# Sanitisation with vapour phase hydrogen peroxide – practical cycle development and future improvements

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## Abstract

Vapour phase hydrogen peroxide (VPHP) has been in use as a sanitising agent, particularly for isolators, for over 20 years. During this time the process has gained a reputation for lengthy and complex cycle development, and for some unreliability. These problems stem from two points:

a. Lack of understanding how the vapour phase hydrogen peroxide process actually works.

b. Lack of consistency in the biological indicators used to challenge the process.

This paper starts by explaining how the vapour phase hydrogen peroxide rapid sporicidal process works and continues with a description of the present methods of cycle development. The paper continues with some suggestions as to how cycle development can be speeded up considerably and introduces enzyme indicators (EIs) as a recent development to add to chemical indicators (CIs) and possibly replace biological indicators (BIs).

The paper offers practical solutions to both the problems mentioned above, based on long experience with the design, construction and validation of vapour phase hydrogen peroxide generators.


## Vapour phase hydrogen peroxide – how the rapid sporicidal process works.

In order to use the VPHP process, it is vital to understand how the process actually works. Since the vapour will have been derived by evaporation from hydrogen peroxide solution, a mixture of air, water vapour and hydrogen peroxide vapour is delivered to the isolator. The molecular weight of hydrogen peroxide (MW 34) is almost twice that of water (MW 18). Thus hydrogen peroxide vapour has a much lower vapour pressure than water vapour. This in turn means that the hydrogen peroxide vapour readily condenses out onto the internal surfaces of the isolator and its contents. Most importantly, this condensate is at high concentration, around 60% or 70%, and it is this liquid condensate that is responsible for the very rapid sporicidal effect of the VPHP process. The condensate forms as very small droplets, such that it is not visible on surfaces, and it is therefore termed "micro-condensation". For these reasons, it has been proposed that the VPHP process should more correctly be termed "micro-condensed hydrogen peroxide" (MCHP)[1].
The hydrogen peroxide vapour is merely the vehicle which delivers micro-condensation to the isolator surfaces. *To amplify this important point, the hydrogen peroxide vapour phase bio-decontamination process is a condensation process.* This paper will therefore hereinafter refer to MCHP as the process in discussion.

## Wet or dry?

Up until recently, there were two alternative descriptions of the vapour phase hydrogen peroxide bio-decontamination process as:
a) a so-called "dry" process, and
b) a so-called "wet" process. This debate was to some extent driven commercially, one group claiming that the process was entirely dry, with no liquid phase present during any part of the cycle, and another group indicating that the process was, at the microscopic level, a liquid process. Given the clear understanding of the MCHP process, this differentiation is no longer relevant.

## The conditions required for MCHP

The conditions required for MCHP are not rigorous, indeed it will form under a wide range of temperature and humidity conditions. However, the operating parameters do need to be governed to give reliable and repeatable bio-decontamination cycles. These operating parameters are listed as follows:

- Concentration of the hydrogen peroxide solution used (%)
- Flow rate of the hydrogen peroxide solution to the evaporating device (g/min)
- Carrier air flow rate ($m^3$/hr)
- Carrier air temperature (°C)
- Carrier air humidity (% RH)
- Isolator surface temperature (°C)
- Time of exposure (min)

The concentration of the hydrogen peroxide solution used is generally fixed at about 35% aqueous solution. Concentrations above this have been used, but present an increasing hazard[i] for transport and use. Concentrations below this have been extensively used with some success, and merit further investigation. This parameter is generally not a variable in cycle development.

If 35% solution is used, and the isolator is of the order of one cubic metre in volume, the flow rate of the hydrogen peroxide solution to the evaporating device is normally around 5 grams per minute. It has been conventional to use a higher flow rate initially in order to raise the vapour concentration quickly in the isolator, and then set a lower flow rate for a period of "dwell" at high concentration. These values are generally variable parameters in cycle development.

The carrier air flow rate for a one cubic metre isolator is likely to be around 20 cubic metres per hour. A number of gas generators have fixed flow rates at for instance, 18 cubic metres per hour. This parameter is generally not a variable in cycle development.

i. With increased concentrations, the hydrogen peroxide solution becomes a steadily more powerful oxidising agent so that there is corrosion risk, fire risk and ultimately, explosion risk

The temperature of the carrier air emerging from the gas generator results from the passage of the carrier air through the hydrogen peroxide evaporating device. It is often around 65 degrees centigrade. This parameter is generally not a variable in cycle development.

