and cumulative (line) applications over the course of the Scheme

Fifty-seven per cent of all participants that had registered for the Scheme were male and 43 per cent were female.
The ages of participants at registration range between 25 and 89 years old, with an average age of 60 years (Figure 2).
Conditions
Eighty six per cent of all participants that had registered were diagnosed with a form of cancer (Figure 3).

Figure 3: Breakdown of participant illnesses

Geographical spread
Approximately 42 per cent of all participants that had registered for the Scheme were located in the Sydney metropolitan region.

Of the remaining participants, approximately 14 per cent were located on the Far North Coast, 12 per cent live in the Central Coast / Newcastle regions and 8 per cent on the Mid North Coast, with the remainder located in other areas of NSW.

Nominated carers
Each registered participant is able to nominate up to three carers.

A total of 599 carers have been registered to the Scheme, with 403 still currently registered.

Participants nominate an average of two carers (statistically, 1.89 carers per registered applicant). The average age of carers is 50 years.

One individual has been nominated as a carer for multiple (two) registered participants.
Certifying medical practitioners
Sixty per cent of all applications had been certified by General Practitioners (Figure 4).

![Figure 4: Specialty of practitioners](image1)

Ninety one per cent of medical practitioners that have certified a person for the Scheme have certified one person only (Figure 5). Six practitioners have registered four or more people.

![Figure 5: Number of patients certified by a medical practitioner](image2)
APPENDIX 3    EXPERT ADVICE: RELIABLE SUPPLY

Reliable supply of medicinal cannabis to patients: analysis and discussion
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With mooted changes to Australian laws to permit the legal medicinal use of cannabis, the issue of reliable supply becomes of immediate interest. It has been proposed that if legal cannabis preparations are too expensive or otherwise perceived difficult to obtain, then patients may cultivate their own supplies, purchase from the black market, or continue to suffer.

Whilst unregulated supplies are undesirable for many reasons, one often publicized reason is the health risk of contaminated supplies. This issue has been raised previously by local researchers, primarily in the context of mental health issues and their perceived exacerbations associated with toxicity from illegal ‘recreational’ cannabis and self-medicated ‘medicinal’ cannabis. The authors reviewed the properties of the uncontrolled plant material and its active cannabinoid content as the primary determinants of the pharmacological potency and health risks. They noted that fungal and bacterial contamination of cannabis is of particular concern for medicinal cannabis users and mentioned the potential toxicity by contamination with heavy metals and agrichemicals. Most of these concerns remain, and data are essentially not available to make clear pronouncements on how they will be addressed by future legal suppliers to permitted patients, but it is clear that some sort of regulation will need to be put in place to address the concerns. Thus, the purpose of this paper is to again raise the issues, specifically in the pharmacological context of the future lawful use of medicinal cannabis.

1. Possible direct harms
Any prescriber or dispenser of any lawful medicinal preparation needs to be aware of the known relevant health risks associated with any drug or medicine, and cannabis is no exception. In writing about the health risks of cannabis three decades ago, at a time when illegal self-medication was the only form available to medical patients, eminent Stanford University pharmacologist Leo Hollister described the then-known effects, salutary and otherwise, and pointed out that there is much ambiguity in the literature. He pointed out that it is difficult to prove or disprove health hazards in humans from animal studies; that much of the research has been performed on essentially healthy young adults in the context of intermittent recreational use where other factors include cannabis use in combination with other substances such as alcohol or tobacco; and that “the whole issue of cannabis use is so laden with emotion that serious investigations of the health hazards of the drug have been colored by the prejudices of the experimenter, either for or against the drug as a potential hazard to health”. Among his conclusions, Hollister noted that “Contamination of marijuana by spraying with defoliants has created the clearest danger to health; such attempts to control production should be abandoned”.

Much valuable research on the toxicity of drugs, has been, and is, adduced from studies in animals, and forms much of the basis for understanding relevant drug actions in humans. So too, with cannabis. Insofar as systematic animal research provides a guide, ∆9-tetrahydrocannabinol (THC), the most studied cannabinoid substance that is generally regarded as the principal psychomimetic component of cannabis, is a relatively low toxicity compound in its own right. Its acute toxicity, as judged by the median lethal doses (LD50), is, like most substances, route of administration dependent.

The LD_{50} values, after intravenous, intraperitoneal and intragastric administration were found, respectively, to be 28.8, 373, and 668 mg/Kg in laboratory rats, and 42.5, 455 and 482 mg/Kg in laboratory mice. Scaled to human weight, these values indicate equivalent median lethal doses of THC on the scale of many grams, compared to pharmacotherapeutic doses on the scale of low 10s of milligrams. This indicates a far less acute toxicity of THC than the majority of conventional drugs that might be utilized for treatment of the same medical condition.

Nonetheless, there is no question that the uncertainty in active cannabinoid content provides a major source of concern should unregulated botanical material be used as medicinal cannabis. There is a common opinion that the THC content, and thus ‘potency’, of ‘street’ cannabis has increased over the years and, as noted by McLaren et al, there is some evidence to support this. Such variability was well-demonstrated in one local study where the THC content of 206 samples police seized or ‘street’ cannabis in NSW, the total THC (i.e., THC + its precursor carboxylic acid) content ranged from 0.94 to 39.76 %w/w, and the analogous cannabidiol (CBD) content ranged from 0 to 6.50 %w/w.

