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Validation of Sterile Water for Injection in Pharmaceutical Industry and Othersterile Facility

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ABSTRACT

Sterile facilities for all pharmaceutical product specially to parentral preparation, is a must important back bone of sterile formulation andor pharmaceutical dosage form. There is most important to sterile of the areas where the formulation process proceed from initial to final stage. The sterile injectable products are very critical and sensitive products as they are administered directly into blood circulation. These products are designed such that it should be free from micro-organisms, pyrogens and unacceptable particulate matter. Any failure in quality and purity of these products may directly affect the safety of patient being treated. FDA, WHO, ISO and Good Manufacturing Practiceshas established the guides to the development of sterile pharmaceutical preparation facilities for health care establishments.This report covers all summaries that the three batches of Methylcobalamine injection 2 ml have been validated with the support of process validation protocol.

Keyword: USFDA, SOPS, CGMP, HVAC, ICFU,FPM.

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INTRODUCTION:

Validation is a concept that has been evolving continuously since its first formal appearance in the United States in 1978. Validation as it is known today has developed from the need to maintain quality, consistency and above all public safety. The present project reflects the current trends and serves as an educational tool in our progressive industry[1].

Definition (USFDA): "Process validation is establishing documented evidence that provides a high degree of assurance that a specific process will consistently produce a product meeting its predetermined specifications and quality characteristics [(2,3)]". Since Methylcobalamine injection (500 mcg) is a new formulation which is going to be administered in the form of IM route for the instant effect.The injectable form is easily accepted, safe, user friendly and palatable dosage form of drug administration, the prospective process validation could be easily and thoroughly studied on this topic. Methylcobalamine is used to produce red blood cells in pernicious anemia and to maintain the good health.

Types of the validation [(6,7)]:

Process validation:-

It is conducted during the manufacturing process of the product.

Types of process validation:-

- Prospective validation
- Concurrent validation
- Retrospective validation
- Revalidation

Validation process [4.5] – flow diagram:-

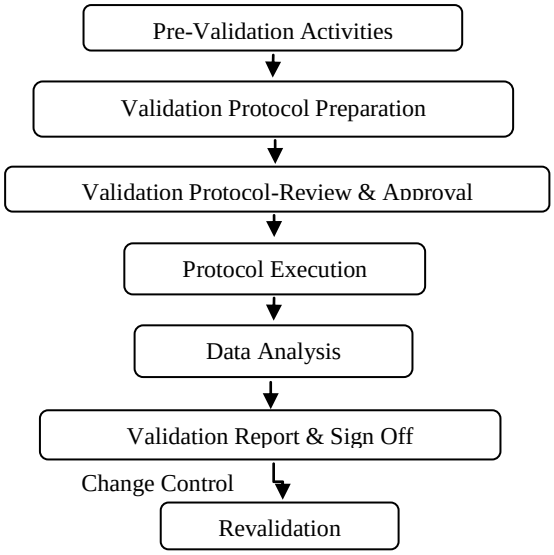

Fig. 1.1: Validation Process- Flow Diagram

Equipment validation:- (Qualification)

The equipment should be designed and/or selected as per the product specifications are consistently achieved.

