CHLORINE DIOXIDE (ClO_2)

THE CHEMISTRY, MICROBIAL RESISTANCE AND IMPORTANCE OF APPROPRIATE BIOCIDE SELECTION

TABLE 1. OXIDANT CAPACITY
*MULTIPLE PART REDUCTIONS

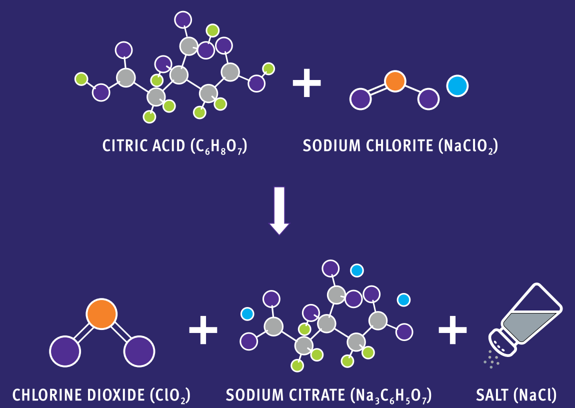
OXIDANT	OXIDATION POTENTIAL (V)	TOTAL OXIDATION CAPACITY
CHLORINE DIOXIDE (ClO_2)	0.95	5 e-*
AQUEOUS CHLORINE	1.48	2 e-
PERACETIC ACID	1.76	2 e-*
HYDROGEN PEROXIDE (H_2O_2)	1.78	2 e-

FIGURE 1. THE REDUCTION OF CHLORINE DIOXIDE

STEP 1. $ClO_2 + e^- \longrightarrow ClO_2^-$

STEP 2. $ClO_2^- + 4H^+ + 4e^- \longrightarrow Cl^- + 2H_2O$

FIGURE 2. CHLORINE DIOXIDE GENERATION



CHLORINE DIOXIDE (ClO_2): THE CHEMISTRY BEHIND THE FUNCTION

Chlorine dioxide has been used in the water treatment industry for the past century. The World Health Organisation approves ClO_2 for the disinfection of drinking water. Tristel's proprietary ClO_2 formulation has become the go-to high-level disinfectant for non-lumened heat sensitive medical devices. Chlorine dioxide is a biocide with the broadest efficacy against microbial organisms such as bacteria, viruses, protozoa, yeasts, fungi, mycobacteria and bacterial spores.

The biocidal activity of ClO_2 is attributed to its oxidative action against microbes. This is highlighted in Table 1. The '**OXIDATION POTENTIAL**' (Potential) of the chemical is its capability to obtain electrons from nearby molecules. The Potential of ClO_2 is lower than that of peracetic acid, hydrogen peroxide and aqueous chorine. Importantly ClO_2 displays a higher biocidal efficacy than other stronger oxidisers. The higher the Potential, the more corrosive the chemical. This means ClO_2 is a powerful, but less corrosive biocide than other oxidisers.

Chlorine dioxide has a higher '**OXIDATIVE CAPACITY**' (Capacity) than any of the other three aforementioned chemicals. The Capacity of chemicals denotes the number of electrons one molecule can accept from its surrounding molecules. In ClO_2's case this means that it can gain five electrons from microbial species per molecule, making it a superior biocide to alternative oxidisers, which typically are only able to gain two. This enhanced effect is attributed to its two-step reduction **(Figure 1)**.

Figure 1 shows the reduction of ClO_2. In the first step, ClO_2 is reduced to a chlorite ion after the acceptance of one electron. The chlorite ion then undergoes another reaction in which it is further reduced by accepting an additional four electrons and four hydrogen atoms. This two-step process allows it to sequester a higher number of electrons from microbes compared to other oxidisers. This means that chlorine dioxide will have a decreased corrosive effect on surfaces it is applied to, whilst having an enhanced ability to kill.

The reason why oxidative agents such as ClO_2 are favoured over non-oxidising disinfectants is due to their proven powerful efficacy against bacterial spores and other microorganisms within short contact times. Substances like alcohols and quaternary ammonium compounds are not sporicidal and do not provide this level of efficacy.

Chlorine dioxide kills pathogens via electron exchange, sequestering electrons from the microorganism's vital structures such as cell walls, membranes, organelles and genetic materials, which causes a molecular imbalance leading to the microorganism's death. Microbes cannot develop resistance to the action of ClO_2 because they are destroyed.

