Labeling Insert for Bioquell Hydrogen Peroxide Sterilant EPA Registration Number 72372-1-86703

Bioquell Rapid Gassing Enclosure (QUBE)

1 Overview

Bioquell Hydrogen Peroxide Sterilant has been registered by Bioquell in accordance with the Federal regulations for use in accordance with the instructions listed in this document. The contents may only be used with Bioquell Rapid Gassing Enclosure in line with the user manual and must not be used for any purpose other than that described.

Before using Bioquell Hydrogen Peroxide Sterilant the operator should ensure that he / she has undergone appropriate training on the Bioquell Rapid Gassing Enclosure and has been certified as such. If unsure, refresher training should be arranged before using the unit to run a bio-decontamination cycle.

2 HPV Bio-decontamination

When bio-decontaminating a rapid processing enclosure (the "Enclosure") using hydrogen peroxide vapor ("HPV"), the operator uses the Bioquell HPV generator to inject HPV into the atmosphere of the Enclosure resulting, once saturation conditions have been reached, with the formation of a very thin layer of 'micro-condensation' onto every exposed surface within the Enclosure. It is the formation of this microscopic layer of hydrogen peroxide condensate that provides the rapid efficacy of the bio-decontamination process and thus the success of the bio-decontamination cycle itself.

Upon completion of the active phase of the bio-decontamination cycle the HPV is catalytically converted into oxygen and water vapor (humidity).

A typical hydrogen peroxide vapor bio-decontamination cycle is made up of 4 distinct phases, each of which is described below.

2.1 Conditioning

The conditioning phase is made up of internal system tests within the unit along with the heating of the vaporizer in preparation for the start of the gassing cycle.

2.2 Gassing

During the gassing phase the Bioquell HPV generator flash evaporates the Bioquell Hydrogen Peroxide Sterilant to generate HPV which is then injected into an air-stream at a specified rate. The active distribution system injects the HPV into the sealed target Enclosure resulting in an increase in the concentration of HPV and, at saturation, producing micro-condensation deposition onto surfaces.

2.3 Dwell

Following the completion of the gassing phase, a pre-established, timed dwell phase results in the HPV circulating throughout the Enclosure ensuring that the

HPV Sterilant has sufficient contact time with the biological agents to ensure a successful bio-decontamination.

2.4 Aeration

The aeration phase results in the removal of the HPV from the Enclosure, reducing the vapor concentration to < 1PPM, the OSHA PEL (Permitted Exposure Limit) in the United States. This is typically achieved by the catalytic conversion of the HPV into water vapor and oxygen.

3 User Safety Requirements

3.1 Handling Bioquell Hydrogen Peroxide Sterilant

Bioquell Hydrogen Peroxide Sterilant contains the active ingredient hydrogen peroxide. Liquid hydrogen peroxide is classified as corrosive and must be handled with the utmost care and whilst wearing appropriate personnel protection equipment, ("PPE"). After handling, users should remove all PPE immediately and wash their hands before eating, drinking, or using the bathroom. Hydrogen peroxide vapor is also harmful in high concentrations and as such liquid hydrogen peroxide should only be handled in open areas or those that have adequate ventilation.
A summary of the health and safety information concerning liquid hydrogen peroxide is shown below, and any PPE used when handling liquid hydrogen peroxide that is not disposable must be maintained in accordance with manufacturers' recommendations.