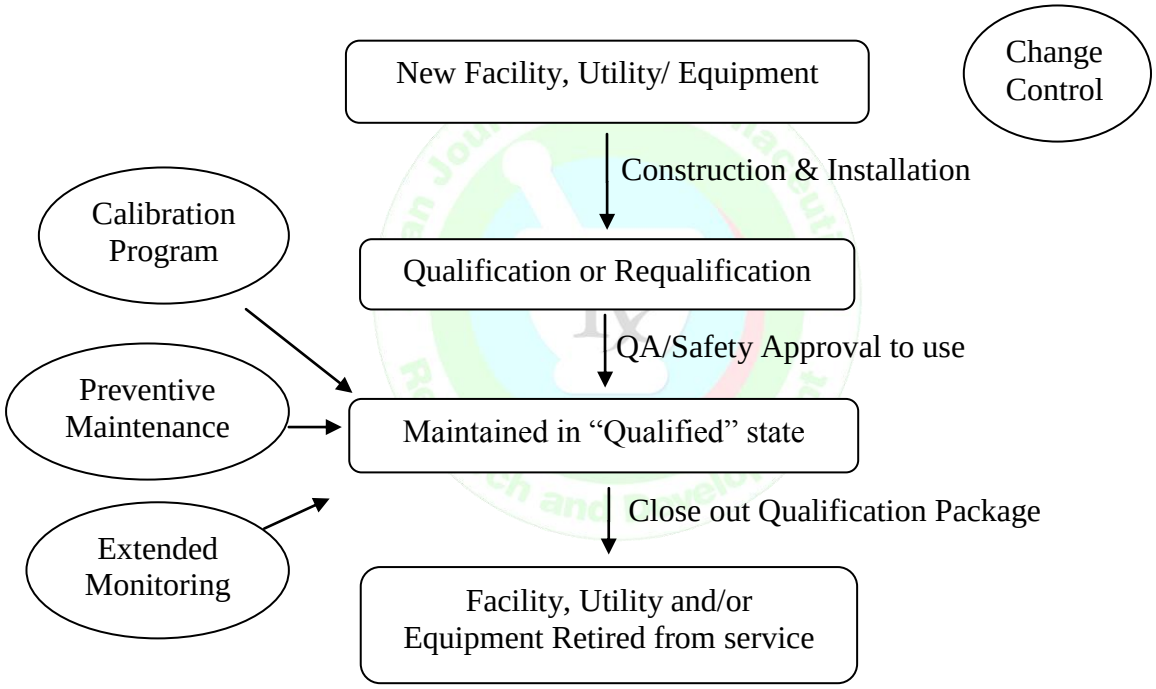

Fig.1.2 Qualification Life Cycle

Types of Equipment Qualification [8,9]

Design Qualification (DQ):

It is the documented verification of the proposed design of the facilities, systems and equipment for the intended purpose. It involves following parameters:make, type, model number, material of construction, size and shape of different parts of the equipments.

Installation Qualification (IQ):

It verifies the installations such as machines, measuring devices, utilities, manufacturing areas used in a manufacturing process.

Operational Qualification (OQ):

OQ checks the facilities, systems and equipment that are operating with standard conditions. It tests whether or not the system works as expected.

Performance Qualification (PQ):

PQ is the documented verification that the facilities, systems and equipment can perform effectively to perform approved process and deliver product specification consistently

Analytical method validation:

Method validation defined as, "The process by which, it is established by laboratory studies, that the performance characteristics of the method meet the requirements for the intended analytical application".

Cleaning validation:-

Cleaning validation is a process of attaining and documenting sufficient evidence to give reasonable assurance given the current state of Science and Technology.

The whole plan of validation of sterile facility is divided into following steps[10,11].

Validation of Utility:

- HVAC system (AHU):
- HEPA filter integrity test (DOP test).
- Air velocity across HEPA filter.
- Air changes per hour.
- Non viable and viable particle count.
- Decontamination time.
- Temperature and humidity monitoring.
- Air flow pattern.

Validation of Equipment:

A) Autoclave validation.

B) Ampoule sterilizing tunnel validation

MATERIALS AND METHODS:

Materials:

Drug-Methylcobalamine Injection- 2 ml
Strip- Bacillus stearothermophilus spore strips
Strip- Chemical integrator strips (Steam –Clox Cards)

Table 1.1: List of Equipments

Sr. No.	Equipments	Manufacturer
1	Weighing balance	Motter Toledo
2.	Ampoules washing machine	Pyroklenz
3.	Autoclave	Metalchem industries
4.	Ampoule sticker labeling machine	Maharshi Udyog
5.	Ampoules filling machine	Kembert
6.	Ampoules sterilizing tunnel	Klenzaieds
7.	Filter integrity test apparatus	Global Eng.
9.	Particle counter	Met one
10.	Carton Packing machine	Pam-Pac120(Hi-Cart machine)

METHODS:-

VALIDATION OF HVAC SYSTEM (Heating Ventilation and Air Conditioning system):

To regulate room temperature, humidity and air flow ensuring that such elements remain within their acceptable ranges is the primary use of HVAC.

DOP Test:

The purpose of performing regularly scheduled leak tests, also to detect leaks from the filter media, filter frame or seal.Leak tests should be performed at suitable time intervals for HEPA filters in the aseptic processing facility.

