Regulatory reforms: 2022 TGA update

CMA Conference – Dec 8 2022

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Deputy Secretary, Australian Department of Health and Aged Care

This presentation

- Complementary medicines updates
  - MMDR reforms - scorecard
  - Performance statistics
  - New Guidances
  - Other reviews and consultations
- Compliance and Enforcement
- New TGA website
- Transformation Program
- New TGA/ODC buildings

Complementary Medicine MMDR reforms now complete – what was their uptake ?

Mechanisms to incentivise research and development

Two-year market exclusivity for new ingredients (Mar 2018)

- 21 ingredients have been given an exclusivity period

Data protection for new Assessed Listed medicines (July 2020)

- Those with a new therapeutic use for an existing permitted ingredient can obtain five years data protection for clinical trial data supporting the new use
- None have qualified for data protection at this stage

Accepting trusted Comparable Overseas Bodies evaluations **(Dec 2019)**

- 9 new ingredients for listed medicines approved utilising COB reports

Online catalogue of approved ingredients for listed medicines (April 2017)

The Permitted Indications list (March 2018, transition to March 2021)

Assessed listed medicines pathway (March 2018)

- Two have been approved:
  - Hydralyte for dehydration associated with gastroenteritis and vigorous exercise
  - Prostate Eze Max - for management of symptoms of benign prostatic hypertrophy
- Three applications rejected and one application under evaluation

New application categories and timeframes (March 2018)

"TGA assessed" claimer for efficacy of non-prescription medicines (Oct 2019)

- 5 registered and 2 listed assessed complementary medicines approved to use claimer

Review and appeal rights for ingredient applicants

A more comprehensive post-market monitoring scheme (Dec 2019)

- Database on the TGA website where compliance review results are published.
- Increase in number of compliance reviews – delayed until mid-2022 due to diversion of staff to the COVID-19 response

Complementary medicines performance statistics

New ingredients permitted for use in listed medicines

	2020-21	2021-22
Application outcome		
Approved	5	14
Rejected	3	4
Withdrawn	5	7
Total completed	13	25

Indications permitted for use in listed medicines

	2020-21	2021-22
Application outcome		
Approved	3	0
Rejected	3	3
Withdrawn	1	1
Total completed	7	4

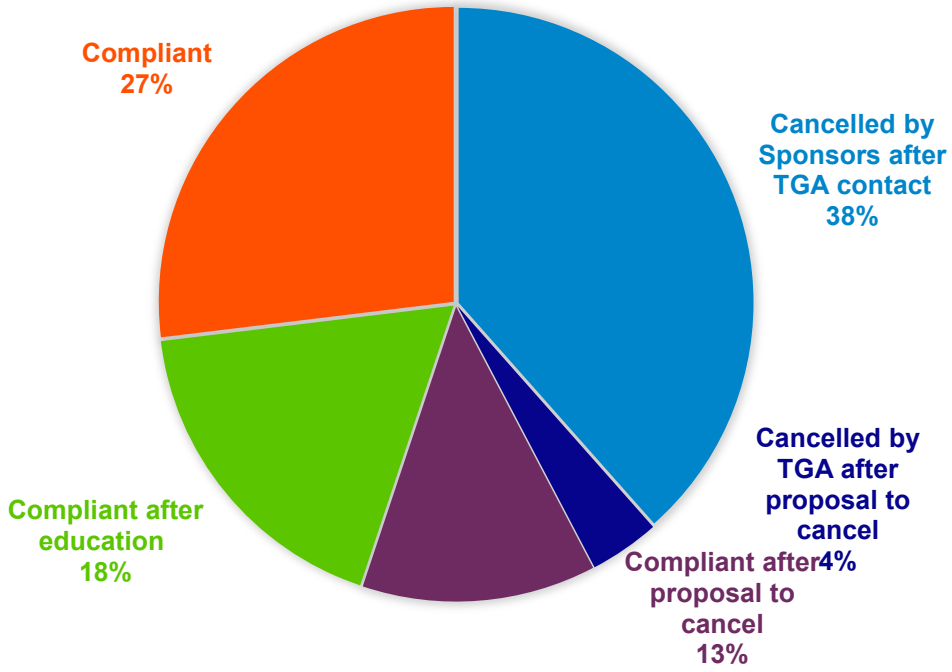
New listings and listing variations

New listed medicines	2020-21	2021-22
	2,184	1,929

Medicine variations	2020-21	2021-22
Approved	142	178 (88%)
Rejected	2	0 (0%)
Withdrawn	18	24 (12%)
Total	162	202 (100%)

