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Dear Sir/Madam

Thank you for the opportunity to comment on the *Proposal for clarifying regulatory requirements for residual claims for disinfectants* put forward by TGA.

Whiteley Corporation is a manufacturer of disinfectant and cleaning products based in New South Wales. The company has an active Research and development team dedicated to new product development. We also actively engage with University research groups in Australia and elsewhere looking for new and innovative products for infection control and prevention. We also participate in the development of Australian and International standards, particularly in the field of medical device reprocessing.

Proposal 1: Definition of residual activity

The proposed definition from TGA for residual activity is as follows:

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

This definition does not include requirements for the surface type. With some disinfectants claiming residual activity, the active ingredient is also capable of covalently attaching to some surface types, specifically metal, glass and some textiles (such as cellulose based textiles such as cotton or rayon). This covalent attachment is unlikely to occur with other surface types (eg polymer surfaces comprising eg polyolefin, polyester, polycarbonate etc.

Other disinfectant systems may also rely on non-covalent bonding to the surface. Again, the strength of bond to the surface is likely to be driven by surface material type.

It is also noted that residual activity has also claimed for both porous and non-porous surfaces. Specifically, materials are available for the treatment of textiles to impart residual biocidal activity. Examples of this type of use can be seen in the US where face masks are treated with materials capable of imparting residual biocidal activity.

Another factor that should be considered in relation to claims for residual activity is the surface maintenance. Given that many of the products being offered in this area are based on quaternary ammonium based biocides, there is a risk that the active material on the surface may be deactivated by inappropriate maintenance such as the use of anionic surfactant based cleaning products.

Any claim for persistent activity should also be considered in conjunction with the manufacturers instructions for use, specifically for routine maintenance.

A suggested definition for residual activity is as follows:

The capability of a product to produce a defined reduction in the number of viable microorganisms on defined surfaces for a defined period of time, and subjected to defined abrasion when applied and maintained according to the manufacturers instructions

Proposal 2: Testing standards

There appears to be two testing standard available for residual activity on surfaces, the PAS 2424.2014 and the EPA protocol #01 1A, *Protocol for Residual Self-Sanitizing Activity of Dried Chemical Residues on Hard, Non-Porous Surfaces.*

There are many similarities between the two protocols, but also some major differences. In the PAS protocol, the surface is inoculated prior to applying the disinfectant treatment, whereas in the EPA protocol, the treatment is applied before the inoculation. Interestingly, the sponsor for the PAS, Byotrol, have a very similar protocol in one of their patents, which has an almost identical protocol to the PAS, the difference being in their patent the treatment is applied to the surface first.

Both testing standards make reference to interfering substances, but only in passing. The PAS mentions anionic surfactants as an interfering substance, but only for cosmetic applications.

Another key difference between the standards is the method of abrasion. The EPA protocol uses a Gardner scrub tester to achieve consistent and repeatable abrasion cycles, whereas the PAS utilises defined cloth held over the mouth of a weighted centrifuge tube. It is recognised that the scrub tester used in the EPA method is expensive (around GBP12,000), and so the PAS represents a pragmatic alternative. The pros and cons of each method should be evaluated and selected on the basis of reproducibility, particularly between testing laboratories.

Appendix 1 lists the differences between the two protocols. It is recommended that both methodologies be considered, and perhaps a hybrid method be derived and validated for use in Australia.

Proposal 3: Acceptance criteria

It is agreed that an acceptance criterion for residual activity of 3 log reduction is acceptable for bacteria.

Proposal 4: Limitations on claimed residual activity period

TGA has 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.

We do not accept this position. Given that many products claimed to provide a residual activity are based on quaternary ammonium chloride, and that there is a real risk that such systems may be adversely affected by anionic surfactants, routine maintenance is clearly an important factor. Whilst it would be a simple matter to maintain a floor in a manner consistent with manufacturer's instructions for short periods (eg 7 days), when the treatment is intended to last for longer periods it becomes harder to ensure that the prescribed maintenance procedures are followed.

There is also the risk that if something happened to a treated surface early on in the claimed use period that compromised its efficacy, the user will be unaware that the surface no longer has biocidal activity, yet has the belief the treatment is still effective. The longer the claim period becomes, the more likely this is likely to occur.

This will also apply to products that have a duration and number of touch claims. Whilst TGA maintains in their stakeholder consultation document 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*", there is at least one

product with these exact claims on the ARTG. This product claims "*residual antibacterial for up to 30 days or 200 touches against gram-negative E. coli and gram-positive S. aureus. Residual Covid-19 kill for up to 7 days*"

How does one determine the number of touches in the real world? If the treatment is applied to a true high touch surface (for instance the push plate on a public toilet door), it is likely that 200 touches will occur in 1 day, yet the time-based claim is for 30 days.

There is also the consideration of abrasion. The current test protocols have a limited number of cycles. However, these are unlikely to match real world experience. How can the limited number of abrasion cycles during testing replicate real world experience? The longer the claim period is, the more acute this issue will become.

Because of the above considerations, claims of activity of "up to X days" should be disallowed, as it leads to the situation where the residual activity has been depleted within the claim period, thus leading the user to believe the surface is still active, when in fact there is no activity left.

A far better claim would be to state minimum periods, as defined by scientific testing. A claim of "residual activity for at least 7 days" is more preferable than "residual activity for up to 7 days"

In terms of actual claims, given the above points, we would suggest limiting claims to a period not longer than 7 days.

With respect to claims for high touch or low touch surfaces, this can be addressed in any adopted test protocol. Claims for high touch surfaces should be justified by significantly more abrasion cycles than low touch surfaces, with allowances made for the relative numbers of wet or dry abrasion cycles.

