

VA Cooperative Studies Program Clinical Research Pharmacy Coordinating Center		Issue Date: 25 Jun 2013	Document:MR-573.04
Authorized by: Jan Hickey CHIEF, CMS		Version: 3	Page 1 of 19
Sub Authorizer: Stanley JOHNSON CHIEF, QCU			
Document Title: Manufacture of Baclofen 20mg Capsules			
INVALID 2 WKS FROM PRINT DATE		Print Date: 2/16/10	

MANUFACTURING PROCEDURES

CSP/Project #: _____	Production Run (Batch/Lot) #: _____	Theoretical Lot Size¹: _____ kg/batch	Start Time: _____ Start Date: _____
MPR #: _____	TID #: _____	Theoretical # units/batch²: _____	End Time: _____ End Date: _____

¹Batch size to be determined at time of production (Procedures suitable for 2.9-4.5 kg batches)

²Theoretical No. of Capsules to be calculated at time of production (see 'bulk quantity required' for capsules in Component ID, Weights and Measures Log section)

Component ID, Weights and Measures Log

COMPONENT	TID	EXPIRATION DATE	QUANTITY PER CAPSULE ¹	FORMULA =	BULK QTY REQUIRED	QUANTITY ON HAND	CALC. PERFORMED BY	CALC. CHECKED BY	QM CHECK
Example (8.89%)			20mg	0.0889 x batch size (kg) x 1,000 =	_____g	_____g			
Avicel PH302 (89.56%)			201.5mg	0.8956 x batch size (kg) =	_____kg	_____kg			
Cab-O-Sil M5P (0.89%)			2mg	0.0089 x batch size (kg) x 1,000 =	_____g	_____g			
Magnesium stearate (0.67%)			1.5mg	0.0067 x batch size (kg) x 1,000 =	_____g	_____g			
Capsules (size 1, light blue opaque)			1	[Batch size (kg) x 1,000] ÷ 0.225g/cap =	_____caps	_____caps			

¹Target powder fill weight = 225mg/capsule

VA Cooperative Studies Program Clinical Research Pharmacy Coordinating Center		Issue Date: 25 Jun 2013	Document:MR-573.04
Authorized by: Jan Hickey CHIEF, CMS		Version: 3	Page 2 of 19
Sub Authorizer: Stanley JOHNSON CHIEF, QCU			
Document Title: Manufacture of Baclofen 20mg Capsules			
INVALID 2 WKS FROM PRINT DATE		Print Date: 2/16/10	

MANUFACTURING PROCEDURES

Step #:	Procedure Description	Specifications-Tolerances	Value	Performed By:	Checked By:
	Safety Precautions: 1. Respirators, gloves, lab coats and booties required. 2. Where possible handle as a Category 3 material 3. Dispose of all disposable gowning, equipment and room cleaning solid materials in containers for incineration. Do NOT discard in normal trash. 4. Avoid release to the environment. 5. Operate within closed systems where practical. 6. In case of a spill, do not release to drains.				

VA Cooperative Studies Program	Issue Date:	Document:MR-573.04
Clinical Research Pharmacy Coordinating Center	25 Jun 2013	
Authorized by: Jan Hickey CHIEF, CMS	Version: 3	Page 3 of 19
Sub Authorizer: Stanley JOHNSON CHIEF, QCU		
Document Title: Manufacture of Baclofen 20mg Capsules		
INVALID 2 WKS FROM PRINT DATE	Print Date: 2/16/10	

