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**Chlorine Dioxide Gas, Effective and Safe for Isolator/Room/Facility Decontamination and for Tank/Pipe Sterilization**




 PDA  
 Parenteral Drug Association  
 New England Chapter

SM Biofilm Revision: PDS-Sub22-230c

 **Overview**

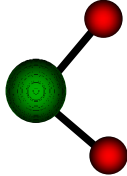
1. Define Chlorine Dioxide
2. What is the Process
3. Chlorine Dioxide Summary
4. Exploration of Applications

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 **What is Chlorine Dioxide (CD) ?**


Properties:

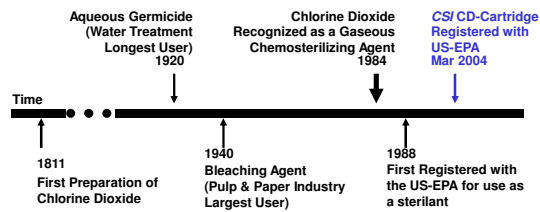
- > Yellow-Green Gas<sup>1</sup>
- > Water Soluble<sup>2</sup>
- > Boiling Point 11°C<sup>3</sup>
- > Tri-atomic Molecule
- > Molecular Weight 67.5



1. Ability to be monitored in real time with a photometric device.  
 Not subject to condensation or affected by temperature gradients.
2. Ability to penetrate water (not all sterilants can penetrate water, vapors can not)
3. Chlorine dioxide is a "true gas" at room temperatures; which means excellent distribution and penetration.

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 **Chlorine Dioxide Time Line**




Timeline events:

- 1811: First Preparation of Chlorine Dioxide
- 1920: Aqueous Germicide (Water Treatment Longest User)
- 1940: Bleaching Agent (Pulp & Paper Industry Largest User)
- 1984: Chlorine Dioxide Recognized as a Gaseous Chemosterilizing Agent
- 1988: First Registered with the US-EPA for use as a sterilant
- Mar 2004: CSI CD-Cartridge Registered with US-EPA

- > World wide consumption of chlorine dioxide – 4.5 million lbs/day (2.04million kg/day).
- > 743,000 lbs (337,000 kg) released to atmosphere in 2000.
- > Example: Maine allows 3 lb's / hour (1.4kg / hour)of CD to be emitted

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 **Types Antimicrobial Pesticides**

**Sterilizers (Sporicides):** Used to *destroy or eliminate all forms of microbial life including fungi, viruses, and all forms of bacteria and their spores.* Spores are considered to be the most difficult form of microorganism to destroy. Therefore, EPA considers the term Sporicide to be synonymous with "Sterilizer."


**Disinfectants:** Used on hard inanimate surfaces and objects to *destroy or irreversibly inactivate infectious fungi and bacteria but NOT necessarily their spores.* Disinfectant products are divided into two major types: hospital and general use.

**Sanitizers:** Used to *reduce*, but not necessarily eliminate, microorganisms from the inanimate environment to levels considered safe as determined by public health codes or regulations.

**Antiseptics and Germicides:** Used to prevent infection and decay by inhibiting the growth of microorganisms. Because these products are used in or on living humans or animals, they are considered drugs and are thus approved and regulated by the Food and Drug Administration (FDA).

[http://www.epa.gov/oppad001/ad\\_info.htm](http://www.epa.gov/oppad001/ad_info.htm)

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 **Current Sterilizer (Sporicides) Registration with US-EPA as of January 2009**

More than 5000 antimicrobial products are currently registered with the US-EPA.  
 Only 40 agents are registered as a Sterilant.

