# The Use of Biological Indicators for validating fumigation processes in High Containment Facilities - types, methods, sampling and statistical interpretation

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**ABSTRACT**
The use of biological indicators is wide in many aspects of high level disinfection and sterilization processes. They are used to monitor the efficacy of entire or part decontamination processes. Biological Indicators (BIs) are an independent source of testing the efficacy of not only the process but also the technology being applied.

The use of biological indicators in decontamination processes vary widely and should be fit for the purpose or process being performed. NAMSA (2007) suggests that the use of a correct biological indicator should follow manufacturer's recommendations and this is further supported by the USP 56 (United States Pharmacopeia, 2003). AS/NZS 2243.3 (2010) states that biological indicators should be used at regular intervals to monitor the microbial killing power of the sterilization process.

Whilst the use of biological indicators is widely known and accepted, there is very little guidance from regulators on the type, number of samples, sampling regime and statistical analysis and final acceptance criteria. This poster aims to present a guide to the use of appropriate biological indicators in high containment laboratory fumigation and the subsequent analysis and acceptance criteria for a successful decontamination/fumigation. The poster is presented a generic guide and not specific to any particular fumigant technology or method.

## HOW TO CHOOSE THE CORRECT BIOLOGICAL INDICATOR FOR THE GASEOUS DECONTAMINATION?

The correct choice of biological indicators is important as the wrong choice may not give correct results or be fit-for-purpose. Sigwarth (2006) suggests that the following parameters are critical when selecting the appropriate biological indicator

1. Sterilization Method
2. Model of Microbial Reduction, i.e. Biological Indicators
3. D-value Determination for Biological Indicators
4. Composition of Biological Indicators (Test Organism; Initial Population; Carrier Material; Primary Packaging)
5. Samples commercially available (e.g. Crosstex, NAMSA, Getinge, 3M, Apex, Mesalabs etc)

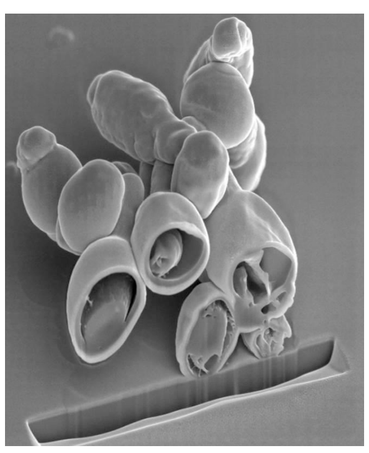
## APPROPRIATE BIOLOGICAL INDICATORS AND DECONTAMINATION PROCESS:

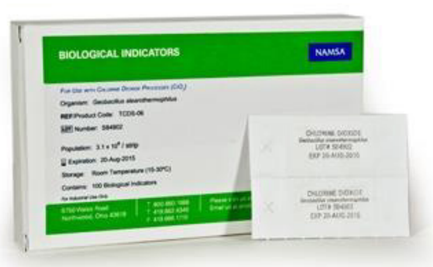
It is important when selecting an appropriate biological indicator that the BI is suitable for process being used. For example, it is fruitless to employ a Tyvek carrier with a glacine envelope for any gaseous decontamination method, as gases cannot effectively diffuse through a glacine envelope and therefore may not give a true indication of the effectiveness of the cycle even though the target parameters were achieved. Further, it would not be truly representative of the cycle success if the biological indicators are too easily killed. The reason for using biological indicators in the first place is to robustly challenge the process and validate its effectiveness.

Below is a table indicating typical biological indicators that maybe used for the various biological decontamination methods. Please note the list below may not represent all biological indicators types available or useful for the methods listed.

**Table 1.1** - Typical indicators for various fumigation methods
Geobacillus stearothermophilus is an appealing indicator in that its incubation process occurs at between 55-600C, making the indicator somewhat more independent of common contamination and thus building in some robustness against false positives that would otherwise grow at 37°C.

| Sterilization Method | Microbial Indicator | Carrier Material | Packaging Material | Reference |
|---|---|---|---|---|
| Formaldehyde | *Geobacillus stearothermophilus* | Tyvek | Tyvek | (Standards Australia/Standards New Zealand, 2010) |
| Chlorine dioxide | *Geobacillus stearothermophilus* | Tyvek | Tyvek | (Luftman, Regits, Lorcheim, Lorcheim, & Paznek, 2008) |
| Hydrogen Peroxide (multiple forms, ie: VHP, HVP, IHP etc) | *Geobacillus stearothermophilus* | Stainless Steel | Tyvek | Bioquell, Steris etc |






CHLORINE DIOXIDE
Geobacillus stearothermophilus
LOT# RU63
EX 30-Mar-2019

**Figure 1.1** - Image of Geobacillus stearothermophilus from George et al. and typical commercially available biological indicators

## PROCESS VALIDATION USING BIOLOGICAL INDICATORS

There is a significant emphasis placed on validation in the Healthcare, Pharmaceutical and Food and Beverage Industries. This includes both biological indicator validation and process validation using biological indicators. For the most part, the suppliers of commercial produced biological indicators will provide technical data or certificates of analysis for each batch of biological indicators produced (North American Science Associates Inc, 2007).

