Cell Culture CO_2 Incubators and Multigas Incubators

Technical Report to verify hydrogen peroxide vapor (H_2O_2) decontamination of CO_2 incubators MCO-170AIC/MCO-170AICL, MCO-230AIC/MCO-230AICL, MCO-170M/MCO-170ML incubators

Development of the industry's fastest cell culture CO_2 incubator decontamination process using hydrogen peroxide vapor (H_2O_2) for highly regulated and general cell culture protocols that require complete, validated decontamination after each use.

CO_2 incubator with built-in H_2O_2 decontamination system integrates UV light, copper-enriched stainless steel construction and a unique cabinet design to permit frequent decontamination in less than three hours with a rapid return to service.

NOTE This validation of the use of hydrogen peroxide vapor for decontamination specifically relates to the decontamination of the CO_2 Incubators. It does not invalidate the specific use of high temperature sterilization protocols for other PHC incubators.

Abstract

The value of the laboratory cell culture incubator used in highly regulated research and clinical protocols is directly related to the proportion of incubator uptime vs. downtime in applications where frequent interior chamber decontamination is required or desired. The need for interior decontamination before initiating new applications for *in vitro* fertilization, stem cell research and regenerative tissue culture is more frequent than longer-term cell culture work. The return on investment favors short, labor-saving decontamination cycles with validation of the decontamination process for GMP applications.

The use of a hydrogen peroxide vapor (H_2O_2) generator *in situ* to decontaminate the cell culture CO_2 incubator without the use of heat decontamination offers significant advantages in routine clinical and highly regulated research laboratories where costly downtime must be avoided. The combination of a seven-minute H_2O_2 vapor in the chamber, circulated by the incubator airflow fan, followed by exposure to narrow-bandwidth ultraviolet light establishes a thorough antimicrobial impact on all incubator walls, shelves, reservoirs, air plenums, sensors and other interior components without the time and expense of high heat cycles, leaving only small amounts of water droplets as a residual. Because all interior components are designed to remain in the chamber for H_2O_2 decontamination during the process, use of a separate autoclave is avoided and the incubator can be returned to service in less than three hours.

MCO-170AIC
MCO-170AICL

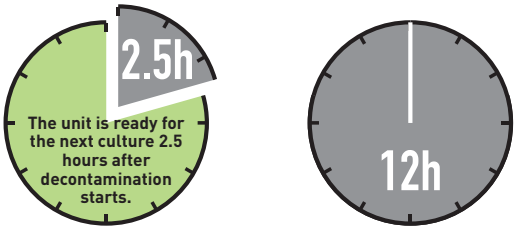
MCO-230AIC
MCO-230AICL

MCO-170M
MCO-170ML

Option 1 Option 2

Option 1 Standard for Model No. including UV.
Option 2 Standard for MCO-170AICUVH/MCO-170AICUVHL

Comparison between the H_2O_2 decontamination process and high temperature sterilization



MCO-170AIC/MCO-230AIC/MCO-170M H_2O_2 decontamination

Average time required for high temperature sterilization.

The cell culture CO_2 incubator with H_2O_2 vapor decontamination was introduced in 2009. The latest incubator complements the company's proactive *in situ* contamination control systems first marketed in 2001. In a layered and orchestrated approach to cell culture incubation predicated on good laboratory technique, the addition of H_2O_2 vapor to existing contamination control techniques meets strict requirements for a wide range of laboratory conditions and culture applications in accordance with standard FDA, EPA, and MDD guidelines.

The Cell Culture Solution

- Good laboratory technique
- Intelligent cabinet design
- InCu-saFe copper-enriched interior walls
- New single-beam, dual array infrared CO_2 sensor with passive sampling
- SafeCell UV decontamination cycling, *in vitro*
- H_2O_2 vapor decontamination process, *in vitro*

PHCbi combines:

(1) Structural and materials engineering
(2) Infrared sensor technology
(3) Self-compensating narrow bandwith ultraviolet light
(4) Multi-purpose airflow

In addition, an integrated microprocessor control unit with *in situ* digital monitoring has created a dynamic cell culture system that is designed to reward good laboratory technique for the most clinical and highly regulated applications.

