KLORTAB NADCC INFECTION CONTROL STUDIES

1.0 INTRODUCTION

Necessity for Infection Control Programs

A successful infection control program consists of many related compounds that contribute to the health and well-being of patients and workers in the medical environment.

The program should be practical, have a scientific impact, and be based on socially acceptable features to prevent cross-infections. There are two basic reason for completing the infection control programs in the hospitals, dental and medical institutions.

First, there is an obvious moral duty to minimize the risk of infection of patients and employees, including nosocomial infections (hospital-transmitted). In generally spoken, the patients are more sensitive against to infection than the general hospital population. This can be due to prolonged illness, treatment that prevents immune reactions from occurring, or medical and surgical procedures. The patients in the hospital are ready especially to get their successful treatment and even life-threatening infections. In additional, In addition, patients who have admitted long-term infections may contact other suspected patients directly or indirectly using the same nurses and doctors. Further, the use of high levels of antibiotics in medical treatment centers facilitates the emergence of more resistant strains of bacteria that lead to the transmission of more virulent species to patients and workers. The most important task is to control the spread of the infection caused by these species to the environment.

Secondly, the infection is more expensive for health authorities. Nosocomial infection increased the treatment costs and the number of bed/days are occupied by patients. It is difficult to assess the cost effects of an infection program, but the necessity and success of a rational program has been proven by the American Study on the Efficacy of Nosocomial Infection Control (SENIC) (1). This project compared the infection frequency of 500 deliberately selected patients in 338 randomly selected clinics, which differ greatly from hospital hygienic supervision in 1970 and 1976. Evaluation of data from 338,000 patients who stayed in hospital for more than 3.5 million days clearly demonstrated the effects of infection control in reducing infection rates in hospitals. The project proves that while the infection rate in clinics without an infection control program is over 18%, the infection rate has decreased by 32% in clinics where an infection control program is applied in the same period.

An infection control program should be both morally beneficial and less cost effective. The program should be considered as part of a detailed policy to create good quality care for patients.

Sterilization and disinfection procedures are an integral part of any infection control program that provides a safe environment for patients and staff. These procedures are reviewed as a reminder in this report.

2.0 STERILIZATION AND DISINFECTION

Sterilization is the complete destruction or destroy of all forms of microbial creatures..

High-grade disinfection describes a process for destroying all microorganisms except most of the bacterial spores.

Medium-grade disinfection inactivates Mycobacteria, vegetative bacteria, viruses and fungi, excluding bacterial spores.

Low-grade disinfection kills bacteria, some viruses and fungi, but it is not a reliable method to kill resistant microorganisms such as tuberculosis bacilli and bacterial spores.

Sterilization and disinfection are terms used to describe the effect on inanimate objects.

Sterilization

Critical materials entering tissues or vascular (vascular) systems, surgical instruments with blood on them, cardiac and urinary catheters, implantation materials, needles, etc. materials such as require sterilization.

Disinfection:

The disinfectants are used for three basic purposes in infection control program.

i) making contaminated materials safe for further use,
ii) Removing or destroying pathogenic microbial organisms from environmental surfaces,
iii) to prevent infection likely to spread from microorganisms through contaminated wastes.

High-grade disinfection is used in semi-critical devices and high-risk areas (ie operating rooms, intensive care, autopsy rooms, clinical laboratories, etc.) that are in direct contact with mucous membranes or skin (i.e. respiratory therapy and anesthesia instruments, endoscopes, etc). Disinfectants to be used in such places need sporicidal (killing spores) effect.

Medium-grade disinfection is used in intermediate risk zones (patient locations, diagnostic rooms, sterile supplies) with some semi-critical items (ie oral and rectal thermometers, latches, etc.). Disinfectants need a tuberculocidal effect.

Low-grade disinfection is used in low-risk areas (administration, cafeteria, kitchens and other sick-free areas) with non-critical materials (ie crutches, bed rails, stethoscopes and pottery, etc.).

ADA AQUA CHEMICAL INDUSTRY AND TRADE INC.
Çamlıca Mah. 47. Cad. Dimas İşyerleri Sitesi No:4-C Yenimahalle Ankara
PHONE: 0312 387 00 47 FAX: 0312 387 00 43 GSM: 0554 870 50 01
E.MAIL: info@adaaqua.com.tr www.adaaqua.com.tr

The following guidelines are recommended when considering the necessary disinfection effect to prevent the local distribution of infection.:

USING AREAS SAHASI	THE REQUIRED MICROBIOCIDAL EFFECT				
	Sporicidal	Tuberculocidal	Virucidal	Fungicidal	Bactericidal
High Risk Areas : Operating rooms, morgue, autopsy rooms, intensive care, isolation units, laboratories, pathology and laboratory residues	√	√	√	√	√
Medium Risk Areas : Areas where patients are located, diagnostic rooms, sterile supplies	-	√	√	√	√
Low Risk Areas : Patient-free environments, kitchens, cafeteria, management units, stretchers, etc.	-	-	-	-	√

There are many key factors to consider in selecting an appropriate disinfectant.

- Given its proper use, it should have a demonstrable broad spectrum effect.
- It should have a quick effect for surface disinfection.
- As far as possible, it should be compatible with environmental factors such as soap, water hardness, organic materials, plastics, stainless steel.
- In the form of use solution, it should be non-toxic, non-corrosive, and not irritating.
- It must have a long-term durability.
- The price should be cheap at the form of using solution.
- Real dilutions must be easy to understand and quickly prepared..
- Storage and transport should be simple and inexpensive, eliminating the need for professional knowledge, weighing / measuring and special dilution solutions.

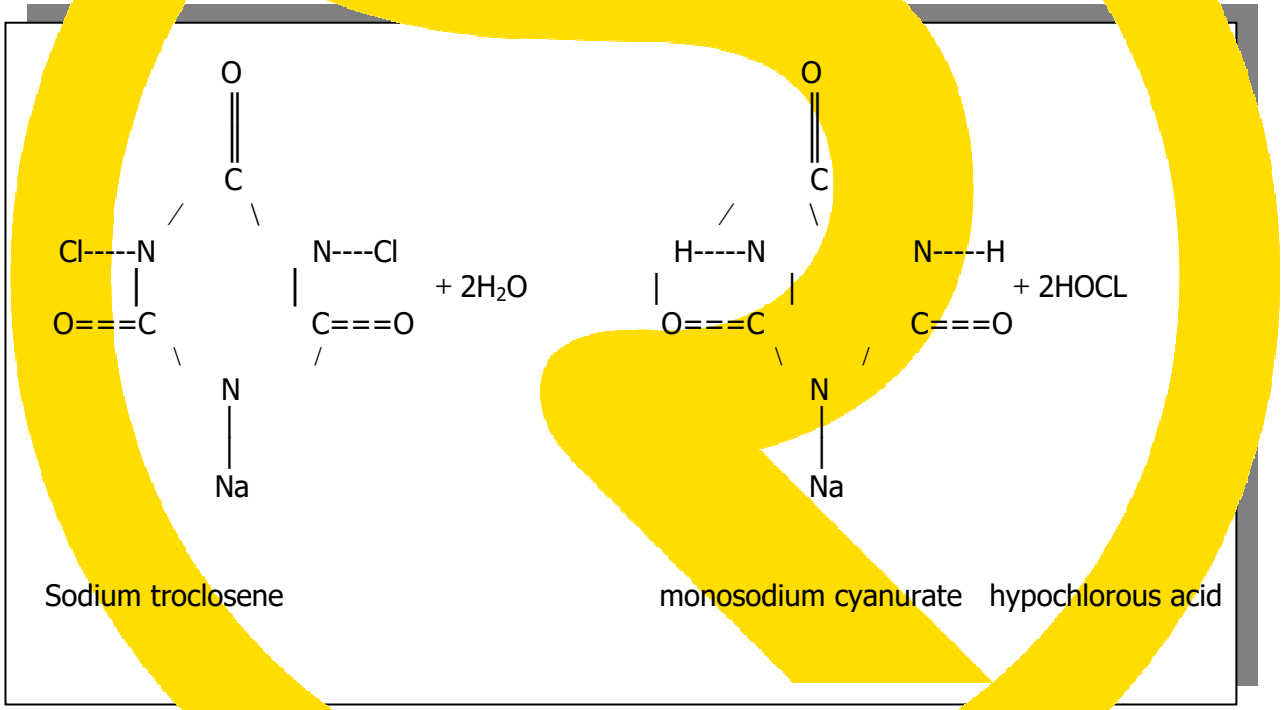
It should be remembered that different disinfectants are never interchanged. The use of unsuitable disinfectants or usage solutions can cause increased costs.