Decontamination equipment manufacturers will also have recommended biological indicators that have been validated against their process and be fit for purpose. As every facility is different and every decontamination process is different, it is important to also validate target locations within the facility to confirm effectiveness of the cycle.

Some users may opt to use a biological indicator that has not been validated by the decontamination equipment manufacture for rapid or reduced incubation times or other reasons. It is important that an internal validation be conducted to compare manufacturers process, recommended biological indicators and user preferred biological indicators to confirm acceptability and comparability. This process is imperative to demonstrate the equitability of effectiveness.

Irrespective of the biological indicator of choice, the minimum acceptance criteria needs to be determined and the appropriate target species population of the BI must be able to demonstrate the level of required efficacy. For example, a chosen acceptance level for a process may be a log-5 reduction (105) and therefore the biological indicator must be a X x 105 strip population. Although a six-log reduction (106) is common, there are several facilities and regulators that are allowing lower reductions such as DAWR Draft BC2 guidelines (DAWR, 2017) that accept log-5. See the table below for log reduction quantification.

| Quantitative Log Reduction | Qualitative Description |
|---|---|
| Log-2 | Sanitation |
| Log-3 | Disinfection |
| Log-4 | High-Level Disinfection |
| Log-5 | Decontamination |
| Log-6 | Sterilization |

**Table 1.2** - Table of Log Reduction and qualitative description (Various authors)

## OTHER METHODS OF VALIDATING PROCESSES

Aside from Biological Indicators, there are a myriad of chemical indicator methods that can also assist in validating processes. Real-time chemical monitoring of the process one form of measure to confirm that the target concentration and exposure was achieved. Appropriately calibrated monitoring, if done in for an appropriate number and position of sampling points is a useful augment to BI's. Another method is the use of colour - changing chemical indicators that will change colour when exposed to a level of concentration of the fumigant. These are excellent supporting tools but should be not used to validate biological efficacy of the process. Ultimately, biological decontamination processes require biological indicators to confirm efficacy.

## SAMPLE NUMBERS AND DUPLICATES (PAIRS VS SINGLE SAMPLES)

The number of samples required to validate or confirm successful decontamination in a facility or room is poorly described. Mostly, the regulators require there to be enough samples to adequately prove efficacy, distribution and penetration of the fumigant. The US-EPA actually use a formula below to determine the required number of sample locations to validate room fumigation processes (US-EPA, 2012).

Determine the number of BI(s) required for testing in the sealed enclosed area by using the following formula:

[(m3 – 10) / 2] + 15, where m3 is the cubic meter area of the sealed enclosure. Note that this equation is only applicable to enclosures ≥60 m3.

The BI(s) are placed inside Tyvek pouches to prevent cross contamination. Biological indicators from the same production lot will be used for all testing including controls. Spore populations will be documented from the accompanying BI Certificate of Analysis.

This formula provides one of the few prescriptive methods of determining appropriate number of locations but when applied to real life fumigation results in 100's of biological indicators per fumigation, even in a small room. This may become time and cost inhibitive and is based solely on volume with no consideration to the idiosyncrasies of each facility. In general, the number of locations within the facility will be determined by the facility operator to adequately determine successful decontamination in discussion with service providers and regulators.

Luftmann et al (2008) highlight the importance of paired samples in each test location as a single sample may provide a false or negative result and therefore deem the process unsuccessful. Gale, Havrilla et al (2005) notes several potential sources of false positives in transfer/handling steps with individual enveloped BI's.

Luftman et al points out that if a pair of samples is used, then if negative result is found and a positive immediately next to it, then there is cause to investigate post-process handling of the indicators as a possible source of contamination rather than failure of the process to achieve the level of sterility.

Luftmann et al (2008) goes further to present statistics that support the proposition that if one or more negative results determined in a sample set, that the process may not be a "failure", rather a reduced, but still satisfactory log reduction. For example, if 2 of 12 samples are negative then a log reduction may have produced a log 5.7 reduction as opposed to a log 6+ reduction. It is important to determine if this type of result is acceptable or not or if a single or small number of negative samples in a larger sample set is an "absolute" failure. The use of paired samples is most important if there are false negatives as opposed to false positives. It is also important to note that it is common industry practice that a PC laboratory fumigation would typically yield a 6 log reduction or sterilisation was achieved.

