Q&A session in relation to new guidance material ‘Demonstrating the quality of listed probiotic medicines’

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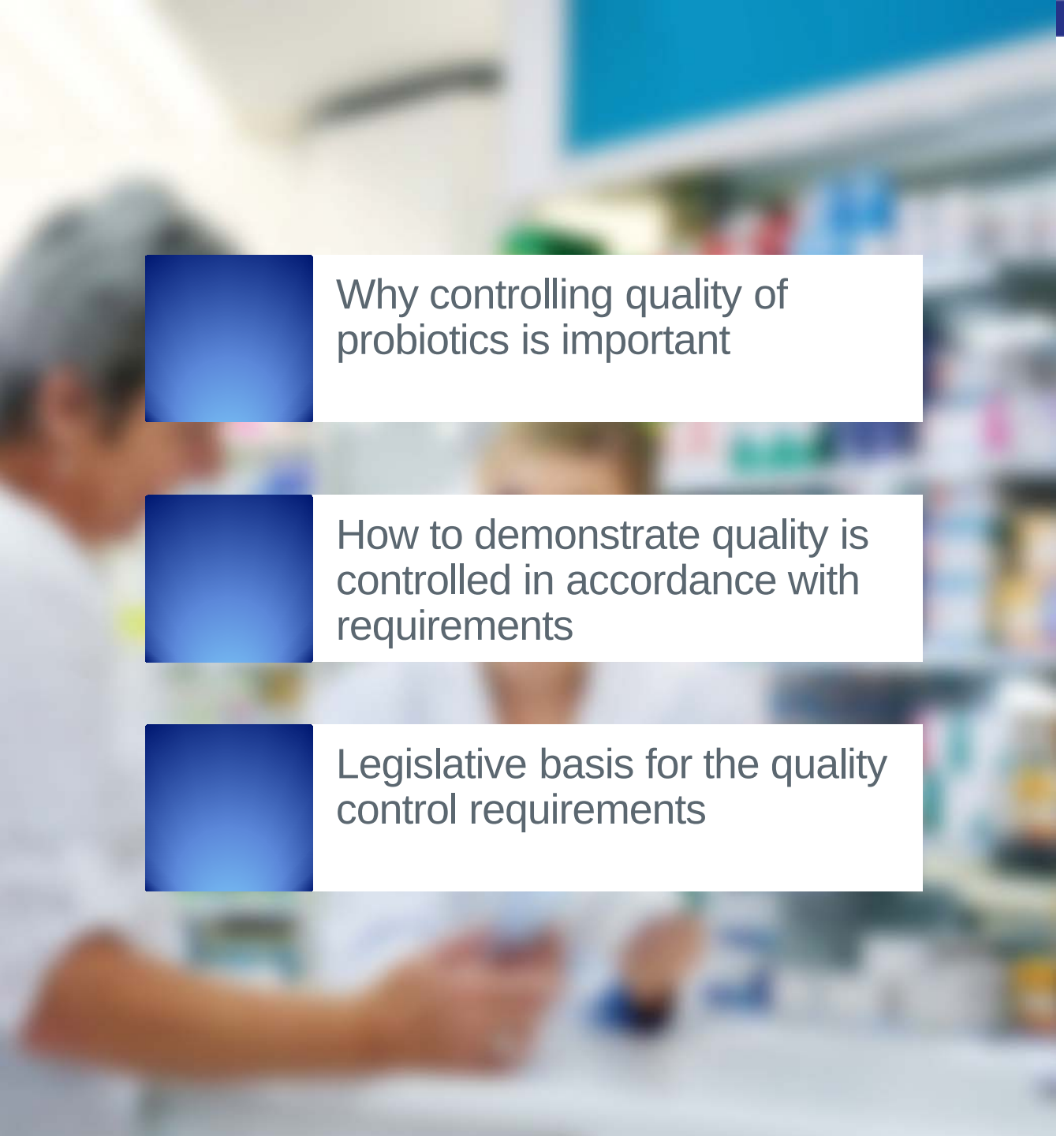
Acknowledgement of Country

In the spirit of reconciliation, the Department of Health and Aged Care acknowledges the Traditional Custodians of country throughout Australia and their connections to land, sea and community.

