GCMC
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July 22, 2013

Rapamune Oral Solution 1 mg/mL

Declaration of Formula

I declare that in order to support the extension of shelf life to 36 months, three batches each of Rapamune 1 mg/mL Oral Solution (V0184A002, LBA003, LBA007) were manufactured at Patheon Inc., Mississauga, Ontario, Canada in accordance with the composition presented in Table 1 below.

Table 1: Composition of Rapamune Oral Solution 1 mg/mL

Names of Ingredient	Unit Dose
Sirolimus	1.0 mg
Polysorbate 80	10.8 mg
Phosphal 50 PG® *	100.0 mL
*Each 100 g of solvent mixture (Phosal 50 PG) contains: Phosphatidylcholine 57 g Soya fatty acids 2 g Ethanol 1.5 g – 2.5 g Monodiglycerides 3 g Propylene glycol 33.8 g – 41.2 g Ascorbyl Palmitate 0.2	

Suzanne Mayr 22-Jul-2013

Suzanne Mayr
Director
Global Chemistry, Manufacturing and Controls
Global Manufacturing Compliance

3.2.P.8. ESTABILIDAD

3.2.P.8.1. RESUMEN DE ESTABILIDAD Y CONCLUSIONES

Resumen

La evaluación de estabilidad de Rapamune solución oral, envasada en frascos de vidrio ámbar se ha completado en un plazo de 36 meses a 5 °C/HR ambiente para 3 lotes comerciales.

Se evaluó la descripción, el ensayo, la secorrapamicina, la pureza, el peróxido, el agua y los límites microbianos de las muestras de estabilidad. Todos los resultados están en conformidad con las especificaciones aprobadas.

Información de los lotes de medicamento

Las tablas de datos de estabilidad detalladas para los siguientes 3 lotes de Rapamune solución oral se incluyen en 3.2.P.8.3 Datos de estabilidad. Todos los lotes se fabricaron y envasaron en Patheon Inc, Canadá.

Tabla 3.2.P.8.1-1 Resumen de lotes de estabilidad

Número del lote	Envasado	Fecha de fabricación	Datos incluidos
V0184A002	Frasco de vidrio ámbar de 60 ml	02 abr 2007	0, 3, 6, 9, 12, 18, 24 y 36 meses a 5 °C ± 3 °C/HR ambiente
LBA003	Frasco de vidrio ámbar de 60 ml	13 ago 2008	0, 3, 6, 9, 12, 18, 24 y 36 meses a 5 °C ± 3 °C/HR ambiente
LBA007	Frasco de vidrio ámbar de 60 ml	4 feb 2009	0, 3, 6, 9, 12, 18, 24 y 36 meses a 5 °C ± 3 °C/HR ambiente

Condiciones de almacenamiento y frecuencia de evaluación

Los lotes se analizaron de acuerdo con el protocolo de estabilidad actualmente aprobado.

Conclusiones para período de validez, almacenamiento y etiquetado

Con base en los datos de estabilidad en tiempo real para Rapamune solución oral 1 mg/ml, se propone una fecha de vencimiento de 36 meses para medicamentos almacenados en condiciones refrigeradas de 5 °C ± 3 °C/humedad relativa (HR) ambiente en frascos de vidrio ámbar.

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SITE: PATHEON LABORATORY SERVICES / PLS

Stability Summary Report

Document Control Number: WYA-SP-095-0607-R3

Product Name: Rapamune Oral Solution, 1.0 mg/mL

Product Code / Lot Number / Customer Lot Number: LBA60/S / LBA003

Client: Wyeth Pharmaceuticals

Study Purpose: 2008 Annual Stability

Storage Condition: 5°C ± 3°C / Ambient R.H.

Time Interval: 0 – 36 Months

Package Size: 60 mL / Bottle

Date of Manufacture: 13/AUG/2008

Date in Chamber: 28/AUG/2008

Stability Start Date: 28/AUG/2008

Expiration Date: N/A

Stability Summary Approvals

Prepared By:	**Rosalind Seong**	**Date:**
Position:	Stability Coordinator	28 SEP 2011
Signature:		
Reviewed By:	**Debbie Nanba**	**Date:**
Position:	QC Supervisor, Stability	28 SEP 2011
Signature:		

