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Residual Claims for Disinfectants TGA response

I wish to thank the TGA for allowing the opportunity to comment on the Consultation on residual claims for disinfectants.

My involvement in the regulation, formulation, development, testing, registration and approvals of disinfectants for the Australian market extends over more than 25 years, including input into both TGO54 and TGO104, and related guidelines.

This submission reflects my insight and perspective on the support for residual efficacy claims taking into account the limits of the technologies involved, the criteria required to demonstrate a consistent and validated efficacy level, the likely effects on public health of these claims, consumer and customer safety, the extent of industry compliance, legislative consistency and the need for improvement in industry standards and practices.

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Summary:

The proposal requiring consideration by the TGA is as follows:

1. a legislated definition of "residual claim";
2. guidance on appropriate testing methods;
3. acceptance criteria for claims being made;
4. guidance or limitations placed on the period over which residual activity is claimed; and
5. limitations on what residual activity claims are made against.

I propose the following additions / amendments to the proposal.

1. The definition of residual activity of a disinfectant product as:

The capability of a disinfectant product to continue to produce a *significant and sustained* reduction in the number of viable cells of relevant test organisms on a surface under use ~~conditions~~ *directions* defined on the label of the product.

2. For testing purposes, adopting the principles set out in PAS 2424:2014 Quantitative surface test for the evaluation of residual antimicrobial (bactericidal and/or yeasticidal) efficacy of liquid chemical disinfectants on hard non-porous surfaces – test method as a preferred methodology for demonstration of residual activity of disinfectants. As the PAS is subject to copyright, it is recommended that it be adopted as is, with additional guidance on extension of the test provisions to cover *requirements for minimum soil loading and* organisms other than bacteria or yeast, *selection and validation of relevant testing surfaces* and periods of greater than 24 hours for residual activity.

3. The acceptance criterion for a claim of *specific* residual activity should be set at a ~~3-log~~ *4-log* difference between the test and the control *for viruses, and 6-log difference for bacteria / yeast*.

4. The period over which residual activity is claimed has to be substantiated by *more than one set of* test data.

5. Residual activity claims can be made against general bacteria and/or specific organisms, if substantiated by test data.

Further comments / summary recommendations:

Residual antibacterial efficacy can be demonstrated with a minimum 3log10 reduction as per PAS 2424.

Residual antibacterial efficacy must be differentiated clearly on the label from any claims of disinfection, and must clearly exclude claims that are made on specific organisms.