We pay our respect to their Elders past and present and extend that respect to all Aboriginal and Torres Strait Islander peoples today

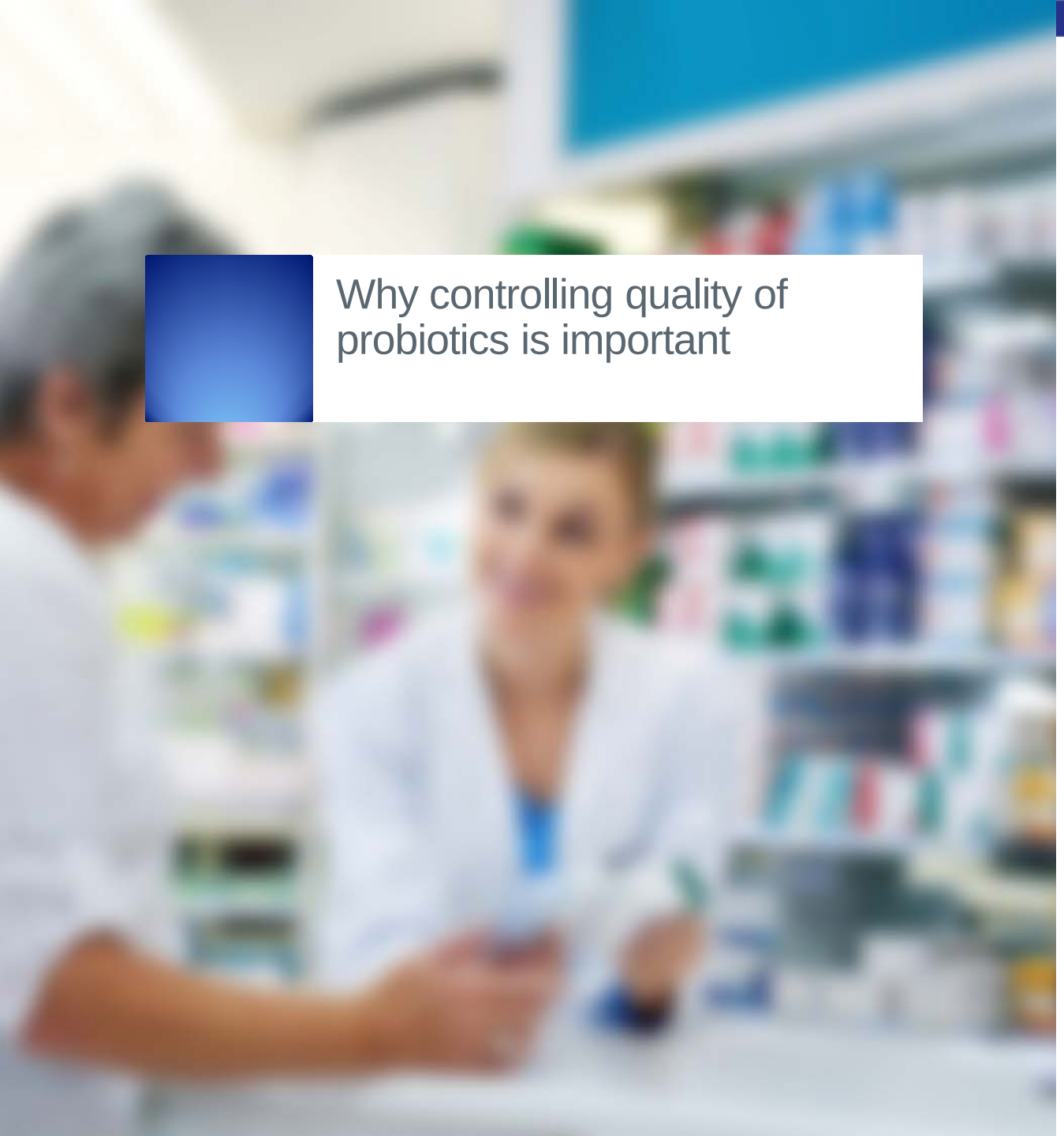
The Guidelines

- Are not mandatory
- Provides transparency for what a TGA delegate would consider in a compliance review
- Individual circumstances will be considered on a case-by-case basis



