STERRAD VELOCITY™
Biological Indicator System

TECHNICAL DOSSIER

PART OF THE Johnson & Johnson FAMILY OF COMPANIES

Please read and follow the Instructions for Use (IFU) prior to using for important information, including contraindications, warnings, and proper directions.

AD-170050-01-CT_A

THE NEW RHYTHM OF REPROCESSING

INTRODUCTION

The purpose of this document is to describe the technology, concepts, operating theory and testing of the STERRAD VELOCITY™ Biological Indicator and Reader System. The STERRAD VELOCITY™ Biological Indicator is a self-contained biological indicator (BI) to be used with an automated reader to achieve a rapid readout time of 30 minutes at 57 ± 2°C. The STERRAD VELOCITY™ BI, used in conjunction with the STERRAD VELOCITY™ Reader, provides a fast and reliable way to verify the effectiveness of STERRAD® System sterilization cycles.

The STERRAD VELOCITY™ BI, in conjunction with the STERRAD VELOCITY™ Reader, is intended to be used as a standard method for frequent monitoring of the following STERRAD® Sterilization Systems:

- STERRAD® 100NX (STANDARD, FLEX, EXPRESS, and DUO Cycles) with and without ALLClear™ Technology
- STERRAD NX® (STANDARD and ADVANCED Cycles) with and without ALLClear™ Technology
- STERRAD® 100S Short and Long cycles

The core technology used by the STERRAD VELOCITY™ system to generate a rapid time-to-result is detection of the α-glucosidase enzymes generated naturally during growth of *Geobacillus stearothermophilus* and released during spore germination (B. Setlow, G. Korza and P. Setlow, 2016).[1] When the BI is processed through the STERRAD® System the enzyme activity is reduced proportionally to the total exposure in the STERRAD® System sterilization process. When exposed to a successful sterilization cycle, the spores and spore-associated enzyme are completely inactivated and the BI will not fluoresce.

TECHNOLOGY OVERVIEW

The STERRAD VELOCITY™ Biological Indicator and the automated reader are designed for frequent monitoring of the 8 STERRAD cycles referenced above. It is compliant, together with the STERRAD® System, with ISO11138-1:2006 (Sterilization of health care products — Biological indicators)[2], and U.S. FDA Guidance for Industry and FDA Staff - Biological Indicator (BI) Premarket Notification [510(k)] Submissions.[3]

STERRAD VELOCITY™ BI SYSTEM DESIGN

1 STERRAD VELOCITY™ Biological Indicator

The STERRAD VELOCITY™ BI consists of a glass fiber disc containing a minimum of 1 x 10^6 *Geobacillus stearothermophilus* (ATCC 7953) spores, a glass ampoule containing nutrient growth medium and non-fluorescent substrate, as well as a vial, cap, cap label, insert, and chemical indicator (Figure 1). The spore disc, growth media ampoule, and insert are contained in a clear plastic vial with a vented cap. The cap is designed with sterilant ingress openings which allow for penetration of hydrogen peroxide vapor into the vial during the sterilization process, and then is used to crush the growth media ampoule and seal the vial when activated for incubation. The small size of the openings, together with the overlying porous functional label, serves as a restriction of flow of hydrogen peroxide into the vial. The chemical indicator (CI), placed on the top of the cap, is a Type 1 process indicator that changes color from red/pink to yellow when exposed to hydrogen peroxide.

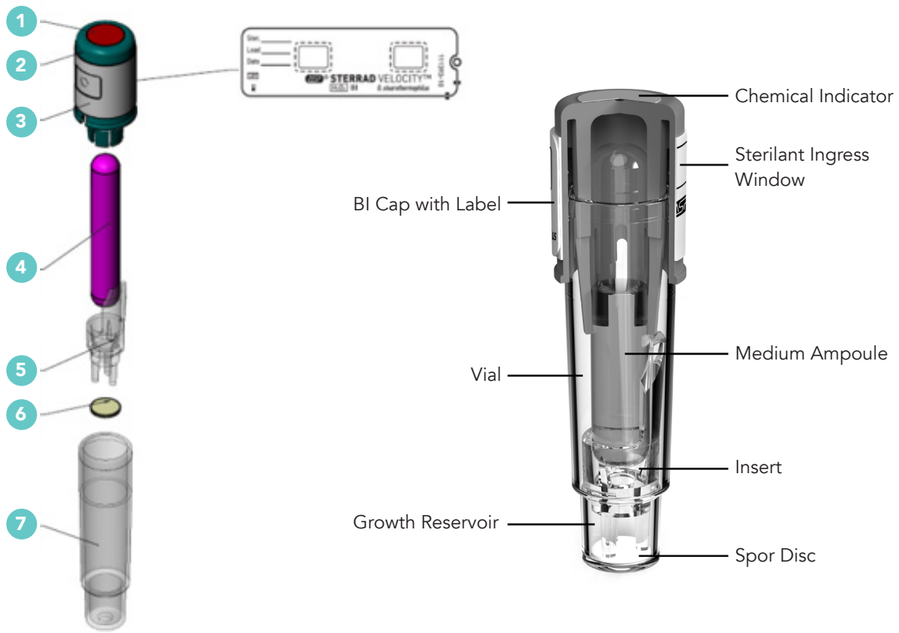


Figure 1: Engineering drawing and Cutaway Illustration of STERRAD VELOCITY™ Biological Indicator

STERRAD VELOCITY™ BI Components and Function

1. **Chemical Indicator**
   Type 1 Process Indicator. Changes color from red/pink to yellow with exposure to hydrogen peroxide.