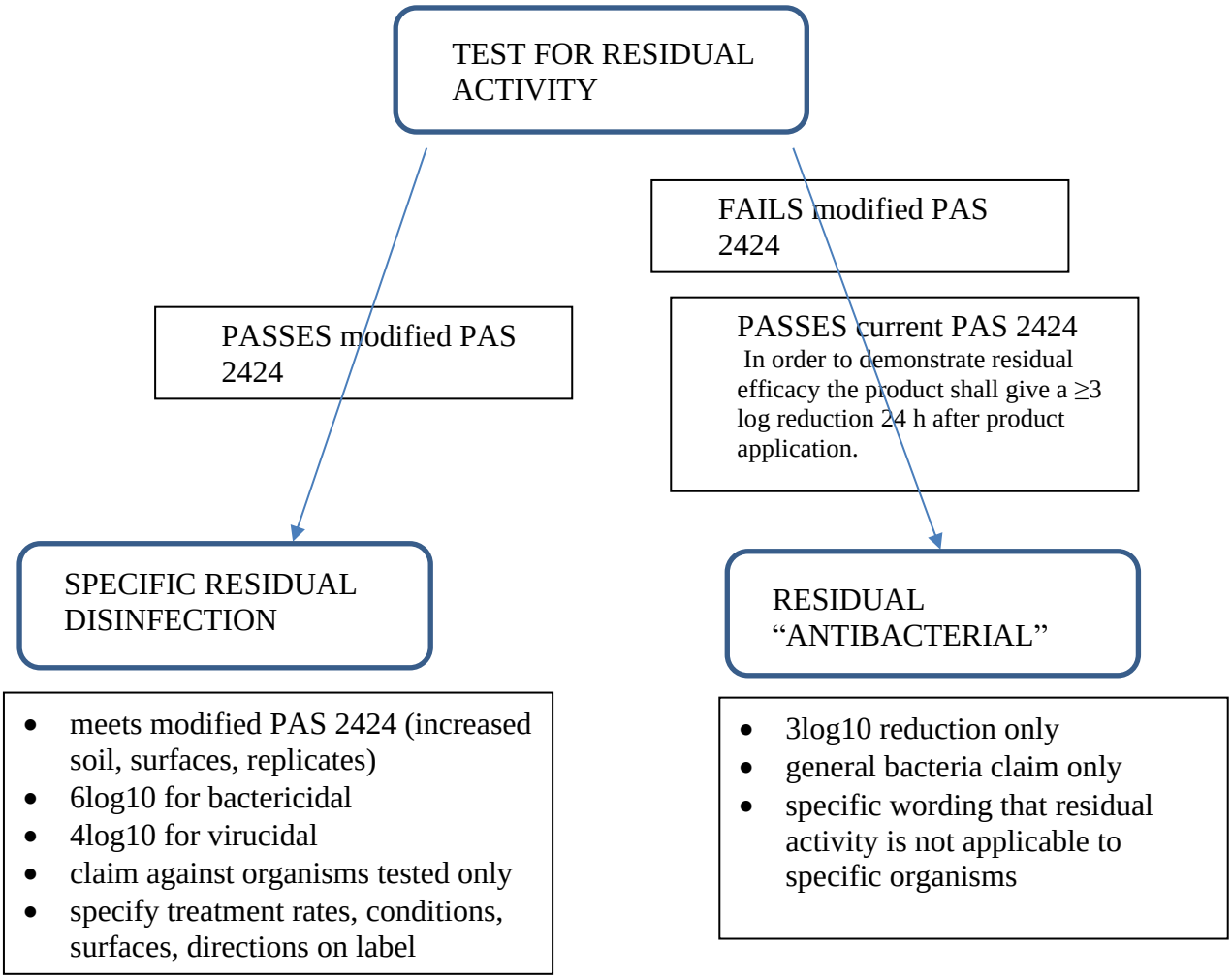
Residual disinfection must be demonstrated using the PAS 2424 test modified as follows:

- under dirty conditions
- with multiple representative surfaces
- with a minimum of 6log10 reduction for bacteria and 4log10 reduction for viruses
- testing in duplicate

The specific conditions under which residual disinfection was achieved must be clearly communicated on the label and must include, but is not limited to:

- the conditions under which the result was achieved (time taken, surfaces tested, temperature and humidity)
- full description of organisms tested
- complete description of the treatment protocol in the directions for use

RESIDUAL ACTIVITY CLAIM FLOW CHART

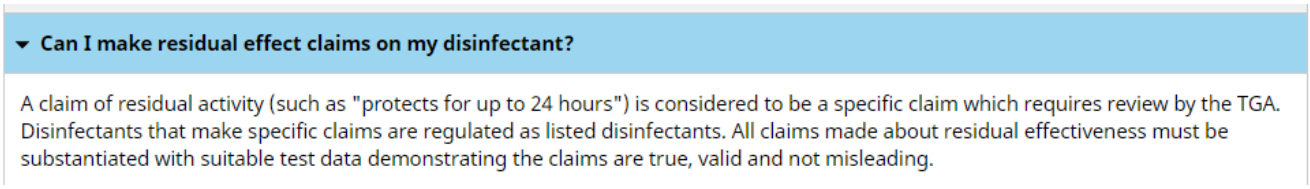


Current regulatory regime review

All disinfectants claiming bactericidal, virucidal, fungicidal or other efficacy must comply with the Therapeutic Goods Act, and must meet the requirements of the relevant Therapeutic Goods Order 104 https://www.legislation.gov.au/Details/F2019L00482

Both Residual and Virucidal claims are specific claims under TGA legislation https://www.tga.gov.au/publication/disinfectant-claim-guide-specific-claims-and-non-specific-claims

This has recently been confirmed by the TGA https://www.tga.gov.au/disinfectants-faq-new-sponsors



Can I make residual effect claims on my disinfectant?

A claim of residual activity (such as "protects for up to 24 hours") is considered to be a specific claim which requires review by the TGA. Disinfectants that make specific claims are regulated as listed disinfectants. All claims made about residual effectiveness must be substantiated with suitable test data demonstrating the claims are true, valid and not misleading.