- Why controlling quality of probiotics is important
- How to demonstrate quality is controlled in accordance with requirements
- Legislative basis for the quality control requirements

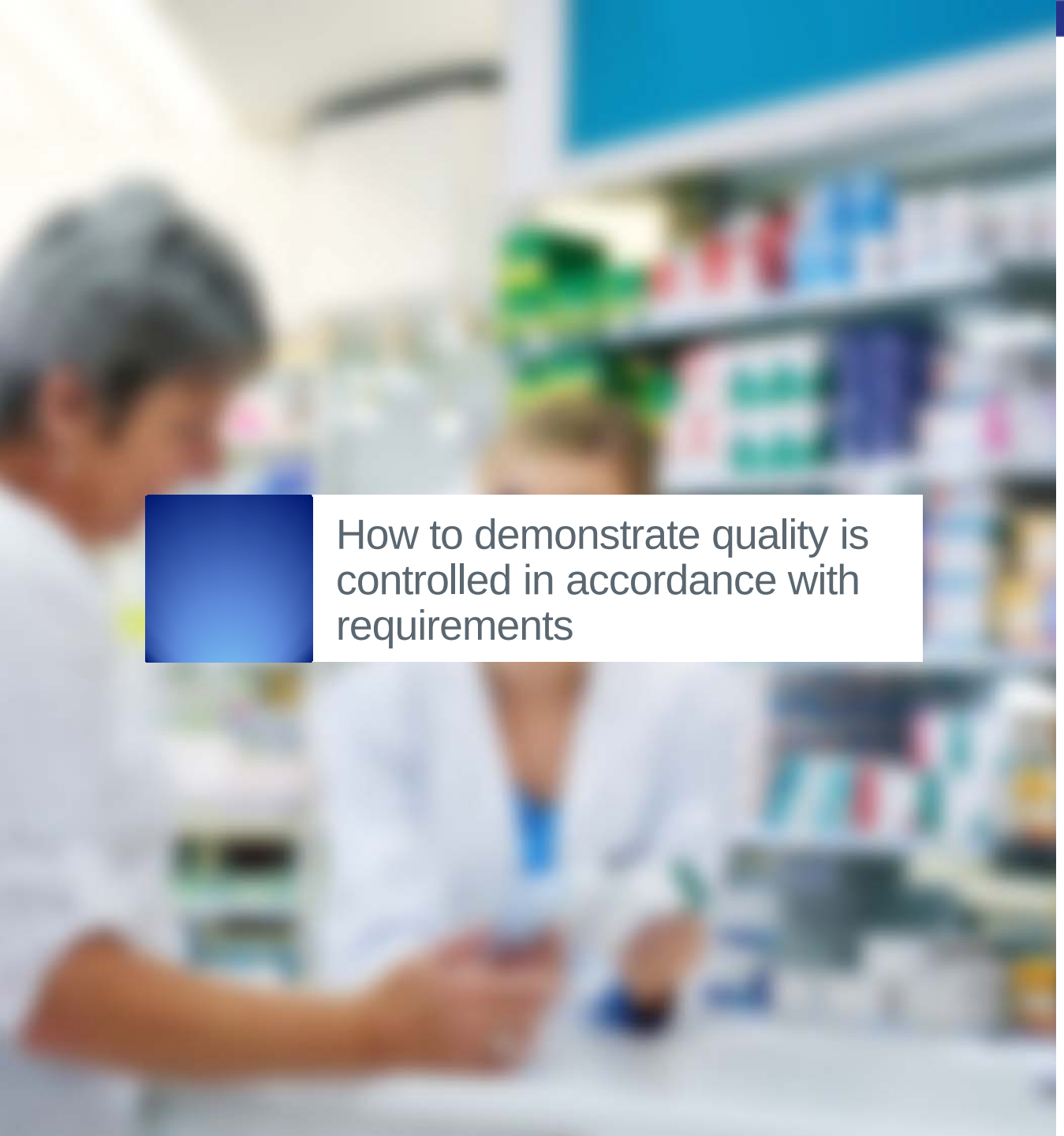
Guidelines divided into 3 parts