Agent	Quantity
Ethylene Oxide	24
Sodium Chlorite (chlorine dioxide)	4
Hydrogen Peroxide Based	12
Total	40

<http://www.epa.gov/oppad001/chemregindex.htm>

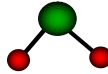
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**ClorDiSys**  
**Current Sodium Chlorite  
(Chlorine Dioxide) Sterilizer Registration**

Company	Produce Name	Registration #	Ingredient %	Sterilization Use
Alcide Corp	Alcide Exspor 4:1:1 - Base	1677-216	1.520%	Immerse in solution for 10 hours @ 20 deg C
ClorDiSys Solutions, Inc.	CSI CD Cartridge	80802-1	72.8%	Follow System Operations Guide
Englehard Corp	Aseptrol S10-Tab	70060-19	20.8%	Immerse or soak in 1000 ppm solution for min 1 hour
Pharmaceutical Research Laboratories Inc	CLIDOX-S BASE	8714-8	0.85%	1:3:1 Dilution for 5 hours @ 25 deg C

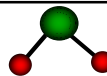
For Anthrax cleanup Under Section 18 of FIFRA, EPA exempted Sabre Technologies from any provision of EPA registration requirement for sale or use.  
<http://www.epa.gov/oppad001/chemregindex.htm>

**ClorDiSys**  
**Chlorine Dioxide Gas**



- Easy process: place generator outside the room or chamber
- Dry gas generation process:
 
$$\text{Cl}_2(\text{g}) + 2\text{NaClO}_2(\text{s}) = 2\text{ClO}_2(\text{g}) + 2\text{NaCl}(\text{s})$$
- 1 Gas Generator for approximately 70,000 cu ft.
- True Gas (boiling point +11°C)
- Requires RH 65+%
- Short cycle times (rooms 3-4 hours)
- Short contact times (isolators 0.5-2 hours)
- Non - Flammable
- Low concentrations (360-1800 ppm)

**ClorDiSys**  
**Chlorine Dioxide Gas**



- Pro's
  - No Residues (no post exposure cleanup required)
  - US-EPA registered process
  - NSF approved for Biological Safety Cabinet (BSC)
  - Inexpensive consumables
  - True Gas (boiling point +11°C)
  - Penetrates water
  - Penetrates HEPA filters
  - Photometric sterilant concentration monitoring and control
  - Carcinogen (ACGIH - NO, OSHA - NO)
- Con's
  - High Cost Capital Equipment
  - Oxidizer

**ClorDiSys**  
**Oxidation Potential of Several Biocidal Agents**

Biocidal Agent	Oxidation Potential (volts)	Oxidation Capacity (electrons)
O <sub>3</sub> (ozone)	2.07	2e <sup>-</sup>
CH <sub>3</sub> COOOH (peracetic acid)	1.81	2e <sup>-</sup>
H <sub>2</sub> O <sub>2</sub> (peroxide)	1.78	2e <sup>-</sup>
NaOCl (sodium hypochlorite)	1.49	2e <sup>-</sup>
ClO <sub>2</sub> (chlorine dioxide)	0.95	5e <sup>-</sup>

*More Corrosive* (indicated by a red arrow pointing up from 0.95 to 1.49)

The above table summarizes key properties of oxidizing biocides. As shown, CD is not as aggressive an oxidizer (oxidation potential data) as chlorine, ozone, peracetic acid, hydrogen peroxide, or bleach — and it is non corrosive to common materials of construction. The fact is that Vapor HP is 1.9 times more corrosive.

1. Barry Wintner, Anthony Contino, Gary O'Neill, Chlorine Dioxide, Part 1 A Versatile, High-Value Sterilant for the Biopharmaceutical Industry, BioProcess International DECEMBER 2005

**ClorDiSys**  
**Gaseous CD is not the same as Liquid CD**

- Liquid CD creates the chlorine dioxide through acidification of sodium chlorite  
Common Liquid Generation Methods: Mixture of Base + Water + Activator = Acidified Sodium Chlorite + Chlorous Acid + Chlorine Dioxide
- Liquid CD is corrosive due to acids involved in the generation process
- Gaseous CD is created through a dry gas process
 
$$\text{Cl}_2(\text{g}) + 2\text{NaClO}_2(\text{s}) \text{ yields } 2\text{ClO}_2(\text{g}) + 2\text{NaCl}(\text{s})$$
  - Only pure gas is delivered to the chamber, the salt solid remains in the CD Cartridge
- Comparison of liquid vs. gas showed a 3.7 log reduction with liquid CD and a 7.4 log reduction with gaseous CD with equal concentrations and exposure times