Specific claims can only be made when tested according to approved TGA protocols, and must be approved by the TGA https://www.tga.gov.au/publication/tga-instructions-disinfectant-testing

There are no TGA approved protocols for Residual Activity, therefore any residual activity claims are not TGA approved.

Any company currently claiming residual disinfection is therefore in breach of the Therapeutic Goods Act. Any business promoting such products are also in breach of the Act.

There are no current TGA approved protocols for Residual Virucidal Activity, therefore any virucidal residual activity claims are not TGA approved.

As residual activity is a specific claim, the TGA should ensure consistency between the efficacy levels and standards of current specific claims, and any proposed residual activity claims, especially for specific organisms.

International Standards Review

There are very few international standards available to demonstrate residual microbial efficacy. These are all, in my opinion, insufficient to support a justifiable claim of residual disinfection. I have also been guided in the assessment of the available standards for residual efficacy on surfaces by the recent publication by the Commonwealth Scientific and Industrial Research Organisation (CSIRO), Australian Centre for Disease Preparedness on the persistence of SARS-CoV-2 on common surfaces.

https://virologyj.biomedcentral.com/articles/10.1186/s12985-020-01418-7

The effect of temperature on persistence of SARS-CoV-2 on common surfaces

1. Protocol for Residual Self-Sanitizing Activity of Dried Chemical Residues on Hard, Non-Porous Surfaces

https://www.epa.gov/sites/production/files/2015-09/documents/cloroxpcol_final.pdf

This protocol allows claims of only 3log10 bacterial reduction, and only for a maximum period of 24 hours. The label claims supported by this Protocol is: *[This product] kills 99.9% of bacteria for 24 hours.*

2. ASTM E2180: "Standard Test Method for Determining the Activity of Incorporated Antimicrobial Agent(s) In Polymeric or Hydrophobic Materials"

This is designed for antimicrobial agents already incorporated into the substrate matrix and does not specify any pass-fail criteria, lag time, contact time or treatment of the surface. It is designed to assess antibacterial efficacy only. The bacterial slurry is used under clean conditions and there is no washing, wiping or any other treatment of the surface between inoculation and sampling.

3. PAS 2424 is designed for bactericidal and yeasticidal efficacy only. As PAS 2424 is the method suggested as the nominal test method by the TGA I will expand on the concerns I have with this method in more detail.

i. Soiling level

The level of soil specified in PAS 2424 is 3.0g/L, or only 0.3%. In contrast the CSIRO has recommended and used a viral : soil ratio of 69% : 31% in their testing of survival rates of Covid-19 on environmental surfaces. The PAS 2424 standard level of soil is clearly significantly less than that assessed as appropriate by the CSIRO. The TGA guidelines also prescribe a minimum soil level of 5% blood serum in hard water for specific claims.

It is also important to note also that a product claiming residual activity over a significant period of time will be exposed to not only frequent touch and cleaning, but also significant contamination from dirt, grime, and other interfering soils throughout the time period where efficacy is claimed.

The option of allowing a "pre-cleaned" use of a residual disinfectant is therefore not appropriate for residual efficacy testing, as by the very nature of the act of contamination (generally from an excretion), any contamination of a surface with a viral or bacterial load will also contain significant soiling. Therefore in order to demonstrate efficacy against transmission any residual activity MUST be performed in dirty conditions.

The residual activity of all organisms should therefore specify **at least** 5% blood serum in hard water (minimum 340ppm) as the soil level. This is consistent with the requirements given in the TGA current guidelines for disinfectant testing for specific biocidal claims:

> If any specific biocidal claims are made (i.e., virucidal, fungicidal, tuberculocidal, sporicidal, or other biocidal activity), the disinfectant must pass appropriate tests as specified below. All tests should be carried out using the exposure time, temperature and pH specified on the label. For products intended for use on surfaces that have not been pre-cleaned, 5% organic soil must be included. For products that are intended for use on surfaces that have been pre-cleaned, organic soil need not be added to the test, with the exception of testing against blood borne viruses, as discussed in the virucidal claim section below.

ii. Surface selection

PAS 2424 uses only one surface, stainless steel discs of type 1.4301, 2.0 cm in diameter with a Grade 2B finish on both sides used in accordance with EN 10088-1 and EN 10088-2. The surfaces shall be of approximately 1.5 mm in thickness.