Stability Summary Report for Rapamune Oral Solution, 1.0 mg/mL

LBA60/S / LBA003 **5°C ± 3°C / Ambient R.H.**

TEST	METHOD	SPECIFICATION		TIME (MONTHS)	
		Time Interval		Initial	6
		Pull Date		28/AUG/2008	02/MAR/2009
		Orientation		Horizontal	Horizontal
Description	Visual	Pale yellow to yellow solution, essentially particulate free.		Yellow solution essentially particulate free.	Pale yellow solution essentially particulate free.
Assay (HPLC) (Sum of Isomers B and C)	CTMLP-1701	0.90 – 1.10 mg/mL		0.97, 0.97 mg/mL X_2 = 0.97 mg/mL	0.99, 1.00 mg/mL X_2 = 1.00 mg/mL
Seco-Rapamycin (WAY-126792)	CTMLP-1701	NMT 8% of Sirolimus Label Claim		ND	2%
Purity[1]	CTMLP-1701	Total Other Degradation Impurities:	NMT 1% of Sirolimus Label Claim	ND	ND
		Largest Single Other Degradation Impurity:	NMT 0.5% of Sirolimus Label Claim	ND	ND
Peroxide Value	BP APP X F	NMT 10		0	0
Water	USP <921>	NMT 0.5%		0.1%	0.1%
Microbial Limit Tests	MM-931	Total Aerobic Microbial Count including Yeasts and Molds	NMT 100 CFU/mL	< 100 CFU/mL	NR
		E. coli	Absent	Absent / 10 mL	NR
		Salmonella species	Absent	Absent / 10 mL	NR
		P. aeruginosa	Absent	Absent / 10 mL	NR
		S. aureus	Absent	Absent / 10 mL	NR

Stability Summary Report for Rapamune Oral Solution, 1.0 mg/mL

LBA60/S / LBA003 **5°C ± 3°C / Ambient R.H.**

TEST	METHOD	SPECIFICATION		TIME (MONTHS)	
		Time Interval		12	18
		Pull Date		28/AUG/2009	01/MAR/2010
		Orientation		Inverted	Inverted
Description	Visual	Pale yellow to yellow solution, essentially particulate free. Should a haze be visible, the solution should be shaken. The presence of this haze does not affect product quality.		Yellow solution essentially particulate free.	Pale yellow solution, essentially particulate free.
Assay (HPLC) (Sum of Isomers B and C)	CTMLP-1701	0.90 – 1.10 mg/mL		1.00, 0.99 mg/mL X_2 = 1.00 mg/mL	0.99, 0.99 mg/mL X_2 = 0.99 mg/mL
Seco-Rapamycin (WAY-126792)	CTMLP-1701	NMT 8% of Sirolimus Label Claim		2%, 2% X_2 = 2%	3%, 3% X_2 = 3%
Purity[1]	CTMLP-1701	Total Other Degradation Impurities:	NMT 1% of Sirolimus Label Claim	ND	ND
		Largest Single Other Degradation Impurity:	NMT 0.5% of Sirolimus Label Claim	ND	ND
Peroxide Value	BP APP X F	NMT 10		0	0
Water	USP <921>	NMT 0.5%		0.1%	0.1%
Microbial Limit Tests[2]	MM-1044	Total Aerobic Microbial Count including Yeasts and Molds	NMT 100 CFU/mL	< 10 CFU/mL	NR
		E. coli	Absent/mL	Absent / mL	NR
		Salmonella species	Absent/10mL	Absent / 10 mL	NR
		P. aeruginosa	Absent/mL	Absent / mL	NR
		S. aureus	Absent/mL	Absent / mL	NR

