

Novel Coronavirus (2019-nCoV)

Scope for Aqualution Hypochlorous Acid Solution for Effective Prevention and Control

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The current outbreak of novel Coronavirus (2019-nCoV) was first reported in Wuhan, China, on 31 December 2019 and has subsequently reached other regions of China and other countries. As of Monday February 3rd 2020, 2019-nCoV has caused 14,557 confirmed cases (14,411 in China, 146 elsewhere) with 305 deaths (304 in China, 1 in the Philippines). Cases have been confirmed in 23 countries across Asia, Europe and North America and the WHO have stated that the risk is “very high” for China and “high” on a global level (WHO website, 3/2/2020). Early outbreak data largely follows an exponential growth pattern (Zhao *et al.*, 2020). Estimates of the R_0 for 2019-nCoV vary with values cited typically between 2.24 and 3.58 (WHO, 2020; Zhao *et al.*, 2020). R_0 is the average number of secondary cases generated by a primary case. If $R_0 < 1$, an epidemic cannot be sustained; if $R_0 > 1$, an epidemic is highly likely (Chowell *et al.*, 2004). The R_0 values for SARS and MERS were retrospectively calculated to be 3 and 0.7 respectively, and Ebola 1.5-2 (Chowell *et al.*, 2004).

Coronaviruses belong to one of two subfamilies: *Coronavirinae* and *Torovirinae*. They are enveloped viruses typically 120-160 μ in diameter. They were first isolated in the 1960s from the nasal cavities of patients suffering with colds. Coronaviruses are said to be responsible for 10-15% of common colds worldwide and have a seasonal pattern (the R_0 value for seasonal influenza is said to be 1.3). They primarily affect the upper respiratory tract of mammals and birds. They cause direct (viral) and secondary (bacterial) pneumonia and bronchitis. The strains of Coronavirus known to affect humans are shown in Table 1.

Coronaviruses, as with Hepatitis, Influenza, Herpes, Newcastle Disease and Orthopox, are enveloped viruses. Enveloped viruses are viruses that possess an envelope or outer coating that is composed of a lipid layer (fat-like substance that is water insoluble). The envelope is needed to aid in attachment of the virus to the host cell. Loss of the envelope results in loss of infectivity. The mode of transmission for enveloped viruses is characterised by the specific virus; however, the most common routes are via indirect or direct contact of infectious virus particles, contact with or inhalation of respiratory droplets. Some enveloped viruses may also be transmitted by airborne transmission. Enveloped viruses are easily inactivated by routine surface cleaning and disinfection. The inactivation mechanisms of several common virucidal agents have been reported. Treatments with ultraviolet (UV) radiation and Aqualution hypochlorous acid usually destroy the viral genome, whereas chlorine dioxide and heat interrupt the process of host cell recognition for virus binding (Wigginton, 2012).

Table 1: The seven strains of Coronavirus known to affect humans

Variant	Genus	Year first reported	Reported number of cases / deaths / mortality rate
Human CoV 229E	AlphaCoronavirus	-	-
Human CoV OC43	BetaCoronavirus	-	-
SARS-CoV	BetaCoronavirus	2003	8098 / 774 / 9.6%
Human CoV NL63	AlphaCoronavirus	2004	-
Human CoV HKU1	BetaCoronavirus	2005	-
MERS-CoV	BetaCoronavirus	2012	2182 / 779 / 36%
2019-nCoV	BetaCoronavirus	2019	14557 / 305 / 2.1% (as of 3/2/2020)

For many years, epidemiologists were only aware of two strains of Coronavirus (Human CoV 229E and Human CoV OC43). Resultant illnesses is fairly mild, affecting just the upper airway. The discovery of SARS-CoV in China added a third. By the end of 2005 two more (mild illness) strains had been identified (Human CoV NL63 and Human CoV HKU1).

Middle Eastern Respiratory Syndrome Coronavirus (MERS-CoV) was identified in 2012 and the new variant (as yet unnamed) 2019-nCoV was first observed in Wuhan, China in late 2019.

