Australian Government
Department of Health
Therapeutic Goods Administration

Information session on the revised evidence guidelines for listed medicines

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TGA Health Safety Regulation

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Welcome

- This webinar is being recorded
- If you need to contact the moderator – please use the **'Chat'** function
- Slides will be made available on the TGA website
- Questions to the **panel** – please use the **Q&A** tool
  - Questions will be answered at the end of the presentation
- Relevant links will be sent to you via the chat function box
- Live poll after presentation – how did we go?.

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Aims for revising the Evidence Guidelines

- Enhance the readability and useability of the guidelines.
- Clarify the way the TGA interprets and analyses the different types of evidence.
- Clarify specific technical concepts that have been unclear for sponsors in the Current Guidelines.

- Provide greater guidance of what is expected in a TGA compliance review in relation to efficacy and assist sponsors mitigate the risk of non-compliance.

Aims for revising the Evidence Guidelines

- The draft Revised Guidelines have not changed existing requirements reflected in the Current Guidelines. The revision provides clearer, more detailed explanation of existing policies and the current regulatory framework.
- The Revised Guidelines do not change the way the TGA conducts post market reviews. Evidence packages that demonstrate efficacy in accordance with the Current Guidelines are not expected to be impacted by the Revised Guidelines.
- The lack of clarity on some technical issues in the current Guidelines have caused a difference in TGA and industry's interpretation of the Guidelines.
- Providing clarity on these issues may be seen by some readers as a change in requirements. Hence, we are conducting a public consultation.

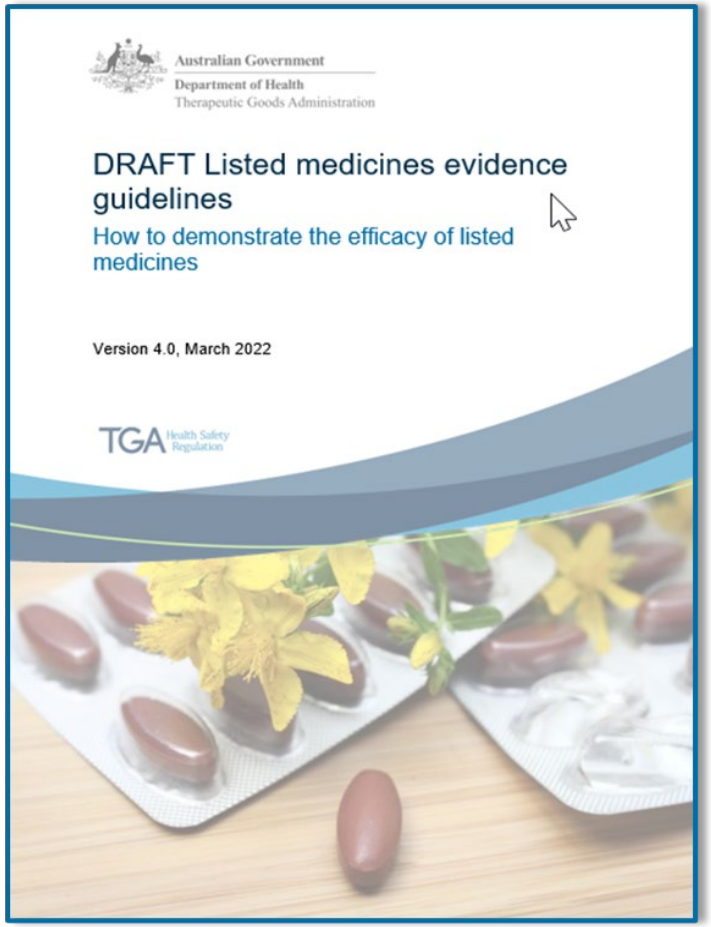
Consultation

- The consultation is open for 4 weeks an closes on 1 April 2022 and is available at the TGA consultation hub https://consultations.tga.gov.au
- Throughout 2021, the TGA has conducted a targeted consultation with an industry working group on specific technical areas in the guidance.
- We have considered the feedback and issues raised by this working group in the revision of the Guidelines.

- The issues discussed in targeted consultation were on the areas where the guidance has been clarified, other areas of the document remain largely unchanged.
- https://consultations.tga.gov.au/medicines-regulation-division/proposed-update-to-evidence-guidelines-listed-meds/

What has changed?

