Title: Training Requirements for Operators Involved in Automated Aseptic Filling Operations

SOP Number: 15140

Revision Number: 03

Supersedes: Revision 02

Effective Date: **JAN** 13 2017

Originator/Date: [redacted]

Approval/Date:

Approval/Date:

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1.0 Purpose

This document specifies the tasks that operators must competently perform to be considered trained for automated aseptic filling operations using the Flexicon FMB 200 Monoblock. This procedure provides a mechanism for documenting the competency of individual operators in these tasks when the skills are demonstrated to a trainer. The forms from this SOP will be used in place of those for Personnel Competency associated with SOP 21600.

Filling Assistant and Basic level operators shall always be supervised by an advanced level operator. The validation of the Flexicon is a test of the ability of the Flexicon Filling system to produces a sterile product with the correct fill volume when operated by trained operators and will be an integral element of the training process.

2.0 Scope

This SOP applies to those who may be an operator during an automated aseptic filling of cGMP/GLP products using the Flexicon FMB 200 Monoblock.

This procedure is made available through federal funds from the National Cancer Institute, NIH, under contract [redacted]

3.0 Authority and Responsibility

3.1 The Manager of Technical Operations (Formulations and Fillings) has the authority and responsibility:

3.1.1 To define the specific tasks to be evaluated for operator competency.

3.1.2 To provide training on the operation of the Flexicon FMB 200 Monoblock to operators.

3.1.3 To evaluate operators for competency in the specific tasks.

3.1.4 To document the competency of operators by completing **Form 15140-01, 15140-2 or 15140-3**.

3.2 Biopharmaceutical Quality Assurance (BQA) is responsible for quality oversight of this procedure.

4.0 Procedure

4.1 Potential assistants and operators for the Flexicon FMB 200 Monoblock will be identified by the Manager of Technical Operations (Formulation and Filling).

4.2 The Manager of Technical Operations (Formulation and Filling) will provide (or arrange for) training of potential operators on the following SOPs:

4.2.1 ***SOP 19406 - Gowning Requirements for Personnel and Visitors: [redacted] Manufacturing and Support Areas***

4.2.2 ***SOP 15113 - Inspection of Unlabeled Vials of Finished Products***

4.2.3 ***SOP 15124 - Cleaning and Sanitization of the Flexicon FMB200 Monoblock***

4.2.4 ***SOP 15127 - Operation of the Flexicon FMB200***

4.2.5 ***SOP 15135 - Operation of the Flexicon FlexSeal 10 Auto-crimper***

4.2.6 ***SOP 15137 - Standard Aseptic Practices for Cleanrooms and BSC's for Production Operations***

4.2.7 ***SOP 15139 - Operating Procedures for Automated Aseptic Filling Using the Flexicon FMB200***

4.2.8 ***SOP 21500 - General Policies and Procedures for Balances***

4.2.9 ***SOP 21600 - Training and Qualification of Personnel in a CGMP Environment***

4.3 There are three tiers of Flexicon Operator; Filling Assistant, Basic, and Advanced allowing operators to perform increasingly complex tasks. Breaking training into tiers shortens the time for training as it otherwise takes a substantial amount of time to demonstrate competency in all aspects of operation and participation is only permitted once training is complete. The approach also promotes depth for the operations that are more numerous and basic. The progressive approach also allows operators to observe higher level operations before performing them.

4.4 Operators must achieve the rank of the lower level prior to independently performing tasks of a higher level. The Manager of Technical Operations (Formulation and Filling) or trainer by their designation will evaluate the competence of potential operators

according to the specified tasks listed on **Form 15140-01, Form 15140-02**, and **Form 15140-03** for Filling Assistant, Basic, and Advanced operators respectively.

4.5 Competency assessment may occur over a series of days. Operators will be evaluated as passed or failed based on their demonstrated competence. To pass, potential operators must demonstrate competence in each specified task without asking the evaluator and with minimal reliance on the SOPs.

4.6 Operator Level Classifications

4.6.1 Filling Assistant - participates in an aseptic fill without in depth operation of the filling equipment and perform the following activities:

4.6.1.1 The new operator will remove and inspect product from the filler and perform vial accountability.

4.6.1.2 Weigh weight check vials and perform necessary calculation to determine if results are correct.

4.6.1.3 Label the pans and submit to the inspection group for further inspection.

4.6.1.4 Complete documentation requested by the Master Production Record (MPR) for the filling of the product.

4.6.1.5 Monitor basic operation of the filling equipment.

4.6.1.6 Demonstrate an understanding of proper aseptic practices per ***SOP 15137 - Standard Aseptic Practices for Cleanrooms and Biological Safety Cabinets for Production Operations*** as they relate to Flexicon Filling Operations.

4.6.2 Basic - approved for general operation but not able to perform all operations including those that are infrequent or require a higher skill level.