MANUFACTURING PROCEDURES

Step #:	Procedure Description	Specifications-Tolerances	Value	Performed By:	Checked By:
1	<p>Manually verify the calibration of each balance to be used with a set of certified masses prior to weighing active ingredient or excipients.</p> <ul style="list-style-type: none"> Only use scales calibrated for the unit of measure to be weighed <ul style="list-style-type: none"> i.e. Kg scale for Kg weight, mg scale for mg weight, g scale for g weight. Use one certified mass for each scale that weighs less than the lowest value to be weighed on that scale. Use one certified mass for each scale that weighs more than the heaviest value to be weighed on that scale. Attach a printout of the results to this page. Actual results shall fall within $\pm 0.5\%$ of the test mass. 	<p>Explorer No. _____</p> <p>Certified Low Mass Weight: _____gms</p> <p>Certified High Mass Weight: _____gms</p> <hr/> <p>Ohaus No. _____</p> <p>Certified Low Mass Weight: _____Kg</p> <p>Certified High Mass Weight: _____Kg</p>	<p>Low Mass Range:</p> <p>Low: _____gms</p> <p>High: _____gms</p> <p>Actual: _____gms</p> <p>High Mass Range:</p> <p>Low: _____gms</p> <p>High: _____gms</p> <p>Actual: _____gms</p> <hr/> <p>Low Mass Range:</p> <p>Low: _____Kgs</p> <p>High: _____Kgs</p> <p>Actual: _____Kgs</p> <p>High Mass Range:</p> <p>Low: _____Kgs</p> <p>High: _____Kgs</p> <p>Actual: _____Kgs</p>		
Step #:	Procedure Description	Specifications-Tolerances	Value	Performed	Checked

VA Cooperative Studies Program Clinical Research Pharmacy Coordinating Center		Issue Date: 25 Jun 2013	Document:MR-573.04
Authorized by: Jan Hickey CHIEF, CMS		Version: 3	Page 4 of 19
Sub Authorizer: Stanley JOHNSON CHIEF, QCU			
Document Title: Manufacture of Baclofen 20mg Capsules			
INVALID 2 WKS FROM PRINT DATE		Print Date: 2/16/10	

MANUFACTURING PROCEDURES

				By:	By:
2	Weigh target amount of _____g of Example powder and record actual weight. Attach printer tape (if available) to the back of this page. Acceptable range $\pm 1\%$ of the bulk quantity determined in the Component ID, Weights and Measures Log (minimum value = target x 0.99; maximum value = target x 1.01)	Minimum : _____g To Maximum: _____g	ACTUAL WEIGHT OF EXAMPLE: _____g (A)		
3	Weigh target amount of _____g of Cab-O-Sil M5P and record actual weight. Attach printer tape (if available) to the back of this page. Acceptable range $\pm 1\%$ of the bulk quantity determined in the Component ID, Weights and Measures Log (minimum value = target x 0.99; maximum value = target x 1.01)	Minimum : _____g To Maximum: _____g	ACTUAL WEIGHT OF CAB-O-SIL M5P: _____g (B)		
4	Weigh target amount of _____kg of Avicel PH 302 and record actual weight. Attach printer tape (if available) to the back of this page. Acceptable range ± 0.02 kg of the bulk quantity determined in the Component ID, Weights and Measures Log	Minimum : _____kg To Maximum: _____kg	ACTUAL WEIGHT OF AVICEL PH 302: _____kg (C)		

Step #:	Procedure Description	Specifications-Tolerances	Value	Performed	Checked
---------	-----------------------	---------------------------	-------	-----------	---------

VA Cooperative Studies Program Clinical Research Pharmacy Coordinating Center		Issue Date: 25 Jun 2013	Document:MR-573.04
Authorized by: Jan Hickey CHIEF, CMS		Version: 3	Page 5 of 19
Sub Authorizer: Stanley JOHNSON CHIEF, QCU			
Document Title: Manufacture of Baclofen 20mg Capsules			
INVALID 2 WKS FROM PRINT DATE		Print Date: 2/16/10	

MANUFACTURING PROCEDURES

				By:	By:
5	Place powders from steps 2 and 3 in the <i>8 qt V-shell</i> blender <i>without the intensifier bar installed</i> . Add approximately 400g of Avicel. Mix powders for 5 minutes ¹ . Add approximately 800 g Avicel. Mix powders for 5 minutes ² . Remove powder from blender and collect in a sanitary plastic bag (Bag A). Pass powder through a 30-mesh screen and collect in a separate plastic bag (Bag B). Place powder back in the blender. Mix for 5 minutes ³ .	Required mix time ¹ ≥ 5 minutes Required mix time ² ≥ 5 minutes Required mix time ³ ≥ 5 minutes	Start Time: _____ Stop Time: _____ Mixing time: _____min. Start Time: _____ Stop Time: _____ Mixing time: _____min. Start Time: _____ Stop Time: _____ Mixing time: _____min.		