**ClorDiSys**

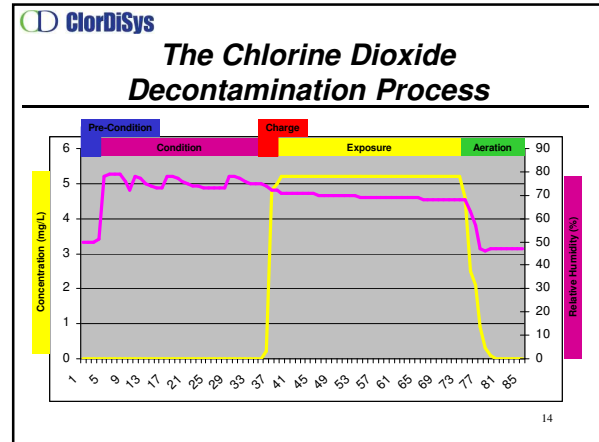
## What is the Process?

**ClorDiSys**

### The Chlorine Dioxide Decontamination Process

- Pre-Conditioning
  - Chamber Leak Test and Raise RH 65%
- Conditioning
  - Dwell time at RH SP
- Charge
  - Raise CD Concentration 1 - 5 mg/L
- Exposure
  - Dwell time at CD SP
- Aeration
  - Remove CD Gas 12-15 air exchanges

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**ClorDiSys**

### Chlorine Dioxide Generation Technology

$$\text{Cl}_{2(g)} + 2\text{NaClO}_{2(s)} \rightarrow 2\text{ClO}_{2(g)} + 2\text{NaCl}_{(s)}$$

- Performed in solid phase
- Gas generated on demand
- Self-Contained reagents
- Simple to replace consumables
- Only pure gas is delivered to the chamber, the salt solid remains in the CD Cartridge

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**ClorDiSys**

### Chlorine Dioxide D-Value Studies (Bacillus atropheus)

Carrier	concentration mg/L	D-Value minutes
Kimguard (plastic)	5	1.7
Paper 991	5	1.6
<i>Condition time 70% for 30 minutes</i>		
Paper	10	0.75
Paper	20	0.27
Paper	30	0.12
<i>Condition 75% for 30 minutes</i>		

D-Value is the time to achieve a 1 log Reduction of microorganisms.

- 1 Log = 90% Reduction
- 2 Log = 99% Reduction
- 3 Log = 99.9% Reduction
- 4 Log = 99.99% Reduction
- 5 Log = 99.999% Reduction
- 6 Log = 99.9999% Reduction

Tyvek/mylar envelopes

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**ClorDiSys**

### Sample CD Antimicrobial Spectrum of Activity

<b>Vegetative Bacteria:</b>	<b>Bacterial Spores:</b>
<ul style="list-style-type: none"> <li>➤ <i>Staphylococcus aureus</i></li> <li>➤ <i>Pseudomonas aeruginosa</i></li> <li>➤ <i>Salmonella choleraesuis</i></li> <li>➤ <i>Mycobacterium smegmatis</i></li> <li>➤ <i>E.Coli</i></li> <li>➤ <i>Listeria Monocytogenes</i></li> </ul>	<ul style="list-style-type: none"> <li>➤ <i>Bacillus atropheus</i> *</li> <li>➤ <i>Bacillus stearothermophilus</i></li> <li>➤ <i>Bacillus pumilus</i></li> <li>➤ <i>Clostridium sporogenes</i></li> </ul>
<b>Fungi:</b>	<b>Viruses:</b>
<ul style="list-style-type: none"> <li>➤ <i>Aspergillus niger</i></li> <li>➤ <i>Candida albicans</i></li> <li>➤ <i>Trychophyton mentagrophytes</i></li> </ul>	<ul style="list-style-type: none"> <li>➤ <i>Herpes simplex Type I (lipid)</i></li> <li>➤ <i>Polio Type II (non-lipid)</i></li> <li>➤ <i>Parvo Virus</i></li> </ul>

\* CD Indicator Organism

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**ClorDiSys**

### Chlorine Dioxide Summary

- Biocidal at Low Concentration and Ambient Temperature
- Efficacious under vacuum or at atmospheric pressure
- Gas Distributes Rapidly
- Gas Penetrates crevices
- Process Tolerates Temperature Fluctuations
- Non-flammable at Use Concentrations
- No Liquids
- Self-contained Reagents
- Short Cycles
- Size Scalable
  - Range of Target Volumes
  - Long Distances
- No Measurable Residuals
- Rapid Aeration (Low-Use Concentration and Minimal Adsorption)
- Gas Concentration is Easily and Accurately Monitored
- No manual wiping required
- No neutralization required
- No mixing of solutions