- The name.
- The structure.
- Clarification of technical concepts.
- Additional guidance, tools and examples.



Structure: What has changed?

Existing guidelines

PART A: Evidence to support indications

- Traditional indications
- Scientific indications
- Cross-evidence base indications

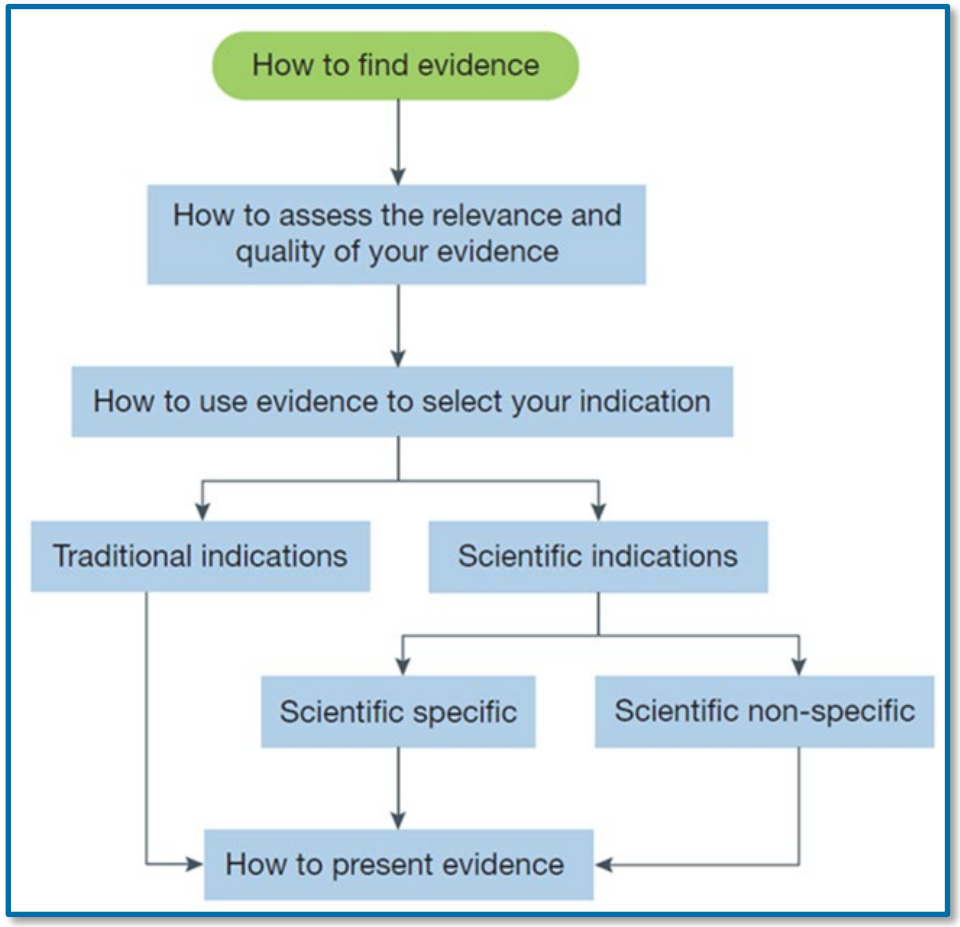
PART B: Further technical guidance

- Equivalency of ingredient
- Scientific studies
- Biomarkers
- Weight loss
- Nutritional supplementation

Appendix 1: How to use evidence checklists
Appendix 2: Journal impact factors
Appendix 3: Examples of resources and texts
Appendix 4: references

Draft revised guidelines

Revised Guidelines: Step through process



Assist sponsors to:

1. Find evidence
2. Critically assess evidence
3. Select indications (as permitted for use in listed medicines) based on evidence
4. Present evidence

Revised guidelines: Section 1 Introduction

Outlines:

- the purpose of the guidelines
- a sponsor's legal obligations to demonstrate efficacy
- how and when the TGA reviews efficacy

In relation to **sponsor's legal obligations**, sponsors must :