Stability Summary Report for Rapamune Oral Solution, 1.0 mg/mL

LBA60/S / LBA003 **5°C ± 3°C / Ambient R.H.**

TEST	METHOD	SPECIFICATION		TIME (MONTHS)	
		Time Interval		24	36
		Pull Date		30/AUG/2010	29/AUG/2011
		Orientation		Inverted	Inverted
Description	Visual	Pale yellow to yellow solution, essentially particulate free. Should a haze be visible, the solution should be shaken. The presence of this haze does not affect product quality.		Pale yellow solution, particulate free. No haze present.	Pale yellow solution, essentially particulate free. Sample solution is clear with no haze.
Assay (HPLC) (Sum of Isomers B and C)	CTMLP-1701	0.90 – 1.10 mg/mL		0.98, 0.98 mg/mL X_2 = 0.98 mg/mL	0.98, 0.94 mg/mL X_2 = 0.96 mg/mL
Seco-Rapamycin (WAY-126792)	CTMLP-1701	NMT 8% of Sirolimus Label Claim		4%, 4% X_2 =4%	5%, 5% X_2 =5%
Purity[1]	CTMLP-1701	Total Other Degradation Impurities:	NMT 1% of Sirolimus Label Claim	<0.2%	ND
		Largest Single Other Degradation Impurity:	NMT 0.5% of Sirolimus Label Claim	<0.2%	ND
Peroxide Value	BP APP X F	NMT 10		0	0
Water	USP <921>	NMT 0.5%		0.1%	0.2%
Microbial Limit Tests[2]	MM-1044	Total Aerobic Microbial Count including Yeasts and Molds	NMT 100 CFU/mL	<10 CFU/ml	<10 CFU/ml
		E. coli	Absent/mL	Absent/ml	Absent/ml
		Salmonella species	Absent/10mL	Absent /10ml	Absent /10ml
		P. aeruginosa	Absent/mL	Absent/ml	Absent/ml
		S. aureus	Absent/mL	Absent/ml	Absent/ml

Notes:
ND = Not Detected
NR = Not Required
1. This does not include process impurities (such as WAY-124854, WAY-155618, WAY-125286) or Group II impurities which have been previously quantitated in the drug substance.
2. Updated for microbial harmonization as per CC #2009-WY-0986.

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SITE: PATHEON LABORATORY SERVICES / PLS

Stability Summary Report

Document Control Number: WYA-SP-095-0607-R3

Product Name: Rapamune Oral Solution, 1.0 mg/mL

Product Code / Lot Number / Customer Lot Number: LBA60/S / LBA007

Client: Wyeth Pharmaceuticals

Study Purpose: 2009 Annual Stability

Storage Condition: 5°C ± 3°C / Ambient R.H.

Time Interval: 0 – 36 Months

Package Size: 60 mL / Bottle

Date of Manufacture: 04/FEB/2009

Date in Chamber: 13/FEB/2009

Stability Start Date: 13/FEB/2009

Expiration Date: N/A

Stability Summary Approvals

Prepared By:	**Dennis A. Ladringan**	**Date:**
Position:	Stability Coordinator, Quality Control	16 APR 2012
Signature:	Dennis A. Ladringan	
Reviewed By:	**Debbie Nanba**	**Date:**
Position:	QC Supervisor, Stability	17 APR 2012
Signature:	Nanba	

Stability Summary Report for Rapamune Oral Solution, 1.0 mg/mL

LBA60/S / LBA007 **5°C ± 3°C / Ambient R.H.**

TEST	METHOD	SPECIFICATION		TIME (MONTHS)	
		Time Interval		Initial	6
		Pull Date		NA	13/AUG/2009
		Orientation		NA	Inverted
Description	Visual	Pale yellow to yellow solution, essentially particulate free. Should a haze be visible, the solution should be shaken. The presence of this haze does not affect product quality.		Yellow solution particulate free.	Yellow solution particulate free.
Assay (Sum of Isomers B and C)	CTMLP-1701	0.90 – 1.10 mg/mL		1.01, 1.03, 1.02 mg/mL X_3 = 1.02 mg/mL	1.07, 1.07 mg/mL X_2 = 1.07 mg/mL
Seco-Rapamycin (WAY-126792)	CTMLP-1701	NMT 8% of Sirolimus Label Claim		ND	1%, 1% X_2 = 1%
Purity[1]	CTMLP-1701	Total Other Degradation Impurities:	NMT 1% of Sirolimus Label Claim	ND	ND
		Largest Single Other Degradation Impurity:	NMT 0.5% of Sirolimus Label Claim	ND	ND
Peroxide Value	BP APP X F	NMT 10		0	0
Water	USP <921>	NMT 0.5%		0.2%	0.1%
Microbial Limit Tests	MM-931	Total Aerobic Microbial Count including Yeasts and Molds	NMT 100 CFU/mL	<10 CFU/mL	NR
		E. coli	Absent	Absent/mL	NR
		Salmonella species	Absent	Absent/10 mL	NR
		P. aeruginosa	Absent	Absent/mL	NR
		S. aureus	Absent	Absent/mL	NR

Stability Summary Report for Rapamune Oral Solution, 1.0 mg/mL

LBA60/S / LBA007

5°C ± 3°C / Ambient R.H.

