OPKO Chile S.A.

ESTUDIO DE ESTABILIDAD

DOXICICLINA CÁPSULAS 100 mg

Subdepartamento Registros y Autorizaciones Sanitarias

Contenido

I. PROTOCOLO

Se realizó una evaluación de la estabilidad de tres lotes de Doxiciclina cápsulas 100 mg fabricado por Emil Pharmaceutical Industries Pvt. Ltd., utilizando materia prima suministrada por Hebei Dongfeng Pharmaceutical Co. Ltd. El estudio se llevará a cabo a dos tiempos y condiciones ambientales.

A continuación los lotes a analizar:

Lote	Fecha de manufactura	Tamaño de lote (comprimidos)	Tiempo de Estudio		
			Inicio	Final (Tiempo real)	Final (Acelerado)
M151	07/2011	850.000	07/2011	06/2014	01/2012
M152	07/2011	850.000	07/2011	06/2014	01/2012
M153	07/2011	850.000	07/2011	06/2014	01/2012

1. Condiciones

El estudio se realizó almacenando muestras, en las siguientes condiciones de temperatura y humedad relativa:

	Estudio Acelerado	Estudio a tiempo real
Temperatura	40ºC ± 2ºC	30ºC ± 2ºC
Humedad	75 % ± 5 % H. R.	65 % ± 5 % H. R

2. Tipo de envase

a) Estuche de cartulina impresa que contiene Blíster ALU/PVC, más folleto de información al paciente, todo debidamente rotulado y sellado.

3. Análisis realizados y frecuencia de testeo:

a) Estudio acelerado

Parámetros medidos	Inicial	3 meses	6 meses
Descripción	√	√	√
Identificación	√	-	√
Promedio de peso	√	-	√
Desintegración	√	√	√
Disolución	√	√	√
Contenido de agua	√	√	√
Uniformidad de contenido	√	-	√
Valoración	√	√	√
Recuento microbiológico	√	√	√
Microbiológico específico	√	√	√

b) Estudio a tiempo real

Parámetros medidos	Inicial	3 M	6 M	9 M	12 M	18 M	24 M	36 M
Descripción	√	√	√	√	√	√	√	√
Identificación	√	-	-	-	-	-	-	√
Promedio de peso	√	-	-	-	-	-	-	√
Desintegración	√	√	√	√	√	√	√	√
Disolución	√	√	√	√	√	√	√	√
Contenido de agua	√	√	√	√	√	√	√	√
Uniformidad de contenido	√	-	-	-	-	-	-	√
Valoración	√	√	√	√	√	√	√	√
Recuento microbiológico	√	√	√	√	√	√	√	√
Microbiológico específico	√	√	√	√	√	√	√	√

NOTA: √ = Parámetro debe ser medido.

4. Especificaciones del producto terminado para estabilidad

EMIL PHARMACEUTICAL INDUSTRIES PVT. LTD.
Reg office: 101 Mangalam, Kulupwadi, Borivali East, Mumbai 400066, INDIA. Tel: +91-22-42090200 Email: info@emilpharma.in
WHO-GMP CERTIFIED
An ISO 9001:2008 Certified Company

Test item	Specification	Control test No.
Description	Hard gelatin capsules size:3, having green cap and green body.	IHS
Identification	The principal peak in the chromatograph obtained with the test solution corresponds to the peak in the chromatograph obtained with the reference solution	USP
Average Weight	250 mg ± 10% (225 – 275 mg)	IHS
Dissolution	Q = NLT 85%(Q) in 60 min	USP
Disintegration	NMT 30 min	USP
Water Content (KF)	N.M.T. 5.5% w/w	USP
Uniformity of Dosage units	Acceptance value : NMT 15.0 when determined on 10 individual units	USP
Assay	90.0 % - 120.0 %	USP
Total aerobic microbial count:		
Bacterial Counts	NMT 1000 cfu/g	IHS
Fungi	NMT 100 cfu/g	IHS
Test for specified microorganisms:		
E. Coli	Absent in 1 g	IHS
Salmonellae	Absent in 10 g	IHS
Pseudomonads	Absent in 1 g	IHS
Stap.aureus	Absent in 1 g	IHS