4.6.2.1 Programming machine operation and performing routine operations via controller.

4.6.2.2 Loading of Stoppers and Aluminum Seals onto Flexicon.

4.6.2.3 Perform routine interventions of clearing select jams for stoppers and aluminum seals.

4.6.2.4 Clean-Up, sanitization, and disassembly of the Flexicon following operations.

4.6.3 Advanced - is the highest level and those that achieve this level may perform any operation.

4.6.3.1 Installation of Flexicon Change Parts including those that are autoclaved to handle the vial size to be filled.

4.6.3.2 Sanitization of the Flexicon using 70% Sterile filtered IPA.

4.6.3.3 Setup and performance of Environmental Monitoring.

4.6.3.4 Installation of filling tubing set(s).

4.6.3.5 Advanced setup, programming and adjustment of the peristaltic pump to deliver the correct volume, and operation of the Flexicon.

4.6.3.6 Performance of additional routine and non-routine interventions, aseptically where required, in order to correct any mechanical issues with the equipment.

4.6.3.7 Advanced level operators will have detailed knowledge of the trouble shooting practices of the filler and will demonstrate these skills during a validation run of the Flexicon. Performing these tasks during a validation ensures 100% inspection of all vials for sterility without potential for product impact as could occur during an actual product fill.

4.6.3.8 Upon successful completion of the validation run the candidate will be verified as having advanced competency in operating the Flexicon and be able to oversee all aspects of operation during Flexicon Filling.

4.7 Certification of Operator

4.7.1 To document the evaluation, the Manager of Technical Operations (Formulation and Filling) or trainers selected by the manager will complete **Form 15140-01, 15140-2**, and or **15140-03**.

4.7.2 The results of the competency assessment will be shared with the potential operator. For a passing evaluation, the operator will indicate (and document) their agreement or disagreement with the assessment results.

4.7.3 Completed and signed assessment training forms are forwarded to BQA.

5.0 References and Related Documents

5.1 **SOP 19406** *Gowning Requirements for Personnel and Visitors: [redacted] Manufacturing and Support Areas*

5.2 **SOP 15124** *Cleaning and Sanitization of the Flexicon FMB200 Monoblock*

5.3 **SOP 15127** *Operation of the Flexicon FMB200*

5.4 **SOP 15135** *Operation of the Flexicon FlexSeal 10 Auto-crimper*

5.5 **SOP 15137** *Standard Aseptic Practices for Cleanrooms and BSC's for Production Operations*

5.6 **SOP 15139** *Operating Procedures for Automated Aseptic Filling Using the Flexicon FMB200*

5.7 **SOP 21603** *Using the PLM Administrator Module*

5.8 **SOP 22315** *Environmental Monitoring in BDP GMP Areas at the [redacted]*

6.0 Attachments

6.1 **Attachment 1 Form 15140-01**, Competency Assessment for Flexicon Operator: Filling Assistant

6.2 **Attachment 2 Form 15140-02**, Competency Assessment for Flexicon Operator: Basic

6.3 **Attachment 3 Form 15140-03**, Competency Assessment for Flexicon Operator: Advanced

This procedure is made available through federal funds from the National Cancer Institute, NIH, under contract [redacted].

Attachment 1

FNLCR, BDP
Form No.: 15140-01
SOP No.: 15140
Revision 03: JAN 13 2017

COMPETENCY ASSESSMENT FOR FLEXICON OPERATOR: FILLING ASSISTANT				
Personnel Name:				
TASK	**EVALUATION**			
	Passed	**Failed**	**Method of Assessment**	**Assessment Date**
Vial inspection				
Perform Weight Checks				
Submit for unlabeled vial inspection				
Documentation				
Equipment Monitoring and Safety				
Aseptic Awareness				

Comments:

METHOD OF ASSESSMENT

1. Process was performed independently (but with supervision) during an actual production. (List lot#)
2. Process was demonstrated to a qualified trainer.
3. Author/trainer of the procedure.
4. Other, describe:

Evaluator Sign-off:

Signature: _____ Name (print)_____

Date: _____

Employee Sign-off (required only for passing competencies)

Agree / Disagree (circle) with evaluation

Signature _____ Date: _____

Passed: Employees demonstrates competency in the specified task without asking the Evaluator and with minimal reliance on the SOP.

This procedure is made available through federal funds from the National Cancer Institute, NIH, under contract [redacted].