The issue of carrier air humidity is somewhat contentious. Earlier gas generators incorporated a system to reduce the humidity of the air in the isolator to a low level, perhaps less than 5% RH. This was thought to allow more "space" for hydrogen peroxide vapour so as to raise the vapour concentration in the isolator to as high a level as possible. This view is erroneous. The MCHP process works by producing micro-condensation and this can perfectly well occur with relatively humid carrier air. Indeed, very dry carrier air combined with low flow rate of solution to the evaporator may give apparently high peroxide concentrations, but disallow micro-condensation. The result of this is a low BI log reduction and a very puzzled operator. Experience shows that if the carrier air is in the region of 20% RH to 50% RH, then micro-condensation will take place and high log reduction can occur. This said, some gas generator manufacturers still dehumidify the carrier air, at least to give a fixed starting point, rather than use whatever the RH of the isolator happens to be. It is suggested that the RH of the carrier air be set ideally at say 35%, and that thereafter this parameter is not a variable in cycle development.

The temperature of the surfaces inside the isolator can be a critical, a factor generally misunderstood by earlier gas generator manufacturers and operators, who thought that the kill of micro-organisms (and the cycle challenging BIs) was purely due to the hydrogen peroxide vapour. Given that MCHP is in fact a condensation process, clearly the temperature of the surfaces could have a significant effect on the efficacy of a given gassing cycle. Surfaces that are relatively warm may not develop micro-condensation at all. Surfaces that are relatively cool may develop excessive condensation, to the extent that frank, visible condensation occurs. This low-concentration liquid then preferentially absorbs incoming hydrogen peroxide vapour, robbing the other surfaces of micro-condensation potential. In either case, a poor micro-biological kill will take place. In practice however, it seems that surface temperatures are not all that critical. Provided that there are no obvious sources of heat (for example, a warm autoclave door on one wall of the isolator) the surfaces inside an isolator housed within a standard cleanroom will be suitably constant. That said, there may be some tendency for the incoming gas to warm certain surfaces, however this effect seems to be limited in practice and therefore surface temperatures are not a variable in cycle development.

Time of exposure is the most important parameter in gassing cycle development. Again using a one cubic metre isolator an example, the "ramp-up time", during which a high peroxide solution injection rate is used, might be in the region of 5 to 10 minutes. The subsequent "dwell time" with a lower injection rate might be in the region of 10 to 15 minutes. The method of setting the appropriate times of exposure is really the central issue of cycle development.

## The "conventional" MCHP cycle development sequences

Cycle development employs resistant biological indicators (BIs) to challenge the MCHP process and thus demonstrate bio-decontamination efficacy. The conventional aim of the bio-decontamination cycle is to demonstrate log 6 reduction of the BI. It has been suggested that log 6 is logically unsupportable and that in fact log 4 would be adequate demonstration of efficacy[2]. The exercise of MCHP cycle development is essentially a three stage process:

1. The "worst case" sites for BIs are identified.
2. Cycles are run to establish up to what point in time BIs survive the cycle, indicating the lower limit of the performance envelope. These are termed partial cycles. Cycle times which are long enough to meet the performance requirement can be used in aseptic isolator operation.
3. Finally, these cycles are conventionally proved by three back-to-back PQ runs.

Up to now, the generally-accepted sequence of MCHP cycle development has been roughly thus:

1. Smoke pattern studies. With suitable smoke introduced as a visible analogue of incoming hydrogen peroxide vapour, areas of apparently low smoke penetration can be noted as suitable "worst-case" sites for BIs, i.e. sites where the gassing process is most challenged.
2. Temperature and humidity studies. These take various forms, some more meaningful than others. In one example, small temperature and humidity loggers are placed throughout the volume of the isolator and its load. A typical gassing cycle is then run but with pure water in place of hydrogen peroxide solution. A study of the readout from the loggers may indicate areas of high or low local temperature, or of high or low local humidity. Such places would be "worst-case" sites for BIs.
3. Chemical indicator studies. Here chemical indicators (CIs) are placed throughout the volume of the isolator and its load. A typical gassing cycle is then run with peroxide solution, the CIs changing colour according to exposure to the vapour. This can be a useful, reasonably rapid and cheap method to find "worst-case" sites for BIs, since CIs located in areas of poor gas penetration will change colour more slowly than those exposed to free gas penetration. Recently-developed CIs actually indicate the BI log reduction that would take place.