Air Velocity Measurement:

To conduct periodic monitoring of uniformity of velocity across the filter (and relative to adjacent filters). Velocity usually increase the possibility of contamination as these can have an effect on unidirectional airflow in validation.

Air changes per hour:

To evaluate the air is exchangedwith fresh or filtered air in each hour (numbers of time).

The air changes is calculated in following ways

Non- viable and viable particulate count: Environmental monitoring

Its include testing of patticle count (number of particles per volume of air)!of various surfaces for microbiological quality.

No. of location = √Area

Table 1.2- Air Classification

Grade	Class	USFDA	ISO Designation	0.5µm/cu ft	5µm/cu ft.
A	100	M3.5	5	100 par/ cu ft	0 par/ cu ft.
B	1000	M4.5	6	1000par/ cu ft	7 par/ cu ft.
C	10000	M5.5	7	10000 par/ cu ft	70 par/ cu ft.
D	100000	M6.5	8	100000 par/ cu ft	700 par/ cu ft.

*Note: par/cu ft- Particles per cubic feet

VALIDATION OF EQUIPMENT:

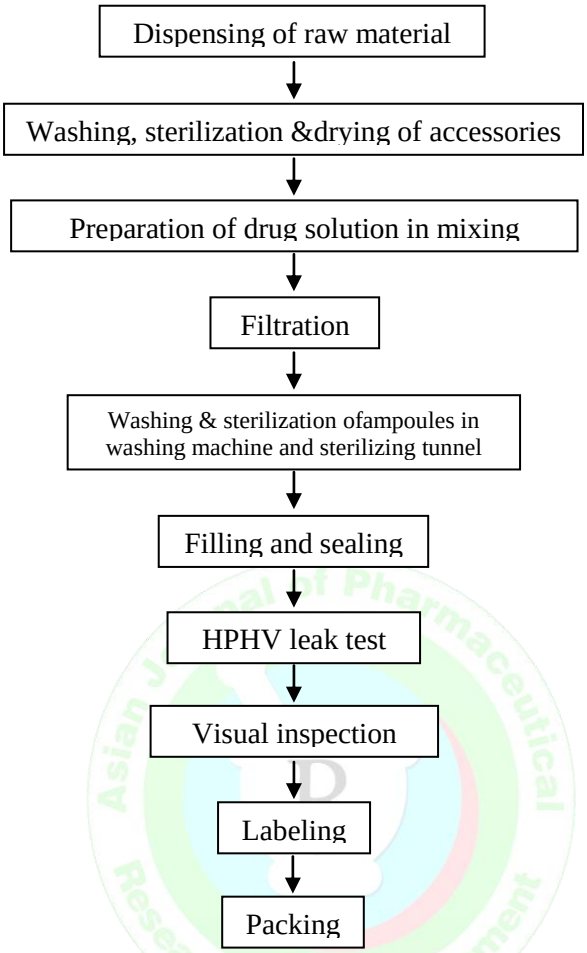

Fig 1.3: Process flow chart of manufacturing operation

Table 1.3: Manufacturing Critical Control Parameter

Test description	Limit
In let WFI temperature	80±5 ºC
Cooled WFI temperature	NLT 35 ºC
Nitrogen pressure	NLT 5 kg/cm^2
Bubble point of membrane filter	NLT 2.5 kg/cm^2
pH	7.2 to 7.5
Final mixing time	NMT 30 min
Nitrogen purging	Whole process

Table 1.4: Machine critical control parameter

Test description	Limit
Washing machine	
Recycled water	NLT 1.5 kg/cm^2
Compressed air	NLT 1.5 kg/cm^2
WFI	NLT 1 kg/cm^2
Tunnel	
Sterile zone temperature	NLT 280 ºC
Pressure differential	
Sterile zone	20 pascal
Cooling zone	12 pascal
Autoclave	
Temperature	121±1 ºC
Steam pressure	1.2 kg/cm^2
Vacuum pressure(leak test)	-0.600 bar