Why controlling quality of probiotics is important

Quality Control

Ensures the safety and efficacy of the probiotic medicine



How to demonstrate quality is controlled in accordance with requirements

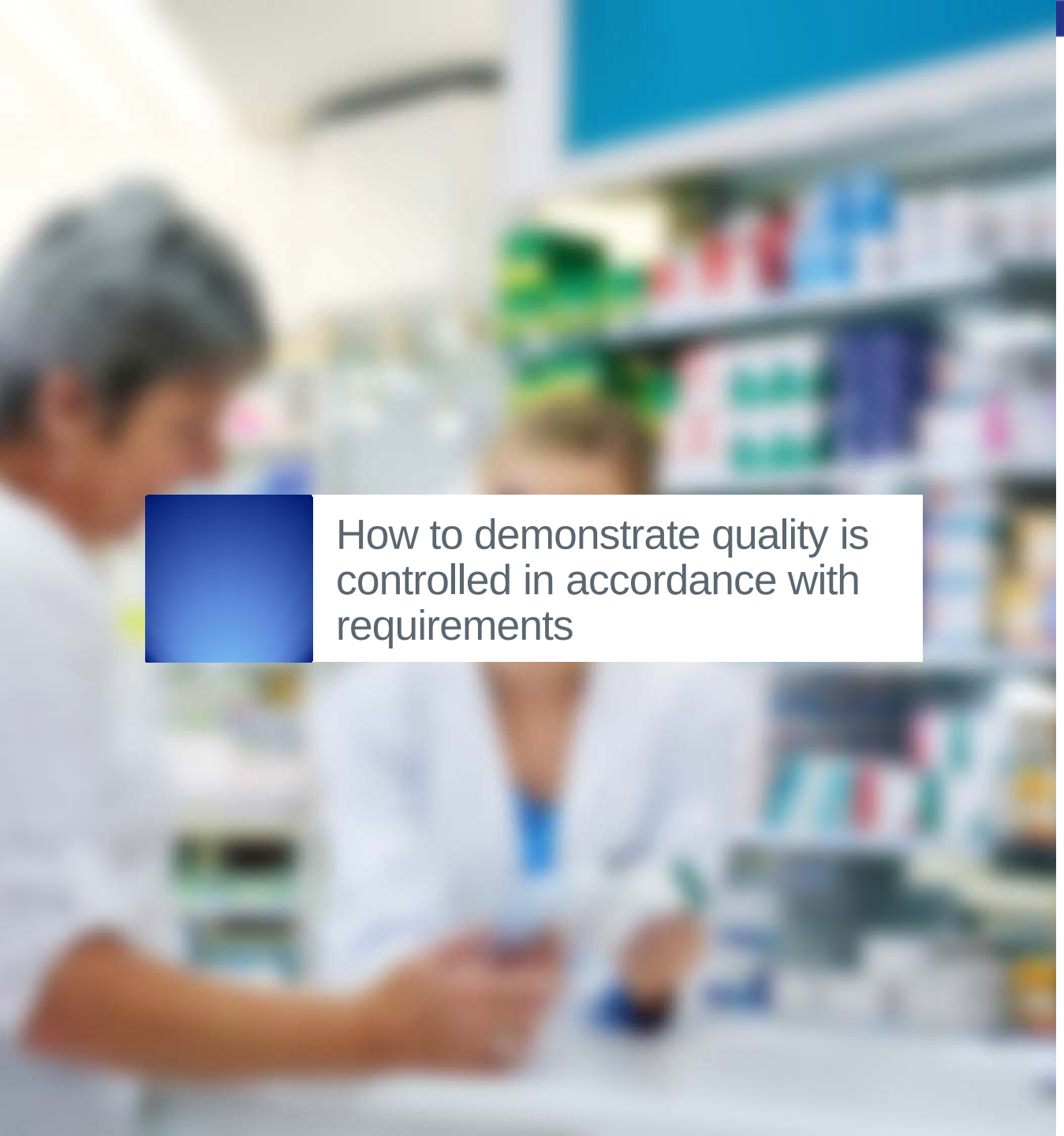
Demonstrating compliance with legislative requirements