Partial cycle studies. These take a variety of forms, and often centre on establishing a D-value[ii] for the BIs. In one method BIs are removed at regular intervals from an isolator during a gassing cycle. They are then incubated and enumerated, and from this data a D-value is calculated. In another method BIs are again removed from an isolator during gassing, and incubated, but this time growth or no growth is noted. Using statistical

ii. The D-value is defined as the time taken to reduce a given spore population by one order of magnitude i.e. to reduce it to one tenth of the starting population. This parallels log reduction such that in theory at least, exposure for six D-values would lead to log 6 reduction

analysis, a D-value is again established. Having obtained a D-value, the cycle developers then multiply the D-value by 6 to give the exposure time required to achieve log 6 reduction of the BIs, or occasionally by 8 to give a theoretical log 8 reduction.

Given the wide variation in D-values for differing batches of BIs, and the consideration that the MCHP process does not put constant stress on the BI, the usefulness of the D-value concept may be questionable in this context.

4. The author prefers the so-called "kill-time" method of partial cycles. Here cycles are run with successively longer dwell times, for example 6, 8, 10 and 12 minutes, in a one cubic metre isolator. Incubation of the BIs with growth or no growth noted, gives an estimate of the kill time, i.e. the time of exposure at which log 6 reduction is achieved. A safety margin of 50% or 100% is then applied to the kill time for the cycles to be used in normal aseptic operation. This method is simple, safe and less costly in operator time and consumables, and does not require skilled technicians to carry out the work.

## The rationalised MCHP cycle development

The "conventional" MCHP cycle development sequences described above have evolved in many cases to become long and complex, with highly detailed protocols to be executed. This has had the unfortunate effect of turning quite a simple process into an expensive and time-consuming exercise. When cycle development for a filling line isolator has costs approaching a quarter of a million pounds, and takes several months to complete, then surely it is time to review the way in which MCHP is applied to bio-decontamination in the pharmaceutical industry.

Whilst we should in no way "cut corners" in cycle development, we can rationalise the process in the light of experience. It is the author's experience that data both from smoke pattern studies, and from temperature/humidity studies, have in no way actively contributed to the subsequent siting of test BIs. The results of these studies have been reviewed, but no clear information or pattern has emerged and, generally-speaking, the choice of BI sites is essentially intuitive. Furthermore, the author has witnessed other specialists executing MCHP development protocols which included these preliminary studies, but then used pre-determined BI sites in any case. We may conclude from this that smoke and temperature / humidity studies are not actually of great use in the MCHP cycle development process, and time should not be expended on this type of work.

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Data from chemical indicators however, may be very helpful in siting BIs and more generally in providing supporting data for the cycle development as such. CIs react quickly as the gassing cycle proceeds, giving the results at the end of the cycle. Thus the results can be reviewed immediately, and the next development cycle modified accordingly, with changes to BI sites and cycle parameters, as required. Information can be accumulated quickly, and then cycles using time-consuming BIs can be run with a greater degree of confidence.

Thus it is suggested that practical cycle development might consist of three phases as follows:

1. Review of Existing Information. This would entail gathering any data from the isolator manufacturers, and the gas generator manufacturers, to indicate what sort of initial values for the operating parameters would be appropriate for the development in hand. These would be the sort of values indicated previously in this paper. Information might also be gathered from the literature, from journals and from consultants, or other experienced personnel. A wealth of data already exists and whilst all isolators and their associated loads are different, it should be possible to predict the cycle parameters fairly accurately before the actual development takes place. At the same time, useful information can be gathered on the sort of distribution of CIs and BIs that has been used for gassing cycles in the past. In the author's opinion, the ideal cycle should show no visible condensation other than slight misting of surfaces at the end of the dwell phase of gassing.
2. Chemical Indicators. An appropriate pattern of chemical indicators can then be placed inside the isolator and the contents, to provide visual information on the performance of the preliminary gassing cycles. The choice of CI sites is largely intuitive, based on locations which appear least likely to receive free gas circulation. This includes top and bottom corners of the isolator, the lower surfaces of gauntlets, between glove fingers, underneath equipment, within loads such as racks of bottles or Steritest cartridges, any "dead end" features such as drains, and the like. Ideally, the CIs should be visible, so that the progressive change in colour can be noted as gassing proceeds. In the ideal gassing cycle, all of the CIs change colour at the same rate, indicating that gas has circulated equally to all the surfaces within the isolator and its contents. Since CIs are relatively inexpensive, fairly large numbers can be used, perhaps fifty or sixty in a one cubic metre isolator and its load. This would provide comprehensive information on the circulation of the gas and thus the likely efficacy of the MCHP process in relation to BIs. Modifications can be made to the cycle parameters and to the isolator load pattern accordingly.
3. Biological Indicators. These are the real test of the bio-decontamination process. Currently the convention is that any MCHP cycle should demonstrate log 6 reduction of *Geobacillus Stearothermophilus* spores,

