Medicinal Cannabis Supply Chains: Know Your Obligations

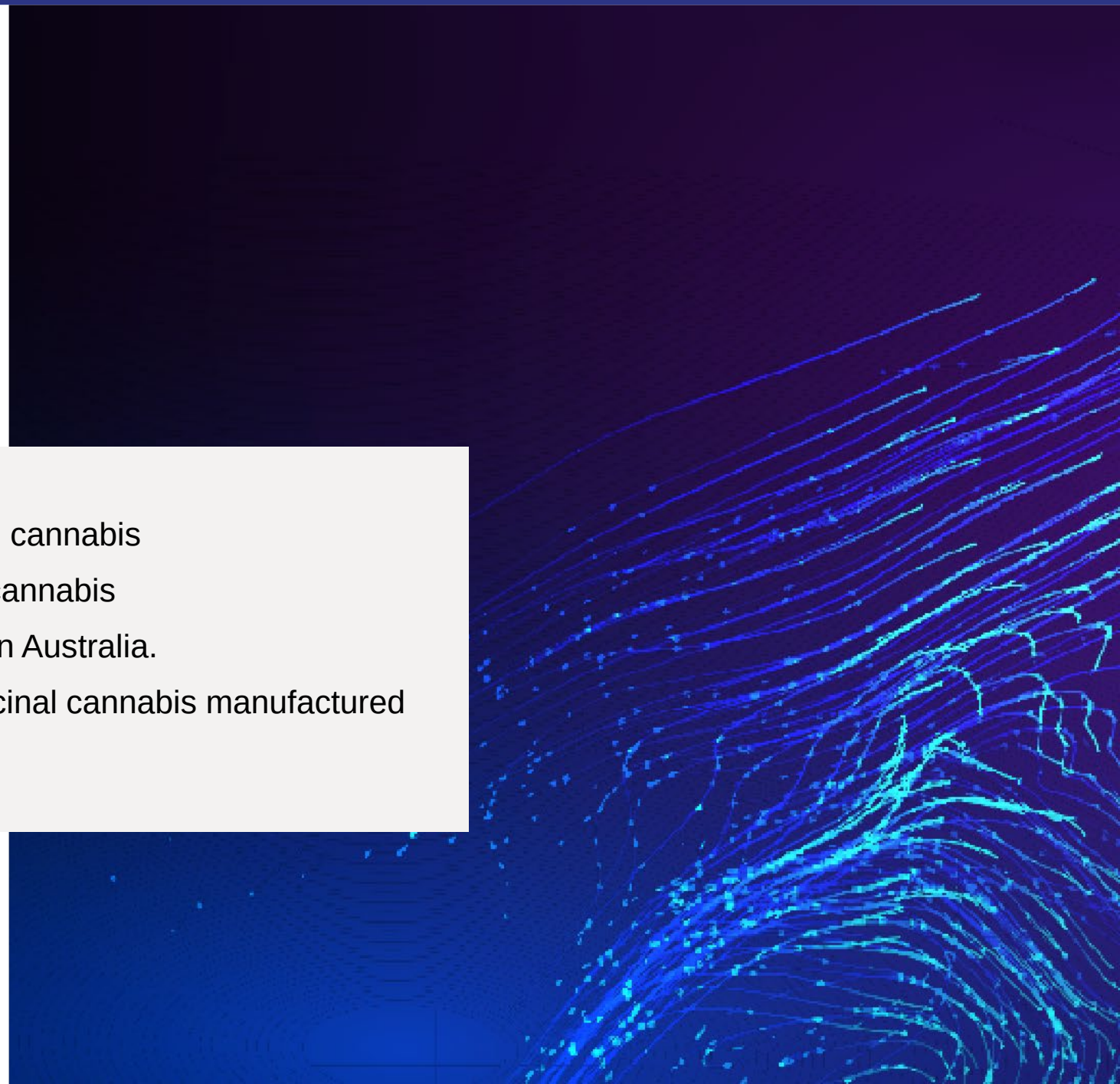
Katherine Clark
Manufacturing Quality Branch
Department of Health and Aged Care, TGA

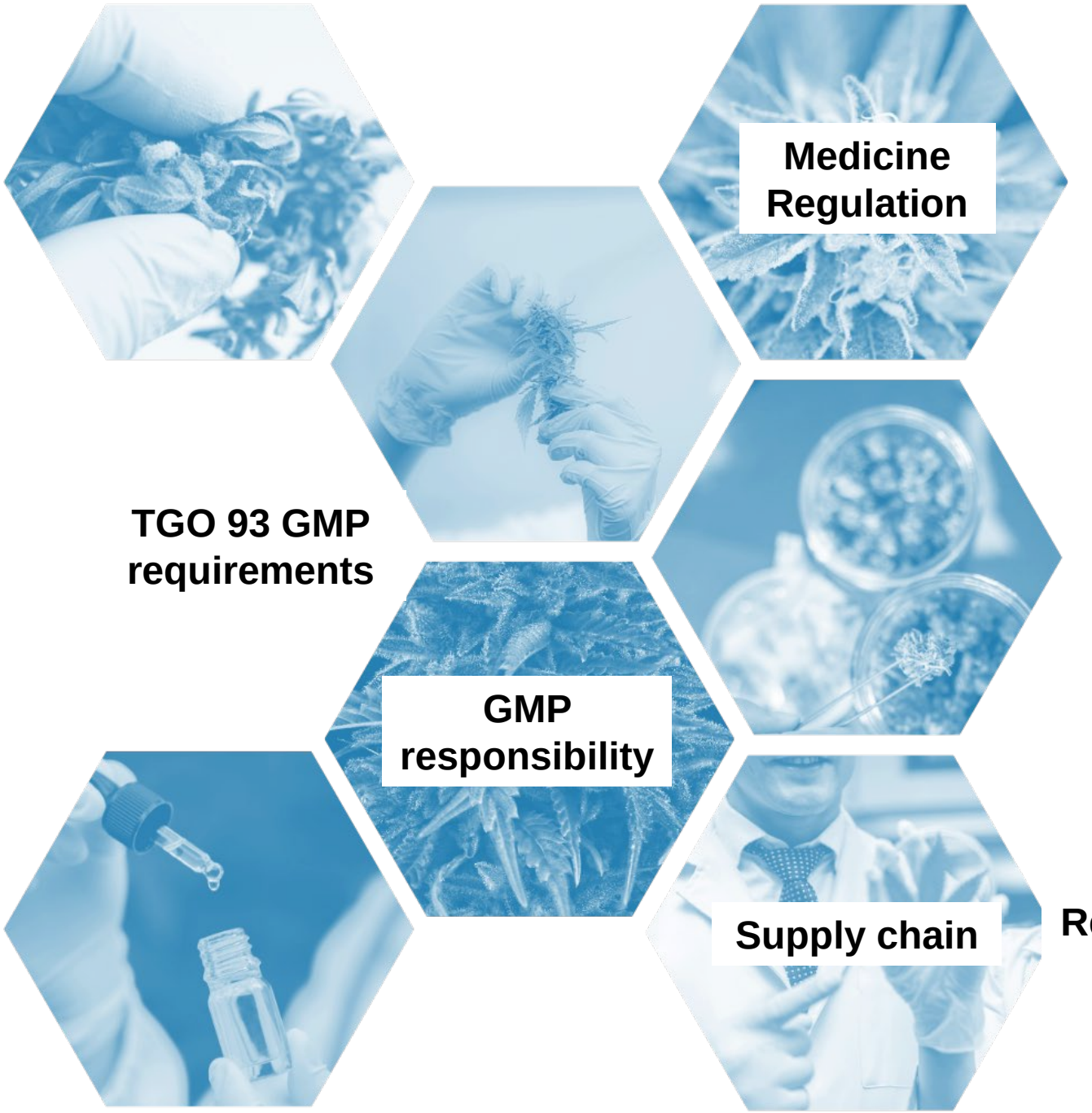
GMP FORUM 2024

Agenda

What will I get out of this session?