- certify [against subparagraph 26A(2)(ja) of the Act] that they **hold evidence to support all indications and comply with all requirements** for those indications
- certify [against subparagraph 26A(2)(j) of the Act] that they **hold evidence to support any claims** (that are not indications) made for the medicine
- adhere to the condition of listing [provided in subparagraph 28(7) of the Act) that they must, **at all times** while the medicine remains listed hold information/evidence that supports the indications

Revised guidelines: Section 1 Introduction

A medicine **can be cancelled from the ARTG** by the TGA, among other things, if:

- the sponsor **certifications** under 26A(2)(ja) and (j) of the Act (that the sponsor holds evidence for all indications and claims) are **found to be incorrect**
- the **efficacy** of the medicine **appears to be unacceptable** [30(2)(a) of the Act]

The TGA can review a medicine at any time it is listed in the ARTG.
During an efficacy review, the key questions the TGA considers include:

1. What therapeutic effect is described by the indication?
2. On what basis can it be concluded that the medicine will result in this therapeutic effect? What are the **reasons** for this conclusion?
3. Is the above conclusion based on data or information that we have **confidence** in **to be true and accurate**?

Revised guidelines: Section 1 Introduction

Consultation questions

- From the information provided in Section 1, did you understand why a sponsor needs to provide a critical analysis of their evidence in an evidence package for their listed medicine?
- Do you have any other comments or feedback regarding section 1?

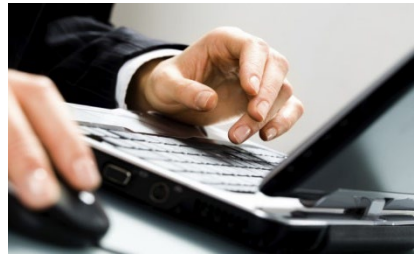
Revised guidelines: Section 2 How to find evidence

Provides guidance on how to conduct and document a literature search

What is new?

Additional guidance on:

- how to conduct a literature search – search methodology
- how and when to conduct a non-systematic literature search
- what to document



Revised guidelines: Section 2 How to find evidence

Consultation questions

- Do you find the information and links presented in section 2 helpful in guiding you to conduct and document a literature search?
- Do you have any other comments or feedback regarding section 2?

Revised guidelines: Section 3 How to assess evidence

Provides guidance on how to assess the relevance and quality of the evidence sources you have found for your medicine.