Contamination of samples during the processing of BIs is not uncommon even with Good Laboratory Practices (GLP) and therefore reinforcing the importance of using pairs of samples in each location rather than single samples.

## EXAMPLE OF SAMPLE NUMBERS AND LOCATIONS

Assume there was a small PC3 facility that required a gaseous decontamination for annual shut down and preventative maintenance (see figure 1.2). In the space there are a small number of benches, a biological safety cabinet (BSC), an incubator and other laboratory equipment, some mobile drawer systems and cupboards and an ante room. The locations of the samples could typically be as follows.

For the initial validation cycle, one might place more pairs of biological indicators in the space to validate penetration, distribution and exposure of the method (see 1.2a) whereas for a subsequent cycle, one might only place a few in the space as validation has been completed. It can be seen that the number of possible BI locations and sample numbers is reduced in subsequent cycles as validation has already been completed.

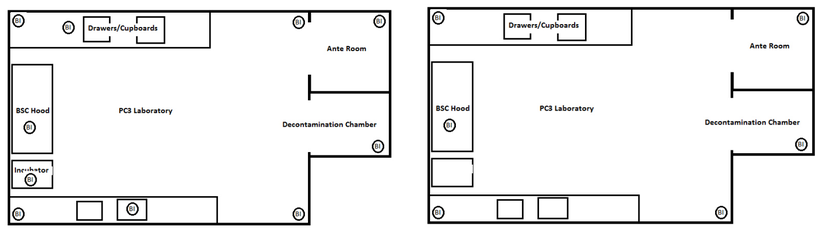



**Figure 1.2a and b** - Small PC3 Laboratory Example indicating possible biological indicator (BI) paired sample locations for a) validation cycle and b) subsequent or routine cycles (Source: Cole, ABSANZ, 2017)

## SAMPLE ANALYSIS AND STATISTICAL REPORTING

Australian Standard AS 2476 (2008) General Fumigation Procedures provides a great reference for the procedures for successful fumigation however only deals with chemical sensors and not biological indicators. AS/NZS 2243.3 (2010) states that biological indicators should be used at regular intervals to monitor the microbial killing power of the sterilization process. In neither case does the standards give any indication of sample design or location for validation of a successful gaseous decontamination cycle. It is important that the discussion is had with all stake holders involved in the decontamination process, that is, users/operators, decontamination sub-contractors and/or regulatory stake holders to determine that appropriate number and locations of BIs prior to the process being completed.

Luftmann et al makes strong statistical case for paired indicators. If both paired samples give a positive, the decontamination failed at that location – however, if one or both give a negative, it indicates at least a 95% probability, that decontamination has produced at least a
5.7 log reduction (above Australian DAWR guidelines of 5 log reduction), as compared with if both strips are negative, that gives a
6.2 log reduction at 95% confidence. A mean statistical log reduction can then be applied to the entire facility rather than just go-no go based on one false positive.

## CONCLUSION

To assure valid results, location, number, and type of biological indicators (BI's) deployed are a critical parameter. The use of "paired" Bis is strongly recommended, and statistically supported, due to known occurrences of false positive results due to contaminants.
Achievement of a "6 log" reduction is a common aim, however, has to be assessed in light of the statistics, and quantity of data, regulator prescribed minimum requirements that support that value to assure valid, defensible conclusions are drawn.

## REFERENCES

A Full Reference List available from authors.

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# A Novel approach to HEPA Housing decontamination for PC3/4 Laboratories using Chlorine dioxide gas and an Automated Mini Chlorine Dioxide Generator.

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## INTRODUCTION

Since the mid 1980s, the use of Chlorine dioxide as a disinfection chemical has been well established (1,2). The reasoning for the wide-spread acceptance, was partially driven by the overall high level of effectiveness. Older treatment chemicals, like formaldehyde had proven effective disinfectants, however, exposure and safety concerns were steadily increasing for Formaldehyde (3).

The added advantages that drove acceptance, were the lack of residue after disinfection, the absence of potentially harmful residues and the penetration ability of a "true-gas" in HEPA filter media, hidden surfaces and difficult to eradicate contaminants/infestations and eggs from species such as Syphacia muris - Pinworm (6,8).

Currently, broad scale disinfection of rooms, decontamination chambers and entire facilities is comparatively routine, using commercially available equipment for chlorine dioxide generation and monitoring (5,7,9,10).

Generally, the physical size, largely manual operation steps, cost and complexity of the equipment, has made the use of this technology the domain of highly trained technicians or commercial services.

This poster outlines a compact, automated system that is ideally suited to use by trained facility users, to decontaminate BSCs and HEPA housings, with the convenience of operation, at any time the facility needs to decontaminate these units and compares them with existing methods.