although as previously indicated, this may be considered excessive, and log 4 reduction could be sufficient in a correctly-cleaned isolator. The sites for BIs can be chosen on the basis of the experience obtained from the CI studies. Sites where CIs have been slower to change colour represent "worst-case" sites for BIs. It should be possible to use fewer sites for BIs, having assessed the gas circulation using CIs. Perhaps thirty to forty BI sites might be used in a one cubic metre isolator, depending on the nature of the load pattern.

The question of duplication or triplication of BIs at each site now arises. This stems from the inherent slight unreliability of BIs whereby so-called "rogue" BIs are found to occur. These are BIs which survive the MCHP process however long the cycle, usually due to "clumping" of the spores on the carrier. Rogue rates have been reported at between 0.3% and 5% of all BIs. Clearly some policy must be adopted to deal with the problem of rogue BIs before starting cycle development. One strategy requires triplicate BIs at each site. It can be shown statistically that of two out of three BIs at a site are killed, then log 6 reduction has taken place. This strategy is quite widely adopted, but the cost for the placement, exposure, incubation and reading of triplicate BIs is significant. Another strategy favoured by the author is to use duplicate BIs at each site, with a clearly-stated acceptance rationale as follows: Up to 0.5% of positive BIs, i.e. BIs which survive the MCHP process, will be accepted provided that no two BIs grow at the same site during subsequent cycles. This has proved practical in a number of cycle development executions.

Having decided the sites for BIs and the use of single, duplicate or triplicate BIs, the central issues of cycle development can be addressed.

## The essential parameters to be established during MCHP cycle development

The parameters which govern the performance of the MCHP cycle have been laid out in an earlier section of this paper. This suggests that a number of these parameters can be pre-set, or pre-established, in the cycle development protocol leaving only two parameters which really have to be derived by development, namely the flow rate of the hydrogen peroxide solution to the evaporating device, and the times of exposure.

***Flow rate of the hydrogen peroxide solution to the evaporating device***

The flow rate of solution needs to be set for both the initial build-up phase, and for the dwell phase of the gassing cycle. These rates can be optimised without recourse to CIs or BIs. Simply start with flow rates indicated by the review exercise described in 1. of the previous section, and use brief cycles, perhaps 5 minutes of build-up time and 10 minutes of dwell time. Increase the flow rate by increments of say, I ml per minute until condensation becomes visible towards the end of the phase. Then reduce the flow rate by 1 ml per minute and use this as the operational value.

***Times of exposure – the build-up phase and the dwell phase***

The length of the build-up phase may be set by using a peroxide concentration instrument such as a Drager sensor. When the concentration reaches around 1,000 ppm, then the dwell phase can be initiated, with its lower solution flow rate.

The length of the dwell phase then becomes the central issue of development, and BIs will be required, for the resulting partial cycle study. As mentioned earlier, the simplest method involves setting up a series of cycles with BIs in place, running progressively increased dwell times. In the case of a one cubic metre isolator, dwell times of 6, 8, 10 and 12 minutes might be used to establish the kill time. Sequences such as this could be run consecutively, to minimise the time required to incubate the BIs. Alternatively, a relatively long cycle (e.g. 12 minutes) and a relatively short cycle (e.g. 6 minutes) might be run consecutively and the BIs incubated. A growth or no growth review will then suggest what further cycles need to be run to establish the kill time more precisely.