Table 1.5: Validation of In Process Parameter

Stages	Test/ Process Parameters	Limit
Rawmaterial verification	Balance calibration	Calibrated
	RM weight verification	Verified
WFI	pH	5-7
	Conductivity	<1.3µs/cm^2
	Bioburden	10 CFU/100ml
	BET	<0.25 EU/ml
Clean steam	BET	< 0.25 EU/ml
	Total bacterial count	10 CFU/100ml
Washing	Before washing bioburden	<10CFU/ampoule
	After washing bioburden	<1 CFU/ampoule
After sterilization	Bacterial endotoxin	<0.25 EU/ml
	Sterility after depyrogenation	<1 CFU/ampoule
	Set temperature of tunnel	>280 ºC
	Conveyor speed	72 mm/min
Mfgpreparation of drug solution	Bioburden of drug solution	< 100 CFU/ml
	pH	7.2-7.5
	Mixing efficiency	10 min (90-110%)
	Temperature	40-50ºC
Filtration	Bioburden	< 4 CFU/100ml
	Sterility	No growth
	Pre integrity pressure	NLT 2.5kg/cm2
	Post integrity pressure	NMT 3.2 kg/cm2
	Filter duration	NMT 2 hour
	Pressure for filtration	1.2kg/cm^2
Compressed air and nitrogen gas	Bioburden	< 1CFU
	Sterility	No Growth
Stages	**Test / Process Parameters**	**Limit**
Filling and sealing	Volume of ampoules	2-2.2 ml
	Sealing	OK
	Nitrogen flushing	OK

	Visual inspection	OK
	Sterility	No Growth
Start filling	Sterility	No Growth
	pH	7.1-7.2
	Assay	90 -110%
Middle filling	Sterility	No Growth
	pH	7.1-7.2
	Assay	90-110%
End filling	Sterility	No Growth
	pH	7.1-7.2
	Assay	90-110%
HPHV leak test	Leak test time	NMT 15 min
	Rejected ampoules	LT 1%
Visual inspection	Clarity	OK
	Output	Ok
Labeling	Clarity of over printing w.r.t. output	OK
Packing	Sealing temperature	170 ºC
	Leak test	OK
	Clarity of over printing w.r.t. blister per minute	Clear
Finished goods analysis	Sterility	No Growth
	Assay	90-110%
Yield	Filling yield	NLT 90%
	Packing yield	NLT 90%
	Visual inspection	NLT 90%
	Batch yield	NLT 90%

Table 1.6: Worst Case Study (Bracketing Method)

Stages	Assets	Test Parameters	Limit
Filling line speed at 150 amp/min	Washing machine	Particulate matter	Absent
		Breakage	NMT 1%
		No. of break down	No major break down
	Tunnel depyrogenation residence time NLT 3min	Sterilit	No Growth
		Endotoxin	< 0.25EU/ml
		No of breakage down	No major break down
	Filling machine	Volume of filled ampoules	2 to 2.2 ml
		Sealing defect	<1%
		Particulate matter	Absent
		Break down	No major break down
Filling line Speed at 250 ampoules/min	Washing machine	Particulate matter	Absent
		Breakage	NMT 1%
		No of break down	No major break down
	Tunnel depyrogenation residence time NLT 3min	Sterility	No Growth
		Endotoxin	< 0.25EU/ml
		No of breakage down	No major break down
	Filling machine	Volume of filled ampoules	2 to 2.2 ml
		Sealing defect	<1%
		Particulate matter	Absent
		Break down	No major break down

RESULT& DISCUSSION:

DOP Test:

Acceptance Criteria: The leakage should not be more than 0.01%

Air Velocity Measurement:

Table 1.7: Air Velocity Result

Room No.	Room Name	Class	Filter No.	Velocity(FPM)					Average Velocity(FPM)
				V1	V2	V3	V4	V5	
PG1.107	Ampoule Filling	B	AHU-29/PG1.107/S/01	102	95	92	89	94	94.4
			AHU-29/PG1.107/S/02	87	95	94	90	85	90.2
			AHU-29/PG1.107/S/03	101	85	94	87	91	91.6
			AHU-29/PG1.107/S/04	94	87	94	101	96	94.4
			AHU-29/PG1.107/S/05	92	95	98	101	97	96.6
			AHU-29/PG1.107/S/06	95	101	85	94	89	92.8
			AHU-29/PG1.107/S/07	104	102	95	97	100	99.6
			AHU-29/PG1.107/S/08	95	106	101	88	87	95.4

Acceptance Criteria: Average velocity must be in range of 90±20% FPM.