NOTE: IHS: In House Specification
USP: United State Pharmacopoeia 33, National Formulary28

II. FÓRMULA CUALI-CUANTITA

Sr. No	INGREDIENTS	SPECIFICATION	QTY PER CAPSULE (Mg)	Reason for Inculsion
1	Doxycycline Hyclate	USP	115.41	Medicament
2	Maize starch	BP	65.88	Diluent
3.	Purified Talc	BP	18.70	Glidant
7.	Empty Hard gelatin capsules *; size :3, having Green cap and Green body	IHS	1 capsule	Encapsulation of Medicament

III. RESULTADOS

a) Estudio de estabilidad acelerado:

Accelerated Stability Study Report

Name of Product	:	Doxycycline Capsules USP 100 mg	**Batch No**	:	M 151
Description of the pack	:	10's ALU-PVC Blister Pack	**Mfg. Date**	:	July 2011
Parameters and test method monitored	:	Description, Identification, average weight, D.T, Dissolution test, Water, CU, Assay, & MLT	**Expiry Date**	:	June 2014
Date of Initiation	:	July 2011	**Storage conditions**	:	40° ± 2°C and 75% ± 5% RH
			Date of completion	:	Jan 2012

TEST	**LIMITS**	**RESULTS OF ANALYSIS**		
		INITIAL	**3 Month**	**6 Month**
Description	Hard gelatin capsules size 3, having green cap and green body	Hard gelatin capsules size 3, having green cap and green body	Hard gelatin capsules size 3, having green cap and green body	Hard gelatin capsules size 3, having green cap and green body
Identification	The principal peak in the chromatograph obtained with the test solution corresponds to the peak in the chromatograph obtained with the reference solution	The principal peak in the chromatograph obtained with the test solution corresponds to the peak in the chromatograph obtained with the reference solution	NA	The principal peak in the chromatograph obtained with the test solution corresponds to the peak in the chromatograph obtained with the reference solution
Average Weight	225 mg – 275mg	251 mg	NA	252 mg
Disintegration test	NMT 30 mins.	5 min	5 min	6 min
Dissolution test	NLT 85 % (Q) in 60 min	1] 101.64% 2] 99.89% 3] 99.68% 4] 101.62% 5] 100.37% 6] 99.53%	1] 99.77% 2] 98.19% 3] 97.66% 4] 99.61% 5] 98.13% 6] 98.24%	1] 96.01% 2] 96.73% 3] 97.63% 4] 98.43% 5] 98.05% 6] 97.13%
Water Content	NMT 5.5%	2.50%	3.10%	3.45%
Content Uniformity	Acceptace value : NMT 15.0 when determined on 10 individual unit	2.5	NA	2.4
Assay	90% to 120%	99.83%	99.13%	98.67%

Accelerated Stability Study Report

Name of Product	:	Doxycycline Capsules USP 100 mg	**Batch No**	:	M 151
Description of the pack	:	10's ALU-PVC Blister Pack	**Mfg. Date**	:	July 2011
Parameters and test method monitored	:	Description, Identification, average weight, D.T, Dissolution test, Water, CU, Assay, & MLT	**Expiry Date**	:	June 2014
Date of Initiation	:	July 2011	**Storage conditions**	:	40° ± 2°C and 75% ± 5% RH
			Date of completion	:	Jan 2012

TEST	LIMITS	RESULTS OF ANALYSIS		
		INITIAL	3 Month	6 Month
Total aerobic microbial count				
Bacteria	NMT 1000 cfu/g	34 cfu/g	38 cfu/g	35 cfu/g
Fungi	NMT 100 cfu/g	Absent	Absent	Absent
Test for specified microorganisms:				
E.Coli	Absent in 1 gm	Absent	Absent	Absent
Salmonellae	Absent in 10 gm	Absent	Absent	Absent
Pseudomonads	Absent in 1 gm	Absent	Absent	Absent
Stap.aureus	Absent in 1 gm	Absent	Absent	Absent

