QUATS:Are you exposed? Quaternary Ammonium Compounds.

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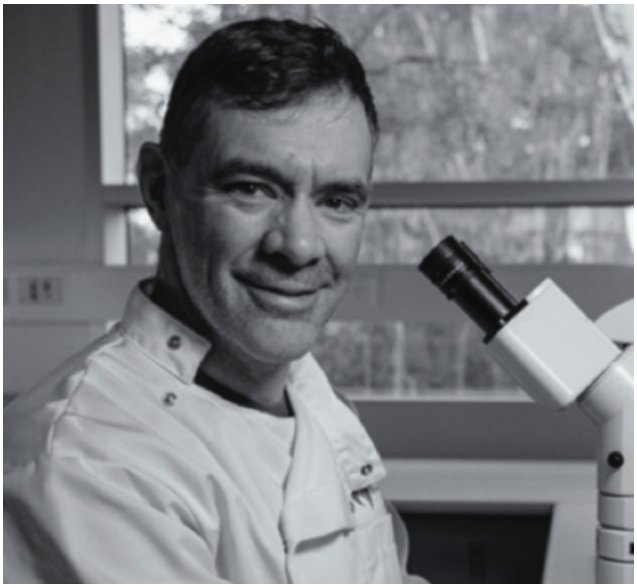
Dr Tony Peacock is the Chairman of Wintermute Biomedical Inc., Wintermute Biomedical Australia Pty Ltd and Ten Carbon Chemistry Pty Ltd. These companies are developing solutions to antimicrobial resistance and marketing the Doxall range of sanitisers, which do not contain quaternary ammonium compounds.

He is a Fellow of both the Australian Academy of Technology and Engineering and the Australian Institute of Company Directors. He is also a Churchhill Fellow and expert on how universities and companies work together.



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Tom is a Wintermute co-founder and inventor, with over 20 years experience in scientific research. He specializes in neuroscience and medical microbiology, with a particular focus on multidrug-resistant bacteria.

He founded Wintermute Biomedical Inc. after seeing a dramatic increase in resistant infections while working in hospitals. He is a Director of Wintermute Biomedical Inc., Wintermute Biomedical Australia Pty Ltd and Ten Carbon Chemistry Pty Ltd.

Note: Dr Tony Peacock is the Chairman and Dr Tom Rau is the Founder and Chief Scientific Officer of Wintermute Biomedical Inc., Wintermute Biomedical Australia Pty Ltd and Ten Carbon Chemistry Pty Ltd. These companies are developing solutions to antimicrobial resistance and marketing the Doxall range of sanitisers, which do not contain quaternary ammonium compounds. Drs Peacock and Rau declare their conflict of interest and invite readers to come to their own conclusions after reading this paper.

About QUATs

You are not alone if you have never heard the term QUATs. But it is almost certain that you are coming in contact with them in increasing frequency, likely daily. The COVID-19 pandemic has seen a huge surge in their use as disinfectants and sanitisers. But are they safe? What is the effect of chronic long-term exposure on humans?

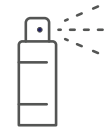
QUATs is the acronym for Quaternary Ammonium Compounds (also kown as QACs) which have been around for over 70 years. Disinfectants and sanitisers are a US$3.4 billion billion global industry with double digit growth experienced during the COVID-19 pandemic[i].

More than half of the disinfectants accepted to kill COVID-19 by regulators in the USA are QUATS[ii]. Australia follows suit. QUATS are also used in hand sanitisers and in disinfectants such as Pine O Clean[iii], Zoono[iv], Viraclean[v] and Tri Nature Sanazone[vi]. QUATS are legal for use. The Poisons Standard administered by the Therapeutic Goods Australia (TGA) allows up to 20% concentration with specified levels of usage safety warnings. Benzalkonium Chloride (ADBAC or BAC) is the most commonly used. This paper largely refers to research on ADBAC, BAC, and DDAC.

Researchers found evidence of harmful, unintended impacts of QUATs over a decade ago. More recently, alarm bells are ringing over a 2020 medical research study finding QUATs in 80% of human blood samples tested. Concerns also exist that QUATs do not deliver their stellar lab test results in the real world. This paper explores these issues and poses the question for anyone responsible for authorising use of QUATs: Is the exposure worth the risk?

Benzalkonium Chloride (ADBAC or BAC) is the most commonly used QUAT.

ALKYLDIMETHYLBENZYLAMMONIUM CHLORIDE (ADBAC, BAC)



Disinfecting spray

Disinfecting wipes

Antibacterial hand soap

Alcohol-free hand sanitiser

QUATs are used as a disinfectant.