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**ClorDiSys**  
**Example Application:**

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**ClorDiSys**  
**Mix-fill, measuring and packaging process Isolators**

**Total Decontamination Cycle**  
 Time - 1.5 hrs (including chamber leak testing)  
 Run 2-3 times per day

**MTF** Musculoskeletal Transplant Foundation

**ClorDiSys**  
**Component Load Transfer Isolator (25 ft<sup>3</sup>)**  
**Total 31 ft<sup>3</sup> (0.9m<sup>3</sup>) with docking station**

**Total Decontamination Cycle Time - 1 hour 20 minutes**

There were a total of 25 biological indicators (*Bacillus subtilis*) placed throughout the chamber and load with NO positives.

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**ClorDiSys**  
**Train of Isolators (279 ft<sup>3</sup> - 7.9m<sup>3</sup>)**

CD Gas Injection

Workstation Isolator    Autoclave Interface Isolator    Autoclave

There were a total of 24 biological indicators (*Bacillus subtilis*) placed throughout the chamber and load with NO positives.

Workstation Isolator / Autoclave Interface Isolator and Autoclave (Total Decontamination Cycle Time - 1 hour 52 minutes)

**ClorDiSys**  
**Workstation Isolator (350 ft<sup>3</sup> - 10m<sup>3</sup>)**

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**ClorDiSys**  
**Filling Line Isolator (250 ft<sup>3</sup> - 7m<sup>3</sup>)**

Amgen  
 Thousand Oaks, CA

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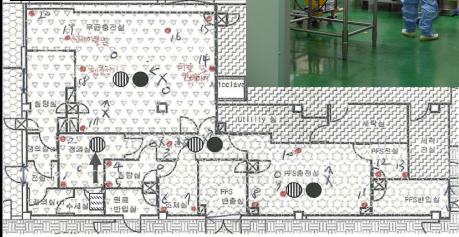


**ClorDiSys Aseptic Filling Room**  
**115 sq m (20,000 ft<sup>3</sup> – 566.3 m<sup>3</sup>)**



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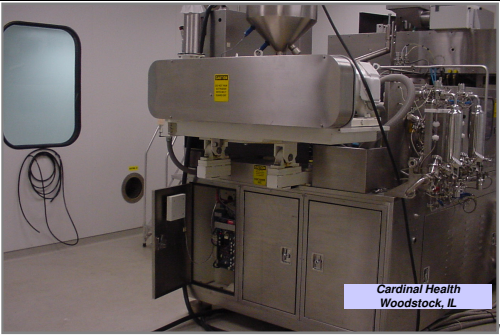
**ClorDiSys Pharmaceutical Aseptic Filling Suite**  
**15,000 ft<sup>3</sup> (424m<sup>3</sup>)**

도면) 선풍기,가습기 설치 구역


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**ClorDiSys Microbial Challenge Room [BFS]**  
**(6000 ft<sup>3</sup> - 170m<sup>3</sup>)**



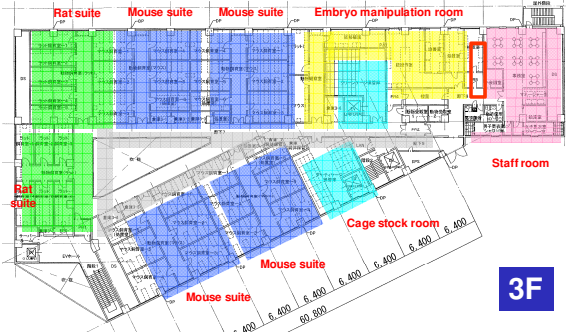
Cardinal Health  
Woodstock, IL

**ClorDiSys Sterilization of Storage Tank with Piping**



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**ClorDiSys Decontamination of New Facility (Japan)**