Evolution of H_2O_2 Decontamination

The emergence of H_2O_2 vapor as a practical decontamination method has been well documented by numerous private and public agencies, and is receiving more attention at the bench level due to improved safety and efficacy when compared to ethylene oxide (EtO)[1, 2]. In a review of commonly accepted decontamination techniques at the USP Annual Scientific Meeting, 2008[3] [presentation on Sterilization and Sterility Assurance], H_2O_2 vapor was unanimously approved for addition to conventional sterilization methods such as chemical, dry heat, filtration, radiation and steam decontamination for consideration in selecting the best technique for various laboratory applications.

As a condensing vapor H_2O_2 is present in multiple phases simultaneously, requiring validation protocols to be constructed within the context of a liquid and gas hybrid. While the efficacy of H_2O_2 vapor assures decontamination, the wide variation in decontamination process parameters among different products and applications requires that validation protocols associated with the cell culture incubator be ascertained from product-specific research in context with known outcomes in vastly different decontamination procedures.

Advantages in GMP and GLP Applications

Design and operation of the incubator units support both clinical and non-clinical applications, starting with research and leading into development, manufacturing and quality control. As laboratories work to maintain contemporary tools and technologies in advance of new demands for both commercial and clinical success, selection of the laboratory incubator must include consideration for scalability and compliance. When retrofitting or building a new laboratory, lab planners must anticipate reporting and data logging performance of laboratory incubators previously classified as commodity equipment, but now recognized as a critical link in the chain of custody for quality management and validation[4].

The PHC incubator offers significant advantages in complying with GMP and GLP criteria imposed by outside and internal regulatory agencies or process manuals.

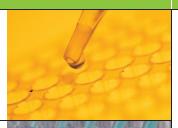
- With respect to GMP, the PHC incubator includes relational operating systems and safeguards designed to protect the cell culture or cell expressed product, particularly when associated with direct human application such as IVF*, stem cells, regenerative tissue processes or autologous cell culture[5].
- GLP criteria promoting continuity in technique and preserving the acquisition and integrity of performance data associated with the typical incubator performance as well as the decontamination cycle is accommodated through the integral control and monitoring system, complete with data point logging and archiving, and optional communications for remote or offsite monitoring.

In developing the contamination control model, PHC engineers based their H_2O_2 decontamination protocol on well-documented efficacy[6] of the increasingly popular hydrogen peroxide vapor decontamination technique often used in decontamination of biological safety cabinets, environmental chambers and other enclosures. When H_2O_2 vapor is utilized in association with the narrow bandwidth ultraviolet light decontamination system already designed into the PHCbi incubator, the complete decontamination process is safe, effective and significantly faster than conventional high-heat decontamination solutions.

The Contamination Control System

The H_2O_2 incubator decontamination system *in vitro* is an extension of the Active Background Contamination Control technique introduced by SANYO Electric Co., Ltd. in 2001. Now part of the incubator series, the cell culture CO_2 incubator employs an isolated narrow-bandwidth ultraviolet (UV) light[7] to destroy airborne contaminants in the incubator chamber, as well as water-borne organisms in the humidity water reservoir. Integrated with copper-enriched interior surfaces and components which inhibit the growth of organisms without surface discoloration.

Typical Applications

Protocol	Requirements	Advantages
Stem cell culture 	• Highly stable temperature and CO_2 and Oxygen control with elevated relative humidity to minimize small sample media desiccation. • Complete decontamination between batch processes. • Continuous mitigation of airborne contaminants following door openings. • Elimination of cross-contamination. • Flexibility for a broad range of cell culture applications.	• Precise temperature control at all shelf levels established through microprocessor controlled Direct Heat and Air air-jacket heating system[9]. • Precise CO_2 and O_2 control, impervious to short-term humidity shifts following door openings. • Safe, hydrogen peroxide vapor 2.5 hour decontamination *in situ* without heat. • Constant scrubbing of chamber air to reduce potential for mycoplasma and other contaminants. • Scalable for use in routine research or for cell cultures highly sensitive to environmental stability and contamination.
IVF* 		
Regenerative tissue culture 		
Conventional cell culture 		

The PHCbi incubator offers an optimum cell culture environment which protects cultures *in vitro*, and minimizes frequent chamber cleaning and downtime.

In 2006, comparative testing commissioned and performed by a certified independent testing laboratory[8] confirmed that the UV light decontamination process is as effective against bacteria, yeasts and molds as high high temperature sterilization at sustained temperatures ranging from 90°C to 180°C in incubators produced by other manufactures.

