MesaLabs

QS-514 Validation Summary
Self-Contained Biological Indicators for H_2O_2 Sterilization Processes
Product Line

Executive Summary

The EZTest-H_2O_2 and ExpoSure manufacturing processes are validated according to QS-501 *Validation Master Plan for the Mesa Labs, Inc., Bozeman Manufacturing Facility 625 Zoot Way.*

The EZTest-H_2O_2 and ExpoSure manufacturing processes, under anticipated conditions, will consistently produce product that meets pre-determined specification requirements.

Process Performance Qualification

Process Performance Qualification (PPQ) conducted under Protocol #180208P *Performance Qualification for the Manufacture of SCBIs for H_2O_2 Sterilization Processes.* This PPQ qualifies manufacturing of the EZTest-H_2O_2 and ExpoSure product lines at 625 Zoot Way, Bozeman MT 59718.

Validation Lots

EZHI/6; GST log 6 100ct/box, Lot H-204
EZHI/6; GST log 6 100ct/box, Lot H-205
EXPO/6; GST log 6 30ct/box, Lot ES-015
EXPO/6' GST log 6 30ct/box, Lot ES-016

Rationale for selection of products

EZTest and ExpoSure manufacturing are a multi-phase processes: inoculation of carrier, assembly into self-contained biological indicators, qualification testing and final packaging. The inoculation phase consists of distributing a known quantity of bacteria onto a product specific carrier. Once assembled, the SCBIs are subjected to qualification testing consisting of population and H_2O_2 resistance testing. The results are used to generate the label claim for each lot of product. Satisfactory completion of the qualification testing results in release of EZTest-H_2O_2 and ExpoSure for distribution.

- The components used to manufacture these lots are representative of the components used to manufacture all variants of EZTest-H_2O_2 and ExpoSure.
- The 4 runs were considered sufficient to simulate conditions that will be encountered during routine manufacturing, such as start-up, shut-downs, breaks, and manufacturing over multiple days.

EZTest-H_2O_2

As compared to the manufacturing process prior to transfer to the new facility, there were no changes to the manufacturing process, components or component suppliers. The only change made to EZTest was the test conditions. The exposure conditions were changed from 2.0mg/L at 45°C to 2.3mg/L at 50°C. Procedures were renumbered to align with the quality system, and a number of minor changes occurred to allow for slightly different workflow in the new facility; they otherwise remained unchanged.

ExpoSure

As compared to the manufacturing process prior to transfer to the new facility, there were no changes to the manufacturing process, performance specifications or component suppliers. There was a change to the unit label material. The polypropylene label previously used for the unit label was discontinued by the manufacturer and it was replaced with a polyester label. There were no changes to the process indicator on the label. The indicator remains red and changes to/toward blue upon exposure to H2O2. Procedures were renumbered to align with the quality system, and a number of minor changes occurred to allow for slightly different workflow in the new facility; they otherwise remained unchanged.

Acceptance criteria and results

Four consecutively manufactured lots (2 EZTest and 2 ExpoSure) meeting the criteria provided below were required to confirm that the EZTest and ExpoSure manufacturing process, under anticipated conditions, will consistently produce product that meets pre-determined specification requirements.

For the QA final inspection per QSWI-103, the Acceptable Quality Level (AQL) for acceptability of a particular lot's inclusion in this qualification was based on criticality and frequency of the defect. If the lot in question fell within these established limits it was deemed acceptable for use as a validation lot. The defects were divided into two tiers. Defects considered *Critical to Performance* were assigned an AQL of 99%. Defects considered as having *No Impact to Performance* were assigned an AQL of 95%. Results are reported below for each validation lot.

EZH/6I, Lot H-204		
Critical to Performance	**Results**	**Pass/Fail**
Population on assayed unit must be the targeted population log: log6	1.8×10^6	PASS
EZTest-H_2O_2 media ampoules must change from purple to bright yellow when growth is present	Units changed to bright yellow upon incubation	PASS
H_2O_2 D-value 2.3 mg/L at 50°C	2.0minutes	NA
Labeling, specific to product traceability (species, lot number and expiration)	0 labeling errors	PASS
No Impact to Performance	**Results**	**Pass/Fail**
No breakage is visible inside the package	No visible breakage was identified during the final inspection	PASS
Inclusion of C of A in package	0 packages without a C of A	PASS

EZH/6I, Lot H-205		
Critical to Performance	**Results**	**Pass/Fail**
Population on assayed unit must be the targeted population log: log6	$1.7x10^6$	PASS
EZTest-H_2O_2 media ampoules must change from purple to bright yellow when growth is present	Units changed to bright yellow upon incubation	PASS
H_2O_2 D-value 2.3 mg/L at 50°C	2.2minutes	NA
Labeling, specific to product traceability (species, lot number and expiration)	0 labeling errors	PASS
No Impact to Performance	**Results**	**Pass/Fail**
No breakage is visible inside the package	No visible breakage was identified during the final inspection	PASS
Inclusion of C of A in package	0 packages without a C of A	PASS

