Australian Government
Department of Health
Therapeutic Goods Administration

Regulatory updates from the TGA

Complementary and Over the Counter Medicines Branch

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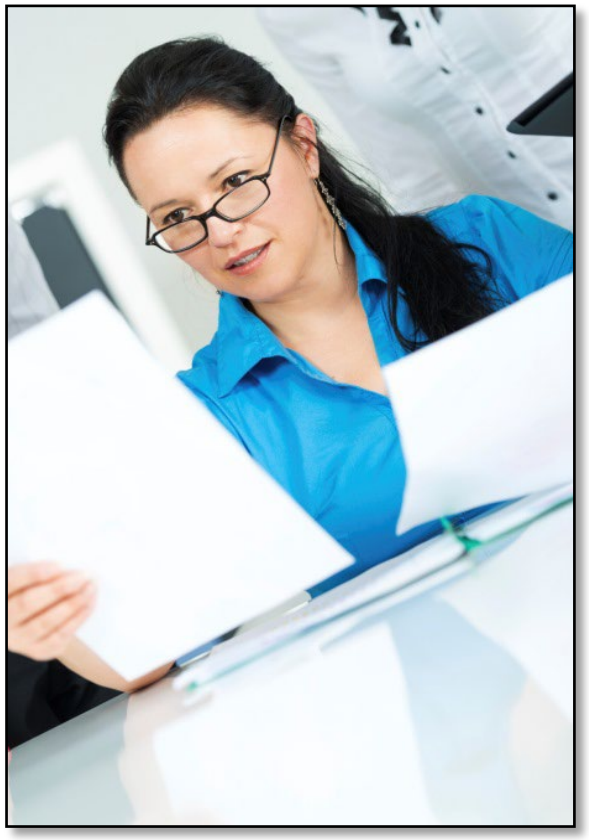
TGA Health Safety Regulation

Key activities in 2022

- Assessed listed medicines – pathway and applications
- Mandatory requirements for new Listed Med ingredient applications
- Guidance for assessment of microorganism strains
- Revised Evidence guidelines for listed medicines
- Guidelines on the quality of listed probiotic medicines
- Targeted compliance activity
- Sunscreen issues
- General Administration of Customs of China registration for exported listed medicines
- TGO 92 clarification
- OTC application timelines
- New TGA website – improved searchability



Assessed listed [Aust L(A)] pathway update

- Legislation for data protection for assessed listed medicines has been implemented and guidance was published in September 2021.
- There are currently 2 L(A) medicines included in the ARTG.
- The change tables for changing a listed or an assessed listed medicine was updated in March 2022. Changes include new categories for:
  - changes to pack size for assessed listed medicines
  - correction of mistakes on the label of assessed listed medicines
- The list of Comparable Overseas Bodies will be updated to include reports from the Pharmaceutical and Medical Devices Agency (PMDA) (Japan) to support efficacy of assessed listed medicines for the L(A)2 application category.

Assessed listed medicines application issues

- Most of the applications received to date have been for listed medicines wanting to be marketed with intermediate indications as assessed listed medicines.

- There are issues with unacceptable presentation if two labels [i.e. AUST L and AUST L(A)] are very similar (e.g. name, presentation, design, indications, umbrella branding) which may lead to confusion about the identification and proper use of the goods, particularly if one product has the TGA assessed claim and the other does not.

- In this case the TGA requires that sponsors cease supplying the listed medicine before they can supply the L(A) medicine.

Assessed listed medicines applications issues

- Another issue is some sponsors have included a large number of indications (e.g. 20 +) of mainly low-level indications:
  - The efficacy evidence supporting each indication of the product needs to be evaluated by the TGA – the more indications, the longer the application will take
  - Indications proposed by sponsors are often vague and not supported by the evidence provided.
  - Intermediate indications need to be supported by the primary outcomes of the study (adequately powered, statistically significant, clinically meaningful). Most studies usually only have one primary outcome.
  - Keep indications simple and clear – not variations with similar intent and meaning, issues with wording will be addressed during evaluation

The TGA therefore advises that sponsors only submit the indications that are supported by evidence on the finished product.