Additionally, the PHCbi incubator isolates the UV emission from cell cultures during normal operation permits decontamination of the internal atmosphere following routine door openings without damaging cell cultures. This is not possible for high heat temperature incubators produced by other manufactures.

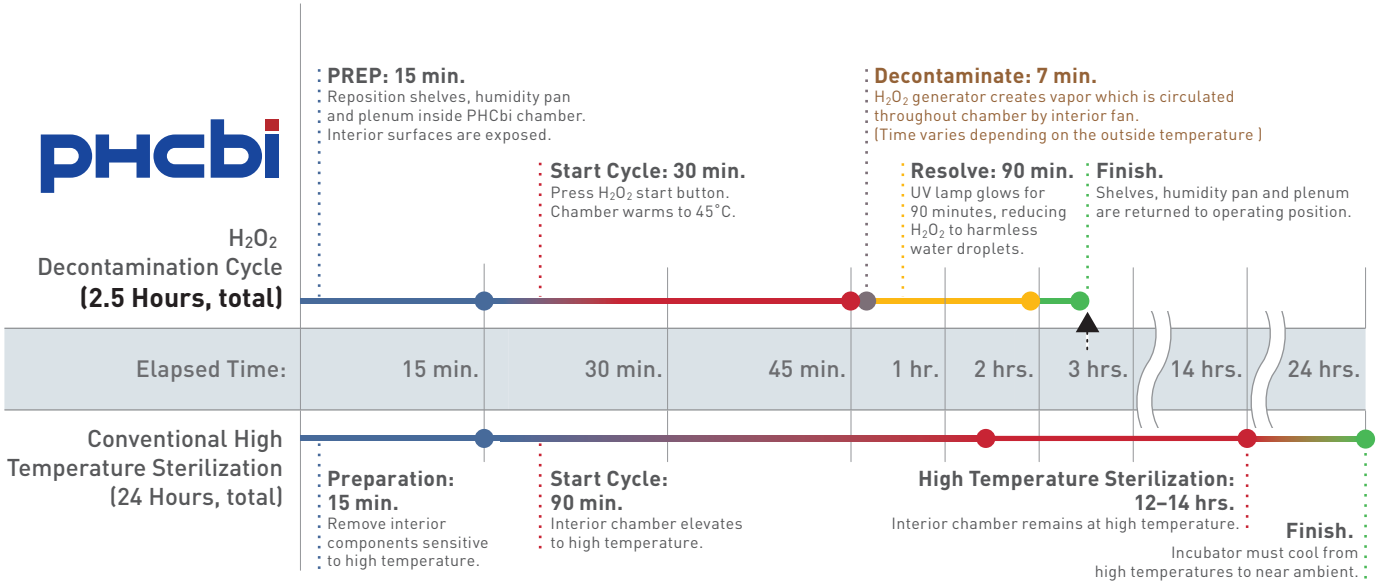
The Productivity Advantage

Automatically coordinated processes within the cell culture incubator work together to maintain optimum *in vitro* conditions of temperature, humidity and CO_2 control while preventing contamination. When complete decontamination is required, the H_2O_2 sequence offers an important uptime advantage over competitive models using high heat or conventional decontamination.

Inherent Factors Assure Maximum

The 2.5 hour *in situ* decontamination sequence returns the incubator to service more quickly and with greater efficiency than competitive models using high heat or other decontamination protocols. In applications that require frequent decontamination between processes, it yields a significant advantage in productivity.

Comparative Process:

