

SEP 10 1998

K974188

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510(k) Summary

**Cetylcode-G® CONCENTRATE
with Diluent Concentrate
For Sterilization and High Level Disinfection**

Cetylite Industries, Inc.
9051 River Road
Pennsauken, New Jersey 08110-3293

Date of Summary: October 27, 1997
Revised August 7, 1998

1. Contact Person

Jeffrey Wachman
609/665-6111

2. Name of Medical Device

Proprietary Name

Cetylcode-G Concentrate
(with Cetylcode-G Diluent Concentrate)

Common or Usual Name

Concentrated glutaraldehyde solution for
sterilization and high level disinfection (used with
diluent solution)

Classification Names

Liquid Chemical Sterilant/Disinfectant

Substantial Equivalence to Predicate Product

Cetylcode-G concentrate is substantially equivalent to Cidex Plus 28-day Solution and MetriCide 28 day Long-Life Activated Dialedehyde Solution. Substantial equivalence is based on the fact that Cetylcode-G has the same intended use (to sterilize and disinfect medical instruments) as the two predicate products and relies on the same active ingredient (glutaraldehyde) to achieve the germicidal effect and has the same demonstrated efficacy. The use dilution of Cetylcode-G has a glutaraldehyde concentration and pH range comparable to that of Cidex Plus and MetriCide. Cetylcode-G is marketed as a concentrate and requires dilution. Cidex Plus and MetriCide both require activation but not significant dilution. When mixed in accordance with their label instructions, the three products have comparable concentrations of glutaraldehyde (3.2% for Cetylcode-G, 3.4% for Cidex Plus, and 2.8% for MetriCide), and overlapping pH ranges. Moreover, based on the performance testing of these products, as described below for Cetylcode-G and as described in the 510(k)s for the two predicate products, Cetylcode-G has demonstrated comparable sterilizing and disinfecting capabilities to the predicates. All three products are labeled with a 28-day reuse period and require a chemical test strip to verify that the active ingredient remains at an effective concentration throughout the 28-day reuse period.

A. **Indications for Use.** Cetylcode-G is intended for use as a liquid chemical sterilant and/or a high level disinfectant to sterilize and disinfect medical devices and instruments in hospitals, medical, dental, and other healthcare facilities when used according to the directions for use in the package insert.

Sterilant: Cetylcode-G is a sterilant when mixed and used in accordance with its directions for use for a maximum of 28 days at 20°C with an immersion time of at least 10 hours at its minimum effective concentration (MEC) of 2.1% glutaraldehyde.

High Level Disinfectant: Cetylcode-G is a high level disinfectant when mixed and used according to its directions for use for a maximum of 28 days at 20°C with an immersion time of at least 40 minutes at its minimum effective concentration (MEC) of 2.1% glutaraldehyde .

Reuse: Cetylcode-G can be reused for a period not to exceed 28 days provided the required conditions of glutaraldehyde concentration, pH, and temperature exist based upon the monitoring described in the package insert directions for use. The minimum effective concentration (MEC) of glutaraldehyde (2.1%) must be verified during the 28-day re-use period by using the Serim Research Corporation's DisIntek™ reagent test strips. The number of days in use should not be solely relied upon for evaluating its efficacy during its reuse period.

Material Compatibility: Cetylcode-G Use Dilution (after dilution with Cetylcode-G Diluent) is an alkaline glutaraldehyde solution. Such solutions have a long history of compatible use with medical instruments made from a variety of materials without corrosive or other apparent damaging effects.¹ They have been found to be compatible with the following materials:

METALS

- Chrome Plated Metals¹
- Nickel Plated Metals¹
- Carbon Steel^{1,8}
- Stainless Steel¹
- Aluminum¹

Elastomers^{1,2}

- Black rubber
- red rubber
- silicone rubber
- polyurethane

PLASTICS^{1,2,7}

- acrylonitrile-butadiene-styrene (ABS)
- polyvinyl chloride (PVC)
- polystyrene
- polyethylene
- polypropylene
- polysulfone
- polymethylmethacrylate (acrylic)
- polyethylene terephthalate (polyester)

Users are instructed to check the labeling of the reusable device for any additional instructions. Cetylcode-G is not recommended for use on unanodized aluminum or for the disinfection of one-piece molded, solvent-bonded or sonic-welded polycarbonate equipment due to possible stress cracking after repeated treatments.