Skin 	Contact with the skin causes irritation and possible burns. May also cause discoloration, swelling and the formation of blisters. Prolonged or repeated contact may cause dermatitis. Drench the skin thoroughly with water (and wash with soap if available). If spilled on clothing, remove immediately and wash before reuse. Skin contact may cause discoloration (whiteness) of the skin, but this is only temporary and the skin will quickly recover its normal color, usually within one hour. **If symptoms persist, seek medical advice.**
Eyes 	Contact is potentially very serious. Eye contact is corrosive and may cause severe burns, corneal damage and blindness. Do NOT allow victim to rub or keep eyes closed. Irrigate with an eye wash kit or water for at least 10 minutes whilst holding the eyelids open. **Seek immediate medical advice.**
Mouth / Ingestion 	Corrosive and irritating to the mouth, throat, and abdomen. Large doses may cause symptoms of abdominal pain, vomiting, and diarrhea as well as blistering or tissue destruction. Stomach distensions (due to rapid liberation of oxygen), and risk of stomach perforation, convulsions, fluid on the lungs or brain, coma, and death are possible. Do NOT induce vomiting. Rinse mouth thoroughly with water and give the casualty plenty of water to drink. **Seek immediate medical advice.**
Vapor 	Hydrogen peroxide vapor can cause irritation to the eyes, nose, throat, lungs and skin. Acute damage to the respiratory tract may also occur at high concentrations. More serious consequences include insomnia, nervous tremors with numb extremities, chemical pneumonia, unconsciousness and death. Remove casualty immediately to fresh air, rest and keep warm. **Seek immediate medical advice.**
Fire 	During a fire, highly toxic gasses may be generated by thermal decomposition. Do not attempt to tackle a hydrogen peroxide fire. **Call the fire department and ask for chemical emergency team.** (Water **only** should be used on a hydrogen peroxide fire).

4 Efficacy

Bioquell Hydrogen Peroxide Sterilant is only to be used with Bioquell HPV generators and when used correctly is a highly effective sterilant, active against spores, bacteria, viruses, and fungi on exposed, pre-cleaned non-porous surfaces in sealed rapid processing enclosures. Bioquell solution can be used in healthcare, pharmaceutical, defense, university and life sciences sectors including hospitals, office blocks, outdoor sheds, aircraft, retail facilities, restaurants, power stations, schools, factories, laboratories, marine craft, army vehicles, bars, sewage works, nursing homes, pharmaceutical buildings, warehouse/storage facilities, governmental buildings. Mobile medical facilities, domestic residences, water treatment plants.

When Bioquell solution is used in conjunction with Bioquell Rapid Processing Enclosures, the following validated cycles shall apply.

For use as a sterilant, sporicide, fungicide, bactericide, and virucide in sealed enclosure of 16ft^3, inject 6g/min until 26g has been injected, followed by a 10 minute dwell (allowing the vapour to remain), followed by aeration.

For use as a sterilant, sporicide, fungicide, bactericide, and virucide in sealed enclosure of 37ft^3, inject 4g/min until 120g has been injected, followed by a 70 minute dwell (allowing the vapour to remain), followed by aeration.

This product is designed to be used in Bioquell HPV generation equipment and may not be used with any other equipment other than for which it was designed. Use of this product in any manner other than for which it was designed is strictly prohibited and may not produce the desired results. This product is not to be used as a terminal disinfectant or sterilant for the processing of critical or semi-critical medical devices.

5 Bio-decontamination Cycle Protocol, (BCP)

Prior to commencing a bio-decontamination cycle of the Enclosure the individual responsible for decontaminating the Enclosure (the "Cycle Manager") must ensure that he / she has adequate and current training and in liaison with the appropriate parties (e.g. the building manager, or supervisor of the proposed Enclosure) a bio-decontamination protocol has been established. This should cover all aspects of the bio-decontamination cycle and may include, but not be limited to:

- Health and safety considerations;
    - monitoring points and frequency,
    - an evacuation plan,
    - any impact on existing evacuation plans (i.e. will isolation of the target enclosure impact on an active fire escape),
    - emergency procedures,

- Practical considerations;
    - ventilation configuration within the target area,

- power requirements,
- access to the target area,
- biological indicator regime, if any, and location plan,
- equipment location plan,

The BCP should be comprehensive and may ultimately take the format of a checklist to ensure that every necessary task has been completed by the Cycle Manager. The BCP should relate to the Enclosure and be appropriately detailed. The aim of the BCP is to ensure that each bio-decontamination cycle is run in a safe, considered and efficient manner - and may also form part of a validation process where consistency and repeatability are important.

