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Case Study

Use of EIs in Vapour Phase Hydrogen Peroxide Decontamination Cycle Optimisation and Rapid Validation

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Abstract

AstraZeneca investigated the use of Enzymatic Indicators (EIs) in order to optimise their Sterility Testing Isolator gassing cycles. The quantitative nature of the EI data has enabled identification and successful validation of an optimised cycle, which has halved the original gassing cycle, leading to reduced costs, reduced periods of Isolator downtime and increased overall productivity. When completing the validation, the EI data was also used to provide greater confidence in the instance of erroneous Biological Indicator results, and as such has also expedited validation of a new 'wet' vaporised H_2O_2 generator. In addition, the EI data provided increased data across the sterility isolator chamber, allowing for confidence that sufficient cycle decontamination is achieved in all challenge locations, and as such there is no risk of BI failures upon requalification. EIs are therefore regarded as a beneficial companion for BI data when looking to optimise productivity of current isolators, and when used for validation of new equipment.

***Keywords:** Isolator, Hydrogen Peroxide, Decontamination, Enzyme Indicators, EIs, Optimisation, Validation, Efficacy.*

1. Introduction

Sterility testing Isolators, and test consumables, are typically decontaminated with gaseous hydrogen peroxide prior to completing sterility testing. This process ensures that the risk of sample contamination during testing is minimised, without impact or risk to the sample itself.

Historically, the decontamination efficacy of gaseous hydrogen peroxide cycles has been validated using Biological Indicators (BIs). 10^6 *Geobacillus stearothermophilus* spore strips are routinely used for their high resistance, creating a higher, "worst-case", challenge than what would be expected from usual environmental bioburden. However, the data that can be gained from BIs is limited due to high intrinsic variation in population and D-value, and qualitative growth/ no growth results. To mitigate these limitations the decontamination cycles are invariably extended, leading to increased costs, elongated periods of Isolator downtime and reduced overall productivity [1].

The use of Enzyme Indicators (EIs) to support decontamination cycle optimisation has been investigated by AstraZeneca [1]. EIs are strips of thermostable adenylate kinase (tAK) which quantitatively assess decontamination efficacy of gaseous hydrogen peroxide [2]. The unique properties of the enzyme enable inactivation to be accurately assessed, using a luminometer to measure the amount of bioluminescence caused by residual enzyme activity. Furthermore, the relative light unit (RLU) results have subsequently been shown to directly correlate with BI spore log reduction. As such, the EI results can be used to robustly assess the decontamination efficacy of the cycle and also provide further insight into the total log reduction achieved [2].

During the initial investigation, AstraZeneca found that the insight into their decontamination cycle from the EI results indicated a high potential for the cycle to be optimised whilst maintaining the efficacy of the cycle [1].

This study aims to build on the initial optimisation works reported by AstraZeneca [1], by validating the optimised cycle parameters using EI and BI data. AstraZeneca are also required to update their current 'wet' vaporised hydrogen peroxide (vH_2O_2) generators to a new model from the same manufacturer and as such the cycle validation will be performed with the new generator system. This study will therefore also explore the use of EIs alongside BIs when validating cycle equivalency.

2. Cycle Optimisation

Initial investigation was performed in 2019 with EIs on an empty sterility testing isolator serviced by a 'wet' vH_2O_2 generator. The investigation identified that the gassing dwell phase could be reduced from 25 minutes to 10 minutes whilst maintaining equivalent efficacy, suggesting that there was substantial opportunity for cycle optimisation (*Fig.1*.)

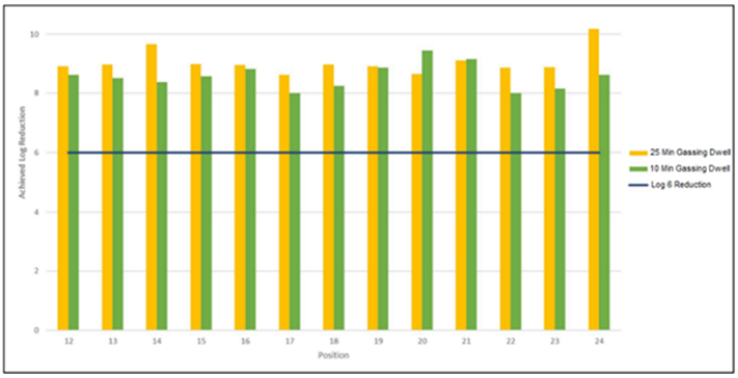

Figure 1: *Initial investigative study results showing maintained cycle efficacy when reducing the gassing dwell phase.*