Rat suite, Mouse suite, Mouse suite, Embryo manipulation room, Staff room, Cage stock room, Mouse suite, Mouse suite

3F

**ClorDiSys**

**Chlorine Dioxide Gas**  
**has good material compatibility**

**For example.....**

**ClorDiSys**  
**Various Equipment**




**ClorDiSys**  
**Transmission Cryo-Electron Microscope (JEOL Cryo-TEM)**  
**\$3,000,000**



utmb Health

**ClorDiSys**  
**Automated Guided Vehicle (AGV)**




**ClorDiSys**  
**Various Equipment**



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**ClorDiSys**  
**Various Computers and Lab Equipment**



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**ClorDiSys**


**How Effective is the Process?**

**When you HAVE to be sure**

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**ClorDiSys**  
*BI Location Inside Open and Closed Cabinets*




BI Placed in OPEN Cabinet      BI Placed in CLOSED Cabinet

**Both BI's Killed**

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**ClorDiSys**  
*BI Location Inside Open and Closed Cabinets*




BI Placed in OPEN Cabinet      BI Placed in CLOSED Cabinet

**Both BI's Killed**

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**ClorDiSys**  
*BI Location Inside Closed Drawer*

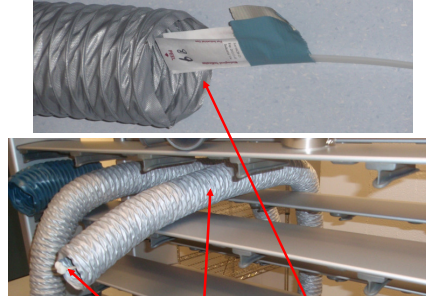


BI Placement      BI Placed in CLOSED Drawer

**Both BI's Killed**

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**ClorDiSys**  
*BI Location Inside Hose*




BI Placed in Hose

**Both BI's Killed**

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**ClorDiSys**  
*BI Location Behind Equipment*




BI Placed behind BSC

**Both BI's Killed**

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**ClorDiSys**  
*BI Location Under Equipment*

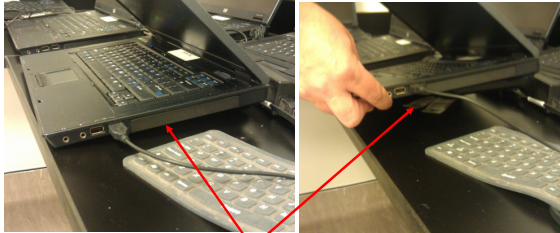


BI Placed UNDER Equipment

**Both BI's Killed**

42

**ClorDiSys**  
**BI Location Under Equipment**




**BI Placed UNDER Equipment**

**Both BI's Killed**

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**ClorDiSys**  
**BI Location Between Components**

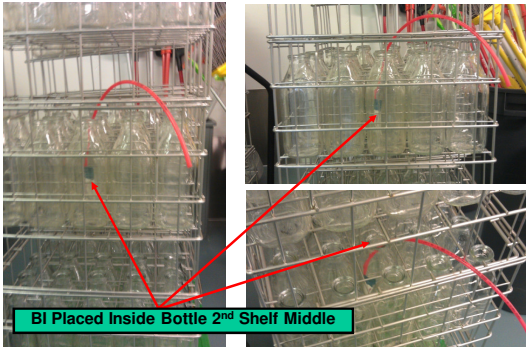


**BI Placed Between Components**

**Both BI's Killed**

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**ClorDiSys**  
**BI Location Inside Bottle 2<sup>nd</sup> Shelf Interior Bottle**




**BI Placed Inside Bottle 2<sup>nd</sup> Shelf Middle**

**Both BI's Killed**

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**ClorDiSys**  
**BI Location Between Packages / Components**



**BI Placed Between Components**

**Both BI's Killed**

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**ClorDiSys**

**Summary**

Safest fumigant available (odor detection, fast cycle time, low concentration levels, non-carcinogen)
Fastest cycle times (start to finish)
Most complete Penetration and Distribution
Most Flexible Process (rooms, BSC's, HEPA Housing, Duct work, isolators, suite of rooms, etc)
Sterilant process
EPA Approved process
NSF Approved process

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**ClorDiSys**

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