2. **Cap**
   Restricts flow of hydrogen peroxide into vial via vents, used to crush ampoule and seal BI when pressed down.

3. **Cap label**
   Tyvek (same material as used for sterilization pouches) functions as a label and a physical barrier when applied to the cap. Two small uncoated windows (non-adhesive area) are aligned with the cap vent holes for hydrogen peroxide penetration.

4. **Media ampoule**
   Sealed glass container holding the sterile growth medium, non-fluorescent substrate and pH indicator. It is crushed prior to incubation, allowing media to contact and immerse the spore disc.

5. **Insert**
   Cradles glass ampoule, facilitates breakage when cap is pressed down.

6. **Spore disc**
   Carrier containing ≥ 1x10^6 *Geobacillus stearothermophilus* spores.

7. **Vial**
   Primary container for BI. Outer container of the device that contains the spore disc, media ampoule, and insert. It serves as a growth reservoir by holding the spore disc and medium during incubation.

After cycle completion, the STERRAD VELOCITY™ BI is activated by pressing down the cap until the glass ampoule breaks and shaken rapidly to ensure that liquid flows into the growth reservoir. The vial and cap have been designed with rigid materials that allow this activation to be completed safely by hand. The BI can be held for up to 2 hours after completion of the sterilization cycle before activating and reading without affecting the results. However, once activated, the BI should be placed immediately into the reader. The STERRAD VELOCITY™ BI is incubated in the STERRAD VELOCITY™ Reader in an upright position at 57 ± 2°C for 30-minute rapid readout detection of any surviving spores.

Optionally, the STERRAD VELOCITY™ BI can also be determined as growth-positive or growth-negative via an optional visual color change results (using bromocresol purple, or BCP). When using this method, the biological indicator must be cultured in an incubator at 55-60°C for 5 to 7 days to get final visual results.

1.1 BI Components and Materials

All materials used in the STERRAD VELOCITY™ BI were selected and verified to be compatible with peroxide. Key considerations for compatibility include the use of materials with minimal peroxide absorption and that do not change in functionality or dimension during exposure. In addition, particular consideration was given to the optical performance of the vial materials, allowing maximum transmittance of fluorescent signals.

1.2 Spore Species and Population

The spore species used in the STERRAD VELOCITY™ BI is *Geobacillus stearothermophilus* (ATCC 7953). This is the microorganism used to validate STERRAD® Systems and has previously been established to be highly resistant to the STERRAD® Sterilization process.

In addition, *G. stearothermophilus* is the microorganism recommended by FDA for the monitoring of hydrogen peroxide sterilization processes per FDA Guidance for Industry and FDA Staff: Biological Indicator (BI) Premarket Notification [510(k)] Submissions, Table 2, October 4, 2007.[3]

The spore population is between 4.0 x 10^6 CFU per disc and 8.3 x 10^6 CFU per disc at product release and will maintain a minimum of 1.0 x 10^6 colony forming units (CFU) per disc throughout the product shelf life.

1.3 Chemical Indicator (Type 1 Process Indicator)

The chemical indicator of the STERRAD VELOCITY™ BI consists of a disc coated with an ink of a proprietary formulation on one side and a co-polymer adhesive on the other side. The ink on the surface of the chemical indicator changes color from red/pink to yellow with exposure to hydrogen peroxide (Figure 2). Some red/orange/brown dots may be present on the chemical indicator after exposure to hydrogen peroxide.

Figure 2: Chemical Indicator Color Change

1.4 Culture Media

The culture media is a proprietary formulation designed to maximize the fluorescent response associated with any residual enzyme while also supporting the growth of any surviving spores. The formula contains casein enzymatic digest and soytone broth with 4-methylumbelliferyl α-D-glucopyranoside (α-MUG) and BCP as a non-fluorescent substrate and a pH indicator, respectively. The non-fluorescent substrate (α-MUG) in the culture media is essential in rapid detection the surviving spores (see Rapid Readout Technology Section). BCP is a pH-sensitive dye that changes from blue-purple to yellow when the pH of the growth medium decreases due to by-products of spore germination and growth (similar to the visual color change of CYCLESURE® 24).

1.5 Rapid Readout Technology

The α-glucosidase enzymes, generated naturally during growth of *G. stearothermophilus* and released during spore germination, hydrolyze the bond between the glucose and 4-methy-lumbelliferyl (4-MU) moieties of α-MUG (Figures 3 and 4). In the combined state α-MUG is not fluorescent. Once the bond between the glucose and 4-MU is hydrolyzed, the 4-MU component becomes fluorescent when excited with 365 nm UV light. Therefore, the α-glucosidase enzyme in its active state can be detected by measuring the fluorescence produced by the enzymatic hydrolysis of α-MUG. The BI is periodically exposed by the STERRAD VELOCITY™ Reader to UV light at 365 nm and the associated emission from the fluorescent by-product (4-MU) of enzyme activity is captured by a photodiode behind a filter centered at 450 nm.

The measured enzyme activity is reduced upon exposure to hydrogen peroxide during the STERRAD® Cycle. With enough exposure, the enzyme will be completely inactivated. As the enzyme activity is directly correlated with the spore outgrowth, the reduction of the enzyme activity below certain level indicates that all the spores have been inactivated. The level of the fluorescence response is determined by applying the algorithm developed for the STERRAD VELOCITY™ BI and used to distinguish between the positive and negative responses.