QA

Approved by:
Mr. S.M. Daptardaar
(QA Manager)

Accelerated Stability Study Report

Name of Product	:	Doxycycline Capsules USP 100 mg	**Batch No**	:	M 152
Description of the pack	:	10's ALU-PVC Blister Pack	**Mfg. Date**	:	July 2011
Parameters and test method monitored	:	Description, Identification, average weight, D.T, Dissolution test, Water , CU, Assay, & MLT	**Expiry Date**	:	June 2014
Date of Initiation	:	July 2011	**Storage conditions**	:	40° ± 2°C and 75% ± 5% RH
			Date of completion	:	Jan 2012

TEST	LIMITS	**RESULTS OF ANALYSIS**		
		INITIAL	**3 Month**	**6 Month**
Description	Hard gelatin capsules size 3, having green cap and green body	Hard gelatin capsules size 3, having green cap and green body	Hard gelatin capsules size 3, having green cap and green body	Hard gelatin capsules size 3, having green cap and green body
Identification	The principal peak in the chromatograph obtained with the test solution corresponds to the peak in the chromatograph obtained with the reference solution	The principal peak in the chromatograph obtained with the test solution corresponds to the peak in the chromatograph obtained with the reference solution	NA	The principal peak in the chromatograph obtained with the test solution corresponds to the peak in the chromatograph obtained with the reference solution
Average Weight	225 mg – 275mg	252 mg	NA	253 mg
Disintegration test	NMT 30 mins.	5 min	5 min	6 min
Dissolution test	NLT 85 % (Q) in 60 min	1] 101.06% 2] 99.11% 3] 99.28% 4] 100.29% 5] 101.07% 6] 99.16%	1] 98.93% 2] 97.34% 3] 96.45% 4] 97.87% 5] 96.35% 6] 97.19%	1] 95.53% 2] 96.74% 3] 94.53% 4] 96.12% 5] 95.32% 6] 96.32%
Water Content	NMT 5.5%	2.14%	2.89%	3.15%
Content Uniformity	Acceptace value : NMT 15.0 when determined on 10 individual unit	2.4	NA	2.4
Assay	90% to 120%	99.47%	98.71%	98.14%

Accelerated Stability Study Report

Name of Product	:	Doxycycline Capsules USP 100 mg	**Batch No**	:	M 152
Description of the pack	:	10's ALU-PVC Blister Pack	**Mfg. Date**	:	July 2011
Parameters and test method monitored	:	Description, Identification, average weight, D.T, Dissolution test, Water , CU, Assay, & MLT	**Expiry Date**	:	June 2014
Date of Initiation	:	July 2011	**Storage conditions**	:	40° ± 2°C and 75% ± 5% RH
			Date of completion	:	Jan 2012

TEST	LIMITS	RESULTS OF ANALYSIS		
		INITIAL	3 Month	6 Month
Total aerobic microbial count				
Bacteria	NMT 1000 cfu/g	40 cfu/g	40 cfu/g	45 cfu/g
Fungi	NMT 100 cfu/g	Absent	Absent	Absent
Test for specified microorganisms:				
E.Coli	Absent in 1 gm	Absent	Absent	Absent
Salmonellae	Absent in 10 gm	Absent	Absent	Absent
Pseudomonads	Absent in 1 gm	Absent	Absent	Absent
Staph.aureus	Absent in 1 gm	Absent	Absent	Absent

QA

Approved by:
Mr. S.M.Daptardar
(QA Manager)

