



ETHICAL AGENTS
VETERINARY MARKETING

EA NEWS

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Edited by:
Dennis Scott BVSc
MACVSc

EA Veterinary Marketing Ltd
54 Hobill Ave Wiri
PO Box 97-110 Manukau City
Manukau 2241

Ph 09-262-1388 Fax 09-262-1411
Freephone 0800 800-624
email info@ethicalagents.co.nz
website www.eavm.nz

A Milestone Year

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The best news about 2020? We have passed the halfway mark!

Not only are the days getting longer but we have gone past the depths of winter and spring is a few short weeks away.

Just as weather predicting is fraught with danger, even NIWA getting El Nino predictions wrong on occasions, making bold statements on outcomes of a swirling pandemic is incredibly risky.

No doubt the weather will have its nasty moments, it is still August after all, but while the Northern hemisphere is

getting itself into knots over going into winter with Covid virus still abounding, we were confident that we had suppressed it before heading to the warmer months.

However this is clearly no time for hubris as our Aussie cousins have shown us just how rapidly this pandemic can plunge a nation back into chaos.

Border security has been lax on occasion and our team of 5 million remained fearful of another outbreak. Sure enough there has been a flare up and we will now see how effective

our containment is. However there is confidence considering our history of disease control, as evidenced later in this newsletter.

2020 already outranks milestone years such as 1968 and 2001 and we have to go back to 1939 to find a year that has had a more cataclysmic effect on the world.

Our offspring will bore their grandchildren in years to come with tales of how they suffered through it.



Special points of interest:

- * CBD the latest in pseudoscience
- * Why use log charts
- * Our biosecurity has actually been very successful.

Looking Ahead

A week is a long time, not only on politics but also in a pandemic.

When it takes approximately a week from writing a newsletter to printing and distribution situations can change dramatically.

Nevertheless our biosecurity article will still ring true as Covid is only a small part of it.

With another lockdown and an election postpone the state of the nation is in constant flux.

We trust you all stay well and we feel secure in the knowledge that our clients, as health professionals, will be taking all suitable precautions.



Cannabinoids

Cannabinoids feature prominently in the news as of late and there has been a lot of misinformation out there. We are not getting into the legalize marijuana debate at all; that is an entirely different issue. What is of interest to the veterinary profession is the massive proliferation overseas of products containing the particular cannabinoid cannabidiol (CBD).

One of the last events pre-Covid lockdown was a pharmacology symposium in the then bustling but now deserted city of Melbourne. The keynote speaker was renowned veterinary pharmacologist Mark Papich Professor of Clinical Pharmacology at North Carolina State University.

Mark has authored/edited eight books on veterinary pharmacology and is one of the editors of the 9th and 10th editions of *Veterinary Pharmacology and Therapeutics*. He is author or co-author of over 235 research papers published in refereed journals and has authored over 130 book chapters, and review papers. In short he is recognized as one of the foremost veterinary pharmacologists in the world.



"In the 19th Century it was snake oil, in the 20th Century deer velvet, and now we have CBD."

During the symposium as a break from hard core subjects like pharmacokinetics Mark gave a short talk on the rise of CBD and backgrounded the science, as opposed to the myriad of pseudoscience claims for the compound.

Based on their origins, cannabinoids can be classified into three groups: phytocannabinoids, endocannabinoids, and synthetic cannabinoids.

Cannabis has more than 100 phytocannabinoids. Phytocannabinoids refer to any cannabinoid that is naturally occurring within the cannabis family of plants. Such cannabinoids include Δ^9 -THC and CBD, but they also include other cannabinoids such as cannabigerol (CBG). Δ^9 -THC is the psychoactive one in cannabis and the other main one of interest is cannabidiol, (CBD), which is non-psychoactive.

Endocannabinoids are produced within the body and serve as intercellular lipid messengers. It is believed that these are synthesized on demand rather than made and stored for later use. Endocannabinol has some relationship with arachidonic acid.

Synthetic cannabinoid receptor agonists are a large family of chemically unrelated structures that act as Δ^9 -THC but are more effective.

