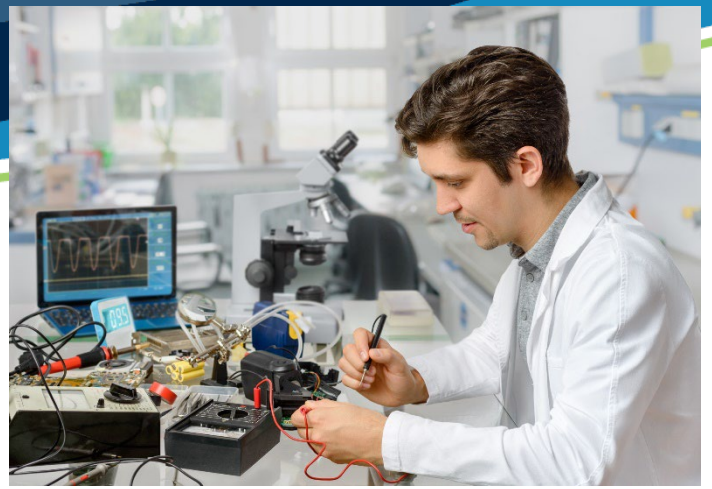
Australian Government
Department of Health
Therapeutic Goods Administration

TGA evidence expectations for medical devices or surfaces with anti-viral or anti-microbial claims



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TGA Health Safety Regulation

Outline

- General regulatory requirements of medical devices
- What antiviral claims can be made
- Types of evidence required
- Guidance on advertising requirements
- What are the risks
- Documentation and record requirements

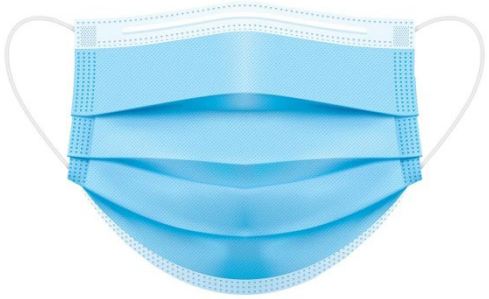
Please note that the Government is in caretaker mode and in accordance with the caretaker conventions I will be limiting my statements today to factual issues and matters of administration.

General regulatory requirements for medical devices

- By the time one apply for inclusion of a medical device into the Australian Register of Therapeutic Goods for supply in Australia, the manufacturer should already have completed the design, laboratory, user and clinical (if applicable) testing, and have validated your processes and verify they are suitable and reproducible. This should be documented in a design dossier, together with QMS manual and quality procedures. If you don't have all of this information you may lose a lot of time/ costs to generate additional data
- The sponsor of a medical device should hold sufficient information at all times to demonstrate it complies with all legislated requirements- this includes the Essential Principles and conformity assessment procedures
  - The **Essential Principles (EPs)** are a set of requirements to demonstrate the safety and performance of a medical device. (Schedule 1, Therapeutic Goods (Medical Devices) Regulations 2002)
  - The **Conformity Assessment Procedures (CAPs)** are additional requirements for the manufacturer to demonstrate devices are manufactured under the appropriate quality control and management system to meet the EPs. (Schedule 3, MD Regulations)
  - Commonly, ISO 13485:2016 is used to demonstrate conformity with CAPs for Class II and above devices. Class I devices can utilise ISO 13485, or ISO 9001 or a compatible set of requirements.

Examples of medical devices requirements

- The amount of evidence required for a device depends upon the class of device and claims made by the manufacturer
- Generally, compliance with a relevant and current technical standard can be used to demonstrate a device meets the **minimum** requirements of its kind.
- As new risks emerges, or where particular claims are made not covered in the standard, other standards or equivalent tests may be required to demonstrate compliance with all of the relevant Essential Principles.



A disposable facemask can nominate conformity with EN 14683 or AS 4381 or equivalent standard
https://www.tga.gov.au/publication/guidance-medicalsurgical-face-masks-and-respirator-standards-key-performance-aspects

A breast implant may nominate conformity with ISO 14630 (implantable devices) and ISO 14607 (mammary implants)
https://www.tga.gov.au/hubs/breast-implants

What evidence is required for antimicrobial and antiviral claims?