3.0 KLORTAB NADCC

Klortab NaDCC are environmental disinfectants that can be used at all levels (it is not recommended to leave metal materials and tools in for long periods). Klortab NaDCC is available in effervescent form which, when thrown into water, delivers disinfectant solutions of known and correct strengths.
The active ingredient of these products is sodium troclosene. (Also known as NaDCC and sodium dichloro-s-triazine trion.)

3.1 Chemistry of NaDCC :

NaDCC; It is the sodium salt of 1,3-dichloro-1,3,5-triazine-2,4,6 (1H, 3H, 5H) -trione and contains about 60% 'available chlorine'. When dissolved in water, hypochlorous acid (active compound) and monosodium cyanurate (non-toxic compound) are rapidly released.



In general, the biocidal killing of organisms occurs by chlorination of protein cells or enzyme systems by means of undissolved hypochlorous acid, which causes hydrolysis of the peptidic chains of pathogenic microbes with cellulosic membranes..

3.2. Comparison of NaDCC and other chlorine donors:

Although hypochlorous acid is the biocidal compound that is released in other chlorinated disinfectants (sodium hypochlorite and calcium hypochlorite, etc.), the effect and biocidal capacity of NaDCC is far superior to theirs due to two important factors.

ADA AQUA CHEMICAL INDUSTRY AND TRADE INC.
Çamlıca Mah. 47. Cad. Dimas İşyerleri Sitesi No:4-C Yenimahalle Ankara
PHONE: 0312 387 00 47 FAX: 0312 387 00 43 GSM: 0554 870 50 01
E.MAIL: info@adaaqua.com.tr www.adaaqua.com.tr

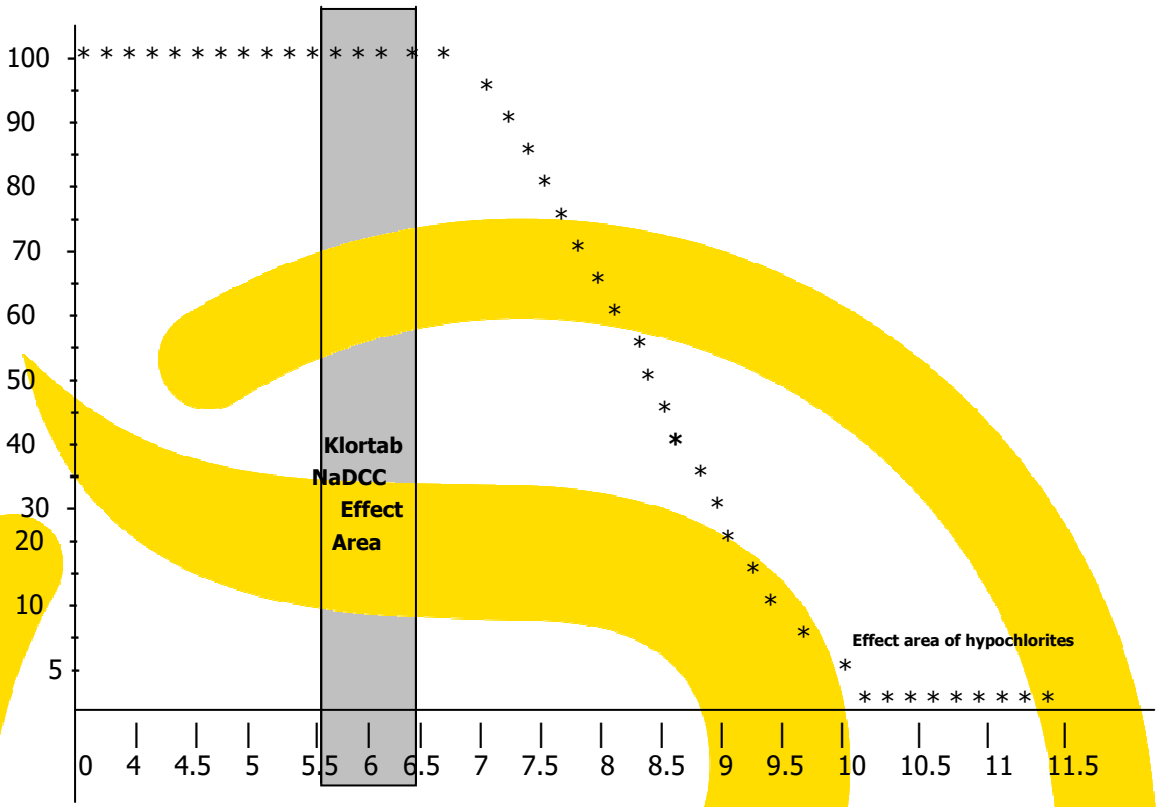
First, NaDCC creates acidic solutions, unlike other chlorinated products such as sodium hypochlorite (bleach) that form alkaline solutions. HOCl thus differs according to the alkalinity and acidity (pH) of the solution as shown below.

$$HOCl \rightleftharpoons OCl^- + H^+$$

HOCl and OCl^- (hypochlorite ion) represent measured free chlorine in solution and are generally defined as milligrams per liter (or parts per million - ppm). However, OCl^- has one percent of undissolved HOCl and therefore has a fairly small biocidal effect. This dissolution depends on pH.

	PH	% HOCl (@ 20^0C)
A C I D	5.0	99.740
	5.5	99.180
	6.0	97.450
	6.5	92.370
Natural (pure water)	7.0	79.290
A L K A L I N E	7.5	54.770
	8.0	27.690
	8.5	10.800
	9.0	3.690
	10.0	1.190
	10.5	0.380
	11.0	0.120
	11.5	0.012

While inorganic hypochlorites produce very alkaline solutions with pH levels above 9.5, the pH levels of Klortab NaDCC products are at the level of 5.5 to 6.5. Thus, while Klortab NaDCC produces free obtainable chlorine containing more than 90% undissolved HOCl, inorganic hypochlorites release free obtainable chlorine with 10% undissolved HOCl.



Secondly, only 50% of the total available chlorine in Klortab NaDCC products is 'free' and the rest is 'bound' as mono or dichloroisocyanurate. This equality between 'free' and 'bound' chlorine remains constant until the need for chlorine in solution arises from microorganisms, organic or nitrogenous substances that replace hypochlorous acid. This disrupts the order of chemical equation, allowing the rapid displacement of more hypochlorous acid used to satisfy the chlorine demand. This process continues until the available 'free' chlorine is exhausted. This whole equation, the increased release of 'free' chlorine has been found with these products, it provides self-regulation, giving improved effect and safety in use compared to other chlorine agents..