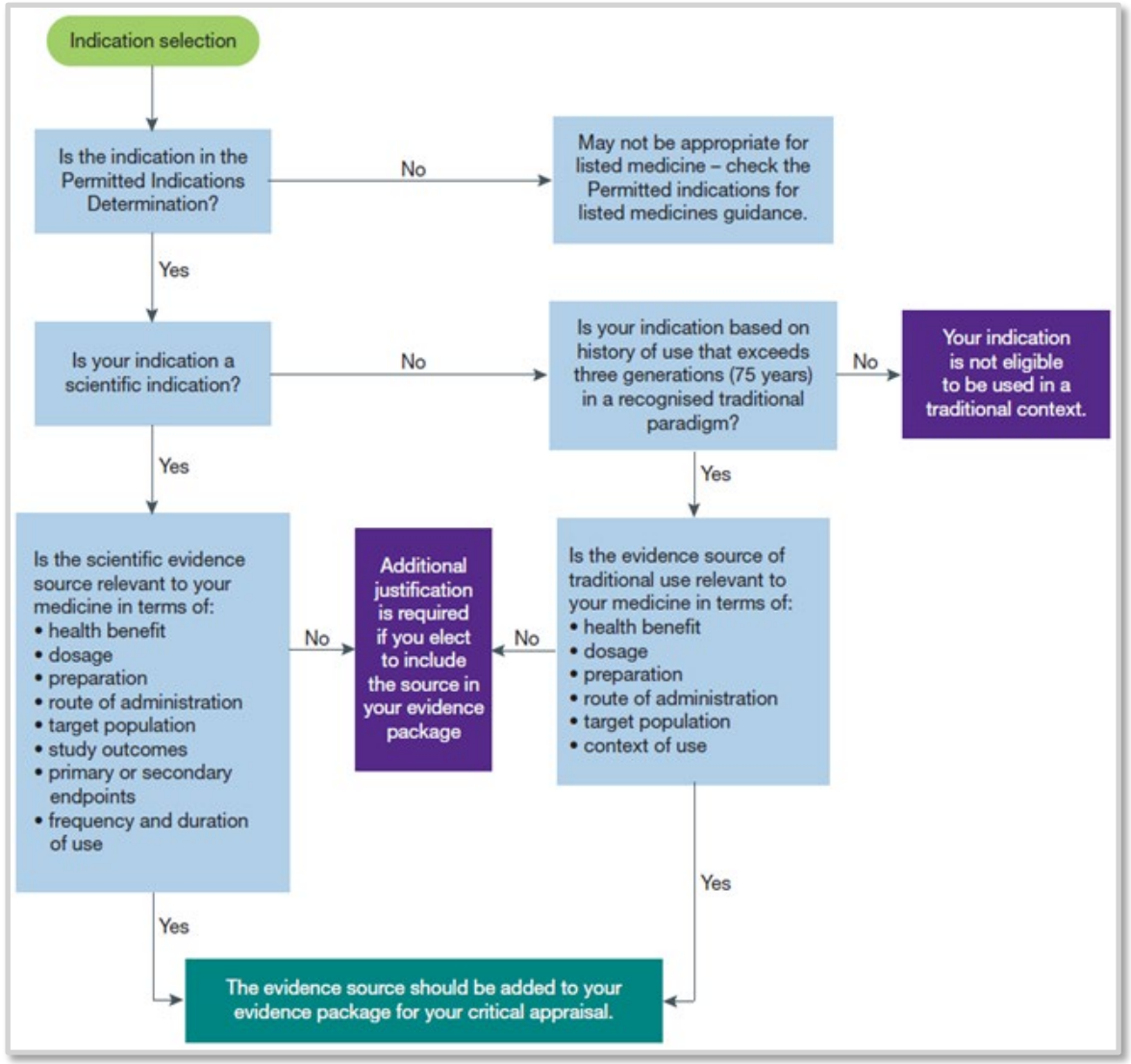
What is new?

- Decision tree to help determine relevance of evidence source to your medicine.
- New categorisation of scientific evidence sources: Categories A, B or C.

Revised guidelines: Section 3 How to assess evidence

NEW:

- Decision tree to help determine relevance of evidence source to your medicine



Revised guidelines: Section 3 How to assess evidence

What is new:

- The existing Evidence guidelines categorise evidence as primary or secondary, which sponsors have found confusing.
- The revised evidence guidelines categorise evidence as Categories A, B or C

Scientific evidence		
Category A	**Category B**	**Category C**
Double blind randomised controlled trials (including cross-over trials)	Observational studies e.g.,. cohort and case-controlled studies	Non-systematic, generalised reviews – including databases
Systematic reviews	Comparative studies (non-control)	Publicised international regulatory authority articles
		Evidence-based reference texts - ***scientific***
		Scientific monographs

Revised guidelines: Section 3 How to assess evidence

Consultation questions

- Are the factors that are important for assessing relevance and quality of evidence sources clear and easy to understand and follow?
- Do you find that the removal of the terms ‘primary’ and ‘secondary’ sources and replacement with the concept of relevance and quality of evidence sources provides greater clarity when selecting evidence sources to include in an evidence package?
- Do you have any other comments or feedback regarding section 3?

Revised guidelines: Section 4 How to use evidence

Describes the different types of claims and indications for listed medicines and outlines the evidence requirements to support them.

What is new?

- Clearer definition of indications and claims.
- Clearer definition of specific and non-specific indications.
- Traditional indications no longer classified as specific or non-specific
- Clarification of what supplementation indications and claims can be supported by at least 25% RDI.
- Low level biomarker indications that describe maintenance of health in a generally healthy population, now classified as non-specific.