Cannabinoid type 1 receptors (CB1) are expressed mainly in the brain, spinal cord, and peripheral nervous system but are also found in organs and tissues, including endocrine glands and parts of the reproductive, urinary, and gastro-

intestinal tracts. CB1 receptors are absent in the medulla oblongata, the part of the brainstem responsible for respiratory and cardiovascular functions, which may account for cannabis-related acute fatalities. CB1 receptors appear to be responsible for the euphoric and anticonvulsive effects of cannabis. CB2 receptors are expressed primarily in the immune system, or in immune-derived cells such as leukocytes. CB2 receptors possibly influence the release of cytokines and therefore are believed to be responsible for the anti-inflammatory and therapeutic effects of cannabis. Because activation of the CB2 receptor does not cause psychological effects, selective agonists have become increasingly investigated for their therapeutic effects. (Reference J. Chilakapati, F.F. Farris, in *Encyclopedia of Toxicology* (Third Edition), 2014)

In summary then the main site of action is the CB1 receptor, which is located both centrally and peripherally and causes most of the effects of cannabis. The CB2 receptor is localized in the immune system. CB1 inhibits the release of neurotransmitters.

The phytocannabinoids Δ^9 -THC and CBD are both in synthetic cannabis. There is some evidence that Δ^9 -THC works on chronic pain if smoked or inhaled, the oral form is not as effective.

CBD seems safe but there is little data. It is absorbed orally but is highly lipophilic so probably has a high first pass effect in both dogs and people. Other than that the pharmacokinetics are unknown.

There is no regulation and there are many claims to it controlling seizures, pain dependency, anxiety

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Cannabinoids

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and insomnia yet it has no CNS effects. CBD is not an agonist of CB1 or CB2 receptors which are responsible for the pharmacological effect.

There has been one study on osteoarthritis in dogs, but the dogs received NSAIDs. In another study there were only 16 dogs and relied upon owner reported differences but veterinary evaluation of lameness and weight bearing resulted in no effect.

Despite this amazing lack of evidence of any efficacy whatsoever there is now a plethora of products in the United States making a multitude of claims that go unchallenged because the market is totally unregulated. There is even dog food containing CBD being widely advertised.

In the 19th Century it was snake oil, in the 20th Century deer velvet, and now we have CBD. It may well have benefits but hard data so far has not been produced but that

has not stopped the pseudoscientists leaping on board with more and more claims. Social media only abets the explosion.

The situation is not helped by the legalize marijuana campaign and the muddying of the waters between recreational and medicinal use (medicinal use under prescription already being legal). In such a climate differences between Δ^9 -THC and CBD seem of little consequence and the efficacy, or lack of, of the latter even less so.

On the Other Hand

What makes the pseudoscience used by the snake oil salesmen so galling is the cynicism and doubt created in the minds of professionals when true science comes up with novel alternatives.

Sometimes this is not helped by marketers jumping on bandwagons with snazzy names.

A great example is the use of hypochlorous acid as an antiseptic.

There is no doubt that it is super efficient and there is enough information on peer reviewed medical journals attesting to this.

The problem has been keeping it stable in solution and that has been achieved by a patented process of electrolysis and pH control.

Marketers overseas adopted the name of electrolyzed water. This coupled by the fact that, to maintain stability, colouring agents are not possible, leaving the product looking remarkably like ordinary water, presents the illusion that there is some hocus pocus here and not hard science.

Nothing could be further from the truth. Hypochlorous acid is what we contain in our white blood to

kill off bacteria, it has been around for millennia and has never met resistance because its action is physical not chemical.

Road Signs

A police officer pulled over Nagy driving a car doing 75 kph in a 60 kph zone, The officer asked Nagy if he realised he was speeding.

"I wasn't speeding," he replied. Look right there - that sign says the speed limit is seventy five."

The officer explained that 75 is the highway number, not the speed limit..

As he was telling Nagy this he looked in the back of the car and saw a woman looking pale and breathing very heavily. He immediately showed concern.

The officer asked her if the was OK and she replied, "Yes, we have just got off highway 155."