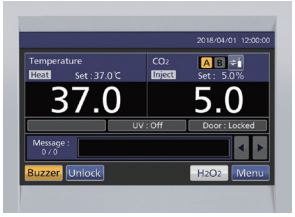


H_2O_2 vs. High Temperature Sterilization

	PHCbi H_2O_2 Decontamination	High Temperature Sterilization	PHCbi Advantage
Speed	Minimal planning required. Entire process can be completed in less than three hours.	Significant downtime expected. Process can take up to 24 hours from start to finish.	PHCbi allows decontamination anytime and permits frequent decontamination with validation for high value GMP protocols.
Construction	No special requirements for materials such as metal surfaces, gaskets, outlets, sensors or other interior components.	Requires high-efficiency insulation and gaskets to withstand cyclical decontamination procedures.	PHCbi's components are not subjected to stress beyond typical operating conditions.
Convenience	All interior components remain inside the incubator to be decontaminated concurrently with the interior surfaces.	Interior components must be removed and sent to an autoclave for decontamination.	PHCbi reduces preparation time and labor for decontamination process; returns incubator to service faster.
Adjacency	No effect on adjacent incubators or other laboratory appliances, instrumentation or equipment.	Adjacent incubator chamber must be vacated or carefully monitored for temperature increases during high heat cycle.	No need to vacate adjacent incubator or other equipment above, below or aside incubator during decontamination process.
CO_2 Sensor	Remains inside chamber. Sensor sampling system is completely decontaminated during cycle.	The CO_2 sensor, HEPA filters and other components must be removed prior to the process, and thoroughly decontaminated or replaced prior to reassembly.	CO_2 sensor uses no moving parts and requires no recalibration following decontamination process.
***In Situ* Protection**	Active Background Contamination Control remains in operation, continuously scouring the incubator of airborne and waterborne pathogens that can cause contamination or cross-contamination among cultures.	Heat decontamination offers no passive benefits to protect cell cultures *in situ*.	PHCbi continues to mitigate against any possible contamination during normal operation.

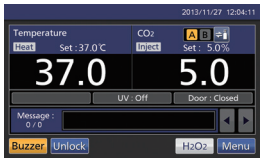
Hydrogen peroxide vapor is more efficient than heat decontamination and requires a fraction of the downtime. Manufacturers of laboratory incubators claim to solve contamination problems with various approaches to incubator design. Some of these operational techniques are moderately successful but limited in terms of long-term efficacy and convenience. Most require periods of downtime during which cultures must be removed and placed in other incubators to maintain temperature, humidity and CO_2 levels. Several manufacturers offer high temperature surface decontamination processes in incubator design. High temperature sterilization appears to be effective against vegetative microorganisms and fungal spores.

Where it Matters: PHCbi Value Increases with Decontamination Frequency: *Beyond conventional clinical and research applications, the advantages of using the PHCbi increase in direct proportion to the critical sensitivity of the cell lines in process, or the frequency of complete decontamination procedures required to separate one lot from another under GMP or other regulatory criteria. The more often decontamination is required, the more comparative avaliability of the PHCbi vs. conventional incubators that use* ***time consuming high heat decontamination systems, and thus, the greater the value in the laboratory.***

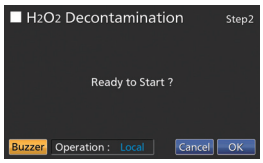


The LCD display panel includes the feature to start the automized decontamination cycle. Upon activation via the START button, the electric door interlock will engage, sealing the door, beginning the cycle. The LCD touch panel will display the current progress and time remaining. In addition, an audible and visual alarm will indicate the cycle completion.

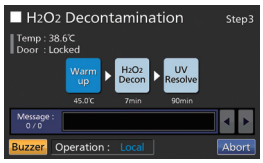
The graphical display indicates decontamination sequence status throughout the process which typically takes less than three hours after shelves, humidity pan and plenum components are repositioned within the chamber for proper exposure.



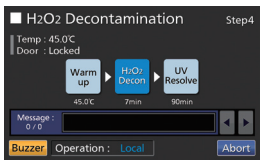
Depress H_2O_2 button



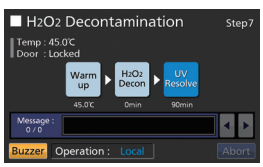
Press OK button to start decontamination



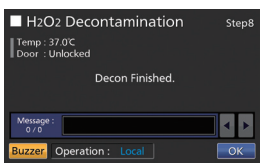
Warm-up



H_2O_2 vapor generation



UV reduction



Decontamination complete

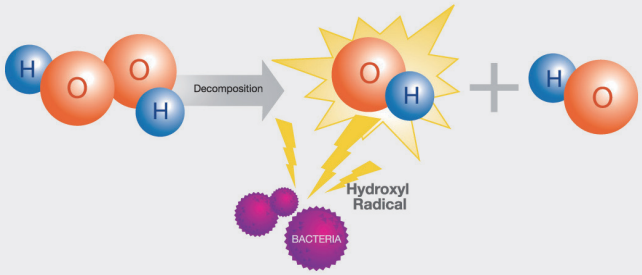
H_2O_2 and Ultraviolet Light: The Fastest Combination

The H_2O_2 decontamination process permits quick turn around of the cell culture incubator from process to process where a complete decontamination is required. Applications include *in vitro* fertilization, tissue regeneration and other highly specific protocols subject to intense scrutiny or regulation.