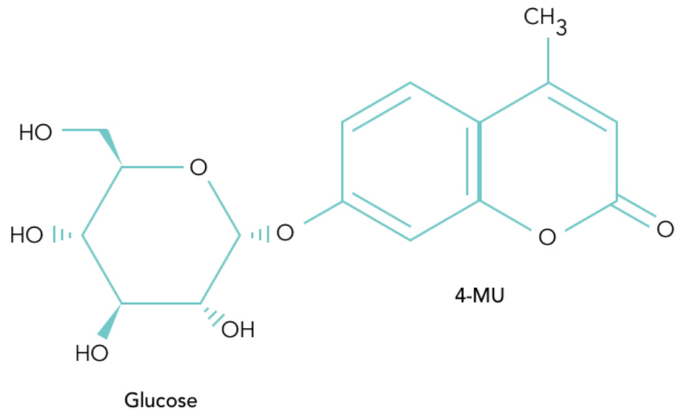


Figure 3: Components of α-MUG

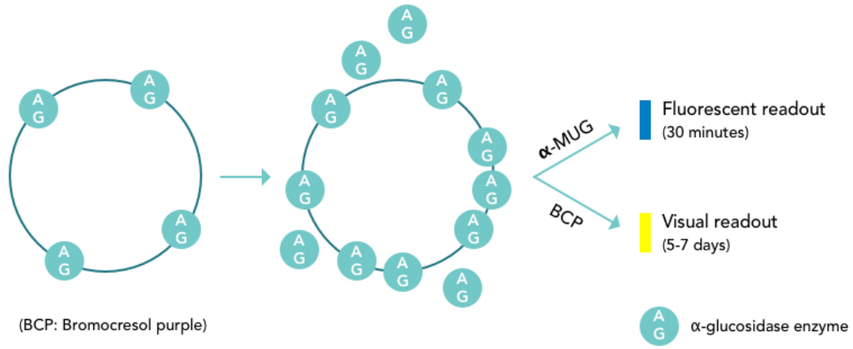
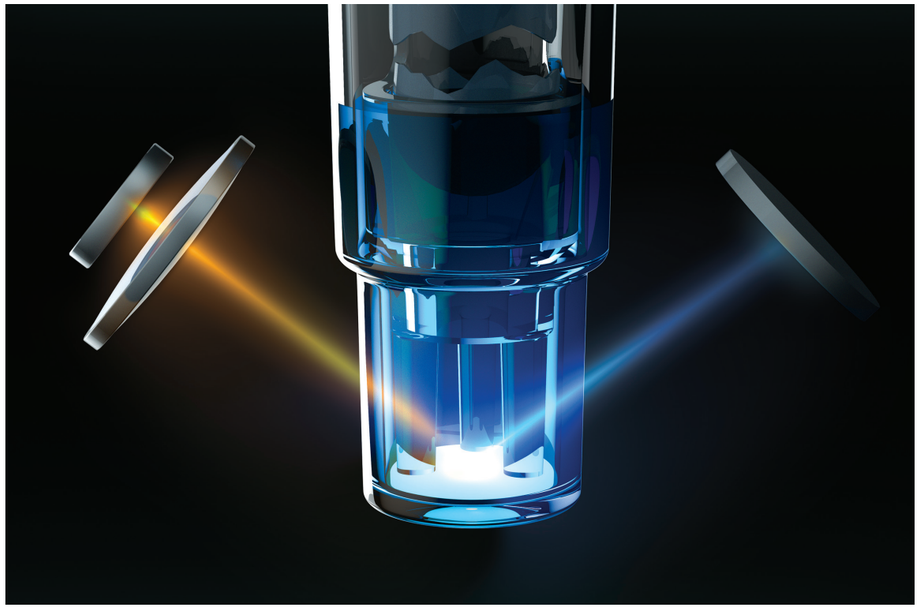


Figure 4: STERRAD VELOCITY™ Biological Indicator Technology
Release and *de novo* synthesis of α-glucosidase enzyme by germinating spores after exposure to a sub-lethal peroxide dose.

Studies using >30,000 BIs run in all indicated STERRAD® System cycles were performed to collect the fluo-rescence and growth data of BIs exposed to sub-lethal (unsuccessful) and full (successful) sterilization cycles. These data were then compared to a database reflecting the use of >50 million CYCLESURE® 24 BIs and >15,000 STERRAD® System cycle data files provided by customers to characterize appropriate fluorescence threshold specification to minimize the false-negative and false-positive BIs in every cycle.

1.6 Sensitivity

The STERRAD VELOCITY™ BI relies on the release of both *de novo* and *in situ* α-glucosidase enzyme associated with or embedded in the spore as well as any *de novo* enzyme produced during the 30-minute incubation period. The release of the enzyme is associated with the very earliest stages of germination.[1] It is expected that even when all spores have been inactivated or damaged sufficiently to prevent growth that sufficient residual enzyme activity may remain to yield a positive fluorescent response. This ensures that the fluorescent response is even more conservative than the growth-based response (further discussed in Section 4). ASP has demonstrated that even when, on average, one viable spore remains in the STERRAD VELOCITY™ BI, the BI will read as positive for fluorescence by the reader.



