Residual Claims for Disinfectants TGA response

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26th March 2021

I wish to thank the TGA for allowing the opportunity to comment on the proposal for clarifying regulatory requirements for residual claims for disinfectants.

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

This submission reflects my insight and perspective on the validity and level of support required 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.

Table of Contents

Background:

As detailed in the Introduction to this consultation, at present, there is no definition of "residual activity" included in the Therapeutic Goods (Standard for Disinfectants and Sanitary Products) (TGO 104) 2019 (the Order) or the TGA published guidance document: TGA Instructions for Disinfectant Testing. There are also no defined test methods or specified acceptance criteria for such testing. To date, claims have been considered (and continue to be considered) by the TGA assessors on a case by case basis.

The TGA are seeking feedback on the following:

1. A definition of residual activity of a disinfectant product
2. Testing standards for residual activity claims
3. Acceptance criteria for residual activity claims
4. Whether there should be a limit on the period over which residual activity is claimed
5. Whether residual activity claims should be restricted to general bacteria only and other specific organisms
6. Whether residual activity claims should be disallowed.

I propose the following *additions / amendments* to the proposals.

Proposal 1: Definition of residual activity

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 and directions defined on the label of the product.

Comments:

The definition must include reference to the parameters of both a significant reduction, in that it must meet the prescribed level of disinfection, and that this significant reduction must be sustained at this level for the claimed life of the effect. In the absence of these parameters the definition allows the scope for variation in the level of reduction, and tacitly allows a decrease in reduction over time. Explicitly stating that the reduction must be both significant and sustained provides both clarity and certainty.

The definition provided in the PAS 2424:20148[8] is only relevant for that test scope, which includes only bacteria and yeast efficacy over a maximum of 24 hours. The scope considered by the TGA proposal is for a greater variety of organisms and times than that covered by PAS 2424:2014[8] – therefore an expansion and clarification of the definition from that of PAS 2424:2014[8] is both expected and required.

Proposal 2: Testing Standards

For testing purposes, adopting the principles set out in PAS 2424:2014[8] *"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. It is recommended that additional guidance be developed to extend the test provisions to cover organisms other than bacteria or yeast, *requirements for minimum soil loading*, *selection and validation of relevant testing surfaces,* and periods of greater than 24 hours for residual activity.

Comments:

i. Soiling level

The level of soil specified in PAS 2424:2014[8] is 3.0g/L, or only 0.3%w/v. In contrast recent work conducted by the CSIRO[1] 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 2424:2014[8] 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[2].

It is also important to note 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 appropriate and relevant 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[2] 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.

Relevant testing surfaces

PAS 2424:2014[8] 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[1] selected 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 critical to recognise 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[3] claims that their product "…*works by coating the surface with a layer of positively charged molecular pins.*" which in turn "*attaches to the surface using a covalent bond which then attracts and kills negatively charged pathogens by rupturing their cells.*". (It is instructive to note that previously the company was making the specific claim that the product "*…can be applied to any surface*" at the following link https://zoono.com/pages/our-technology-efficacy-testing which is now disabled, and now make no claim on what surfaces the product can be applied to, other than mentioning generic "surfaces".).

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[4].

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 consistent with the TGA requirement for testing on specific claims on viruses being required on at least two batches of product to assure efficacy[2] *(One surface is required to be tested for each of two batches of product.).* This is also consistent with the US EPA requirements for bactericidal (3 lots) and virucidal (2 lots) residual efficacy[10].

Surface limitations:

I do not support any residual claim for soft surfaces as 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. Despite the TGA tacitly approving soft-surface disinfection[5], I believe the application of residual efficacy should be restricted to hard surfaces only. I note also that there is no provision in PAS 2424:2014[8] for any soft surface testing.

Proposal 3: Acceptance Criteria

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

Comments:

Confidence in specific claims for Listed disinfectants are of extremely high importance in public health. These products are used not only routinely by the general public but are also heavily marketed, sought after and used in key industries such as transport, education, commercial and industrial facilities. Consistency and surety in the efficacy of these products must be paramount, especially as global industries such as aviation emerge out of the global pandemic disruption. The use of these products is already proliferating in such industries, and it is essential that there is both confidence and consistency in the efficacy claimed.

Hard surface listed disinfectants with specific claims are also ubiquitous 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 a further specific claim of 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. Note that the same microbial efficacy requirements are in place for listed disinfectants and Class IIb Device disinfectants[2], therefore logically this should be extended to residual disinfectants.

The efficacy expected of a residual disinfectant must be equal to that required by a non-residual hard surface disinfectant.

I recommend that any specific organism **residual** activity claim must meet the current 6log10 reduction requirement for bactericidal efficacy[2] and the 4log10 requirement for virucidal efficacy[2] in place for both Class IIb Device and Listed disinfectants in order to be approved.

