HEMOCLEAN® C Reference Manual

Huons Medicare

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I. INTRODUCTION

The medical purpose Citric Acid Disinfection Abstergent has been widely used as a disinfectant & abstergent for artificial hemodialysis equipments since the middle of 1980 centering around the U.S., beginning the applications on hemodialysis therapy operations for the End Stage Renal Disease patients. There are certain differences in various disinfectants & abstergents of artificial hemodialysis devices depending on the recommendations of respective equipment manufacturer, however the most commonly used method is to independently perform the disinfection and cleaning functions with [Acid + Sodium Hypochlorite] or [Citric Acid(boiling water) + Sodium Hypochlorite], which accompanies with the certain high level of user inconvenience and disadvantage of low performance.

Particularly, the use of Sodium Hypochlorite has been quickly decreasing due to the corrosion problem subject to the metal elements, and become the focus of public regulations both in domestic and overseas countries owing to the various issues such as the environment pollution problems caused by the second order reaction & purification capability loss of septic tank. As for the Tokyo Prefecture, they stipulated it as the one of 48 elements subject to heavily focused surveillance system of waste liquids at the public facilities including the medical clinics, concentrating the effort in managing and regulating the used volumes.[1)]

HEMOCLEAN®C is the first, sole medical specialty product registered and developed by in-house technology in Korea, as the agent removing calcium & magnesium precipitates from the dialysis solution passage of dialysis machine. The primary characteristics of **HEMOCLEAN®C** Solution are, the fast disinfecting speed as an acidic disinfectant with the citric acid, organic acid & etc. as major ingredients, showing excellent disinfecting & cleaning effect in citric acid – boiling water sterilization and ease of density management in diversified conditions. Besides, **HEMOCLEAN®C** Solution also is proven for superior & lengthy stability in preserving the product effectiveness, remarkable environmental friendliness resolving the elements completely in natural circumstance proud of continuous & effective removing capability of the scale within the piping & components of equipment.

This Reference Manual is made for the correct understanding and convenience of users & operators of dialysis machine & facilities, based on the various test results performed since the beginning of product development.

II. SUBSTANCE OF STUDY AND EXAMINATION PRODUCT

1. GENERAL INFORMATION OF HEMOCLEAN® C

(1) Composition

- Main ingredient: Citric acid 25.0%
- Sub ingredient: Other organic acid and stabilizer Proper quantity
- Solvent: Purified water Proper quantity

(2) Physical properties

- Appearance : Light yellow, transparent liquid filled in white plastic container.
- Non-flammable, Incombustible
- Convenience for rinse after disinfection due to the ease of mixing it water.
- pH: < 2.0
- Density: 1.10 g/cm^3

2. EFFICACY OF HEMOCLEAN® C

Remove Calcium and Magnesium Deposits from Dialysis Solution Passage of dialysis machine.

(1) STERILIZATION EFFECT OF HEMOCLEAN® C

FDA recognizes as the high level disinfectant when an agent shows certain level of disinfection capability on spore exterminating the tuberculous bacillus by over 10^6. [2] The test table shown below summarizes the results of tests performed at the KRD's Research Team Laboratory, which confirms the perfect extermination of tuberculous bacillus, fungi & bacteria, including the spore.

1) Pathogenic microorganism In-vitro test of HEMOCLEAN® C

Table 1. Test result of bactericidal activity

Test organism	Inocolumns size	Clean condition		Dirty condition	
		5 min	10 min	5 min	10 min
Bactericidal					
Staphylococcus aureus (ATCC 6538)	1.5×10^9	-	-	-	-
Enterococcus hirae (ATCC 10541)	1.2×10^9	-	-	-	-
Pseudomonas aeruginosa (ATCC 15442)	3.2×10^9	-	-	-	-

According to the measurement of disinfection capability as per the EN 14561 Test Method, **HEMOCLEAN® C** showed the disinfection effect of over 5 Log for 85℃ reacting temperature within 5 & 10 minutes of contact time period respectively, which is way beyond the standard as required by EN 14561 Test Method, on Staphylococcus aureus, Enterococcus hirae,

Pseudomonas aeruginosa. [3) 4)]

2) **Fungicdal Test Result of HEMOCLEAN® C**

Table 2. Test result of Fungicidal activity

Test organism	Inocolumns size	Clean condition		Dirty condition	
		5 min	10 min	5 min	10 min
Fungicidal					
Candida albicans (ATCC 10231)	1.9×10^{9}	-	-	-	-
Aspergillus niger (ATCC 16404)	1.5×10^{8}	-	-	-	-