In contrast the CSIRO used the following surfaces:

Australian polymer bank notes, de-monetised paper bank notes and common surfaces including brushed stainless steel, glass, vinyl and cotton cloth were used as substrates in this study. Both polymer and paper banknotes were included in the study to gather information on the possible roles of note based currency in general for the potential for fomite transmission.
Stainless steel is used in kitchen areas and public facilities and is the substrate used in some disinfectant testing standards [14, 15]. Glass was chosen due to its prevalence in public areas, including hospital waiting rooms, public transport windows and shopping centres, and high contact surfaces such as mobile phone screens, ATMs and self-serve check-out machines. Vinyl is a common substrate used in social settings, tables, flooring, grab handles on public transport, as well as mobile phone screen protector material. Cotton was chosen as a porous substrate, often found in clothing, bedding and household fabrics.

It is a critical detail also that the technologies used for promoting residual disinfection rely heavily on various methods of adherence between the substrate and the chemical to achieve both residual adherence of the product, and continued efficacy.

For example Zoono claims that "*a layer of positively charged molecular pins coat the surface…*" which in turn "*attracts negatively-charged pathogens*". This "*…can be applied to any surface*" https://zoono.com/pages/our-technology-efficacy-testing

Bacoban claims that "*The technology used here is the sol-gel process that develops a solid gel phase on the basis of a liquid phase. The biocides used to kill germs are embedded in the porous structure of the developing sponge-like sol-gel".* All test results however appear to be done only on ceramic as the test surface.

It is recommended therefore that in order to demonstrate both sustained adherence and activity across a representative surface group at least three hard surfaces must be tested, i.e. stainless steel, glass and vinyl plastic. This testing must be conducted at least in duplicate to confirm the efficacy. This is analogous to testing on specific claims being required on at least two batches of product to assure efficacy.

Surface limitations:

I do not support any residual claim for soft surfaces for the following reasons.

Soft surfaces are very varied in their nature and composition in terms of porosity, chemical make-up and ease of assay. It is extremely difficult to ensure that soft surfaces have been dosed evenly and correctly, disinfected evenly and correctly and the resulting microbial load extracted effectively. In this regard the TGA should restrict the application of residual efficacy to the current definition of hard surfaces only.

Level of efficacy:

Confidence in specific claims for Listed disinfectants are of extremely high importance in public health. These products are used not only routinely in the general population but are also heavily marketed, sought after and used in hospital and healthcare facilities in many areas, except on Devices, in which case they must be approved as a Class IIb Device disinfectant. To illustrate this point, a general ward in a hospital can use a Listed disinfectant with specific claims e.g. against norovirus on all hard surfaces within the ward, e.g. tables / chairs / bedside drawers, but when moving to bedrails, IV poles or other surfaces deemed "devices" then these must be disinfected with a Class IIb approved disinfectant. Given the physical distance from the non-device surface to the patient and the touch point frequency of the non-device surfaces, any claim for residual efficacy must AT LEAST meet the same criteria of other specific claims in terms of definition, protocol, scope, validation and efficacy. This is especially so when the residual claims are on products that claim other specific activities (e.g. virucidal) as part of their Listing credentials.

I therefore propose that any specific organism residual activity claim must meet the current 6log10 reduction requirement for bactericidal efficacy and the 4log10 requirement for virucidal efficacy in order to be approved.

A residual activity claim that does not meet these criteria must be restricted to a general antibacterial claim only, provided a 3log10 reduction on gram positive and gram negative bacteria can be demonstrated according to PAS 2424. The sponsor must also clearly state that the residual activity is not applicable to the organisms for which the specific claims are made.

Further considerations

For the claim of residual efficacy to be valid the precise conditions and specifications of the test performed must be clearly and fully known and presented to the TGA for approval. This is both so that the applicability of the test to the product and claim can be fully evaluated, and so that the test can be fully duplicated by the TGA as part of their post-market surveillance audit program.

This must include at least:

- Full formulation disclosure
- Batch numbers of the product tested
- Testing conditions throughout the whole trial (temperature and humidity)
- Full material descriptions and specifications
- Inoculation specifications and instructions
- Full description of organisms tested
- Complete description of the treatment regime and directions for use

Please do not hesitate to contact me or any further clarification or information.

Yours sincerely,

Dr. Paul Wynn-Hatton
Dynamic Innovations Specialised Services