Log Charts

Not all disinfectants are created equal and the major measure of efficacy is the reduction in microbial numbers after application of a specific concentration of the disinfectant. This reduction is generally measured on log reduction. A logarithm calculation is a mathematical device utilized to graphically compare large disparities in numbers.

In mathematical terms the logarithm of a given number x is the exponent to which another fixed number, the base b , must be raised, to produce that number x . Putting that in more simple terminology, the logarithm counts the number of occurrences of the same factor in repeated multiplication; e.g., since $1000 = 10 \times 10 \times 10 = 10^3$, the "logarithm base 10" of 1000 is 3, or $\log_{10}(1000) = 3$. Note that 10 is a very common base to use in log calculations.

Why do mathematicians employ such devices? Although seemingly

to over complicate they actually make graphic depictions much simpler to display. A great recent example was the Covid 19 graphs in the media.

By using logarithms instead of a linear scale it is possible to compare changes over time in New Zealand to those in much higher population density countries. On a linear scale graph our figures would not register at all so no comparison could be made.

With this non-linear graph from the Stuff website, each interval on the vertical axis represents a 10-times increase.

This is a better way to compare percentage changes. For instance, when case numbers double from 10 to 20 or from 100 to 200, they will be represented by the same vertical jump on the chart.

From this we can see that our initial spike was as sharp as any other country even though total num-

bers were low. It also shows how quickly and successfully we 'flattened the curve.'

The non-linear graph also indicates that the rise in Australia after initial flattening is actually steeper than the progressive rise in the United States even though the actual numbers are almost infinitesimal in comparison.

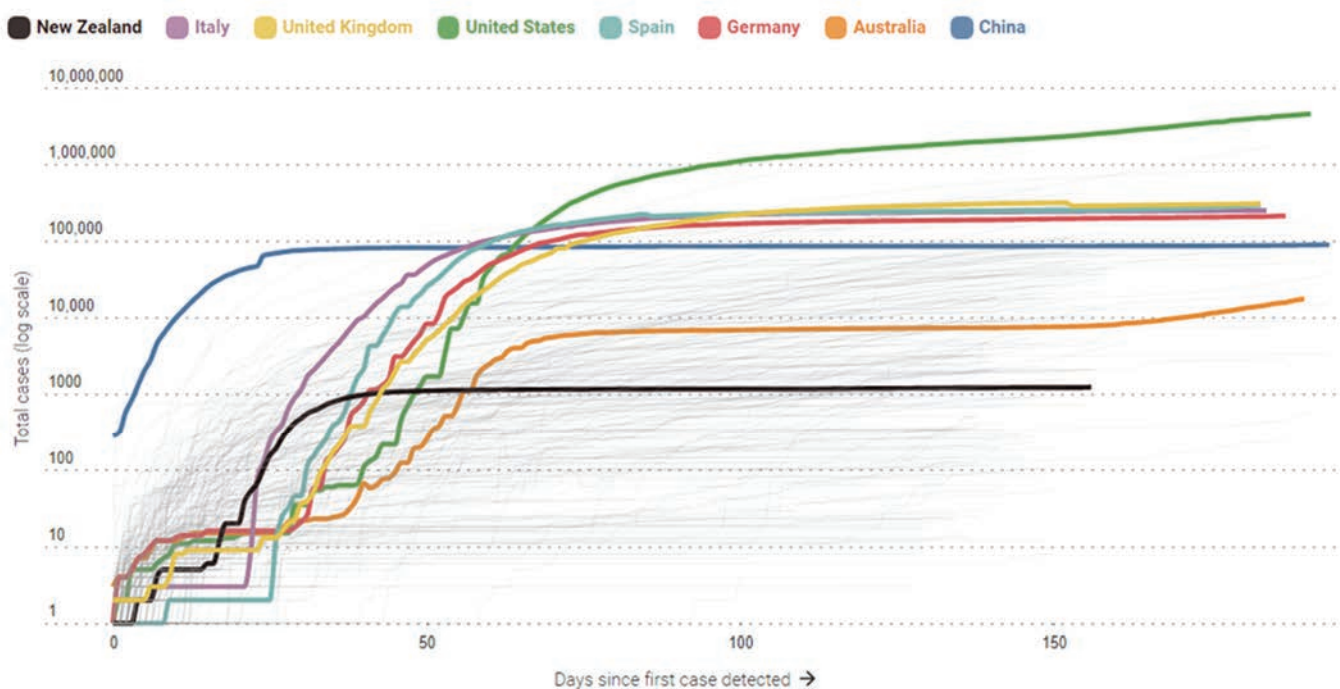
Another great example of a logarithmic scale is the Richter scale for measuring seismic activity, where again each whole number increase in magnitude represents a tenfold increase in measured amplitude; as an estimate of energy, each whole number step in the magnitude scale corresponds to the release of about 31 times more energy than the amount associated with the preceding whole number value.