Compliance reviews and top compliance issues

- Advertising
- Labelling
- Efficacy evidence
- Unacceptable presentation
  (suggestion that product has ingredients or characteristics it does not have)



78 compliance reviews conducted in 2021/22

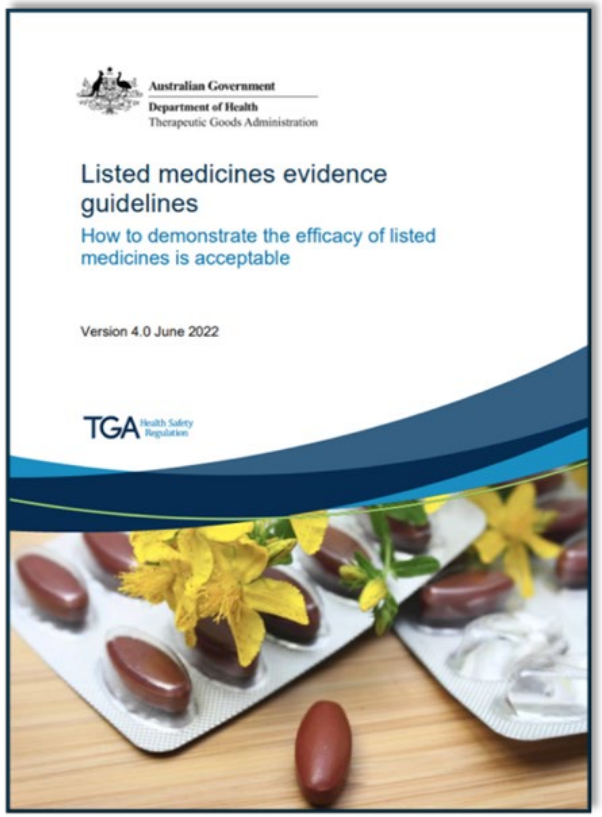
We have a dedicated team reviewing newly listed products

	2020-21	2021-22
Signals monitored		
Newly listed medicines monitored	1,947	2,115
Leads (complaints and referrals) received	54	42
Signals of non-compliance risk assessed and investigated	78	221
Signals of non-compliance resolved through obligations notices or educational correspondence	54	41
Signals of non-compliance moved to a compliance review	21	19

Phoenixes are not usually a good thing

Listed Medicines Evidence Guidelines

Revised guidelines published in June 2022



Do not involve any policy changes, nor change existing legal requirement for sponsors to substantiate evidence for indications

Updated to:

- ✓ enhance readability and utility
- ✓ clarify the legislative basis for listed medicine efficacy
- ✓ clarify specific technical concepts that had been unclear
- ✓ clarify the way TGA interprets and analyses different types of evidence
- ✓ show sponsors what TGA considers in a compliance review and what will more likely result in a successful review outcome

The Evidence Guidelines help sponsors compile robust evidence packages to support efficacy claims

- ✓ Restructured to follow a ‘step-through’ process.
- ✓ Additional information for literature searches.
- ✓ New guidance on compiling a critical appraisal.
- ✓ Revised hierarchy of evidence sources.
- ✓ New decision tool to classify specific/non-specific indications
- ✓ New case studies

What the updated Guidelines don’t do

- ✗ Do NOT change regulatory requirements for listed medicines.
- ✗ Do NOT include mandatory requirements for how evidence must be presented

Structure of the evidence guidelines

- **How to find evidence**
- **How to assess evidence –** relevance, quality, search strategy
- **How to use evidence –** types and levels of indications
- **How to document and present evidence -** critical appraisal of the body of evidence
- **15 Case studies are presented** (plus a case study of a search strategy)

  1: Health benefit does not match
  2,3: Active ingredient dose does not match
  4,5: Preparation method does not match
  6: Dosage form does not match
  7,8,9: Relevant evidence source
  10,11,12: Evidence relevance and quality
  13: Appropriate justification
  14: Non-validated measurement method
  15: Study duration inconsistent

Section 31 requests for information

- set out **what TGA will be looking for**
- provides **recommended formats** in which to provide that information
    - but these are not mandatory
- **providing transparency** around compliance review requirements a recent focus of improving Commonwealth regulatory practice
    - they should request specific rather than general information
- **if a sponsor is unclear** what is requested, please contact us

