

APO-PREGABALIN Capsules 75 mg and 150 mg

6. FINISHED PRODUCT

6.4 Stability

6.4.1 Stability Summary and Conclusion

The following batches of APO-PREGABALIN Capsules 75 mg and 150 mg manufactured at Apotex Research Private Limited, packaged in blisters are placed on stability study.

Summary of Stability Studies Submitted is provided in the table below

Batch Number	Strength	Pack Type	Pack Size	Storage Conditions (°C / % RH)	Completed Test Intervals
PGCF/10240	75 mg	Blister	10's	25°C/60%RH	24 months
PGCF/10240		Blister	10's	40°C/75%RH	6 months
PGCF/10255		Blister	10's	25°C/60%RH	24 months
PGCF/10255		Blister	10's	40°C/75%RH	6 months
PGCF/10267*		Blister	10's	25°C/60%RH	24 months
PGCF/10267*		Blister	10's	40°C/75%RH	6 months
PGCD/10238	150 mg	Blister	10's	25°C/60%RH	24 months
PGCD/10238		Blister	10'S	40°C/75%RH	6 months
PGCD/10253		Blister	10's	25°C/60%RH	24 months
PGCD/10253		Blister	10'S	40°C/75%RH	6 months
PGCD/10265*		Blister	10's	25°C/60%RH	24 months
PGCD/10265*		Blister	10'S	40°C/75%RH	6 months

Note:

*Batches mentioned above were manufactured and charged for stability study for other market however the formulation and manufacturing process are identical to the proposed formulation and manufacturing process proposed in this application.

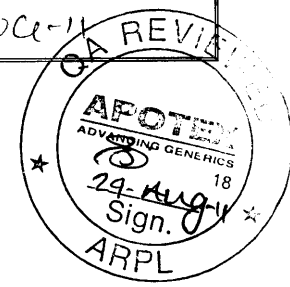
CONTROLLED ROOM TEMPERATURE CONDITIONS STABILITY SUMMARY REPORT

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ADVANCING GENERICS

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ACCELERATED CONDITIONS STABILITY SUMMARY REPORT												
Product Name: Pregabalin capsules 75 mg			Drug Substance Manufacturer: Srinu pharmaceuticals Ltd.,			Manufacturing Date: NOV-2010			Batch No.: PGCF/10240			
Product Description: Hard gelatin capsules with opaque orange cap and opaque white body. Imprinted APO P75 in black ink. Filled with white powder.			Manufacturing Site: SRINI PHARMACEUTICALS LTD Plot No.10, Road. No:8, film nagar Jubilee Hills, Hyderabad-500033, AP, India. ACTIVE RM BATCH NO.:JN9054, JN9055			Batch Size: 1,40,000 Capsules			Pack Size: Blister 10's (Alu-PVC)			