References:

1. Miner, N.A., McDowell, J.W., et al: Antimicrobial and other properties of a new stabilized alkaline glutaraldehyde disinfectant/sterilizer, *Am. J. Hosp. Pharm.* 34: 376-382 (Apr.) 1977.
2. Borrick, P.M.: Chemical Sterilizers (Chemosterilizers) *Advan. App. Microbiol.* 10: 291-311, 306 (1968).
3. Scott, E.M., Gorman S.P.: Sterilization with glutaraldehyde, *In Disinfection, Sterilization, and Preservation*, 3rd. Ed., Lea & Febiger, Philadelphia, 1983, p. 65-88.
4. O'Brien, H.A., Mitchell, J.D.: The use of activated glutaraldehyde as a cold sterilizing agent for urological instruments, *J. Urol.* 95: 429-435 (Mar.) 1966.
5. Babb, J.R., Bradley, C.R., et al: Sporicidal activity of glutaraldehydes and hypochlorites and other factors influencing their selection for the treatment of medical equipment, *J. Hosp. Infect* 1: 63-75 1980.
6. Russell, A.D.: Bacterial spores and chemical sporicidal agents, *Clin. Microbiol. Rev.* 3: 99-199 (Apr.) 1990.
7. Stonehill, A.A., Krop., S., et al: Buffered glutaraldehyde 10 a new chemical sterilizing solution, *Am. J. Hosp. Pharm.* 20: 465-585 (1963).
8. Blackwood, A.W., Duerr, J.S.; Technical Report 52760 Before/after research study of scalpel blade edge using scanning electron microscopy techniques: 1989 (unpublished).

Pre-Cleaning Agent Compatibility: Cetylcode-G is compatible with enzymatic detergents which are mild in pH, low foaming, and easily rinsed from equipment. Detergents that are either highly acid or alkaline are contraindicated as pre-cleaning agents since improper rinsing could affect the efficacy of the Cetylcode-G 28-day solution by altering its pH.

Warnings: Cetylcode-G Concentrate and its use dilution is hazardous to humans and domestic animals. Danger: Keep out of reach of children. Contains glutaraldehyde.

- 1) Do not get in eyes, on skin or on clothing. Glutaraldehyde is corrosive to exposed eye and skin tissue, and can cause damage. In case of contact with eyes, immediately flush with water and continue flushing for at least 15 minutes. Obtain medical attention immediately. For skin, wash immediately with soap and water.
- 2) HARMFUL IF SWALLOWED. If ingested, drink large quantities of water. Do not induce vomiting. Obtain medical attention immediately.
- 3) Use in well ventilated area in closed containers.

Precautions:

- 1) Use rubber or nitrile gloves, eye protection, face mask and chemical apron when cleaning and disinfecting/sterilizing devices.
- 2) Contaminated, reusable devices **MUST BE THOROUGHLY CLEANED** prior to disinfection or sterilization, since residual contamination will decrease the effectiveness of the germicide.
- 3) The user must follow the Directions for Use since any modifications will affect the safety and effectiveness of the germicide.
- 4) To optimize the effective reprocessing of reusable devices, the user must follow a validated reprocessing procedure for any device disinfected or sterilized in Cetylcode-G Use Solution.

Performance Testing: Cetylcode-G Concentrate, after dilution with Cetylcode-G Diluent, was evaluated in several efficacy tests after 28 days of manual stressing to simulate worst-case conditions encountered during its reuse. Cetylcode-G was tested for sporicidal, bactericidal, fungicidal, tuberculocidal, and virucidal activity, and the results are summarized below.

a. Sporicidal Tests

Cetylcode-G passed the AOAC Sporicidal Test against *B. subtilis* spores and *C. sporogenes* spores carried on silk suture loops and porcelain penicylinders in 10 hours at 20°C.

In a sporicidal test involving an end-point analysis of silk suture carriers inoculated with *B. subtilis*, Cetylcode-G was found to be sporicidal at 20°C and exposure times ranging from 9 hours to 10 hours and 30 minutes.