Legal basis

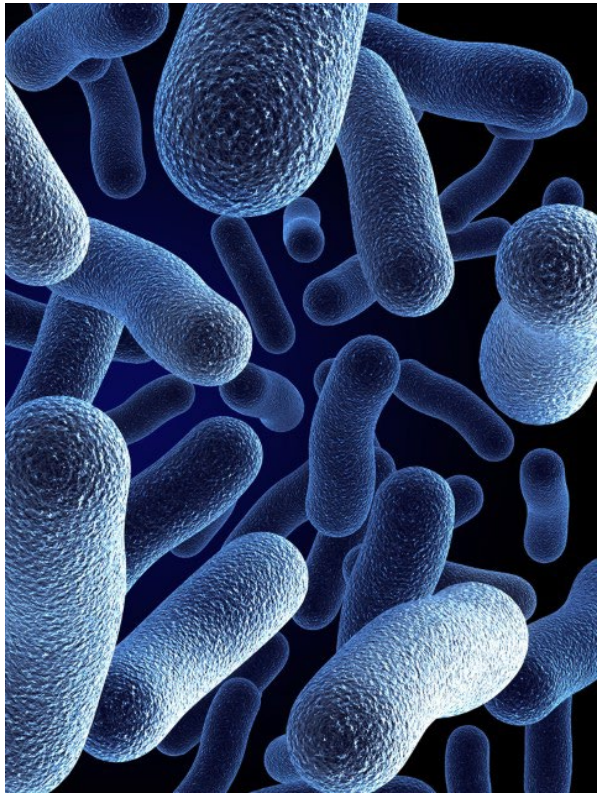
TG Act s31(2)h and Regs 16AA(2) -
"The Secretary may by notice in writing…require information or documents relating to…the efficacy of the goods for the purposes for which the goods are to be used"

TG Act s26A(2)ja –
At the time of listing the sponsor certifies "the applicant holds information or evidence to support each indication"

TG Act s28(7) –
"the sponsor … has at all times information or evidence that supports the indication…" and "will, if asked to do so give the information or evidence to the Secretary"

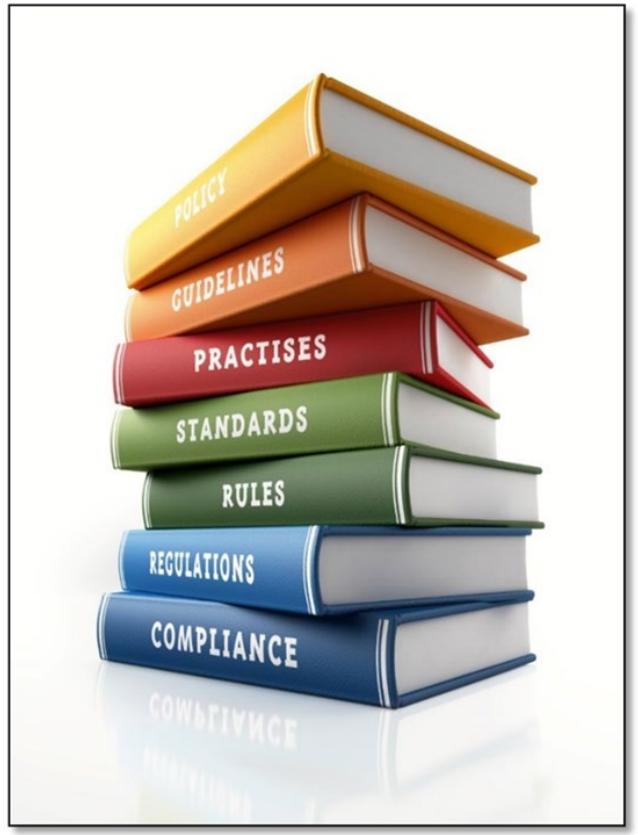
Listed probiotic medicine quality guidelines

- **Compliance reviews** identified insufficient justification for quantification of active strains/species per dosage form for the duration of the product's shelf-life
- **The new guidelines explain**
  - ✓ existing legislation for probiotic medicine quality
  - ✓ quality control through good manufacturing practices (GMP), testing and labelling
  - ✓ testing – including microbial ingredient identification and quantification, product stability and bioburden
  - ✓ Quantification by input supported by scientific justifications is permitted that achieves the intent of Ph Eur monograph 3053 (without following the Ph testing exactly as described)
- **More consultation will be undertaken** in Jan-Feb 2023