- Understand quality requirements for medicinal cannabis
- Understand regulatory controls for medicinal cannabis
- Understand your obligations for manufacture in Australia.
- Understand your obligations if importing medicinal cannabis manufactured overseas





Framework

TGO 93 GMP requirements

Responsibilities for supply

Medicines regulatory framework

Approved medicines

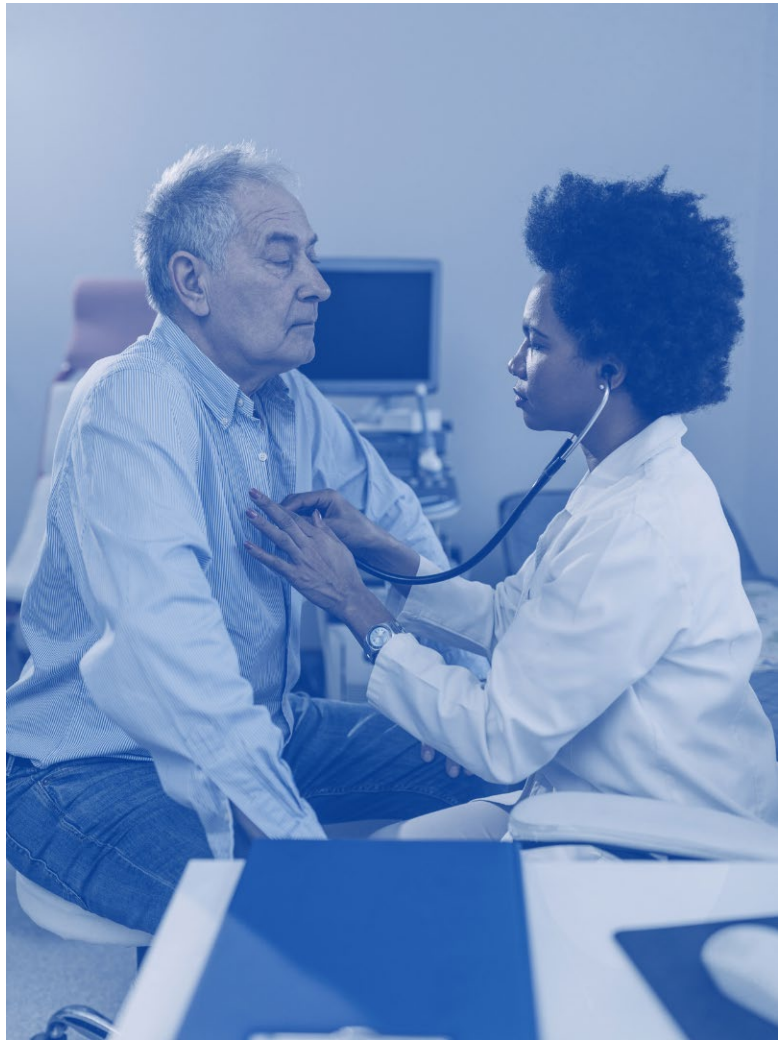
TGA's role

- Quality, safety, efficacy and timely supply under *Therapeutic Goods Act 1989*
- Generally, TGA evaluation and marketing authorisation are required prior to supply
- Approved medicines are entered on the Australian Register of Therapeutic Goods (ARTG)

Medicines regulatory framework

Special access to unapproved medicines

- When approved treatments are not available
  - Special Access Scheme - SAS
  - Authorised Prescriber – AP
- Usually pharmaceuticals with market authorisation in an overseas jurisdiction.
- Responsibility for selecting appropriate medicine is held by the medical practitioner



Medicines regulatory framework

Quality standards

- Default standards
  - Established in the *Therapeutic Goods Act 1989*
  - Monographs in major pharmacopoeia: BP, EP, USP-NF

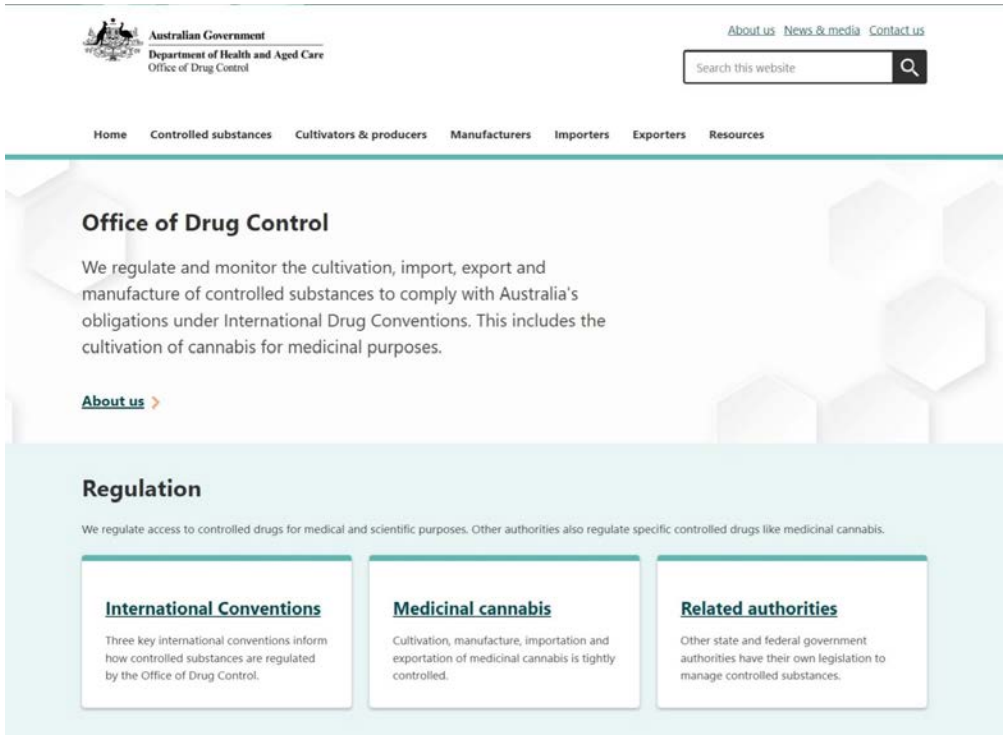
- Ministerial standards
  - Provisions in the *Therapeutic Goods Act 1989* to create new legislative instrument
  - Therapeutic Goods Orders – ‘TGO’
  - Australian-specific requirements