Removing an incubator from service is an expensive laboratory procedure that requires significant downtime for the decontamination process, prep before and after, and additional time for the chamber to reach a measured equilibrium suitable for cell culture.

While H_2O_2 is effective for a complete decontamination required separating protocols, the need for a continued protection during the cell culture process is acute. Following years of research and testing, the PHCbi. introduced the SafeCell UV decontamination system. SafeCell is a unique decontamination technology described as Active Background Contamination Control. This process arrests and destroys contaminants within the incubator chamber, and also compares favorably to high heat decontamination offered by leading industry competitors at 90°C and 180°C.

Ultraviolet Light Neutralization of H_2O_2[10]



When hydrogen peroxide is added to an aqueous solution that is simultaneously irradiated with ultraviolet light (UV) the result is that the hydrogen peroxide more readily breaks down into •OH free radicals than when UV is not present, as illustrated in equation

$$H_2O_2 \xrightarrow{UV} 2\ \bullet OH$$

Therefore, there are significantly more hydroxyl free radicals to enter into chain initiation steps than is the case without UV. UV light thus greatly increases the oxidative power of hydrogen peroxide in a manner similar to that of metal activation (Fenton's reagent). Although it has not been made clear how the reaction proceeds, it seems likely that the ultraviolet energy enables hydrogen peroxide to either separate into two hydroxyl free radicals, each having nine protons and nine electrons, as suggested by equation

$$H_2O_2 \xrightarrow{UV} 2\ \bullet OH$$

or to obtain an electron from some source, probably the target organic compounds, and thus dissociate into one hydroxide ion (nine protons and ten electrons [OH^-] and one hydroxyl free radical (nine protons and nine electrons [•OH] as shown in equation

$$H_2O_2 + e^- \longrightarrow \bullet OH + OH^-$$

The hydroxyl free radicals then go on to enter or perpetuate a chain reaction.

Independent Test Results Document the Efficacy of H_2O_2 Technique

Independent testing supports the efficacy of the concentric contamination control technique based on H_2O_2 vapor followed by ultraviolet light exposure to render the H_2O_2 to trace amounts of water and oxygen. The decontamination of the inner chamber of the incubator by hydrogen peroxide gas was verified with no BI (biological indicator) growing as observed in every BI collected from all setting locations inside the chamber.

Test Protocol and Results

Objective: *To certify the decontamination effect to the inner chamber of an incubator by hydrogen peroxide gas.*

Client: *PHC Corp. 370-0596 1-1-1 Sakada Oizumi Oura-gun Gunma, Japan*

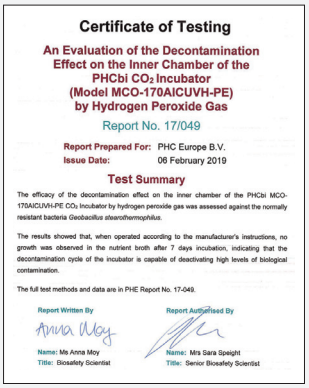
Test Microorganism: *Geobacillus stearothermophilus ATCC 12980 (spore) selected by PHC. This microorganism is used as an index microorganism in verification of H_2O_2 vapor technologies for decontaminating indoor surfaces contaminated with biological or chemical agents issued by the United States Environmental Protection Agency.*

Biological Indicator (BI) for H_2O_2 gas from Apex Laboratories, Inc., Lot H1838.

Test Method: *The test method is conducted as following the decontamination effect validation protocol that is attached to the product. Following the protocol, biological indicators were positioned at strategic locations in the inner chamber of the incubator. The inner chamber was decontaminated using the product H_2O_2 decontamination mode. After decontamination, biological indicators were put into Tryptic Soy Broth (BBL) and cultured at 55°C for one week. Location map detailed in report. Contact PHC for detailed test results.*

Test Result: *No growth was observed for any of the biological indicators after decontamination of the inner chamber by hydrogen peroxide gas certified below.*

Testing Institution: Confidential test report No.17/049 carried out by Public Health England on 17, April 2018