2 STERRAD VELOCITY™ Reader

The STERRAD VELOCITY™ Reader is designed to incubate and automatically read the STERRAD VELOCITY™ BI to obtain a final fluorescence result in 30 minutes at the incubation temperature of 57 ± 2°C. There are eight individual BI incubation wells in the STERRAD VELOCITY™ Reader, each containing a fixed light source and photodetector. While incubating, the BI is periodically exposed by the reader to UV light at 365nm and the associated emission from the fluorescent by product (4-MU, described in section 1.5) of any residual enzyme activity is captured by a photodiode behind an optical bandpass filter. The fluorescence is then converted into a voltage reading. The voltage readings are assessed by the detection algorithm in the Reader to determine the final result (positive or negative). If the fluorescent signal is determined to be significantly higher than that associated with a fully inactivated BI, the BI result can be assessed as positive. If, after 30 minutes, the increase in fluorescence of the BI is below a certain threshold, the BI result will be assessed as negative.

2.1 Ecosystem

The reader is designed to recognize individual STERRAD VELOCITY™ BIs via the serialized 2D barcode on each BI label. This allows association of individual test BI results with specific STERRAD® System cycle(s). The reader will transmit the BI interrogation record via ASP ACCESS™ to the clinic's instrument tracking system (ITS) or other designated recipient(s), such as the Sterile Process Department (SPD) manager. A failed test BI will result in notification of the user via the reader display, and if connected to ASP ACCESS™, alerts via user-designated electronic means. The failed test BI result will also result in a notification of affected cycles on the affected STERRAD® System with ALLClear™ Technology screen(s).

2.2 Compliance

The STERRAD VELOCITY™ Reader incorporates multiple features to enhance compliance, usability and ease of record-keeping. It features a touch screen graphical user interface. Directly under each well is a well-number illuminated by a status indicator light. Three colors (white, green, and red) and two states (off and solid line) are used for the indicator light on the touch screen to show the status of the BI processing. The reader has a thermoplastic exterior which makes it easy to clean and maintain. The built-in barcode scanner coupled with network connectivity automates maintenance of sterilization records.

The reader is also designed to detect and respond to various user mis-use scenarios while also ensuring compliance with the institution's procedures. Recognition of individual BIs helps prevent use of the BI in ways inconsistent with the IFU, such as use of BIs from an expired lot, use of BIs from a lot on which a control has failed, re-use of a particular BI, reading of a BI more than 2 hours after removal from the STERRAD® System cycle or failure to properly activate a BI. Furthermore, compliance with institutional requirements regarding the frequency of BI usage can be tracked using the STERRAD VELOCITY™ Reader. As part of a self-diagnostics system, the reader will also inform the user of any detected system or sub-system failures, and will prevent the user from using reader any well(s) that cannot accurately incubate or read a BI. Finally, when used in conjunction with ASP ACCESS™ and the STERRAD® 100NX with ALLClear™ Technology or STERRAD NX® with ALLClear™ Technology, information regarding the BI, test results, and associated loads will be automatically recorded by the system rather than requiring manual record-keeping.

3 Testing and Validation

Testing and validation of the STERRAD VELOCITY™ System was conducted to ensure both accuracy and performance of the BI in monitoring in STERRAD® System cycle performance as well as compliance with applicable industry and governmental standards, including ISO11138[2] and Guidance for Industry and FDA Staff - Biological Indicator (BI) Premarket Notification [510(k)] Submissions.[3]

3.1 STERRAD VELOCITY™ BI Validation

Validation testing for the BI includes:

Dose-response in all indicated STERRAD® System cycles: ensures that the BI responds appropriately to various exposure levels of peroxide in each STERRAD® System cycle for both fluorescence and growth-based readouts. Exposure levels range from those in which no BIs are inactivated to those that completely inactivate the BI. This testing is done under "worst-case" conditions, including loading of the STERRAD® Systems to the cycle weight limits, reduced chamber temperature, and using reduced peroxide concentrations. This testing ensures that the BI will perform both within, and even beyond, the validated limits of what a user could experience using a STERRAD® system.

D-value (Holcomb-Spearman-Karber procedure, or HSK, and survivor-curve): Consistent with ISO11138-1 guidance, ASP tests two D-values for the STERRAD VELOCITY™ BI (ASP also reports these values for each individual lot of BIs manufactured). This D-value reflects the spore growth result only, not fluorescence (for which a standard method does not yet exist). Both HSKP and survivor-curve are tested according to methodology specified in the ISO11138 guidance.[2] It is ASP's position that these two methods are the most accurate measure of each lot's resistance as compared to the survival-kill method used for STERRAD® CYCLESURE® 24 BI which incorporated a "fixed" kill-time value that does not change between lots.

Fluorescent response: This testing consists of two aspects—sub-lethal exposure and "kill" cycles. This testing is designed to ensure that the BI, when used in conjunction with the STERRAD VELOCITY™ Reader, will read fluorescent-positive as long as any spores remain viable (preventing false-negative results) and will be fluorescent-negative after exposure to a successful sterilization cycle (preventing false-positive results).