Proposal 5: Restricting residual activity claims to specific organisms

We would propose that residual claims can be made against a range of organisms if supported by appropriate and defensible test data. The current system of general bactericidal and virucidal claims as defined in TGO 104 would be a suitable framework for this.

Proposal 6: Allowing residual activity claims

As discussed above, we have reservations about allowing claims beyond 7 days, and we see no need to extend these to 30 days or longer.

Yours sincerely

Dr Greg S Whiteley

Executive Chairman

Dr Trevor Glasbey

Research and Intellectual Property Manager

Table 1: Differences between UK and US protocols for the assessment of residual activity of detergents

	PAS2424:2014	EPA protocol 01-1A
Test surface	Stainless steel disks, Grade 2B finish	Non-porous, precleaned Glass, non-frosted Mirrored stainless steel Polycarbonate ¼" (0.64cm) thick
Test sample dimensions	2cm diameter, 1.5cm thick	1" x 1" (2.54cm x 2.54cm)
Obligatory Test organisms	*Pseudomonas aeruginosa* (ATCC 15442/NCTC13359) *Escherichia coli* (ATCC10536/NCTC 10788) *Staphylococcus aureus (ATCC6538/ NCTC10788)* *Enterococcus hirae* (ATCC 10541/NCTC 13383) *Candida albicans* (ATCC 1023/NCPF3179)	*Staphylococcus aureus* (ATCC6538) *Klebsiella pneumoniae* (ATCC4352) *Enterobacter aerogenes* (ATCC 13048)
Optional test organisms	*Listeria monocytogenes* (ATCC35152/NCTC7073) *Salmonella typhimurium* (ATCC 13311/NCTC 13277) (Methicillin Resistant) *Staphylococcus aureus* (NCTC13277)	As desired
Preparation of test substance	As per manufacturer's directions	As per manufacturer's directions
Interfering substances	Bovine albumin (obligatory) Milk (dairies etc) Yeast extract (breweries etc)	Organic soil (e.g. serum)

	Sucrose (beverage industry Sodium dodecyl sulfate (cosmetics industry) Buffer solutions (cleaning)	
Preparation of test surface	Rinse in running water for 5 minutes then place in 70% ethanol for 15 minutes. Dry in laminar flow then sterilise by autoclave. Do not clean with any product that might inhibit the action of the test substance, e.g. surfactant	Clean all plastic surfaces in mild detergent, then alcohol and rinse thoroughly in distilled water and then dry. Clean metal and glass surfaces by rinsing in alcohol, then distilled water and allow to dry. Decontaminate glass, metal and plastic surfaces by immersing in absolute ethanol, wiping and allowing to dry. Check for absence of inhibitory species. Clean all plastic surfaces in mild detergent, then alcohol and rinse thoroughly in distilled water and then dry. Clean metal and glass surfaces by rinsing in alcohol, then distilled water and allow to dry. Decontaminate glass, metal and plastic surfaces by immersing in absolute ethanol, wiping and allowing to dry. Check for absence of inhibitory species.
Application of test substance	Following initial inoculation (see note 1)	Prior to initial inoculation
Control substance	Sterile hard water	0.01% Triton X-100 (non-ionic surfactant) solution applied to both test and control test surfaces
Initial inoculum	10^6 for bacteria, 10^5 for yeast: mixed 1:1 with interfering substance	48-54 hour culture, 2x serial dilutions (1:10)
Repeat inoculum	10^4 for bacteria, 10^3 for yeast: mixed 1:1 with interfering substance	18-24 hour culture, 2x serial dilutions (1:10): dilute 1:1 with water and add soil (0.5ml serum to 9.5% culture)
Abrasion regime	Dry: polypropylene wipe folded in half lengthways x2 to give 4 sheet thickness. Attach to centrifuge tube weighted to 210g. wipe each test surface once forward and once back. Use wipe only one time Wet: as for dry but wet wipe by spraying with hard water. Repeat for each test surface so each has received a total of 3 dry abrasions, 23 wet abrasions and 5 reinoculations	Dry: Gardner scrub tester fitted with cotton cloth and foam liner 1 cycle (pass to left then return to right). Reinoculate surface after 15 minutes Allow 30 min drying time

		Wet: Gardner scrub tester fitted with cotton cloth and foam liner 1 cycle (pass to left then return to right). Reinoculate surface after 15 minutes At least 12 wear cycles to be performed and 5 reinoculations
Suggested modifications	none	As per consumer usage habit survey to define worse case usage
Final assessment time	24 hours after test substance application	Minimum 24 hours after test substance application
Final assessment	Use repeat inoculum: 5 minute contact time then enumerate survivors	Use repeat inoculum: 5 minute contact time then enumerate survivors
Acceptance criteria	$\geq$ 3 log reduction (99.9%) reduction compared to controls in 5 minutes at 20^{o}C (15 minutes for yeasts)	$\geq$ 3 log reduction (99.9%) reduction compared to controls in 5 minutes at 20^{o}C
Label claims	No specific claims suggested	A. [This product] kills 99.9% of bacteria for 24 hours B. [This product] sanitises for 24 hours C. [This product] kills 99.9% of odour causing bacteria for 24 hours D. [This product] keeps killing 99.9% of bacteria for 24 hours E. [This product] continues to kill 99.9% of bacteria for 24 hours F. [This product] also kills 99.9% of bacteria for 24 hours

Note 1. In the PCT patent application filed by Byotrol (WO2013061082) it is noted the test substance is applied to the test surface prior to inoculation with the bacterial suspension.