Coronaviruses cause a wide range of disease in farm animals and domesticated pets: porcine CoV, bovine CoV (both cause diarrhoea in young animals), avian CoV (respiratory tract), Canine CoV (two types), Feline CoV (two types, both associated with high mortality rates), ferret CoV (two types) and murine CoV (high mortality rate). Coronaviruses are also present in wild animal species e.g. bats, camels and snakes. Some of these CoV have effective vaccinations (e.g. IBV vaccines are widely used in the commercial poultry industry). These animal diseases are zoonotic and freely mutate, so new viral pandemics continue to pose a very real threat to humans and animals. Consequently, there is much academic and government interest in emerging viruses.

The term “emerging viruses” is used to describe the appearance of viruses whose presence has increased over the past twenty years or whose presence threatens to increase in the years to come (Artika and Ma’roef, 2017). Emerging viruses include those that have been newly diagnosed in the civil population or those that may have been present before but have mutated. High profile viruses that meet this definition include the highly pathogenic avian influenza (HPAI) virus of subtype H5N1, severe acute respiratory syndrome (SARS-CoV), Ebola, the Middle East respiratory-syndrome Coronavirus (MERS-CoV), Zika and most recently the new variant Wuhan Coronavirus (2019-nCoV). Diseases caused by emerging viruses threaten human and animal health. The majority of emerging viruses are zoonotic. Their appearance is believed to be driven by a number of factors such as socio-economic, environmental and ecological changes (Jones *et al.*, 2008). More local interaction with wildlife in undeveloped countries, greater levels of global travel and trade, and different land use have also been identified as contributing factors for their rapid emergence. Such factors, together with a substantial increase of human population over the past five decades, and urbanisation in developing countries, have contributed to the increased chance of viral diseases emergence and re-emergence.

Of the six previously known strains, two have been associated with serious outbreaks: SARS and MERS.

SARS-CoV was first reported in China in 2002 and caused severe illness (muscle ache, headache, fever followed by respiratory symptoms including pneumonia). WHO state that approximately 25% of cases were seen in health care professionals due to the highly contagious nature of the virus. Whilst most of the cases were in China, it affected over 30 countries. No new outbreaks have been reported since 2014.

MERS-CoV was first discovered in 2012 in Saudi Arabia. Although it has been reported in 27 countries, 85% of the cases have been in Saudi Arabia. Infected patients present with a range of symptoms including fever, shortness of breath, cough, nausea, headache, vomiting and diarrhoea. Epidemiological data suggest that those affected are predominantly males who also suffer with co-morbid disease (eg diabetes) (Hui *et al.*, 2018).

SARS-CoV has been shown to persist on hard surfaces for up to 96 hours (Duan *et al.*, 2003) and up to 5 days if dry (Rabenau *et al.*, 2005b); MERS-CoV persists for at least 48 hours on surfaces (Hui *et al.*, 2018). Environmental contamination is considered a serious reservoir of infection in hotels, public places and health care settings (Radun *et al.*, 2003). Environmental contamination by MERS-CoV in patients' rooms has been reported in South Korea, with positive MERS-CoV RT-PCR results for cultures from environmental swabs taken from bed sheets, bed rails, intravenous fluid hangers and tables (Bin *et al.*, 2016). In the same study viable MERS-CoV viruses could still be isolated from three of the four enrolled patients studied on days 18–25 after symptom onset. Another study (Cho *et al.*, 2016) detected the presence of MERS-CoV by RT-PCR in viral cultures from four of seven air samples taken from two patients' rooms, one patient's bathroom, and one common corridor. MERS-CoV was also detected in the viral cultures for 15 of 68 surface swabs. A third study showed low concentrations of MERS-CoV RNA for environmental swabs taken from bed guardrails and monitors. Even after cleaning the monitors with 70% alcohol based disinfectant, RT-PCR showed low concentrations of MERS-CoV RNA remained: the samples only became negative for MERS-CoV after the monitors were wiped with diluted sodium hypochlorite (Song *et al.*, 2015). This is consistent with the findings of other researchers eg Rabenau *et al.* (2005) found that (under laboratory conditions) alcohol gels were effective against feline calicivirus in the presence of fetal calf serum but not effective in the presence of sheep erythrocytes or serum albumin: clearly alcohol gels are not efficacious under all “dirty” conditions.