Reduced Incubation Time (RIT): Consistent with FDA guidance, this test is used to validate the rapid fluorescent read-out time of 30 minutes as well as the 5-7 day readout time for the optional visual readout. After exposure to a peroxide dose in which 30-80% of the BIs read positive for growth (visual) after 7 days, for each growth-positive BI the fluorescent result obtained at 30 minutes, and the 5-day growth result is compared to the 7-day growth result. The FDA guidance requires that no more than 3% of the growth-positive BIs can be read as negative at the specified time (30 minutes and 5 days for fluorescence and growth results, respectively). An example data set, collected for the STERRAD® 100NX STANDARD cycle (Table 1) confirmed that no (0%) false-negatives were detected in 100 BIs (Guidance for Industry and FDA Staff - Biological Indicator (BI) Premarket Notification [510(k)] Submissions) subjected to sub-lethal doses of peroxide in 3 different lots of indicators.[3]

Table1: Comparison of fluorescent versus growth (visual) positive STERRAD VELOCITY™ BIs exposed to a sublethal peroxide dose in the STERRAD® 100NX Standard Cycle.

BI Lot	1	2	2
Total # of BIs per cycle	100	200	100
# of Fluorescence-positive BIs	100	100	10
# of Fluorescence-positive BIs that are Growth-positive (numerator)	49	64	64
Total # of Growth-positive BIs on Day 7 (denominator)	49	49	64
% Read-out for Fluorescence	100% (49/49)	100% (64/64)	100% (64/64)

Bacteriostasis: This test is conducted to ensure that the materials used in the biological indicator do not inhibit the outgrowth of small numbers (10-100) of spores after exposure to the sterilant. ASP has verified that after exposure to even the highest concentration of peroxide used in STERRAD® Systems in a sub-lethal cycle, remaining viable spores will grow and be detected.

Population: This test is used to confirm that the number of spores contained in each BI meets the minimum requirements (>1 million spores/carrier) through shelf-life. In fact, each STERRAD VELOCITY™ BI is inoculated with 4-8.3 x 10^6 spores, which, when combined with the enzyme specifications, results in the optimal performance of the STERRAD VELOCITY™ BI in each cycle.

Shelf-life: Several lots of the STERRAD VELOCITY™ BI were tested to ensure that the BI meets all specifications throughout the labeled shelf-life at the labeled storage conditions. These include population, resistance, enzyme levels, fluorescent response and growth media performance, among other parameters. In addition, the performance of the BIs after exposure to more extreme temperatures (-12°C to 65°C) ("excursions") encountered during shipping was tested. These studies verified that the STERRAD VELOCITY™ BI will perform as intended throughout its labeled shelf-life.

Enzyme: The manufacturing process for the STERRAD VELOCITY™ BI was validated to yield spores that produce the required levels of enzyme to maintain the BI performance, even in "worst-case" testing conditions, throughout the labeled shelf-life. This enzyme level is also tested in every BI lot released from ASP.

Hold time: The length of time that the BI can be held after completion of the sterilization cycle and before activation and incubation was determined to be 2 hours or less. Within this hold time, the growth and fluorescence results are the same as for processing of the BI immediately after cycle completion.

3.2 STERRAD VELOCITY™ Reader Validation

Mechanical: The reader was verified to have the appropriate sound and visual indicators for the operating environment, as well as withstand the mechanical (e.g. vibration) and chemical exposures (including dust or moisture ingress) that might be expected in its use environment.

Electrical: This testing verified performance of the reader's electrical characteristics including input power and current consumption, functionality of the device digital interfaces, functionality of the device user interfaces, functionality of the device audio interfaces and the heating profile of the Incubation Cycle.

Thermal: This testing verified heater block temperature maintenance and monitoring, the number of BIs that may be assessed concurrently, heater block temperature monitoring systems, fault handling, and thermal runaway protection.

Optical: The performance of the optical subsystem was verified, including the ability of the system to detect insertion and removal of the BI, delivery of the appropriate wavelengths and intensity of UV light, the ability of the fluorescence detector to filter out extraneous light and capture the wavelength of light being emitted by the 4-MU.

System-level error checks: This testing verified that the reader can either accurately measure the BI under various use and mis-use scenarios or provide the user with a message indicating that the BI cannot be accurately read. These scenarios include such things as improper insertion of the BI, mechanical disruption of the BI reading, contamination of the wells, etc.

Software verification: Testing was conducted of the software, including the software used to control the operation of the reader, Graphical User Interface (GUI) flow and error messaging to ensure proper functioning of the system under a wide range of use and mis-use scenarios and the ability to accurately read a BI or, in the event of a critical system or sub-system failure, message the user appropriately and prevent use of any well(s) that cannot accurately read a BI. In all cases, the software was demonstrated to function correctly.

Robustness: The ability of the reader to withstand exposure to shipping, water or dust ingress, extreme environmental conditions, vibration and shock, aging, and other events, while either maintaining functionality or providing the appropriate error messages to the user was tested. In all cases, the reader demonstrated the ability to function properly.

Safety: testing was performed by an external laboratory to demonstrate compliance with:

- EN 61010-1[7]
- IEC 61010-1[8]
- UL 61010-1[9]
- EN 61010-2-010[10]
- IEC 61010-2-010[11]
- UL 61010-2-010[12]
- CAN/CSA-C22.2 No. 61010-1-12[13]
- CAN/CSA-22.2 No. 61010-2-010:15[14]

Electromagnetic compatibility (EMC)/Electromagnetic Interference (EMI): EMC/EMI testing was performed by an accredited external testing laboratory. Test cases executed verified compliance of the STERRAD VELOCITY™ Reader with requirements of the EN 61326-1:2013 standard and EMC Directive.[5, 6, 15, 16] The reader was found to not cause any electromagnetic disturbance that could affect the functionality of other interfaced and nearby devices and was able to perform without any performance degradation in the presence of electromagnetic disturbance.