## METHOD

### EQUIPMENT

The system used in this study, consisted of a 1.1m3 decontamination chamber, to replicate a typically large BSC or HEPA housing.

The chambers' Chlorine Dioxide concentrations were monitored throughout the study with a calibrated tuned wavelength spectrometer (EMS System; Clordisys NJ USA). Data on concentration levels were recorded over time and presented as concentration (mg/L) over time and cumulative exposure (ppm-hrs).

Chlorine dioxide was generated with a compact, automated gas generator and scrubber (Mini-CD System (MCS), DRS Laboratories, Lehigh Valley, PA. USA).

Biological indicators for use with Chlorine Dioxide Processes, Bacillus Stearothermophilus. Crosstex Rush NY USA

**Figure 1** - Experimental units, concentration monitoring (EMS) image left, MCS system to generate and scrub, image right.


### PROCESS

The setup of the MCS, followed safe connection to the test chamber with two 1" gas tight tubing assemblies with camlock terminations (supply and return). The required PPE was arranged and checked for appropriateness and condition. Safety glasses, an appropriate respirator, gloves and lab coat are minimum requirement for the operator, who has had appropriate training in the systems use. Chlorine dioxide gas detection sensors were deployed (ATI portasense). A clear area of at least 2m was created using safety tape and appropriate signs. Biological indicators (pair) Bacillus Stearothermophilus were deployed in the chamber, and a control was deployed outside the decontamination zone.

Reference to the MCS manual (11), indicates the quantity of CD generation tablets to be used, based on the volume of the chamber to be treated. In this case, 8 tablets were indicated to be appropriate for the chamber volume of 1.1m3 (0 to 1.1m3 requires 8 tablets). The tablets are a commercial formulation supplied in foil wrappings to maintain effective storage life, and appropriate performance in terms of gas release when mixed with water.

Wearing appropriate PPE (gloves, gown, respirator-mask), a chlorine dioxide gas sensor was enabled then the MCS unit was powered up, through the simple-to-understand, user interface, then the generation vessel was filled with 1 litre of room temperature, laboratory tap water. The chamber was then threaded to the MCS unit and hand tightened to provide a sealed vessel.

Process chemicals were then added to separate chambers in the MCS system, the pre-packaged neutralisation chemical was added to the appropriately indicated holding chamber. Eight CD tablets were added to the CD dispensing cylinder.

The system was then reviewed for correct set-up and sealing. As chlorine dioxide is degraded by light (visible and UV) the chamber was covered with a light blanket material.

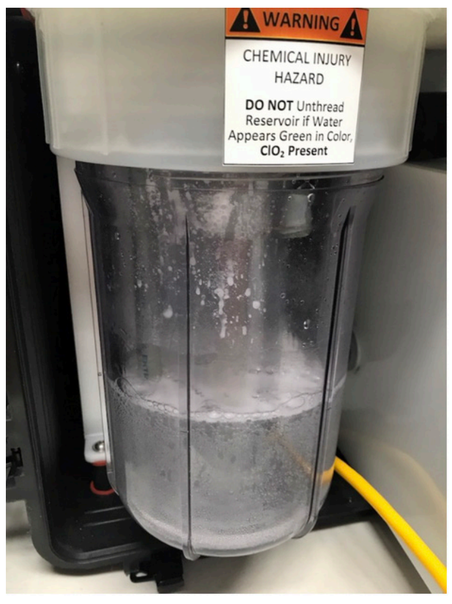


**Figure 2** - Gas generation cylinder.

The CD generation switch on the MCS was depressed, activating humidified air-flow through the system (target of 60-85% RH). This preconditioning stage allows a visual inspection, to assure there are no significant leaks in the chamber or connection points. A brief test of the scrubbing blower is to confirm readiness is done by depressing the manual scrubbing button.

Having verified all important functions, the Auto Start button is depressed, initiating an automated and timed process of decontamination, including gassing and scrubbing. The system deploys the CD generation tablets into the water containing chamber, generating a controlled charge of Chlorine Dioxide gas. This is circulated to the chamber via the inbuilt air-flow blower fan.

Gas sensors are used at this time to check for minor cabinet and connection leaks. Correction of leaks if they occur is generally done by application of tape. In this study, data collection regarding concentration and total exposure was done through the cycle, by use of a Clordisys EMS unit. .


**Figure 3** - Simple User Interface Panel.

Part way through the gassing exposure, the system re-activates the blower pump to "bump" the chamber to assure good gas distribution.

Once the predetermined exposure time is completed, the system activates the scrubbing cycle. Drawing chamber gas through a MCS installed carbon cartridge, effectively trapping the generated Chlorine Dioxide gas. After an appropriate period of scrubbing, the cycle is completed and the unit pauses. The operator then releases the neutralisation chemical into the generation chamber and allows 15 min for full neutralisation.