Medicines regulatory framework

Manufacturing requirements

- Domestic medicine manufacturing sites need TGA licence
- Applications for registration or listing on the ARTG rely on an *assessment of manufacturing and quality controls* at overseas sites:
    - Reliance framework – ‘clearances’
    - Inspections – ‘certificates’

Legalisation of cultivation



2016

Introduction of new licensing scheme for Australian cultivators

Regulated by the Office of Drug Control

Supply only:

- to clinical trials

or

- under the SAS or AP pathway

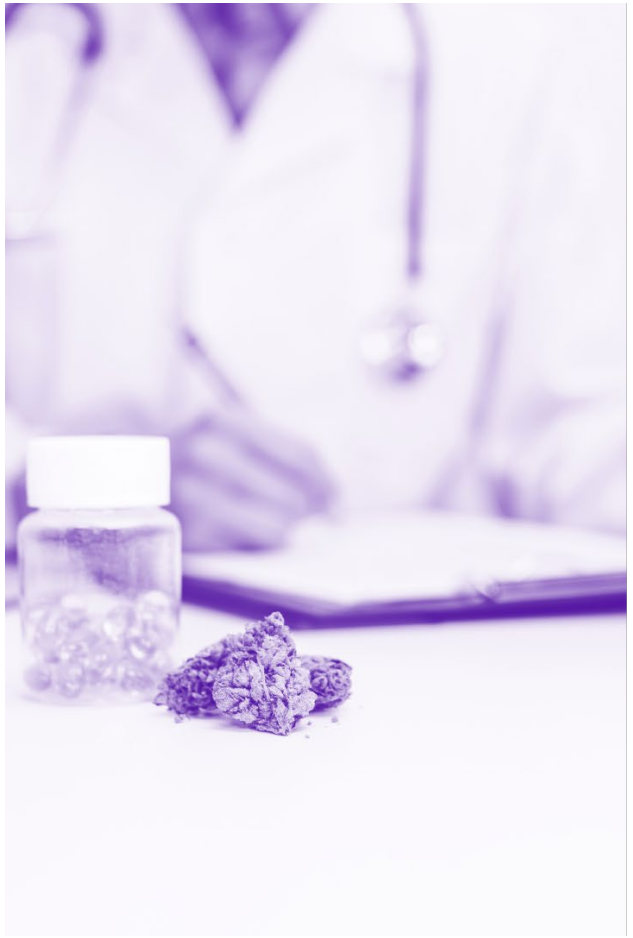
Need for quality requirements

Quality standard for medicinal cannabis

- Not regulated as medicine in many jurisdictions
- Unapproved pathways don’t allow TGA review of quality

- New Therapeutic Goods Order for ‘medicinal cannabis products’

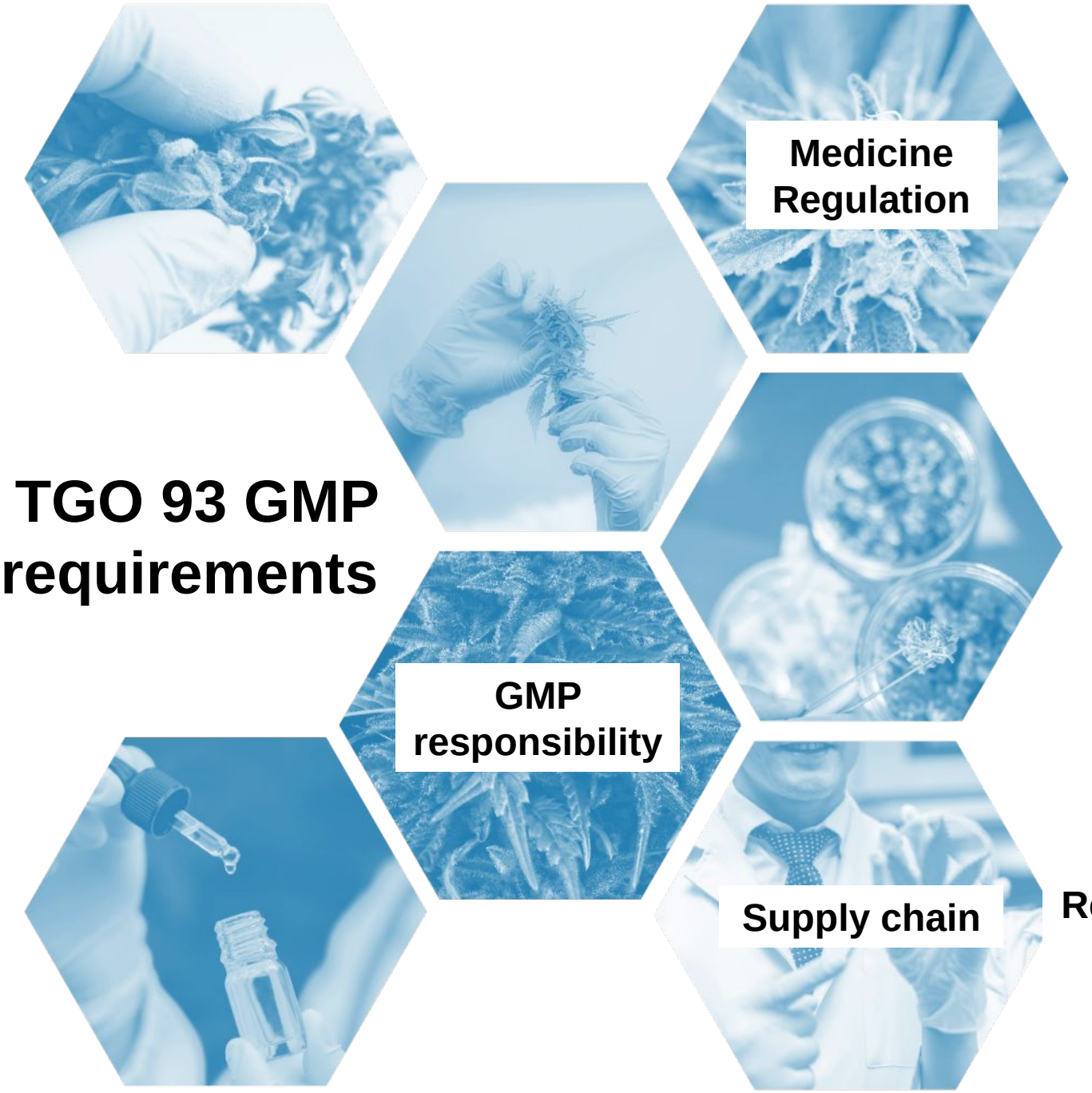
Quality requirements for medicinal cannabis



TGO 93

- All medicinal cannabis products must comply with TGO 93 when they are released for supply in Australia.
- There are offence provisions in the Therapeutic Goods Act 1989 (the Act) for import and supply of medicines not complying with a relevant standard.
- These provisions apply to everyone in the supply chain, not just the importer or sponsor

TGO 93 GMP requirements



Framework

Responsibilities for supply

Evidence of GMP

What is evidence of GMP?