The release of this 'latent' chlorine provides a greater biocidal effect found with NaDCC compared to inorganic hypochlorites, and defines that NaDCC is less inactivated by organic substances. It further explains why NaDCC solutions are less corrosive and less toxic[2].

Many studies confirm the superbiosidal effect of NaDCC.

3.3 Comparative biocidal effect of NaDCC and Sodium Hypochlorites (NaOCl):

Bacteria and Fungus :

In one study[3], the effect of NaDCC solutions was compared with a hypochlorite solution containing an equal amount of available chlorine concentration (125ppm) against Escherichia coli strain. While effective in both formulations, NaDCC has a killing capacity at least twice as much as the hypochlorite formulation, ie the retained bactericidal capacity at half strength of

NaDCC (62.5ppm) is equal to the full strength of the hypochlorite solution. Furthermore, there is a marked difference in how both formulations are affected by milk. While 2% milk actually inactivates the product, 1% milk is sufficient to reduce the bactericidal ability of hypochlorites to less than 10^6 organisms per milliliter. NaDCC retains its bactericidal ability to retain more than 10^8 organisms per milliliter, even against 2% milk.

In another study[4], the disinfection capacities of both NaDCC and NaOCl formulations were compared with bacterial species such as Pseudomonas aeruginosa, Escherichia coli, Staphylococcus aureus and Klebsiella aerogenes and fungi species such as Candida albicans at 'use' concentrations containing 125ppm of available chlorine. Disinfecting capabilities for all bacterial species are greater than 10^9 organisms per milliliter, while for C. albicans more than 10^7 organisms per milliliter. Ability tests have also been achieved using 50% NaDCC 'use' solution to obtain an exact estimate of the 'killing site' using the same inoculation for both NaDCC and NaOCl formulations. Both formulations showed a high disinfectant ability, but as tested further in E. coli, NaDCC showed a significantly higher effect against bacterial strains, but no significant change against C. albicans.

In a later study[5], a comparison was made between NaDCC and NaOCl solutions versus Pseudomonas aeruginosa versus horse serum. The degree of inactivation with various concentrations of horse serum was measured and declared under a neutralization coefficient condition. Inactivation of NaDCC solutions is demonstrably much less than NaOCl solutions, separated by unevenness. In a 30% serum, a NaDCC solution containing 4000ppm of available chlorine showed the same bactericidal effect as a NaOCl solution containing 17000ppm of available chlorine. This superior ability of the NaDCC is exemplified better in regions where organic contamination is by blood and an inequality is expected due to the expectation to cause more inactivation from the same level of serum.

Spores :

Many studies[6] have supported previous studies by proving the super effect of NaDCC on NaOCl against plasma concentrations of 2.5% to 20% (v / v). A NaDCC solution with 3000 ppm available chlorine, pH 6.6, gave a sufficient effect against 20% plasma, while NaOCl solution concentrations of 5000 ppm available chlorine at 7.2, 9.0 and 10.6pH were inactivated. In the same study, a NaDCC solution containing 5000ppm of available chlorine and at pH 6.6, in a suspension of 3.6 x 108 Bacillus subtilis spores organisms per milliliter within 5 minutes, 5-6 log reduction (99.999% to 99.9999% reduction) and 200ppm concentration. It produced 5 log reduction within 30 minutes. The concentration of a NaOCl solution containing 5000 ppm achievable chlorine at pH 10.6 showed a reduction of only 3-4 log within 5 minutes, with a concentration of 200 ppm showing little or no effect within 30 minutes.

Mycobacteria :

The effect of 6.000ppm achievable chlorine-containing concentrations of NaOCl and NaDCC was compared as mycobactericidal agent on Mycobacterium tuberculosis - contaminated suspensions (suspension test) and stainless steel surfaces (carrier test). In a sputum-free environment, after 1 minute of contact time, NaOCl achieved 2 log-reduction in both suspension and vehicle test, while NaDCC achieved 4 log-reduction in suspension test and 3

log-reduction in vehicle test. As a result of tests with sputum addition, there was only 2 log-reductions in both suspension and vehicle tests with NaOCl, while with NaDCC, 4 log-reductions in the suspension test and 2 log-reductions in the vehicle test.

Viruses :

A test has been developed to calculate the surface effect value of disinfectants against coverslip-dried viral preparations containing NaDCC and NaOCl formulations[7]. Each coverslip containing Herpes simplex virus Type 1, approximately 3 x 10^9 sheet forming units, was dried before being immersed in the disinfectant solution. At 2500ppm available chlorine level, the NaOCl solution showed 2.5 log-reduction after 1 minute, while the NaDCC solution produced 4.9 log-reduction. No virus was detected in either formulation after 5 minutes. At the 1000ppm level, no virus was detected in both formulations after 5 minutes, while the NaDCC formulation again showed a log-reduction approximately 2 times better than the NaOCl formulation after 5 minutes.

Using a quantitative suspension test method, the antiviral effects of NaOCl and NaDCC were investigated against Human Immunodeficiency Virus (HIV)[9]. Viral suspensions containing between 10^4 and 10^5 virus particles per milliliter in 0.9% saline solution were prepared to simulate clean and dirty conditions, with and without the addition of 10% volume / volume plasma. 4-5 log-reduction was achieved by both formulations containing 50ppm obtainable chlorine under 'clean' conditions, and both formulations with 2500ppm achievable chlorine concentrations showed the same success in the environment with 10% plasma. Additional NaDCC and NaOCl solutions containing 10,000 ppm of available chlorine were sufficient for a total kill within 2 minutes to equalize to the contaminated blood volumes (giving the blood a final achievable concentration of chlorine of 5,000 ppm).

All the above test results show the fast and broad spectrum effect of NaDCC as a microbicide and its super effect on NaOCl, especially where there is organic contamination.

4.0 PUBLISHED GUIDE DILUTIONS

Infection control programs clearly define and standardize methods for decontamination (ie sterilization, disinfection and cleaning) of equipment and the environment. Infection control programs must ensure that the same disinfectants and concentrations are used everywhere for similar purposes.

The use of chlorine products to control infections in medical areas has a long and successful history. The first records of chlorine gas treatment in hospitals with smoke date back to 1791. However, the widespread use of chlorine solutions in medical environments began in the second half of the 19th century and continues to be used in the same way all over the world. The popularity of chlorine is justified due to its wide range of effects as a biocide and its proven power. It is very easy to apply, measure and control, completely free from toxic and physiological effects and very cheap. Other agents are either equal to or slightly superior to any of these properties, but none of them can combine these properties in an advantageous manner.
This long story of use gives strength to the authoritative manuals recommended by various international approval organizations. Some of these published guides are listed below.

4.1. Human Immunodeficiency Virus (HIV) and Hepatitis B Virus (HBV)

Blood or excess fluid spills. The spillage is washed thoroughly with solution and the surface is subsequently wiped.

Recommended solution strength: 5.000 - 10.000ppm available chlorine power[10,11,12,13,14,15,16,17]

Alternatively, chlorine-containing granules are recommended to absorb and disinfect the spill.

4.2. Laboratory Waste Jars, pipettes

Disinfection of laboratory pipettes, jars
Recommended solution strength: 2.500ppm available chlorine[10]

4.3. General Environmental Disinfection at the High Level Risk Areas

Disinfection of high risk areas as Operation rooms, autopsy rooms, laboratories

Recommended solution strength : 1.000 – 5000ppm available chlorine[10,11,12,13,14,16,17]

All surfaces clean and disinfect.