As standard procedure, prior to undertaking a bio-decontamination cycle the Cycle Manager and any other operators should re-acquaint themselves with this packaging material, the user manual and any additional training materials supplied with the Bioquell HPV generator. These should be read in context with any existing BCPs that have been established for use within the Enclosure, and any applicable local or state laws.

For facilities that are using HPV bio-decontamination technology for the first time a new BCP should be produced. Subsequent bio-decontaminations of the same Enclosure may be conducted using an existing BCP. The following sections provide a template that a typical BCP may follow although it must be noted that each bio-decontamination and target facility are inherently different and, as such, this list is not exhaustive and each prospective cycle must be considered individually and will present its own points to address.

- A global plan/sketch of the area surrounding the Enclosure showing evacuation routes and the location of emergency equipment (e.g. fire extinguishers, fire alarm 'break-glass' points, emergency shower/eye-wash stations, telephones).
- An evacuation plan in the event of an emergency listing muster points and a list of appropriate emergency contact telephone numbers including:
  - Cycle manager.
  - Target area responsible person (e.g. Unit Manager / supervisor).
  - On-site emergency personnel (if applicable).
  - Local emergency services (Fire, ambulance, police, hospitals).

Whilst it is essential that all areas are independently assessed for suitability, if there are a number of identical Enclosures, or Enclosures which are representative of each other, it is not essential that a new or full BCP is completed for every decontamination. However, the Cycle Manager must ensure that all processes and procedures are carried out in accordance with a generic dossier, with any Enclosure specific alterations adhered to.

5.1 Step 2: Notification

5.1.1 Personnel Briefing

Prior to commencing any HPV bio-decontamination cycle it is of the utmost importance that all personnel who may have access to the target Enclosure are made aware of the process. All staff/personnel should be briefed in-terms of the logistical factors (cycle timings, areas designated out-of-bounds, restricted access areas, monitoring points) and how their normal working practices may be impacted for the cycle duration and, of course, the health and safety aspects of HPV bio-decontamination.

If appropriate a briefing session should be arranged with key personnel that may routinely have access to the target Enclosure and they should be made aware of relevant aspects of the bio-decontamination to be performed including:

- Proposed cycle timings and timescales.
- Emergency procedures and evacuation routes.
- Any impact on existing emergency procedures
- A background of HPV and the bio-decontamination process.

5.1.2 Cycle Operator Briefing

Prior to the cycle start the cycle operators should have a separate briefing in which all aspects of the BCP are discussed in order to ensure that all cycle personnel are familiar with the detail of the proposed bio-decontamination schedule.

5.2 Step 4: Target Enclosure Preparation

Prior to commencing any bio-decontamination cycle the target Enclosure should be optimized in order to maximize the efficacy and achieve a rapid and consistent bio-decontamination. There are a number of steps to be taken and these are listed and discussed below.

5.2.1 Cleaning

Hydrogen peroxide vapor has limited penetrating power into dirt and other gross contamination and thus prior to commencing the bio-decontamination cycle the target Enclosure must be subject to a minimum level of cleaning to ensure that the target Enclosure is *visibly clean* – i.e. free from all gross contamination including dust, dirt, blood, faeces, animal feed. If large levels of dust or dirt are present upon commencing the cycle then viable micro-organisms may well be present below the gross contamination and could possibly survive the bio-decontamination process.

5.2.2 Absorbent Materials

Absorbent materials must be removed from within the target area and not be exposed to the bio-decontamination cycle.

5.2.3 Occluded Surfaces

HPV is not freely penetrating through many materials; as such it is vitally important that the occurrence of occluded (i.e. covered) surfaces is minimized

5.2.4 Extremes of Temperature

The hydrogen peroxide vapor bio-decontamination process relies on saturation of the atmosphere of the sealed target Enclosure with vapor in order to form a layer of micro-condensation of hydrogen peroxide that in turn affects the bio-decontamination; as such any factors that can affect the formation of the condensate layer must be controlled. Temperature gradients within the target area should be avoided as cooler surfaces will see the formation of micro-condensation sooner and more plentifully than warmer areas. Failure to do so may potentially lead to reduced efficacy of the bio-decontamination cycle due to uneven vapor distribution throughout the target Enclosure.