Further investigation was pursued in order to ascertain if a reduced cycle could be developed on the sterility testing isolator with a standard load. The aim was to develop a cycle which maintained the decontamination efficacy, whilst reducing the length of the cycle and the volume of hydrogen peroxide injected. The EI results demonstrated that the optimised cycle parameters were achieving sufficient decontamination efficacy, with a general increase in EI inactivation (*Fig.2*) across the locations. There was a slight change in distribution profile noted, however this was to be expected following the addition of load items in the sterility test isolator.

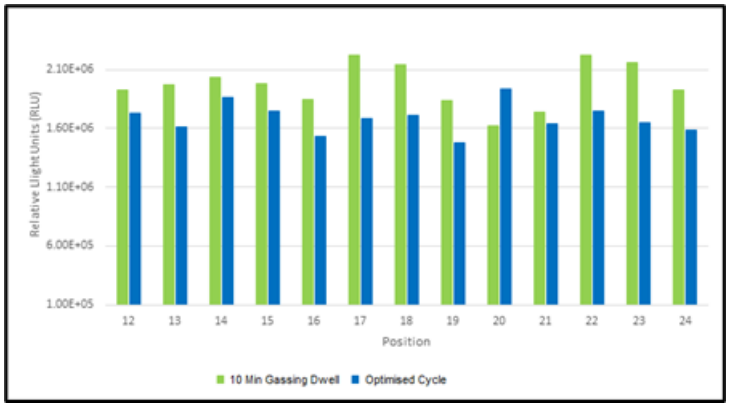

Figure 2: *Optimised cycle shows a general increase in EI inactivation to the reduced cycle from the initial study. Only Isolator chamber locations have been compared as the Sterility Isolator was not loaded in the initial study.*

The optimised cycle was then repeated in triplicate, and the EIs were able to demonstrate that the cycle maintained a consistent decontamination efficacy.

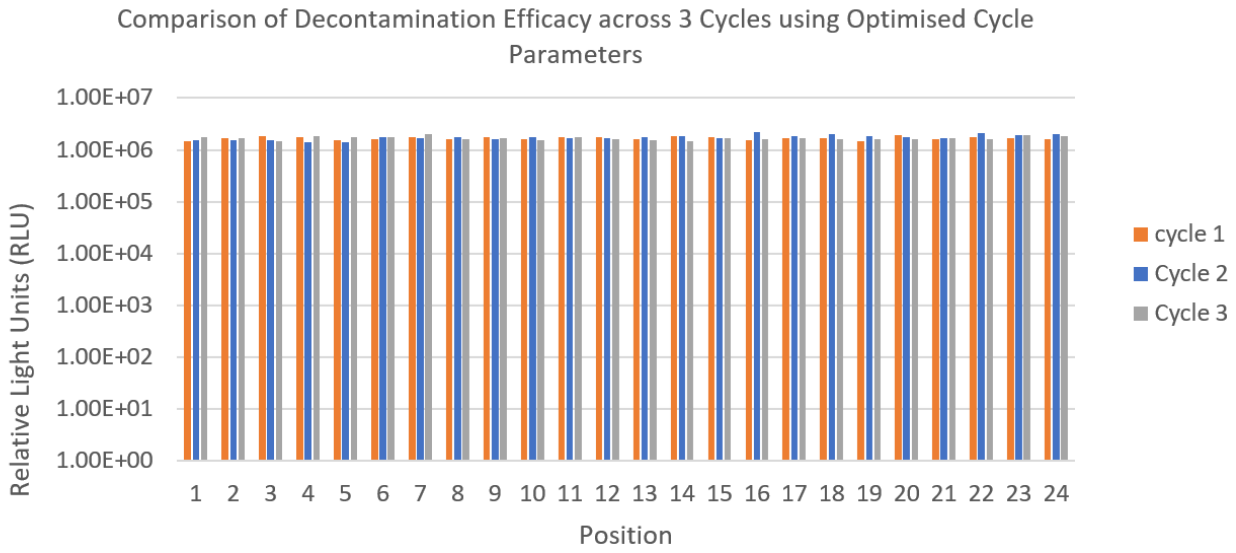

Figure 3: *Optimised cycle shows consistent decontamination efficacy across triplicate cycles on a loaded Sterility Testing Isolator.*

