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**IMPROVEMENTS IN THE CONTROL
OF BIO-DECONTAMINATION CYCLES**

This invention relates to improvements in the method of
5 controlling bio-decontamination cycles used for the bio-
decontamination of enclosed spaces, such as pharmaceutical
clean rooms, isolators and hospital wards.

Vapour phase bio-decontamination is generally a four
10 phase process. During the first "conditioning" phase the
equipment is brought up to working temperature, and in the
case of small enclosures the relative humidity inside the
enclosed space can be brought to a pre-set value. This is
followed by the "gassing" phase during which the active
15 vapour concentration inside the enclosed space is raised.
In the "dwell" phase the vapour is distributed inside the
enclosed space for a sufficient period of time to ensure
that bio-decontamination is achieved. The fourth and final
phase is the "aeration" phase in which the active vapour is
20 removed from the enclosed space generally by dilution with
clean air.

The most commonly used vapour for bio-decontamination
is hydrogen peroxide which is generated by evaporating an
25 aqueous solution of about 30 to 35% w/w. The usual
technique for producing a "flash" evaporated vapour is to
drop the aqueous solution onto a heated plate held at a
temperature above the boiling point of the liquid thus
generating a vapour with the same weight ratio as the source
30 liquid. There are two theories as to the action of the
hydrogen peroxide; the earlier thinking was that the vapour
should be maintained at a concentration below the dew point

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thus avoiding condensation, the other theory suggests that condensation is necessary to give a rapid bio-decontamination.

5 There are numerous patents covering the use of gaseous and vapour phase bio-decontamination of enclosed spaces, the most important of which are US-B-5173258, US-B-7014813 and US-B-7790104.

10 US-B-5173258 describes a single loop closed system in which the carrier gas is circulated from the vapour generator to the chamber to be bio-decontaminated and then back to the vapour generator. On returning to the vapour generator the carrier gas and vapours pass through a device
15 to remove the active vapour and the water vapour thus allowing more hydrogen peroxide to be evaporated into the circulating carrier gas.

 US-B-7014813 describes a similar process but has a by-
20 pass loop inside the vapour generator. Thus the vapours are not removed from the circulating carrier gas on returning to the vapour generator during the second and third phases of the cycle. This allows a more rapid build up of vapour concentrations and is normally used in cycles when
25 condensation is required.

 In both types of bio-decontamination cycles (in which condensation is to be avoided or encouraged respectively) it is essential that the active vapours are distributed evenly
30 throughout the chamber. In some systems the vapours are delivered from rotating nozzles at high velocities and in

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others external fans are used to move the vapour mixture around the chamber.

Short cycle time is a key commercial driver for
5 hydrogen peroxide vapour generators. The target assets for
bio-decontamination within a hospital are often extremely
expensive and hence there is a substantial opportunity cost
of closing a facility. Figures that have been produced for
the USA suggest that revenues of \$5k per day per bed are not
10 atypical. Consequently, the time saving needs to be
maximised while still guaranteeing the efficacy of bio-
decontamination.

In the prior art processes, the control of the cycles
15 has been based on monitoring the concentration of the bio-
decontaminant to determine when saturation conditions have
been reached. However this can lead to misleading results,
for example if the space undergoing bio-decontamination
contains highly absorbent surfaces, or the space is not
20 properly sealed and fresh air is able to enter.

In many states of the USA the relative humidity (RH)
drops during the winter months to around 5%; the low
starting RH means that the time to reach dew point is
25 extended and can lead to unacceptably long cycles.
Conversely, many Asian countries experience extremely high
relative humidity conditions, with 95% not unheard of.
These extremely difficult conditions, due to the rapid onset
of condensation, cause control methods based entirely on RH
30 measurements to under-dose and jeopardise efficacy.

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It is therefore an object of the present invention to provide a method of control of bio-decontamination cycles which reduces user input and enables the cycle time to be minimised, whilst maintaining the efficacy by bio-
5 decontamination.

The present invention therefore provides a method of controlling a bio-decontamination cycle to decontaminate an enclosed space, said bio-decontamination cycle comprising a
10 number of phases including at least one gassing phase, during which sterilant vapour is generated and circulated within the enclosed space;

characterised by the steps of continuously measuring the modified relative humidity of the air in the enclosed
15 space, the modified relative humidity being the ratio of water and sterilant vapour: capacity of water and sterilant vapour in the air, and using the measured modified relative humidity to control the steps of the process.

20 The basic decontamination process which preferably uses hydrogen peroxide as the sterilant is described in WO-A-2008145990, and is summarised as follows. During the first "conditioning" phase of the decontamination cycle evaporator and nozzle fans of the decontamination apparatus are
25 switched on together with an evaporator heater. This allows the gas generator and the space to be decontaminated to come to a stable temperature. Once thermal stability has been achieved the gas generator moves to a second phase of the decontamination cycle, the "gassing phase", during which a
30 hydrogen peroxide liquid pump is switched on and hydrogen peroxide solution is "flash" evaporated and mixed with the air leaving the decontamination apparatus.