TEST	METHOD	SPECIFICATION		TIME (MONTHS)	
		Time Interval		12[2]	18
		Pull Date		16/FEB/2010	13/AUG/2010
		Orientation		Inverted	Inverted
Description	Visual	Pale yellow to yellow solution, essentially particulate free. Should a haze be visible, the solution should be shaken. The presence of this haze does not affect product quality.		Yellow solution particulate free.	Yellow solution, particulate free, no haze.
Assay (Sum of Isomers B and C)	CTMLP-1701	0.90 – 1.10 mg/mL		1.02, 1.01 mg/mL X_2 = 1.02 mg/mL	0.99, 1.02 mg/mL X_2 = 1.01 mg/mL
Seco-Rapamycin (WAY-126792)	CTMLP-1701	NMT 8% of Sirolimus Label Claim		2%, 3% X_2 = 3%	2%, 2% X_2 = 2%
Purity[1]	CTMLP-1701	Total Other Degradation Impurities:	NMT 1% of Sirolimus Label Claim	ND	ND
		Largest Single Other Degradation Impurity:	NMT 0.5% of Sirolimus Label Claim	ND	ND
Peroxide Value	BP APP X F	NMT 10		0	ND
Water	USP <921>	NMT 0.5%		0.1%	0.3%
Microbial Limit Tests	MM-1044	Total Aerobic Microbial Count including Yeasts and Molds	NMT 100 CFU/mL	<10 CFU/mL	NR
		E. coli	Absent/mL	Absent/mL	NR
		Salmonella species	Absent/10 mL	Absent/10 mL	NR
		P. aeruginosa	Absent/mL	Absent/mL	NR
		S. aureus	Absent/mL	Absent/mL	NR

Stability Summary Report for Rapamune Oral Solution, 1.0 mg/mL

LBA60/S / LBA007 **5°C ± 3°C / Ambient R.H.**

TEST	METHOD	SPECIFICATION		TIME (MONTHS)	
		Time Interval		24	36
		Pull Date		14/FEB/2011	13/FEB/2012
		Orientation		Inverted	Inverted
Description	Visual	Pale yellow to yellow solution, essentially particulate free. Should a haze be visible, the solution should be shaken. The presence of this haze does not affect product quality.		Yellow solution, essentially particulate free, free of haze.	Yellow solution, essentially particulate free, free of haze.
Assay (Sum of Isomers B and C)	CTMLP-1701	0.90 – 1.10 mg/mL		1.00, 1.01 mg/mL X_2 = 1.01 mg/mL	0.99, 0.99 mg/mL X_2 = 0.99 mg/mL
Seco-Rapamycin (WAY-126792)	CTMLP-1701	NMT 8% of Sirolimus Label Claim		4%, 4% X_2 = 4%	6%, 6% X_2 = 6%
Purity[1]	CTMLP-1701	Total Other Degradation Impurities:	NMT 1% of Sirolimus Label Claim	ND	ND
		Largest Single Other Degradation Impurity:	NMT 0.5% of Sirolimus Label Claim	ND	ND
Peroxide Value	BP APP X F	NMT 10		0	0
Water	USP <921>	NMT 0.5%		0.1%	0.1%
Microbial Limit Tests	MM-1044	Total Aerobic Microbial Count including Yeasts and Molds	NMT 100 CFU/mL	<10 CFU/mL	<10 CFU/mL
		E. coli	Absent/mL	Absent/mL	Absent/mL
		Salmonella species	Absent/10 mL	Absent/10 mL	Absent/10 mL
		P. aeruginosa	Absent/mL	Absent/mL	Absent/mL
		S. aureus	Absent/mL	Absent/mL	Absent/mL

Notes:

1. This does not include process impurities (such as WAY-124854, WAY-155618, WAY-125286) or Group II impurities which have been previously quantitated in the drug substance.
2. Revised microbial limit test due to harmonization of method (WYA-SP-095-0607-R3 and CC #2009-WY-0986).

NA = Not Applicable ND = Not Detected NR = Not Required

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Stability Summary Report

Document Control Number: WYA-SP-050-0307-R2

Product Name: Rapamune Oral Solution, 1.0 mg/mL

Product Code / Lot Number / Customer Lot Number: V0184A/S / V0184A003

Client: Wyeth Pharmaceuticals

Study Purpose: Validation Stability

Storage Condition: 5°C ± 3°C / Ambient R.H.