Inanimate surfaces can be as infective as people so prudent and correct use of disinfectants is paramount in environmental control. SARS-CoV can be inactivated (4 log reduction) “quite easily” with many commonly used disinfectants (Rabenau *et al.*, 2005). These workers reported a 30 - 60 minute contact time at in use concentrations of disinfectants based on glutaraldehyde and benzalconium chloride. They did not test any chlorine based products. Dellano *et al.* (2009) tested a range of household disinfectants against Murine Hepatitis Virus (a SARS-CoV surrogate), including sodium hypochlorite. They found that a 30 second contact time was sufficient to achieve a 4.5 log reduction of MHV dried onto stainless steel coupons. Fogging has also been tested as a viricidal vehicle for disinfectants: Knotzer and workers (2015) fogged stainless steel coupons with dry residue of a range of viruses (enveloped and non-enveloped). They demonstrated that 5 minutes fogging with hydrogen peroxide / peracetic acid (at a rate of 0.4ml/m³) was sufficient to achieve inactivation. However, this disinfectant is very aggressive and, if not used in the correct quantity can be very dangerous to humans. Aqualution Aqualution hypochlorous acid is safe for humans and the environment. Published work (Clark *et al.*, 2006) has demonstrated excellent log

reductions of up to 10^7 against MRSA (on ceramic tiles). Our informal studies have repeatedly demonstrated that Aqualution products are effective against bacteria and viruses in a wide range of applications (e.g. food safety, animal production, health care) and methods of use (e.g. spray, dip, fog).

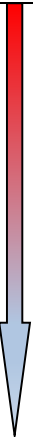
One of the most commonly studied viruses is Feline calicivirus (FCV) as it is relatively easy and safe to work with under laboratory conditions. It is also used as a surrogate for norovirus. Both norovirus and FCV are non-enveloped viruses which are harder to kill than enveloped viruses such as Coronaviruses. Many studies have reported on various compounds used for the inactivation of FCV, including acids and alcohols (Whitehead and McCue, 2010), ozone gas (Hudson *et al.*, 2007), H_2O_2 vapors, and chlorine dioxide gas (ClO_2) (Morino *et al.*, 2009). Whitehead and McCue (2010) showed that bleach and acid-based disinfectants could inactivate FCV within 1 min ($>4 \log_{10}$ reduction). The use of ClO_2 has been shown to reduce FCV titers by $>3 \log_{10}$ within 10 h (Morino *et al.*, 2009), and ozone can inactivate FCV in less than 1 h (Hudson *et al.*, 2007). Some of these compounds are toxic, some expensive and most require an extended time for virus inactivation. Aqualution hypochlorous acid (150ppm) achieved $>5 \log$ reduction in FCV titres in less than a minute (Chander *et al.*, 2012).

Various virucides are commonly used to disinfect environmental contact surfaces implicated in viral outbreaks. The material safety data sheets and labels for these virucidal compounds rarely allow for their aerosolization, spraying, or fogging due to their toxicity and adverse health effects for given exposure durations and concentrations. Many of these chemical compounds, such as sodium hypochlorite, chlorine gas, and glutaraldehyde, have been associated with occupational illnesses. For example, exposure to glutaraldehyde is associated with contact dermatitis in health workers, and the use of quaternary ammonium compounds has been found to cause occupational asthma in users (Purohit *et al.*, 2000; Ravis *et al.*, 2003). For cases in which aerosolization is approved, the use of personal protective equipment and a self-contained breathing apparatus is required, which makes the use of these compounds difficult, especially in public places such as hospitals or schools. Aqualution hypochlorous acid has been demonstrated as a powerful disinfectant and has been shown to be efficacious against a wide range of microorganisms in solution and when sprayed in the air. Another significant benefit of Aqualution hypochlorous acid is its lack of toxicity at ready-to-use (RTU) concentrations. In-house testing has repeatedly shown that fogging of Aqualution RTU Aqualution hypochlorous acid products achieves safe and consistent log reductions in bacterial and viral loading, both on environmental surfaces (eg aged care facilities) and food products (eg eggs, fresh raspberries).

SARS-CoV and MERS-CoV were emerging diseases so no medical treatment or vaccines were available and control of the epidemics relied on rapid diagnosis, isolation of patients and attention to infection control. This will also be the case for any future pandemics caused by emerging viruses. According to WHO (2015) cleaning surfaces with water and detergent followed by application of a commonly used disinfectant is an effective and sufficient procedure to ensure good environment hygiene.