EXPO/6, Lot ES-015		
Critical to Performance	**Results**	**Pass/Fail**
Population on assayed unit must be the targeted population log: log6	$1.7x10^6$	PASS
ExpoSure media ampoules must change from purple to bright yellow when growth is present	Units changed to bright yellow upon incubation	PASS
H_2O_2 D-value at 2.5 mg/L at 50°C must be within 0.75-6.0seconds	0.8seconds	PASS
Labeling, specific to product traceability (species, lot number and expiration)	0 labeling errors	PASS
No Impact to Performance	**Results**	**Pass/Fail**
No breakage is visible inside the package	No visible breakage was identified during the final inspection	PASS
Inclusion of C of A in package	0 packages without a C of A	PASS

EXPO/6, Lot ES-016		
Critical to Performance	**Results**	**Pass/Fail**
Population on assayed unit must be the targeted population log: log6	$1.2x10^6$	PASS
ExpoSure media ampoules must change from purple to bright yellow when growth is present	Units changed to bright yellow upon incubation	PASS
H_2O_2 D-value at 2.5 mg/L at 50°C must be within 0.75-6.0seconds	0.9seconds	PASS
Labeling, specific to product traceability (species, lot number and expiration)	0 labeling errors	PASS
No Impact to Performance	**Results**	**Pass/Fail**
No breakage is visible inside the package	No visible breakage was identified during the final inspection	PASS
Inclusion of C of A in package	0 packages without a C of A	PASS

Deviations to protocol

There was one deviation encountered during the execution of protocol 180208P.

- 180208P-D001: The protocol stated that 30 boxes of EZH/6 shall be assembled from each of two lots to complete the PPQ process. This planned deviation was to change the item from EZH/6 to EZH/6I and the quantity from exactly 30 boxes of each lot to a minimum of 30 boxes from each lot.
    - There is no negative impact to the protocol. The manufacturing process for EZH/6 and EZH/6I is identical. Changing the quantity from exactly 30 boxes to a minimum of 30 boxes allows for the production of more product based on business need.

Method Verification

The following Compendial Method Verifications were completed as part of this protocol:

- Population assay testing on stainless steel carriers in self-contained biological indicators per ISO 11138-1 and Mesa procedure LP-306.
- Population assay testing on quartz carriers in self-contained biological indicators per ISO 11138-1 and Mesa procedure LP-305.
- H_2O_2 resistance testing on self-contained biological indicators per ISO 11138-1 and Mesa procedure LP-302
    - There is no compendial method for exposure conditions or acceptable resistance range for biological indicators intended for use in hydrogen peroxide sterilization processes

Equipment Qualification

The following equipment qualifications were completed in order to execute this protocol:

Equipment Number	Equipment	Qualification document(s)	Protocol Deviations	Conclusion
STZ-101	Steam Autoclave	STZ101-IOQ-001	None	The Steam Autoclave has been installed successfully. The installation, operation, and performance criteria have been met.
		STZ101-PQ-003	None	
RES-108	H_2O_2 Resistometer	RES108-IOQ-001	None	The H_2O_2 resistometer has been installed successfully. The installation and operation qualification criteria have been met.
RES-110	H_2O_2 Resistometer	RES110-IOQ-001	None	The H_2O_2 resistometer has been installed successfully. The installation and operation qualification criteria have been met.
INC-103	30-35°C Incubator	INC103-IOQ-001	None	The 30-35°C incubator has been installed successfully. The installation and operation qualification criteria have been met.
INC-105	55-60°C Incubator	INC105-IOQ-001	None	The 55-60°C incubator has been installed successfully. The installation and operation qualification criteria have been met.
ASM-105	Assembly Machine	ASM105-IOQ-001	None	The assembly machine has been installed successfully. The installation and operation qualification criteria have been met
LBR-106	AXUS Label Applicator	LBR106-IOQ-001	None	The labeler has been installed successfully. The installation and operation qualification criteria have been met.

Equipment Number	Equipment	Qualification document(s)	Protocol Deviations	Conclusion
LBR-109	Autolabe Label Applicator with Hot Stamp Printer	LBR109-IOQ-001	None	The labeler has been installed successfully. The installation and operation qualification criteria have been met.
LBR-110	Autolabe Label Applicator with Hot Stamp Printer	LBR110-IOQ-001	None	The labeler has been installed successfully. The installation and operation qualification criteria have been met.