Step #:	Procedure Description	Specifications-Tolerances	Value	Performed By:	Checked By:
6	Remove powder from blender and collect in Bag A.	Required mix time ¹ ≥ 5	Start Time: _____		

VA Cooperative Studies Program Clinical Research Pharmacy Coordinating Center		Issue Date: 25 Jun 2013	Document:MR-573.04
Authorized by: Jan Hickey CHIEF, CMS		Version: 3	Page 6 of 19
Sub Authorizer: Stanley JOHNSON CHIEF, QCU			
Document Title: Manufacture of Baclofen 20mg Capsules			
INVALID 2 WKS FROM PRINT DATE		Print Date: 2/16/10	

MANUFACTURING PROCEDURES

	Pass powder through a 30-mesh screen and collect in Bag B.	minutes	Stop Time: _____		
	Place powder in the 16 qt. V-shell blender <i>without the intensifier bar installed</i> .		Mixing time: _____min.		
	Add approximately 1500 g of Avicel to Bag B.				
	Gently shake the bag.				
	Place contents of bag in 16 qt V-shell.		Start Time: _____		
	Mix for 5 minutes ¹ .	Required mix time ² ≥ 5 minutes	Stop Time: _____		
	Add any remaining Avicel.		Mixing time: _____min.		
	Mix for 5 minutes ² . (If no additional powder added, omit this step)				
	Remove powder from blender and collect in Bag A.				
	Pass powder through a 30-mesh screen and collect in Bag B.		Start Time: _____		
	Place powder back in the blender.	Required mix time ³ ≥ 5 minutes	Stop Time: _____		
	Mix for 5 minutes ³ .		Mixing time: _____min.		

Step #:	Procedure Description	Specifications-Tolerances	Value	Performed By:	Checked By:
7	Calculate the theoretical concentration of Example in the powder blend:				

VA Cooperative Studies Program	Issue Date:	Document:MR-573.04
Clinical Research Pharmacy Coordinating Center	25 Jun 2013	
Authorized by: Jan Hickey CHIEF, CMS	Version: 3	Page 7 of 19
Sub Authorizer: Stanley JOHNSON CHIEF, QCU		
Document Title: Manufacture of Baclofen 20mg Capsules		
INVALID 2 WKS FROM PRINT DATE	Print Date: 2/16/10	

MANUFACTURING PROCEDURES

	<p>i. Convert Example weight to kg:</p> $= \frac{\text{_____}(A)}{1,000} = \text{_____} \text{ kg } (D)$ <p>ii. Convert Cab-O-Sil weight to kg:</p> $= \frac{\text{_____}(B)}{1,000} = \text{_____} \text{ kg } (E)$ <p>iii. Calculate the % Example in powder blend:</p> $= \frac{\text{_____}(D)}{\text{_____}(C) + \text{_____}(D) + \text{_____}(E)} \times 100 =$ $= \text{_____} \% (F)$		<p>THEORETICAL CONCENTRATION OF EXAMPLE =</p> <p>_____ % (F)</p>		

Step #:	Procedure Description	Specifications-Tolerances	Value	Performed By:	Checked By:
8	Obtain pre-weighed 25ml volumetric flasks from BPLS		Obtain %RSD of the 6 samples from FM-MFR-016		
	Remove samples of the powder blend from the <i>top and bottom</i> of the				

VA Cooperative Studies Program Clinical Research Pharmacy Coordinating Center		Issue Date: 25 Jun 2013	Document:MR-573.04
Authorized by: Jan Hickey CHIEF, CMS		Version: 3	Page 8 of 19
Sub Authorizer: Stanley JOHNSON CHIEF, QCU			
Document Title: Manufacture of Baclofen 20mg Capsules			
INVALID 2 WKS FROM PRINT DATE		Print Date: 2/16/10	

MANUFACTURING PROCEDURES

	powder bed on <i>both sides</i> of the blender. Weigh approximately 250mg of each directly into preweighed 25ml volumetric flasks obtained in advance from BPLS. Attach printer tape (if available) to the back of this page. Provide samples to BPLS for testing. STOP production until the blend uniformity assay (BUA) results of these samples are obtained and within acceptable limits. Include the completed FM-MFR-16, Manufacturing Record, In-Process Blend Assay in the MR Percent of theoretical concentration: $= \frac{\text{_____}(G)}{\text{_____}(F)} \times 100 = \text{_____} \% (H)$	Acceptance criteria: %RSD NMT 4.0% Percent of theoretical concentration 95-105%	%RSD of the 6 samples: _____% Actual Example Conc.: Obtain Average Calculated Example Concentration _____ (X) from FM-MFR-016: _____ (G) Percent of Theoretical Concentration _____ % (H)	IQM APPROVAL REQUIRED	