Packaging Description: Blister: Forming foil: PVC CLEAR FILM 250 MIC Lidding Foil: Highly heat resistant lacquer on the basis of polyester pure aluminum, hard tempered(0.025 mm) Carton: Super chrome white duplex board without varnish						Packaging Date: 15-DEC-10			Stability Start Date: 15-DEC-10			
TIMEPOINT	Initial**	1 month	2 months	3 months	6 months	9 months	12 months	18 months	24 months	36 months	IDENTIFICATION	
Date due	N/A	17-JAN-11	15-FEB-11	15-MAR-11	15-JUN-11	N/A	N/A	N/A	N/A	N/A	Compound Name : PRB-II: 3-Isobutyl glutaric acid (Synthetic impurity/ Degradation product) PRB-III: 4-Isobutyl - pyrrolidin-2-one (Degradation product)	
Date started	15-DEC-10	17-JAN-11	15-FEB-11	15-MAR-11	15-JUN-11	N/A	N/A	N/A	N/A	N/A		
Date finished	31-DEC-10	10-FEB-11	16-MAR-11	26-MAR-11	16-JUL-11	N/A	N/A	N/A	N/A	N/A		
Specifications used *	PRB-FP-CAP-75MG-GLOBAL-RD, Version 1	PRB-TP-ST-CAP-GLOBAL-RD, Version 1	PRB-TP-ST-CAP-GLOBAL-RD, Version 1	PRB-TP-ST-CAP-GLOBAL-RD, Version 1	PRB-TP-ST-CAP-GLOBAL-RD, Version 1	N/A	N/A	N/A	N/A	N/A		
Appearance	Complies	Complies	Complies	Complies	Complies	N/A	N/A	N/A	N/A	N/A		
Identification (HPLC)	Complies	Complies	Complies	Complies	Complies	N/A	N/A	N/A	N/A	N/A		
Assay: 90.0 - 110.0% (% of claim)	99.5%	99.6%	100.2%	99.7%	99.7%	N/A	N/A	N/A	N/A	N/A		
Dissolution : Q=80% Time = 15 min	99%	99%	97%	97%	99%	N/A	N/A	N/A	N/A	N/A		
Dissolution range	97%-102%	96%-102%	94%-100%	94%-100%	95%-103%	N/A	N/A	N/A	N/A	N/A		
Dissolution-S1/S2/S3	S1	S1	S1	S1	S1	N/A	N/A	N/A	N/A	N/A		
Degradation products						N/A	N/A	N/A	N/A	N/A		
i. PRB-II: NMT 0.2%	ND	ND	ND	ND	ND	N/A	N/A	N/A	N/A	N/A		
ii. PRB-III: NMT 0.2%	ND	BRT	BRT	BRT	BRT	N/A	N/A	N/A	N/A	N/A		
iii. Unidentified Impurity : NMT 0.2% each	BRT(0.06%)	0.1%	0.2%	0.2%	0.3%##	N/A	N/A	N/A	N/A	N/A		
iv. Total Impurities : NMT 1.0%	BRT	0.1%	0.2%	0.2%	0.3%	N/A	N/A	N/A	N/A	N/A		
Comments: Expiry Date: OCT-2012 * Specification as per the current test profile PRB-TP-ST-CAP-DOM-RD, Version 1, effective on 16-Aug-2011 ## Degradation products results reported as per OOS11-25												
N/A=Not applicable; ND=Not detected; NMT=Not more than; NLT=Not less than; BRT = Below Reporting Threshold. ** As per Specification and COA.												
Reviewed by:	Date:				Approved by:				Date:			
D. Srinivasulu	29-Aug-11				A. S. Reddy				28-Aug-11			