Calculation of Air Changes:
RoomName:Filling area
Room Volume:2160 .86 Cu ft
Area of Filters: 2 ft X 2 ft= 4 Sq ft
CFH: Average velocity X area of filter X 60 min

Table 1.8: Calculation of Air Changes

Filter No.	Average Velocity(FPM)	CFH
AHU-29/PG1.107/S/01	94.4	22656
AHU-29/PG1.107/S/02	90.2	21648
AHU-29/PG1.107/S/03	91.6	21984
AHU-29/PG1.107/S/04	94.4	22656
AHU-29/PG1.107/S/05	96.6	23184
AHU-29/PG1.107/S/06	92.8	222272
AHU-29/PG1.107/S/07	99.6	23904
AHU-29/PG1.107/S/08	95.4	22896
	∑ CFH	**181200**

Air changes per hour = ∑ CFH ÷Room Volume in Cu ft
= 181200÷2160.86
=83.85 air changes
Acceptance Criteria: Min 25 air changes per hour.

Viable Particle Count: Settle Plate Method

Table 1.9: Viable Particle Count

Sr. No.	Location	Grade	No. of Samples	Count /plate				
				L1	L2	L3	L4	L5
1.	Under LAF	A	2	<1	<1	-	-	-
2.	Filling Room	B	5	<1	<1	<1	<1	<1
3.	Filtration Room	B	4	<1	<1	<1	<1	-
4.	Cooling Zone	B	3	<1	<1	<1	-	-
5.	Leak Test Room	B	3	<1	<1	<1	-	-

Pressure Differential:

Table 1.10: Pressure Differential

Area w.r.t. area	Diff Pressure				Limit
	Morning	Reading	Evening	Reading	
Filling Vs Filling Corridor	9.00 A.M.	8	6.30 P.M.	8	NLT 6 Pa
Cooling Vs Cooling Corridor	9.05 A.M	8	6.35 P.M.	8	NLT 6 Pa
Filling Vs Staging	9.10 A.M.	18	6.40 P.M.	18	NLT 15 Pa
Filtration Vs Sterile Corridor	9.15 A.M.	20	6.45 P.M.	20	NLT 15 Pa
Amp Filling Vs Amp washing	9.25 A.M.	18	6.55 P.M.	18	NLT 15 Pa

Temperature and Humidity Monitoring:

Room Name: Filling Room

Table 1.11: Temperature and Humidity Monitoring

Time	Temperature	Humidity	Limit
10.00 A.M.	21.3ºc	53%	Temp:23±2ºc Humidity:NMT55%
3.00 P.M.	24.5ºc	49%	Temp:23±2ºc Humidity:NMT55%
6.00 P.M.	22.6ºc	47%	Temp:23±2ºc Humidity:NMT 55%

Validation of the Sterilization Process in Autoclave:

Table 1.12: Temperature recorded in Autoclave

Sterilization time	RTD1 (ºC)	RTD2 (ºC)	RTD3 (ºC)	RTD4 (ºC)	RTD5 (ºC)	RTD6 (ºC)	RTD7 (ºC)	RTD8 (ºC)
10:31:01	121.2	121.4	121.3	121.5	121.4	121.2	121.6	121.5
10:32:02	121.8	121.9	121.7	121.9	121.8	121.6	121.8	121.7
10:33:01	121.6	121.7	121.7	121.9	121.8	121.7	121.7	121.6
10:34:02	121.5	121.5	121.6	121.7	121.8	121.6	121.5	121.4
10:35:01	121.4	121.6	121.7	121.6	121.8	121.5	121.6	121.5
10:36:01	121.6	121.7	121.7	121.5	121.6	121.4	121.5	121.6
10:37:01	121.5	121.6	121.7	121.4	121.4	121.3	121.2	121.4
10:38:01	121.4	121.7	121.6	121.5	121.5	121.4	121.3	121.3
10:39:01	121.5	121.6	121.7	121.4	121.2	121.3	121.4	121.5
10:40:01	121.6	121.7	121.6	121.3	121.3	121.2	121.5	121.6
10:41:01	121.7	121.8	121.7	121.4	121.5	121.4	121.6	121.7
10:42:01	121.6	121.9	121.8	121.6	121.6	121.7	121.8	121.9
10:43:01	121.7	121.6	121.5	121.5	121.4	121.6	121.7	121.8
10:44:01	121.8	121.7	121.7	121.4	121.3	121.5	121.3	121.5
10:45:01	121.6	121.5	121.3	121.5	121.2	121.2	121.2	121.6
Average	**121.6**	**121.7**	**121.6**	**121.5**	**121.5**	**121.4**	**121.5**	**121.6**
MIN. (ºC)	**121.2**	**121.4**	**121.3**	**121.3**	**121.2**	**121.2**	**121.2**	**121.3**
MAX. (ºC)	**121.8**	**121.9**	**121.8**	**121.9**	**121.9**	**121.7**	**121.8**	**121.9**
Coolest point	**121.2ºC**							