Step #:	Procedure Description	Specifications-Tolerances	Value	Performed By:	Checked By:
9	If blend uniformity results are NOT within acceptable limits:	Required mix time (1 st re-blend) \geq 10 minutes ^a	Start Time:_____		

VA Cooperative Studies Program Clinical Research Pharmacy Coordinating Center		Issue Date: 25 Jun 2013	Document:MR-573.04
Authorized by: Jan Hickey CHIEF, CMS		Version: 3	Page 9 of 19
Sub Authorizer: Stanley JOHNSON CHIEF, QCU			
Document Title: Manufacture of Baclofen 20mg Capsules			
INVALID 2 WKS FROM PRINT DATE		Print Date: 2/16/10	

MANUFACTURING PROCEDURES

	<ul style="list-style-type: none"> Remove powder from blender into Bag A. Pass powder through 30-mesh screen and collect into Bag B. Place powder into the 16 qt. V-shell blender <i>without the intensifier bar installed</i>. Blend for an additional 10 minutes. Conduct Step 9 only if this step was conducted. 		Stop Time:_____		
			Total mix time:_____min.		

Step #:	Procedure Description	Specifications-Tolerances	Value	Performed By:	Checked By:
---------	-----------------------	---------------------------	-------	---------------	-------------

VA Cooperative Studies Program Clinical Research Pharmacy Coordinating Center		Issue Date: 25 Jun 2013	Document:MR-573.04
Authorized by: Jan Hickey CHIEF, CMS		Version: 3	Page 10 of 19
Sub Authorizer: Stanley JOHNSON CHIEF, QCU			
Document Title: Manufacture of Baclofen 20mg Capsules			
INVALID 2 WKS FROM PRINT DATE		Print Date: 2/16/10	

MANUFACTURING PROCEDURES

10	<p>Conduct this step only if Step 9 was conducted.</p> <p>Obtain pre-weighed 25ml volumetric flasks from BPLS</p> <p>Remove samples of the powder blend from the <i>top and bottom</i> of the powder bed on <i>both sides</i> of the blender.</p> <p>Weigh approximately 250mg of each directly into preweighed 25ml volumetric flasks obtained in advance from BPLS.</p> <p>Attach printer tape (if available) to the back of this page.</p> <p>Provide samples to BPLS for testing.</p> <p>STOP production until the blend uniformity assay (BUA) results of these samples are obtained and within acceptable limits.</p> <p>Include the completed FM-MFR-16, Manufacturing Record, In-Process Blend Assay in the MR</p> <p>Percent of theoretical concentration:</p> $= \frac{\text{_____}(G)}{\text{_____}(F)} \times 100 = \text{_____} \% (H)$ <p>Reject the batch if blend uniformity fails the second time.</p>	<p>Acceptance criteria:</p> <p>%RSD NMT 4.0%</p> <p>Percent of theoretical concentration</p> <p>95-105%</p>	<p>Obtain %RSD of the 6 samples from FM-MFR-016</p> <p>%RSD of the 6 samples:</p> <p>_____ %</p> <p>Actual Example Conc.:</p> <p>Obtain Average Calculated Example Concentration</p> <p>_____ (X) from FM-MFR-016:</p> <p>_____ (G)</p> <p>Percent of Theoretical Concentration</p> <p>_____ % (H)</p>	<p>IQM APPROVAL REQUIRED</p>	
----	--	--	--	-------------------------------------	--

Step #:	Procedure Description	Specifications-Tolerances	Value	Performed	Checked
---------	-----------------------	---------------------------	-------	-----------	---------

VA Cooperative Studies Program	Issue Date:	Document:MR-573.04
Clinical Research Pharmacy Coordinating Center	25 Jun 2013	
Authorized by: Jan Hickey CHIEF, CMS	Version: 3	Page 11 of 19
Sub Authorizer: Stanley JOHNSON CHIEF, QCU		
Document Title: Manufacture of Baclofen 20mg Capsules		
INVALID 2 WKS FROM PRINT DATE	Print Date: 2/16/10	