Our greatest earthquake ever was in Wairarapa in 1855 at a huge magnitude of 8.2 but this is

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How coronavirus case trends compare worldwide

Confirmed infections since first case detected on a non-linear scale¹



Log Charts

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 dwarfed by last century's Chile quake of 9.5.

One can only image the devastation caused by these giant tremors when we reflect on the horrific results of the 6.3 magnitude quake in Christchurch in 2011.

So logarithms are not just a toy for the mathematically minded but an extremely valuable tool.

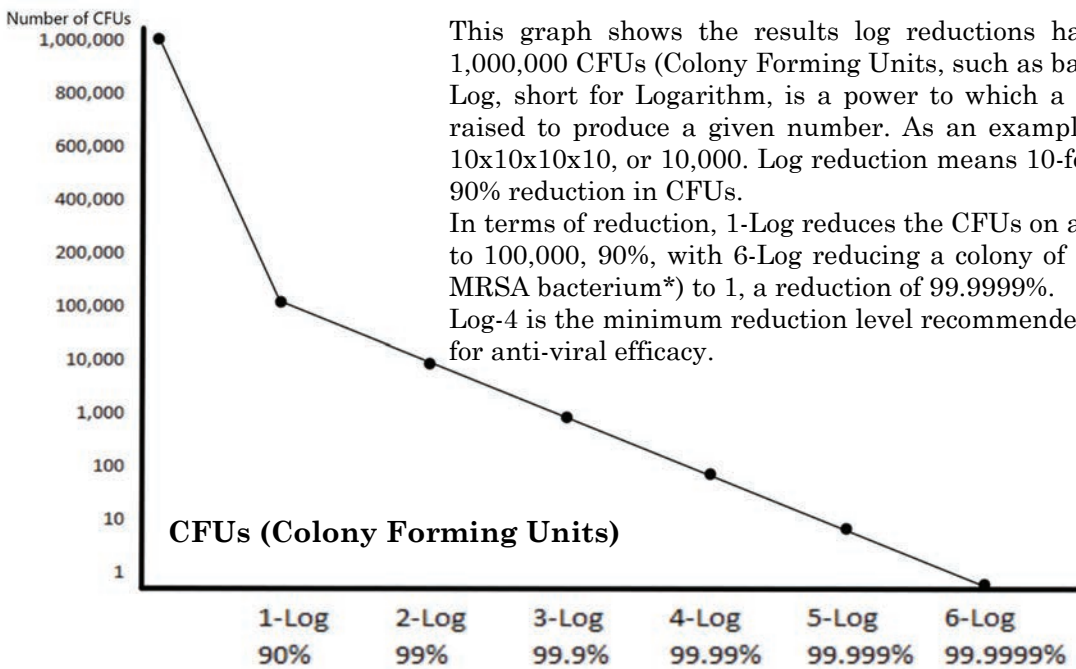
Just as the Richter scale provides a convenient measure of seismic events a log reduction can give a

very accurate and meaningful guide to disinfectant killing power.

It also makes recommendations simpler for health authorities, for example the minimum European standard for antiviral activity is a log 4 reduction. Those claiming a log 3 reduction are not just a little short of the mark, they are a massive 10 times less effective than the minimum standard.

The graph below sums it up with the y axis showing CFUs (Colony Forming Units) and the x axis indicating the reduction.