The consistency observed provided confidence that the cycle parameters could be optimised to reduce the cycle length, and volume of hydrogen peroxide injected, without compromising the efficacy of the cycle. This confidence was further bolstered 7 days later, when the co-located BIs showed no growth after incubation.

Comparing the parameters of the optimised cycle to the validated cycle (Table 1) it became apparent that optimising the cycle would enable the cycle to be halved, reducing the decontamination cycle costs by 50% and doubling the production potential of the isolator. As such the optimised cycle parameters were put forward for validation.

Table 1: vH_2O_2 Generator Cycle Parameters for Original and Optimised Cycles.

Cycle details	Original Cycle	Optimised cycle
Gassing	3g/min x 15 min (45g total H_2O_2)	5g/min x 3 min (15g total H_2O_2)
Gassing Dwell	1.5g/min x 25 min (37.5g total H_2O_2)	2g/min x 10 min (20g total H_2O_2)
Aeration	420 mins	240 mins
Total Time	470 mins	263 mins
Total H_2O_2	82.5g	35g

3. Optimised Cycle Validation Strategy

In order to stress the gassing cycle into worse-case conditions, the sterility testing isolator was prepared with the maximum consumable loading required, creating the highest surface area. Furthermore, BIs of the highest permitted D-value (2.0 minutes in 2.0mg/L gaseous H_2O_2), were sourced to ensure the validation was performed with the greatest defined microbial challenge. The validation was then performed using both fractional and distribution studies in triplicate to assess the cycle efficacy and robustness of the cycle, using the new 'wet' vH_2O_2 generator.

Distribution studies were completed to ensure that the required decontamination efficacy is achieved across all areas of the sterility testing isolator. This is important during cycle evaluation as it assesses if consistent and repeatable decontamination is achieved across the whole of the isolator chamber. To perform the distribution study, one BI and EI were co-located in 27 pre-defined challenge locations across the isolator, which included 12 chamber locations and 15 load item locations. A decontamination cycle programmed with the optimised cycle parameters was then completed and the samples retrieved. Upon retrieval the EIs were assayed immediately, and the BIs were inoculated into 10ml TSB vials and incubated at 55-65°C for 7 days. One positive and negative control was performed for each BI and EI test set.

Fractional studies, also known colloquially as time-point removal studies, were completed to ascertain the exact point of BI inactivation (6 Log Reduction). This is important during cycle evaluation as it assesses which phase in the cycle the required decontamination is achieved, and ascertains the extent of the cycle overkill. For example, if BI inactivation is achieved during the 'gassing' phase, where the generator is rapidly injecting high volumes of vH_2O_2 into the Isolator, the overall vH_2O_2 concentration is likely to be too high, risking inconsistent decontamination efficacy from 'H_2O_2 pooling'- an affect which occurs when the concentration is pushed past the precipitation point. Too high vH_2O_2 concentration and exposure will also have long term impacts, such as increased damage to the isolator materials (including gloves, HEPAS, etc), increased running costs and elongated aeration phases. Therefore, when proving a vH_2O_2 cycle, it is prudent to ensure that cycle inactivation occurs during the 'gassing dwell' phase which enables increased consistency in decontamination efficacy. Furthermore, the extent of the overkill can then be controlled, as it is known exactly how long the 'gassing dwell' is maintained past the BI 'kill point'.