STABILITY SUMMARY REPORT

CONTROLLED ROOM TEMPERATURE CONDITIONS STABILITY SUMMARY REPORT

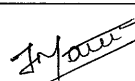
Product Name: Pregabalin capsules 75 mg			Drug Substance Manufacturer: Srini pharmaceuticals Ltd.,			Manufacturing Date: DEC-2010			Batch No.: PGCF/10255
Product Description: Hard gelatin capsules with opaque orange cap and opaque white body. Imprinted APO P75 in black ink. Filled with white powder.			Manufacturing Site: SRINI PHARMACEUTICALS LTD Plot No.10, Road. No:8, film nagar Jubilee Hills, Hyderabad-500033, AP, India.			Batch Size: 1,40,000 Capsules			Pack Size: Blister 10's (Alu-PVC)
Packaging Description: Blister: Forming foil: PVC CLEAR FILM 250 MIC Lidding Foil: Highly heat resistant lacquer on the basis of polyester pure aluminum, hard tempered(0.025 mm) Carton: Super chrome white duplex board without varnish			ACTIVE RM BATCH NO.: JR9473, JR9474			Packaging Date: 21-JAN-11			Stability Start Date: 03-FEB-11

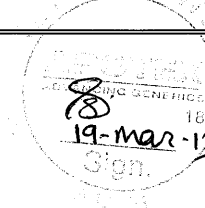
TIMEPOINT	Initial**	3 months	6 months	9 months	12 months	18 months	24 months	36 months	IDENTIFICATION
Date due	N/A	03-MAY-11	03-AUG-11	03-NOV-11	03-FEB-12	03-AUG-12	04-FEB-13		Compound Name :
Date started	22-JAN-11	03-MAY-11	03-AUG-11	03-NOV-11	03-FEB-12	03-AUG-12	04-FEB-13		PRB-II: 3-Isobutyl glutaric acid (Synthetic impurity/ Degradation product)
Date finished	31-JAN-11	03-JUN-11	23-AUG-11	06-DEC-11	08-MAR-12	30-AUG-12	06-MAR-13		PRB-III: 4-Isobutyl -pyrrolidin-2-one (Degradation product)
Specifications used *	PRB-FP-CAP-75MG- GLOBAL-RD, Version 1	PRB-TP-ST-CAP- GLOBAL-RD Version.1	PRB-TP-ST-CAP- GLOBAL-RD Version.1	PRB-TP-ST-CAP- DOM-RD, Version.2	PRB-TP-ST-CAP- DOM-RD, Version.2	PRB-TP-ST-CAP- DOM-RD, Version.3	PRB-TP-ST-CAP- DOM-RD, Version.4		PRB-V: 1-((2S,3R,4R,5R,6R)-4,5-dihydroxy-6-(hydromethyl)-2- ((2R,3S,4R,5R,6S)-4,5,6-trihydroxy-2- (hydroxymethyl)tetrahydro-2H-pyran-3-yloxy)tetrahydro-2H- pyran-3-yl)-4-isobutylpyrrolidin-2-one.
Appearance	Complies	Complies	Complies	Complies	Complies	Complies	Complies		
Identification (HPLC)	Complies	Complies	Complies	Complies	Complies	Complies	Complies		
Assay: 90.0 - 110.0% (% of claim)	99.7%	99.6%	99.7%	98.1%	99.5%	102.1%	101.3%		
Dissolution : As per USP/EP Q=80% Time = 15 min	101%	101%	101%	98%	98%	99%	100%		
Dissolution range	100% - 102%	97% - 106%	100% - 104%	96% - 100%	96% - 101%	97% - 100%	99% - 102%		
Dissolution-S1/S2/S3	S1	S1	S1	S1	S1	S1	S1		
Degradation products									
i. PRB-V:NMT 0.2%	-	-	-	-	-	0.1%	BRT		
ii. PRB-II:NMT 0.2%	ND	ND	ND	ND	ND	ND	BRT		
iii. PRB-III:NMT 0.2%	ND	BRT	BRT	BRT	BRT	BRT	BRT		
iv. Unidentified Impurity : NMT 0.2% each	BRT	BRT(0.064%)	BRT (0.087%)	0.1%	BRT (0.070%)	ND	ND		
v. Total Impurities : NMT 1.0%	BRT	BRT	BRT	0.1%	BRT	0.1%	BRT		

Comments: Expiry Date: NOV-2012
 * Specification as per the current test profile PRB-TP-ST-CAP-DOM-RD, Version 4, effective on 25-Jan-2013

N/A=Not applicable; ND=Not detected; NMT=Not more than; NLT=Not less than; BRT = Below Reporting Threshold.

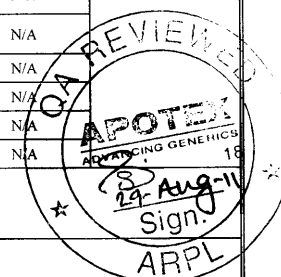
** As per Specification and COA.

Reviewed by: 	Date: 12-MAR-13	Approved by: 	Date: 12-MAR-13
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STABILITY SUMMARY REPORT