In a spore rate-of-kill (D-value) test, Cetylcode-G was found to have a D-value of 6-8 minutes for *C. sporogenes* and 90 minutes for *B. subtilis* at 20°C.

b. AOAC Tuberculocidal Tests

When tested under the quantitative tuberculocidal test protocol, stressed Cetylcode-G was concluded to achieve a six log reduction in *Mycobacterium bovis* in 40 minutes at 20°C.

c. AOAC Fungicidal Test

When tested under the AOAC Fungicidal test protocol, stressed Cetylcode-G was found to kill *Trichophyton mentagrophytes* within 5 minutes at 20°C.

e. Simulated In-Use Test

In tests designed to simulate the actual use of stressed Cetylcode-G on medical devices, Cetylcode-G effectively disinfected flexible fiber optic endoscopes with no microorganisms recovered from the instruments after 20 minutes of exposure at 20°C.

f. AOAC Viricidal Efficacy Test

In the most recent round of testing, stressed Cetylcode-G was shown to be effective against the Polio Type II virus and the Herpes simplex Type I virus in ten minutes at 20°C.

Safety

Toxic effects depend on a variety of factors and the interplay between them, including the number of exposures, concentration of materials, route of exposure and the particular formulation of the test materials. In order to be toxic, the material must be ingested or come into contact with an exposed body surface: the skin, the eyes, or the mucous membrane linings of the alimentary or respiratory systems. To produce systemic effects, the test material must be absorbed, distributed and metabolized in whatever test animal is selected.

Effects may be observed after a single exposure or after chronic, repeated exposure. These effects may be described as cumulative, latent, persistent or transient.

Hazard analysis is used to estimate the potential for producing harmful effects and this analysis is defined for glutaraldehyde by examining a variety of important factors. These include: 1) the concentration and formulation of glutaraldehyde-based chemical sterilant solutions, 2) the route of likely exposure, 3) the number, magnitude and duration of exposure, and 4) the identity of the population affected.

Acute toxic effects are usually observed in 14-day studies. The following studies were performed:

1. Acute Peroral Toxicity.

Approximately 50 tests were performed in a range of glutaraldehyde concentrations. The results showed that aqueous solutions containing 5 percent or more of glutaraldehyde showed moderate peroral toxicity. Larger volumes of glutaraldehyde solution are required to produce effects as the concentration increases from 5 to 50 percent.

2. Acute Percutaneous Toxicity.

Glutaraldehyde in water at concentrations of 45-50 percent showed moderately active percutaneous toxicity. A potential hazard exists from the absorption of this concentration of glutaraldehyde from the skin. When the concentration is reduced to 25 percent, the effects from systemic absorption are greatly reduced; at 10 percent or less, there is no systemic risk from absorption from the skin.

3. Acute Inhalation Toxicity.

Various types of acute inhalation studies revealed that glutaraldehyde vapor generated at ambient conditions produced sensory irritant effects, but was not acutely injurious. However, vapor concentrations produced by elevating the vapor generation temperature may be harmful in a single sustained exposure.

4. Primary¹ Eye Irritation.

Based on a single 24-hour post-instillation observation of rabbit eyes treated with varying concentrations of glutaraldehyde solutions, the threshold for producing inflammatory effects is approximately 0.25 percent glutaraldehyde (rabbit eye). An obvious dose response was found in the production of corneal and conjunctival injury. Transient minor corneal injury was produced at 1.0 percent, while conjunctival irritation was produced at 0.2 percent. The no-effect concentration for acute eye irritation was 0.1 percent.

5. Primary Skin Irritation.

Again, a dose response for acute irritative effects was seen for both severity and duration. At 45-50 percent, the effects of solutions were moderately severe and persistent. At 25 percent, the effects were less but persisted 14 days. When the concentration was reduced to 5 percent, less severe and less persistent mild to moderate irritation was found. One percent was the no-effect level, while 2 percent was the threshold for irritant effects, and 45 and 50 percent exposure was associated with local corrosive effect.

^{1/} Primary irritancy refers to the acute inflammation produced by a material in contact with a surface membrane and the effects produced in the exposed tissues.