4.4. Moderate and Low Risk Areas

There are ample and varied recommendations for cleaning and / or disinfection of Medium and Low Risk Zones.

Even though they are named as 'Moderate' and 'Low Risk', these regions must be clearly defined in infection control procedures.

5.0 STANDARDS OF ASSOCIATION FRANÇAISE DE NORMALISATION (AFNOR) :

When selecting a standard method for testing NaDCC products, a flawless, productive and standardized technique selection criteria with clearly defined microbial species, substances, inoculation and cultures were taken into account. The French AFNOR Standards, which are used all over Europe and accepted in international markets, are a homogeneous system based on standardized methods and an alphabetical ranking that calculates the positive value or degree of bactericidal, fungicidal, sporicidal and virucidal activity. Each stage of the activity criterion is based on a 5 log-reduction (99.999%) of microorganisms under standardized experimental conditions (inoculation, contact time, temperature, materials, media and reagents) using suspension and carrier tests with or without mixing agents.
In the majority of disinfectant samples (for medium and low risk zones - see Section 2), it is in principle necessary to reduce the amount of bacteria and limit their spread on surfaces. In other cases (for high risk areas) disinfection should have a killing effect on bacteria, viruses, fungi and spores

5.1 Moderate and Low Risk Areas (General Environment)

For dosage requirements in low-risk and intermediate-risk zones, assessments are made for bacterial species such as ***Pseudomonas aeruginosa, Escherichia coli, Stphylococcus aureus, Enterococcus faecium*** and ***mycobacterial species*** such as ***Mycobacterium smegmatis*** in suspension tests with or without ingredients (reference Annex I), 100ppm can be obtained (NFT 72 151) and a concentration with 150ppm of available chlorine (NFT 72 170) compliant with the standard (milk).

When testing a fungal species ***Candida albicans*** in suspension, the 50ppm achievable chlorine-containing concentration complies with the NFT 72 201 standard.

In the surface carrier test (glass disc), the 100ppm available chlorine-containing concentration complies with the NFT 72 190 standard against the 5 bacterial strains mentioned above.

In addition, the NaDCC was tested at a maximum 140ppm achievable chlorine concentration in a suspension test with both 20% human serum as a mixing agent and no mixing agent, in order to comply with the Italian Ministry of Health Circular No. 100 dated 24 November 1978[25]. The product was tested against ***Stphylococcus aureus, Escherichia coli, Pseudomonas aeruginosa, Pseudomonas mirabilis, Klebsiella pnemoniae, Salmonella typhi, Salmonella paratyphi A., Salmonella typhimurium, Salmonella faecalis, Proteus microorganism***[10]. In the absence of human serum, complete inactivation was achieved within 3 to 10 minutes, whereas in the presence of human serum, this was achieved within 6 to 30 minutes.

It should be borne in mind that a use concentration containing 200ppm obtainable chlorine is sufficient for low and medium-risk areas, giving adequate mycobicidal, fungicidal and bactericidal activity.

5.2. High risk Areas

For dosage requirements in high-risk areas, the product must be sporicidal. In a suspension test, a concentration of 650ppm obtainable chlorine meets the NFT 72 231 standard.

Sporicidal effect has been evaluated in accordance with the Italian Ministry of Health's circular dated November 20, 1978 and numbered 100[25]. The tests are carried out in the presence and absence of 20% blood serum, according to the methods defined by Borick et.al.[26] and Synder et.al.[27], ***Bacillus subtilis (a and b types), Bacillus sphaericus, Bacillus arothermophylus, Bacillus globigii, Clostridium tetani, Clostridium perfiringenes*** was obtained against USDA type spores. Inactivation is less than one hour in the absence of blood serum and less than two hours in the presence of blood serum against all microbial spores. In accordance with AOAC Official Analysis Reports (U.S. EPA registration)[28], ***Bacillus subtilis*** and ***Clostridium sporogenes spores*** were fertilized in silk suture knots and porcelain cylinders by establishing an exposure of 10 hours at 20^0C. Ninety copies of each test were undertaken, with no surviving sport found in any replicate.

It should be noted that a use concentration of 1000ppm obtainable chlorine is sufficient for high-risk areas, giving proven sporicidal, mycobicidal, fungicidal and bactericidal activity. This is consistent with many published guidelines recommendations.[10,11,12,14,16,17]

5.3. HIV and HBV

Body Fluid Spills

The use of chlorine containing granules has been calculated and recommended in many studies.[9,11,18,20].
For oversized spills, 10000ppm available chlorine-containing solution is recommended [10,11,12,15,16,17].

Virucidal effect has been evaluated in accordance with the circular number 100 dated November 24, 1978 of the Italian Ministry of Health[25]. Activity was evaluated against ***Hepatitis B Virus*** and ***Herpes simplex Virus*** on devices in the presence and absence of blood serum as mixing agent at a maximum available chlorine concentration of 140ppm. With the ***Herpes simplex virus***, the virus was incubated for 30 minutes after disinfection and then observed over a ten minute period. No activity was found at the end of the period. With the ***hepatitis B virus***, destruction rates were observed by electron microscopy. It was observed that complete elimination was completed within 45 minutes in serum-free medium and within 60 minutes in serum-free medium.
(Note that for a concentration of 10,000ppm achievable chlorine, the inactivation time is less than one minute in serum or serum-free media.)

(Chlorine-releasing products are not recommended to be poured on urine debris as it will react with uric acid to release chloride gas.)[21].

6.0 KLORTAB NADCC DILUTION GUIDES

For disinfection residues, distribution and control of guideline dilutions and recommendations are assigned to the individual responsibility of medical authorities and infection control personnel..

The following guides are recommendations based on useful studies and published guidelines..

KULLANIM SAHASI	KULLANIM METODU	SOLUTION STRENGTH OF KLORTAB NADCC Available Chlorine
HIV and HBV	The surface is first covered with a paper towel or other absorbent material, and then Klortab NaDCC solution is poured on the absorbed material and left for 10 minutes. Then, all waste is wiped with a new absorbent material and thrown into the infectious-waste carrier. The surface must then be disinfected with Klortab NaDCC solution.	**10.000ppm**
Infectious surfaces and equipment	All surfaces are wiped with Klortab NaDCC solution. Metal surfaces should be rinsed after application. The materials are immersed in the solution for 60 minutes.	**5.000ppm**
HIGH RISK AREAS Disposed jars, pipettes, slides	The materials to be discarded are left in solution for 60 minutes before being discarded.	**2.500ppm**
Operating rooms, autopsy rooms, burn units, intensive care, isolation units, clinical and pathology laboratories, etc.	Surfaces are cleaned and then wiped with Klortab NaDCC solution. Metal surfaces should be rinsed after application.	**1.000ppm**
GENERAL ENVIRONMENT, MEDIUM AND LOW-RISK ZONES Diagnostic rooms, sterile services, kitchens, cafeterias, around hydrotherapy pools, toilets, stretchers, etc. Sliders, bedpans, mats, food items ...	Surfaces are wiped with Klortab NaDCC solution. All materials, Sheets etc. It is pressed into the solution for 15 minutes.	**200ppm**
Notes : Klortab NaDCC is not recommended for materials that require sterilization. Extended immersion times are not recommended for metal materials as they can cause corrosion. Instructions and warnings inside the boxes should be followed carefully.		

7.0 PRESENTATION OF KLORTAB NADCC

Effectiveness of Klortab NaDCC products is an essential feature. However, it is also necessary for practical application and use.

It is imperative for dilutions to be obtained easily without the need for complete evaluations or the need to weigh or measure concentrated forces or liquids.