5.3 Step 5: Cycle Start

Before commencing the bio-decontamination cycle the Cycle Manager should go through the BCP as a checklist acknowledging that all necessary steps have been completed ensuring the safety of the cycle.

The cycle manager should also confirm that all personnel who work with the target Enclosure and any personnel who may have cause to access the area (e.g. cleaning or security staff) have been notified about the cycle and all evacuation and emergency procedures.

Upon completion of the acknowledgement procedures the Cycle Manager may then begin the bio-decontamination cycle.

5.4 Step 6: Monitoring

Monitoring the bio-decontamination cycle takes two distinct phases, monitoring the perimeter of the target Enclosure for vapor leakage, and monitoring the vapor concentration within the target Enclosure to monitor the cycle progress, and ultimately to confirm the end of the cycle.

5.4.1 Leak Monitoring

The cycle operators should use a hand held hydrogen peroxide sensor in order to verify that there is no escape of vapor from the target Enclosure, by monitoring

the perimeter of the target Enclosure. Leak monitoring should continue through the gassing and dwell phases of the bio-decontamination cycle.

5.4.2 Cycle Monitoring

The progress of the bio-decontamination cycle itself should (where applicable) be monitored using remote sensory equipment placed within the target Enclosure. The sensors should be configured such that they provide real-time data of the cycle parameters within the target Enclosure. This data should then be logged at regular intervals throughout the cycle to record the cycle progress. On completion of the gassing and dwell phases, as the cycle moves into aeration the sensors allow verification of the vapor concentration for post-cycle re-entry.

5.5 Step 7: Cycle Completion

5.5.1 Cycle Finish Verification

A bio-decontamination cycle is completed once the cycle is in the aeration phase and the vapor concentration is below the applicable local exposure limit for personnel re-entry, (<1PPM). The vapor concentration should first be verified using the remote sensors (where applicable) and if they read < 1PPM (or other appropriate local exposure limit) then personnel may re-enter the target enclosure.

5.5.2 Cycle Success Criteria

A bio-decontamination cycle may be declared successful if the validation standards defined in the BCP have been satisfied, and the aeration phase has been completed with the vapor concentration within the target Enclosure confirmed as < 1PPM.

6 Validated and Non-Validated Use

6.1 Validated Use in Rapid Processing Enclosures up to 37ft^3

Validated bio-decontamination cycles utilizing Bioquell solution and Bioquell Rapid Processing Enclosures have been developed for use as a sterilant, sporicide, fungicide, bactericide, and virucide in sealed enclosures up to 37ft^3.

The cycle parameters are:

For use as a sterilant, sporicide, fungicide, bactericide, and virucide in sealed rapid processing enclosures of 16ft^3, inject 6g/minute until 26g has been injected, followed by a 10 minute dwell (allow vapour to remain), followed by aeration.

For use as a sterilant, sporicide, fungicide, bactericide, and virucide in sealed rapid processing enclosures of 37ft^3, inject 4g/minute until 120g has been injected, followed by a 10 minute dwell (allow vapour to remain), followed by aeration.

6.2 Validated Use in Enclosures greater than 37 ft^3

Bioquell hydrogen peroxide solution may also be used as a sterilant, sporicide, fungicide, bactericide, and virucide in sealed enclosures of various volumes (including enclosures greater than 37ft^3) with the development of a customized validated bio-decontamination cycle.

The set-up and cycle management phases of customized cycles are identical to those for a validated cycle with regard to the preparation of the bio-decontamination cycle protocol, ("BCP"), and target area set-up and sealing procedures.