Observations on human skin revealed that it may be more responsive to the irritative effects of glutaraldehyde than the rabbit skin. A 5 percent solution produced moderate erythema, but 1 and 2 percent did not.

The dermal irritant effects of glutaraldehyde depends on the site on the body, the thickness of the skin, concentration of glutaraldehyde, solvent, time of contact and whether the site was occluded. The threshold for dermal irritation is 0.2 to 0.5 percent glutaraldehyde in water. Effects vary as the conditions listed above vary.

6. Skin Sensitization and Allergic Contact Dermatitis.

Allergic contact dermatitis is an immune-mediated hypersensitivity reaction produced by concentrations of glutaraldehyde at much lower concentrations than the initial induction exposure. The information from human contact has been accumulated from worker exposure and skin sensitization studies in human volunteers. The threshold elicitation dose for dermal hypersensitivity is 0.5 percent in water. No cross-sensitization with formaldehyde was found.

7. Peripheral Sensory Irritation.

Exposure recognition is important to avoiding toxic or irritating effects of glutaraldehyde. The odor recognition threshold is 0.04 ppmv, while the threshold for sensory irritation to the eye and respiratory tract is 0.3 ppmv. Noticeable eye irritation occurs at 1 ppmv. The Threshold Limit Value for glutaraldehyde has been established at 0.2 ppmv (as an 8-hour, time-weighted average concentration) by the American Conference of Governmental Industrial Hygienists.

8. Teratology and Mutagenicity.

Studies in animals have shown that glutaraldehyde is not teratogenic and evidence is extensive that it is also not mutagenic.

Residue Study

A recent study is presented in which glutaraldehyde residues were measured on three Olympus endoscopes following 10 hours of soaking in Cetylcode-G and rinsing. Glutaraldehyde concentration in the final soak/rinse water was either undetectable or in the low mg/L (parts per million) range.

Another residue study shows measurements of glutaraldehyde present in (1) the endoscope rinse water after the second rinse (i.e., the rinse following the initial residue reduction step originally called for in the labeling) and (2) the solution used to extract the glutaraldehyde from the five swabs that were wiped over the endoscopes to remove any glutaraldehyde remaining after the second rinse.

From the raw data presented, it is estimated that the endoscopes had, on average, 25 mg of glutaraldehyde remaining on their surfaces after being immersed for 10 hours in Cetylcide-G and undergoing the single-rinse residue reduction step.

Of all the ingredients present in the Cetylcide-G use dilution, glutaraldehyde (3.2%) is the ingredient of greatest toxicological concern. Other ingredients are present below 1% in the use dilution. In light of the low levels at which other ingredients are present in the use dilution, and the even lower levels at which those substances would be present as residues on instruments, separate residue tests for these components were not performed. These additional ingredients are soluble in water and would be expected to rinse easily.

Testing of the Indicator Strip

Cetylite tested the accuracy of the DisIntek test strip for measuring the glutaraldehyde concentration in the Cetylcide-G use dilution under simulated conditions of use. Samples of Cetylcide-G use dilution were manually stressed for 28 days, with the pH and glutaraldehyde concentration measured periodically. Test strip readings were recorded on days 1, 8, 15, 19, 21, 23, 25, and 27. The test report also shows the glutaraldehyde concentration of the stressed material on each of those days, as determined by chemical titration.

The test results show that a comfortable safety margin exists between the MEC and the test strip readings. On day one, for example, nearly all test strips were read as high. This corresponds to an actual glutaraldehyde concentration of 3.03% and 3.25% in the two lots. Most importantly, the DisIntek test strip produces "high" glutaraldehyde readings only when the glutaraldehyde concentration in Cetylcide G is above the MEC.

D. Conclusion

Exposure to glutaraldehyde may produce toxic, irritant, inflammatory and allergic responses. Warnings and precautions in labeling can adequately inform users of these hazards. Frequently, the personnel handling Cetylcide-G will be medical professionals, or healthcare personnel trained to handle glutaraldehyde products. Although the concentrations being handled (with the exception of Cetylcide-G prior to dilution) are not highly toxic, they may be irritating. Warning and precaution statements must be read and followed. In sum, Cetylcide-G is a safe and highly effective product when used in accordance with its labeled directions for use and precautionary information.