According to the fungicidal capability test result per the EN 14562 Test Method, **HEMOCLEAN® C** demonstrated the strong fungicidal power of over 4 Log for 85℃ reacting temperature within 5 & 10 minutes of contact time period respectively, which is way beyond the standard as required by EN 14562 Test Method, on Candida albicans, Aspergillus niger.[5)]

3) **Sporicidal Test Result of HEMOCLEAN® C**

Table 3. Test result of sporicidal activity

Test organism	Inocolumns size	Clean condition		Dirty condition	
		5 min	10 min	5 min	10 min
Sporicidal					
Bacillus subtilis (ATCC 19659)	5.6×10^{9}	1.9×10^{2}	-	1.2×10^{3}	-

According to the sporicidal capability test result per the EN 13727, AOAC 966.04 Test Method, **HEMOCLEAN® C** demonstrated the Sporicidal effect of over 5 Log for 85℃ reacting temperature within 5 & 10 minutes of contact time period respectively. [6)]

(2) CLEANING OF HEMOCLEAN® C

1) **Decalcification and magnesium salt elimination**

HEMOCLEAN® C has been analyzed using XRD by extracting the 2 duplicated test pieces per each equipment model in order to check the expected calcium & magnesium salt, and confirmed the peak values of $CaCO_3$ and $MgCO_3$. The XRD Phase Analysis on the Gambro AK90, FMC 4008B & B/BRAUN has been executed for the internal dialysis solution passage of dialysis machine, where the calcium & magnesium deposits are confirmed existing, after sterilization with the 20% citric acid solution & **HEMOCLEAN® C**, using the citric acid – boiling water disinfection mode in accordance with the manual of equipment manufacturer.

It is checked that the peak characteristic of $CaCO_3$, $MgCO_3$ & $CaMg(CO_3)_2$ has been reduced, and for the case of **HEMOCLEAN® C** the elimination effect of inorganic salt which is more superior than the 20% citric acid of reference solution is confirmed.

In order to compare the decalcification capability of **HEMOCLEAN® C** in comparison with other competitive products, the solubility test result is shown as below

Table.4 Desolved $CaCO_3$ compared with citric acid and **HEMOCLEAN® C**

	Purified water	C Product		HEMOCLEAN® C	
		Dissolution Rate	Average	Dissolution Rate	Average
Calcium carbonate (0.1 g)	No Change	100.0 %		100.0 %	
Calcium carbonate (0.2 g)	No Change	91.5 %	89.1 %	92.3 %	93.2 %
		90.5 %		93.1 %	
		85.3 %		94.1 %	

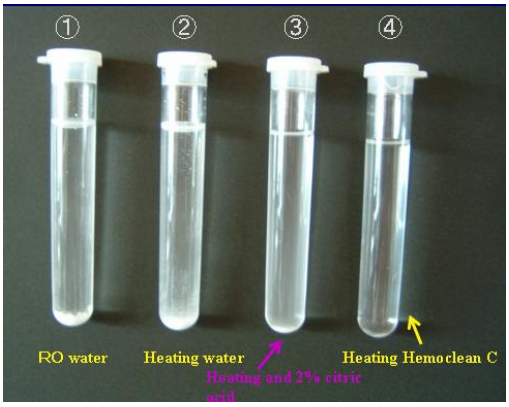


Fig. 1 Comparison of solubility for $CaCO_3$

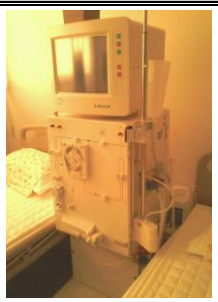
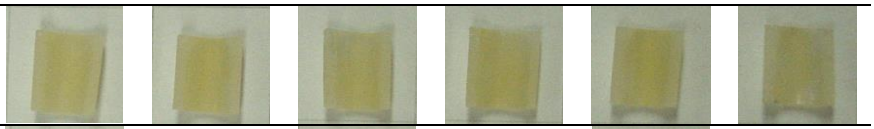
Manufacturer/ Name of Equipment	Gambro AK90	FMC 4008B	B/Braun
Equipment			
Location of Test Piece			
Test Piece before Sterilization			
Test Piece after Sterilization (20%Citric Acid)		-	-	-
Test Piece after Sterilization (HEMOCLEAN®C)	-		-	-