- 1-Log reduction: Number of CFUs is 10 x smaller
- 2-Log reduction: Number of CFUs is 100 x smaller
- 3-Log reduction: Number of CFUs is 1,000 x smaller
- 4-Log reduction: Number of CFUs is 10,000 x smaller
- 5-Log reduction: Number of CFUs is 100,000 x smaller
- 6-Log reduction: Number of CFUs is 1,000,000 x smaller.



This graph shows the results log reductions have on a test area with 1,000,000 CFUs (Colony Forming Units, such as bacteria).

Log, short for Logarithm, is a power to which a base, such as 10, can be raised to produce a given number. As an example, Log 4 represents 10⁴, 10x10x10x10, or 10,000. Log reduction means 10-fold (one decimal place) or 90% reduction in CFUs.

In terms of reduction, 1-Log reduces the CFUs on a test area from 1,000,000 to 100,000, 90%, with 6-Log reducing a colony of 1,000,000 CFUs (such as MRSA bacterium*) to 1, a reduction of 99.9999%.

Log-4 is the minimum reduction level recommended by the European Union for anti-viral efficacy.

A Panda

A panda walks into a restaurant and orders a sandwich. When it comes he eats the sandwich, pulls out a gun and shoots the waiter dead.

As the panda stands up to go the manager shouts, "Where are you going? You have just shot my waiter and you haven't paid for the sandwich."

The panda says, "hey man, I'm a panda, look it up."

The manger gets out his tablet and Googles 'panda'. He sees the following definition:

"A tree dwelling marsupial of Asian origin. Eats shoots and leaves."



NZ Biosecurity

Despite some notable lapses, such as Psa in kiwifruit and varroa mite in bees, (and now the second wave of Covid 19 all of a sudden) biosecurity in New Zealand is extremely strong and this, coupled with our being an island nation far from the major population centres on the planet make us very good at eliminating potential threats.

History proves this to be true and what we are currently seeing with our, up until recently, successful Covid 19 struggles has been reflected in the veterinary world many times.

Small successes like Equine Viral Arteritis (EVA) being eradicated in the last decade followed the massive success of brucellosis in the 20th century with bovine tuberculosis also being almost eradicated until it unfortunately became established in the wild fauna.

The biggest threat of all has always been foot and mouth disease in even toed ungulates. Experts in the mid 20th Century always believed it would be a matter of when not if the disease would strike in New Zealand. Over half a century later, despite a couple of false alarms, it has not reared its ugly

head.

Credit for this can be given to strict border controls and a friendly but brutally efficient customs service.

Maybe there is a lesson here for the current Covid 19 security regime. MPI border staff would surely not have let those quarantine breaches occur.

Currently we have had a scare with equine piroplasmiasis which looks like being a scare only and we will hopefully be able to declare the country disease free sooner rather than later.

What is interesting is the fact that the tactics used to control this problem are virtually the same as those employed in human medicine against Covid 19, i.e. contact tracing and testing.

A single mare was found to be affected. This horse was imported from France with a supposedly negative test but was positive when she was being sent on to Australia.

Whatever the doubts about her initial testing procedures MPI Biosecurity, in conjunction with the Equine Health Association, swung rapidly into action. The mare's movements in New Zealand were tracked and a program set up to identify and test possible contacts.

The disease is transmitted by ticks and the main tick responsible is not present in New Zealand. Despite this the cattle tick present here, *Haemaphysalis longicornis*, could not be totally disregarded as a possible vector with overseas literature demonstrating that the tick could carry the protozoa involved but there had been no recorded incidences of it being able to transfer it to another

host. The upshot being that, although tick transmission was highly unlikely in New Zealand, it could not be definitively ruled out.

The mare had been based in two separate establishments in her

"As with Covid 19 in Australia the biggest factor in the spread was non-compliance"

time here, an agistment farm in Karaka and a stud farm in Cambridge. Ticks have been known in both areas but much more so in Karaka.