Mandatory requirements for new ingredient applications

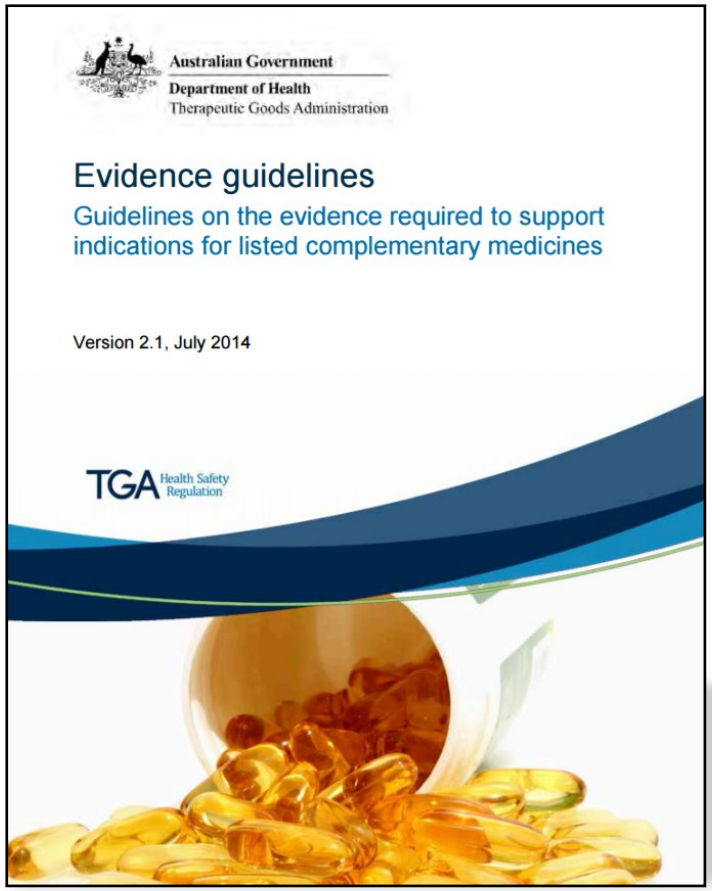
- Minimum data requirements for new ingredient applications based on core data requirements
- Clarify TGA expectations to ensure consistent treatment of all applications, while still offering flexibility
- Prevent deficient applications that are unlikely to succeed from delaying evaluation of other applications in the queue
- Applicants can provide justifications for unique circumstances and the merits of these will be assessed during the evaluation
- Publication expected late 2022

Guidance for assessment of microorganism strains (bacteria and fungi) for LM and RCMs.

- Relates to applications for new microorganism strains and responds to requests for clarity on TGA expectations
- The TGA has consulted extensively with stakeholders to develop guidance: ComTech, FSANZ, ACCESS, ASM, ACCM
- Reviewed international approaches e.g. FAO WHO, EFSA, HC, IPA
- The guidance bridges a significant gap in current application guidelines and ensures that microorganisms, when identified and characterised, are safe for their intended use
- Publication will align with Guidance on Mandatory requirements for new ingredient applications and update to the list of Comparable Overseas Bodies

Evidence guidelines for listed medicines

- A public consultation on draft revised Guidelines closed on 1 April 2022.
- The guidelines were restructured to be more user friendly, clarify content and reduce ambiguity.
- 29 submissions were received from industry, consumer and professional organisations.
- Submissions and TGA response will be published in late May/ early June.
- Guidelines to be finalised later in 2022



Aims for revising the evidence guidelines

- The draft Revised Guidelines have not changed existing requirements reflected in the Current Guidelines.
- The lack of clarity on some technical issues in the current Guidelines has caused a difference in TGA and industry's interpretation of the 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.

Proposed evidence guidelines for listed medicines

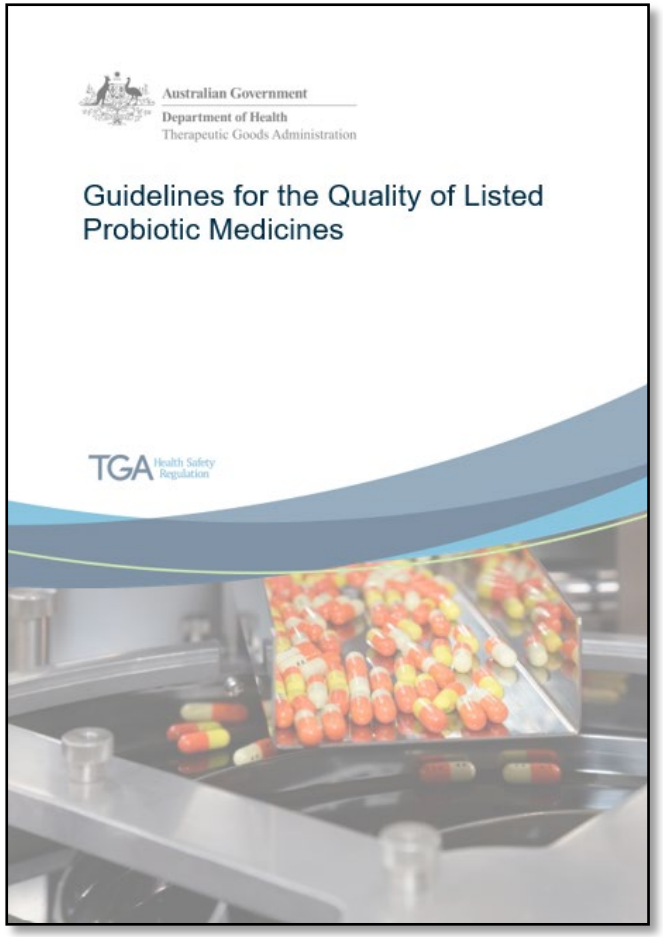
- Additional guidance on literature searches; assessment of evidence; the value of a critical appraisal; justifications
- New decision trees, case studies and examples
- New categorisation of scientific evidence sources as Categories A, B or C
- Clearer definitions of: indications, claims, specific, non-specific indications
- Low level biomarker indications now classified as non-specific.
- Traditional indications no longer classified as specific or non specific
- Clarification of evidence for claims and indications for supplements