Cybersecurity: Completed cybersecurity activities for the STERRAD VELOCITY™ Reader software are consistent with the cybersecurity framework core functions (Identify, Protect, Detect, Respond, and Recover) recommended in the FDA Guidance *Content of Premarket Submissions for Management of Cybersecurity in Medical Devices* dated October 2.[4] Information security has been addressed by applying the specific concepts of confidentiality, integrity, availability, and accountability (CIAA).

4 Accuracy/performance

With respect to the sterilization process, the STERRAD VELOCITY™ BI is precisely designed to provide the appropriate level of challenge to each of the cycles for which it is indicated. It is neither too weak—completely inactivated before the appropriate sterilization conditions are met, nor too strong—indicating a positive result even after a successful sterilization cycle has completed.

This ideal performance of a biological indicator in an individual STERRAD® System cycle is illustrated in Figure 5. Ideally, the BI should represent the most challenging medical devices approved for use in that cycle. The most-challenging devices are typically those with the longest, narrowest lumens and are represented in our testing by the "biological model"—a standardized set of inoculated lumens of various materials and dimensions, unique to each cycle, and tested together with a heavily loaded instrument tray representing maximum allowed loading of the chamber. This biological model serves as a critical reference point for comparison of BI performance to ensure a robust challenge to the sterilization process. The STERRAD VELOCITY™ BI is not fully inactivated before the conditions required to sterilize the most challenging medical devices approved for use in that cycle are achieved. At the same time, it will be fully inactivated before the completion of the cycle.

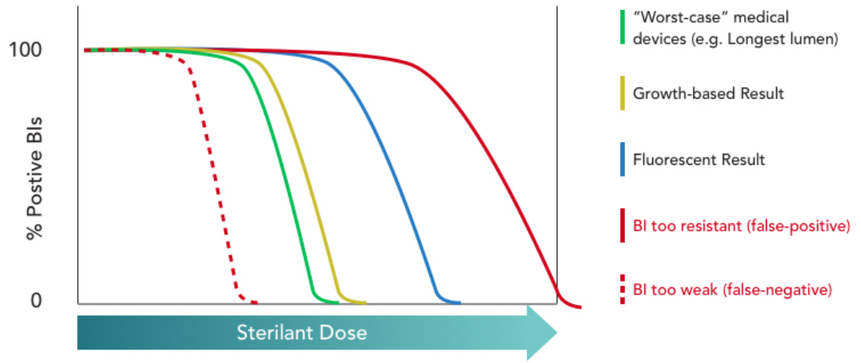


Figure 5: Ideal dose-response curve of a biological indicator in STERRAD® System cycles (illustrative only). Green represents the worst-case medical devices, or biological model. The growth-based (visual) response is illustrated by the yellow line, whereas the fluorescent result is shown in blue. A full sterilant dose (complete cycle) is indicated by the right-most vertical line.

In general, as illustrated in Figure 5, the fluorescence (enzyme-based) response is a more conservative challenge of the STERRAD® System cycle than the visual response (pH indicator of metabolism), meaning that a higher dose of peroxide is required to achieve a fluorescent-negative than the visual-negative STERRAD VELOCITY™ BI. This design is intentional to ensure that the rapid-read technology will never underestimate the growth of spores and allow the visual read for color change to be optional only. It is also important to note that, for the STERRAD VELOCITY™ BI, the use of rapid-read technology does not sacrifice the accuracy or rigor with which the cycles are being monitored.

Furthermore, these performance targets—benchmarked by the medical devices indicated for each cycle and the total efficacy of the cycle, are different for each indicated STERRAD® System cycle. Thus, the performance of the BI must be tightly constrained to provide the appropriate challenge for all indicated cycles. These offset "goal-posts" are illustrated in Figure 6.

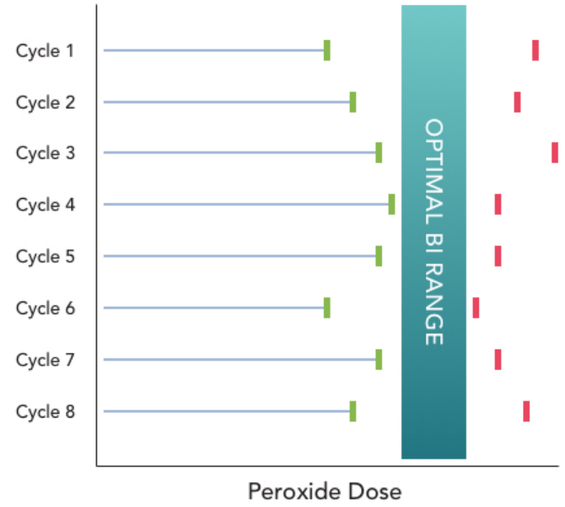


Figure 6: Optimal performance range of a biological indicator in STERRAD® System cycles (illustrative only). Teal indicates the range in which the BI should be fully inactivated. The green line indicates the peroxide dose in which the "worst-case" medical devices are sterilized while the red line indicates the peroxide dose achieved in a full cycle.