Certificate of Testing

An Evaluation of the Decontamination Effect on the Inner Chamber of the PHCbi CO_2 Incubator (Model MCO-170AICUVH-PE) by Hydrogen Peroxide Gas

Report No. 17/049

Report Prepared For: PHC Europe B.V.
Issue Date: 06 February 2019

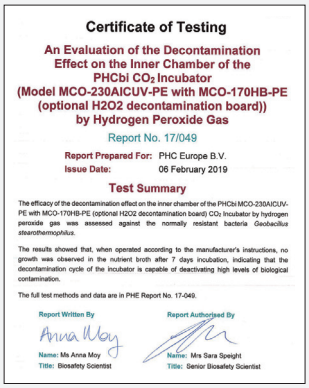
Test Summary

The efficacy of the decontamination effect on the inner chamber of the PHCbi MCO-170AICUVH-PE CO_2 Incubator by hydrogen peroxide gas was assessed against the normally resistant bacteria *Geobacillus stearothermophilus*.

The results showed that, when operated according to the manufacturer's instructions, no growth was observed in the nutrient broth after 7 days incubation, indicating that the decontamination cycle of the incubator is capable of deactivating high levels of biological contamination.

The full test methods and data are in PHE Report No. 17-049.

Report Written By — Name: Ms Anna Moy, Title: Biosafety Scientist
Report Authorised By — Name: Mrs Sara Speight, Title: Senior Biosafety Scientist



Certificate of Testing

An Evaluation of the Decontamination Effect on the Inner Chamber of the PHCbi CO_2 Incubator (Model MCO-230AICUV-PE with MCO-170HB-PE (optional H2O2 decontamination board)) by Hydrogen Peroxide Gas

Report No. 17/049

Report Prepared For: PHC Europe B.V.
Issue Date: 06 February 2019

Test Summary

The efficacy of the decontamination effect on the inner chamber of the PHCbi MCO-230AICUV-PE with MCO-170HB-PE (optional H2O2 decontamination board) CO_2 Incubator by hydrogen peroxide gas was assessed against the normally resistant bacteria *Geobacillus stearothermophilus*.

The results showed that, when operated according to the manufacturer's instructions, no growth was observed in the nutrient broth after 7 days incubation, indicating that the decontamination cycle of the incubator is capable of deactivating high levels of biological contamination.

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Report Written By — Name: Ms Anna Moy, Title: Biosafety Scientist
Report Authorised By — Name: Mrs Sara Speight, Title: Senior Biosafety Scientist

Table 1

Cell culture Incubator Model Number: MCO-170AICUVH

	RUN1	RUN2	RUN3
Interior	-	-	-
Control	+	+	+
Biological Indicator	Supplier	Concentration	D-value
Geobacillus Stearothermophilus	MesaLabs	1.8 x 10^6 CFU/mL	1.2 minutes
Batch No. H0038			

Cell culture Incubator Model Number: MCO-230AICUV**

	RUN1	RUN2	RUN3
Interior	-	-	-
Control	+	+	+
Biological Indicator	Supplier	Concentration	D-value
Geobacillus Stearothermophilus	MesaLabs	1.8 x 10^6 CFU/mL	1.2 minutes
Batch No. H0038			

**Attaching the optional MCO-170HB and MCO-170EL to MCO-230AICUV will add the H_2O_2 decontamination function.

***All of the H_2O_2 cycles (and other testing) performed in the "-PE" models perform equivalently to the "-PA" and "-PK" models.

Advantages in GMP and GLP Applications

The UV system is based upon an isolated, narrow bandwidth (253.7nm) ozone-free ultraviolet lamp interlocked with the incubator door. The interior is comprised of copper-enriched stain- less steel with copper-enriched stainless steel shelves, brackets and plenum components. A directional airflow and containment plenum surrounds the UV exposed humidity reservoir in a removable, stainless steel pan. The multi-faceted approach to contamination control is designed to destroy airborne particulates introduced during door openings, as well as contaminants that grow in the water reservoir. With active and passive systems working together in the performance model, contaminants that inevitably enter the chamber through routine door openings or other means are intercepted and destroyed while cell culture continues uninterrupted.

Efficacy of UV Exposure on Humidity Water

SafeCell UV tests on humidity pan water demonstrate how periodic exposure to narrow bandwidth ultraviolet light destroys bacterial and fungal contaminants, including thermophilic organisms, which migrate to the humidity pan water during routine door openings.