Eye drops

QUATs are used as a preservative.

DIDECYLDIMETHYLAMMONIUM CHLORIDE (DDAC)

Disinfecting spray

QUATs are used as a disinfectant.

Fabric refreshers

QUATs are used as an antimicrobial.

QUATs Questioned

QUATs came under increasing pressure in 2008 after an interview with an "accidental toxicologist", Professor Patricia Hunt in Nature magazine[vii]. Professor Hunt, a medical researcher, moved research mice from Ohio to Washington State University. The mouse colony experienced a substantial decline in fertility and increased birth defects. After an exhaustive search, Professor Hunt identified the culprit as the lab disinfectant which contained the QUAT benzalkonium chloride (BAC) and didecyl dimethyl ammonium chloride (DDAC).

A year later Dr Terry Hrubec, a reproductive toxicologist at Virginia Tech and Edward Via College of Osteopathic Medicine, made similar findings. She only expected to find neural tube defects in embryos of pregnant mice in her test group exposed to drugs known to cause defects. However, Professor Hrubec found neural tube defects in 10% of the embryos which came from the control group of healthy, unexposed mice. Experiments were repeated with variables tested and, consistent with Professor Hunt's findings, a change to a QUAT disinfectant a few months earlier was the culprit.

"80% of people in the study had disinfectant residues in their blood... we found increased inflammation and decreased mitochondrial function"[ix]

Dr Hrubec has continued to research the effects of QUATs. Further study exposed mice to conditions mimicking everyday exposure (pre-covid) such that people might experience in buildings cleaned with QUATs. She concluded that key cellular processes were disrupted.

"Male mice living in the QUAT-using building had about a 25% lower sperm count and 10% lower sperm motility."[viii]

Her latest study was of humans, not mice. Dr Hrubec joined with other medical researchers to study QUATs in human blood. Eighty percent of randomised blood samples from 43 people contained measurable concentrations of QUATs[ix]. "I found that 80% of people in the study had disinfectant residues in their blood... we found increased inflammation and decreased mitochondrial function in people who had disinfectant in their blood. We need to study this further to see if these changes contribute to disease. These findings are of particular concern to the medical community as the disinfectant is used extensively in healthcare settings", says Dr Hrubec.

Exposure of the human population to QUATs has increased due to the COVID-19 crisis. An analysis of household dust in 2020 showed an increase in levels of quaternary ammonium compounds, compared with 2018 and 2019[x]. QUATs have long been linked to asthma[xi], and nurses exposed to high levels of disinfectant have reduced fecundity, which is mitigated by use of protective equipment[xii].

Researchers consistently report difficulty in attracting research funding to study the health impacts of QUATs.