There is no wide limit of application rates for essentially the same end users. This only serves to complete the infection control program and eliminate the confusion users encounter. The dilutions recommended in previous sections describe this need and finally published recommendations and efficacy tests.

Klortab NaDCC offerings are formulated to ensure that usage dilutions are easily understood and obtained.

Tablet	Dilution Ratio		Available Chlorine Ppm
	Water quantity	Tablet	
Klortab NaDCC 5GR x 100 TABLET	7,5	1	200ppm
	1,5	1	1.000ppm
	1,5	5	5.000ppm
	1,5	10	10.000ppm
Klortab NaDCC 3,4GR x 30 TABLET	5	1	200ppm
	1	1	1.000ppm
	1	5	5.000ppm
	1	10	10.000ppm

8.0 ADVANTAGES OF KLORTAB NADCC

Klortab NaDCC has proven rapidity and broad spectrum activity. This activity has been independently verified (ISTANBUL YEDITEPE UNIVERSITY, IZMIR EGE UNIVERSITY)
The effect limits are suitable for disinfection in low, medium and high risk areas, in the form of effervescent tablets that dissolve safely and quickly
Effervescent tablets can be obtained to be combined with a suitable detergent
Klortab NaDCC series are very easy to transport and transport (they do not splash and leak) and require much less storage space than liquid products take up.
Usage solutions are easily understood and available and comply with many published guidelines.
Unlike many other disinfectants, especially chlorinated products, Klortab NaDCC has great stability: Klortab NaDCC - 2 years (Hypochlorites characteristically lose activity within months..)
Usage solutions are easily priced and very inexpensive[14]. In addition, there are many cost benefits implications of reduced waste (liquids and powders are frequently overdosed, KLORTAB NADCC is at full dosage) and reduced working time (such as measuring liquids or powders or calculating dilution and requirement dosages)..
Klortab NaDCC has a consistent quality and reliable strengths. Liquids and powders are produced in various strengths and compositions (e.g. bleaches, hypochlorites can be obtained in quantities of 1%, 2%, 5%, 5.25%, 10% 12%, these inconsistencies are very difficult to apply to an effective infection control program.
The Klortab NaDCC tablet strengths are tailored to meet the dilution requirements in an easily understandable manner. For example; Like 1 tablet per 7.5 liters (bucket). This process provides practical applications.
Derivatives of the active ingredient of Klortab NaDCC are relatively non-toxic and biodegradable in the environment (biodegradable).[22,23,24].

9.0 STABILITY

Sodium hypochlorite solutions are not stable due to their chemical structure; they are degraded by light, heat and heavy metal ions[29]. The strength of sodium hypochlorites does not only change with its decrease, but also, from brand to brand, precisely measuring "use" solutions with any confidence puts it in difficult situations. 10% strength (100.000ppm) NaOCl solutions lose 30% strength after 20 weeks and 60% after 1 year [30]

Klortab NaDCC, however, is very stable with a storage life of two years when stored in its original container and in dry conditions. Real 'use' solutions can be prepared simply and safely at any time and place.

10.0 TOXICOLOGY

Klortab NaDCC; It is compounded with sodium dichloroisocyanurate (NaDCC) into an inert effervescent base.
When dissolved in water, these products form effective chlorine solutions (see Section 3.3).

The use of chlorine in the form of hypochlorous acid as a surface disinfectant in infection control and water disinfection for human consumption has a long and successful history. For chlorine products, toxicity reasons have long been properly recognized. Therefore, this report does not include toxicity studies for chlorine.

The ingredients used for the inert effervescent base are pharmaceutical or food grade materials.

10.1 Sodium cyanurate

Sodium Cyanurate (also known as monosodium cyanurate, sodium isocyanurate, akvenosit B, NaCy) is the sodium salt of 1,3,5-triazine -2,4,6 (1H, 3H, 5H) - trion.

Acute Toxicity: Acute oral toxicity of sodium cyanurate in mouse studies[31] per kg. showed an LD50 of more than 7.5 grams per kilogram in rabbits and more than 20 grams per kilogram in rabbits. The LD50 for cats is given at 21.44 grams per kilogram[32].

The dermal LD50 in rabbits is more than 7.94 grams per kilogram[33].

Chronic / subchronic Toxicity : A diet containing 8% w / w sodium cyanurate was given to 3 dogs over a period of more than 2 years. No adverse effects were detected in growth, hematological parameters, chemical or microscopic urine analysis and pathology during the first 6 months. 2 of the dogs died after 16 months and 21 months, respectively. Microscopic examination; showed renal fibrosis, focal enlargement and epithelial proliferation (enlargement) in Bellini ducts. Autopsy of the third dog sacrificed after 2 years showed thyroid atrophy with lymphocyte infiltration but no hyperplasia, in addition to the same kidney changes. In contrast, when a diet containing 0.8% w / w sodium cyanurate was given to 3 dogs for 6 months, there was no proven adverse effect. Thyroids are not enlarged and kidney tissues and organ weights are normal[34].

Of the 20 male and 20 female rats fed with 8% w / w sodium cyanurate for 20 weeks, 14 males and 4 females died during the experimental period. Autopsy showed histological changes in the kidneys, possibly caused by the diuretic action of cyanuric acid - the focal regions of epithelial proliferation and the distal accumulation tubes and Bellini ducts were enlarged. In a parallel experiment, however, 0.8% w / w sodium cyanurate diet caused no toxic symptoms or pathological effects[34].

Pharmacokinetic data (rat, dog, human) have shown that oral cyanurate is rapidly excreted through excretion, while the ability of a tissue or organ to structure a certain substance is minimal in dermal exposure.[33,35]

Sodium cyanurate was given to rats at levels of 400, 1200, 2400 and 5375 ppm (maximum solubility) in randomly selected groups of - 24 months, 80 - 100 / breed / group for most of their lifetimes. Body weight and food and water consumption were measured at regular intervals. Hematology, clinical chemistry, and clinical parameters of chemical or microscopic analysis of urine were evaluated for each group sacrificed at 6, 12, 18 and 24 months. Treatment-related deaths were investigated in 13% of male mice given the 5375ppm dosage that died during the first 12 months. The deaths were attributed to stone formation in the

urinary tract of test animals at maximum resolution. This high concentration of cyanurate causes sedimentation to form stones, which causes inhibition and secondary effects such as uremia and pathological changes, as sensitive males cannot easily pass through the urinary tract (the male's urethra is anatomically more susceptible to blockage than females). During the second twelve months, there were no examination-related deaths. No intense dose-related evidence or microscopic pathological changes occurred in the tissues of test animals that died or were slaughtered during the last 12 months. Body weights, food consumption and clinical parameters have been compared both control and process groups. The water consumption is increased for high dosage cyanurate and sodium control groups. Based on tests, it was concluded that sodium cyanurate does not cause cancer in large male and female rats. During the first 12 months, no effect was observed at 2.400ppm (daily average consumption 154mg/kg for males and 266mg/kg for females). During the last 12 months, there was no effect at 5.375ppm (371mg/kg for males, 634mg/kg for females)

In a chronic mouse study, sodium cyanurate was administered to 80 - 100 mice / breed / treatment groups in drinking water at levels of 100, 400, 1200 and 5375ppm over 2 years[33]. The experimental design is the similar rat study previously described. Sodium cyanurate is a noncancerous agent for mice and absolutely no treatment-related effects occurred at any level tested. In addition, sodium cyanurate has been found to be unable to cause tumors in mice.