Accelerated Stability Study Report

Name of Product	:	Doxycycline Capsules USP 100 mg	**Batch No**	:	M 153
Description of the pack	:	10's ALU-PVC Blister Pack	**Mfg. Date**	:	July 2011
Parameters and test method monitored	:	Description, Identification, average weight, D.T, Dissolution test, Water , CU, Assay, & MLT	**Expiry Date**	:	June 2014
Date of Initiation	:	July 2011	**Storage conditions**	:	40° ± 2°C and 75% ± 5% RH
			Date of completion	:	Jan 2012

TEST	LIMITS	RESULTS OF ANALYSIS		
		INITIAL	3 Month	6 Month
Description	Hard gelatin capsules size 3, having green cap and green body	Hard gelatin capsules size 3, having green cap and green body	Hard gelatin capsules size 3, having green cap and green body	Hard gelatin capsules size 3, having green cap and green body
Identification	The principal peak in the chromatograph obtained with the test solution corresponds to the peak in the chromatograph obtained with the reference solution	The principal peak in the chromatograph obtained with the test solution corresponds to the peak in the chromatograph obtained with the reference solution	NA	The principal peak in the chromatograph obtained with the test solution corresponds to the peak in the chromatograph obtained with the reference solution
Average weight	225mg–275mg	251 mg	NA	255mg
Disintegration test	NMT 30 mins.	4 min	4 min	6 min
Dissolution test	NLT 85 % (Q) in 60 min	1101.70% 2] 99.67% 3] 99.91% 4] 100.99% 5] 99.88% 6] 98.75%	1] 98.61% 2[99.50% 3] 98.19% 4] 99.45% 5] 98.08% 6] 98.71%	1] 97.67% 2] 96.07% 3] 95.27% 4] 97.87% 5] 95.07% 6] 96.67%
Water content	NMT 5.5%	3.51%	4.05%	4.37%
Content Uniformity	Acceptace value : NMT 15.0 when determined on 10 individual unit	3.0	NA	2.8
Assay	90% to 120%	99.58%	98.74%	98.19%

Accelerated Stability Study Report

Name of Product	:	Doxycycline Capsules USP 100 mg	**Batch No**	:	M 153
Description of the pack	:	10's ALU-PVC Blister Pack	**Mfg. Date**	:	July 2011
Parameters and test method monitored	:	Description, Identification, average weight, D.T, Dissolution test, Water , CU, Assay, & MLT	**Expiry Date**	:	June 2014
Date of Initiation	:	July 2011	**Storage conditions**	:	40° ± 2°C and 75% ± 5% RH
			Date of completion	:	Jan 2012

TEST	LIMITS	RESULTS OF ANALYSIS		
		INITIAL	3 Month	6 Month
Total aerobic microbial count				
Bacteria	NMT 1000 cfu/g	30 cfu/g	35 cfu/g	35 cfu/g
Fungi	NMT 100 cfu/g	Absent	Absent	Absent
Test for specified microorganisms:				
E.Coli	Absent in 1 gm	Absent	Absent	Absent
Salmonellae	Absent in 10 gm	Absent	Absent	Absent
Pseudomonads	Absent in 1 gm	Absent	Absent	Absent
Staph.aureus	Absent in 1 gm	Absent	Absent	Absent

Approved by:
QA Mr. S.M. Daptardaar
(QA Manager)

b) Estudio de estabilidad a tiempo real:

REAL TIME STABILITY STUDY REPORT

Name of Product		:	Doxycycline Capsules USP 100 mg			**Batch No.**	:	M 151		
Description of the pack		:	10's ALU-PVC Blister Pack			**Mfg. Date**	:	July 2011		
Parameters and Test methods monitored		:	Description, Identification, average weight, D.T, Dissolution test, Water , CU, Assay, & MLT			**Expiry Date**	:	June 2014		
Date of Initiation		:	July 2011			**Storage conditions**	:	30°C ± 2°C and 65%± 5% RH		
						Date of completion	:	Oct 2014		
TESTS	**LIMITS**	**RESULTS OF ANALYSIS**								
		INITIAL	**3 Month**	**6 Month**	**9 Month**	**12 Month**	**18 months**	**24 Month**	**36 Month**	**39 month**
Description	Hard gelatin capsules size 3, having green cap and green body	Hard gelatin capsules size 3, having green cap and green body	Hard gelatin capsules size 3, having green cap and green body	Hard gelatin capsules size 3, having green cap and green body	Hard gelatin capsules size 3, having green cap and green body	Hard gelatin capsules size 3, having green cap and green body	Hard gelatin capsules size 3, having green cap and green body	Hard gelatin capsules size 3, having green cap and green body	Hard gelatin capsules size 3, having green cap and green body	Hard gelatin capsules size 3, having green cap and green body
Identification	The principal peak in the chromatograph obtained with the test solution corresponds to the peak in the chromatograph obtained with the reference solution	The principal peak in the chromatograph obtained with the test solution corresponds to the peak in the chromatograph obtained with the reference solution	NA	NA	NA	NA	NA	NA	The principal peak in the chromatograph obtained with the test solution corresponds to the peak in the chromatograph obtained with the reference solution	The principal peak in the chromatograph obtained with the test solution corresponds to the peak in the chromatograph obtained with the reference solution
Average Weight	225mg–275mg	252 mg	NA	NA	NA	NA	NA	NA	253 mg	254 mg
Disintegration test	NMT 30 mins.	5 min	5 min	6 min	6 min	6 min	7 min	7 min	7 min	8 min
Dissolution test	NLT 85 % (Q) in 60 min	1] 101.64% 2] 99.89% 3] 101.68% 4] 99.62% 5] 100.37% 6] 100.53%	1] 100.35% 2] 100.03% 3] 99.29% 4] 98.36% 5] 100.50% 6] 98.13%	1] 97.58% 2] 98.66% 3] 97.74% 4] 98.97% 5] 99.51% 6] 97.20%	1] 97.21% 2] 96.86% 3] 98.19% 4] 96.48% 5] 98.83% 6] 97.21%	1] 96.46% 2] 95.82% 3] 95.47% 4] 96.29% 5] 96.58% 6] 95.52%	1] 94.69% 2] 95.06% 3] 94.26% 4] 95.59% 5] 96.94% 6] 94.79%	1] 93.56% 2] 95.48% 3] 94.88% 4] 95.68% 5] 93.35% 6] 95.58%	1] 92.32% 2] 91.97% 3] 91.54% 4] 92.52% 5] 93.67% 6] 93.54%	1] 91.32% 2] 91.81% 3] 91.47% 4] 91.47% 5] 93.14% 6] 93.74%
Content Uniformity	Acceptace value : NMT 15.0 when determined on 10 individual unit	2.5	NA	NA	NA	NA	NA	NA	2.6	2.6

REAL TIME STABILITY STUDY REPORT

Name of Product		:	Doxycycline Capsules USP 100 mg			**Batch No.**	:	M 151		
Description of the pack		:	10's ALU-PVC Blister Pack			**Mfg. Date**	:	July 2011		
Parameters and Test methods monitored		:	Description, Identification, average weight, D.T, Dissolution test, Water , CU, Assay, & MLT			**Expiry Date**	:	June 2014		
Date of Initiation		:	July 2011			**Storage conditions**	:	30°C ± 2°C and 65%± 5% RH		
						Date of completion	:	Sept 2014		
TESTS	**LIMITS**	**RESULTS OF ANALYSIS**								
		INITIAL	**3 Month**	**6 Month**	**9 Month**	**12 Month**	**18 months**	**24 Month**	**36 Month**	**39 month**
Water Content	NMT 5.5%	3.12%	3.21%	3.42	3.48	3.52	3.62%	3.63%	3.58%	3.85%
Assay	90% to 120%	99.31%	99.15%	98.73%	98.29%	97.95%	97.69%	97.34%	96.95%	96.49%
Total aerobic microbial count										
Bacteria	NMT 1000 cfu/g	34 cfu/g	38 cfu/g	40 cfu/g	40 cfu/g	42 cfu/g	45 cfu/g	45cfu/g	50 cfu/g	50 cfu/g
Fungi	NMT 100 cfu/g	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent
Test for specified microorganisms:										
E.Coli	Absent in 1 gm	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent
Salmonellae	Absent in 10 gm	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent
Pseudomonads	Absent in 1 gm	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent
Staph.aureus	Absent in 1 gm	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent

Approved by:
Mr. S.M.Deptardar
(QA Manager)

REAL TIME STABILITY STUDY REPORT

Name of Product : Doxycycline Capsules USP 100 mg		**Batch No.** : M 152	
Description of the pack : 10's ALU-PVC Blister Pack		**Mfg. Date** : July 2011	
Parameters and Test methods monitored : Description, Identification, average weight, D.T, Dissolution test, Water , CU, Assay, & MLT		**Expiry Date** : June 2014	
Date of Initiation : July 2011		**Storage conditions** : 30°C ± 2°C and 65%± 5% RH	
		Date of completion : Oct 2014	

TESTS	LIMITS	RESULTS OF ANALYSIS								
		INITIAL	3 Month	6 Month	9 Month	12 Month	18 months	24 Month	36 Month	39 month
Description	Hard gelatin capsules size 3, having green cap and green body	Hard gelatin capsules size 3, having green cap and green body	Hard gelatin capsules size 3, having green cap and green body	Hard gelatin capsules size 3, having green cap and green body	Hard gelatin capsules size 3, having green cap and green body	Hard gelatin capsules size 3, having green cap and green body	Hard gelatin capsules size 3, having green cap and green body	Hard gelatin capsules size 3, having green cap and green body	Hard gelatin capsules size 3, having green cap and green body	Hard gelatin capsules size 3, having green cap and green body
Identification	The principal peak in the chromatograph obtained with the test solution corresponds to the peak in the chromatograph obtained with the reference solution	The principal peak in the chromatograph obtained with the test solution corresponds to the peak in the chromatograph obtained with the reference solution	NA	NA	NA	NA	NA	NA	The principal peak in the chromatograph obtained with the test solution corresponds to the peak in the chromatograph obtained with the reference solution	The principal peak in the chromatograph obtained with the test solution corresponds to the peak in the chromatograph obtained with the reference solution
Average Weight	225mg–275mg	251 mg	NA	NA	NA	NA	NA	NA	253 mg	253 mg
Disintegration test	NMT 30 mins	5 min	5 min	5 min	6 min	7 min	6 min	6 min	7 min	7 min
Dissolution test	NLT 85 % (Q) in 60 min	1] 99.06% 2] 101.11% 3] 100.28% 4] 99.29% 5] 101.07% 6] 99.16%	1] 99.41% 2] 98.04% 3] 98.56% 4] 99.41% 5] 98.51% 6] 98.82%	1] 98.06% 2] 97.48% 3] 97.11% 4] 98.27% 5] 98.90% 6] 97.48%	1] 97.74% 2] 96.68% 3] 98.92% 4] 96.26% 5] 97.30% 6] 98.93%	1] 95.24% 2] 96.86% 3] 95.48% 4] 96.27% 5] 95.46% 6] 96.92%	1] 94.06% 2] 95.00% 3] 96.17% 4] 93.11% 5] 95.62% 6] 94.95%	1] 93.31% 2] 94.13% 3] 93.56% 4] 93.00% 5] 92.43% 6] 93.80%	1] 92.82% 2] 93.56% 3] 92.18% 4] 93.42% 5] 91.28% 6] 92.51%	1] 90.82% 2] 92.46% 3] 91.28% 4] 92.32% 5] 92.18% 6] 91.41%
Content Uniformity	Acceptace value : NMT 15.0 when determined on 10 individual unit	2.4	NA	NA	NA	NA	NA	NA	2.6	2.4