MANUFACTURING PROCEDURES

				By:	By:
11	<p>Continue with the procedures after blend uniformity results meet specifications.</p> <p>Sieve magnesium stearate through a 40-mesh screen.</p> <p>Weigh target amount of _____g of sieved magnesium stearate and record actual weight. Attach printer tape (if available) to the back of this page.</p> <p>Acceptable range: $\pm 1\%$ of the bulk quantity determined in the Component ID, Weights and Measures Log</p>	<p>Minimum : _____g</p> <p>To</p> <p>Maximum: _____g</p>	<p>Actual weight of Magnesium Stearate:</p> <p>_____g (I)</p>		
12	<p>Add the magnesium stearate to the blender.</p> <p>Mix with the powder blend for 5 minutes.</p>	<p>Required mix time ≥ 5 minutes</p>	<p>Start Time: _____</p> <p>Stop Time: _____</p> <p>Total mixing time:</p> <p>_____min.</p>		
13	<p>Empty the powder blend from the mixer into a sanitary plastic bag (Bag C).</p> <p>Record the weight of the powder.</p>		<p>WEIGHT OF POWDER BLEND:</p> <p>_____ kg (J)</p>		
Step #:	Procedure Description	Specifications-Tolerances	Value	Performed By:	Checked By:
14	Calculate a percent yield for the blending process:	Acceptance criteria: 95-102.5%	Yield for the blending process:		

VA Cooperative Studies Program	Issue Date:	Document:MR-573.04
Clinical Research Pharmacy Coordinating Center	25 Jun 2013	
Authorized by: Jan Hickey CHIEF, CMS	Version: 3	Page 12 of 19
Sub Authorizer: Stanley JOHNSON CHIEF, QCU		
Document Title: Manufacture of Baclofen 20mg Capsules		
INVALID 2 WKS FROM PRINT DATE	Print Date: 2/16/10	

MANUFACTURING PROCEDURES

	Convert Magnesium Stearate weight to kg: $= \frac{\text{_____}(I)}{1,000} = \text{_____} kg (K)$ $= \frac{\text{_____}(J)}{\text{_____}(C) + \text{_____}(D) + \text{_____}(E) + \text{_____}(K)} \times 100$ $= \text{_____} \% (L)$		_____ % (L)		
15	Manually verify the calibration of each balance to be used with a set of certified masses prior to weighing active ingredient, excipients or capsules. <ul style="list-style-type: none"> Only use scales calibrated for the unit of measure to be weighed <ul style="list-style-type: none"> i.e. Kg scale for Kg weight, mg scale for mg weight, g scale for g weight. Use one certified mass for each scale that weighs less than the lowest value to be weighed on that scale. Use one certified mass for each scale that weighs more than the heaviest value to be weighed on that scale. Attach a printout of the results to this page. Actual results shall fall within $\pm 0.5\%$ of the test mass. 	Sartorius No. _____ Certified Low Mass Weight: _____mg Certified High Mass Weight: _____mg	Low Mass Range: Low: _____mg High: _____mg Actual: _____mg High Mass Range: Low: _____mg High: _____mg Actual: _____mg		
Step #:	Procedure Description	Specifications-Tolerances	Value	Performed By:	Checked By:
16	Weigh 10 size 1 empty gelatin capsules. Attach printer tape (if available) to the back of this page.		Weight of 10 capsules:		

VA Cooperative Studies Program Clinical Research Pharmacy Coordinating Center		Issue Date: 25 Jun 2013	Document:MR-573.04
Authorized by: Jan Hickey CHIEF, CMS		Version: 3	Page 13 of 19
Sub Authorizer: Stanley JOHNSON CHIEF, QCU			
Document Title: Manufacture of Baclofen 20mg Capsules			
INVALID 2 WKS FROM PRINT DATE		Print Date: 2/16/10	