- For **Australian manufacturers** it is a TGA manufacturing licence, demonstrating compliance with Australian Good Manufacturing Principles (GMP).

- For **overseas manufacturers** the sites must comply with one of the GMP standards set out in section 13(2) and the Australian sponsor (the importer) of the medicinal cannabis product must hold evidence of GMP compliance, as specified in section 13(3) of TGO 93

GMP licence for manufacture in Australia

Section 35 Criminal offences relating to manufacturing therapeutic goods

(1) A person commits an offence if:

(a) the person, at premises in Australia, carries out a step in the manufacture of therapeutic goods (other than goods exempt under section 18A or 32CB); and

(b) the goods are for supply for use in humans; and

(c) none of the following applies:

(i) the goods are exempt goods;

(ii) the person is an exempt person in relation to the manufacture of the goods;

(iii) the person is the holder of a licence that is in force that authorises the carrying out of that step in relation to the goods at those premises; and

(d) either:

(i) the use of the goods has resulted in, will result in, or is likely to result in, harm or injury to any person; or

(ii) the use of the goods, if the goods were used, would result in, or would be likely to result in, harm or injury to any person; and

(e) the harm or injury has resulted, will result, is likely to result, would result, or would be likely to result, because the person carried out the step in the manufacture of the goods.

Penalty: Imprisonment for 5 years or 4,000 penalty units, or both.

GMP licence for manufacture in Australia

Section 35 Criminal offences relating to manufacturing therapeutic goods

(4) A person commits an offence if:

(a) the person, at premises in Australia, carries out a step in the manufacture of therapeutic goods (other than goods exempt under section 18A or 32CB); and

(b) the goods are for supply for use in humans; and

(c) none of the following applies:

(i) the goods are exempt goods;

(ii) the person is an exempt person in relation to the manufacture of the goods;

(iii) the person is the holder of a licence that is in force that authorises the carrying out of that step in relation to the goods at those premises.

Penalty: Imprisonment for 12 months or 1,000 penalty units, or both.

GMP licence for manufacture in Australia

Section 35 Criminal offences relating to manufacturing therapeutic goods

(4A) A person commits an offence if:

(a) the person, at premises in Australia, carries out a step in the manufacture of therapeutic goods (other than goods exempt under section 18A or 32CB); and

(b) the goods are for supply for use in humans; and

(c) none of the following applies:

(i) the goods are exempt goods;

(ii) the person is an exempt person in relation to the manufacture of the goods;

(iii) the person is the holder of a licence that is in force that authorises the carrying out of that step in relation to the goods at those premises.

Penalty: 100 penalty units.

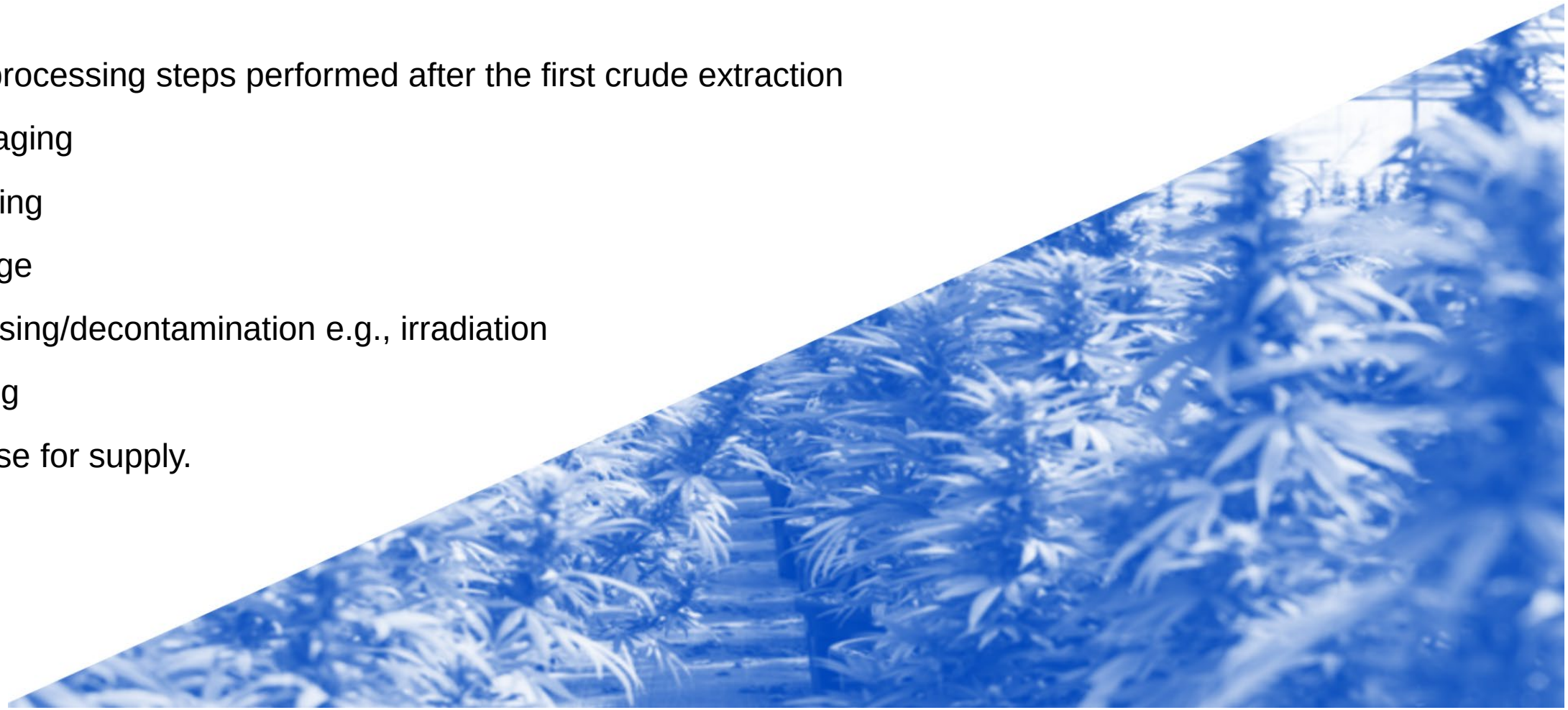
(4B) An offence against subsection (4A) is an offence of strict liability.

Manufacturing steps that require a TGA licence or GMP evidence

Steps that require GMP

Include:

- any processing steps performed after the first crude extraction
- packaging
- labelling
- storage
- sterilising/decontamination e.g., irradiation
- testing
- release for supply.



Exemptions

When a TGA licence or GMP evidence is not required

- There are some exemptions under Schedule 7 to the Therapeutic Goods Regulations 1990 (the Regulations) that allow the manufacture of herbal materials in Australia to occur without a GMP licence, this includes the manufacture of most excipient ingredients and plant material or the first crude oil extract under certain conditions.

- For overseas manufacture of medicinal cannabis products subsection 13(1) of TGO 93 applies the same exemption for cannabis plant material and the first crude oil extract for overseas manufacturing as Schedule 7

- These exemptions apply when cannabis plant or first crude extract is used as starting material for further manufacture at a licensed site.