Table 1.13: Manufacturing critical control parameter

Test description	Batch No. X	Batch No. Y	Batch No. Z
In let WFI temp	84.2 ºC	84.0ºC	83.2ºC
Cooled WFI temp	28.3ºC	26.2ºC	28.00ºC
Nitrogen pressure	5.0 kg/cm^2	5.2 kg/cm^2	5.3 kg/cm^2
Bubble point of membrane filter	3.0 kg/cm^2	3.2 kg/cm^2	3.3 kg/cm^2
pH	7.9	7.8	7.9
Final mixing time	30 min	30 min	30 min
Nitrogen purging	Whole process	Whole process	Whole process

Table 1.14: Machine critical control parameter

Test description	Batch No. X	Batch No. Y	Batch No. Z
Washing machine			
Recycled water	2.0 kg/cm^2	2.0 kg/cm^2	2.0 kg/cm^2
Compressed water	2.0 kg/cm^2	2.0 kg/cm^2	2.0 kg/cm^2
WFI	1.2 kg/cm^2	1.2 kg/cm^2	1.2 kg/cm^2
Tunnel			
Sterile zone temp(ºC)	330,328,326,324	330,328,326,324	330,328,326,324
Pressure differential			
Sterile zone(pa)	23	26	23
Cooling zone(pa)	14	14	14
Autoclave			
Temp.(ºC)	121.4	121.3	121.4
Steam pressure(kg/cm2)	1.2 kg/cm^2	1.2 kg/cm^2	1.2 kg/cm^2
Vacuum pressure(Leak test)	-0.600 bar	-0.600 bar	-0.600 bar

Table 1.15: Validation of In Process Parameter Result

Stage	Test/Process parameter	Result		
		Batch No. X	**Batch No. Y**	**Batch No. Z**
Raw material weight verification	Balance calibration	Calibrated	Calibrated	Calibrated
	RM weight verification	Verified	Verified	Verified
WFI	Bacterial endotoxin	<0.25 EU/ml	<0.25 EU/ml	<0.25 EU/ml
	pH	6.17	5.44	5.67
	Bioburden	<1CFU/100ml	<1CFU/100ml	<1CFU/100ml
	Conductivity	0.5423µs/cm^2	0.7483µs/cm^2	0.7463µs/cm^2
Clean steam	Bacterial endotoxin	<0.25 EU/ml	<0.25 EU/ml	<0.25 EU/ml
	Total bacterial count	<1CFU/100ml	<1CFU/100ml	<1CFU/100ml
Ampoule washing & sterilization/depyrogenation	Before washing bioburden	03 CFU/ampoule	07 CFU/	05 CFU/ ampoule
	Particulate matter	absent	absent	absent
	After washing bioburden	<1CFU/amp	<1CFU/amp	<1CFU/amp
	After sterilization/depyrogenation			
	Bacterial endotoxin	<0.25 EU/ml	<0.25 EU/ml	<0.25 EU/ml
	Sterility	No growth	No growth	No growth
	Set temp. of tunnel(ºC)	330,328,326,324	330,328,326,324	330,328,326,324
	Conveyour speed	67 mm/min	67 mm/min	67 mm/min
Mfgpreparation of drug solution	Bioburden of drug solution	2 CFU/100ml	4 CFU/100ml	3 CFU/100ml
	pH	7.2	7.1	7.1
	Mixing efficiency	100.1%	96.5%	98.5%