Mandatory requirements for applications for new listed medicine substances – publication due Jan 2023

- Australian regulation **underpins a high quality, safe product**
- **Minimum core data requirements** for **new ingredient applications**
- Will **clarify TGA expectations**, while offering flexibility and prevent deficient applications from delaying evaluation of other applications
- **Consequential updates made to other documents** to ensure all are synchronised
- **Multiple industry consultations** e.g. on use of acceptable alternative requirements, difference in requirements between active and excipient ingredients, the COB process, quality requirements etc.
- Propose to amend IN1 applications to **allow use of monographs** to support quality evaluation
- **Applicants can provide justifications for unique circumstances** and these will be assessed in evaluation



Conditions of Listing (section 28) Instrument

- A number of **conditions of listing** are applied to all listed medicines at the time of listing
  - while other conditions are only applied to certain products after the medicine is listed
- A determination that will set out the conditions of listing for listed medicines will enable sponsors will to see the conditions to which their products will be subject to **before they apply to list their products** in the ARTG
- **Conditions included** in the instrument will apply automatically to the goods that the instrument relates to

Permissible Ingredients Determination (26BB) review

- **Determination imposes requirements for use of some ingredients** that reflect requirements imposed by other instruments (e.g. Poisons Standard, TGO 92, TGO 95)
- **Reviewed** to ensure requirements in the 26BB Determination are consistently worded and are in the most appropriate instrument(s)
  - 876 ingredients in the Determination reviewed and some inconsistencies and duplications with the Poisons Standard found
  - continuing to work with industry to resolve individual ingredient issues
- Does not change the **requirements for eligibility for listing**
  - medicine must not contain a scheduled substance
  - ingredient must be included in 26BB
- **Child resistant packaging** requirements don't just apply to individual ingredients, but also if the product claims to be child resistant

Evaluation reports from Comparable Overseas Bodies

- **The COB pathway is an abridged pathway** (less data requirements, fees and timeframes)
- **9 new substances** for listed medicines approved relying on a COB evaluation report – most based on EFSA on reports under the IN1 category (safety and quality)
- List of COBs and guidance on using reports published Dec 2019
- **Updated, clearer COB guidance** coming Jan 2023, clarifying
  - how to use COB reports that have **not** been generated based on a submission dossier
  - that copies of the clinical trials, toxicology studies etc. that support the COB report is not required for applications for new substances for use in listed medicines.
  - Recognises that many evaluation reports generated for substances are not initiated by an applicant

TGO 92 – depiction of medicine trade names

- In a targeted consultation in June 2022, we proposed to update TGO 92 to provide clarification on the use of brand names on medicine labels – in particular the **requirement for medicine names to be displayed in a continuous uninterrupted manner** and not broken up by additional information or background text
- A range of issues emerged along with requests for changes to other parts of the medicines labelling requirements
- Therefore, **a broader review and consultation will need to be undertaken** - TGO 92 sunsets on 1 Oct 2026 and will need to be re-made before this date
- In the meantime, **section 14 exemptions** have been extended for affected products using brand names

Review of access to green tea extract

- **Concerns around liver damage** from green tea extracts, especially when concentrated in sports supplement or weight loss products
- **Proposal under public consultation:** Complementary medicines with > 5 % green tea extract to be sold in a pharmacy UNLESS they are labelled with warnings
- **Some Alternatives:**
  - should there be no pharmacy sale requirement but instead a warning on all green tea products ?
  - should warnings relate to specific substances instead ?

Next steps:

- First public consultation held September 2022
- Interim decision and second public consultation Feb-Mar 2023
- Final decision April 2023

Vitamin B6 and peripheral neuropathy

- **Peripheral neuropathy** is a known side effect of vitamin B6 at low doses although there is a lack of awareness.