It should be noted that in developing these two basic parameters, no highly skilled technicians are needed, and no difficult, potentially dangerous, in-cycle BI removals are required.

## Note on aerosol MCHP systems

A number of bio-decontamination systems are available in which hydrogen peroxide solution is introduced into an isolator as a fog, or mist. The correct term for this form is an aerosol. These systems variously use compressed air nozzles, ultrasonic nozzles or a combination of both. The author pioneered the use of ultrasonic nebulisation some 30 years ago, producing technology still in use today.

Aerosol hydrogen peroxide works in the same way as that delivered as a vapour. The large surface area of the small droplets allows preferential evaporation of hydrogen peroxide, which then forms micro-condensation on the isolator surfaces. Thus the aerosol systems are essentially just another version of the MCHP process.

It should be noted that some hydrogen peroxide spray systems do not produce a true aerosol, and thus do not reliably lead to micro-condensation. Such systems, which are characterised by the formation of visible streams of droplets that may coalesce on surfaces opposite the delivery nozzle, are to be avoided.

## Enzyme indicators – the future of MCHP cycle development

Over the last decade, Public Health England (PHE), Porton Down, has carried out extensive study on some enzymes produced by highly thermophilic bacteria. One enzyme in particular, thermostable adenylate kinase (tAK) has the unique property of denaturing progressively and predictably, on exposure to bio-decontamination processes such as MCHP. The activity of the enzyme following exposure to MCHP can be measured by a luciferin/luciferase reaction. The result is given as relative light units, but this can be readily converted to a direct numeric equivalent value for log reduction of Stearothermophilus spores. This device is now termed an enzyme indicator (EI) as an equivalent to biological indicators (BIs)[3].

The major advantage of EIs is that they can, like chemical indicators, be read as soon as the gassing cycle is complete. A typical set of EIs from an isolator can be read in an automatic instrument, in a matter of a few minutes. This completely avoids the lengthy process of incubation

for BIs which takes seven days. A further and very significant advantage of EIs is that they are not subject to "rogues" in the same way as BIs, therefore duplicates or triplicates are not required.

EIs are now readily available commercially[iii], as are the reader instruments. Given the very significant advantages of EIs it seems likely that they will eventually take over from BIs in MCHP cycle development.

## Conclusion – practical MCHP cycle development and routine re-qualification

It is suggested that the time is now right for rationalised, simplified, and accelerated, but none-the-less robust, MCHP cycle development and re-qualification to be applied throughout the industry.

The rationalised MCHP cycle development would consist basically of two phases. First of all, studies would be carried out using chemical indicators to gain an overall view of the isolator, load pattern, and gas generator performance. Ideally CIs which give an indication of the log reduction value achieved would give maximum support to the subsequent phase. The second phase would use enzyme indicators to give more precise numeric values to the equivalent log reduction achieved. This rationalised development might be entitled Chemical/Enzyme Indicator Development (C/EID).

Such a cycle development process would be very much quicker than the current conventional sequences described at the beginning of this paper. Development that has hitherto taken weeks or months, could be completed in days. Relatively unskilled technicians could carry out the bulk of the work. Furthermore, the documentation would also be very much simpler and more comprehensible to all concerned. But this documentation would be as supportable and robust as that produced by the current development process, possibly more so.

The populations of the Western world are ageing, the need for healthcare is increasing, and costs are rising alarmingly. If ways to cut costs are not explored, Western healthcare will approach the brink of collapse. Rationalised qualification must be invoked, and simplified MCHP development could form a small part of that.

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**Tim Coles,** BSc (Hons), M.Phil., Technical Director, Pharminox Isolation Ltd., has worked in the field of isolator technology for over twenty years. He was a founding member of the UK Pharmaceutical Isolator Working Party that produced Pharmaceutical Isolators, Pharmaceutical Press, 2004, and more recently of the PDA committee that produced Technical Report No 51. "Biological Indicators for Gas and Vapour Phase Decontamination Processes" [for the validation of isolator sanitisation]. His book Isolation Technology - a Practical Guide, CRC Press Inc. 2004, is now in its second edition.

iii. Editor's note: From Protak Scientific

# Enzyme Indicators proven as valuable tool for validation of hydrogen peroxide decontamination processes

May 25, 2017

Enzyme Indicators (EI's) have been proven as a revolutionary viable alternative to biological indicators (BI's) for Hydrogen Peroxide decontamination validation. A white paper published today by the Parenteral Drug Association (PDA) Journal of Pharmaceutical Science & Technology, and written by Public Health England (PHE), states that Enzyme Indicators are a "potentially valuable tool for rapid VPHP bio-decontamination cycle development and subsequent re-qualification."