Time Interval: 0 – 36 Months

Package Size: 62 mL / Bottle

Date of Manufacture: 12/APR/2007

Date in Chamber: 30/APR/2007

Stability Start Date: 30/APR/2007

Expiration Date: N/A

Stability Summary Approvals

Prepared By:	**Rosalind Seong**	**Date:**
Position:	Stability Coordinator	
Signature:	Rosalind Seong	19/MAY/2010
Reviewed By:	**Debbie Nanba**	**Date:**
Position:	QC Supervisor, Stability	
Signature:	Debbie Nanba	19 MAY 2010

Stability Summary Report for Rapamune Oral Solution, 1.0 mg/mL

V0184A/S / V0184A003

5°C ± 3°C / Ambient R.H.

TEST	METHOD	SPECIFICATION		TIME (MONTHS)	
		Time Interval		Initial	3
		Pull Date		N/A	30/JUL/2007
		Orientation		N/A	Horizontal
Physical Appearance	Visual	Pale yellow to yellow solution, essentially particulate free.		Yellow solution that is particulate free.	Yellow solution that is particulate free.
Moisture	USP <921>	NMT 0.5%		0.2%	0.2%
Peroxide Value	BP APP X F	NMT 10		0	0
Potency Assay	CTMLP-1701	0.90 – 1.05 mg/mL		1.02, 1.02, 1.02 mg/mL	1.02, 1.01 X_2 = 1.02 mg/mL
Related Substances[1]	CTMLP-1701	Seco Rapamycin:	NMT 8% of Sirolimus Label Claim	Beg =ND Mid = ND End = ND	1%
		Total Other Degradation Products:	NMT 1% of Sirolimus Label Claim	Beg = 0% Mid = 0% End = 0%	1%
		Largest Single Other Degradation Product:	NMT 0.5% of Sirolimus Label Claim	RRT0.85 = 0.2% 0.2%, 0.2%,	RRT0.31 = 0.3% RRT0.38 = <QL RRT0.56 = 0.3% RRT0.69 = <QL RRT0.84 = <QL
Microbial Limit Tests	MM-931	Total Aerobic Microbial Count including Yeasts and Molds	NMT 100 CFU/mL	< 10 CFU/mL	NR
		E. coli	Absent	Absent / 10 mL	NR
		P. aeruginosa	Absent	Absent / 10 mL	NR
		S. aureus	Absent	Absent / 10 mL	NR
		Salmonella species	Absent	Absent / 10 mL	NR

Stability Summary Report for Rapamune Oral Solution, 1.0 mg/mL

V0184A/S / V0184A003

5°C ± 3°C / Ambient R.H.

TEST	METHOD	SPECIFICATION		TIME (MONTHS)	
		Time Interval		6	9
		Pull Date		30/OCT/2007	30/JAN/2008
		Orientation		Horizontal	Horizontal
Physical Appearance	Visual	Pale yellow to yellow solution, essentially particulate free.		Yellow solution essentially particulate free.	Pale yellow solution essentially particulate free.
Moisture	USP <921>	NMT 0.5%		0.2%	0.2%, 0.2%
Peroxide Value	BP APP X F	NMT 10		0	0
Potency Assay	CTMLP-1701	0.90 – 1.05 mg/mL		1.01, 1.02 X_2 = 1.02 mg/mL	0.99, 0.99 X_2 = 0.99 mg/mL
Related Substances[1]	CTMLP-1701	Seco Rapamycin:	NMT 8% of Sirolimus Label Claim	1%, 1% X_2 = 1%	1%, 1% X_2 = 1%
		Total Other Degradation Products:	NMT 1% of Sirolimus Label Claim	RRT0.84: <QL, <QL X_2 = <QL	ND
		Largest Single Other Degradation Product:	NMT 0.5% of Sirolimus Label Claim	RRT0.84: <QL, <QL X_2 = <QL	ND
Microbial Limit Tests	MM-931	Total Aerobic Microbial Count including Yeasts and Molds	NMT 100 CFU/mL	NR	NR
		E. coli	Absent	NR	NR
		P. aeruginosa	Absent	NR	NR
		S. aureus	Absent	NR	NR
		Salmonella species	Absent	NR	NR

Stability Summary Report for Rapamune Oral Solution, 1.0 mg/mL

V0184A/S / V0184A003

5°C ± 3°C / Ambient R.H.