Evidence guidelines: industry concerns/feedback:

- “Document too long and complex”
- “Justifications and critical analysis are increased requirements”
- Nutritional supplementations:
  - Removal of 10% RDI for content claims
  - Lack of clarity between content and supplementation claims requirements
  - Some supplementation claims requiring more evidence than just 25% RDI
- More clarity is required on equivalence of traditional herbal ingredients
- Change in how evidence presented- checklists removed
- More case studies on herbal materials needed

Guidelines on the quality of listed probiotic medicines

- The guidelines will provide greater clarity for how quality of probiotics is expected to be demonstrated.
- Targeted consultation throughout 2021 with: industry representatives; ACCM, EDQM and USP
- Industry continues to provide valuable feedback to help shape the contents and structure of the guidelines.
- Work ongoing



General Administration of Customs of China (GACC) registration

- In 2021 China issued decrees requiring imported foods to be registered. The goods captured by the decrees are largely foods, for which Department of Agriculture, Water and Environment is the competent authority.
- However, a number of the goods are regulated in Australia as listed medicines and for these the TGA is the competent authority.
- For listed medicines in scope, the TGA will endorse the sponsor of the medicine, as they are the entity legally responsible for the overall manufacture of the goods
- The GACC registration is in addition to other regulatory requirements in China (e.g. registration under the red cap system)
- The TGA has been working with sponsors to understand and help facilitate the registration process

Sunscreens – current and upcoming issues

- Adoption of new Australian Sunscreen Standard into Therapeutic Goods legislation (expected later 2022)
- Aerosol dosage forms – efficacy issues
- Data requirement for evaluation of new listed medicine ingredients for dermal use
- International developments e.g., FDA GRASE status.
  - sunscreen ingredients that are no longer on the US FDA's GRASE list.
  - reports of benzophenone and benzene in sunscreens

2022 targeted compliance activity

- COMB: targeted compliance reviews of a selection of listed medicines:
  - requiring a pregnancy warning statement
  - aerosol sunscreen products
  - containing caffeine
  - newly listed medicines at risk of non-compliance
- TGA: non compliant sports supplements - e.g. containing substances included in the Poisons standard

TGO 92 clarification

- TGO 92 to be updated to provide clarification on
  - Use of brand names in the medicine name
  - Make some editorial corrections (to errors)
- Consultation expected 2nd half 2022