2. Other possible harms

Despite its illegality, it is acknowledged that many patients presently self-medicate with cannabis products, often with their own-grown material or with black market-obtained material. When they do so, they may rationally choose particular cultivars or chemovars, or they may be totally unaware of any such properties of the material being used. Despite any expectations by many users then, there is no assurance of a reasonable standard of purity or freedom from contamination of drug substances that are not subjected to the rigorous testing procedures required by governmental regulatory agencies. It is clear that selective breeding of plants for the desired phytochemical content needs to be, and can be, the standard practice for medicinal purposes.

In comparison, the issue of contamination of ‘street’ drugs has been recognized for many years, and anecdotes as well as urban myths abound. Such ‘street’ drugs are often diluted or adulterated for profit, and the materials used may themselves be the source of toxicity. Among such materials, heavy metals are necessary for normal plant physiology, but excess due to contamination is a common concern.

Cannabis is known to contain zinc, iron, copper and manganese, largely reflecting the abundance in the growing soil. One, perhaps extreme, report found the presence of lead as fine particles, presumably added to cannabis intentionally to increase the weight.

With many states of the USA now legalizing the use of cannabis, renewed interest is being given to the freedom from contaminants of cannabis used both for recreational and medical purposes, as well as occupational safety protection for people involved in production and administration. For cannabis, the principal known contamination risks include pesticides, herbicides and microorganisms.

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Potter\textsuperscript{11}, in describing the experience of GW Pharmaceuticals, the first cannabis-based medicine to be approved in the UK, related both the human difficulties (such as the needs to protect from those with a curious, acquisitive or malicious intent) and the agricultural difficulties (such as the vagaries of the weather, pests, disease, and contamination) on the outdoor growing of cannabis. He pointed out that similar problems would face producers of illicit cannabis, that indoor growing enables GW Pharmaceuticals to grow with more exacting control, and that the Good Agricultural Practise Guidelines dictate quality standards in medicinal crop growing and processing, permit limited pesticide use, and institute rigorous cleaning regimes are routine and growing conditions so infections and infestations are avoided\textsuperscript{12}. It is clear that whether indoor or outdoor grown, rigid standards need to be applied to minimise risk to patients from contamination.

Pesticides may be used by growers during cultivation to increase their yields and, not surprisingly, traces of various pesticides can be found reflecting the local use of these agents. For example, one recent survey from Uruguay revealed that seized and legally produced cannabis samples contained pesticides, and residues of diazinon (0.03 mg.kg\textsuperscript{-1}), tebuconazole (0.19 mg.kg\textsuperscript{-1}) and teflubenzuron (0.11 mg.kg\textsuperscript{-1}) were simultaneously detected in one sample\textsuperscript{13}; others have found that residual pesticides will transfer into inhaleable cannabis smoke\textsuperscript{14}.

Herbicides, often the result of crop eradication procedures used by various law enforcement authorities, include paraquat and glyphosate which have both been found in seized cannabis samples\textsuperscript{15}. At this stage, it is difficult to place the measured such agrochemical levels on a scale of toxicity to humans, but a clear maxim is that humans are better without them\textsuperscript{16}.

Microorganisms have been implicated in various reports of broncho-pulmonary infections. A number of reports have implicated \textit{aspergillus} spp., mainly in cannabis cigarettes, and the likely cause of such infections\textsuperscript{17}. Moreover, the risk may be increased due to the production of aflatoxins which may reach sufficient a mycotoxin level to present a health hazard to those in daily contact\textsuperscript{18}.

\begin{thebibliography}{99}

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While it is recognized that cannabis contains substances with antibacterial properties, contamination of unprocessed medicinal botanicals by microorganisms is to be expected, but such contamination can be of particular concern in already compromised patients, such as immunosuppressed patients receiving chemotherapy. It was noted in one report that such contamination is unlikely to be removed from smoked cannabis by the use of a water pipe. Although it has been suggested that heat sterilization of cannabis by heating to 150°C for 5 minutes will kill potentially harmful fungal spores, it also may be problematic to the regulation of the cannabinoid content. Gamma irradiation treatment of cannabis has been shown to not materially affect the content of THC and CBD, and has thus become standard practice in the government-supported medicinal cannabis programs of The Netherlands as well as Canada. While the overall qualitative composition of the samples was unaltered, differences in several terpene components could be detected after irradiation in the cannabis varieties studied. Treatment by gamma irradiation currently seems the only method available to meet these requirements, at least until other more generally accepted methods have been developed and validated. With the increasing demand for cannabis oil and other preparations, an additional risk factor is that of residual extracting solvents in material.

3. Some conclusions.

In those states of the USA where legalization of recreational cannabis has driven a new industry, it is recognized that it is essential to provide customers with a safe, consistent and pure product with regard to potency (THC and CBD), purity (with regard to harmful pesticides, moulds and other residuals).

This involves licensing of facilities for testing some or all of (i) potency/homogeneity, (ii) residual solvents contamination and (iii) microbial contamination. Colorado, among such states, is slowly beginning to enforce the regulatory requirements for pesticide testing of recreational and medical marijuana but is meeting with inadequate quality among some testing facilities.

It seems that there are several main lessons from the literature. (i) If controlled supply legal cannabis is not readily available at a reasonable price, the many patients will obtain black market or grow-your-own cannabis for medicinal use. (ii) The potential for cannabis microbial contamination is high, but can be dealt with by gamma irradiation, at least. (iii) The potential for cannabis agrichemical and heavy metal contamination depends on the growing conditions, and ought to be manageable. (iv) Licensed laboratory testing using validated methods would seem mandatory, at least during the early phases of learning how to manage medicinal cannabis supply and distribution.