MANUFACTURING PROCEDURES

	Determine the average weight of one empty capsule shell.		_____mg AVE. CAPSULE WEIGHT: _____mg (M) (weight of 10 capsules ÷ 10)		
17	<p>Calculate the target weight (in mg) of the finished capsule.</p> <p>Record the weight.</p> <p>Target weight = Average weight of 1 empty capsule + weight of powder containing 20mg of drug (based on BUA results):</p> <p>Weight of powder containing 20mg of drug = 2000 divided by (G)</p> <p>= 2,000 ÷ _____(G) = _____mg (N)</p> <p>_____mg (M) + _____mg (N) = _____mg (O)</p>		TARGET CAPSULE WEIGHT: _____mg (O)		
18	<p>Calculate the acceptable range (in mg) for the weight of finished capsules and record the range.</p> <p>Target weight of capsule (O) ± 8 %</p>	FINAL SPEC Minimum : _____mg to Maximum: _____mg			
Step #:	Procedure Description	Specifications-Tolerances	Value	Performed By:	Checked By:
19	Calculate the acceptable range (in mg) for the weight of finished capsules during the in-process set-up of the Bosch and record the range.	IN-PROCESS SPEC Minimum : _____mg			

VA Cooperative Studies Program		Issue Date:	Document:MR-573.04
Clinical Research Pharmacy Coordinating Center		25 Jun 2013	
Authorized by: Jan Hickey CHIEF, CMS		Version: 3	Page 14 of 19
Sub Authorizer: Stanley JOHNSON CHIEF, QCU			
Document Title: Manufacture of Baclofen 20mg Capsules			
INVALID 2 WKS FROM PRINT DATE		Print Date: 2/16/10	

MANUFACTURING PROCEDURES

	Target weight of capsule (O) \pm 4 %	to			
		Maximum: _____mg			
20	<p>Set up Bosch machinery with size 2 tamping pins and dosing disk and bowl height to 5.</p> <p>Set tamping pins for 0 compression as initial set up, NOTE – compression of tamping pins will be needed to minimize capsule weight variability.</p> <p>Fill the capsule hopper.</p> <p>Fill the powder hopper with powder from Bag C.</p>				
21	<p>Turn on Bosch encapsulator and operate in the 'jog' position for at least 2 full revolutions.</p> <p>Collect 10 capsules and record the total capsule weight. Attach printer tape (if available) to the back of this page.</p> <p>Calculate the average capsule weight.</p>		<p>Total weight of 10 capsules:</p> <p>_____mg</p> <p>Ave. capsule weight:</p> <p>_____mg</p> <p>(wt of 10 capsules \div 10)</p>		

Step #:	Procedure Description	Specifications-Tolerances	Value	Performed By:	Checked By:
22	<p>Adjust tamping pins and/or bowl height as necessary to achieve an average capsule weight within the acceptable in-process specification.</p> <p>Repeat steps 20 and 21 until the average capsule weight is within the</p>		<p>Total weight of 10 capsules:</p> <p>_____mg</p>		

VA Cooperative Studies Program Clinical Research Pharmacy Coordinating Center		Issue Date: 25 Jun 2013	Document:MR-573.04
Authorized by: Jan Hickey CHIEF, CMS		Version: 3	Page 15 of 19
Sub Authorizer: Stanley JOHNSON CHIEF, QCU			
Document Title: Manufacture of Baclofen 20mg Capsules			
INVALID 2 WKS FROM PRINT DATE		Print Date: 2/16/10	

MANUFACTURING PROCEDURES

	acceptable in-process specification.		Ave. capsule weight: _____mg (wt of 10 capsules ÷ 10)		
23	Operate Bosch at full speed. Allow for at least 2 full revolutions. Collect 10 capsules and record the total capsule weight. Calculate the average capsule weight.		Total weight of 10 capsules: _____mg Ave. capsule weight: _____mg (wt of 10 capsules ÷ 10)		
24	Make minor adjustments to tamping pins/bowl height if necessary. Repeat step 22 and 23 until the average capsule weight is within the acceptable in-process specification. Set aside capsules from the set-up process for destruction.		Total weight of 10 capsules: _____mg Ave. capsule weight: _____mg (wt of 10 capsules ÷ 10)		

Step #:	Procedure Description	Specifications-Tolerances	Value	Performed By:	Checked By:
25	Set capsule polisher alongside the Bosch encapsulator such that the filled capsules are fed directly into the polisher. Collect filled/polished capsules in a sanitary plastic bag.				