ACCELERATED CONDITIONS STABILITY SUMMARY REPORT											
Product Name: Pregabalin capsules 75 mg			Drug Substance Manufacturer: Srini pharmaceuticals Ltd.,			Manufacturing Date: DEC-2010			Batch No.: PGCF/10255		
Product Description: Hard gelatin capsules with opaque orange cap and opaque white body. Imprinted APO P75 in black ink. Filled with white powder.			Manufacturing Site: SRINI PHARMACEUTICALS LTD Plot No.10, Road. No:8, film nagar Jubilee Hills, Hyderabad-500033, AP, India ACTIVE RM BATCH NO.:JR9473, JR9474			Batch Size: 1,40,000 Capsules			Pack Size: Blister 10's (Alu-PVC)		
Packaging Description: Blister: Forming foil: PVC CLEAR FILM 250 MIC Lidding Foil: Highly heat resistant lacquer on the basis of polyester pure aluminum, hard tempered(0.025 mm) Carton: Super chrome white duplex board without varnish						Packaging Date: 21-JAN-11			Stability Start Date: 03-FEB-11		
TIMEPOINT	Initial**	1 month	2 months	3 months	6 months	9 months	12 months	18 months	24 months	36 months	IDENTIFICATION
Date due	N/A	03-MAR-11	05-APR-11	03-MAY-11	03-AUG-11	N/A	N/A	N/A	N/A	N/A	Compound Name :
Date started	22-JAN-11	03-MAR-11	05-APR-11	03-MAY-11	03-AUG-11	N/A	N/A	N/A	N/A	N/A	PRB-II 3-Isobutyl glutaric acid (Synthetic impurity/ Degradation product)
Date finished	31-JAN-11	01-APR-11	03-MAY-11	03-JUN-11	23-AUG-11	N/A	N/A	N/A	N/A	N/A	PRB-III 4-Isobutyl - pyrrolidin-2-one (Degradation product)
Specifications used *	PRB-FP-CAP-75MG- GLOBAL-RD, Version.1	PRB-TP-ST-CAP- GLOBAL-RD Version.1	PRB-TP-ST-CAP- GLOBAL-RD Version.1	PRB-TP-ST-CAP- GLOBAL-RD Version.1	PRB-TP-ST-CAP- GLOBAL-RD Version.1	N/A	N/A	N/A	N/A	N/A	
Appearance	Complies	Complies	Complies	Complies	Complies	N/A	N/A	N/A	N/A	N/A	
Identification (HPLC)	Complies	Complies	Complies	Complies	Complies	N/A	N/A	N/A	N/A	N/A	
Assay:90.0 - 110.0% (% of claim)	99.7%	100.2%	100.7%	100.4%	98.6%	N/A	N/A	N/A	N/A	N/A	
Dissolution : Q=80% Time = 15 min	101%	97%	98%	96%	99%	N/A	N/A	N/A	N/A	N/A	
Dissolution range	100% - 102%	95% - 100%	94% - 104%	85% - 99%	95% - 100%	N/A	N/A	N/A	N/A	N/A	
Dissolution-S1/S2/S3	S1	S1	S1	S1	S1	N/A	N/A	N/A	N/A	N/A	
Degradation products						N/A	N/A	N/A	N/A	N/A	
i. PRB-II:NMT 0.2%	ND	ND	ND	BRT	BRT	N/A	N/A	N/A	N/A	N/A	
ii. PRB-III:NMT 0.2%	ND	BRT	BRT	BRT	BRT	N/A	N/A	N/A	N/A	N/A	
iii. Unidentified Impurity : NMT 0.2% each	BRT	BRT(0.074%)	0.1%	0.2%	0.2%	N/A	N/A	N/A	N/A	N/A	
iv. Total Impurities : NMT 1.0%	BRT	BRT	0.1%	0.2%	0.2%	N/A	N/A	N/A	N/A	N/A	
Comments: Expiry Date: NOV-2012 * Specification as per the current test profile PRB-TP-ST-CAP-DOM-RD, Version 2, effective on 16-Aug-2011											
N/A=Not applicable; ND=Not detected; NMT=Not more than; NLT=Not less than; BRT = Below Reporting Threshold.											
** As per Specification and COA.											
Reviewed by: D. S. S. S. S.		Date: 29 Aug 11			Approved by: A. S. S. S. S.			Date: 28-Aug-11			