Figure 2 shows the reaction by which Tristel's proprietary ClO_2 chemistry is generated. The generation of Tristel's ClO_2 leaves no harmful by-products after use. The reaction itself generates ClO_2, sodium citrate and salt. Sodium citrate and salt are common food additives/ preservatives that pose no threat to the patient, user or equipment. In addition to the primary reaction products, water is also formed.

MICROBIAL RESISTANCE AND THE IMPORTANCE OF APPROPRIATE BIOCIDE SELECTION

Antimicrobial resistance occurs when organisms evolve to grow in the presence of chemicals which would ordinarily kill them. Excessive and improper use of antibiotics and biocides alike, across human clinical settings and animal breeding, has led to a dramatic increase in antimicrobial resistance.

The rising prominence of antimicrobial resistance in pathogenic microorganisms has in time become a major health concern and a severe risk for patients. The role of biocides in the increase of antimicrobial resistance has in recent years been a key research area, with several studies identifying the low-level biocide discharge in biosystems as a driver for selection of antimicrobial resistant organisms[1]. The risks of using inappropriate or sub-optimal biocides has additionally been shown to directly affect physiological traits in microbes, with studies finding for example, that exposure to sub-optimal biocides caused an increased expression of drug efflux pumps in Salmonella strains[2]. Mutations such as these would subsequently lead to increased antibiotic and biocidal resistance. For patient and staff safety it is imperative that the appropriate biocides are used.

Biocides such as quaternary ammonium compounds and triamines have been shown in multiple studies to contribute to the rise of antimicrobial resistance, with several resistant strains being identified, including *E.coli*[3] and *C.difficile* spores[4]. Whereas with biocides such as ClO_2, microbial resistance is not possible[5]. This is due to the chemistry's mode of action, acting as a strong oxidiser, sequestering electrons form microbial structures and attacking the cells molecular integrity. This breaks down the membrane, disrupting protein function, inhibiting RNA synthesis and killing the microbes[6].

One could say that ClO_2 is a remarkable molecule. It provides the complete solution for disinfection: killing the widest range of microbes in short contact times, whilst having fewer corrosive effects on surfaces. Furthermore, using ClO_2 avoids the threat of microbial resistance.

WE HAVE CHEMISTRY.

[1] Morrissey, I., Oggioni, M., Knight, D., Curiao, T., Coque, T., Kalkanci, A. and Martinez, J. (2014). Evaluation of Epidemiological Cut-Off Values Indicates that Biocide Resistant Subpopulations Are Uncommon in Natural Isolates of Clinically-Relevant Microorganisms. PLoS ONE, 9(1), p.e86669.

[2] Whitehead, R., Overton, T., Kemp, C. and Webber, M. (2011). Exposure of Salmonella enterica Serovar Typhimurium to High Level Biocide Challenge Can Select Multidrug Resistant Mutants in a Single Step. PLoS ONE, 6(7), p.e22833.

[3] Hansen, L. S., Jensen, L. B., and Sørensen, H. I. (2007). Substrate specificity of the OqxAB multidrug resistance pump in Escherichia coli and selected enteric bacteria. J. Antimicrob. Chemother. 60, 145–147.

[4] Macleod-Glover N, Sadowski C. Efficacy of cleaning products for C. difficile: environmental strategies to reduce the spread of Clostridium difficile-associated diarrhea in geriatric rehabilitation. Can Fam Physician. 2010;56(5):417–423.

[5] Noszticzius, Z., Wittmann, M., Kály-Kullai, K., Beregvári, Z., Kiss, I., Rosivall, L. and Szegedi, J. (2013). Chlorine Dioxide Is a Size-Selective Antimicrobial Agent. PLoS ONE, 8(11), p.e79157.

[6] Block, S., Knapp, J. and Battisti, D. (2001). Disinfection, sterilization, and preservation. Philadelphia: Lippincott Williams & Wilkins, pp.215-227.

Created by: T +44 (0) 1638 721500 - **E** mail@tristel.com - **W** www.tristel.com

For Tristel patent information please visit: http://www.our-patents.info/tristel

Copyright © Tristel Solutions TRS-019-1 - September 2019