VA Cooperative Studies Program Clinical Research Pharmacy Coordinating Center		Issue Date: 25 Jun 2013	Document:MR-573.04
Authorized by: Jan Hickey CHIEF, CMS		Version: 3	Page 16 of 19
Sub Authorizer: Stanley JOHNSON CHIEF, QCU			
Document Title: Manufacture of Baclofen 20mg Capsules			
INVALID 2 WKS FROM PRINT DATE		Print Date: 2/16/10	

MANUFACTURING PROCEDURES

	<p>At approximately 10 minute intervals, randomly select 10 capsules and weigh each individually.</p> <p>If weights fall outside of the target capsule weight, stop the run. Segregate capsules that may have incorrect weights, adjust the Bosch to the correct setting and restart the run.</p> <p>Record individual weights on form MFR-002C. Attach printer tape (if available) to the back of the form.</p> <p>Continue capsule production until the majority of available powder has been encapsulated.</p> <p>Refill capsule hopper as necessary.</p> <p>Refill powder hopper as necessary.</p>				
26	<p>Remove remaining powder from hopper and collect in a sanitary container. Attach printer tape (if available) to the back of this page.</p> <p>Weigh remaining powder blend and record the weight.</p> <p>Set powder aside for destruction.</p>		<p>WEIGHT OF POWDER REMAINING:</p> <p>_____ g (P)</p>		

Step #:	Procedure Description	Specifications-Tolerances	Value	Performed By:	Checked By:
26	<p>Weigh the finished capsules. Attach printer tape (if available) to the back of this page.</p> <p>Record the weight of the finished capsules.</p>		<p>WEIGHT OF FINISHED CAPSULES:</p> <p>_____ kg (Q)</p>		

VA Cooperative Studies Program Clinical Research Pharmacy Coordinating Center		Issue Date: 25 Jun 2013	Document:MR-573.04
Authorized by: Jan Hickey CHIEF, CMS		Version: 3	Page 17 of 19
Sub Authorizer: Stanley JOHNSON CHIEF, QCU			
Document Title: Manufacture of Baclofen 20mg Capsules			
INVALID 2 WKS FROM PRINT DATE		Print Date: 2/16/10	

MANUFACTURING PROCEDURES

27	Remove powder from vacuum. Weigh the powder and record the weight. Attach printer tape (if available) to the back of this page. Set powder aside for destruction.		Weight of powder collected from vacuum: _____g		

Step #:	Procedure Description	Specifications-Tolerances	Value	Performed By:	Checked By:
28	Calculate a percent yield based on the number of capsules produced. Actual: i. Calculate the average weight from in-process testing $= \frac{\sum \text{Individual capsule weights}}{\text{Total number of capsules weighed}} = \text{_____} mg(R)$	Acceptable range: 75-110% of theoretical	PERCENT YIELD = _____ % (V)		

VA Cooperative Studies Program	Issue Date:	Document:MR-573.04
Clinical Research Pharmacy Coordinating Center	25 Jun 2013	
Authorized by: Jan Hickey CHIEF, CMS	Version: 3	Page 18 of 19
Sub Authorizer: Stanley JOHNSON CHIEF, QCU		
Document Title: Manufacture of Baclofen 20mg Capsules		
INVALID 2 WKS FROM PRINT DATE	Print Date: 2/16/10	

MANUFACTURING PROCEDURES

	<p>ii. Estimate the total number of capsules produced</p> $= \frac{\text{_____}(Q) \times 1,000,000}{\text{_____}(R)} = \text{_____} \text{ capsules}(S)$ <p>Theoretical:</p> <p>Convert target powder fill (N) to grams:</p> $\text{_____}(N) \div 1000 = \text{_____}(T)$ $= \frac{([\text{_____}(J) \times 1,000] - \text{_____}(P))}{\text{_____}(T)} = \text{_____} \text{ caps}(U)$ <p>Percent of theoretical</p> $= \frac{\text{_____}(S)}{\text{_____}(U)} \times 100 = \text{_____} \%(V)$				

Step #:	Procedure Description	Specifications-Tolerances	Value	Performed By:	Checked By:
29	Double bag, label and quarantine capsules until released by IQMU.				