- The exemptions allow cultivation sites to grow, cut and dry cannabis and to remove a crude extract for further manufacture without themselves holding an approved GMP evidence

GMP for products manufactured overseas

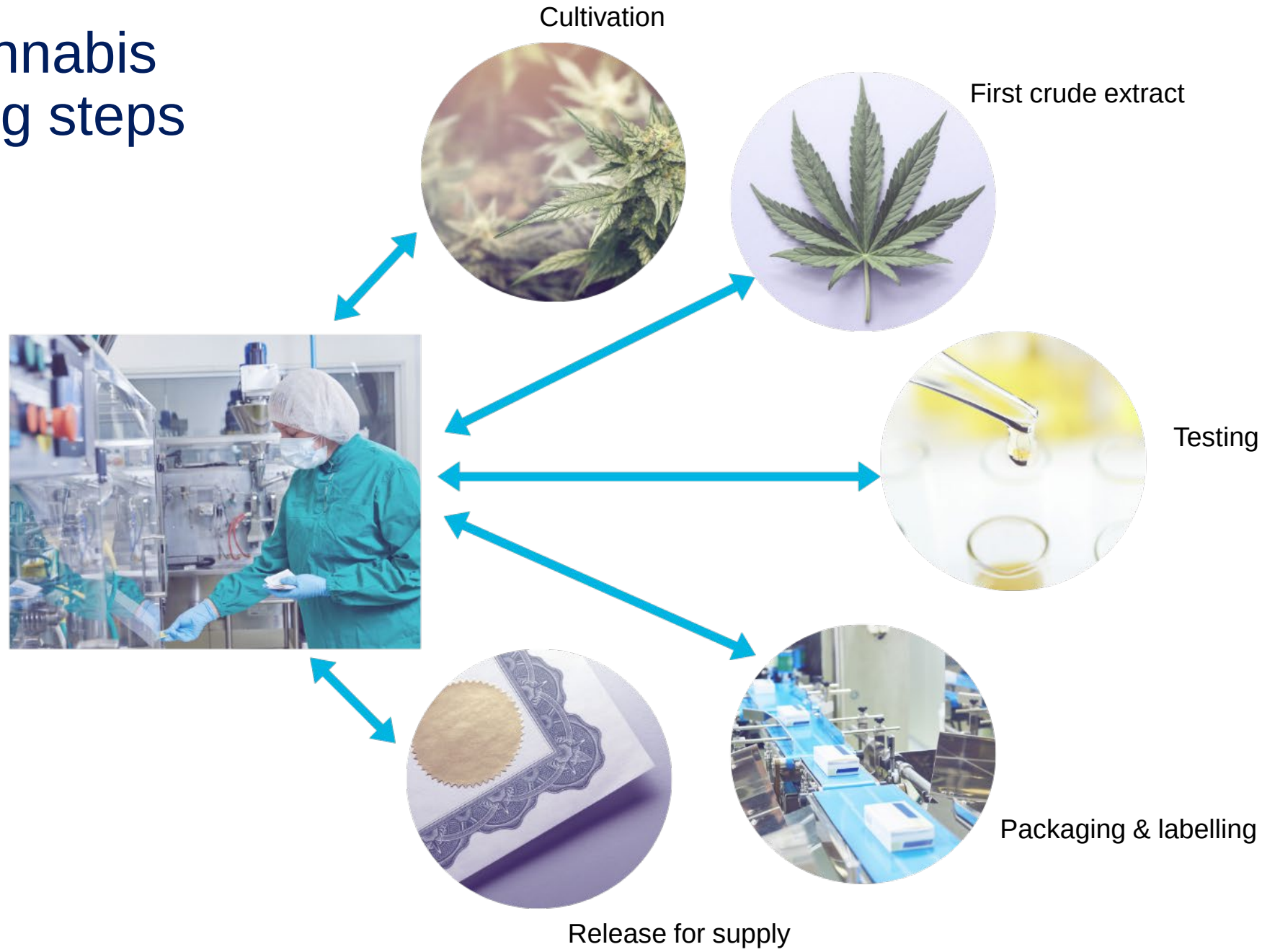
- Evidence that overseas manufacturing has taken place under approved GMP
- Includes irradiation and testing sites
    - Concern with accuracy of cannabinoid claims
- Exemption for herbal material supplied to Australian licenced site or overseas site with approved GMP

Evidence of GMP

Overseas manufacturers

- For **overseas manufacturers** the sites must comply with one of the GMP standards set out in section 13(2) and the Australian sponsor (the importer) of the medicinal cannabis product must hold evidence of GMP compliance, as specified in section 13(3) of TGO 93

Medicinal cannabis manufacturing steps



TGO 93 Section 13(2)

Manufacturing standards for medicinal products

Each step of manufacture in relation to a medicinal cannabis product that occurs outside Australia must be in accordance with one or more of the following:

a. the PIC/S Guide to GMP;

b. Article 47 of EU Directive 2003/94/EC;

c. Article 47 of EU Directive 2001/83/EC;

d. the South African Guide to GMP;

e. *Part 211—Current Good Manufacturing Practice for Finished Pharmaceuticals* of *Subchapter C—Drugs: General*, in *Chapter I—Food and Drugs Administration* of *Title 21—Food and Drugs*, in the United States *Code of Federal Regulations*, as in force or existing from time to time;

f. *Division 2 – Good Manufacturing Practices* in Part C of the *Food and Drug Regulations* (Canada), as in force or existing from time to time*;*

g. the New Zealand Code of GMP.

TGO 93 Section 13(3)

GMP Evidence equivalent to an Australian GMP licence

A medicinal cannabis product that is manufactured outside Australia must be manufactured at a site that is the subject of one or more of the following:

(a) for a medicinal cannabis product manufactured in the United Kingdom—a valid certificate of good manufacturing practice **issued to the manufacturer of the product by the Medicines and Healthcare products Regulatory Agency of the United Kingdom or a licensing authority of an EU Member State**;

(b) for a medicinal cannabis product manufactured in an EU Member State—a valid certificate of good manufacturing practice **issued to the manufacturer of the product by a licensing authority of an EU Member State;**

TGO 93 Section 13(3)

GMP Evidence equivalent to an Australian GMP licence

for a medicinal cannabis product manufactured in Canada—either:

(i) written confirmation from Health Canada that the manufacturing site operates in accordance with Part 5: Good Production Practices of the Cannabis Regulations SOR/2018-144 (Canada), as in force or existing from time to time, **and:**

(A) a valid certificate of good manufacturing practice issued to the manufacturer of the product by a licensing authority of an EU Member State; or

(B) written confirmation from the Therapeutic Goods Administration that the manufacturing site operates in accordance with the PIC/S Guide to GMP; or

(ii) a Drug Establishment Licence issued by Health Canada for the relevant medicinal cannabis product manufactured at the site;

So that means I can import medicinal cannabis from Canada?