The design and performance of the STERRAD VELOCITY™ BI was characterized using data gathered from millions of CYCLESURE® 24 BIs run in STERRAD® Systems, testing of >30,000 of STERRAD VELOCITY™ prototype indicators and drawing on a database containing the detailed cycle parameters of more than 15,000 cycles run by users in hundreds of STERRAD® Systems representing a wide range of loads and devices. Using this approach, ASP ensured that the likelihood of experiencing a false-positive and false-negative are both minimized.

This is also illustrated in Figure 7, in which the STERRAD VELOCITY™ BI was tested for both growth and fluorescence-based results after exposure to increasing doses of hydrogen peroxide in a STERRAD® System. The results indicate that even when all spores are fully inactivated, a substantial number of BIs will read as fluorescent-positive.

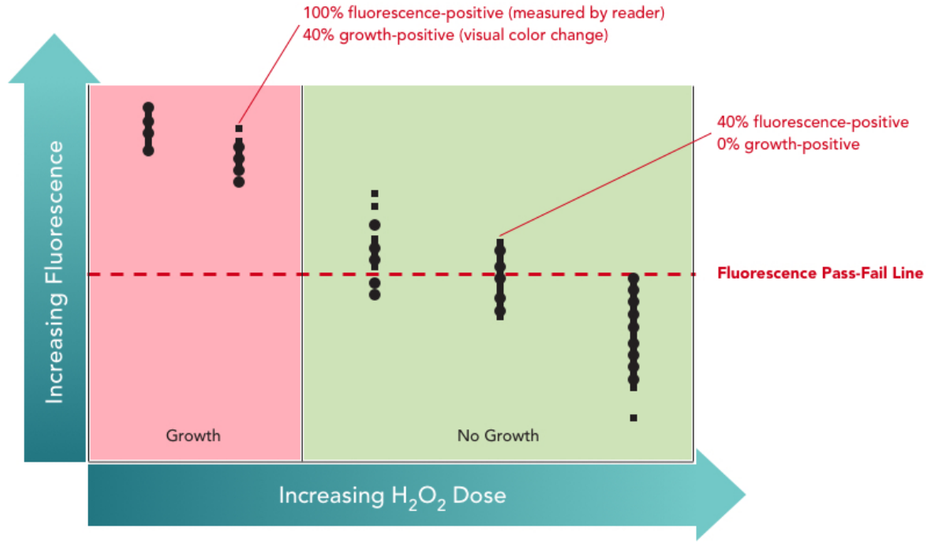


Figure 7: Exposure of STERRAD VELOCITY™ to increasing doses of peroxide. Each point in the graph represents a BI read for growth and fluorescence (representing residual enzyme activity).

Beyond verification of the STERRAD VELOCITY™ BI, release testing is conducted on every lot of biological indicators to ensure that it fully meets ASP specifications for spore population, enzyme level, fluorescent response (including tests for false-positives and false-negatives), and resistance of spores to the sterilization process.

In addition, the STERRAD VELOCITY™ Reader has been designed and validated such that it maintains its performance as long as it remains in use. This is achieved through several means, particularly for monitoring of the critical thermal and optical subsystems required to accurately monitor BI performance. These means include the use of system self-diagnostics, triply redundant monitors of temperature, performance checks of the optical subsystems, such as "dark voltage", and algorithms designed to react if the signal being read from a BI is not within the expected ranges, or if a BI reading is disrupted. If any system issue is identified that could result in an inaccurate reading, the reader will notify the user and render the affected well(s) inoperable. The reader also employs high-performance parts in critical subsystems, such as the optical and thermal subsystems, that have been subject to extensive testing both by the component manufacturer and through development by ASP. Part of this process is reliability and Highly Accelerated Life Testing (HALT) and Highly Accelerated Stress Screening (HASS) testing meant to test the design limits of the product. Throughout validation, reliability, environmental and ship testing of the electrical, hardware, optical, and thermal subsystems of the reader, no failures resulting in an inaccurate reading were detected.

4.1 False-positive and false-negative rates

The STERRAD VELOCITY™ BI was designed to have an overall false-positive rate equivalent or better than the estimated false-positive rate (based on complaint data) for CYCLESURE® 24 (1 in 30,000). The actual false-positive rate will vary among the cycles, with the non-concentrated hydrogen peroxide cycles

(STERRAD® 100NX EXPRESS and DUO, STERRAD® 100S SHORT) likely to experience higher rates than the concentrated cycles. To mitigate the likelihood of false-positives, ASP recommends that the BI not be placed inside a pouch (rather taped to the load or placed in a small container or tray), and for the STERRAD® 100S SHORT cycle, recommends that the BI be placed in the front of the chamber. Even by placing the BI in the front of the chamber, the BI represents a stronger challenge to the cycle than the biological model (or "worst-case devices") placed in anywhere in the chamber.

The STERRAD VELOCITY™ BI was designed to have an overall false-negative rate of less than 3% per the FDA Guidance document.[3] Through characterization testing of the product, it was determined that the false-negative rate with low levels of enzyme is 0.2% or less. The likelihood of a STERRAD® System failing in such a way as to not cancel the cycle and convert the CI but also not deliver the appropriate amount of peroxide into the chamber is estimated to be <0.1%. Thus, the combined likelihood of a failure that is not detectable to the user via either a STERRAD® cancellation or a positive BI result is conservatively estimated at 0.2% (probability of an individual BI yielding a false-negative) multiplied by 0.1% (probability of a multi-level STERRAD® system failure not resulting in cycle cancellation), or <0.0002% (1 in 500,000).[18]

REFERENCES

1. Setlow, G. Korza and P. Setlow, 2016. Analysis of ⍰-glucosidase enzyme activity used in a rapid test for steam sterilization assurance. Journal of Applied Microbiology Journal of Applied Microbiology 120, 1326--1335.