The design of the sterility testing isolator at AstraZeneca does not allow for the safe removal of EI and BI samples during the gassing cycle, and so the 'quench' method was employed for the fractional studies. With this method, all of the EI and BI samples were carefully positioned in one location of the isolator, ensuring that the samples did not occlude each other. A decontamination cycle programmed with the optimised cycle parameters was initiated, and a positive and negative control was performed for both EI and BI, prior to initiation of the gassing phases. One BI and one EI were then sampled at specified time intervals throughout the 'gassing' and gassing dwell' phases. For each time interval, one BI was retrieved, inoculated, and sealed into a labelled 10ml TSB vial; and one EI was retrieved, immersed and sealed into a labelled test tube containing the first reagent of the bioluminescence assay. In this way, at each specified timepoint the oxidation of the EI and BI by the vH_2O_2 was quenched by the corresponding reagent, without elongated exposure of the reagent to the vH_2O_2. The operator was careful to perform this with minimal movement so as to not disrupt the vH_2O_2 distribution, however the sterility testing isolator is accessed via a half-suit and so a low level of airflow disruption could not be eradicated. Once all the specified time points had been sampled, the vials and test tubes containing the EI and BI samples were retained in the isolator until cycle completion. The BIs were then incubated at 55-65°C for 7 days, the EIs were assayed immediately upon retrieval.

4. Fractional Results & Discussions

Table 2: Fractional Cycle 1: Enzyme Indicator Results and 7-day Biological Indicator Results.

Time minutes	BI Results (Growth/No Growth)	EI Results (RLU)	EI Results- Achieved Log Reduction (ALR)
Negative Control*	No Growth	152903	N/A
Positive Control*	Growth	105773816	N/A
2 min	Growth	114624365	0
4 min	Growth	45977560	0
6 min	Growth	18089656	0
8 min	No Growth	7775729	1.5
10 min	No Growth	4146989	3.5
12 min	Growth	2968492	4.5

*EI results pass negative and positive control limits; 80000-340000 RLU and 41300000-164000000 RLU respectively.

Initial fractional cycle (Table 2) showed BI inactivation appeared to be around 8 minutes into the gassing cycle (5 minutes into the 'gassing dwell' phase). However BI growth was then identified at 12 minutes. It should be noted that the 12-minute BI sample was dropped onto the base of the isolator during sampling, close to the half suit where there was high risk of airflow movement causing potential occlusion. To ensure the BI growth result was erroneous the gassing dwell was extended by 3 minutes and BI sampling was increased to 1-minute intervals.

Table 3: Fractional Cycle 2: Enzyme Indicator Results and 7-day Biological Indicator Results.

Time minutes	BI Results (Growth/No Growth)	EI Results (RLU)	EI Results- Achieved Log Reduction (ALR)
Negative Control*	No Growth	165300	N/A
Positive Control*	Growth	125894993	N/A
4 min	Growth	54672652	0
5 min	Growth	43338176	0
6 min	Growth	14200024	0
7 min	Growth	7620638	1.6
8 min	Growth	3840880	3.7
9 min	No Growth	3806371	3.8
10 min	No Growth	4327643	3.3
11 min	No Growth	2981168	4.5
12 min	No Growth	2689735	4.8
13 min	No Growth	2854438	4.7
14 min	No Growth	2631841	4.9
15 min	No Growth	1990008	5.8
16 min	No Growth	1836590	6.0

*EI results pass negative and positive control limits; 80000-340000 RLU and 41300000-164000000 RLU respectively.

Fractional cycle 2 (Table 3) showed BI inactivation at 9 minutes into the gassing cycle (6 mins into the 'gassing dwell' phase). No BI growth was then identified across the rest of the sampling. Therefore, it is considered that the growth recovered at 12 minutes in fractional cycle 1 is erroneous. This was confirmed by a further fractional cycle. As the kill point could be identified as between 8-9 minutes, the sampled time points were reduced respectively.

Table 4: Fractional Cycle 3: Enzyme Indicator Results and 7-day Biological Indicator Results.

Time minutes	BI Results (Growth/No Growth)	EI Results (RLU)	EI Results- Achieved Log Reduction (ALR)
Negative Control*	No Growth	165300	N/A
Positive Control*	Growth	132517370	N/A
2 mins	Growth	113203578	0
4 mins	Growth	69577096	0
6 mins	Growth	34313653	0
8 mins	Growth	11554271	0.3
9 mins	No Growth	6221469	2.2
10 mins	No Growth	4347227	3.3
12 mins	No Growth	3394169	4.1

*EI results pass negative and positive control limits; 80000-340000 RLU and 41300000-164000000 RLU respectively.