Attachment 1 (Continued)

FNLCR, BDP
Form No.: 15140-01
SOP No.: 15140
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Filling Assistant		
TASK	ELEMENT OF TASK EVALUATED	DEMONSTRATED? (circle)
Vial inspection	Remove product from the filler	yes no
	Inspect vial Closure	yes no
	Accountability of vials filled	yes no
Perform weight checks	Weigh empty vials and label to create weight check vials.	yes no
	Receive weight check vials from filling line, remove the closure, and weigh the vial and perform calculations for filling volume.	yes no
Submit for unlabeled vial inspection	Label pans of glassware	yes no
	Submit vials to unlabeled vial inspection	yes no
Documentation	Complete documentation of the BPR	yes no
Equipment Monitoring and Safety	Read equipment display to assess basic operational status	yes no
	Stop the filling machine to interrupt operations	yes no
Aseptic Awareness	Proper knowledge of aseptic practices per ***SOP 15137 – Standard Aseptic Practices for Cleanrooms and Biological Safety Cabinets for Production Operations*** as they relate to Flexicon Filling Operations. Areas of concern include handling of tools and instruments, positioning of tables and carts, handling of trash, and movement.	yes no

This procedure is made available through federal funds from the National Cancer Institute, NIH, under contract [redacted].

Attachment 2

FNLCR, BDP
Form No.: 15140-02
SOP No.: 15140
Revision 03: JAN 13 2017

COMPETENCY ASSESSMENT FOR FLEXICON OPERATOR: BASIC				
Personnel Name:				
TASK	**EVALUATION**			
	Passed	**Failed**	**Method of Assessment**	**Assessment Date**
Question: Autoclavable Parts				
Programming				
Loading Stoppers				
Loading Aluminum Seals (Crimps)				
Filling Operation				
Clearing Jams from Stopper Bowl				
Clearing Jams from Seal Bowl at Chute Location				
Clean-up and Sanitization				

Comments:

METHOD OF ASSESSMENT
1. Process was performed independently (but with supervision) during an actual production. (List lot#)
2. Process was demonstrated to a qualified trainer.
3. Author/trainer of the procedure.
4. Other, describe:

Evaluator Sign-off:

Signature: _____ Name (print)_____

Date: _____

Employee Sign-off (required only for passing competencies)

Agree / Disagree (circle) with evaluation

Signature _____ Date: _____

Passed: Employees demonstrates competency in the specified task without asking the Evaluator and with minimal reliance on the SOP.

This procedure is made available through federal funds from the National Cancer Institute, NIH, under contract [redacted].

Attachment 2 (Continued)

FNLCR, BDP
Form No.: 15140-02
SOP No.: 15140
Revision 03: JAN 13 2017

Basic		
TASK	ELEMENT OF TASK EVALUATED	DEMONSTRATED? (circle)
Question: Which parts are autoclavable?	Answer: The bowls, the chutes and dispensing heads for the stoppers and aluminum seals are autoclavable.	yes no
Programming machine operation	Turn power on	yes no
	Check that air is on	yes no
	Select proper load program	yes no
	Select proper vibration setting	yes no
	Select proper fill mode	yes no
Loading Stoppers	Spraying off hands	yes no
	Spraying off autoclave bags	yes no
	Removing inner autoclave bag without touching pouring area of inner autoclave bag	yes no
	Opening inner bag and pouring stoppers into bowl without touching bowl or mouth of bag	yes no
	Minimizing particle generation (resist shaking bag to retrieve every last stopper)	yes no
Loading Aluminum Seals	Spraying off hands	yes no
	Spraying off autoclave bags	yes no
	Removing inner autoclave bag without touching pouring area of inner autoclave bag	yes no
	Opening inner bag and pouring Aluminum Seals into bowl without touching bowl or mouth of bag	yes no
	Minimizing particle generation (resist shaking bag to retrieve every last Aluminum Seal)	yes no
Filling Operation	Reset status to zero (PLC)	yes no
	Reset function 8 to zero (MC12P)	yes no
	Activate Start Button	yes no
	Stop filling so additional glassware may be added	yes no
	Empty line of filled glassware	yes no
Clearing jams from stopper bowl.	Demonstrates proper use of forceps,	yes no
	Remove stoppers that are stuck together.	yes no
	Proper discard of stuck stoppers so that they are not reused.	yes no
Clearing jams from seal bowl at chute location	Move seals back into bowl using sterile forceps	yes no
Clean-up and Sanitation of Flexicon	Removal of vials, stoppers, seals from unit	yes no
	Disassembly of unit	yes no
	Disposition of unused vials, stoppers, seals and autoclavable parts	yes no
	IPA disinfection of Flexicon	yes no

This procedure is made available through federal funds from the National Cancer Institute, NIH, under contract [redacted].