Gas sensors are used to verify the treated chamber and connection lines are free of Chlorine Dioxide (<0.1ppm), before disconnection the system and sealing components. The packaging, and neutralised aqueous waste are disposed of appropriately and PPE is discarded.

The entire sequence of events takes less than 150 minutes, with the display representing the status and time remaining at any time the user requires the information. At any time the sequence can be aborted and the scrubbing cycle initiated.

## RESULTS

The chamber decontamination was biologically successful as indicated by the Biological indicators (2) Bacillus Stearothermophilus compared to the control indicator.


**Figure 4** - Greater than 6-Log decontamination. Paired test BI's – negative to growth (left and centre) Control - positive to growth (right).

Concentration over time is shown in figure 5. Graph indicates that the gas is generated and deployed comparatively swiftly, with a stable period of exposure above 2mg/L, then a sharp drop to zero values when the scrubbing phase is automatically initiated by the system.

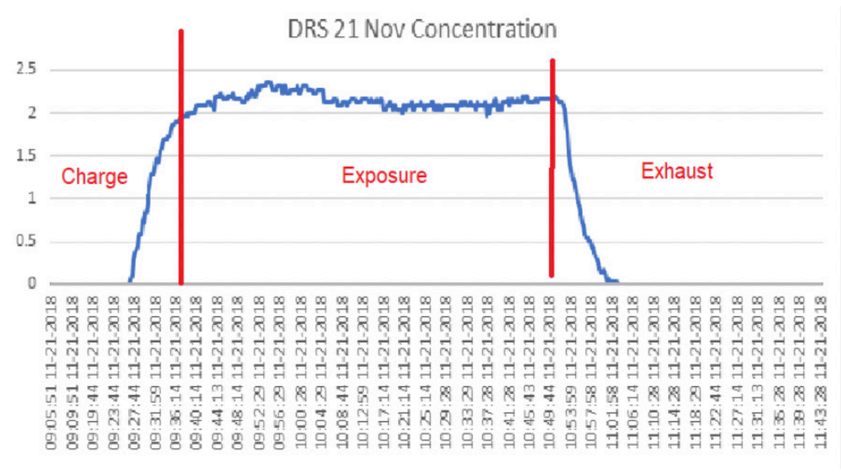


**Figure 5** - Chlorine Dioxide Concentration during the automated decontamination sequence.

Total exposure is demonstrated in figure 6. Total exposure of in excess of 1100 ppm-hrs is demonstrated for the 1.1m3 chamber volume. Generally, values of above 720 ppm-hrs would be regarded as more than sufficientto allow effective decontamination of most commonly encountered contaminants.

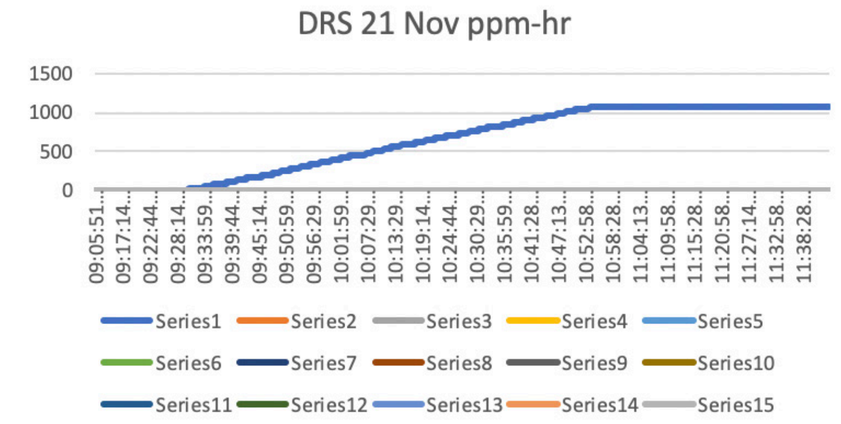


**Figure 6** - Exposure values over time recorded for the 1.1m3 chamber.

## DISCUSSION

The use of a fully automated, compact, gas generation and scrubbing system was successfully demonstrated. The controlled generation of chlorine dioxide gas, coupled with pre-packaged chemicals is a viable alternative to more manual, somewhat uncontrolled, open bowl generation processes. A significant user safety factor is added by the inclusion of a scrubbing system, that may be initiated at any time in the sequence of decontamination. The rapid time frame of operation, comparative mobility, freedom from residue, penetration power of the gas and clear ease-of-use features of the system, permit facility users an effective and accessible disinfection by chlorine dioxide.

The decontamination chamber is an appropriate model to replicate BSCs and HEPA housings. The connections and processes for these devices is identical. Calculations of tablet load are done on the basis of the volume of the devices, as was the case for the decontamination chamber. If present, HEPA filter materials will be decontaminated, as the gas is fully capable of penetrating the filter media. The use of MDS units for BSCs and HEPA housings has been done and shown to have comparable results to this systematic study.