Fig. 2 Target Test Equipment and Test Piece

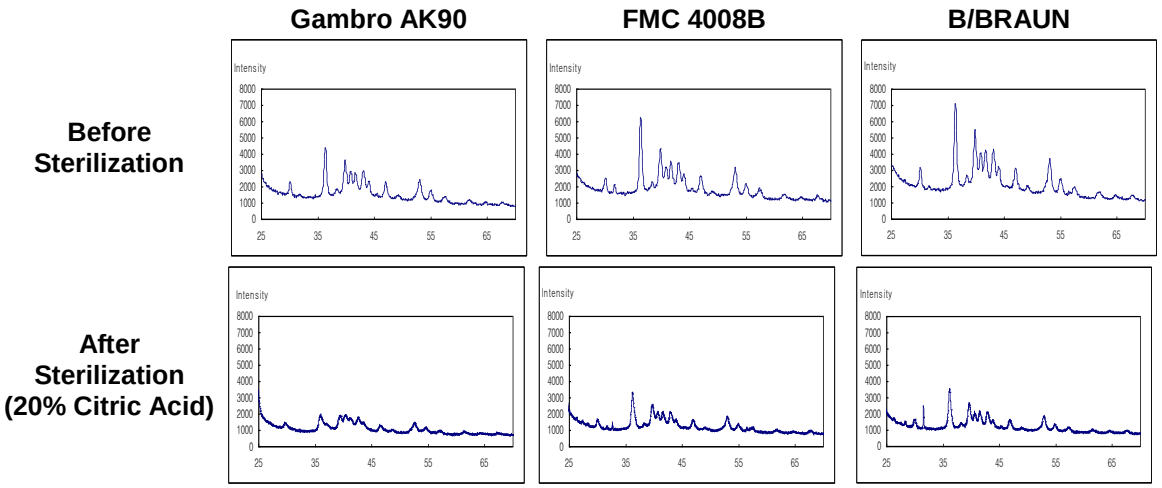


Fig. 3 XRD Phase Analysis before & after Sterilization with 20% Citric Acid

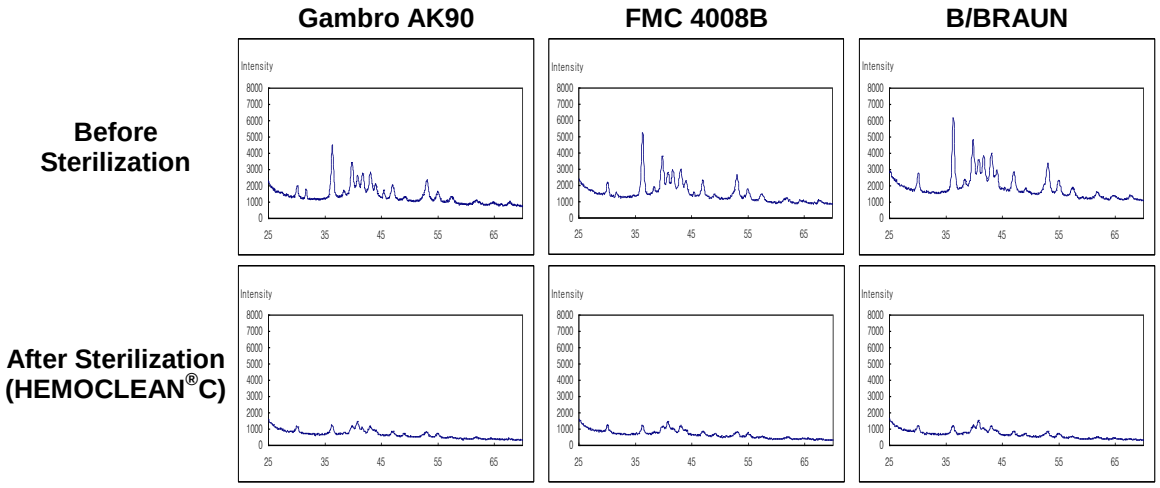


Fig. 4 XRD Analysis before & after the Sterilization with **HEMOCLEAN®C**

2) Cleaning about polluted tube

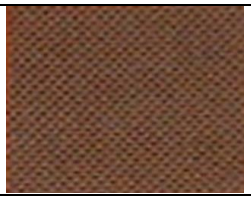
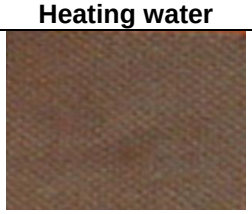
Conc. : 1/30 dilution, Temp. : 85℃, Time : 5 min

Fig. 5 Cleaning on the polluted tube

After we compared **HEMOCLEAN® C** to other citric acid disinfectant apply for the heating mode of HD Units, **HEMOCLEAN® C** disinfection showed better result on the solubility for protein and decalcification

3) Solubility for protein

Sample: EMPA-111 (attached protein on the sheet)

Before use	Water	Heating water
		

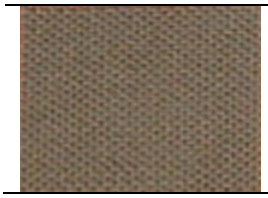
2% citric acid	Heating water 2% citric acid	NaClO 300ppm 3 hours	Heating water HEMOCLEAN®C (diluted 30times)
			

Fig. 6 Comparison of solubility for protein

4) The pump regions in dialysis machine

We have used **HEMOCLEAN®C** for 7 months, there was no effects to ETCF. Also, there was no corrosion or aging problems, etc.