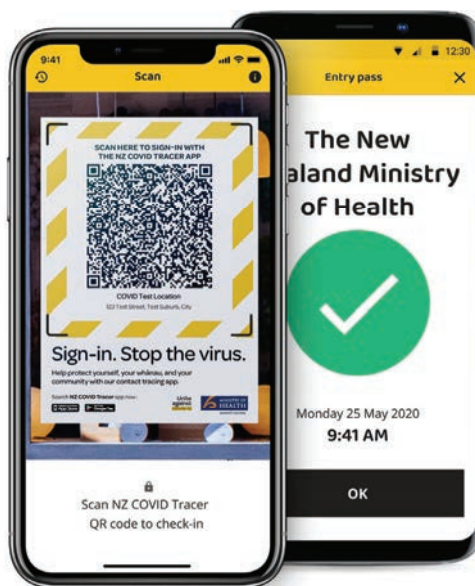
Contacts were put into different categories depending on risk profile, for example Category A contacts shared a paddock, Category B may have subsequently grazed the pasture, Category D were on the property but not in contact and category D were horses like walk in mares, coming to the stud for service only and returning immediately home.

In the end the mare herself was transported back to France, luckily for her, and all possible contacts have so far tested negative.

Identification proved critical with track and trace vitally important just as it has been crucial in the Covid 19 response, which leads us on to the other huge success story – the possible elimination of *Mycoplasma bovis*!

Many said it could not be done as eradication had been singularly unsuccessful throughout the world. The naysayers were definitely in the ascendancy early on as it was discovered that the much vaunted NAIT system of identification had broken down due to non-compliance on the part of many

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NZ Biosecurity

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 farmers, making track and trace exceedingly difficult.

This only emphasized how important track and trace is, as recognized by our medical colleagues.

However a couple of years down the road the track and trace system is now functioning better and farmers are tracing more animals after changes were made to NAIT and compliance improved.

So despite all predictions to the contrary, New Zealand is very close to eradicating the disease and this would be a world first for a country where it had gained a proper foothold.

We are not quite there yet but, with only a handful of farms now designated as affected we can certainly see light at the end of the tunnel.

As with Covid 19 in Australia the biggest factor in the spread was non-compliance making track and tracing difficult.

There have been several cases recently of fines of several thousand dollars on farmers not register-

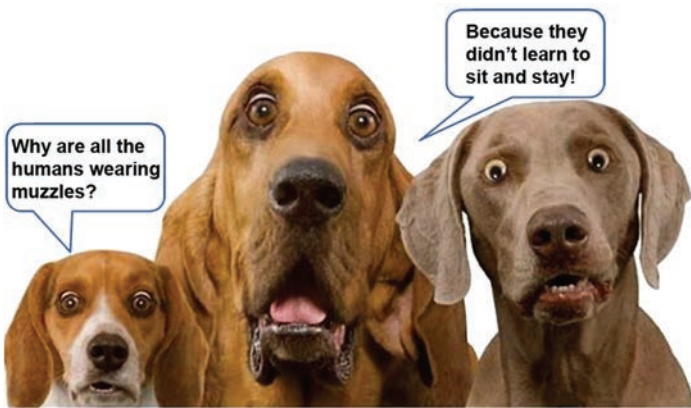
ing stock so control is gradually been taken over on the process.

Again as with Covid 19 now the biggest enemy is complacency when we are on the cusp of elimination. With both diseases it is apparent that the disease can be eliminated but the risk will not be.

50 years ago bovine tuberculosis was on the verge of elimination only to re-ignite and is now endemic.

However our track record and advantages are very good and the similarities between human and veterinary disease eradication are striking.

The one major advantage the animal health field has in some cases is a slaughter policy. Right now some medicos in Victoria probably wish they had the same policy in those instances of people deliberately flouting the rules!



Lost and Found

A teenager lost a contact lens while playing basketball in his driveway. After a brief, fruitless search he gave up.

His mother took up the cause and within minutes found the lens.

“How did you manage that?” the teenager asked.

“We weren’t looking for the same thing,” his mother quietly explained.

“You were looking for a small piece of plastic, I was looking for \$250.”

Preying Lion

While walking through the jungle a man encountered a lion.