- **Warning statement** required:

  "Stop taking this medication if you experience tingling, burning or numbness and see your healthcare practitioner as soon as possible (contains vitamin B6)"

- **Changes to listed medicines** implemented in March 2022
  - Threshold for label statement decreased from 50 mg to 10 mg/day
  - The maximum daily dose reduced from 200mg/day to 100mg/day

- Existing medicines have a **transition period** until 1 Mar 2023

Listed Medicine Compliance Priorities - 2023

- to address areas that undermine integrity of the self-listing framework

1. Not holding adequate **evidence to support efficacy**
2. **Advertising indications** not in the ARTG entry
3. Missing **mandatory warning** statements

4. Not complying with the **Permissible Ingredients Determination**
5. **Relisting of a non-compliant product** with no change after cancellation
6. Investigation of **sponsors who are consistently non-compliant**

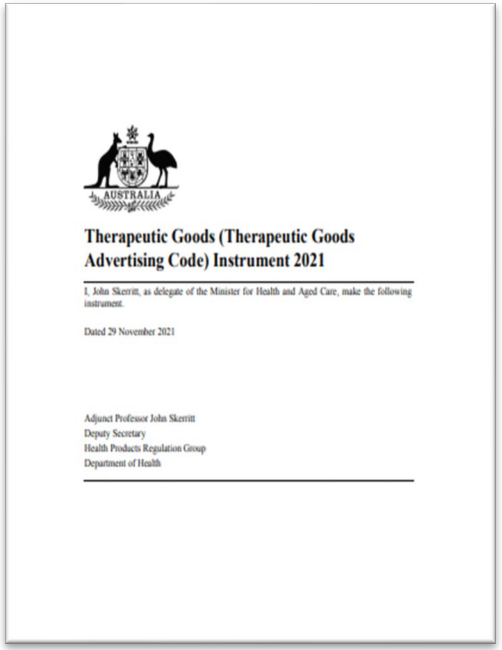
Compliance priorities – specific product types

- **Medicines with higher risk** if the medicine does not work as advertised
- **Vitamin D** for bone health claims
- **Lysine hydrochloride** for cold sores
- **Sports supplements**
- **Glucosamine** for joint health
- **Hangover relief** products
- **NAD+ presentations** for anti-ageing
- **Iron medicines** indicated for children
- Medicines targeting **pregnancy**

Regulation of therapeutic goods advertising

Therapeutic Goods Act and Regulations

- References to serious conditions require TGA permission (restricted representations)
- Prohibited representation listed in the Regulations, e.g. cancer
- Cannot imply Government endorsement
- Compliance powers, civil and criminal penalties



AUSTRALIA

Therapeutic Goods (Therapeutic Goods Advertising Code) Instrument 2021

I, John Skerritt, as delegate of the Minister for Health and Aged Care, make the following instrument.

Dated 29 November 2021

Adjunct Professor John Skerritt
Deputy Secretary
Health Products Regulation Group
Department of Health

Therapeutic Goods Advertising code

Updated – effective from July 1 2022 - main changes

- Simplification of requirements for mandatory statements
- Warnings required by legislation on labels (or IFUs) only required to be in advertisements that the facilitate the direct sale of the product
- Expansion of list of samples that may be offered
- Clarification of rules around testimonials and endorsements

Advertising of complementary medicines

Advertisements must comply with Act, Regulations and Code:

- be accurate and not misleading
- not be advertised to children
- not be inconsistent with product's ARTG entry
- include mandatory statement (e.g. for medicine: 'Always read the label and follow the directions for use.')
- include applicable health warnings where the product cannot be inspected prior to purchase
- health warnings and mandatory statements must be prominently displayed or communicated
- ensure appropriate use of testimonials and endorsements

Compliance priorities for advertising, import and supply have some similarities

- Unapproved references to **restricted or prohibited representations** (serious conditions requiring diagnosis, monitoring or treatment by a healthcare)
- **Unapproved therapeutic goods on digital platforms -** including for pregnancy and prenatal goods, weight loss products and hangover cures
- **Examples of potential contraventions** include:
  - Import, advertising or supply of products not on the ARTG
  - Non-compliance with the Therapeutic Goods Advertising Code, including in relation to testimonials
- **To ensure your products are compliant**, consider obtaining legal advice, assistance of a regulatory affairs consultant, or asking us !!