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Once the space has been decontaminated the generator moves to the third "aeration phase" of the cycle. In the aeration phase the hydrogen peroxide liquid pump is switched
5 off, as is the evaporator heater. The evaporator fan is also switched off but an aeration fan is started. The operation of the aeration fan opens flap valves in the apparatus casing and draws in large quantities of air through filters, which decompose the hydrogen peroxide to
10 water and, oxygen and at the same time, absorb the water vapour. The aeration fan is left running to ensure good distribution of the air during aeration. The high air flow generated by the aeration fan reduces the time taken for aeration of the space. Once the hydrogen peroxide vapour
15 concentration within the space to be decontaminated has reached a safe level the generator is switched off.

During further development of this process it has been found, surprisingly, that using "modified relative humidity"
20 (MRH), i.e. the ratio of [water and H₂O₂ vapour] to [capacity for water and H₂O₂ vapour in the air], as the main control parameter is more accurate than using the parameters of the prior art methods. Thus 100% MRH indicates that the air is maximally saturated with mixed water and H₂O₂
25 vapours when dew point is reached (whereas 100% RH refers to water vapour only). The method of control of the present invention has been shown to provide 6-log kill of Biological Indicators ("BIs") using *G. stearothermophilus* at starting relative humidity between 5 and 95%, i.e. thus compensating
30 for extremes and preventing overgassing which can damage materials and undergassing which leads to ineffective decontamination. Significantly the algorithm used by the

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method is also capable of adapting to different hydrogen peroxide injection rates resulting from varying power supplies globally.

5 The method of control of the present invention therefore utilizes an algorithm which divides the bio-decontamination process into five distinct phases. This is illustrated in Figure 1 which shows the concentration of sterilant, preferably hydrogen peroxide (H_2O_2), in the
10 enclosed space (as parts per million (ppm)) against cycle time in minutes.

As described above the first phase is still the "conditioning" phase, during which the vaporiser heats up,
15 and the H_2O_2 , relative humidity (RH) and temperature sensors are allowed to stabilise. However, the previously described "gassing" phase is divided into two distinct phases, "G1" and "G2", which become the second and third phases of the cycle respectively. The gassing commences at the start of
20 G1, during which an H_2O_2 solution is vaporised up to a point where the conditions immediately surrounding the generator are considered to be suitable for bio-decontamination. G2 involves continued gassing such that the entire enclosed space, be it room, chamber or enclosure, is considered to be
25 at a condition suitable for bio-decontamination. The next phase is the "dwell" phase, which optionally involves the cessation of H_2O_2 vaporisation and a fixed time period in which the contaminant may take up the H_2O_2 present and be deactivated. The fifth and final phase is the same
30 "aeration" phase as is described above which involves the catalysis of the H_2O_2 vapour present such that the enclosed space is returned to a condition safe for re-occupation/use.

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In order to control the G1 phase a relative humidity sensor capable of measuring both water and H₂O₂ vapour is used, i.e. an atmosphere water content sensor. The measurement of the modified relative humidity (MRH) allows the identification of the point in time where the onset of condensation (dew point) occurs.

The "target MRH" is set at the value to be reached to ensure that condensation occurs and therefore accelerated kill conditions are ensured. The "threshold RH" is set to be the value at which the algorithm changes its approach, i.e. given the high start MRH conditions, it needs to gas longer than it otherwise would in order to compensate for the reduced H₂O₂ concentration in any condensate formed.

Target MRH has been found experimentally to be optimally set at between 70 and 80%.

Threshold RH has been found experimentally to be optimally set at between 80 and 90% of Target MRH, i.e. between 56 and 72% RH.

The reason "target" is in terms of MRH and "threshold" is in terms of RH is that the threshold is only used at the start of the cycle therefore there is no H₂O₂ vapour present, i.e. the two units will be the same.

The end of G1 is defined by reaching the target MRH.

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Thus it is the G1 phase that is adapted to compensate for variations in relative humidity and temperature which may occur depending on the location or time of the year etc.

5 The present method also requires certain other parameters to be pre-set by the user. These are:-

1. the volume of the space to be decontaminated (room_volume);

2. whether or not the space is "loaded" or "normal" (cycle_type), i.e. an empty room would be normal and a room
10 containing any equipment and/or mattresses or the like providing extra surfaces to be decontaminated, on anything which affects the circulation and/or distribution of the sterilant vapour would be loaded.

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Therefore during the conditioning phase, and before vaporisation of H₂O₂ solution commences in the G1 phase, the actual RH and temperature in the space are measured and the process controller performs the following calculations to
20 define the following limits.

First, the controller calculates the theoretical mass of H₂O₂ solution required to be vaporised to reach the target MRH in the enclosed space, using the actual starting
25 RH and temperature.

Secondly, the calculated mass of H₂O₂ solution is multiplied by the volume of the space and the lower gas limit multiplier to give a Lower Limit. This is used to
30 prevent under-gassing in high starting RH environments.