- The amount of evidence required for antibacterial, antimicrobial and antiviral claims depend upon the claims made by the manufacturer. E.g. antiviral additive coating on a mask, or a anti-fouling surface of an implant
- Claims guide (intended for disinfectants, but most content is translatable to medical devices): https://www.tga.gov.au/publication/disinfectant-claim-guide-specific-claims-and-non-specific-claims
- Consider the depth of claim
  - ‘effective against bacteria’ could be inferenced based on a reduction compared against control;
  - ‘kills 99.99% of bacteria’ requires specific experiments showing the reduction in the specified timeframe and conditions
- Consider the specificity of the claim-
  - ‘Kills SARS-CoV-2’ is specific, and requires evidence against SARS-CoV-2
  - ‘Kills viruses’ is general and requires evidence against each major group of communicable viruses
  - Antimicrobial- in addition to above, include evidence for bacteria, fungus and spores

Are the antimicrobial and antiviral claims misleading?

- The TGA guidelines provides cautions about advertising claims- all COVID claims are ‘restricted representation’ require evaluation of evidence and TGA approval
  - https://www.tga.gov.au/media-release/warning-about-products-claiming-treat-or-prevent-novel-coronavirus

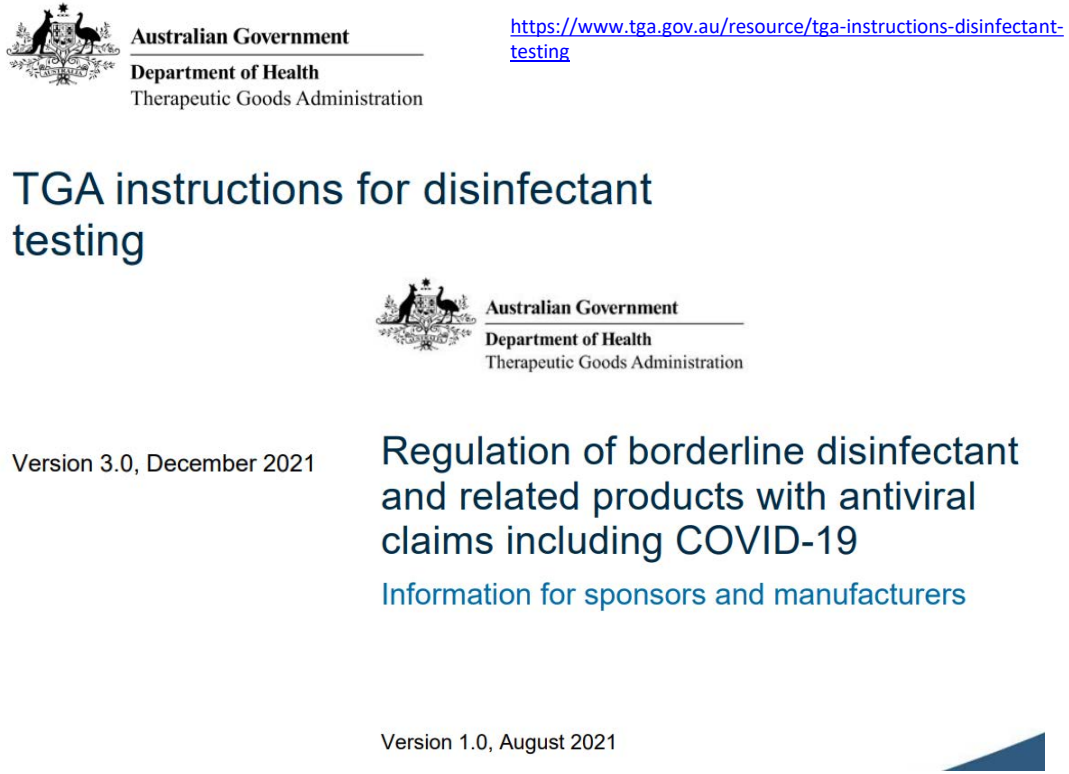
- Consider the likelihood that the claim may be misleading to the consumer:
  - ‘Effective against viruses’ may not mean much or confer meaningful protection to a consumer and may be rejected as it is likely an advertorial claim that does not bring about a clear benefit
  - Statistically significant data does not necessary mean clinical relevance. A 60% reduction in live viruses after 24 hours is meaningless in a face mask application where the use time is a few hours, and the risks of transmission is still high
  - A 99% reduction may not be meaningful, e.g. if you start with a colony size of 10^8 and reduce to 10^6, that is still a very high volume and sufficient to cause infection/ transmission of disease
  - ‘Made of antiviral fabrics’ may be a kind of claim that again presents little measurable and tangible benefit to the consumer if it is not quantifiable and measurable

What evidence is needed to demonstrate benefit?