CM Advertising compliance and enforcement 2020-2022

	Financial year 20-21	Financial year 21-22	1 July – 15 Oct 2022
Reports of alleged non-compliance received	711	649	374
Not a matter for the TGA - insufficient evidence to validate allegations •No breach identified, •Not relevant to TGA regulatory framework	341	235	111
Cases created	370	255	181
Number of products involved in cases	985	425	336

Cases this financial year dominated by:

- Post and prenatal supplement
- Weight loss
- Mushroom supplements
- Ayurvedics

Compliance and enforcement – update on activities

e.g. from 1 July to late October 2022:

- Received over 370 reports of alleged non-compliance for complementary medicines:
  - 113 related to advertising offences involving 233 products
  - Another 68 for supply, export or manufacturing concerns involving 103 products
- **103 entities warned** regarding their regulatory obligations
- **Issued 5 infringement notices** to 3 entities, over $45,200
- **Working with state and territory regulators on safety of complementary medicines**, particularly unregistered products e.g. ayurvedic medicines with high levels of lead

AUSTRALIAN BORDER FORCE

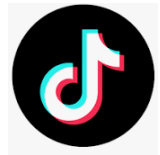
Also looking at listed medicine names that may be non-compliant, for example:

- Numbers in names with **no meaning or which could be misleading**
- Making **indications/claims** not included in the ARTG entry, or those not included in the Determination and outside of what is acceptable for listed medicines
- Making reference to **restricted/prohibited representations** without approval from TGA
- **Targeting pregnant women** when not all indications in the ARTG entry are permitted for pregnancy
- Referring to **ingredients that are not in the product**

Compliance and enforcement

Unapproved therapeutic goods on e-commerce platforms

- Unapproved complementary medicines being **advertised and sold through online stores and e-commerce platforms**, some of which use unlawful testimonials and unsupported claims
- **Working with online stores and social media platforms** to remove unlawful advertisements, and will take enforcement action where appropriate
- **Between July and mid Nov 2022 alone**, worked with platforms such as eBay and Amazon to **remove over 3,600 allegedly unlawful listings**
  - Around two thirds of these were complementary medicines including pregnancy and pre-natal, weight loss, and hangover products



Do's and Don'ts in therapeutic goods advertising

Do

- Ensure the therapeutic good is included on the ARTG
- Ensure ads are compliant with the Advertising Code, e.g. includes mandatory statements and warnings
- Use only indications or intended purposes that are in the ARTG for that product
- Verify testimonials and remove paid testimonials
- Remove testimonials or endorsements given by people excluded under the Code
- Seek regulatory advice, or submit an advertising enquiry to the TGA, when unsure

Don't

- Use paid testimonials
- Use magical/miraculous/unfailing language
- Imply a product is safe or has no side-effects
- Exaggerate the efficacy or performance of goods
- Imply Government endorsement in the ad e.g. TGA Approved
- Offer unpermitted product samples
- Use scientific/ clinical representations without citing and enabling access to the reference material
- Refer to serious conditions or diseases unless specifically permitted by the TGA
- Ignore emails or phone calls from the TGA

New TGA Laboratories

- **State of the Art Laboratory Facility** – co-locates similar functions and shares equipment
- Supports more efficient testing
- **Track samples** from receipt to disposal through RFID tags – where have they been, who had the samples
- **Supports Collaboration**
- Increased Security
- **Flexible Design** to respond to future priorities - services can be disconnected and reconnected for a new layout

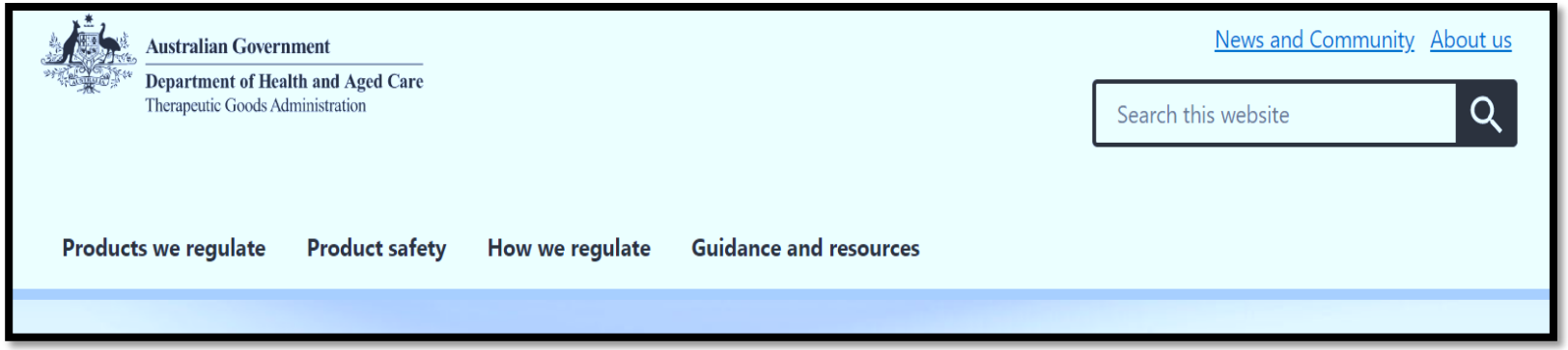
1. Removed 4000+ pages of old content
2. Moved to modern web platform
3. Rearranged existing content
4. Laid the foundations for content work

TGA Website re-developmemt

Challenge – it is one of the biggest government websites – e.g. more content than the Tax Office and the main Health department websites !