Furthermore, the proposed level of efficacy described in the consultation *(…a 3-log reduction for residual activity.)* for bacteria is the same that prescribed as the standard for Antibacterial Cleaning Products[6], which fall outside of the jurisdiction of the TGA. It is therefore both inconsistent and confusing to have the same level of efficacy (a 3-log reduction) being regulated by the TGA for Listed disinfectants claiming residual activity, but the same level of efficacy can be excluded from regulation if the same product is marketed as an antibacterial cleaner. Requiring only a 3-log reduction leads to an inconsistent and confusing hierarchy of efficacy between sanitisers / antibacterial products, residual specific claims, and non-residual specific claims.

Proposal 4: Limitations on claimed residual activity period

It is proposed that no limitations be placed on the period over which residual activity is claimed, as long as the claims are substantiated by test data*, however the period over which residual activity is claimed has to be substantiated by more than one set of test data. Conditions during the period must incorporate real life applications as claimed for the product.*

Comment:

Information from the TGA as provided in this current consultation clearly indicates that while there have been multiple applications made for products achieving residual disinfection, none of these applications have incorporated any assessment of the conditions likely to be encountered during actual use of these products by the end-user.

"There have been no examples in the applications made to TGA that include test data to support the claims of residual activity after a number of "touches".

This significant absence in my opinion invalidates any claim for residual disinfection made on any of these products. The range of examples of test methods presented so far to the TGA, as detailed in this consultation, provide evidence only of delayed disinfection, not ongoing residual disinfection.

To illustrate, in the BS EN 13697 example given, the disinfectant was applied to a surface, stored for 30 days and then liquid inoculum applied to the surface. The ensuing result can be readily explained as being achieved by the liquid inoculum dissolving and releasing the biocide from the dried surface. **This does not constitute evidence of residual disinfection** which must be achieved through multiple challenges of the surface through regular washing, touching, wiping, abrasion and repeated exposure to liquid inoculum.

The same comment is relevant for the examples given for the ASTM method and the Staph aureus / E coli 12 month residual applications. Neither presents any evidence to support the claims of residual activity after either a number of "touches", or multiple challenges such as those described in the previous paragraph. They all demonstrate only a single delayed disinfection event, not a continued significant and sustained reduction as required by the definition.

Any claimed residual activity period must incorporate limitations not just in terms of time, but also in terms of challenges with conditions likely to be encountered during actual use of these products by the end-user.

It is instructive that the suggested standard PAS 2424:2014[8] specifies over a period of 24hrs that the disc undergoes a series of abrasion cycles and re-inoculations which are designed to simulate the abrasion and re-contamination (via touch and exposure) of a surface in between treatment with a disinfectant product.

Furthermore, the related US EPA standard Protocol # 01-1A *"Protocol for Residual Self-Sanitizing Activity of Dried Chemical Residues on Hard, Non-Porous Surfaces"*[7] requires a minimum of 12 wear cycles with an abrasion tester fitted with a moist cloth to be performed on the surface treated with the test product.

Given that there exist two validated protocols for residual efficacy testing already established globally that require wear and abrasion testing in between inoculations, in order to be relevant and consistent the final approved protocol required by the TGA must also incorporate appropriate abrasion cycle methodology.

It is noted that the current position of the US EPA on residual disinfection[10] is that qualifying products for residual disinfection must meet the requirements of the residual self-sanitization protocol[7], which incorporates the minimum 12 wear abrasion cycles.

It is noted that there is a current US EPA notification of one product approved for residual antiviral activity not meeting these guidelines[11]. This is however a temporary exemption under Section 18, and is valid only in TX, AR, and OK until August 24, 2021. After that the product will be required to meet the interim guidelines as described above[7,10]. Note that the EPA guidance for this product is as follows: *"According to its updated labels, SurfaceWise2 provides residual surface control of the coronavirus SARS-CoV-2 on surfaces that are undisturbed for up to 30 days. However, SurfaceWise2 should be reapplied every time surfaces are disinfected to ensure continuous product performance. Exposure to prolonged wetness may adversely impact the efficacy of the product."* This application method required by the US EPA does not meet the proposed TGA definition of a residual disinfectant.

Validation of Residual Activity by the biocide:

The position of the US EPA regarding exposure to prolonged wetness adversely impacting product efficacy is especially important in light of recent independent work undertaken by the University of Hong Kong[9] on the commonly used residual disinfectant active octadecylaminodimethyltrihydroxysilylpropyl ammonium chloride, CAS 27668-52-6, showing that after a single water wipe 50% of the compound is removed from the surface, no detectable compound remains on the surface after 14 wipes, and that **virus survival without treatment** drops by 1000 fold on most surfaces after 24 hours. It is also noted that recent work by the CSIRO[1] has shown that SARS CoV-2 virus titres drop by 50% with no treatment on most surfaces within 2 days at 20°C, and a 4-log reduction from starting titres is observed within 2 hours at 40°C.

Claims of residual activity over a period on time should therefore also be validated to confirm that the residual activity is arising from the action of at least minimum concentration amounts of the biocidal active, rather than simply the lack of viability of the virus or bacteria to survive in the particular conditions (environment, surface) used.

For Listed disinfectants the microbial efficacy must be validated with appropriate stability data, including assay of the active ingredient. As a claim of residual efficacy is a specific claim, the efficacy of residual disinfectants requires commensurate validation. This will require the sponsor to demonstrate through acceptable scientific means that the biocide is both present and active at both the beginning and the end of the claimed residual activity period.