Revised guidelines: Section 4 How to use evidence

Minimum levels of traditional evidence

Traditional indications	
Minimum evidence requirements	Minimum of two from 'Traditional Evidence to support tradition of use'
Traditional Evidence to support tradition of use	
• Materia medica • Official pharmacopoeias • Monographs • Publications from various international regulatory authorities • Texts that are relevant to the traditional paradigm • Well-recognised evidence-based reference texts	

Revised guidelines: Section 4 How to use evidence

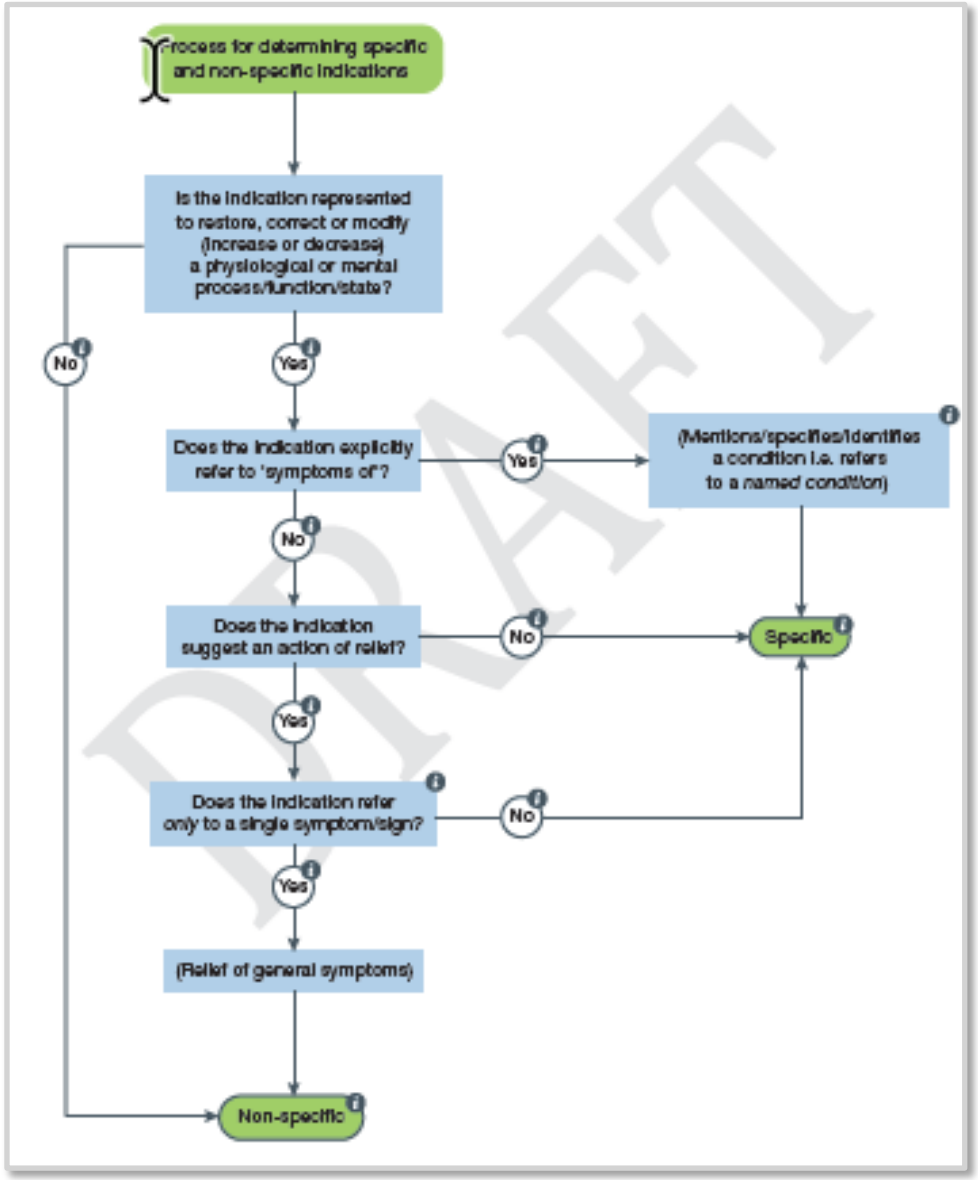
Minimum levels of scientific evidence

Minimum evidence requirements		
Scientific indications		
Minimum evidence requirements	**Non-specific indications:**	**Specific indications:**
	Minimum of two from Category B or Category C	Minimum of one from Category A **OR** Minimum of one from Category B AND two from Category C
Category A	**Category B**	**Category C**
Double blind randomised controlled trials (including cross-over trials)	Observational studies, for example: cohort and case-controlled studies	Non-systematic, generalised reviews – including databases
Systematic reviews	Comparative studies (non-controlled)	Publicised international regulatory authority articles
		Evidence-based reference texts - ***scientific***
		Scientific monographs

Revised guidelines: Section 4 How to use evidence

NEW

Decision tool for determining specific/non specific indications



Revised guidelines: Section 4 How to use evidence

Supplementation

New:

- Clarification on what is a supplementation claim and an indication.
- Clarification of what claims and indications can be supported by providing at least 25% RDI without the requirement for additional evidence.