Chlorine Dioxide is widely regarded as the most effective disinfection treatment available at present, with demonstrated efficacy for challenging species such as Syphacia muris.

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# Rapid decontamination, biological validation, HEPA and Pressure degradation testing to reduce shut-down time in a PC3/4 annual maintenance shutdown

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**ABSTRACT**

The maintainance of a PC3/4 facility is a challenging and complex task. The need for up-time, reliable containment, multiple stake holders and the inherent risks of these facilities, presents a very high level of difficulty for all involved.

A general part of the maintenance strategy is an annual shut down, where all major works are compressed into as narrow a window as possible. One of the more time consuming elements in this shut down is the steps involving decontamination, biological verification testing, thence HEPA testing and Pressure Degredation testing.

This poster outlines a number of novel steps that allow a compression of downtime of this process, without any compromise in the resulting safety or efficacy of the individual steps. Explanation of how a traditional 7-10 day decontamination/testing time can be compressed into a 4 day duration for this stage of the shutdown will be detailed, along with data to demonstrate efficacy of these processes.

## INTRODUCTION

For any Facility Manager, the annual shutdown of a High containment facility; PC3/PC4; requires precision planning, scheduling and execution to enable the facility to be up and running in the shortest time possible. The multitude of specialist and generalist trades that are involved, timing in terms of works scheduled and execution of said works followed by the required documentation and validation for Regulators (OGTR/DAWR) is a highly involved process requiring long term planning.

Any delay or issue encountered as part of the annual maintenance shutdown can result in length delays resulting in extended shut down of these much required facilities. Additional pressure is sometimes placed on an already highly sensitive environment, is when the facility is involved in clinical diagnostic work or critical timed research.

This poster looks at some novel approaches to reducing the amount of time the annual shut down is required by utilising available and approved methods especially in the preliminary decontamination and critical testing at the beginning of any High Containment shut down period.

A typical schedule for shutdown may look like Figure 1 indicating the major components of a shut down period.

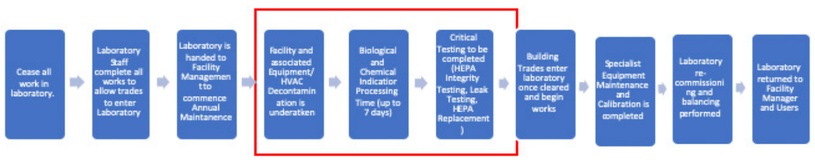


**Figure 1** - shows typical shutdown period of PC3/PC4 facility (not in detail). This poster concerns itself with the section highlighted in red whereby many days can be saved using a more rapid decontamination process, rapid biological efficacy validation and intelligent scheduling and testing.

A traditional approach to biological decontamination would typically require at least 12-24 hours aeration post decontamination (Formaldehyde, $H_2O_2$ etc) and would typically occurred on day 1 of the shutdown period. Please see Figure 2 that demonstrates, in principle, the first 12 days of a typical a) traditional method shutdown and b) a rapid method shutdown process outlined in this poster.

**Figure 2** - shows typical shutdown period in days activities of PC3/PC4 facility (not in detail).

| Traditional Method | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Shut down Days | | | | | | | | | | | | |
| 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | ... |
| Decontaminate Lab & exhaust overnight | Return to wipe down & clear lab. Collect & Process BI's | Await BI Results | Await BI Results | Await BI Results | Await BI Results | Await BI Results | BI Results & Acceptable | Commence Leak Testing & Critical Testing | Facility Maintence | Facility Maintence | Facility Maintence | Facility Maintence |

| Rapid Method | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Shut down Days | | | | | | | | | | | | |
| 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | ... |
| Decontaminate Lab & exhaust on same day. Collect BI's and Process | Await BI Results | BI Results & Acceptable (AM). Commence Leak Testing & Critical Testing (PM) | Facility Maintence | Facility Maintence | Facility Maintence | Facility Maintence | Facility Maintence | Facility Maintence | Facility Maintence | Facility Maintence | Facility Maintence | Facility Maintence |

Methodology:

By adopting the following principles and decontamination process, there can be up to a 6 day saving alone on the first step of the shut process.