REAL TIME STABILITY STUDY REPORT

Name of Product : Doxycycline Capsules USP 100 mg		**Batch No.** : M 152	
Description of the pack : 10's ALU-PVC Blister Pack		**Mfg. Date** : July 2011	
Parameters and Test methods monitored : Description, Identification, average weight, D.T, Dissolution test, Water & Assay		**Expiry Date** : June 2014	
Date of Initiation : July 2011		**Storage conditions** : 30°C ± 2°C and 65%± 5% RH	
		Date of completion : Oct 2014	

TESTS	LIMITS	RESULTS OF ANALYSIS								
		INITIAL	3 Month	6 Month	9 Month	12 Month	18 months	24 Month	36 Month	39 month
Water Content	NMT 5.5%	2.14 %	2.21%	2.42	2.48	2.52	2.42%	2.74%	2.85%	3.02%
Assay	90% to 120%	99.84%	99.65%	99.123%	98.88%	98.76%	98.42%	98.14%	97.83%	97.24%
Total aerobic microbial count										
Bacteria	NMT 1000 cfu/g	40c ia/g	42 cfu/g	40 cfu/g	40 cfu/g	42 cfu/g	40 cfu/g	40cfu/g	45 cfu/g	50 cfu/g
Fungi	NMT 100 cfu/g	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent
Test for specified microorganisms:										
E.Coli	Absent in 1 gm	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent
Salmonellae	Absent in 10 gm	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent
Pseudomonads	Absent in 1 gm	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent
Staph.aureus	Absent in 1 gm	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent

Approved By:
Mr.S.M.Daptardar
(QA Manager)

REAL TIME STABILITY STUDY REPORT

Name of Product	:	Doxycycline Capsules USP 100 mg	**Batch No.**	:	M153
Description of the pack	:	10's ALU-PVC Blister Pack	**Mfg. Date**	:	July 2011
Parameters and Test methods monitored	:	Description, Identification, average weight, D.T, Dissolution test, Water , CU,Assay, & MLT	**Expiry Date**	:	June 2014
Date of Initiation	:	July 2011	**Storage conditions**	:	30°C ± 2°C and 65%± 5% RH
			Date of completion	:	Oct 20174

TESTS	LIMITS	RESULTS OF ANALYSIS								
		INITIAL	3 Month	6 Month	9 Month	12 Month	18 months	24 Month	36 Month	39 month
Description	Hard gelatin capsules size 3, having green cap and green body	Hard gelatin capsules size 3, having green cap and green body	Hard gelatin capsules size 3, having green cap and green body	Hard gelatin capsules size 3, having green cap and green body	Hard gelatin capsules size 3, having green cap and green body	Hard gelatin capsules size 3, having green cap and green body	Hard gelatin capsules size 3, having green cap and green body	Hard gelatin capsules size 3, having green cap and green body	Hard gelatin capsules size 3, having green cap and green body	Hard gelatin capsules size 3, having green cap and green body
Identification	The principal peak in the chromatograph obtained with the test solution corresponds to the peak in the chromatograph obtained with the reference solution	The principal peak in the chromatograph obtained with the test solution corresponds to the peak in the chromatograph obtained with the reference solution	NA	NA	NA	NA	NA	NA	The principal peak in the chromatograph obtained with the test solution corresponds to the peak in the chromatograph obtained with the reference solution	The principal peak in the chromatograph obtained with the test solution corresponds to the peak in the chromatograph obtained with the reference solution
Average Weight	225mg–275mg	252 mg	NA	NA	NA	NA	NA	NA	254 mg	254 mg
Disintegration test	NMT 30 mins.	5 min	5 min	5 min	5 min	6 min	6 min	7 min	7 min	8 min
Dissolution test	NLT 85 % (Q) in 60 min	1] 101.56% 2] 99.82% 3] 100.40% 4] 99.13% 5] 101.45% 6] 99.82%	1] 99.22% 2] 98.01% 3] 98.54% 4] 97.01% 5] 99.77% 6] 98.47%	1] 98.21% 2] 97.75% 3] 97.33% 4] 96.12% 5] 98.03% 6] 96.72%	1] 97.74% 2] 96.68% 3] 98.92% 4] 96.26% 5] 97.30% 6] 98.93%	1] 95.88% 2] 94.52% 3] 96.85% 4] 96.09% 5] 95.22% 6] 95.23%	1] 93.89% 2] 94.07% 3] 95.69% 4] 93.11% 5] 94.95% 6] 94.29%	1] 94.72% 2] 91.24% 3] 92.78% 4] 93.26% 5] 93.56% 6] 92.10%	1] 91.32% 2] 92.50% 3] 93.14% 4] 93.12% 5] 91.62% 6] 92.58%	1] 90.32% 2] 91.71% 3] 92.58% 4] 92.42% 5] 90.82% 6] 91.87%
Content Uniformity	Acceptace value : NMT 15.0 when determined on 10 individual unit	3.0	NA	NA	NA	NA	NA	NA	3.1	3.1