Filtration	Temperature	32 ºC	33 ºC	35 ºC
	Sterility	No growth	No growth	No growth
	Post integrity pressure	3.2 kg/cm^2	3.2 kg/cm^2	3.2 kg/cm^2
	Filter duration	60 min	75 min	70 min
	Bioburden	<1CFU	<1 CFU	<1 CFU
	Pressure for filtration	3.2 kg/cm^2	3.2 kg/cm^2	3.2 kg/cm^2
Compressed air &nitrogen gas	Bioburden	<1 CFU	<1 CFU	<1 CFU
	Sterility	No growth	No growth	No growth
Filling and sealing	Volume of ampoule	2.2 ml	2.2 ml	2.2 ml
	Sealing	OK	OK	OK
	Nitrogen flushing	OK	OK	OK
	Visual inspection(rejection)	07	04	08
	Sterility	No growth	No growth	No growth
HPHV leak test	Leak test time	11 min	12 min	10 min
	Rejected ampoule	05	08	07

Assay of Methyl Cobalamine during start, middle and end of filling:

Table 1.16: Assay of Methyl Cobalmine

Series	**Assay of Methyl Cobalamine (%)**								
	Batch No.								
	X			**Y**			**Z**		
	S	M	E	S	M	E	S	M	E
01	100.72	100.73	104.45	100.64	98.62	97.32	99.71	98.72	101.78
02	100.65	101.28	100.06	99.47	100.82	99.76	100.33	98.21	100.62
03	99.22	100.25	101.44	100.05	101.17	98.07	100.94	97.44	100.16
04	101.34	102.14	100.05	98.15	98.82	101.36	100.86	97.94	100.19
05	101.09	100.39	101.49	100.74	101.12	99.91	99.54	100.14	99.03
06	100.56	100.79	99.09	98.05	102.07	99.27	99.06	97.67	100.96
07	101.08	100.47	98.94	102.35	101.22	100.41	100.11	99.11	100.66
08	99.91	100.96	98.82	100.79	98.47	99.12	100.74	98.35	100.95
09	100.22	101.37	101.83	98.29	98.67	102.01	100.28	99.61	100.13
10	101.04	99.73	99.78	98.68	101.32	98.27	101.34	97.98	99.44
Max	101.34	102.14	104.45	102.35	102.07	102.01	100.94	100.14	101.78
Min	99.22	99.73	98.82	98.05	98.47	97.32	99.06	97.44	99.03
Mean (%)	100.58	100.87	100.60	99.72	100.23	99.55	100.29	98.52	100.39
% RSD	0.84	0.67	1.72	1.44	1.40	1.47	0.71	0.87	0.79