Rutala and Weber (2014) proposed a hierarchy approach to anticipating the effectiveness based on the general resistance to disinfection of various microorganisms, shown in the table below.

Table 2: Hierarchy of Microbial Resistance to Disinfectants and Sterililants

Most Resistant	Microorganism	Aqualution BS EN tests
	Spores (eg <i>C. difficile</i>)	BS EN 13704:2002; BS EN 13727:2003
	Mycobacteria (eg <i>M. tuberculosis</i>)	BS EN 14204:2012; BS EN 14348:2005
	Non-Enveloped Viruses (eg norovirus, polio)	BS EN 14476:2013
	Fungi (eg <i>Candida albicans</i>)	BS EN 13697:2001; BS EN 1275:1997
	Bacteria (eg MRSA, VRE, Acinetobacter)	BS EN 1040:2005; BS EN 1276:2009; BS EN 13697:2001; BS EN 1656:2009
	Enveloped Viruses (eg HIV, influenza,)	BS EN 14476:2013
Most Susceptible	Adapted from Spaulding, 1957 and Rutala and Weber, 2014	

In the table above, enveloped viruses are at the bottom of the table in the most susceptible group ie the easiest class of microorganisms to kill. 2019-nCoV is an enveloped virus and falls into this group, therefore we would expect disinfectants effective against this group to also be effective against Coronavirus, when used as per directions of use. We are not currently able to test Aqualution products against 2019-nCoV as the strain is not available for laboratory testing. In addition, even if samples were available, it is not possible to make any definitive claims until regulators review and approve those claims, this is the situation with the newly identified Coronavirus.

However, Aqualution products have passed British Standards tests for virus efficacy and we have conducted our own in-house testing against a wide range of viruses, both enveloped and non-enveloped. We constantly strive to ensure that Aqualution products are efficacious and as such have performed many tests against a wide range of organisms. We have passed all the BS EN tests highlighted in the table above and have not failed to achieve a positive test result to date. We have also carried out tests on a wide range of other organisms to satisfy the very vigorous demands of the Biocidal Products Regulation (BPR) under which our active substance is approved and for which we own the dossiers submitted to ECHA regulating Aqualution hypochlorous acid throughout the European Union.

Selecting the most suitable disinfectant is one of the two components essential for effective environmental disinfection. The other component is ensuring that the disinfectant contacts all surfaces, is given the correct dwell time and that manufacturers label instructions are followed. This relies on proper training of hospital staff, especially environmental staff and infection control nurses. The combination of product and practice results in effective surface disinfection, the reduction of patient risk and improved patient outcomes. The five key considerations when selecting a disinfectant are summarized in the table below. The authors of the guidance framework (Rutala and Weber, 2014) suggest giving potential disinfectant products a score in each of the five categories and recommend that the optimal product is the one with the highest score. Aqualution hypochlorous acid manufactured by



Aqualution Systems achieves very high scores and as such could offer a safe and efficacious disinfection option in domestic, community and healthcare settings.

Our findings demonstrate that it consistently performs well under both laboratory and field conditions and as such is fit for purpose. We have passed many efficacy tests, including the stipulated BS EN tests. We have achieved the required >3 log reductions in viral loads both under laboratory and commercial “real life” conditions. Alcohol-based sanitizers and disinfectants are effective against viruses in laboratory-based tests, and therefore recommended to prevent viral transmission. However they do not always appear to be effective in “real life” situations. Similarly, the glutaraldehydes tested by Rabenau and workers (2005) achieved good log reductions of viral loading on surfaces. However, their very long contact times (30 -60 minutes) mean that they may be of limited “real world” use as it is not practical nor in some cases safe, to leave them on the surface for that length of time. Aqualution hypochlorous acid achieves >5 log viral reductions in less than a minute and is therefore effective in a spray and wipe cleaning regime.

Aqualution’s Aqualution hypochlorous acid is safe for people and the environment. It can be misted into the environment when people and animals are in place with no deleterious effects. It can be sprayed onto a surface and left with no fear of toxic residues. Workers do not need any PPE to handle it. It can be used on soft and hard surfaces. It is extremely versatile and can be used as a dip, spray, mist or fog. It is simple to use therefore compliance is high. It does not lose efficacy at low temperatures. It has a 12 month shelf life if kept at suitable storage conditions.