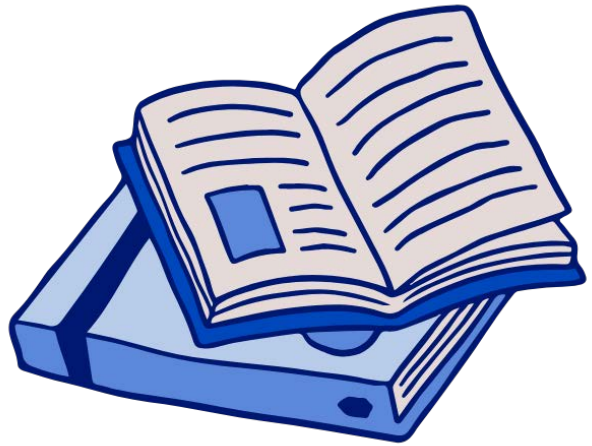
No - not unless

- The medicinal cannabis product has been manufactured at a site with a Drug Establishment Licence that includes the medicinal cannabis dosage form on the licence; OR
- The medicinal cannabis product has been manufactured at a site with a licence issued by the Canadian Government AND;
  - has a GMP certificate issued by an EU member state, or
  - has been inspected by the TGA.
- The testing of medicinal cannabis must be done under the same standards

Requirements for medicinal cannabis

Manufacturing requirements

- Recreational use has been legalised in some countries
- The countries included in TGO 93 have equivalent to the Australian regulatory framework. Manufacturers must produce medicines and have:
    - A licence issued by the Government that allows for compliance actions such as revocation of licence for non-compliance; and
    - Authorises medicine manufacture

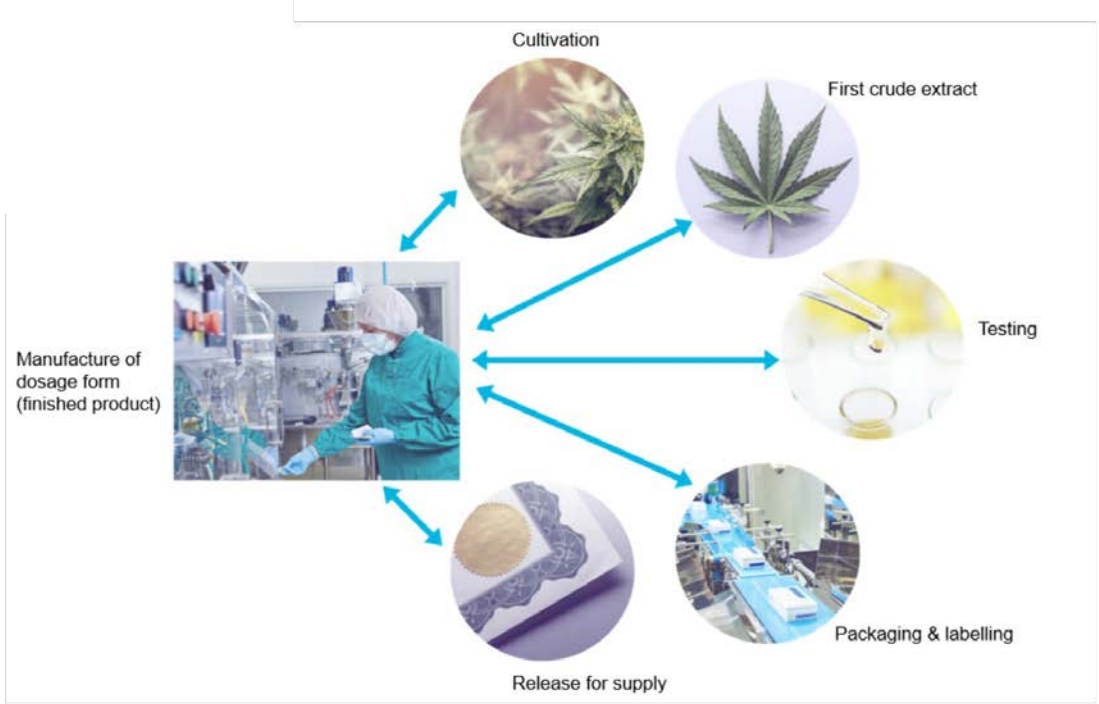


TGO 93 Section 13(3)

GMP Evidence equivalent to an Australian GMP licence

(f) for a medicinal cannabis product manufactured in any other country—written confirmation from the Therapeutic Goods Administration that the manufacturing site operates in accordance with the PIC/S Guide to GMP.

“written confirmation from the Therapeutic Goods Administration that the manufacturing site operates in accordance with the PIC/S Guide to GMP”



- Apply to the TGA for a TGA GMP inspection of your manufacturing site(s)
- TGA GMP inspectors will inspect overseas manufacturing sites for compliance with PIC/S Guide to GMP
- Issue a **Certificate of GMP Compliance for the purposes of Therapeutic Goods Order 93**
- Requirements for GMP evidence the same as for TGA licence in Australia – includes testing, irradiation, packaging and release for supply sites

Framework

Responsibilities for supply

Medicinal cannabis supply

Domestic product

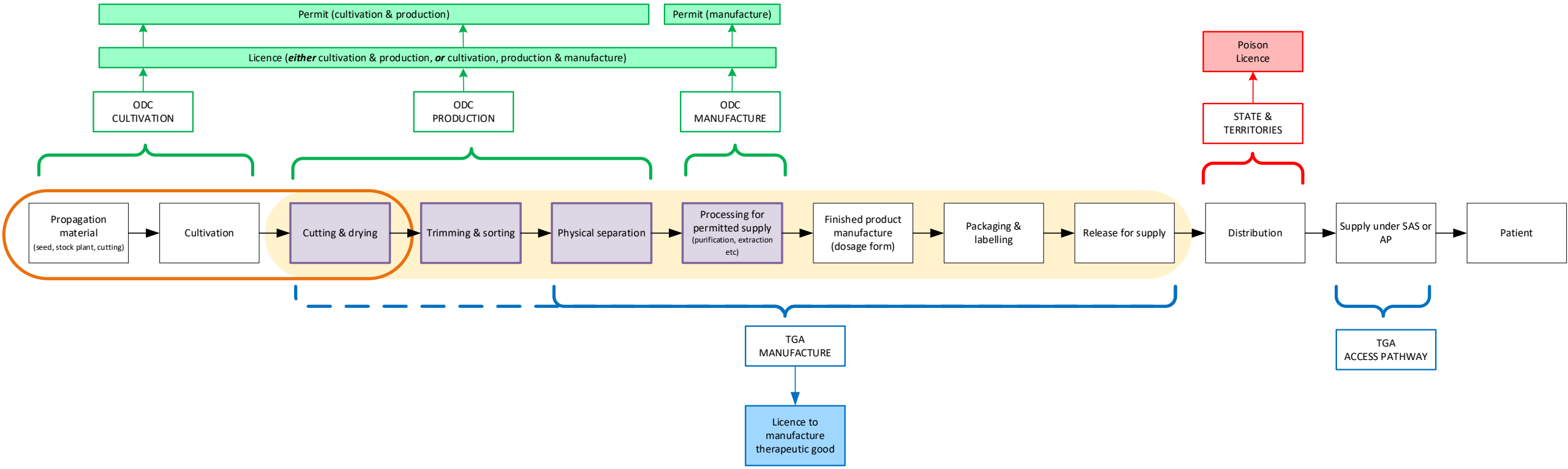
- Office of Drug Control
    - Licence and permit to cultivate, produce and/or manufacture and related supply
- GMP licence to manufacture drug substance or finished product
- State and territory legislation
- Supply to compounders, SAS and AP