QUATs and Antibiotic Resistance

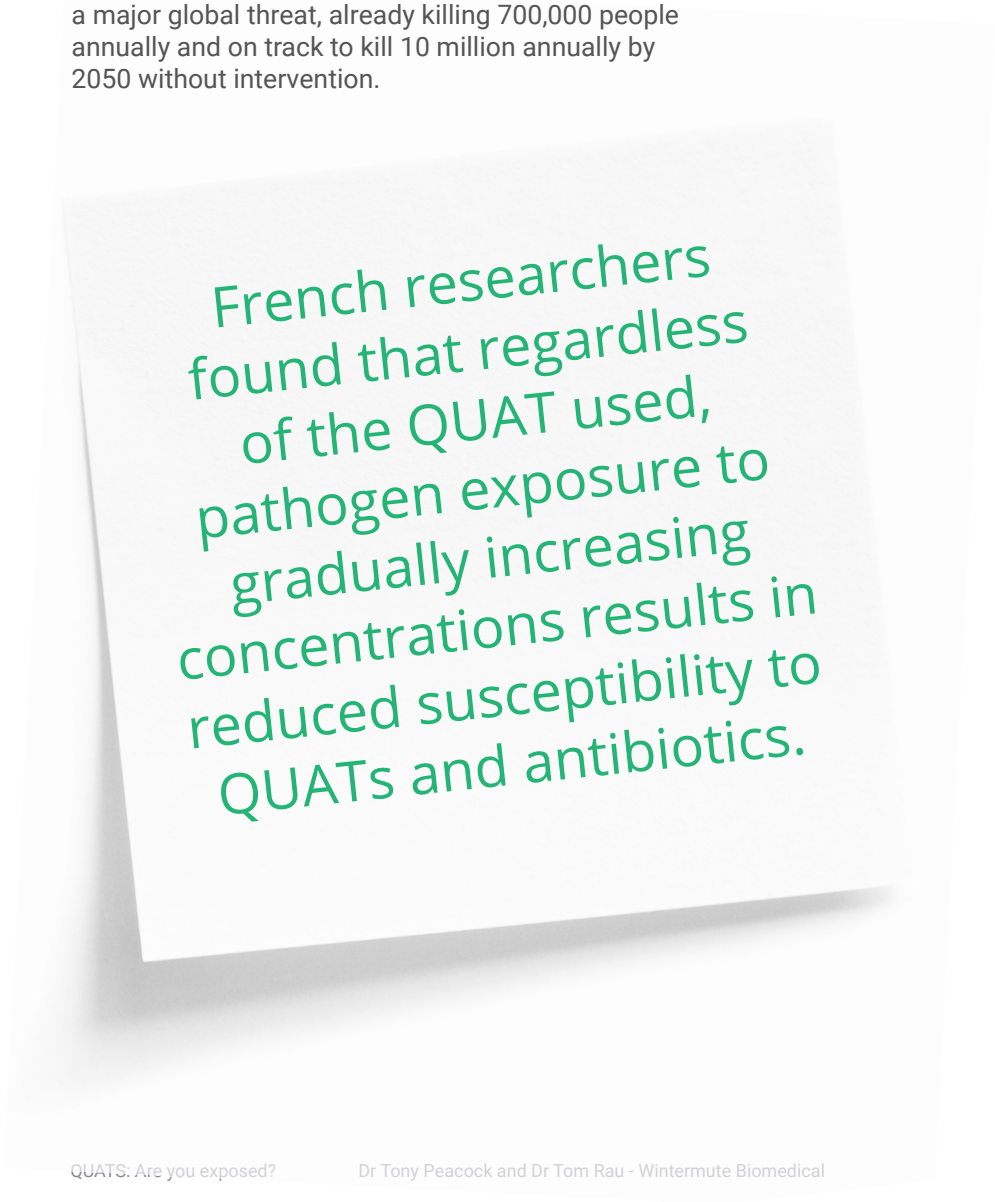
Perhaps the most concerning and least studied aspect of the increased use of QUATs is their contribution to bacteria developing resistance to antibiotics (AMR). Bacteria can pass on their resistance gene to other bacteria, even bacteria of a different species. A study in 2019 concluded that QUATs may facilitate the evolution and transfer of antibiotic resistance genes[xiii].

In a nightmare future scenario, the most basic of infections will again be deadly if bacteria, viruses, fungi and parasites become drug resistant. Vancomycin-resistant Enterococcus (VRE) is already at that point, being resistant to virtually all antibiotics.

The World Health Organisation has identified AMR as a major global threat, already killing 700,000 people annually and on track to kill 10 million annually by 2050 without intervention.

The chemical industry argues that QUATs are a wide class of compounds and we should not draw conclusions about the whole class, based solely on individual members. But French researchers found that regardless of the QUAT used, pathogen exposure to gradually increasing concentrations results in reduced susceptibility to the QUATs and antibiotics as well.[xiv]

In another research paper, Hora and co-authors reflected on the irony of using QUATs to fight COVID-19, which "could lead to increased infections from antibiotic resistant bacteria if elevated QAC (QUAT) exposure jolts the spread of antibiotic resistance"[xv].



Do QUATs work on dirty surfaces?

The answer lies in the difference between the laboratory and the real world.

An essential prerequisite for most QUATs is that the surface must be clean before application. This means a multi-step application process is needed. The surface needs to be cleaned, the QUAT applied and allowed to dry.

According to a US industry-supported website www.quats.org:

> "...make sure you are starting with a clean surface as dirt and dust will inactivate the QUATs disinfecting ability."

Testing of disinfectants for regulation requires them to knock down bacteria in laboratory test conditions. Those conditions do not include the varied mix of body oils, dirt and grime that occur in the "real world".

In food preparation areas, most QUATs require the further step of a final rinse-off before use to avoid contaminating the food.

Used correctly, QUATs should live up to label claims. However, when cleaners are pressed for time, shortcuts to multistep processes are almost certain to occur. The result can be failure to kill the germs targeted, failure to remove toxic QUAT residue... or both.

With the need for both pre-cleaning and rinsing, it is easy to imagine cleaners under time pressure skipping steps needed to ensure QUATs are effective.

Responses to research on QUATs

The arc of concern about QUATs ranges from environmental and health lobby groups calling for a complete ban to industry organisations with well-honed rebuttals of criticism.

At one end of the spectrum is People Against QUATs, part of a group called Women's Voice for the Earth, concerned about the disproportionate impact of toxic chemicals on women and girls. They call for a ban or severe restriction[xvi].