Claims/indications	Minimum evidence requirements
Supplementation claims	a. Provides at least 25% of RDI, AI or NRV b. Nutrient is in a form that can be absorbed by the body c. Medicine must also have at least one permissible indication in the medicine's ARTG entry and on the medicine label.
Permissible indications with special evidence requirements 1. 'Maintain/support (state vitamin/mineral/nutrient) levels in the body' 2. 'Maintain/support (state vitamin/mineral) within normal range'	a. Provides at least 25% of RDI, AI or NRV b. Nutrient is in a form that can be absorbed by the body

Revised guidelines: Section 4 How to use evidence

Low level Biomarker indications classified as non-specific

- The Therapeutic Goods (Permissible Indications) Determination only includes low level biomarker indications relating to general health:
  - ‘Helps maintain/support healthy blood sugar/glucose’
  - ‘Helps maintain/support healthy cholesterol’
- The decision tool classifies low level biomarker indications that describe a **maintenance of existing health in a generally healthy population** as non-specific.

Revised guidelines: Section 4 How to use evidence

Weight loss indications

Study duration for temporary weight loss indications

For indications specifically referring to temporary weight loss, which must carry the mandatory label statement advising consumers that the 'Weight loss may not be maintained for longer than 3 months' (which clarifies for consumers that the weight loss they achieve may only be for a short term), may be appropriate to rely on clinical studies that show at least a 5% reduction of the initial body weight over a minimum duration of three months.

Revised guidelines: Section 4 How to use evidence

Consultation questions

- Do you find the decision tool helpful for classifying indications?
- According to the decision tool, low-level biomarker indications (such as '*helps maintain/support healthy cholesterol*' and '*helps maintain/support healthy blood sugar/glucose*') are classified as 'non-specific', while previously these indications have been generally regarded as specific. Do you agree that the efficacy of listed medicines with these indications should be supported by Category B or C type evidence only?

Revised guidelines: Section 4 How to use evidence

Consultation questions continued

- Does section 4.4.2. clarify when it might be appropriate for a supplement to only provide a minimum 25% of the Recommended Dietary Intake (RDI) (of a specified vitamin/mineral/nutrient) without the sponsor needing to hold additional evidence sources to support their medicine's efficacy? Do you agree with this proposed clarification?
- What do you interpret the indication 'maintain vitamin levels' to mean?
- Do you find the evidence requirements for weight loss indications clear and easy to understand?
- Do you have any other comments or feedback regarding section 4?

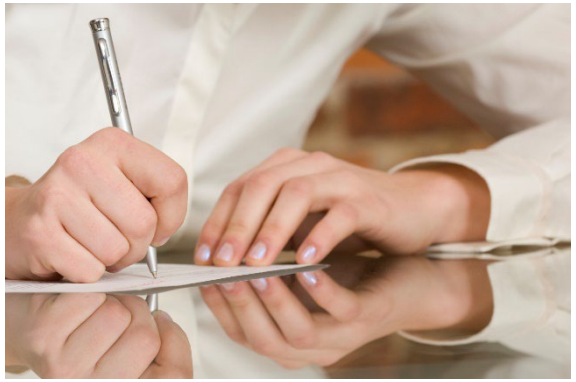
Revised guidelines: Section 5 How to present evidence

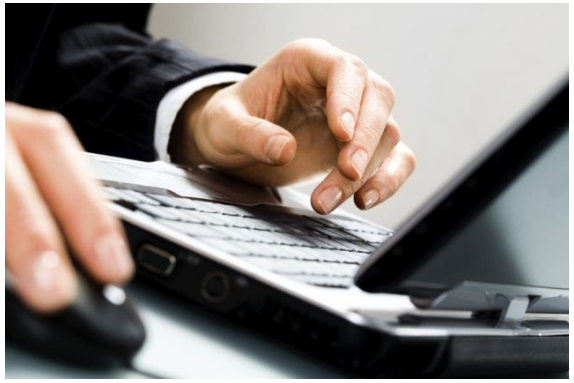
Provides guidance on how to document and present a critical appraisal of the evidence, including providing justifications where appropriate.