The subchronic (between chronic and half-hull) toxicity of sodium cyanurate was evaluated in a 13-week study in rats and mice[33]. Sodium cyanurate was given at a concentration of 5375ppm at maximum resolution. At this concentration, daily compound consumption 500 to 700 mg/kg for the rats and 2.000 to 2.200mg/kg for mices. The only adverse effect is the presence of bladder stones accompanying hyperplasia of the bladder epithelium. This is not surprising because of the precipitation at the maximum solubility level of sodium cyanurate. In a study related to this study, sodium cyanurate was administered by nasal gavage to rats and mice at a level of 500 to 6,000mg / kg / day for 14 weeks. No evidence of compound-related clinical changes and large microscopic lesions was found in tissues of high dosed rats and mice.

Irritation: The instillation of 0.1ml suspension of 8% sodium cyanurate daily in one eye of 5 albino rabbits for 5 days each week for 3 months did not cause any damage to the eyes[34]. Daily application of 5ml suspension containing 8% sodium cyanurate, 5 days a week for 3 months, did not cause any local irritation on approximately 10% of the body surfaces of albino rabbits, but caused a minor dilation in the Bellini ducts[34].

Teratogenicity (Freak formation) : Sodium cyanurate is given 50, 200 and 500mg per kilogram during the most important period of organogenicity (development of animal and plant organs) to pregnant Dutch belted rabbits via oral rubber gavage during the 6th - 18th days of pregnancy[33]. No compound-related deaths and adverse reactions were observed during the study period. A minor reduction in body weight was noted in animals given medium and high dosages. A compensatory weight gain occurred in these groups after finishing treatment on day 18. No evidence of fetal poisoning was seen on day 28 of pregnancy. The substantial amount of live fetus / mother animal and sex ratio was basically comparable in all groups. Body weights and crown / rump lengths of the fetus decreased insignificantly in animals given high dosages when compared for controls, however, these

values occurred within the important and historical limits of laboratory studies. No evidence of external and internal malformation (defective formation) or dosage-related growths at the extent of occurrence of the skeletal anomaly. Therefore, this process ended as sodium cyanurate was neither toxic nor teratogenic in rabbits.

Sodium cyanurate was administered to a group of 25 pregnant rats at levels of 200, 1,000 and 5,000 mg per kilogram from the 6th to the 15th day of pregnancy by nasal gavage during the most important period of organogenicity[36]. No deaths, changes in body weight and adverse reactions have been observed[31].

Mutagenicity (The ability to produce mutations related to genes or aberrations to chromosomes): The mutagenic possibility of sodium cyanurate is evaluated using In-vitro and in-vivo tests[37]. All in-vitro tests were performed in the presence or absence of metabolic activation. In each assay, the highest concentration of sodium cyanurate was generally tested when its solubility was excessive. In the Salmonella microbial assay, sodium cyanurate was not mutagenic up to a concentration of 10,000µg / platelic across all four test types. Sodium cyanurate L5178Y at 2,000µg / platelic concentration did not produce mutations (changes) in the TK locus of mouse lymphoma (tumor originating from lymphoid tissue) cells. In an in-vivo examination of the chromosome structure of the bone marrow by laboratory methods, rats were administered a single dose of 5,000mg / kg sodium cyanurate via a nasal gavage and were sacrificed 24 and 48 hours after this dosage administration. Bone marrow cells, chromosomal abnormalities are pooled and examined. As a result of these examinations, no evidence of chromosomal anomaly caused by sodium cyanurate was found.

Sodium cyanurate was administered to a group of 12 albino male mice as a single dose of 250ml per kilogram of body weight injected into the peritoneal sac. Each male mouse was placed in the breeding cage together with 3 virgin female mice. These female mice replaced 3 other females for six weeks. Male mice were sacrificed after six weeks and females were removed from the cage 1 week later. No significant differences were observed between the test and control groups in terms of embryos, mutation rates, implantation and resorption points. No treatment has caused a dominant (inherited superiority - dominant) death reaction [31].

Sodium cyanurate was not mutagenic in the in-vitro induction of cister chromatid change in a Chinese hamster's ovary (CHO) cell test (ensuring the proper and normal formation of various tissues and organs in an embryo)[38]. In this study, CHO cells exposed to 1.500µg/ml concentration.

Metabolism (Chemical changes occurring continuously in living matter): In a number of metabolism studies, it has been shown that cyanurate is easily excreted from the body without any changes.

Sodium cyanurate (^{14}C) was given to rats orally as a single dose of 5 or 500mg / kg and 5mg / kg intravenously every day for 15 days[39]. Sodium cyanurate was absorbed completely at 5mg / kg as a single dosage but partially at 500mg / kg. The substance is rapidly removed from the body, the elimination half-life is 30 to 40 minutes after IV at 5mg / kg, 40 to 60 minutes at 5mg / kg PO and 2.5 hours at 500mg / kg PO. No ^{14}C was revealed in tissues

except traces in the adrenal glands, fats, bladder and intestines within seven days following single exposure at 500mg / kg PO. Sodium cyanurate did not cause pathological changes in metabolically normal tissues in rats. After daily applications, no appreciable bioaccumulation occurred, and after 15 days of oral administration of 5mg / kg daily, no significant changes in sensitivity to certain effects and diseases or in metabolism were found.

The metabolic fate of sodium cyanurate was investigated in the dog using the same experimental procedures[33]. A low dosage of 5mg / kg was completely absorbed, whereas a dosage of 500mg / kg was partially absorbed. The dispersion of sodium cyanurate, which is somewhat greater than the total volume of water in the body, of 0.7 liter / kg was dispensed into an easily understandable volume. The half-life of excretion is set at 1.5 to 2 hours.

Cyanurate was easily excreted into urine without any changes. Radioactive inclusions in tissues are below emergence levels for single and repeated dosages. Cyanurate is not bio-accumulate in tissues and there is no evidence that cyanurate is not biodegreaded in dogs.

It has been shown that cyanurate can be clearly administered to humans since it is found that it is easily and quantitatively excreted from the urine of subjects given as an oral dosage, without any change[40].

Reproduction (Reproductive) : To quantify the long-term effects of sodium cyanurate on reproductive performance, the substance was administered to three successive groups of rats. [33]. Sodium cyanurate was administered to groups of rats of 12 males and 24 females at 400, 1,200 and 5.375ppm (maximum solubility) levels in drinking water. Treatment started in the 30-day period for the parents and continued for a minimum of 100 days before mating. Parents mated to give birth to 2 babies (A, B). The newly weaned (B) was randomly selected to become a parent for the next generation and continued treatment for the next 120 days. These animals later mated to give birth to two offspring (C, D). The newly weaned D was chosen at random as parents for the last generation and these animals were treated for the next 120 days and mated to produce a litter (E). The newly weaned (E) was treated for the added four weeks and then sacrificed. As far as possible, all littermates obtained from different matings were examined by autopsy.

No compound-related deaths or adverse reactions were observed in these studies. Body weight and food consumption are similar across all groups. No evidence was found of dosage - related or cross breeding changes in gestational length, offspring size, number of surviving babies to be weaned, sex ratio, or infant weights. High-dosage compound of cyanurate causing epithelial hyperplasia or chronic cystitis - no macroscopic or microscopic pathological changes or organ weight variations associated with it. It was concluded that sodium cyanurate did not interfere with reproductive performance in rats.

Risk assessment: Various studies show that cyanurate exhibits very little toxicity. Cyanurate is not fetotoxic in addition to its specifications such as teratogenic, mutagenic, carcinogenic, tumor-forming properties in animal studies. Moreover, it does not interfere with reproductive performance. Chronic or subchronic studies have shown no significant toxicity. The only significant finding that resulted in the precipitation of 5.375ppm (mg / lt) sodium cyanurate at the maximum solubility level is the formation of stones in susceptible rats causing death and secondary pathological effects, leading to urinary tract obstruction.