- No one size fits all strategy to control quality

Legislative basis for the quality control requirements

Applicable legislation

- Steps through legislation that underpins the quality requirements



How to demonstrate quality is controlled in accordance with requirements

Demonstrating compliance with legislative requirements

- No one size fits all strategy to control quality

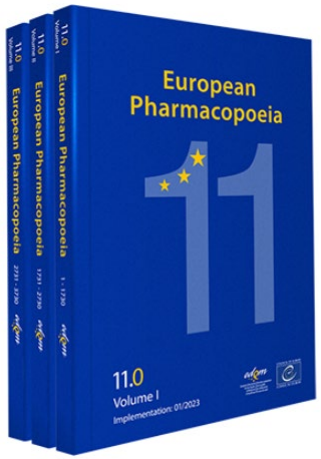
Demonstrating quality control

Quality parameters

- Active ingredient identity and quantity
- Stability
- Microbial Contamination
- Labelling

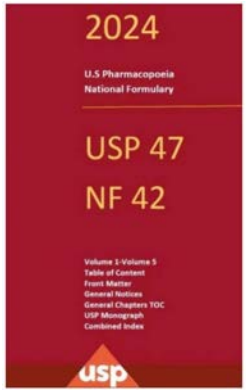
Background on applicable standards

- '**Ministerial standards**' – Therapeutic Goods Orders (TGO)
- '**Default standards**' – British, European and US Pharmacopoeias:
  - '**Individual monographs**' apply to final product or raw/starting materials
  - '**General monographs**' apply to anything that falls within the scope/definition described in the general monograph



Current TGOs

- Therapeutic Goods Order No. **91** - Standard for labels of prescription and related medicines
- Therapeutic Goods Order No. **92** - Standard for labels of non-prescription medicines
  - Guidance for TGO 91 and TGO 92
- Therapeutic Goods (Standard for Medicinal Cannabis) (TGO **93**) Order 2017
  - Guidance on quality requirements for medicinal cannabis products - Conforming with TGO 93
  - The PIC/S Guide to GMP - The following PIC/S guide must be read in conjunction with Section 13 of the amended order above.
    - GMP for Medicinal Products Introduction
    - GMP for Medicinal Products Part I
    - GMP for Medicinal Products Part II
    - GMP for Medicinal Products Annexes
- Therapeutic Goods Order No. **94** (Standard for Haematopoietic Progenitor Cells derived from Cord Blood)
- Therapeutic Goods Order No. **95** - Child-resistant packaging requirements for medicines 2017 (TGO 95)
  - Child-resistant packaging requirements for medicines - Guidance on TGO 95
- Therapeutic Goods Order No. **99** - Therapeutic Goods (Standard for Menstrual Cups) Order 2018
- Therapeutic Goods Order No. **100** - Therapeutic Goods (Microbiological Standards for Medicines) Order 2018
- Therapeutic Goods (Standard for Tablets, Capsules and Pills) (TGO **101**) Order 2019
  - Guidance for TGO 101: Standard for tablets, capsules and pills