What is new?

Additional guidance on:

- Critical appraisal
- Justifications in your critical appraisal





Revised guidelines: Section 5 How to present evidence

Critical appraisal

- An evidence package should include a convincing argument that demonstrates how the body of evidence supports the efficacy of a medicine.
- It is reasonable to expect that a sponsor has undertaken a critical appraisal of the evidence – consumers would expect that a company marketing a particular medicine would have appraised the evidence for its claimed indications.
- Including a convincing argument reduces the substantial amount of communications that currently occurs between the sponsor and the TGA during a compliance review and thus will reduce regulatory burden on sponsors.

Revised guidelines: Section 5 How to present evidence

Consultation questions

- Is it clear what the TGA might consider as gaps and discrepancies in the evidence source?
- Is it clear why it is important to include a persuasive critical appraisal of the body of evidence in an evidence package?
- Do you have any comments or feedback regarding section 5?

Revised guidelines: Appendices

- Provides additional technical guidance on specific evidence issues and case studies.
- Appendix 1: Examples of resources and texts
- Appendix 2: Case studies
- Appendix 3: Example evidence package for vitamin B12

What is new?

- Case studies
- Vitamin B12 example evidence package

Revised guidelines: Appendixes

Consultation questions

- A case study showing an example evidence package for vitamin B12 has been developed for the Guidelines, demonstrating an example critical appraisal format that sponsors may wish to follow for their own medicine evidence package. Do you have any comments or feedback on the example evidence package for vitamin B12?
- Is there a case study that you would like to see included in the Guidelines that would help you better understand the evidence requirements for listed medicines?
- Do you have any other comments or feedback on the Appendices of the proposed Guidelines?

Diane and Jenny are currently reading over your submitted questions.

We'll be back shortly for **Q&A**

We appreciate your participation in our live poll.

LIVE POLL

More information – Social media

	Website	https://www.tga.gov.au
	Facebook	https://www.facebook.com/TGAgovau/
	Twitter	https://twitter.com/TGAgovau
	YouTube	https://www.youtube.com/channel/UCem9INJbMSOeW1Ry9cNbucw
	Topic blogs	https://www.tga.gov.au/blogs/tga-topics
	Linkedin	https://www.linkedin.com/company/therapeutic-goods-administration/
	Instagram	https://www.instagram.com/tgagovau/?hl=en