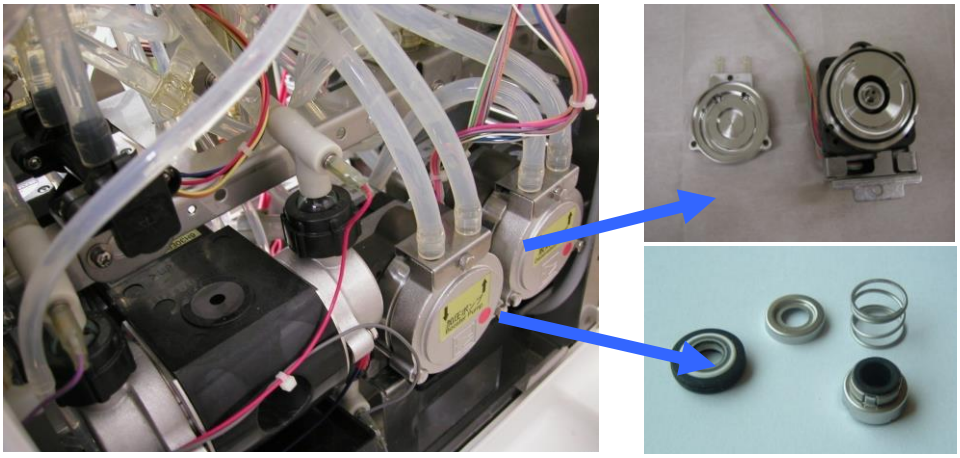
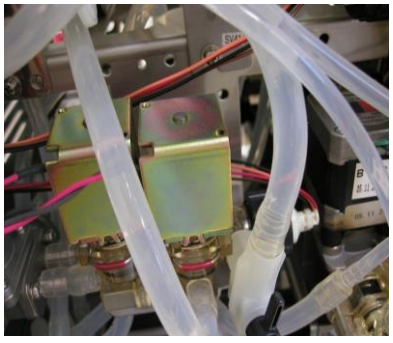
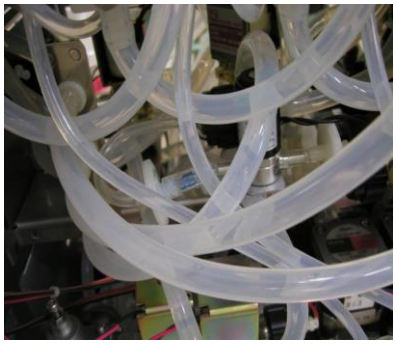


Fig. 7 pump regions in dialysis machine

5) The silicon tubes in dialysis machine





3. SAFETY OF HEMOCLEAN® C

(1) Biocompability

The Citric Acid, primary element of **HEMOCLEAN® C**, is proven for high level of safety feature with Non-Human Toxicity Values.

LD_{50} Rat [7]	oral	6,730 mg/kg
LD_{50} Mouse [8] [9]	iv	42 mg/kg
	oral	5,040 mg/kg
LD_{50} Rabbit [10]	iv	330 mg/kg

(2) Biodegradability

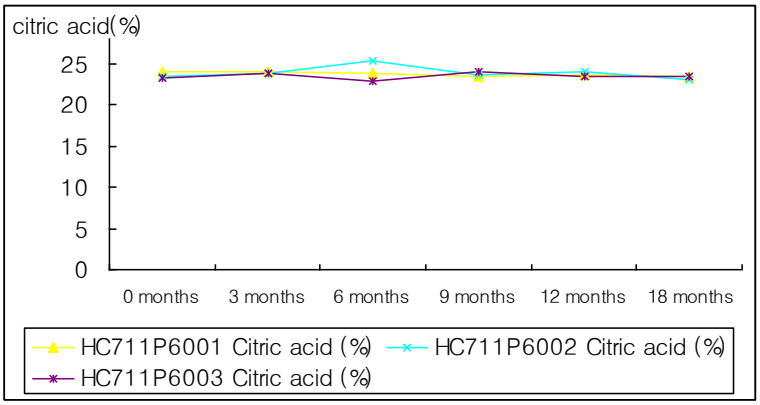


Figure 8. Stability of **HEMOCLEAN® C** (3 Lot)