The Environmental Working Group, a Washington based non-profit group established "to protect human health and the environment" recommends using safer alternatives and avoiding quats even during COVID-19 noting links to asthma, reproductive toxicity, and birth defects[xvii].

Good Environmental Choice Australia (GECA) is fussy about accepting QUATs into their eco label program. At present no BAC QUATs have been accepted by GECA[xviii].

In 2016, the European Union banned most QUATs from products contacting skin, food preparation surfaces and in human and veterinary hygiene.[xix]

Regulators have been slow to change. However, in 2016, the European Union banned most QUATs from products contacting skin, food preparation surfaces and in human and veterinary hygiene[xix]. QUATs have virtually disappeared from the food service sector in the UK as a result of residue testing limits imposed in 2015. In March 2020, after hearing Dr. Hrubec and other scientists present research and counterarguments, a Californian panel of nine scientists voted unanimously to place QUATs in their biomonitoring program.

QUATs have been a workhorse of disinfectant practices for over 70 years. The pandemic has seen their use increase by an order of magnitude beyond what public health officials could have envisioned when setting regulatory limits. Questions need to be asked:

- Are the regulation settings still right?
- Do QUATS pose adverse fertility hazards?
- Are they endocrine disruptors?
- Are they still safe to be used around humans?
- Should we be following the UK and EU on bans and restrictions?

There are responsible companies that present serious safety warnings in both marketing and labelling of QUATs. However, some present QUATs as a worry-free choice. One Australian QUAT (BAC) is advertised as "naturally derived", "fully biodegradable", "no harsh chemicals", "suitable for those suffering from skin conditions such as eczema, dermatitis and psoriasis" and "family friendly". The CEO of one publicly listed company is on YouTube saying his QUATS are "the same toxicity as orange juice or a Starbucks coffee, you can actually drink the product it is so safe."[xx]

It could be argued that end users have choice. However, current regulatory settings for disinfectants in Australia make fully informed purchasing decisions impossible. Only the active ingredient must be disclosed on a disinfectant label. QUATs, or any other toxic chemical, could be used as a proprietary exipient and not mentioned on a label. Also, QUATs do not need to be included on a Safety Data Sheet if present at less than 1% total volume. An active statement "Contains no Quaternary Ammonium Compounds or QUATs" is the only assurance.

Like other big industries, QUAT manufacturers fund industry bodies. These are at the other end of the arc of concern over QUATs and go the furthest in defending them. Relying on regulatory rulings and criticising research is not uncommon.

Accord, the relevant Australian industry association, runs a website called Furphies. The purpose is to "address unfounded public alarm arising from common myths and misconceptions." Among these, Accord considers it a myth that "household cleaning products, especially sprays, increases the risk of asthma."[xxi] This is at odds with a 2017 study which examined the link between asthma and exposure to quaternary ammonium compounds on nurses, aides and cleaners in healthcare settings. The authors concluded QUATs exposure increased the risk of asthma, the high-risk tasks being disinfection of surfaces, preparation of soaking solutions, dilution of products and the use of sprays[xxii].

Furphies challenges research that "some specific QUATs may be linked to potential health issues" citing Professor Hunt's mouse experiments. Furphies argues the studies lack relevance and cite lack of human trials. Accord relies on regulators saying, "regulatory agencies around the world monitor for new scientific evidence, and act if necessary…It is not yet time to panic!... More research is needed… The bottom line: There is no scientific evidence warranting further regulatory action".

At the time of writing, there are no known research studies or regulation reviews underway in Australia specific to QUATs. Calls from environmental and health groups are understandably fragmented. Entrenched market leaders run for cover behind existing regulation preferring to "shoot the messenger" rather than create safer products or fund independent research. Only a small minority of the most sophisticated consumers would have any inkling about the possible risks of exposure to QUATs.

It is confronting to read research expressing serious concerns about QUATs. It is alarming to read evidence of their presence in random human blood samples linked to negative health markers. Quality, safety and fit for purpose are assumed pillars of achieving Government approval to sell a product in Australia. It is worrying that consumers are largely in the dark.

There is a near perfect storm brewing over QUATs. Their use has skyrocketed since the COVID-19 pandemic. The industry tells us "it is not yet time to panic". But, mounting evidence points to serious health concerns. QUATs can trigger antimicrobial resistance, an even bigger threat to humans than COVID-19. There has rarely been a stage better set with imperatives for change.

Mounting evidence points to serious health concerns. QUATs can trigger antimicrobial resistance, an even bigger threat to humans than COVID-19.

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