Proposal 5: Restricting residual activity claims to specific organisms

It is proposed that residual activity claims can be made against general bacteria and/or specific organisms, if substantiated by test data.

Comment:

Residual activity claims can be allowed against any organism, as is the case for current Listed disinfectants. However except for a general bactericidal claim, each and every specific organism must be individually tested, assessed and prior approval obtained from the TGA. Surrogates for specific organisms will not be accepted unless specifically allowed by the TGA[2] e.g. murine hepatitis virus for SARS-COV-2, calicivirus for poliovirus, M.terrae for M.tuberculosis.

This is consistent with the current TGA Instructions for Disinfectant Testing[2], where specific claims require individual assessment and approval prior to being allowed. As noted in this consultation the TGA considers a residual efficacy claim as a specific claim.

Proposal 6: Allowing residual activity claims

~~It is proposed that residual activity claims be allowed in the interim, and be assessed on a case by case basis. Should a test method or multiple test methods be defined, the new testing requirements will apply to new listings.~~

All current residual activity claims currently approved must be revoked, and these claims will be re-instated on a case by case basis according to the test method(s) defined and approved. The new testing requirements will apply to all previous and subsequent listings.

Comment:

It has already been explicitly noted by the TGA in this consultation that *"There have been no examples in the applications made to TGA that include test data to support the claims of residual activity after a number of "touches".* Protocols already exist globally[7,8] for residual activity that require multiple abrasion methodology in order to be valid and relevant. Any product that is currently approved does not meet the requirements of these global standards, even for sanitation after 24 hours. It is both inconsistent and a significant concern to public health therefore to continue allow the same technology to be approved for a residual disinfection claim in Australia that concurrently will not be allowed to be used as either a residual antimicrobial or sanitising product according to established approved protocols.

The scope of the current consultation is for residual activity against both highly pathogenic and low pathogenic organisms. The possible application of use of these products extends across all applications, from in-home use, business, transport (covering all modes including buses, trains and aircraft), and healthcare facilities, up to and including critical care units in hospitals and surgeries. Therefore allowing current approved products to be continued to be used presents a significant public health risk, and cannot be allowed to continue.

Significant work on the survival rates on Covid-19 has been done by many organisations and bodies in the past 12 months. Notably the CSIRO has conducted their own recent investigation[1] into the survival rate of Covid-19 under a variety of environmental conditions. This work also incorporated the use of significant soiling present with the virus and the contribution of the type of surface on which the virus was inoculated onto. Significant difference in results were seen in this study depending upon the surface used. It is therefore reasonable, appropriate and consistent to require a similar variety of surfaces also be incorporated into any testing for residual disinfection efficacy. As none of the current products appear to meet this criteria they do not reflect good scientific practice and the claims must be immediately revoked until such time as they do. Note that many industries have a variety of critical areas and surfaces that require disinfection. For example, in hospitals & aged care the surfaces are mainly bed fabrics, metals and plastic; in dentists & clinics the surfaces are mainly chairs and metal. Seating that is comprised of vinyl & eleather is the main surface in global public transport : buses, trains & aircraft. Products that have not validated their efficacy on the variety of surfaces on which they are proposed to be used on are at the least false and misleading, and more pertinently a potential endangerment to public health.

Finally the application of any new testing method to new listings only creates an inappropriate and commercially unacceptable hierarchy in the market between those products that will be well regulated and supported (new listings) and those products “grandfathered” with inadequate or inappropriate data (interim listings). The subsequent regulatory and cost burden on new listings is both unfair and inconsistent. The allowing of interim listings to be able to make specific claims under a lesser regulatory oversight than that required for new listings is also counter to good public health outcomes.

Alternative recommendation for products with currently approved residual claims:

An alternate proposal for the current products with residual disinfection claims is that their claims are amended to one of general residual antibacterial or sanitising efficacy only, provided that residual antibacterial efficacy can be demonstrated with a minimum 3log10 reduction as per PAS 2424:2014[8], or a pass against the EPA protocol[7].

If this is permitted then the residual antibacterial efficacy claim must be differentiated clearly on the label from any claims of disinfection, and must on the label and in all promotional material clearly exclude any residual disinfectant claims that are made on specific organisms.

Further comments on data requirements and level of evidence / communication:

For a 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 descriptions and specifications of the surfaces used
- Inoculation specifications and instructions
- Full description of organisms tested
- Complete description of the treatment regime and directions for use, including a rationale for the applicability of the results to the proposed marketing and end-user requirements

Residual disinfection must be demonstrated:

- 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 promotional material 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
- description of the treatment protocol in the directions for use

Summary:

In summary the proposal to provide clarity on residual disinfectant claims is generally supported. The final guidance must however be consistent with already existing and established validated protocols, align with best practices for surface selection and testing, ensure proper validation of the activity and use, recognize that these products will be used in a multitude of industries, environments and situations for public health benefit including high end medical and healthcare situations, and provide both clarity and consistency with existing TGA disinfection requirements that are a major contributor to sound public health outcomes.

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

Yours sincerely,

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