Fractional cycle 3 (Table 4) confirmed BI inactivation at 9 minutes into the gassing cycle. No BI growth was then identified across the rest of the sampling. Therefore, it is considered confirmed that the growth recovered at 12 minutes in fractional cycle 1 is erroneous. The cycle is therefore considered to have BI inactivation at 6 minutes into the gassing dwell phase, enabling an overkill of 40% (4 minutes).

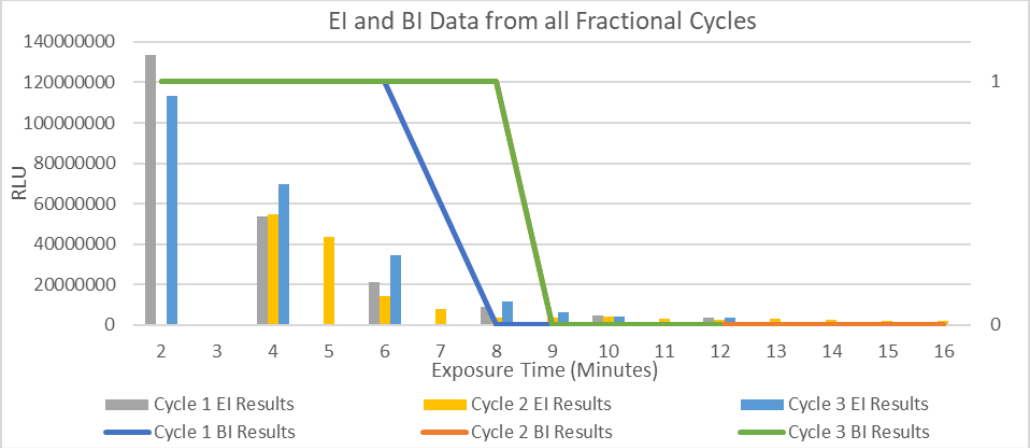

Figure 4: *Fractional Cycle 1,2,3 BI and EI Results*.

Note: Erroneous data point 12 has been excluded from Cycle 1 BI result analysis.

The EI results from the fractional cycles supported the BI results found. Figure 4 clearly shows a general inactivation across the time periods monitored which plateau from 10-minute exposure, demonstrating that the 3 cycles had reached the limit of the inactivation potential of the system. Review of the EI achieved log reduction (ALR) showed that use of a correction factor was required to correlate the EI ALR to the BI system D-Value.

The default EI ALR is automatically calculated upon completion of an EI assay using the correlation curve equation y= -3.152ln(x)+51.51(where y= log reduction and x= RLU), determined during initial correlation research [2]. However, due to BI D value variation, the level of BI challenge varies across different vH_2O_2 systems (an affect known as system D-value), and as such the level of EI inactivation that results in a BI kill also varies. Therefore, to correlate the EIs to BI inactivation in a specific system, the system correction factor needs to be ascertained and applied to the ALR to give a corrected log reduction (CLR). One way to determine the system correction factor (CF) is to correct the value of discrepancy between the EI ALR, and the BI kill point from the BI data. This is determined as follows:

$$Correction\ Factor = \frac{6\ (representing\ the\ minimum\ spore\ \log reduction)}{EI\ Achieved\ Log\ Reduction\ at\ timepoint\ of\ BI\ KIll}$$

Using this against the results obtained in Fractional cycles 1, 2 and 3, correction factors of 4.00, 1.60 and 2.73 can be obtained respectively. The difference in the correction factors is a cumulative effect from slight alterations in the BI challenge (caused by the inherent variability of the BI) and the gassing cycle variation introduced from environmental parameters and equipment control tolerance, which subsequently cause different corresponding EI RLUs. Therefore, a level of error in alignment between EI CLR and BI growth is expected around the BI kill point when utilising limited data. To assess which correction factor is most applicable, the CLR is calculated across each fractional run for each correction factor and checked for alignment with the BI results. The correction factor of 2.73 was then chosen to evaluate the distribution data, as this was the most conservative correction factor which provided greatest alignment across all the results gathered in the three fractional cycles (Table 5). This then ensures greatest accuracy in corelation whilst ensuring against over-compensation which could lead to further misalignment with future BI test results.