He fell to his knees and began praying for salvation from the terrifying beast.

All of a sudden the lion bent down right next to him and started to

pray as well. The man was astonished at this sight.

“It’s a miracle!” he shouted.

“Excuse me,” said the lion, “would you mind keeping quiet while I am saying grace.”



Selection of test results

ORGANISM	Dil'n	Method	Reduction
Sporicidal Activity			
Bacillus Subtilis	1:100	EN14347	>Log 6
Clostridium difficile	1:100	EN14347	>Log 5
Clostridium sporogenes	1:100	EN13704	>Log 6
Clostridium perfringens	1:100	EN13704	>Log 6
Mycobactericidal Activity			
Mycobacterium avium	1:100	EN14348	>Log 6
Mycobacterium bovis	1:100	EN14348	>Log 5
Mycobacterium fortuitum	1:100	EN14348	>Log 6
Mycobacterium terrae	1:100	EN14348	>Log 6
Virucidal Activity			
Hepatitis B	1:100	EPA Protocol	complete deactivation
Norovirus (Feline calicivirus)	1:100	EPA Protocol	complete deactivation
HIV	1:100	EPA Protocol	complete deactivation
Adenovirus type 5	1:100	EPA Protocol	complete deactivation
Coronavirus (SARS/COVID-19)	1:100	EPA Protocol	complete deactivation
H5N1	1:200	Harbin Veterinary Research Institute	Total kill
Fungicidal Activity			
Aspergillus niger	1:200	EN13624	>Log 4
Candida albicans	1:200	EN13624	>Log 4
Penicillium verrucosum	1:200	EN1675	>Log 4
Trichophyton rubrum	1:200	EN13624	>Log 4

ORGANISM	Dil'n	Method	Reduction
Bactericidal Activity			
Pseudomonas aeruginosa	1:200	EN1276 by HIRL	>Log 5
Staphylococcus aureus	1:200	EN1276 by HIRL	>Log 5
Escherichia coli	1:200	EN1276 by HIRL	>Log 5
Enterococcus hirae	1:200	EN1276 by HIRL	>Log 5
Pseudomonas aeruginosa	1:200	EN1276 by HIRL	>Log 5
Staphylococcus aureus	1:200	EN1276 by HIRL	>Log 5
Enterococcus hirae	1:200	EN1276 by HIRL	>Log 5
Acinetobacter calcoaceticus	1:200	EN13727	>Log 5
Campylobacter jejuni	1:200	EN13727	>Log 5
Enterococcus faecium	1:200	EN13727	>Log 6
Helicobacter pylori	1:200	EN13727	>Log 5
Klebsiella pneumoniae	1:200	EN13727	>Log 5
Legionella pneumophila	1:200	EN13623	>Log 6
Listeria monocytogenes	1:200	EN13727	>Log 6
MRSA	1:200	EN13727	>Log 6
Proteus vulgaris	1:200	EN13727	>Log 6
Salmonella dublin	1:200	EN13727	>Log 6
Salmonella enteritidis	1:200	EN13727	>Log 6
Salmonella typhimurium	1:200	EN13727	>Log 6
Serratia marcescens	1:200	EN13727	>Log 6

Tested by Warwick University to inactivate and destroy DNA/RNA

SteriGENE test results,

- 1) expressed as log numbers,
- 2) Note that 'complete deactivation means total destruction, i.e. > log 6



The Bloody Bat

A vampire bat came flopping in from the night with its face covered in fresh blood and parked himself on the roof of the cave to get some sleep.

Pretty soon all the other bats smelled the blood and began harassing him about where he got it..

"Go away and let me get some sleep," the bat said but they persisted until he finally gave in.

"OK then, follow me," he said and he flew out of the cave with hundreds of excited bats fanatically following him.

Down through a valley they went, across a river and into a huge forest of trees.

Finally he slowed down and the other bats milled excitedly around him, tongues hanging out in anticipation.



"Do you see that large oak tree over there?" he asked.

"Yes, yes, yes!" the bats screamed in a frenzy.

"Good," said the first bat, "because I jolly well didn't!"