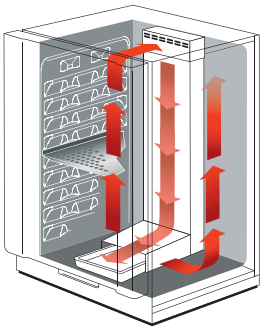
Humidity Water Test Methodology

Efficiency of decontamination for any bacteria is determined by the D value. D value is the time needed to achieve 1 log reduction in bacteria number. The corresponding D values for *E.coli* and *S.aureus* were in 5 minutes and 9 minutes respectively. Below table show effectiveness of the UV light for decontaminating bacteria in the humidifying water.

	After 5 min.	After 30 min.	D value
E.coli,	1.1 x 10^6 CFU/mL	0	5 minutes
S.aureus	3.6 x 10^5 CFU/mL	1.7 x 10^3 CFU/mL	9 minutes

Active Background Contamination Control

Together with the passive resistance of copper-enriched stainless steel, the active effort to destroy airborne contaminants *in vitro* forms an effective Active Background Contamination Control unique to the PHCbi incubator with UV decontamination function. As the cell culture process proceeds in the incubator chamber, the work of germicidal protection from airborne organisms continues unabated without costly downtime. This protection extends to thermophilic organisms as well.



Added Benefit: UV Safe and Effective During In Situ Operation

During normal operation when cells are being incubated within the chamber, the UV lamp is visibly isolated from the cell culture chamber by a plenum cover over the humidity pan, permitting UV decontamination of circulated, humidified air and humidity pan surface water to remain in process without damaging the cells. The UV cycle is factory set to glow for several minutes following each door opening. The lamp ON time is programmable depending on user preference. The position of the UV lamp, as well as the relationship between the lamp, plenum, humidity reservoir and airflow system is integral to the performance of thePHCbi incubator.

InCu-saFe Construction for Germicidal Protection

PHCbi offers exclusive use of InCu-saFe copper-enriched stainless steel alloy interior surfaces within a technical design created to eliminate contamination sources and to mitigate the effect of airborne contaminates introduced through normal use.

- Selected to provide natural germicidal protection without rust or corrosion, InCu-saFe expresses a natural germicidal attribute to inhibit the growth of molds, fungi, mycoplasma and bacteria when exposed to humidity and CO_2.
- All interior components, easily removable without tools if required.
- During the H_2O_2 decontamination cycle interior components can be repositioned within the chamber for in situ decontamination.
- All interior surfaces are exposed for conventional wipe down.
- Large curve corners and electropolished surfaces are easy to clean.
- Pass-thru ports accommodate probes or instrumentation leads as required for specialized cell culture protocols. Each chamber includes a port positioned in the rear wall, upper left, with dual silicone stoppers inside and outside the cabinet for added protection.

Mycoplasma Stain	Positive Control	Conventional Stainless Steel 304	PHCbi inCu-saFe	Conventional Copper C1100
Mycoplasma fermentans PG18	YES	YES	NO	NO
Mycoplasma orale CH19299				
Mycoplasma arginini G230				
Mycoplasma hominis PG21				

"YES" *mycoplasma strains grew on the material.*
"NO" *no mycoplasma strain grew on the material.*

How PHCbi InCu-saFe Inhibits Mycoplasma: Survival Results
Chart summarizes test results with four strains of mycoplasma. Results demonstrate how PHCbi InCu-saFe copper-enriched stainless steel alloy offers germicidal properties of conventional C1100 copper while maintaining both corrosion-proof and discoloration-resistant properties of conventional Type 304 stainless steel. Detailed test results are available from PHCbi.

Passive Contamination Control Benefits of PHCbi InCu-saFe Copper Enriched Stainless Steel

Test results comparing PHCbi InCu-saFe copper-enriched stainless steel with conventional copper construction illustrate the passive resistance of InCu-saFe interior surfaces against common Mycoplasma contamination.

Comparative Antibacterial Characteristics of PHCbi InCu-saFe Copper-Enriched Stainless Steel

The inherent germicidal efficacy of PHCbi InCu-saFe copper-enriched stainless steel (copper alloy) versus conventional C1100 copper and conventional Type 304 stainless steel is demonstrated through both film cover and drop methodology, and summarized below.