Table 5: Correlation Correction Factor Assessment of EI corrected log reduction (CLR) against BI data. All misalignments are highlighted in red.

Correction Factor	Time (Minutes)	Cycle 1*		Cycle 2		Cycle 3	
		BI Results (Growth/ No Growth)	EI Results-CLR	BI Results (Growth/ No Growth)	EI Results-CLR	BI Results (Growth/ No Growth)	EI Results-CLR
1.60	2 min	Growth	0			Growth	0
	4 min	Growth	0	Growth	0	Growth	0
	5 min			Growth	0		
	6 min	Growth	0	Growth	0	Growth	0
	7 min			Growth	2.6		
	8 min	No Growth	2.4	Growth	5.9	Growth	0.4
	9 min			No Growth	6.1	No Growth	3.5
	10 min	No Growth	5.6	No Growth	5.3	No Growth	5.3
	11 min			No Growth	7.2		
	12 min			No Growth	7.7	No Growth	6.6
	13 min			No Growth	7.5		
	14 min			No Growth	7.8		
	15 min			No Growth	9.3		
	16 min			No Growth	9.7		
2.73	2 min	Growth	0			Growth	0
	4 min	Growth	0	Growth	0	Growth	0
	5 min			Growth	0		
	6 min	Growth	0	Growth	0	Growth	0
	7 min			Growth	4.4		
	8 min	No Growth	4.1	Growth	10.1	Growth	0.8
	9 min			No Growth	10.4	No Growth	6.0
	10 min	No Growth	9.6	No Growth	9.0	No Growth	9.0
	11 min			No Growth	12.3		
	12 min			No Growth	13.1	No Growth	11.2
	13 min			No Growth	12.8		
	14 min			No Growth	13.4		
	15 min			No Growth	15.8		
	16 min			No Growth	16.4		

Table continued.....

Correction Factor	Time (Minutes)	Cycle 1*		Cycle 2		Cycle 3	
		BI Results (Growth/ No Growth)	EI Results- CLR	BI Results (Growth/ No Growth)	EI Results- CLR	BI Results (Growth/ No Growth)	EI Results- CLR
4.00	2 min	Growth	0			Growth	0
	4 min	Growth	0	Growth	0	Growth	0
	5 min			Growth	0		
	6 min	Growth	0	Growth	0	Growth	0
	7 min			Growth	6.4		
	8 min	No Growth	6.0	Growth	14.8	Growth	1.2
	9 min			No Growth	15.2	No Growth	8.8
	10 min	No Growth	14.0	No Growth	13.2	No Growth	13.2
	11 min			No Growth	18.0		
	12 min			No Growth	19.2	No Growth	16.4
	13 min			No Growth	18.8		
	14 min			No Growth	19.6		
	15 min			No Growth	23.2		
	16 min			No Growth	24.0		

**Note: Erroneous data point 12min has been excluded from Cycle 1 result analysis*

5. Distribution Results & Discussions

Table 6: Distribution Cycles: Enzyme Indicator Results and 7day Biological Indicator Results.

Location No.	Distribution Cycle 1			Distribution Cycle 2			Distribution Cycle 3		
	BI Results (Growth/ No Growth)	EI Raw Result (RLU)	EI Result - CLR	BI Result (Growth/ No Growth)	EI Raw Result (RLU)	EI Result - CLR	BI Results (Growth/ No Growth)	EI Raw Result (RLU)	EI Result- CLR
Negative Control*	No Growth	162546	N/A	No Growth	161811	N/A	No Growth	181510	N/A
Positive Control*	Growth	96820434	N/A	Growth	82960842	N/A	Growth	90839839	N/A
1	No Growth	2556032	13.7	No Growth	1997046	15.8	No Growth	1697217	17.2
2	No Growth	2553134	13.7	No Growth	2437493	14.1	No Growth	2265208	14.7
3	No Growth	2611164	13.5	No Growth	2225103	14.9	No Growth	2826277	12.8
4	No Growth	2685483	13.2	No Growth	1559599	17.9	No Growth	1861395	16.4
5	No Growth	2026771	15.7	No Growth	1653579	17.4	No Growth	2012531	15.7
6	No Growth	2775595	13.0	No Growth	1920653	16.1	No Growth	2062606	15.5
7	No Growth	2163216	15.1	No Growth	2519343	13.8	No Growth	3021995	12.2
8	No Growth	1771821	16.8	No Growth	1530663	18. 1	No Growth	1759416	16.9
9	No Growth	2968184	12.4	No Growth	2129373	15.2	No Growth	2091368	15.4

Table continued.....