Attachment 3

FNLCR, BDP
Form No.: 15140-03
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COMPETENCY ASSESSMENT FOR FLEXICON OPERATOR: ADVANCED				
Personnel Name:				
TASK	**EVALUATION**			
	Passed	**Failed**	**Method of Assessment**	**Assessment Date**
Removal of Screw Drive				
Removal of Star Wheel and Ejector				
Flexicon sanitization				
Environmental Monitoring				
Installation of Autoclavable Parts				
Installation of Tubing Sets*				
Programming MC12P				
Filling Operation				
Clearing Jams from Seal Bowl at Dispensing Head				
Handling Spills or breakage*				

Comments:

METHOD OF ASSESSMENT

1. Process was performed independently (but with supervision) during an actual production. (List lot#)
2. Process was demonstrated to a qualified trainer.
3. Author/trainer of the procedure.
4. Other, describe:

Evaluator Sign-off:

Signature: _____ Name (print)_____

Date: _____

Employee Sign-off (required only for passing competencies)

Agree / Disagree (circle) with evaluation

Signature _____ Date: _____

Passed: Employees demonstrates competency in the specified task without asking the Evaluator and with minimal reliance on the SOP. *Denoted activities must be performed during a validation run.

This procedure is made available through federal funds from the National Cancer Institute, NIH, under contract [redacted].

Attachment 3 (Continued)

FNLCR, BDP
Form No.: 15140-03
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Advanced Operator		
TASK	ELEMENT OF TASK EVALUATED	DEMONSTRATED? (circle)
Removal of screw drive	Turning off power to Flexicon	yes no
	Removing photosensor	yes no
	Disassembling	yes no
	Remove Screw system from machine.	yes no
	Disinfect replacement parts prior Installation of new screw drive assembly	yes no
	Reinstallation of photosensor.	yes no
	Powering up.	yes no
Removal of star wheel and ejector	Releasing trussing system	yes no
	Raising tool plate,	yes no
	Removal of bolts holding star wheel	yes no
	Loosened Set screws on the rejector Arm	yes no
	Removal of star wheel and ejector.	yes no
	Disinfect with 70% IPA replacement Parts	yes no
	Replacing star wheel and ejector,	yes no
	Putting correct height spacer in place	yes no
	Lowering tool bar	yes no
	Securing the trussing system	yes no
Flexicon sanitization	Use Sterile 70% and a saturated clean room wipe to sanitize all exposed work surfaces of the filler prior to installation of Autoclaved components.	yes no
Environmental Monitoring	Proper positioning of continuous non-viable and viable air monitoring equipment.	yes no
	Proper touch plating of Flexicon surface and sterilization of the area after touch plating and proper labeling of the sample.	yes no
Installation of autoclavable parts	Proper installation of autoclavable parts	yes no
Installation of tubing sets	Proper removal of tubing set from sterile packaging	yes no
	Inserting tubing in peristaltic pump assuring that tubing is straight and taut.	yes no
	Making proper aseptic connection to supply bag.	yes no
	Insertion of empty sterile vial into star wheel	yes no
	Proper orientation of dispensing canula into the vial. (Needle properly oriented over vial, proper height over \vial for no-dive, proper dive depth for the bottom fill)	yes no
	Demonstrate how to set up the dispensing canula for a “no-dive” or “bottom fill”	yes no
Programming MC12P (peristaltic pump) and verification that fill volume is accurate and filling line is ready for operation	Bring out of standby mode	yes no
	Press dispense button	yes no
	Check that operational parameter match MPR requirements (fill volume, tubing diameter, etc.)	yes no
	Determine that the filler is forming acceptable crimps, make adjustments as necessary. Perform a practice run of 20 vials, make adjustment as necessary. If bad crimps were form do a second practice run with 10 vials.	yes no
	Determine if guides are lined up with star wheel and vial moves easily through guides, make adjustments as necessary.	yes no
	Determine if fill volume is acceptable, make adjustments as necessary, confirm with 2 weight checks	yes no
	Check for foaming, splashing, overflow, adjust controls as necessary to correct problem.	yes no

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Attachment 3 (Continued)

FNLCR, BDP
Form No.: 15140-03
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Advanced Operator			
Filling Operation	Start fill	yes	no
	Proper stocking of vials, crimps, weight checks, stoppers	yes	no
	Ongoing reconciliation of filled vials by pan, including proper documentation.	yes	no
	Perform filling associated interventions such as insertion of check weigh vial, recovery of a downed or jammed vial, and adjustment of crimp head.	yes	no
	Know when to stop fill	yes	no
	Disable fill function and complete the finishing of last vial.	yes	no
Clearing jams from seal bowl at dispensing head	Hold seals back	yes	no
	Dispense materials from dispensing head	yes	no
	Take dispensing head and chute off the machine	yes	no
Handling spills or breakage	Confirm either by discussion or simulation that operator understands how to aseptically resolve the following situations including clearing an appropriate number of vials from machine during a:		
	Spill without glass breakage	yes	no
	Spill with breakage, no shattering	yes	no
	Shattered vial with no spill	yes	no
	Shattered vial with spill	yes	no
	Proper disposition of affected materials	yes	no
	Proper documentation in MPR	yes	no

This procedure is made available through federal funds from the National Cancer Institute, NIH, under contract [redacted].