Product Comparison

A comparison of key features of Cetylcode-G with the predicates, Cidex Plus and MetriCide is presented in Table I. The information regarding MetriCide and Cidex Plus is taken from publicly available 510(k) summaries and labeling.

Table I

Features	Cetylcode-G	MetriCide	Cidex Plus
target glutaraldehyde concentration of use dilution	3.2%	2.5%	3.4%
claimed minimum effective concentration	2.1%	1.8%	2.1%
reuse period	28 days	28 days	28 days
exposure conditions for sterilization	10 hours 20°C	10 hours 25°C	10 hours 20-25°C
exposure conditions for high level disinfection	40 minutes at 20°C	90 minutes 25°C	20 minutes 25°C
dilution required	yes	no	no
activation required	yes (with dilution)	yes	yes
test strip available	yes	yes	yes



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

SEP 10 1998

Food and Drug Administration
9200 Corporate Boulevard
Rockville MD 20850

Cetylite Industries, Incorporated
C/O Mr. John S. Eldred
Law Offices of Keller and Heckman LLP
1001 G. Street, N.W.
Suite 500 West
Washington, D.C. 20001

Re: K974188
Trade Name: Cetylside-G Concentrate and Diluent
Concentrate
Regulatory Class: Unclassified
Product Code: MED
Dated: June 12, 1998
Received: June 15, 1998

Dear Mr. Eldred:

We have reviewed your Section 510(k) notification of intent to market the device referenced above and we have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration.

If your device is classified (see above) into either class II (Special Controls) or class III (Pre-market Approval), it may be subject to such additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 895. A substantially equivalent determination assumes compliance with the Good Manufacturing Practice for Medical Devices: General (GMP) regulation (21 CFR Part 820) and that, through periodic GMP inspections, the Food and Drug Administration (FDA) will verify such assumptions. Failure to comply with the GMP regulation may result in regulatory action. In addition, FDA may publish further announcements concerning your device in the Federal Register. Please note: this response to your pre-market notification submission does not affect any obligation you might have under sections 531 through 542 of

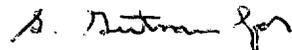
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the Act for devices under the Electronic Product Radiation Control provisions, or other Federal laws or regulations.

This letter will allow you to begin marketing your device as described in your 510(k) premarket notification. The FDA finding of substantial equivalence of your device to a legally marketed predicate device results in a classification for your device and thus, permits your device to proceed to the market.

If you desire specific advice for your device on our labeling regulation (21 CFR Part 801 and additionally 809.10 for in vitro diagnostic devices), please contact the Office of Compliance at (301) 594-4692. Additionally, for questions on the promotion and advertising of your device, please contact the Office of Compliance at (301) 594-4639. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR 807.97). Other general information on your responsibilities under the Act may be obtained from the Division of Small Manufacturers Assistance at its toll-free number (800) 638-2041 or (301) 443-6597 or at its internet address "<http://www.fda.gov/cdrh/dsmamain.html>".

Sincerely yours,



Timothy A. Ulatowski
Director
Division of Dental, Infection Control,
and General Hospital Devices
Office of Device Evaluation
Center for Devices and
Radiological Health

Enclosure

510(k) Number (if known): K974188

Device Name: Cetylcode-G

Indications For Use:

Cetylcode-G is a liquid chemical sterilant and high-level disinfectant intended for use on medical devices. For use as a sterilant, immerse instruments in Cetylcode-G Use Solution for 10 hours at 20°C. For use as a high-level disinfectant, immerse instruments in Cetylcode-G Use Solution for 40 minutes at 20°C.

(PLEASE DO NOT WRITE BELOW THIS LINE-CONTINUE ON ANOTHER PAGE IF NEEDED)

Concurrence of CDH, Office of Device Evaluation (ODE)

George A. Miller for
(Division Sign-Off) *Chin S. Lin, PhD*
Division of Dental, Infection Control,
and General Hospital Devices
510(k) Number K974188

Prescription Use _____
(Per 21 CFR 801.109)

OR

Over-The-Counter Use _____

(Optional Format 1-2-96)