The biodegradability of Citric Acid under aerobic condition has been tested with 6 itemized experiments showing the positive results of high biodegradability in all tests. With Citric Acid, the 93% of DOC has been removed at the Couple Units Test (sludge inoculum), 85% removed after one day period with the Zahn-Wellens Test, 100% removed with the AFNOR Test, Sturm Test, OECD Screening Test and 90% removed with the BODT in a closed bottle test.[11]

4. STABILITY OF HEMOCLEAN® C

In order to test the stability of **HEMOCLEAN® C**, the Medi-Chemical Institute of Huons Medicare Co., Ltd. has performed the product stability test for one year period using the High Performance Liquid chromatography(HPLC) proving the stability within the specified effective date.

5. DIRECTIONS FOR USE

(1) Use only for the dialysis machine stipulating the specified dilution density and cleaning time, enabling the cleaning with citric acid.

(2) Content to be used, dilution density & cleaning time must be followed by the relevant

manual instructions of dialysis machine.

(3) As the rinsing is a process enabling the **HEMOCLEAN® C** play the effectiveness in full, make sure to rinse for over 10 minutes after the dialysis therapy, and execute sterilization.

6. STORAGE AND PRECAUTION

(1) Warning

Do not use the dialysis machine for patients listed below.

(2) Patients who are sensitive to the contents of HEMOCLEAN® C.

(3) General Caution

1) Do not use the medication in other ways different from the specified directions & contents.
2) In the event of taking the medication, provide fresh air & rinse the nose, mouth and throat with water if required.
3) The medication may be subject to stimulating to the human skin. If the skin is exposed to the medication, take off the polluted clothing and rinse the skin with the plenty of water.
4) The medication is subject to stimulating to the eyes, rinse with water immediately after contacting for 10 ~ 15 minutes with wide opening the eyes and follow the directions of doctors.
5) If digested, as the medication may cause burning feeling on mouth & throat accompanied with the stomachache, wash the mouth with water and drink either water or 2 cups of milk. Do not induce vomiting and follow the direction of doctors.
6) Must use the medication only for dialysis machine.
7) The product must be used together with heated sterilization program of dialysis machine.
8) When using the medication, must avoid the medication to contact with skin & eyes, and wear the appropriate protective devices or costume such as glove, eye protective glass & etc.
9) Always refer to the Reference Manual of dialysis machine in use.

(4) Maintenance and Handling Cautions

1) Store in the locations out of children's reach.
2) Do not store for long period of time under the direct sun ray or high temperature.
3) Do preserve the medication in the original container, not touching the cap of container, as the change of the medication container may cause accidents and is not recommended in terms of quality maintenance.
4) Dispose the used medication without exception, not re-injecting into the container.

(5) Package/Storage condition/Shelf life

1) Package : 5 L X 2 / Box
2) Storage condition : Room temperature(1~30℃)
3) Shelf life : 24 months (in original, sealed package)

III. CONCLUSION

There are plenty of research reports generated and available on environmental pollution and toxic character of aldehyde & chlorine sterilizers from the variety of research institutes world wide. Particularly out of economic reason, the chlorine sterilizer used with dialysis machine, water purifiers & purified water supplying equipments for sterilization & cleaning applications has been commonly used, not able to sufficiently remove the calcium carbonate (CaCO3) & ferrous metals and bio-films which is the primary corrosive materials of scaling rather inducing the equipment corrosion thereby shortening the life cycles of equipments and facilities. Besides, it generates the organic halogen carcinogen compounds such as THM (trihalomethane), trichloroethylene & tetraethylene causing secondary environmental pollution, by reacting with organic materials. The aldehydes have strong toxic character requiring lengthy time for sterilization and generating carcinogenic materials reacted with chlorines.

The primary features of **HEMOCLEAN® C** , the acidic disinfecting agent, comes from the fast disinfecting speed along with remarkable disinfecting & cleaning capabilities, superior stability preserving the product effectiveness for long period of time, environmental friendliness completely dissolving in the nature, continuous & effective scale preventing & removing capability inside the piping & equipments. **HEMOCLEAN® C** has been proven for the product excellence with all the tests performed to experiment the performance. According to the test results, **HEMOCLEAN® C** demonstrated effective disinfecting capability throughout the wide range of microorganisms including spores, together with outstanding effect in removing & preventing the calcium carbonate & corrosive characters of scale attached inside the piping & equipments.

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