Traditional biological indicator incubation times would be

1. Rapid Decontamination Process – Chlorine dioxide (as per AS/NZS 2243.3)
2. Rapid & Validated Biological Indicator Technologies and Incubation Times
3. Intelligent Scheduling and Planning to minimize downtime in Critical Testing (Pressure Degradation and HEPA Integrity Testing)
4. Rapid Reporting of Results and Quality Gates

### RAPID DECONTAMINATION PROCESS – Chlorine dioxide (as per AS/NZS 2243.3)

The use of more rapid biological decontamination methods (such as Chlorine dioxide in this case), can reduce the amount of time a facility is down in terms of time. Chlorine dioxide offers some unique chemical and physical characteristics that make it preferable in terms of cycle lengths. The fact that it is a true gas at room temperature means that it will quickly fill the target space. Given that it is a true gas, it will not condense out onto cold surfaces and therefore only requires minimal aeration times. Figure 3 indicates a typical cycle in a large space showing the charge, exposure and aeration back to below 0.1ppm in a little over 3 hours for the complete cycle. There is no need to leave aeration for 12-24 hours like other methods and therefore saving precious shutdown time.

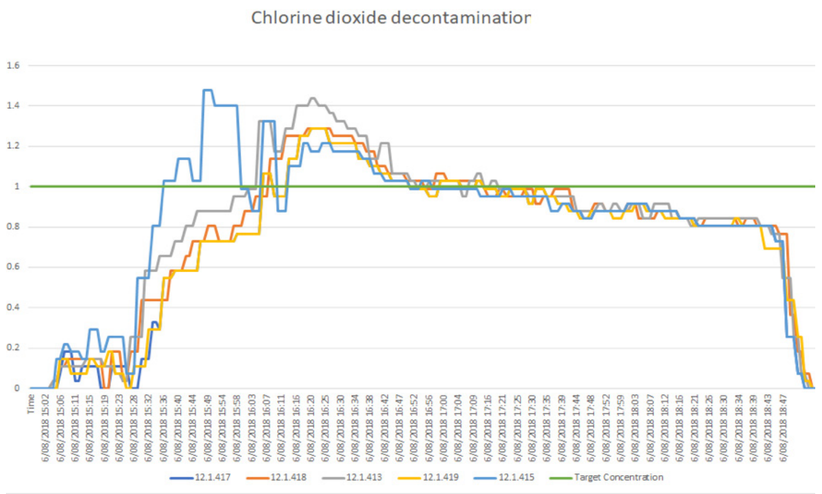


**Figure 3** - A typical biological decontamination cycle for a large space and cycle stages. Note cycle time is 3.5 hours.

It's gaseous properties also allow it to be mechanically moved in the space and therefore able to decontaminate air handling units such as BSC2 Cabinets, Laminar Flow Cabinets and HEPA Housings during the same cycle time eliminating the need to perform these decontamination cycles after the main target area. This can again save up to 24 hours by eliminating multiple decontamination cycles using traditional methods. This, of course, relies on the facility design allowing for such mechanical movement. Figure 4 shows a typical HEPA housing arrangement with the addition of side-channel blowers to assist the movement of the Chlorine dioxide through the HVAC ductwork and HEPA Housings during the main cycle. Scheduled intelligently, the Chlorine dioxide decontamination cycle allows for the retrieval of biological indicators on the same day as the cycle is performed and therefore able to be processed the same day eliminating unnecessary delays in the schedule.

**Figure 4** - A typical HEPA Housing and Side-Channel Blower set up in actual in-situ image.

### RAPID & VALIDATED BIOLOGICAL INDICATOR TECHNOLOGIES AND INCUBATION TIMES

There are many available and emerging rapid biological indicators (BI) that allow for rapid detection of biological decontamination efficacy. Many BI manufacturers have designed and validated rapid systems that will detect growth within as little as 3-4 hours (3M, Getinge etc) and where validated for the facility and process, can shave days off the shutdown period. For the sake of this paper, the use of Crosstex Medical Geobacillus stearothermophilus (Product Code TCDS-06) Tyvek spore strip enclosed in Tyvek pouches; Batch No. RU86, expiry 31/5/2020 – see Figure 4.5) were used which have been validated by the manufacturer to 36 hours. Used in conjunction with the manufacturers specified TSP Prepared Media allows the incubation times for the BI to be reduced from traditional 7 days to as little as 36 hours eliminating up to 4 days from the traditional shut down period. It can be seen in Figure 2 that the testing may be commenced as soon as day 3 using these methods rather than the traditional day 8 or 9.

Of course this requires intelligent scheduling and execution to allow BI to be removed from the facility and processed by the laboratory in potentially the same day. 24 hours laboratory inspections for positive growth of control samples and treated samples can indicate early alarms for positive growth and therefore scheduling of other trades based on these results. Previous papers by the authors suggest the use of paired samples to minimise confusion and build a more robust statistical interpretation when a single positive BI is discovered especially with accompanying chemical indicators/ data in support.

**Figure 4.5** – shows the Biological Indicators validated to 36 hour incubation and pairs of samples in each location (Luftmann et al, 2010)


### INTELLIGENT SCHEDULING AND PLANNING TO MINIMIZE DOWNTIME IN CRITICAL TESTING (Pressure Degradation and HEPA Integrity Testing).