We realise that with such a big website redevelopment, there may be some broken links etc – so please tell us …..

Structure of the new website



- **Products we regulate** - types of therapeutic goods, Information hubs for special topics, COVID-19 related products, Unapproved product schemes, Travelling, importing and buying online
- **Product safety** - recalls, alerts and shortages; how the TGA monitors safety
- **How we regulate** - Information for sponsors and manufacturers, how to complete a task
- **Guidance and resources** - Publications, Portals, Reference information, Notices, exemptions, permissions, Laboratory reports. Cancellations and suspensions, Decision tools
- **News and Community** pages - News, media releases, recalls and alerts, COVID-19 and vaccine information; Events – webinars, presentations, Consultations, Compliance notices
- **About Us** - Committees, International collaboration, Legislation, Corporate info and reports

Non-prescription medicines

Depending on their risk to consumers, non-prescription medicines can be bought off the shelf from health food shops, supermarkets and pharmacies or over the counter after a pharmacist's advice.

OTC medicines

Find out about over-the-counter medicines and what they are.

Listed medicines

Find out more about listed medicines and what they are.

Assessed listed medicines

Find out more about assessed listed medicines and what they are.

Registered complementary medicines

Find out more about registered complementary medicines and what they are.

Reduce regulatory burden and costs for businesses

Improve responsiveness to the needs of industry, patients, consumers and healthcare practitioners

Make faster, more consistent decisions

Better inform health consumers through greater data accuracy

Reduce risk to Government service delivery e.g. security risks

TGA Digital and Business Transformation Program
Planned outcomes

Transformed TGA Website
Improvements to help users find the information they need, including improved search and consolidation of content

ARTG
Completed trial of Beta version which included new search and filtering options. Enhancements planned based on user feedback

Laboratory Modernisation
Process review underway and future streamlining. Instruments connected to the building network in the new laboratory

Process Transformation
Review of several processes including Complementary and OTC Medicines completed

Health Products Portal and Case Management project
Business Services Experience Research completed – identified user needs and potential prototypes

… and achievements in many areas unrelated to complementary medicines

Relevant work planned for 2023 and 2024

Labs Modernisation

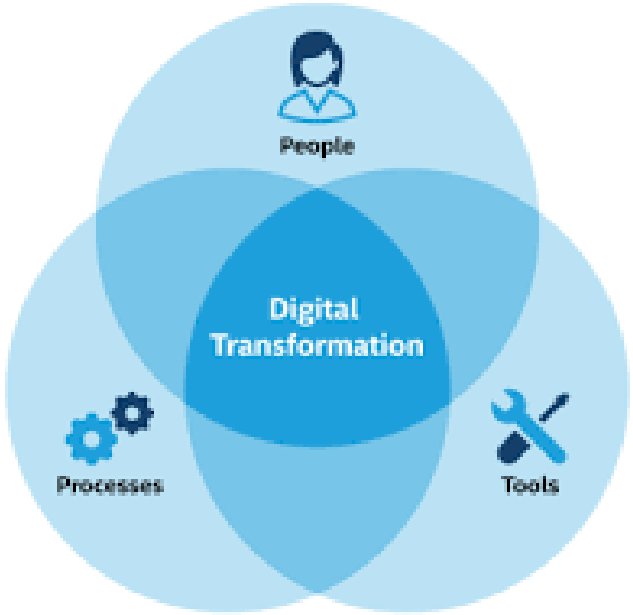
Trial and implementation of new software, design and build of new instrument network.

Health Products Portal

Creation of more efficient transactions through a new digital front-door. Establish Industry Working Group.

Enquiry Management

Completed review and identification of options to simplify enquiry management.



Transformed TGA Website

Continue to improve the content and functions to help users find what they need.

Enhanced ARTG Search

Negotiate performance improvements and enhancements to improve Beta tool.

Poisons Standard Prototype

Current review of solution options.