Control of active ingredient identity and quantity

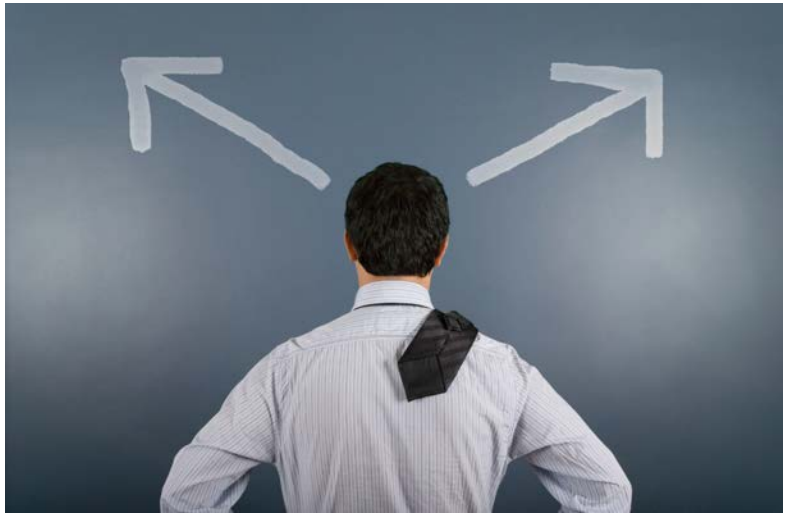
Standards applicable to probiotics

- Under the *Therapeutic Goods Act 1989* (the Act), medicines must comply with applicable standards
- European/British Pharmacopoeia general monograph 3053 ‘Live biotherapeutic products for human use’
  - Applicable to all probiotics, including multi-strain
- Therapeutic Goods Order 101
  - Only applicable to probiotics that are tablets or capsules
- US Pharmacopoeia general chapter 64 ‘Probiotics’ only applies if it’s referenced in an applicable individual monograph
  - Currently only one single strain USP individual monograph exists (*Bacillus coagulans capsules*)
  - Not applicable to multi-strain probiotics (until multi-strain individual monographs are created)

Control of active ingredient identity and quantity

Testing vs alternative strategies

- Irrespective of dosage form, for multi-strain and most single-strain probiotics - Ph Eur/BP 3053 is the most applicable standard
- Ph Eur/BP 3053 requires probiotic active ingredients to be controlled at strain level
- This can be through testing the final product **OR through ‘other means’ by which the same outcome is achieved**



Control of active ingredient identity and quantity

Alternative strategy – Quantified by Input (QBI)

- QBI – where testing the strain identity and quantity in the final product is not conducted
- Control of strain identity and quantity is conducted earlier on in the manufacturing process through compliance with GMP, such as (not exhaustive):
  - Vendor/supplier qualification
  - Blending process validation
  - Control of water activity

Stability of active ingredients

Quantified by Input (QBI)

- Also expected to be controlled at strain level – but this does not mean testing of strains is necessary throughout shelf life
- If relying on a total genus or species count at different timepoints, additional data is needed to show that particular strains are not out-competing other strains such that the total genus or species count is a good reflection that each strain is still present at the correct proportions
- This can include (not exhaustive):
  - Stability data generated from individual strains
  - Relevant water activity data to show that changes in strain quantity will be minimised when water activity is below a certain value

Microbial contamination

Ph Eur/BP 3053

- Chapter 2.6.36 ‘Microbiological examination of live biotherapeutic products: Tests for enumeration of microbial contaminants’
- Chapter 2.6.38 ‘Microbiological examination of live biotherapeutic products: Tests for specified microorganisms’.
- Chapter 5.1.6 ‘Alternative methods for control of microbiological quality’

- TGO 100 refers to Ph Eur/BP and USP-NF test methods that are **not applicable** to medicines containing viable microorganisms as active ingredients

Labelling

Strain or species?

- Labelling Order (TGO 92) requires use of Australia Approved Name (AAN) of the active ingredient (currently only available at species level) as a cohesive unit with the medicine name and active ingredient quantity
- Ph Eur/BP 3053/USP-NF – requires labelling of active ingredients at strain level

► Technically, both needs to be on the label. However…

Example label:

BEAN'S PROBIOTIC–A

Active ingredient: ***Lactobacillus acidophilus*** **50 billion CFU/capsule**

[other label text or graphics]

L. acidophilus strains: **NCFM and La-14, each 25 billion CFU/capsule**

Labelling

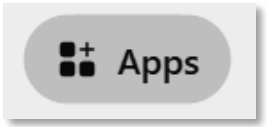
s14 consent to not comply with a standard

- Can either comply with:
  - Labelling Order (TGO 92) – at species level

    OR
  - Ph Eur/BP 3053/USP-NF – at strain level
- Cannot mix and match on the one label
- Same rules apply on the side label
- s14 consent decision expires 1 October 2026 (TGO 92 sunset date)
- Once expires, both AAN+quantity and strain name+quantity are to be shown on the label

How did we go?