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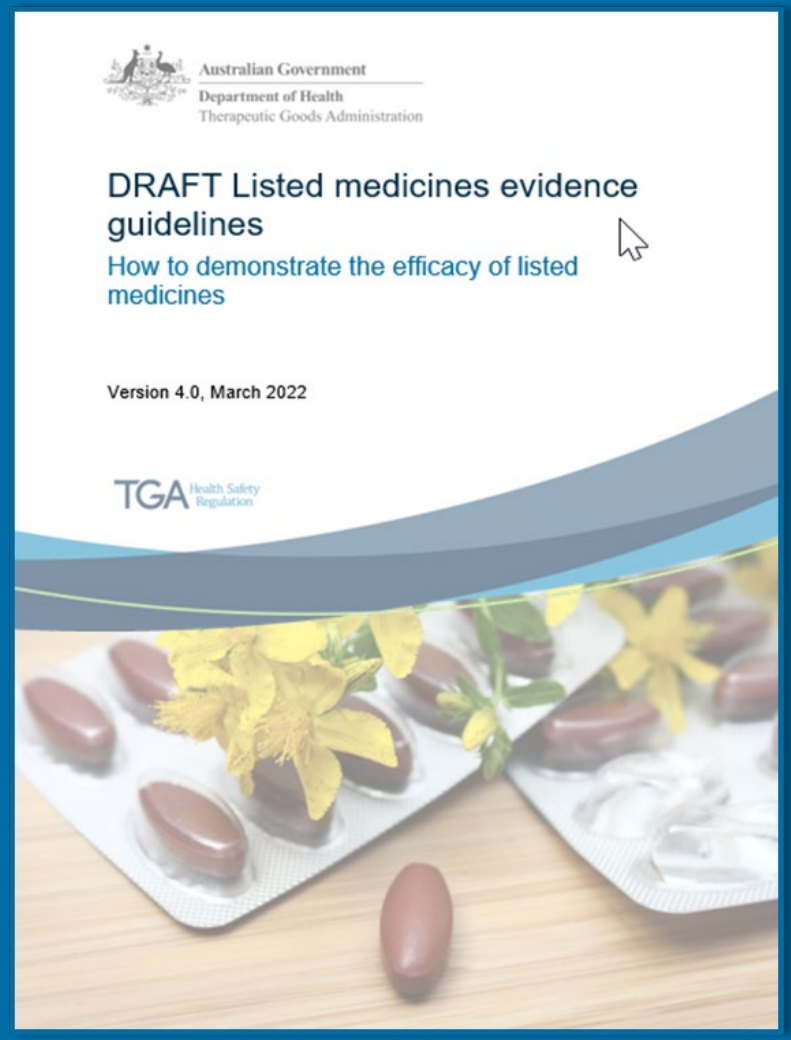
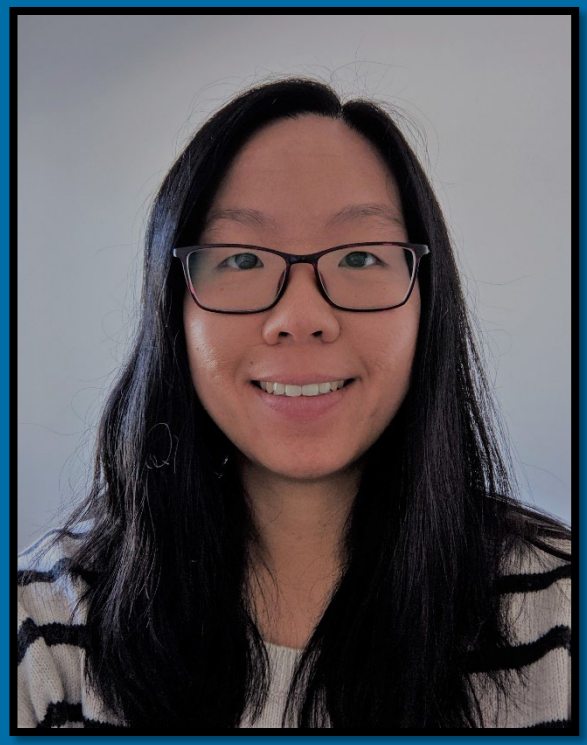
Questions

Diane Wilkinson

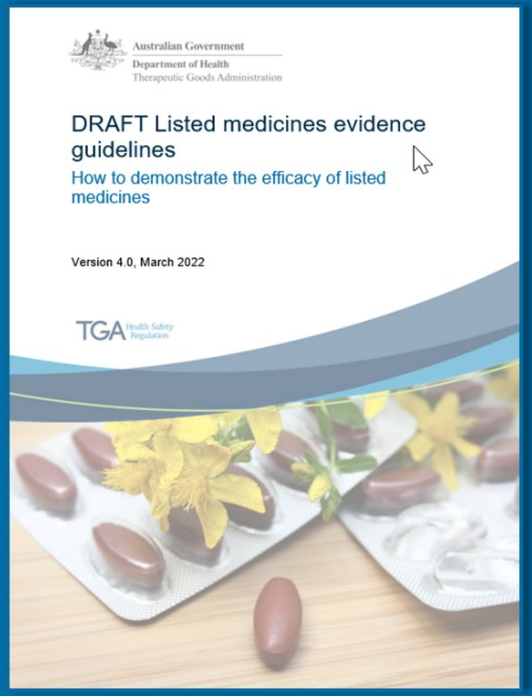




Jenny Cheng

Next Q & A session

After today's session, we will be conducting an additional Q & A session on the revised evidence guidelines for listed medicines on the 28th of March – details are on our website https://www.tga.gov.au/information-our-proposed-updated-evidence-guidelines-listed-medicines-28-march



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