The 5.375ppm level obtained from a NaDCC solution contains 4.480ppm of available chlorine (83.3%). The direct and possible long-term effects of ingestion of this obtained chlorine (hypochlorous acid) level are all the more important when considering the risk assessment.

10.2 Sodium Dichloroisocyanurate

The toxicity data that can be obtained from NaDCC are formally explained below. However, it should be kept in mind that NaDCC in solution produces cyanurate or chlorine. The amount of cyanurate has been evaluated independently in the previous section without any interference from any effect depending on the chlorine present in the same solution.

The toxicity data in the NaDCC is extremely appropriate given the risk conditions associated with the transport and use of its dry form.

Acute toxicity : Acute oral toxicity of NADCC showed an LD50 of 1.67[31] grams per kilogram in rats and 2.0 grams per kilogram in rabbits. The LD50 value for humans is given as 3.57 grams per kilogram[32].

Dermal LD50 is consistently greater than 5.0 grams per kilogram when administered to rabbit skin as a single dosage[33].

Chronic / Subchronic Toxicity: No chronic toxicity were found at rats and dogs[31]. After the administration of diets containing 16.6 and 333ppm NaDCC to a group of 10 male and 10 female rats for 6 months, 16, 67 and 333ppm, and also to a group of 3 dogs (2 males, 1 female), hematological values, sugar and protein in the urine, body Increases in weight, organ weights and histological appearance of tissues no toxicity was observed.

Respiratory studies from groups of 10 male and female rats exposed to dichloroisocyanurate powders at levels of 3, 10, and 30 mg / m^3 for 6 hours per day, 5 days a week for 4 weeks, produced no fatalities in the test animals[33], although adverse reactions have been observed at moderate and high doses. A low concentration of 3mg / m^3 exposed was considered an ineffective level with an average daily dosage of 0.64mg / kg. The comparable dosage in humans was appreciated at 0.074mg / kg for more than 8 hours, a factor 8 lower than the ineffective level in the rat.

In the study findings in the administration of dichloroisocyanurate in drinking water to male and female rats at levels of 0, 400, 1200, 4000 and 8000ppm for 59 days, it was decided that the dosages limited to 50 to 130 mg / kg are ineffective, depending on the gender. In another subchronic study[33], dichloroisocyanurate was formulated in a diet to large albino rats at concentrations of 0, 2,000, 6,000 and 12,000ppm for 13 weeks. No effect level has been taken into account, which equates to a daily consumption of 100mg / kg.

Irritation: No irritation was observed on the intact skin after the application of NaDCC in dry powder form, undiluted, for 24 hours[31]. The 333ppm NaDCC solution instilled into the eyes of each of 5 albino rabbits daily for 3 months, 5 days of the sheet, did not cause any damage or irritation to the eyes. Daily application of 5ml of 333ml of solution per liter on

average 10% of the body surfaces of albino rabbits for 3 months, 5 days a week did not reveal any adverse effects[31].

NaDCC solutions at concentrations of 1,400 and 4,000ppm have been found to be non-irritating when used in humans[41,42]. Indeed, the solutions have been continuously applied to infected wounds and have been found to aid healing procedures.

Teratogenicity: Dichloroisocyanurate was administered to 30 pregnant rats at daily dosages of 0, 25, 100 and 400 mg / kg by a rubber catheter during the 6th and 15th days, the most important period of the organogen of pregnancy. Death occurred in approximately 50% of the high-dosed animals due to irritation of the gastrointestinal tract. As a mean of the amount of live / dead fetus, no evidence of foetotoxicity was found and resorption occurred comparatively for the control and examination groups. Sex ratio and newborn body weights also appeared to be similar. No visible difference was found in the degree of occurrence of external malformations or internal anomalies. The delay in ossification of the skeleton was seen in fetuses in the high dosage group. Delays in ossification occur frequently at high dosages causing maternal toxicity and were not considered compound-related. There is no evidence that dichloroisocyanurate is foetotoxic or teratogenic in mice[33].

Mutagenicity: Isocyanurates showed no mutagenicity when tested in four Salmonella species in the presence or absence of liver extracts from five rats[43].

Studies using SOS Chromotest have shown that sodium dichloroisocyanurate is not genotoxic[44].

Risk assessment: NaDCC was considered to be non-genotoxic, mutagenic or even teratogenic in the studies mentioned. It is irritating to the skin and eyes due to the chlorine capacity contained in the raw material, and is corrosive if inhaled in sufficient quantity. Therefore, the substance is formulated in tablet form, minimizing the possibility of severe reactions.

The LD_{50} for humans is given as 357 grams per kilogram, which corresponds to 214 grams for a 60 kg adult and 17.85 grams for a 5 kg child. From Klortab NaDCC 3,4gr tablets, adults should swallow 62 tablets and children 5 tablets. While this number is determined as 43 tablets for adults and 3.5 tablets for children in Klortab NaDCC 5 gr tablets, Klortab NaDCC requires 12 tablets for adults and 1 tablet for children for 17.4 gr tablets. Especially when the unpleasant taste, size and effervescent properties of the tablets are taken into consideration, swallowing these amounts will become impossible.

In the meantime, if the solution comes into contact with the eyes, they should be washed with plenty of water.

11.0 REFERENCES

1. Hospital Hygiene – A New Challenge. H.G. Sonnatag, Hygiene-Institute, University of Heidelburg, Germany. J. Sterile Services Management. 1993, 10-12 (570).

2. COATES, D. A Comparison of Sodium Hypochlorite and Sodium Dichloroisocyanurate Products. J. Hospital Infection. 1985, 6, 31-40 (33).

3. BLOOMFIELD, S.F. and MILES, G.A. The Relationship between Residual Chlorine and Disinfection Capacity of Sodium Hypochlorite and Sodium Dichloroisocyanurate Solutions in the presence of ***Escherichia coli*** and milk. Microbios Letters, 1979, 10, 33-43 (19).

4. BLOOMFIELD, S.F. and MILES, G.A. The Antibacterial Properties of Sodium Dichloroisocyanurate and Sodium Hypochlorite Formulations. Journal of Applied Bacteriology, 1979, 46, 65-73 (18).

5. COATES, D. Comparison of Sodium Hypochlorite and Sodium Dichloroisocyanurate Disinfectants: Neutralisation by Serum. Journal of Hospital Infection, 1988, 11, 60-67,(48).

6. BLOOMFIELD, S.F. and USO, E.E. The Antibacterial Properties of Sodium Hypochlorite and Sodium Dichloroisocyanurate as Hospital Disinfectants, J. Hospital Infection, 1985, 6, 20-30, (34)

7. BEST, M., SATTAR, S.A., SPRINGTHORPE, V.S. and KENNEDY, M.E., Efficacies of Selected Disinfectants against ***Mycobacterium tuberculosis***. J. Clin Microbiology. 1990, 28, 2234-2239 (371).

8. TYLER, R and AYLIFFE, G.A.J., A Surface Test for Virucidal Activity of Disinfectants: Preliminary Study with Herpes virus. Journal of Hospital Infection, 1987, 9, 22-29 (44).

9. BLOOMFIELD, S.F., SMITH-BURCHNELL, C.A. and DALGLEISH, A.G., Evaluation of hypochlorite-releasing disinfectants against the human immunodeficiency virus (HIV). Journal of Hospital Infection, 1990, 15, 273-278 (369)

10. AYLIFFE, G.A.J., COATES, D. and HOFFFMAN, P.N., Chemical Disinfection in Hospitals. Public Health Laboratory Service. 1984 (B1).