In order for a customized cycle to be effective it is vital that the Cycle Manager gives due consideration to global vapor distribution throughout the target facility in order to ensure uniform formation of micro-condensation. As such, due consideration must be given to the number and location of Bioquell HPV generators deployed during the cycle, and the appropriate use of oscillating distribution fans or other appropriate equipment to ensure good vapor distribution. In accordance with the procedures described above the positions of all equipment used within the bio-decontamination cycle should be recorded on a facility plan within the BCP.

When performing customized validated cycles the cycle must be capable of attaining the required bio-burden reduction (as specified in the BCP), and have appropriate use of pre-determined indicators to ensure that the specified level is reached throughout the target facility.

On completion of the target area set-up and sealing procedures (including indicator placement) (sections 5.1 to 5.4), the Cycle Manager can begin the cycle; the cycle itself will have the same structure as a validated cycle with discrete conditioning, gassing, dwell and aeration phases.

Upon successful completion of the 'conditioning' phase (including system test) the cycle moves into the 'gassing' phase with HPV injected into the enclosure. The Cycle Manager should monitor the cycle environmental data from within the target enclosure recorded via the on-board sensory equipment in order to recognize the point of onset of micro-condensation, the dew-point. Once micro-condensation has been achieved within the enclosure the cycle then moves into the 'dwell' phase in which the vapor is allowed to circulate within the target enclosure and ensure adequate contact time is allowed between the sterilant and the biological agents to affect a successful bio-decontamination.

Upon completion of the dwell phase the cycle moves in the aeration phase removing the HPV from the target area, reducing the vapor concentration to < 1PPM, the OSHA PEL (Permitted Exposure Limit). Once the vapor concentration has been confirmed as <1PPM, the restricted access status of the target facility may be revoked and the facility 'released' back into normal operation.

Should a cycle fail to meet the pre-determined target challenge then the cycle has not been successful and the cycle should be repeated with the gassing and/or dwell periods increased, and the validation process repeated.

When conducting any bio-decontamination cycle validated or non-validated all user safety procedures listed in section 3 and operational procedures in section 5 (including monitoring and post cycle re-entry) must be adhered to and overseen by the Cycle Manager.

6.2.1 Biological Indicators, BIs

In order to assess the success of bio-decontamination cycles a standard challenge is used to ensure that the cycle has been effective. Whilst various validation methods can be used biological indicators, (BIs), are the industry standard method for validation of hydrogen peroxide bio-decontamination cycles as they present the most consistent, and repeatable challenge.

A number of organisms may be used although the accepted organism is *Geobacillus stearothermophilus;* Bacillus endospores are the most resistant class of organisms to deactivation and thus provide suitable challenge organisms. *Geobacillus stearothermophilus* also has inherent practical operational advantages in that it is thermophilic with an optimum incubation temperature of 57ºC, limiting the possibility of false positives due to the high incubation temperature. It is also a category 1 organism so is not harmful to humans and thus may be easily and safely handled.

The industrially accepted biological indicator challenge is a 6-log (i.e. > 1,000,000 spores per indicator) inoculum of *Geobacillus stearothermophilus* although lower challenge BIs (i.e. 4-log – 10,000 spores) are also commercially available. Experience has shown that the most consistent BIs are those that are inoculated onto a stainless steel substrate; other inoculum substrates including paper are available but experience has shown them to be less consistent and repeatable.

BIs should be placed throughout the target Enclosure typically placed in the corners of rooms where a 'dead spot' in terms of vapor distribution is formed at the point where three walls meet. The number of indicators used is at the discretion of the cycle manager, and each location should be recorded on a plan of the target Enclosure and should be kept with the bio-decontamination plan.

Upon completion of the bio-decontamination cycle the BIs should be retrieved and incubated as per the organism protocols and the results available after the defined incubation period.

6.2.2 Chemical Indicators, CIs

Chemical indicators, (CIs) that change color in the presence of hydrogen peroxide vapor are also commercially available and may be used in cycle verification if calibrated to an appropriate biological challenge.