REAL TIME STABILITY STUDY REPORT

Name of Product	:	Doxycycline Capsules USP 100 mg	**Batch No.**	:	M 153
Description of the pack	:	10's ALU-PVC Blister Pack	**Mfg. Date**	:	July 2011
Parameters and Test methods monitored	:	Description, Identification, average weight, D.T, Dissolution test, Water , CU, Assay, & MLT	**Expiry Date**	:	June 2014
Date of Initiation	:	July 2011	**Storage conditions**	:	30°C ± 2°C and 65%± 5% RH
			Date of completion	:	Oct 2014

TESTS	LIMITS	RESULTS OF ANALYSIS								
		INITIAL	3 Month	6 Month	9 Month	12 Month	18 months	24 Month	36 Month	39 month
Water Content	NMT 5.5%	1.21%	2.51%	2.68%	3.16%	3.52%	3.84%	4.10%	4.22%	4.12%
Assay	90% to 120%	99.78%	99.55%	98.73%	98.45%	98.18%	97.83%	97.62%	96.91%	96.42%
Total aerobic microbial count										
Bacteria	NMT 1000 cfu/g	30 cfu/g	32cfu/g	35cfu/g	35 cfu/g	40 cfu/g	40 cfu/g	45cfu/g	45 cfu/g	50 cfu/g
Fungi	NMT 100 cfu/g	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent
Test for specified microorganisms:										
E.Coli	Absent in 1 gm	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent
Salmonellae	Absent in 10 gm	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent
Pseudomonads	Absent in 1 gm	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent
Staph.aureus	Absent in 1 gm	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent

QA

Approved By:
Mr. S.M.Daptardar
QA Manager

IV. DISCUSIÓN

De acuerdo a los resultados obtenidos en el Estudio de Estabilidad, tanto Acelerado como a Tiempo Real de los lotes M151, M152 y M153, se puede verificar que los lotes estudiados no muestran deterioro físico o químico en el envase utilizado (Blíster ALU/PVC). No se evidencia una disminución significativa en la valoración del activo, y los parámetros analizados se mantuvieron dentro de los límites especificados, durante al menos 36 meses en el estudio a tiempo real y durante 6 meses en el estudio acelerado.

V. CONCLUSIÓN

Basado en los datos adquiridos de los estudios de estabilidad a tiempo real y acelerado, se concluye que el producto analizado es estable por un periodo de 36 meses si se almacena en su envase original cerrado, a una temperatura no mayor a 30°C ± 2°C y una humedad ambiental de 65% ± 5%.

VI. ESPECIFICACIÓN DE LA VIDA ÚTIL

Se propone un periodo de eficacia para Doxiciclina cápsulas 100 mg de 36 meses a partir de su fecha de fabricación almacenándolo en su envase original (Estuche de cartulina impresa que contiene Blíster ALU/PVC), más folleto de información al paciente, todo debidamente rotulado y sellado, a una temperatura ambiente no mayor a 30°C ± 2°C, protegido de la luz y la humedad.