The paper entitled *"Evaluation of novel process indicators for rapid monitoring of hydrogen peroxide decontamination processes"* explains the process of comparing Enzyme Indicator performance against the current industry standard approach of using biological indicators (BI's). Given ongoing concerns about the reliability and response time of BI's, PHE explored the potential for an enzyme-based approach decontamination process evaluation.

The Enzyme Indicator is based on thermostable Adenylate Kinase, an enzyme whose presence and activity can be rapidly measured by luminescence assays. This enzyme, unlike many proteins, is very thermostable and resistant to oxidizing agents. It has a very predictable biphasic inactivation profile. These characteristics make it suitable for monitoring and quantification of oxidation decontamination processes such as $VH_2O_2$. Indicators with thermostable Adenylate Kinase (tAK), once processed, are used to catalyse a biochemical reaction with Luciferin / Luciferase. Such a reaction produces bioluminescence instantaneously. The individual photons of light produced by this reaction are recorded with a special Lunometer and an accurate measure of the degree of inactivation of the tAK indicator is achieved.

Protak Scientific are the globally exclusive licensee of this technology for gaseous decontamination validation with PHE and are working hard to educate pharmaceutical manufacturing companies about how Enzyme Indicators can benefit them from the Bio-technician to the CFO.

Phillip Godden, CEO, Protak Scientific explains:

> *The Enzyme Indicator is a surrogate of the Biological Indicator (Geobacillus Stearothermophilus). In order to check their reliability, they can initially be combined with Biological Indicators, both for cycle development and for validation. Once validation is concluded and its reliability verified, this new technology offers three great advantages. It gives quantitative results, one test offering a scale of <2.5log to >9log, for example a degree of reduction i.e. Log 6.55 reduction. It is instantaneous – amazingly in less than 3 seconds - and Enzyme Indicators do not suffer rogue syndrome. No false positives - in fact EI technology offers positive and negative controls! The Enzyme Indicators provide immediate and quantitative proof that the decontamination cycle has achieved the expected results. And this is a game-changing revolution that radically transforms decontamination validation as we know it. The Net result? This could potentially save pharmaceutical manufacturers millions of dollars per year, thousands of hours, reduce risk, remove a run to fail process and increase process understanding instantly.*

**Source:**

http://www.protakscientific.com/

# Enzyme Indicators – The Revolutionary New Technology for Decontamination Validation

# Enzyme indicators – new technology for decontamination validation

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## Pharmacy News Article

### 5/16/17 - Enzyme Indicators - New technology for decontamination validation

The conventional 7 day wait for Biological Indicator (BI) decontamination results is over. There is an alternative way to really measure and validate decontamination performance instantly.

Enzyme Indicators (EI's) are an industry-changing advance in measuring decontamination performance. No longer will the pharmaceutical industry suffer financial losses, wasted man hours, and the burden of high risks associated with BI's. EI's offer a fast, cost-effective, accurate, and risk-free alternative to biological indicators.

**ADENYLATE KINASE** - Adenylate kinase is an enzyme - its presence and activity can be measured using a rapid and sensitive luminescence assay. The technology originated from the isolation of thermostable Adenylate Kinase (AK) from thermophilic bacteria found in hot springs (Sulpholobus acidocaldarius).

**tAK** - tAK is a remarkably stable enzyme that has a high tolerance to processes that would quickly inactivate most other proteins such as high temperature and oxidising agents. The enzyme has a predictable inactivation profile which can be measured across a wide dynamic range. These characteristics make tAK ideal as a surrogate marker for monitoring decontamination processes.

Using an Enzyme Indicator as a supporting tool for cycle development immediately major performance to a data scale. This effectively enables validators, assessment or pretty much anything that uses HO as a decontamination tool to be fully mapped on the first cycle. The data is calculated immediately, taking just 3 seconds per test to collate. From the first cycle, typically within less than an hour in total, the OCD process is clearly mapped out, least penetrative spots are located and positive action can be taken.