Location No.	Distribution Cycle 1			Distribution Cycle 2			Distribution Cycle 3		
	BI Results (Growth/ No Growth)	EI Raw Result (RLU)	EI Result-CLR	BI Result (Growth/ No Growth)	EI Raw Result (RLU)	EI Result-CLR	BI Results (Growth/ No Growth)	EI Raw Result (RLU)	EI Result-CLR
10	No Growth	2953002	12.4	No Growth	2087416	15.4	No Growth	2239016	14.8
11	No Growth	2911666	12.5	No Growth	2044909	15.6	No Growth	2551723	13.7
12	No Growth	3137463	11.9	Growth	2128765	15.2	No Growth	2820688	12.8
13	No Growth	2168727	15.1	No Growth	1798565	16.7	No Growth	2586922	13.6
14	No Growth	1280584	19.6	No Growth	2163216	15.1	No Growth	2722819	13.1
15	No Growth	1854507	16.4	No Growth	2340545	14.4	No Growth	2743208	13.1
16	No Growth	2267341	14.7	No Growth	2295529	14.6	No Growth	2138408	15.2
17	No Growth	1883445	16.3	No Growth	2341951	14.4	No Growth	2524976	13.8
18	No Growth	2175831	15.1	No Growth	2433356	14.1	No Growth	2502270	13.8
19	No Growth	2802766	12.9	No Growth	2488371	13.9	No Growth	3060016	12.1
20	No Growth	2703784	13.2	No Growth	2495383	13.9	No Growth	2613923	13.5
21	No Growth	3199781	11.7	No Growth	2432058	14.1	No Growth	2617898	13.5
22	No Growth	3886655	10.1	No Growth	2740735	13.1	No Growth	3387273	11.2
23	No Growth	2368578	14.3	No Growth	2713642	13.2	No Growth	2413752	14.2
24	No Growth	2532016	13.7	No Growth	2164594	15.1	No Growth	2341010	14.4
25	No Growth	1651928	17.4	No Growth	2460214	14.0	No Growth	2636202	13.4
26	No Growth	1873170	16.3	No Growth	2329985	14.5	No Growth	2494002	13.9
27	No Growth	2408549	14.2	No Growth	2633385	13.4	No Growth	2284229	14.6

*All EI assays passed negative and positive control limits; 8000-340000 RLU and 41300000-164000000 RLU respectively.

Distribution studies were performed in triplicate. As can be seen in Table 6, Distribution Cycle 2 showed growth at location 12, whilst all other locations repeatedly showed no growth across all 3 cycles. Location 12 is found on the base of the isolator in front of the suit and is therefore not impacted by shadowing or occlusion. Investigation into the EI results of location 12, against nearby locations 10, 11 and 20, show that there is no evidence of decreased cycle efficacy in this location. Furthermore, the EI showed a high level of inactivation, which is higher than that achieved during cycle 1 and 3, which provided negative BI results. Therefore, it is suspected that the BI growth observed at location 12 is erroneous. To ensure this, a 4th cycle was completed with 3 BIs and 3 EIs in the location. The results from this cycle prove that the BI growth recovered was an erroneous result (Table 7), as no growth was recovered from the BIs and the EI results are consistent with those achieved across the cycles 1, 2 and 3.

Table 7: Distribution Cycle 4: Mapping of Location 12.