2. ISO11138-1:2006 Sterilization of health care products — Biological indicators. Retrieved from: www.iso.org/standard/33956.html October 10, 2017.

3. U.S. FDA Guidance for Industry and FDA Staff - Biological Indicator (BI) Premarket Notification [510(k)] Submissions, October 4, 2007. Retrieved from: https://www.fda.gov/MedicalDevices/ucm071261.htm. October 16, 2017

4. Content of Premarket Submissions for Management of Cybersecurity in Medical Devices (2014). Retrieved from: https://www.fda.gov/downloads/medicaldevices/deviceregulationandguidance/guidancedocuments/ucm356190.pdf October 10, 2017

5. Directive 2014/30/EU of the European Parliament and of the Council of 26 February 2014 on the Harmonization of the Laws of the Member States Relating to Electromagnetic Compatibility. Retrieved from: http://eur-lex.europa.eu/legal-content/EN/TXT/?uri=celex%3A32014L0030 October 10, 2017

6. EN 61326-1:2013 EMC Directive: Evaluation of Lab, Test & Measurement Equipment. Retrieved from: http://www.metlabs.com/emc/en-61326-1-2013-replacing-2006-version-for-emc-directive-evaluation-of-lab-test-measurement-equipment/ October 16, 2017

7. EN 61010-2-010:2014. Safety requirements for electrical equipment for measurement, control and laboratory use - Part 2-010: Particular requirements for laboratory equipment for the heating of materials. Retrieved from: https://www.iecee.org/dyn/www/ x?p=106:49:0:::FSP_STD_ID:4283 October 16, 2017

8. IEC 61010-1:2010. Safety requirements for electrical equipment for measurement, control, and laboratory use - Part 1: General requirements. Retrieved from: https://www.iecee.org/dyn/www/f?p=106:49:0:::FSP_STD_ID:4279 October 16, 2017

9. UL 61010-1:2012. Safety requirements for electrical equipment for measurement, control, and laboratory use - Part 1: General Requirements. Retrieved from: http://www.dlsemc.com/safety/61010-3rd-Ed.htm?gwds-laboratory October 16, 2017

10. EN 61010-1:2010. Safety requirements for electrical equipment for measurement, control, and laboratory use. General requirements. Retrieved from: http://www.dlsemc.com/safety/61010-3rd-Ed.htm, October 16, 2017

11. IEC 61010-2-010:2014. Safety requirements for electrical equipment for measurement, control and laboratory use - Part 2-010: Particular requirements for laboratory equipment for the heating of materials. Retrieved from: https://www.iecee.org/dyn/www/f?p=106:49:0:::FSP_STD_ID:4283 October 16, 2017

12. UL 61010-2-010:2015. Safety requirements for electrical equipment for measurement, control, and laboratory use - Part 2-010: Particular requirements for laboratory equipment for the heating of materials. Retrieved from: http://standards.globalspec.com/std/9880492/ul-61010-2-010-bulletin October 17, 2017

13. CAN/CSA-C22.2 No. 61010-1-12 (2012). Safety requirements for electrical equipment for measurement, control, and laboratory use - Part 1: General requirements (Tri-national standard, with UL 61010-1 and ANSI/ISA-61010 Retrieved from: https://webstore.ansi.org/RecordDetail.aspx?sku=CAN%2FCSA+C22.2+No.+61010-1-2012+(R2017) October 17, 2017

14. CAN/CSA-22.2 No. 61010-2-010:15 (2015). Safety requirements for electrical equipment for measurement, control and laboratory use - Part 2-010: Particular requirements for laboratory equipment for the heating of materials. Retrieved from: http://shop.csa.ca/en/canada/measurement-control-and-signaling-apparatus/cancsa-c222-no-61010-2-01015/invt/27021092015, October 17, 2017

15. EN 61326-1:2013/IEC 61326-1:2012. EMC Emissions/Immunity Requirement Changes for Laboratory Equipment. Retrieved from: https://shop.bsigroup.com/ProductDetail/?pid=000000000030291592, October 17, 2017

16. EMC Directive (2014/30/EU). Directive 2014/30/EU of the European Parliament and of the Council of 26 February 2014 on the harmonisation of the laws of the Member States relating to electromagnetic compatibility. Retrieved from: http://f2labs.com/low-voltage-directive testing?_vsrefdom=ppcgooglece&utm_source=google&utm_medium=cpc&utm_term=ce%20low%20voltage%20directive&utm_campaign=ce&gclid=Cj0KCQjwsZHPBRClARIsAC-VMPD2njOEPsJPbnRP_PE6Gg_97SDnh2F0O1wpmzAXddfTzmT9EUBNH4oaAsXoEALw_wcB. October 16, 2017

17. FCC Part 15, Subpart B, Class A. Code of Federal Regulations, Title 47, Part 15 (47 CFR 15) Subpart B: Unintentional Radiators. Retrieved from: https://www.fcc.gov/general/rules-regulations-title-47 October 16, 2017

18. SR-43210 and SR-43220, Advanced Sterilization Products, Irvine, CA. October 17, 2017