This is versus a BI model where at this point you would still be putting the BI's into tooth and preparing to incubate. You would then wait days - up to seven to collate assumed data. Even when you have that data all you would know is that you did or didn't achieve a 6 Log reduction. You would have no real idea about how close of far from this goal you really are.

EZ PQ / IQ / SAT just became a lot quicker and easier. Using EI's gives confidence in cycle. This ensures that when processing with end users and developing a cycle, as a manufacturer you already know the outcome of your cycle and can then easily demonstrate the performance of your system to customers with complete confidence. Using EI's alongside a BI also gives immediate assurance that you are not suffering Rogue syndrome too. EI's offer a direct correlation to the performance of Bi Geobacillus Stearothermophilus using a developed standard curve and you can 'test the test' at any time, with positive and negative control built into the EI reader.

Enzyme Indicators take away all the frustration and wasted time associated with Cleaning Cycle Development. Enzyme Indicators are never fully denatured so are always able to provide a true measure of cycle performance. That alone is a massive boost to the process but the fact that data is captured immediately and enables multiple cycles per day and immediate action - that is where the true value lies.

If you are not already nodding your head, then here is a summary of the reasons why Enzyme Indicators a simply better than conventional practices.

**Instant results** - This is THE most important factor in why this new science will change the world. Instant results mean instant action. And instant action is what's needed to reduce waste, improve productivity and so, in the end contribute to save lives.

**Accurate data capture** - EI READERS provide quantifiable, linear readings that provide users with substantially more information than the current BI's. Enzyme Indicators can act as early warning systems - allowing performance monitoring, threshold release and automatic data capture.

**Simple & easy-to use** - EI Tests are simple and easy to use and so can be used regularly by medical and pharmaceutical users and technicians alike. A simple test strip is used alongside a bespoke luminometer, which reads and delivers results instantly.

**Life-changing implications** - From being faster to bring operating theatres back into service to ongoing surgical equipment validation and immediate medical batch release of medicines, the benefits are tangible - this revolutionary science may save lives.

**Satisfies audit process** - EI's and IAR validation provide the information needed to satisfy the audit process quickly and easily - and satisfy the regulator's scrutiny.

**Performance assurance** - EI's are manufactured to eliminate rogue results and include an optional onsite self-validation process. The Enzyme Indicator Readers offer more accurate quantifiable data than traditional Biological Indicator tests.

**Reasonably priced** - The EI technology, readers and test strips are reasonably priced and the results far outweigh the costs. They also have a long and stable shelf life compared with traditional BI's.

**Developed and Extensively tested by Public Health England (PHE)** - PHE, a part of the UK Department of Health has been researching and testing this technology for 15 years with significant investment and over sixty patents granted.

It's clear this technology is worth investigating and putting head to head with current biological indicator validation processes for truly see the results.

http://blog.tape.org/enzyme-bio-indicators-revolutionary-new-technology





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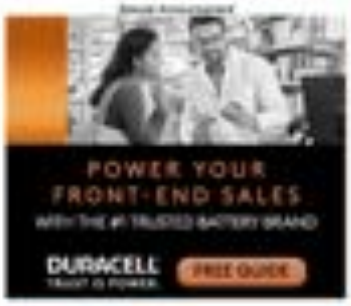


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# HVP cleanroom decontamination validation in minutes not days

6-Jul-2017

*EUROPE · TESTING*

Enzyme indicators (EI) look like biological indicator (BI) strips, are biological like BIs and are used for decontamination performance monitoring – but that is where the similarities end. Phillip Godden, CEO, Protak Scientific, explains why he believes EIs deliver superior performance and benefits

*EIs are an industry-changing advance in measuring the decontamination performance of vaporised hydrogen peroxide*

Biological indicators (BIs) are essentially a microbiological test system made up of a known viable population of particular bacterial spores, inoculated onto a carrier, which provides a defined resistance to a specific sterilisation process. It is used by pharmaceutical companies to check whether a sterilisation process is working effectively or not.

The industry-standard wait of up to 7 days for the BI decontamination results, however, can mean productivity and financial losses are incurred with the delay.

Now, there is an alternative way to measure and validate decontamination performance instantly. Following some 15 years of research and testing by Public Health England (PHE), enzyme indicator (EI) technology is now commercially available, and Protak Scientific is the globally exclusive licensee.



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