Location No.	Cycle 4		
	BI Results (Growth/ No Growth)	EI Result (RLU)	EI Result- CLR
12-1	No Growth	1775952	16.8
12-2	No Growth	2246221	14.8
12-3	No Growth	3095008	12.0

Furthermore, the results also reflected the range in localised efficacy around location 12. In distribution cycle 4, all of the 3 EIs were positioned in as close proximity as possible (without causing occlusion) around location 12, however the results recorded a range of CLRs from 12.0-16.8. A similar range to this is also mirrored across the first 3 cycles where the location recorded a range of CLRs from 11.9-15.2, which provides evidence that the observed variation at location 12 across cycles 1-3 is more likely caused by localised gas distribution changes than by variation in gassing cycle efficacy. This therefore provides evidence that there is sufficient localised gassing cycle efficacy across all of the cycles to ascertain BI kill in location 12 and, as such, provides further evidence that the BI growth observed in this location is erroneous.

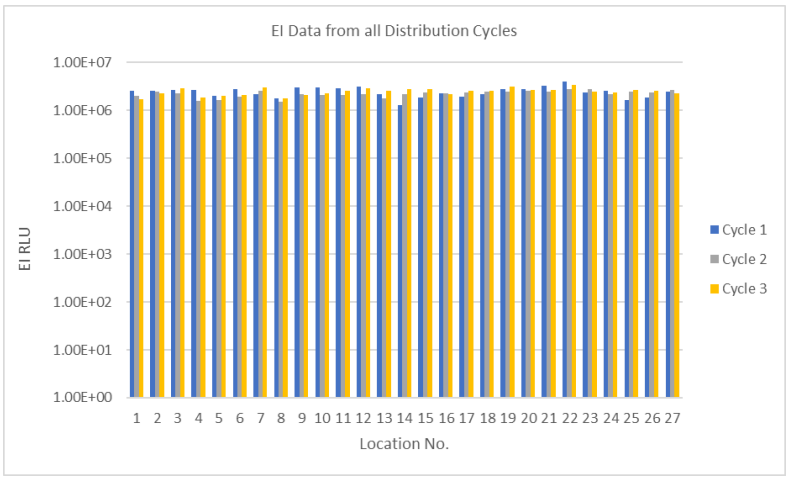

Figure 5: *Distribution Cycles: Enzyme Indicator Results.*

Assessment of the EI data across the distribution cycles, show that the optimised cycle parameters have provided consistently high decontamination efficacy, across the isolator enclosure when stressed with maximum loading. Furthermore, when comparing these results obtained using the new 'wet' vaporised H_2O_2 generator (Fig. 5), to those obtained during cycle optimisation on the older model (Fig. 3), there is no discernible difference in decontamination efficacy. Therefore, the EI and BI data can give confidence that the optimised cycle parameters and the 'wet' vH_2O_2 generator are sufficient to perform decontamination of the sterility testing isolator, and as such the cycle is regarded as validated.

Conclusion

The use of EIs in cycle optimisation and validation has proven a powerful tool. The quantifiable nature of the EI data allows greater insight into the decontamination efficacy of vH_2O_2 enabling rapid identification of cycle optimisation and subsequent validation across 10 working days. This has enabled the cycle parameters to be halved which in turn halves the cost of the cycle and doubles the productivity potential of the isolator. This could not have been possible with BI data alone, as additional cycles would have been required during the development of the optimised cycle. In addition, without EI data you would be unable to assess if cycle inactivation was nearing plateau, and so even if an optimised cycle were developed with BI data alone, the cycle would most likely have been extended longer than what has been achieved in this study to provide additional confidence.

Furthermore, the validation of the new 'wet' vH_2O_2 generator was also expedited using EI data, especially where instances of erroneous BI results were observed. With EIs co-located at each sample point, additional confidence of the erroneous nature of the BI result can be achieved, as there is additional data from the impacted location that the result was observed in. This is then much more powerful when trending across cycles as you can trend the magnitude of decontamination efficacy across the other isolator locations and other cycles performed, and confidently assess the error without requiring multiple repeat cycles.

Overall, the EI data provided increased insight across the sterility isolator chamber, allowing for confidence that sufficient cycle decontamination is consistently achieved in all challenge locations. As such, the cycle is considered to be validated with limited risk of BI failures upon requalification.

Therefore, AstraZeneca regards the use of EI technology as a beneficial companion to BI data when investigating opportunities to optimise productivity of current isolators, or validating new cycles or equipment.

Conflict of Interest

The author declares that this paper was written in conjunction with Enzyme Indicator manufacturer, Protak Scientific.

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