PRODUCT NAME: Pregabalin Capsules 75mg		BATCH NO.: PGCF/10267		PACKAGING DESCRIPTION:					
ACTIVE INGREDIENT(S): Pregabalin		BATCH SIZE: 70,000 Capsules		FORMING FOIL: PVC CLEAR FILM 250 MIC					
LABEL CLAIM: 75mg		PACKAGING SIZE: 10 X 10 Capsules		LIDDING FOIL: Highly heat resistant lacquer on the basis of polyester pure aluminum, hard tempered(0.025mm)					
PACKAGE TYPE: Blister(Alu-PVC)		MFG. SITE: ARPL, Bangalore		UNIT DOSAGE CARTONS: Super chrome white duplex board without varnish					
ACTIVE RM SOURCE: Srinu pharmaceuticals Ltd.,		MFG. DATE: DEC-2010		PACKAGING DATE: 21-JAN-11					
ACTIVE RM BATCH NOS.: JR9475, JR9476		STORAGE CONDITIONS: 25°C / 60%RH		PACKAGING SITE: ARPL, Bangalore					
STABILITY PROTOCOL NO.: ARI/01/PRT/STB/277/A									
PRODUCT DESCRIPTION: Hard gelatin capsules with opaque orange cap and opaque white body. Imprinted APO P75 in black ink. Filled with white powder.									
STUDY START DATE: 03-FEB-11	TIME POINTS:	INITIAL	3 MONTHS	6 MONTHS	9 MONTHS	12 MONTHS	18 MONTHS	24 MONTHS	36 MONTHS
	DATE PULLED:	N/A	03-MAY-11	03-AUG-11	03-NOV-11	03-FEB-12	03-AUG-12	04-FEB-13	
	TESTING START DATE:	22-JAN-11	03-MAY-11	03-AUG-11	03-NOV-11	03-FEB-12	03-AUG-12	04-FEB-13	
	TESTING END DATE:	31-JAN-11	03-JUN-11	23-AUG-11	06-DEC-11	08-MAR-12	31-AUG-12	06-MAR-13	
TEST	ACCEPTANCE CRITERIA								
Specifications used *		PRB-FP-CAP-75MG-GLOBAL-RD, Version 1	PRB-TP-ST-CAP-GLOBAL-RD Version.1	PRB-TP-ST-CAP-GLOBAL-RD Version.1	PRB-TP-ST-CAP-AUS-RD, Version 3	PRB-TP-ST-CAP-AUS-RD, Version 3	PRB-TP-ST-CAP-AUS-RD, Version 4	PRB-TP-ST-CAP-AUS-RD, Version 4	
Appearance	Refer to product description	Confirms	Confirms	Confirms	Confirms	Confirms	Confirms	Confirms	
Identification	HPLC Retention Time: Corresponds to standard	Confirms	Confirms	Confirms	Confirms	Confirms	Confirms	Confirms	
Assay	92.5 - 107.5% (% of claim)	101.8%	100.6%	100.5%	101.6%	98.6%	99.5%	100.0%	
Dissolution	As per USP/EP	104%, 104%	100%, 99%	99%, 100%	96%, 97%	97%, 96%	99%, 99%	101%, 102%	
	Q=80%, Time = 15 min	101%, 100%	107%, 100%	99%, 100%	100%, 95%	95%, 98%	100%, 102%	97%, 99%	
		102%, 101%	100%, 99%	99%, 100%	98%, 95%	96%, 101%	99%, 99%	101%, 99%	
	Mean (% dissolved)	102%	101%	100%	97%	97%	100%	100%	
	Dissolution range (min-max)	100% - 104%	99% - 107%	99% - 100%	95% - 100%	95% - 101%	99% - 102%	97% - 102%	
Degradation Products	Dissolution stage	S1	S1	S1	S1	S1	S1	S1	
	PRB-II : NMT 0.2%	ND	ND	ND	ND	ND	ND	BRT	
	PRB-III : NMT 0.2%	ND	BRT	BRT	BRT	BRT	BRT	BRT	
	Unidentified Impurity :NMT 0.2% each	BRT	BRT(0.062%)	BRT (0.096%)	0.1%	BRT (0.068%)	0.1%	BRT	
	Total Impurities : NMT 1.0%	BRT	BRT	BRT	0.1%	BRT	0.1%	BRT	
Microbial Limits	a) Total Aerobic Microbial Count : NMT 1000 cfu/g	20 cfu/g	N/A	20 cfu/g	N/A	20 cfu/g	N/A	20 cfu/g	
	b) Total Yeast and Mould Count : NMT 100 cfu/g	Less than 10 cfu/g	N/A	Less than 10 cfu/g	N/A	Less than 10 cfu/g	N/A	Less than 10 cfu/g	
	c) E.coli : Absent in 1 g	Absent/g	N/A	Absent/g	N/A	Absent/g	N/A	Absent/g	
Water Content	NMT 5.0% (200 mg of sample)	-	-	-	-	-	1.55%	1.78%	

** As per Specification and COA
 * Specification as per the current test profile PRB-TP-ST-CAP-AUS-RD , Version.4, effective on 14-Jun-2012

ND = Not Detected	N/A = Not Applicable	NMT = Not More Than	NLT = Not Less Than	cfu = Colony forming units	BRT = Below Reporting Threshold
Verified by:		Date: 12-MAR-13	Approved by:		Date: 12-Mar-13