Species	InCu-saFe Copper-Enriched Stainless Steel	Conventional Stainless Steel
E. Coli (ATCC8739)	99.928%	0%
E. Coli (IFO3301)	99.847%	0%
S. Aureus (ATCC6538P)	99.998%	0%
B. Subtilis (ATCC6633)	99.997%	—
B. Stearothermophilus (ATCC7953)	99.870%	0%

Typical results are shown.
*(N=3) *Bacteria killing rate = (1-Test Sample Colony No./ Control Colony No.) x 100*

Conclusion

The PHCbi Model MCO-170AIC/MCO-170AICL, MCO-230AIC/MCO-230AICL, MCO-170M/MCO-170ML CO_2 incubators incorporates a series of internal systems, processes and design factors that work together to maintain a multi-layered defense against contamination in the *in vitro* environment. Integration of a safe and effective two-hour decontamination process, the fastest in the industry, using an H_2O_2 vapor generator offers total decontamination of all interior surfaces and return to service more quickly than conventional incubators that use high heat decontamination. As a result, the PHCbi incubators can be used for a broader range of cell culture applications, including the industry's most highly regulated protocols.

For additional product details visit

https://www.phchd.com/global/biomedical/incubation/CO2incubators
https://www.phchd.com/eu/biomedical/incubation
https://www.phchd.com/us/biomedical/incubators

1 D.Mistry; Siebert, Matt, Busujima, Hiroki et al.

2 Caputo, Ph.D.,Ross A.; Robert Reich, Jim Fisher, Robert E. Byrnes, Ph.D.; March 3, 2009; Contamination Control for the Life Sciences; VHP: The Sterilant of Choice, Characterization, Properties and Biological Effects of Vapor Phase Hydrogen Peroxide.

3 Agalloco, James, 2008; Member, USP Microbiology and Sterility Assurance Expert Committee: Quality of Manufactured Medicines, General Session II, Wednesday, September 24, 2008; Performance Testing, Microbiology Topics - A Look to the Future: USP Activities Impacting Decontamination & Sterility Assurance [71, Sterility Testing; 1211, Decontamination/Sterility Assurance; 1229 Decontamination Methods].

4 Aldridge, Ph.D., Susan; February 15, 2007; Genetic Engineering News; Techniques for Cell Culture Improvement.

5 Typical applications such as in vitro fertilization, stem cell culture, regenerative tissue culture, autologous cell culture or proprietary pharmaceutical processes require the CO_2 incubator to be vacated, completely decontaminated and validated at the conclusion of one process or batch and preceding the next. The speed and efficacy of the PHCbi H_2O_2 system permits frequent decontamination with validation under these mandates with the benefit of short lead time, minimal preparation, quick cycle and resolve and fast return to service, usually within three hours.

6 Confidential decontamination report paper for PHC April 2018, available in accordance with non disclosure agreement.

7 Marketed as SafeCell UV, US Patent 6,255,103.

8 Where indicated, independent testing funded by PHCbi Commercial Solutions and performed by Celsis Analytical Services, 6200 S. Lindbergh Blvd., St. Louis, MO, 63123 USA, Celsis is an FDA registered cGMP analytical services laboratory and functions under current Good Manufacturing Practices (cGMP) and applicable Good Laboratory Practices (GLP). Celsis has been successfully audited by regulatory agencies (FDA, EPA, DEA). www.celsis.com/lab.

9 Direct Heat and Air Jacket U.S. Patent 5519188.

10 Industrial Waste Treatment Handbook. Woodard & Curran, Frank Woodard, Woodard & Curran, Inc.; Edition: 2, illustrated, revised; Published by Butterworth-Heinemann, 2006; ISBN 0750679638, 9780750679633; Page 182.

For USA:
* IVF applications only for MCO-170M-PA
MCO-170AICL-PA / MCO-170AICUVL-PA / MCO-230AICL-PA / MCO-230AICUVL-PA are for laboratory use.

For EU:
MCO-170AIC-PE / MCO-170AICUV-PE / MCO-170AICUVH-PE / MCO-230AIC-PE / MCO-230AICUV-PE series are certified as a Class IIa Medical Device (93/42/EEC and 2007/47/EC) for medical purposes of culturing cells, tissues, organs and embryos.

PHCbi

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https://www.phchd.com/us/biomedical/incubators
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