Imported product

- Office of Drug Control
    - Import licence and permit
    - Reporting obligations under Single Convention
- Held under control of importer until authority to supply
- State and territory legislation
- Supply to compounders, SAS and AP

Regulatory controls across the supply pathway

ODC and TGA licensing required in Australia



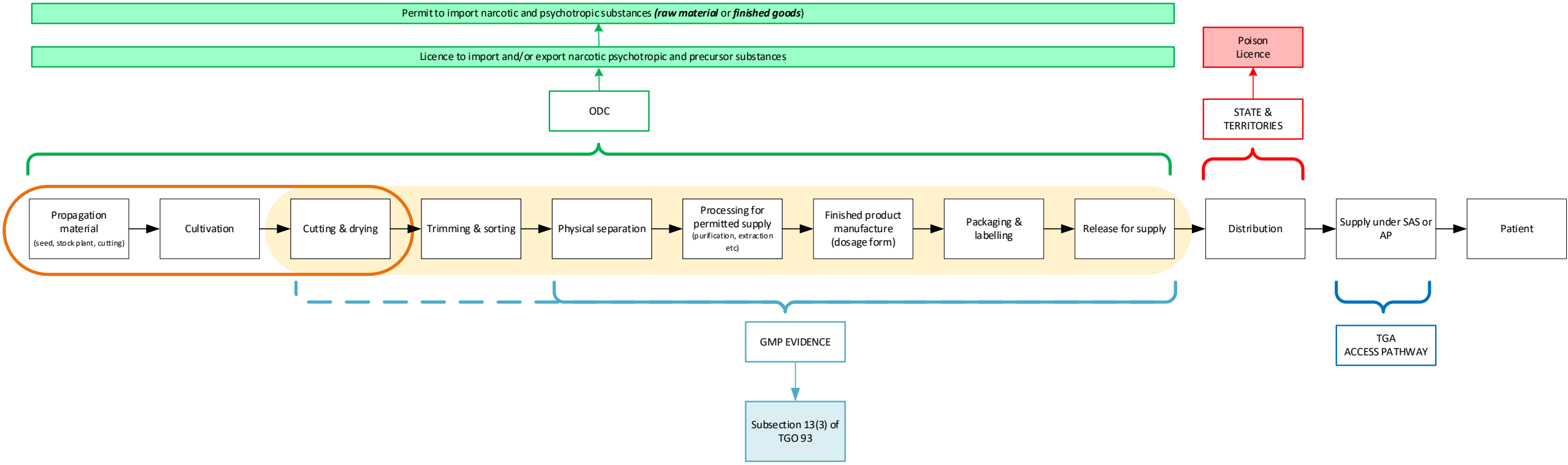
Licences and permits

What licence and permits do I need?

Cannabis manufacturing steps	TGA manufacturing licence	Overseas manufacturing licence/certificate[2]	ODC Licence & Permit	
Propagation materials (e.g., seed, cuttings, plants)	✗	✗	✓	cultivation
Cultivation of cannabis plant	✗	✗	✓	cultivation
Cutting and drying	✗	✗	✓	production
Trimming and sorting	▲	▲	✓	production
First expression e.g., crude extract	✓	✓	✓	manufacture
Further processing	✓	✓	✓	manufacture
Finished product manufacture	✓	✓	✗	
Storage	✓	✓	✓	Cultivation, production & manufacture
Testing	✓	✓	✓	Cultivation, production & manufacture
Packaging and labelling	✓	✓	✗	
Release for supply	✓	✓	✗	

Regulatory controls across the supply pathway

TGO 93 GMP evidence required for imported product



TGO 93 Compliance obligations

Importers / Sponsors

Legally responsible for ensuring products comply with TGO 93

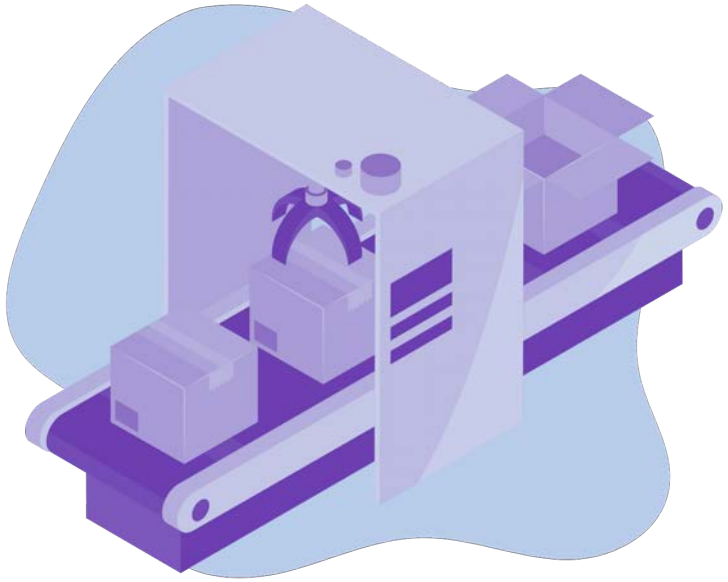
Reporting requirements for sponsors supplying goods under SAS and AP

We strongly encourage sponsors to report any side effects (adverse events) from medicinal cannabis products.

Australian sponsor (the importer) of the medicinal cannabis product must hold evidence of GMP compliance in accordance with TGO 93.

‘Direct Control’ obligations

Wholesale



If you import or manufacture **finished** medicinal cannabis products that are not entered in the Australian Register of Therapeutic Goods, you can only supply those products:

- if they are held under your **direct control** until they are supplied under an **approved pathway** to an Authorised Prescriber or Special Access Scheme approval holder
- if you comply with certain conditions.
- In Australia, the supply of unapproved medicinal cannabis products through wholesale arrangements is prohibited. A sponsor of an unapproved therapeutic good will commit a criminal offence, and may be liable for civil penalties, if they supply that therapeutic good to another person and it is not subject to a relevant exemption, approval or authority.

‘Direct Control’ obligations

Direct Control

For a sponsor to hold medicinal cannabis products under its 'direct control', it must:

- maintain legal ownership of the product, and
- make decisions as to where and how the products are to be kept, and to whom (i.e. the Authorised Prescriber (AP) or the Special Access Scheme (SAS) approval holder) the products are to be supplied.

The goods are kept in a warehouse or a properly secured area under the control of the sponsor.

If multiple products are stored together in a warehouse each sponsor has not met the direct control requirements.

Importing medicinal cannabis to Australia

Section 14 Criminal offences for importing, supplying or exporting goods that do not comply with standards

Offences relating to importing goods into Australia

(1) A person commits an offence if:

(a) the person imports therapeutic goods into Australia; and

(b) the goods are imported without the consent in writing of the Secretary; and

(c) the goods do not conform with a standard applicable to the goods (other than by reason of a matter relating to labelling or packaging); and

(d) either:

(i) the use of the goods has resulted in, will result in, or is likely to result in, harm or injury to any person; or

(ii) the use of the goods, if the goods were used, would result in, or would be likely to result in, harm or injury to any person; and

(e) the harm or injury has resulted, will result, is likely to result, would result, or would be likely to result, because the goods do not conform with the standard.