- All claims must be backed by robust and relevant clinical or laboratory studies
- Test evidence needs to relate to the product itself, rather than a proof of concept.
  - E.g. culture studies of the finished mask product itself rather than the fabric or additive
  - Culture studies of an implantable polymer surface, rather than the same coating on a metal disc
  - Test evidence needs to be specific and consider how the device is used
  - Static culture may not be sufficient for a facemask where there is continuous passage of air
  - Implantable surfaces may need to consider the microenvironment where it is implanted- e.g. further studies to consider *in vivo* immune response conditions and biofilm/ capsule formation
- The time of action needs to be considered
  - For face mask applications, clinical literature indicates the infectious period is ~8-17 min. Reduction timeframes over 15 minutes may not provide appreciable benefit to the user
  - For an implantable polymer, consider the lifetime the device is implanted, and how long we should expect antimicrobial action to last to cover the vulnerable period. Is this effect stable over time or reduces? Characterise the length of time protection is consistently achievable

Planning and collecting evidence

- Review information in state of the art on suitable studies but also manage the gaps
- TGA guidance and website
- Overseas regulator guidance
- Relevant standards e.g. ISO 18184- antiviral activity of textile products, but consider how air flow and design of a face mask may impact results of a study
- Consider worst case scenario
- Choose appropriate sample size, sampling plan and sampling timeframe. Sample size of 3 is not sufficient especially if uncertainty is high
- Is the protection consistent across batches? Need validation and verification evidence that processes are effective and repeatable



https://www.tga.gov.au/resource/tga-instructions-disinfectant-testing

https://www.tga.gov.au/sites/default/files/regulation-borderline-disinfectant-related-products-with-antiviral-claims-including-covid-19_0.pdf

Are there new risks introduced?

- The introduction of compounds, or coating to confer the benefit may also introduce risk to the user
- Pharmaceutical/ pharmacological ingredients adds regulatory complexity and requires further evidence, including GMP clearance and evidence expected of the medicinal ingredient
- ‘New chemical entities’ may require characterisation and evidence generation
- All risks of a medical device must be risk assessed and minimised by the manufacturer in the appropriate risk management framework, e.g. ISO 14971:2019. Essential Principles 2, 3, 4, 6, 7, 8…
  - If risk is not adequately considered with appropriate evidence, application may be rejected

Are there new risks introduced?

- What is the risk of the coating/ compound itself? When new, and over the service/ implant life of device
- Is the compound stable? Will it degrade, oxidise, create particles, flakes, delamination, volatile organic compounds (VOCs), change pH? Are degradation products harmful? If it is cleaned or exposed to other devices/ surgical techniques, will that damage/ or effect the coating/ device?
- Account for incorrect or improper use. E.g. if facemask worn inside out and coating is directly exposed to skin
  - For facemasks- require manufacturer's risk assessment of risk of coating/ compound via ingestion, inhalation, skin reactivity/ sensitivity over duration of wear in worst case (8 hrs a day, multiple days)
  - For breast implant- consider adverse biocompatibility reaction, toxicological data, studies vs ISO 10993 series, long term safety data, cases known in the state of the art e.g. risk of breast cancer, breast implant illness, breast implant associated anaplastic large cell lymphoma (BIA-ALCL). Likely require animal and clinical studies

Documentation and records

- Evidence and documentation should be part of the Design Dossier or Design History File or Technical documentation
  - Collection of information about the device, the product specifications, the requirements
  - Records about materials, coatings, technologies applied
- Test reports, with details of traceability, and manufacturer's analysis of test evidence- multiple test reports to show repeatability, but also findings of each test. The analysis is important, result should be contextualised and limitations considered and stated clearly
- Records for risk management- risk assessment document, failure mode effect analysis, proposed mitigations
  - Records of risk mitigation- validation/ verification testing, in process controls, batch controls, validation of product specifications
- Release records, ongoing post-market surveillance, procedures to handle complaints/ adverse events, continue risk assessment
- Consideration of impacts and changes, e.g. from literature, or variants of viruses that could impact risk/ benefit profile of device
- Keep documents updated systematically based on manufacturer's QMS

Take home message

Come to my poster presentation on TGA activities and for a chat– **Friday F15**

- Think broadly about experiments and studies to demonstrate technologies confer a tangible and measurable benefit before making antimicrobial and antiviral claims
- Collect evidence against potential risks of additives/ coatings and conduct thorough risk assessment including additional studies to show there is no added harm, or that it is acceptable and outweighed by benefits.
- Claims must be appropriate and not misleading, noting TGA advertising obligations
- **We are hiring!** Multiple employment opportunities available across TGA https://www.apsjobs.gov.au/ - come make a difference

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