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Thirdly, the same calculated mass of H_2O_2 solution is multiplied by the volume of the space and the upper gas limit multiplier to give an Upper Limit. This is used to prevent over-gassing in low starting RH environments.

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In environments with high starting RH conditions, the first bead of condensate will be at a lower peroxide concentration than that formed at a lower starting RH. By looking at how close the start RH is to the target value, the system can decide whether to increase the peroxide dosing. Should the system measure and confirm that the start conditions meet this criterion, it decides upon a higher nominal value for G1, and accordingly calculates a higher minimum gassing limit for G1.

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The controller then starts the G1 phase and commences the gassing of the H_2O_2 solution (ideally, although not exclusively, at a constant rate) until the Lower Limit is reached. This ensures that the atmosphere is suitable to effectively decontaminate the space. Should the MRH measured at this point exceed the preset target MRH G1 is terminated and G2 is started. Otherwise the vaporisation continues until either the MRH target is met or the Upper Limit is reached.

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In this way the controller advantageously adapts to its environments such that neither ineffective nor overly long cycles are brought about by extreme humidity conditions.

30 The G2 phase is time-based and is a function of the volume and loading of enclosed space to be bio-decontaminated. G2 is thus controlled to allow the H_2O_2

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vapour to disperse, having been experimentally confirmed as sufficient to allow full distribution of vapour in an "unloaded" enclosure and therefore sufficient to allow the entirety of said enclosure to reach deactivation conditions.

5 In effect conditions close to the generator exceed deactivation conditions to ensure complete bio-decontamination of the entire enclosure. As such its duration is proportional to the size of the enclosure, such that each cubic metre of volume requires the addition of a
10 specific mass of H_2O_2 vapour.

Should the enclosed space be considered to be loaded the G2 phase time is extended by multiplication by a parameter (loaded factor) to allow for the reduced vapour
15 mobility and more importantly the increased surface area expected.

As this phase is limited by the volume of the enclosed space undergoing decontamination it requires no limits.

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Should it be required, injection of H_2O_2 vapour during the dwell phase can also be specified. Otherwise, vaporisation of H_2O_2 ceases and the phase involves a timed countdown until aeration begins.

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Preferably in the method of the present invention two distinct phases are calculated and monitored; the first one is concerned with getting up to the required MRH and the second with laying down the condensate. Whilst these phases
30 are preferably run sequentially, they could be run in parallel as one phase in which the target condensate is achieved.

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CLAIMS:-

1. A method of controlling a bio-decontamination cycle to decontaminate an enclosed space, said bio-
5 decontamination cycle comprising a number of phases including at least one gassing phase, during which sterilant vapour is generated and circulated within the enclosed space;

characterised by the steps of continuously measuring
10 the modified relative humidity of the air in the enclosed space, the modified relative humidity being the ratio of water and sterilant vapour: capacity of water and sterilant vapour in the air, and using the measured modified relative humidity to control the steps of the process.

15

2. A method as claimed in claim 1 in which there are two gassing phase parameters, the first of which is controlled to compensate for variations in the relative humidity and temperature and the second of which is to
20 compensate for the volume of the enclosed space, and any adverse distribution effects.

3. A method as claimed in claim 1 or claim 2 in which there are two gassing phases.

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4. A method as claimed in claim 3 in which the gassing phases are run sequentially or in parallel.

5. A method as claimed in any one of the preceding
30 claims further comprising the step of calculating in which a mass of sterilant solution, which is the theoretical amount

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of sterilant solution required to be vaporised to reach a preset target modified relative humidity.

6. A method as claimed in claim 5 further comprising
5 the step of calculating a lower limit to prevent under-gassing in high starting relative humidity conditions, and the step of calculating an upper limit to prevent over-gassing in low starting relative humidity conditions,

10 7. A method as claimed in claim 6 in which the sterilant vapour is generated during the first gassing phase until the first gassing phase is terminated when either the volume of sterilant vapour generated is greater than the upper limit or if the measured relative humidity exceeds a
15 predetermined modified relative humidity conditional on the lower limit having been exceeded.

8. A method as claimed in any one of claims 2 to 7 in which the single or multiple gassing phase parameters are
20 modified to compensate for the loading and volume of the enclosed space, which loading is determined by any content of the enclosed space to be decontaminated which affects the circulation and/or distribution of the vapour.

25 9. A method as claimed in any one of the preceding claims in which a relative humidity sensor is used to measure the modified relative humidity.

10. A control module for controlling a bio-
30 decontamination cycle to decontaminate an enclosed space comprising means for measuring the relative humidity or modified relative humidity of air in an enclosed space,

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means for performing calculations based on the relative
humidity measurement means for generating control signals to
activate or deactivate a gassing phase during which
sterilant vapour is generated and circulated within the
5 enclosed space.

11. A control module as claimed in claim 10 comprising
means to enable a number of parameters to be preset by an
operator.