Scheduling, planning, execution and Project Management is crucial to any maintenance shutdown period but much time can be saved by intelligent Management of the project.

Early engagement of the stake holders by the Project Manager is crucial to maintaining the project requirements, scheduling and execution and subsequent communication between each trade/service provider. Procurement of long lead-time parts and labour needs to be planned well in advance and be taken into consideration during the scheduling process. Of course, it is imperative that the Project Manager has a full and comprehensive knowledge of the r egulatory requirements of PC3/PC4 facilities, the required outcomes and regulatory responsibility the operator has to produce accurate records to Regulators. All this information can then be shared in a project schedule that is communicated to each stakeholder, their responsibilities and outcomes are and what communication is required back. Figure 5 shows a part of a typical shutdown schedule or Gannt chart.

Once the results of the biological decontamination have come back to confirm efficacy, the next testing phase of the facility/equipment can be commenced. Utilizing qualified and experienced Consultants for the scheduling and testing can lead to savings in time. The Consultant will make sure that all parts and staff are available and ready for the next phase of thae maintenance shutdown. Working with the decontamination service provider or internal staff in the case where this is done in house, not removing room selaing material after the decontamination cycle means this can be utilized for a secondary purpose of room/laboratory pressure degradation testing saving valuable time in terms of secondary set up processes. This requires trades to work closely together and communication through a series of predetermined quality gates to confirm readiness for the next phase of the shut down.

From Figure 2, Specialist Testing Consultants are able to move their equipment in and be ready to undertake testing as soon as the biological indicator results are available. Once received, consultants are able to immediately commence testing and this saves down time once again. With strategic planning and execution, much of this testing work can be carried out in unison and in one day saving several days on a typical schedule. This can involve leak testing of rooms and HEPA Housings (AS/NZS 2243.3, 2010) (See Figure 6) or HEPA Filter change over or Integrity Testing to AS1807. These results can be available immediately after testing is completed rather than waiting for days after the testing has been completed.

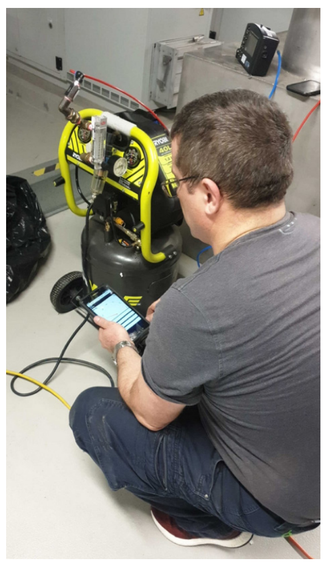

**Figure 6** - shows the pressure degradation testing being performed on a facility.

### RAPID REPORTING OF RESULTS AND QUALITY GATES

For any plan to come together, it requires prompt communication from stake holders on each stage of the shutdown period. This includes reporting from various trades and service providers on progress and outcomes at each stage of the project. To maintain the shortest possible downtime of the facility, the critical dates for each report/communication should be nominated by the Project Manager in consultation with each stakeholder and prescribed in the Project Schedule, similar to the one in Figure 5. Each stage of the project will require the report/results from the Service provider to be provided as this reporting can then trigger the next phase of the project, ie: Quality Gates. The Project Manager is then able to instigate the next phases of the project.

The need for rapid reporting needs to be discussed and confirmed prior to the project commencement as part of the Stakeholder engagement process. As the reporting can sometimes involve third-party laboratories and external processes, the need to have this communicated to said providers is required pre-process so that there can be no or minimal delays when executed. Providing a central communication and file sharing system will allow Service Providers to be able to upload their reports to the Project Manager whilst storing all Reulatory required documents in a central system. The Project Manager will have preliminary knowledge of the overall shutdown reporting requirements from the Facility Operator and by Service Providers providing these rapidly, the Project Manager can better control the schedule and compile the overall report during and not after the shutdown period has ended.

## CONCLUSION

It can be seen in Figure 2, that by following all or some of these methods/ processes, that many days can be saved in a traditional PC3/PC4 annual maintenance shut down period. Each step requires stakeholder engagement and outcome communication, intelligent scheduling and quality gates nominated and rapid communication down and upline between stakeholders at critical times during the project. The use of rapid decontamination processes like Chlorine dioxide and adoption of rapid and validated Biological indictators can vastly save many days from a traditional shutdown methodology.

Critical to all the above processes is Intelligent and experienced Project Management to bring together Facility Operators and Service Providers to clearly plan, communicate, execute and deliver a rapid and comprehensive shut down whilst providing prompt reporting of testing, maintenance and data to fulfill operator regulatory requirements.

## REFERENCES

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