OTC Medicines - RASML update

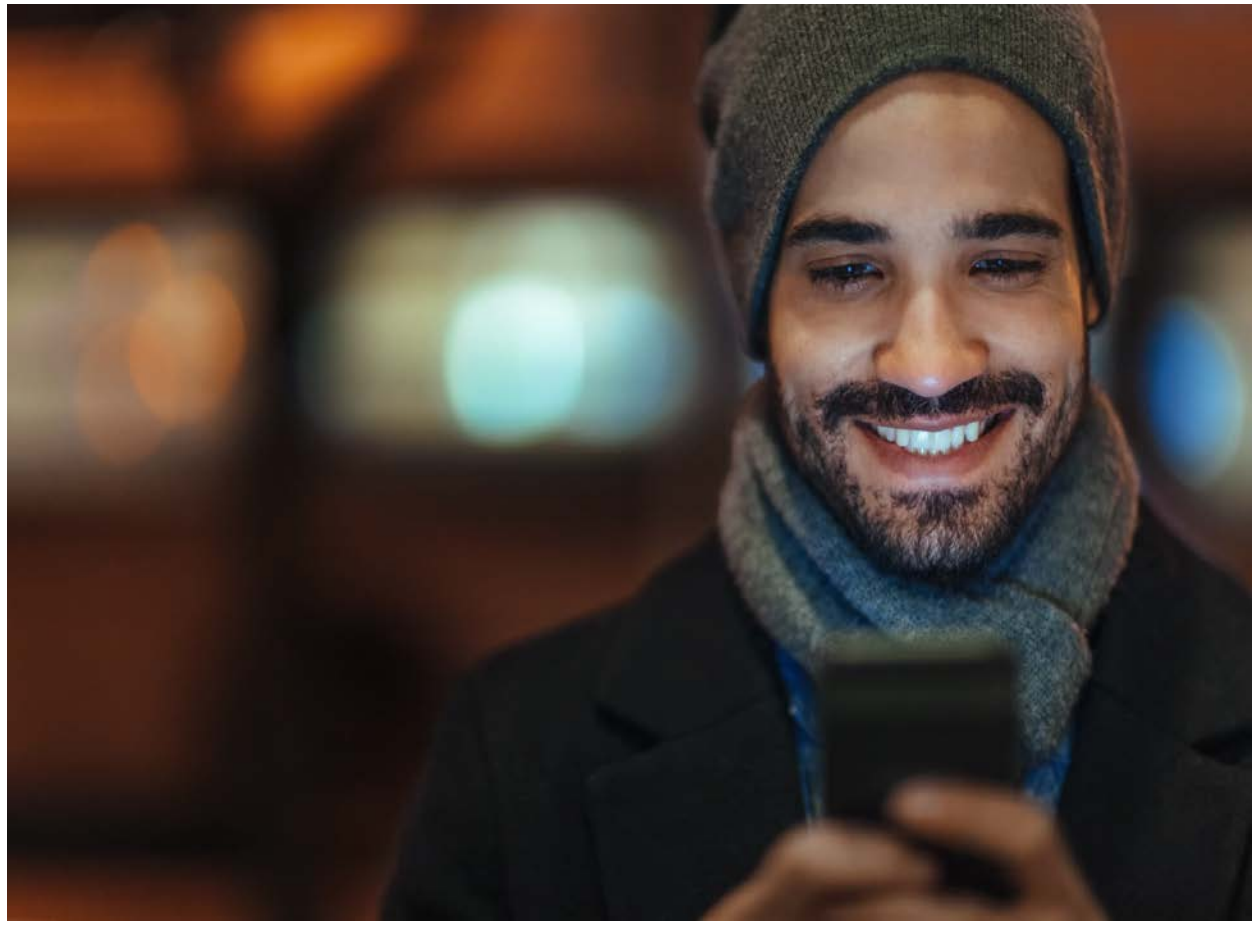
- Public consultations conducted in April and September 2021 to include new and amended warning/cautionary statements for:
  - Menthol for dermal use – to align with 26BB
  - Melatonin – due to down-scheduling from s4 to s3
  - Mometasone – due to down-scheduling of dermal use preps from s4 to s3, & addition of warnings for nasal sprays preps
  - Triptans (sumatriptan, zolmitriptan, eletriptan and rizatriptan) - due to down-scheduling from s4 to s3
  - Methyl salicylate – to align with 26BB
- Changes to entries for:
  - sedating antihistamines indicated for insomnia (diphenhydramine, doxylamine and promethazine)
  - Lidocaine – to contraindicate use for teething pain in children, as consequence of TGA safety review
  - Chlorhexidine, ibuprofen & hydrocortisone – corrections, clarity, remove ambiguities
- RASML No. 6 published 1 January 2022, full effect 1 July 2023 after 18 month transition period.
- During the transition period, labels may comply with either RASML No. 5 or RASML No. 6.

OTC Medicines - application timeframes

- Number of OTC applications received, July 2021 to April 2022 = **646**
- Number of applications approved, July 2021 to April 2022 = **672**
- For C1, C2, C3 & N2 - more than 80% of applications completed within target timeframes
- For N1, N3, N4 and N5 - 63-71% of applications completed within target timeframes
- Higher number of N1, N2 & C1 applications received in this period
- Measures taken to address timeframes:
  - More resourcing - Redirected a senior evaluator to focus on N1 and N2; Recruited a permanent evaluator
  - Applications in progress is trending down. For example,
    - in progress in April 2021 = 331
    - in progress in April 2022 = 306*
- **high no. C1 applications received in April ’22 (45), normally receive about 20 on average/month.**

TGA digital transformation: revised website

- Modern look and features
- Accessible, helpful language
- Structured content that supports common tasks
- Automated collections
- Responsive to device being used
- New search capabilities



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