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Table. Key Considerations for Selecting the Optimal Disinfectant for Your Facility.

Consideration	Questions to Ask	Score (1-10)
Kill Claims	<p>Does the product kill the most prevalent healthcare pathogens, including those that:</p> <ul style="list-style-type: none"> • Cause most HAIs? • Cause most outbreaks? • Are of concern in your facility? 	
Kill Times and Wet-Contact Times	<ul style="list-style-type: none"> • How quickly does the product kill the prevalent healthcare pathogens? • Does the product keep surfaces visibly wet for the kill times listed on its label? 	
Safety	<ul style="list-style-type: none"> • Does the product have an acceptable toxicity rating? • Does the product have an acceptable flammability rating? • Is a minimum level of Personal Protective Equipment (PPE) required? • Is the product compatible with the common surfaces in your facility? 	
Ease-of-Use	<ul style="list-style-type: none"> • Is the product odor considered acceptable? • Does the product have an acceptable shelf-life? • Does the product come in convenient forms to meet your facility's needs (e.g. liquids, sprays, refills, and multiple wipe sizes, etc.)? • Does the product work in the presence of organic matter? • Is the product water soluble? • Does the product clean and disinfect in a single step? • Are the directions for use simple and clear? 	
Other factors	<ul style="list-style-type: none"> • Does the supplier offer comprehensive training and ongoing education, both in-person and virtual? • Does the supplier offer 24-7 customer support? • Is the overall cost of the product acceptable (considering product capabilities, costs of infections that may be prevented and costs per compliant use)? • Can the product help standardize disinfectants used in your facility? 	

CONCLUSION

SARS-CoV, MERS-CoV and 2019-nCoV were and are emerging diseases with no immediate availability of medical treatment or vaccines. This will also be the case for any future pandemics caused by emerging viruses. There is a strong likelihood that other emergent zoonotic viral pandemics will occur in the future. Little evidence is available in the literature concerning inactivation of viruses by disinfectants. What is available indicates that viruses, especially enveloped ones, are relatively easy to inactivate and a wide range of disinfectants may be effective. Important potential areas of contamination / transfer include people (isolation, face masks), animals (hand hygiene), food (thorough cooking, pasteurisation) and the environment (hard surfaces). Rapid case identification, isolation of patients and infection control measures are essential to prevent the spread of these emerging viral diseases within households, the community and health care facilities. Aqualution hypochlorous acid is not specifically tested against 2019-nCoV – no disinfectant is - but it is tested and efficacious against a wide range of microorganisms including spores, bacteria and other viruses (enveloped and non-enveloped) leading to the reasonable conclusion that it will be effective.

Controlling environmental hygiene in homes, public places and health care facilities is paramount. Viruses are able to persist in the environment for days but are relatively easy to kill, especially enveloped ones. Disinfectants need to have complete virucidal activity against both enveloped and non-enveloped viruses. Data on the efficacy of disinfectants against coronavirus are very limited. The BS for virucidal activity (BS EN 14476:2013) uses Adenovirus and Poliovirus as the test organisms, both of which are non-enveloped. Aqualution hypochlorous acid has been tested against viruses and has been shown to have virucidal properties (Pineau, 2000). It has achieved >5 log reductions against orthopoxvirus (enveloped), adenovirus (non-enveloped) and poliovirus (non-enveloped). Disinfectants work best in clean conditions so it is important to clean (with a detergent) then disinfect for optimal results. Although some products pass lab based virucidal tests, they do not work well in “real life” conditions, especially in the presence of soil / organic material. Many products are effective in lab tests but need extended contact times (30 minutes to several hours) to be effective. Again, this is not compatible with “real life” needs for a disinfectant.

Aqualution hypochlorous acid is fast acting with contact times typically less than a minute. It is safe for people and safe for the environment. It is versatile and can be used as a dip, skin irrigant, spray, mist or fog. There may be opportunity to fog areas with disinfectant in an attempt to reduce / inactivate viral load in the air and environment. It is extremely effective against a wide range of micro-organisms, including enveloped viruses. As such it is suitable for use as a broad spectrum, easy to use, efficacious and safe disinfectant.

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