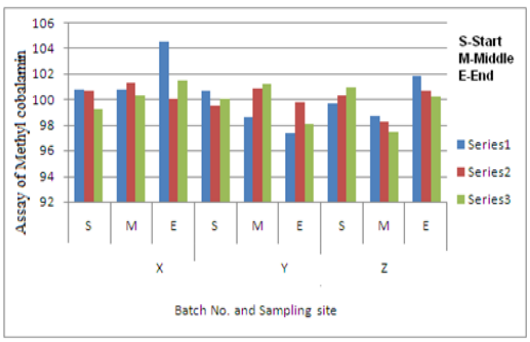

Fig 1.4: Assay of Methylcobalamine series 1-3

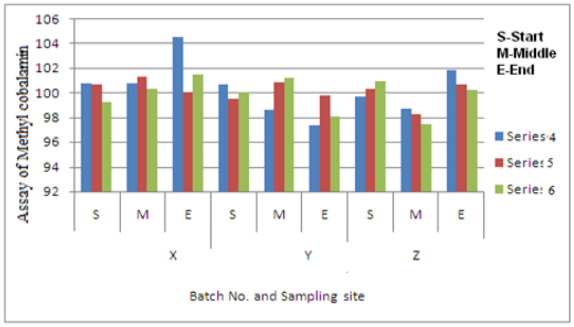

Fig 1.5: Assay of Methylcobalamineseries 4-6

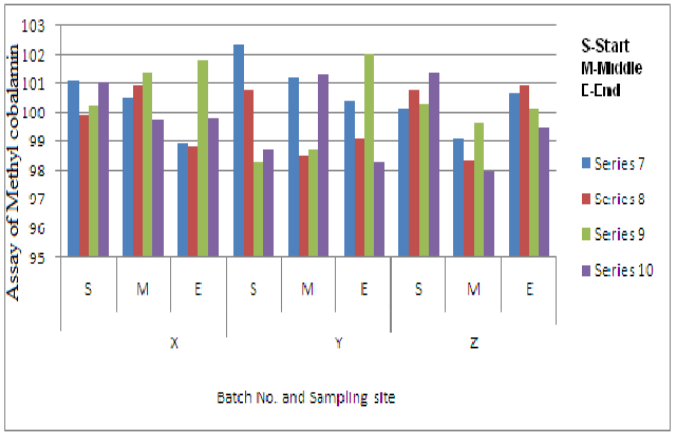

Fig1.6: Assay of Methylcobalamineseries 7-10

Filling Line Speed Validation at 150 ampoule/min

Table 1.17: Result of filling line speed validation at 150 ampoule/min

Assets	Test parameter	Batch No		
		X	Y	Z
Washing machine	Particulate matter	No particulate matter	No particulate matter	No particulate
	Breakage	LT 1%	LT 1%	LT 1%
	No. of break down	No major break down	No major break down	No major break
Tunnel	Sterility	No growth	No growth	No growth
	Endotoxin	<0.25EU/ml	<0.25EU/ml	<0.25EU/ml
	Breakage	LT 1%	LT 1%	LT 1%
	No. of breakage down	No major break down	No major break down	No major break
Filling machine	Volume	2.2 ml	2.2 ml	2.2 ml
	Sealing defect	LT 1%	LT 1%	LT 1%
	Particulate matter	LT 2%	LT 2%	LT 2%
	Break down	No major break down	No major break down	No major break
Labelling machine	Coding on label	OK	OK	OK
	Breakage	LT 1%	LT 1%	LT 1%
	No .of break down	No major break down	No major break down	No major break
Cartooning machine	Coding on carton	OK	OK	OK
	Breakage	LT 1%	LT 1%	LT 1%
	No .of break down	No major break down	No major break down	No major break

Filling Line Speed Validation at 250 ampoule/min

Table 1.18: Result of filling line speed validation at 250 ampoule/min

Assets	Test parameter	Batch No.		
		X	Y	Z
Washing machine	Particulate matter	No particulate matter	No particulate matter	No particulate matter
	Breakage	LT 1%	LT 1%	LT 1%
	No. of break down	No major break down	No major break down	No major break down
Tunnel	Sterility	No growth	No growth	No growth
	Endotoxin	<0.25EU/ml	<0.25EU/ml	<0.25EU/ml
	Breakage	LT 1%	LT 1%	LT 1%
	No. of breakage down	No major break down	No major break down	No major break down

Filling machine	Volume	2.2 ml	2.2 ml	2.2 ml
	Sealing defect	LT 1%	LT 1%	LT 1%
	Particulate matter	LT 2%	LT 2%	LT 2%
	Break down	No major break down	No major break down	No major break down
Labelling machine	Coding on label	OK	OK	OK
	Breakage	LT 1%	LT 1%	LT 1%
	No .of break down	No major break down	No major break down	No major break down
Cartooning machine	Coding on carton	OK	OK	OK
	Breakage	LT 1%	LT 1%	LT 1%
	No .of break down	No major break down	No major break down	No major break down

SUMMARY:

Validation of HVAC system ensures that all these parameter are within the predetermined specification.

Test/Critical parameter	Acceptance criteria
DOP test	NMT 0.01%
Air velocity	90±20 % FPM
Air changes	NLT 25 air changes
Pressure differential	For same class NLT 6 Pa and different class NLT 15 Pa
Temp and humidity	Temp:23±2°c , Humidity:NMT55%
Non-viable count	As per ISO specification
Viable count	As per IHS guideline
Air flow pattern	Uniform up to the operational level
Decontamination time	NMT 8 minutes

CONCLUSION:

Based on the validation test results, review, assessment and evaluation it is concluded that the manufacturing process of Methylcobalamine injection is validated (as per cGMP guidelines) for the predetermined acceptance criteria. For the intended indication of new drug (accurate and reliable assessment) for its effectiveness and safety, it is necessary before approval of new drug Pharmaceutical validation and process control are required facilities.

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