Penalty: Imprisonment for 5 years or 4,000 penalty units, or both.

Importing medicinal cannabis to Australia

Section 14 Criminal offences for importing, supplying or exporting goods that do not comply with standards

Offences relating to importing goods into Australia

(4) A person commits an offence if:

(a) the person imports therapeutic goods into Australia; and

(b) the goods are imported without the consent in writing of the Secretary; and

(c) the goods do not conform with a standard applicable to the goods (other than by reason of a matter relating to labelling or packaging).

Penalty: Imprisonment for 12 months or 1,000 penalty units, or both.

Importing medicinal cannabis to Australia

Section 14 Criminal offences for importing, supplying or exporting goods that do not comply with standards

Offences relating to importing goods into Australia

(4A) A person commits an offence if:

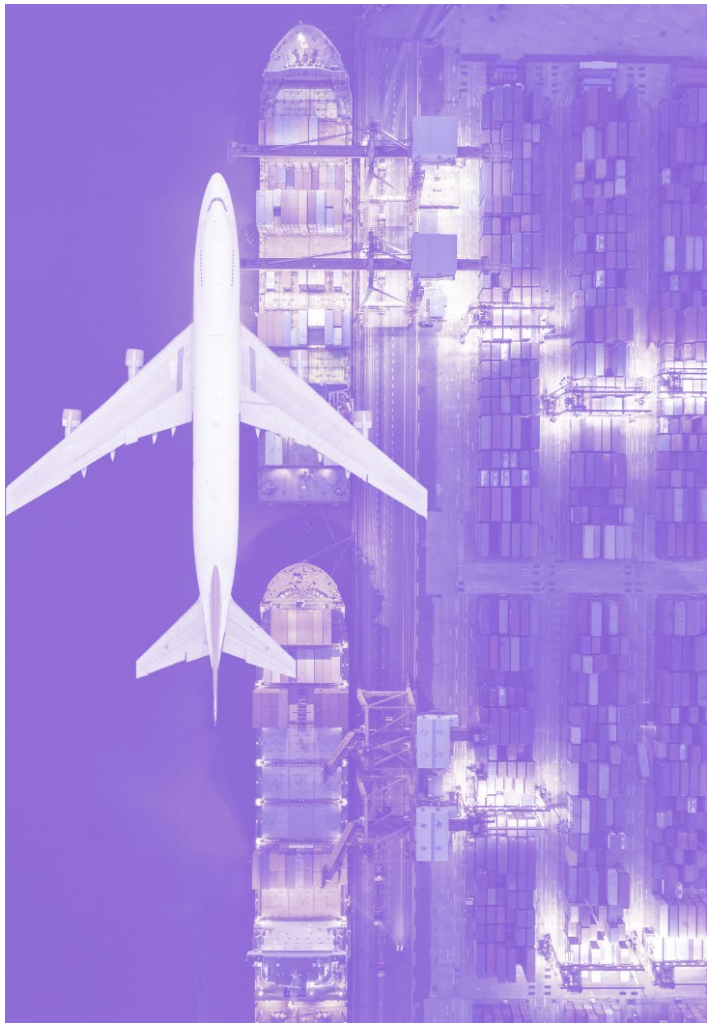
(a) the person imports therapeutic goods into Australia; and

(b) the goods are imported without the consent in writing of the Secretary; and

(c) the goods do not conform with a standard applicable to the goods (other than by reason of a matter relating to labelling or packaging).

Penalty: 100 penalty units.

(4B) An offence against subsection (4A) is an offence of strict liability.



Supplying medicinal cannabis in Australia

Section 14 Criminal offences for importing, supplying or exporting goods that do not comply with standards

Offences relating to supplying goods for use in Australia

(6) A person commits an offence if:

(a) the person supplies therapeutic goods for use in Australia; and

(b) the goods are supplied without the consent in writing of the Secretary; and

(c) the goods do not conform with a standard applicable to the goods; and

(d) either:

(i) the use of the goods has resulted in, will result in, or is likely to result in, harm or injury to any person; or

(ii) the use of the goods, if the goods were used, would result in, or would be likely to result in, harm or injury to any person; and

(e) the harm or injury has resulted, will result, is likely to result, would result, or would be likely to result, because the goods do not conform with the standard.

Penalty: Imprisonment for 5 years or 4,000 penalty units, or both.

Supplying medicinal cannabis in Australia

Section 14 Criminal offences for importing, supplying or exporting goods that do not comply with standards

Offences relating to supplying goods for use in Australia

(9) A person commits an offence if:

(a) the person supplies therapeutic goods for use in Australia; and

(b) the goods are supplied without the consent in writing of the Secretary; and

(c) the goods do not conform with a standard applicable to the goods.

Penalty: Imprisonment for 12 months or 1,000 penalty units, or both.

Supplying medicinal cannabis in Australia

Section 14 Criminal offences for importing, supplying or exporting goods that do not comply with standards

Offences relating to supplying goods for use in Australia

(9AA) A person commits an offence if:

(a) the person supplies therapeutic goods for use in Australia; and

(b) the goods are supplied without the consent in writing of the Secretary; and

(c) the goods do not conform with a standard applicable to the goods.

Penalty: 100 penalty units.

(9AB) An offence against subsection (9AA) is an offence of strict liability.

Confidence in quality

For all stakeholders

- Better labels improve knowledge and understanding for patients and healthcare professionals
- Education campaign to encourage reporting of poor quality products
- Increased visibility of compounded medicinal cannabis products

- GMP to support testing requirements in TGO 93
- TGA conducting inspections of overseas medicinal cannabis manufacturing sites where needed
- Additional sources of equivalent GMP evidence can be added to TGO 93 if needed

Labelling guiding principles

Labels should facilitate the quality use of medicines by consumers and health professionals

- Precise obligations are in section 15 of TGO 93
- Not comprehensive because ‘unapproved’ medicines
- Australian requirements for labels on prescription and non-prescription medicines are ‘best practice’ – TGO 91 and 92

Descriptions of ingredients on labels

- Binomial of species or hybrid
- Plant part
- If a preparation, the type of preparation
- Content of THC/CBD
- Content of any other cannabinoid >1%
- If extract,
    - quantity of extract
    - and
    - minimum dry weight of the plant part from which the extract came (if applicable)

Evidence of GMP

Labelling is a step of GMP

- Labelling of medicines must occur at a site with a TGA manufacturing licence.
- Relabelling, ‘”over-stickering”, extending expiry dates must be done at a TGA licensed sites.
- Exemptions for the application of supplementary labelling, where the supplementary label contains only a name and address, the registration or listing number of goods, or the biological number of a biological in Schedule 7 Item 5 of the Regulations

Questions?

Scan the QR code with your device to submit a question

GMP FORUM 2024

Australian Government

Department of Health and Aged Care

Therapeutic Goods Administration