TEST	METHOD	SPECIFICATION		TIME (MONTHS)	
		Time Interval		12	18
		Pull Date		30/APR/2008	30/OCT/2008
		Orientation		Horizontal	Horizontal
Physical Appearance	Visual	Pale yellow to yellow solution, essentially particulate free.		Yellow solution essentially particulate free.	Pale Yellow solution that is particulate free.
Moisture	USP <921>	NMT 0.5%		0.2%, 0.2%	0.2%
Peroxide Value	BP APP X F	NMT 10		0	0
Potency Assay	CTMLP-1701	0.90 – 1.05 mg/mL		1.00, 1.00 X_2 = 1.00 mg/mL	0.99, 0.99 X_2 = 0.99 mg/mL
Related Substances[1]	CTMLP-1701	Seco Rapamycin:	NMT 8% of Sirolimus Label Claim	2%, 2% X_2 = 2%	1%, 1% X_2 = 1%
		Total Other Degradation Products:	NMT 1% of Sirolimus Label Claim	<QL, <QL X_2 = <QL	ND
		Largest Single Other Degradation Product:	NMT 0.5% of Sirolimus Label Claim	RRT0.8: <QL, <QL X_2 = <QL	ND
Microbial Limit Tests	MM-931	Total Aerobic Microbial Count including Yeasts and Molds	NMT 100 CFU/mL	< 10 CFU/mL	NR
		E. coli	Absent	Absent / 10 mL	NR
		P. aeruginosa	Absent	Absent / 10 mL	NR
		S. aureus	Absent	Absent / 10 mL	NR
		Salmonella species	Absent	Absent / 10 mL	NR

Stability Summary Report for Rapamune Oral Solution, 1.0 mg/mL

V0184A/S / V0184A003

5°C ± 3°C / Ambient R.H.

TEST	METHOD	SPECIFICATION		TIME (MONTHS)
		Time Interval		24
		Pull Date		30/APR/2009
		Orientation		Horizontal
Physical Appearance	Visual	Pale yellow to yellow solution, essentially particulate free.		Yellow solution that is particulate free.
Moisture	USP <921>	NMT 0.5%		0.2%
Peroxide Value	BP APP X F	NMT 10		0
Potency Assay	CTMLP-1701	0.90 – 1.05 mg/mL		0.98, 0.98 X_2 = 0.98 mg/mL
Related Substances[1]	CTMLP-1701	Seco Rapamycin:	NMT 8% of Sirolimus Label Claim	3%, 3% X_2 = 3%
		Total Other Degradation Products:	NMT 1% of Sirolimus Label Claim	ND
		Largest Single Other Degradation Product:	NMT 0.5% of Sirolimus Label Claim	ND
Microbial Limit Tests	MM-931	Total Aerobic Microbial Count including Yeasts and Molds	NMT 100 CFU/mL	2 CFU/mL
		E. coli	Absent	Absent / 10 mL
		P. aeruginosa	Absent	Absent / 10 mL
		S. aureus	Absent	Absent / 10 mL
		Salmonella species	Absent	Absent / 10 mL

Stability Summary Report for Rapamune Oral Solution, 1.0 mg/mL

V0184A/S / V0184A003 **5°C ± 3°C / Ambient R.H.**

TEST	METHOD	SPECIFICATION		TIME (MONTHS)
		Time Interval		36[2]
		Pull Date		30/APR/2010
		Orientation		Horizontal
Physical Appearance	Visual	Pale yellow to yellow solution, essentially particulate free.		Yellow solution, essentially particulate free.
Moisture	USP <921>	NMT 0.5%		0.3%
Peroxide Value	BP APP X F	NMT 10		0
Potency Assay	CTMLP-1701	0.90 – 1.05 mg/mL		0.98, 0.98 X_2 = 0.98 mg/mL
Related Substances[1]	CTMLP-1701	Seco Rapamycin:	NMT 8% of Sirolimus Label Claim	2%, 2% X_2 = 2%
		Total Other Degradation Products:	NMT 1% of Sirolimus Label Claim	ND
		Largest Single Other Degradation Product:	NMT 0.5% of Sirolimus Label Claim	ND
Microbial Limit Tests	MM-1044	Total Aerobic Microbial Count including Yeasts and Molds	NMT 100 CFU/mL	<10 CFU/mL
		E. coli	Absent/mL	Absent / mL
		P. aeruginosa	Absent/mL	Absent / mL
		Salmonella species	Absent/10 mL	Absent / 10 mL
		S. aureus	Absent/mL	Absent / mL

Notes:
1. This does not include process impurities (such as WAY-124854, WAY-155618, WAY-125286) or Group II impurities which have been previously quantitated in the drug substance.
2. Microbial test limit and method revised as a result of harmonized method as per WYA-SP-050-0307-R2 and CC #2009-WY-0986.

NA = Not Applicable ND = Not Detected NR = Not Required QL = Quantitation Limit