Take a moment to complete our survey, and we'll be back with you shortly for Q&A



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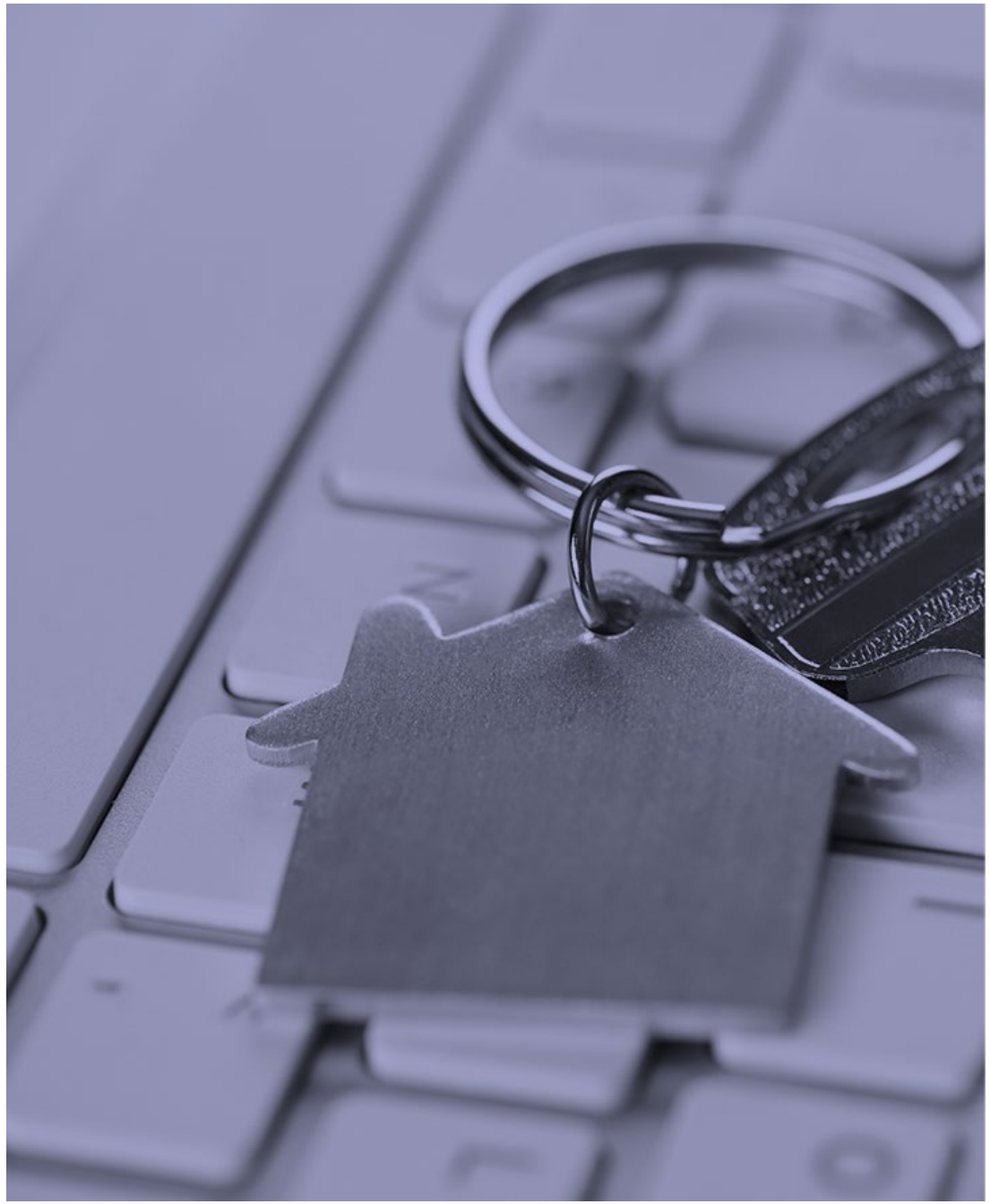
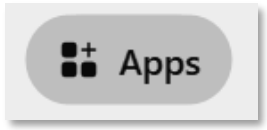
nonprescriptionmedicines@health.gov.au



Questions?

Ask us through Slido



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