Utility Qualification

The following utility qualifications were completed in order to execute this protocol:

System Number	Utility	Qualification document(s)	Protocol Deviations	Conclusion
AIR-101	Compressed Air System	AIR101-IOQ-001	None	The Compressed Air System has been installed successfully. The installation and operation qualification criteria have been met.
STM-101	Steam System	STM101-IOQ-001	None	The Steam System has been installed successfully. The installation and operation qualification criteria have been met.
WPU-101	RO/DI Water System	WPU101-IOQ-001	None	The RO/DI Water System has been installed successfully. The installation and operation qualification criteria have been met.
		WPU101-PQ-002	Six deviations, described below. No impact to protocol	The RO/DI water system meets acceptance criteria. Data confirmed that the system generates water that meets or exceeds Type II RO/DI water specifications

Deviations to WPU101-PQ-001:

- WPU-101-PQ-001-D-01 was opened to document that microbial data gathered before 11Jul2017 were determined to be invalid, as it was discovered that the filters used for testing were not sterile. No impact to the protocol; the required 30 business days of testing was completed.
- WPU101-PQ-001-D-02 was opened for using expired test strips to record the ozone levels. Data were invalidated. No impact to the protocol; the required 30 business days of testing were completed.
- WPU101-PQ-001-D-03 was opened for having a detectable level of ozone present in the water when ozone wasn't being generated. Data was invalidated. No impact to protocol; the reason ozone was detected was that Facilities had run the ozone cycle less than 90 minutes before the testing was performed.
- WPU101-PQ-001-D-04 was opened to document that the form used to record data for this study included an action limit for a sampling point before the RO tanks. No action limit should have been set, as this data was being gathered for information only, is not part of the RO system, and was not included in the performance qualification. No impact to the protocol, as all data required for the protocol were gathered and are reported.
- WPU101-PQ-001-D05 was opened to document that all microbial testing was performed at 10 Evergreen Drive instead of at 625 Zoot Way. No impact to protocol; testing was performed and documented according to procedures and forms identified in the protocol.
- WPU101-PQ-001-D-06 was opened to document that microbial samples were incubated at room temperature instead of in a 20-25°C incubator as specified in the protocol. No impact to protocol; room temperatures were confirmed to have remained within 20-25°C for the period of the study.

Standard Operating Procedures

The protocol was executed under the following standard operating procedures:

Document Number	Revision	Title
LP-205	4	Preparation of Spore Dilution for Production
LP-209	1	Hand Inoculation
LP-302	4	Resistance Determination of Biological Indicators
LP-305	3	Population Assya of Biological Indicator Products
LP-306	2	Population Assay on Non-Cellulose Carriers
LP-438	2	Operation of the New Forge Hydrogen Peroxide BIER
LP-444	1	Operation of SteriFast H2O2 BIER
AP-101	1	Labeling of Biological Indicators and Media Tubes
AP-104	1	Labeling of BIs and Media Tubes using AXUS Labeler
AP-201	7	Packaging of Product
AP-202	4	Inspection of Biological Indicators and Releasat Media Tubes
AP-203	3	Hand Assembly of Biological Indicators
AP-306	1	H2O2 Assembly Machine
QSWI-103	6	QA Release of Finished Product Inventory

Training

The operators in the table below completed qualification training on the SOPs identified above during the PPQ.

Operator	Procedure(s)	Status of read-and-understand training on SOPs	Status of qualification training on SOPs
DS	LP-205, LP-209, LP-302, LP-306, LP-438, LP-444	Complete	Complete
EA	LP-205, LP-209, LP-302, LP-305, LP-306	Complete	Complete
NA	LP-205, LP-209, LP-305, LP-306	Complete	Complete
RM	LP-305, LP-306	Complete	Complete
CV	LP-205, LP-209	Complete	Complete
HG	AP-101, AP-201, AP-202, AP-203, AP-306	Complete	Complete
JS	AP-101, AP-202, AP-306	Complete	Complete
LG	AP-101, AP-201, AP-202	Complete	Complete
AT	AP-201, AP-202, AP-306	Complete	Complete
KR	AP-101, AP-201, AP-202, AP-203	Complete	Complete
HR	AP-101, AP-202, AP-203	Complete	Complete
BT	AP-202	Complete	Complete
DF	AP-101, AP-201, AP-202	Complete	Complete
DG	AP-201, AP-202, AP-203	Complete	Complete
GS	AP-104, AP-201, AP-202, AP-203	Complete	Complete
EA	AP-202, AP-306	Complete	Complete
CS	AP-202, AP-203, AP-306	Complete	Complete
ED	AP-202	Complete	Complete
CW	AP-203	Complete	Complete
VK	AP-202, AP-203	Complete	Complete
CJB	AP-202, AP-203	Complete	Complete

Attachments:

List of Catalog Numbers Validated Under Protocol 180208P Rev. 2

Approvals:

Validation: _____ Date: 26OCT2018

Kurt McCauley - Director of Manufacturing

Production: _____ Date: 26/10/2018

Robert Bradley - Director of Manufacturing

QA: _____ Date: 29OCT2018

Kira Gardner – QA Manager

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List of Catalog Numbers Validated Under Protocol #180208P Rev. 2

EZH5
EZH/5I
EZH/6
EZH/6I
EXPO/6