25-Mar-13
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PRODUCT NAME: Pregabalin Capsules 75mg		BATCH NO.: PGCF/10267		PACKAGING DESCRIPTION:			
ACTIVE INGREDIENT(S): Pregabalin		BATCH SIZE: 70,000 Capsules		FORMING FOIL: PVC CLEAR FILM 250 MIC			
LABEL CLAIM: 75mg		PACKAGING SIZE: 10 X 10 Capsules		LIDDING FOIL: Highly heat resistant lacquer on the basis of polyester pure aluminum, hard tempered(0.025mm)			
PACKAGE TYPE: Blister(Alu-PVC)		MFG. SITE: ARPL, Bangalore		UNIT DOSAGE CARTONS: Super chrome white duplex board without varnish			
ACTIVE RM SOURCE: Srinipha pharmaceuticals Ltd.,		MFG. DATE: DEC-2010		PACKAGING DATE: 21-JAN-11			
ACTIVE RM BATCH NOS. JR9475, JR9476		STORAGE CONDITIONS: 40°C / 75%RH		PACKAGING SITE: ARPL, Bangalore			
STABILITY PROTOCOL NO.: ARJ/01/PRT-STB/277/A							
PRODUCT DESCRIPTION: Hard gelatin capsules with opaque orange cap and opaque white body. Imprinted APO P75 in black ink. Filled with white powder.							
STUDY START DATE 03-FEB-11	TIME POINTS:	INITIAL	1 MONTH	2 MONTHS	3 MONTHS	6 MONTHS	
	DATE PULLED:	N/A	03-MAR-11	05-APR-11	03-MAY-11	03-AUG-11	
	TESTING START DATE:	22-JAN-11	03-MAR-11	05-APR-11	03-MAY-11	03-AUG-11	
	TESTING END DATE:	31-JAN-11	01-APR-11	03-MAY-11	03-JUN-11	23-AUG-11	
TEST	ACCEPTANCE CRITERIA						
Specifications used *		PRB-FP-CAP-75MG- GLOBAL-RD, Version 1	PRB-TP-ST-CAP- GLOBAL-RD Version 1	PRB-TP-ST-CAP- GLOBAL-RD Version 1	PRB-TP-ST-CAP- GLOBAL-RD Version 1	PRB-TP-ST-CAP- GLOBAL-RD Version 1	
Appearance	Refer to product description	Confirms	Confirms	Confirms	Confirms	Confirms	
Identification	HPLC Retention Time: Corresponds to standard	Confirms	Confirms	Confirms	Confirms	Confirms	
Assay	90.0 to 110.0% (% of claim)	101.8%	100.6%	101.4%	100.5%	102.6%	
Dissolution	As per USP/EP	104%, 104%	98%, 98%	99%, 93%	99%, 100%	98%, 94%	
	Q=80%, Time = 15 min	101%, 100%	100%, 99%	96%, 97%	96%, 96%	92%, 91%	
		102%, 101%	101%, 99%	97%, 100%	96%, 97%	96%, 97%	
	Mean (% dissolved)	102%	99%	97%	97%	95%	
	Dissolution range (min-max)	100% - 104%	98% - 101%	93% - 100%	96% - 100%	91% - 98%	
	Dissolution stage	S1	S1	S1	S1	S1	
Degradation Products	PRB-II : NMT 0.2%	ND	ND	ND	BRT	BRT	
	PRB-III : NMT 0.2%	ND	BRT	BRT	BRT	BRT	
	Unidentified Impurity :NMT 0.2% each	BRT	BRT(0.075%)	0.2%	0.2%	0.2%	
	Total Impurities : NMT 1.0%	BRT	BRT	0.2%	0.2%	0.3%	
Microbial Limits	a) Total Aerobic Microbial Count : NMT 1000 cfu/g	20 cfu/g	N/A	N/A	40 cfu/g	10 cfu/g	
	b) Total Yeast and Mould Count : NMT 100 cfu/g	Less than 10 cfu/g	N/A	N/A	Less than 10 cfu/g	Less than 10 cfu/g	
	c) E.coli : Absent in 1 g	Absent/g	N/A	N/A	Absent/g	Absent/g	
** As per Specification and COA * Specification as per the current test profile PRB-TP-ST-CAP-AUS-RD, Version 2, effective on 25-Aug-2011							
ND = Not Detected N/A = Not Applicable NMT = Not More Than NLT = Not Less Than cfu = Colony forming units BRT = Below Reporting Threshold							
Verified by: D. S. Srinivasulu		Date: 30-Aug-11		Approved by: A. S. Reddy		Date: 30-Aug-11	