11. Acquired Immuno Deficiency Syndrome (AIDS): Recommendations of a Working Party of Hospital Infection Society. Journal of Hospital Infection, 1990, 15, 7-34 (333).

12. Decontamination of Equipment, Linen or Other surfaces contaminated with Hepatitis B or HIV. Dept. of Health and Social Security, Health Notice, January 1987 (82).

13. Acquired Immuno Deficiency Syndrome (AIDS): Precautions for Clinical and Laboratory Staffs: Morbidity and Mortality Weekly. Centres of Disease Control. U.S. Department of Health and Human Services. 1982, 31, 577-580 (109)

14. Guidelines on Sterilization and Disinfection methods effective against Human Immunodeficiency Virus (HIV). WHO Aids Series 2. 2nd Edn. WHO Geneva 1989 (B10).

15. Safety in Pathology Laboratories. Department of Health and Social Security and Welsh Office. May 1972, 19-65 (10).

16. WHO Technical Report Series No. 512. Viral Hepatitis. WHO. 1973, 48-52 (14).

17. Advisory Committee on Dangerous Pathogens. LAV/HTLVIII – the Causative agent of AIDS and Related Conditions – Revised Guidelines, June 1986 (B13).

18. BLOOMFIELD, S.F. and MILLER, E.A., A Comparison of Hypochlorite and Phenolic Disinfectants for Disinfection of Clean and Soiled Surfaces and Blood Spillages. Journal of Hospital Infection, 1989, 13, 231-239 (246).

19. COATES, D. and WILSON, M. Use of Sodium Dichloroisocyanurate Granules for Spills of Body Fluids. Journal of Hospital Infection, 1989, 13, 241-251 (247)

20. COATES, D. Disinfection of Body Fluids: How Effective is a Level of 10,000ppm Available Chlorine? Journal of Hospital Infection, 1991, 18, 319-332 (426)

21. Safety Action Bulletin. Dept. of Health, Scottish Home and Health Dept., Welsh Office, Dept. of Health and Social Services. May 1990, No.59 (359).

22. SALDICK, J., Biodegredation of Cyanuric Acid. App. Microbiology. 1974, 28, 1004-1008 (302).

23. COOK, A.M., BEILSTEIN, P., GROSSENBACHER, H. and HÜTTER, R., Ring Cleavage and Degradative Pathway of Cyanuric Acid in Bacteria. Biochem. J. 1985, 231, 25-30 (362).

24. MYSCOW, W., LASOTA, T and STACHYRA, A., Cyanuric Acid – a S-triazine Derivative as a Nitrogen Source for some soil microorganisms. 1982, 32, 177-183 (363).

25. Universita Degli Studi di Bologna. Departimento di Farmacologia. Presidio Medico-Chirurgico Klortab NaDCC Tavolette (22 January 1993) and Presidio Medico-Chirurgico Sterinova (2 February 1993) Bologna, Italy.

26. BORICK, P.M., DONERSHINE,F.H. and CHANDIER, V.L. Alkalinized gluteraldehyde, a new Antimicrobial Agent. J. Pharm. Sci. 1964, 53, 1273-1275.

27. SNYDER, R.W. and CHEATLE, E.L. Alkaline Gluteraldehyde – an Effective Disinfectant. Am. J. of Hosp. Pharm. 1965, 22, 321-327.

28. HORWITZ, W. Official Methods of Analysis of the Association of Official Analytical Chemists, 11th Edition, 1970, 59-72.

29. HOFFMAN, P.N., DEATH, J.E., COATES, D., The stability of Sodium Hypochlorite Solutions in Disinfectants : Their Use and Evaluation of Effectiveness. Academic Press, 1981, 77 – 83.

30. COATES, D.A., A Comparision of Sodium Hypochlorite and Sodium Dichloroisocyanurate Products. Journal of Hospital Infection. 1985, 6, 31 – 40.

31. CANELLI, E. Chemical, Bacteriological and Toxicological Properties of Cyanuric Acid and Chlorinated Isocyanurates as Applied to Swimming Pool Disinfection : A Review. Am. J. Public Health, 1974, 64, 155 – 162. (95).

32. EPA TSCA Chemical Inventory, June 1990, 105810 / 11 / 12, (493

33. HAMMOND, B.G., BARBEE, S.J., INOUE, T., ISHIDA, N., LEVINSKAS, G.J., STEVENS, M.W., WHEELER, A.G., and CASCIERI, T. A Review of Toxicology Studies on Cyanurate and its Chlorinated Derivatives. Environ. Health Perspec. 1986, 69, 287 – 292 (402).

34. HODGE, H.G., PANNER, B.J., DOWNS, W.L., INOUE, and MAYNARD, E.A. Toxicity of Sodium Cyanurate. Toxicol. Appl. Pharmacology, 1965, 7, 667 –674 (108)

35. CASCIERI, T., BARBEE, S., HAMMOND, B., INOUE, T., ISHIDA, N., and WHEELER, A.G. A Comprehensive Evaluation of the Urinary Tract after Chroric Exposure to Cyanurate in Drinking Water. Toxicologist, 1985, 5, 58 (417)

36. CASCIERI, T., BARBEE, S., HAMMOND, B., INOUE, T., ISHIDA, N., WHEELER, A.G., and SCHARDEIN, J.L. Absence of a Teratogenic Response in rats with Monosodium Cyanurate. Toxicologist, 1983, 3, 65 (411).

37. HAMMOND, B.G., BARBEE, S.J., WHEELER, A.G., and CASCIERI, T. Absence of Mutagenic Activity for Monosodium Cyanurate. Fund. And Appl. Toxicol. 1985, 5, 655 – 664 (421)

38. Fi-Clor Toxicity Data, Chlor-Chem Ltd., Cheshire, UK 1987

39. BARBEE, S.J., CASCIERI, T., HAMMOND, B.G., INOUE, T., ISHIDA, N., WHEELER, A.G., CHADWICK, D., HAYES, J., MACAULEY, M., & McCOMISH, A. Metabolism and Disposition of Sodium Cyanurate. Toxicologist, 1983, 3, 80, (412)

40. ALLAN, L.M. Absorption and Excretion of Cyanuric Acid in Long-Distance Swimmers. Drug Metab. Rev. 1982, 13, 499 – 516 (422)

41. FREEDMAN, S.F., HERALD, Z., KAPLAN, I. The Use of Troclosene Sodium Solution of Infected Wounds (Hospital Rreport) (39).

42. BLOOMFIELD, S.F., SIZER, T.J. Eusol BPC and other Hypochlorite Formulations Used in Hospitals. The Pharmaceutical Journal. Aug. 3, 1985, 153 – 157 (35)

43. LUSBY, A.F., SIMMONS, Z AND McGUIRRE, P.M. Variation in mutagenicity of s-Triazine Compounds Tested for Four Salmonella Strains. Environ. Mutagen. 1979, 1, 287 – 290 (376)

44. YIN, M., CHEN, Y., WANG., J. Studies on Genotoxicity of Disinfectants with SOS Chromotest. Environ. Mol. Mutagen. 1989, 14 (Suppl. 15), 225 – 226 (392)

45. WINDHOLZ, M (Ed). The Merck Index, Tendth Edition. 1983, 8446, 1234

46. LITTLE, A.D. ENVİRONMENTAL AND Human Safety of Major Surfactants. Vol. 1. anionic Surfactants, Part I. Linear Alkylbenzene Sulfonates. February 1991, 16 – 28 (661).