

Stability protocol for Xanomeline / Trospium HCl Pellets											
Manufacturing date: 2016DE12, Incubation date: 2016DE16											
Project	Lot (Strength)	Packaging	Stability conditions			Time points (month)					
			25°C/ 60% RH	30°C/ 65% RH	40°C/ 75% RH	0	1	2	3	6	EXTRA
286-02	OT20 Xanomeline 50mg (lb) Trospium HCl 20mg	30cc HDPE bottles with sealed PP cap	6 bottles (20 capsules/bottle)			2016DE16	2017JA16	2017FE16	2017MR16	2017JN16	TBD
				6 bottles (20 capsules/bottle)			2017JA16	2017FE16	2017MR16	2017JN16	TBD
					4 bottles (20 capsules/bottle)		2017JA16	2017FE16	2017MR16	2017JN16	TBD
	5 bottles (20 capsules/bottle)				2017JA16		2017FE16	2017MR16	2017JN16	TBD	
			6 bottles (20 capsules/bottle)		2017JA16		2017FE16	2017MR16	2017JN16	TBD	
				3 bottles (20 capsules/bottle)	2017JA16		2017FE16	2017MR16	2017JN16	TBD	
Sample to be analyzed for:											
Appearance, Assay, Related Substances, KF and Dissolution.											
At the Client request, sample will be removed from chamber and analyzed.											

FIG 1

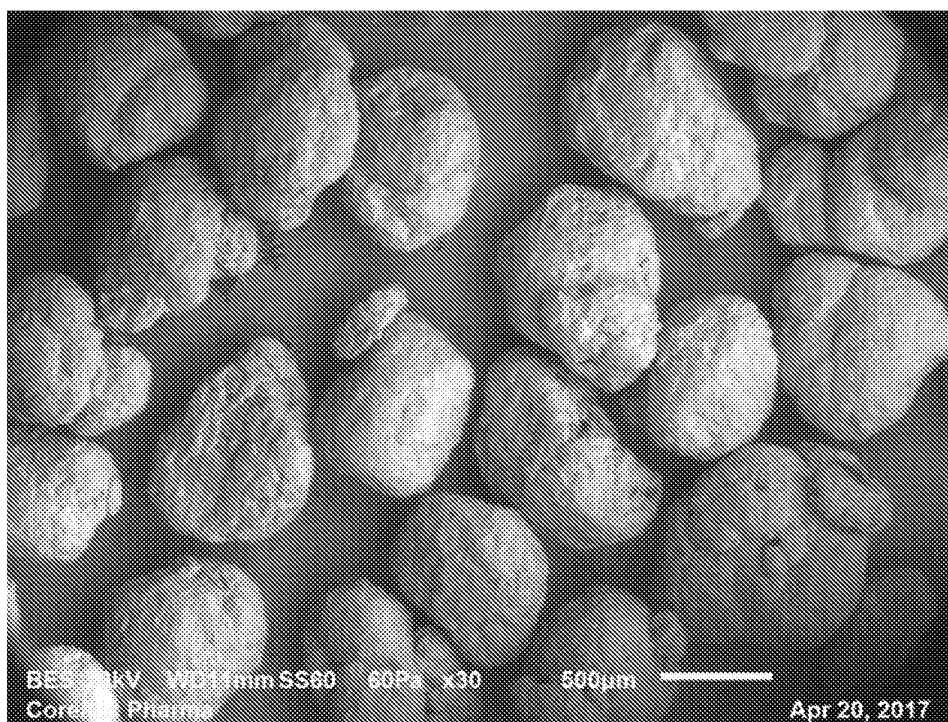


FIG. 2



FIG. 3

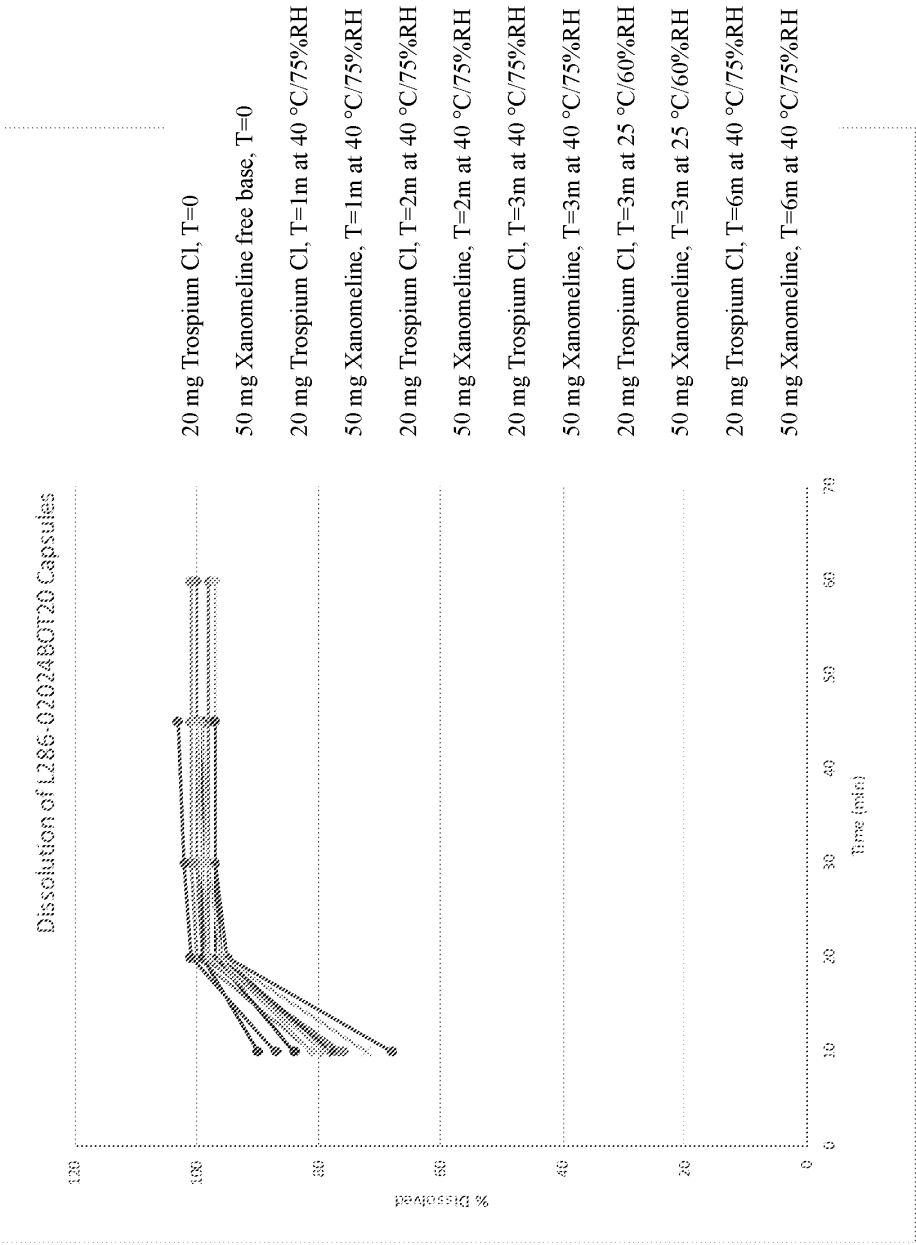


FIG. 4

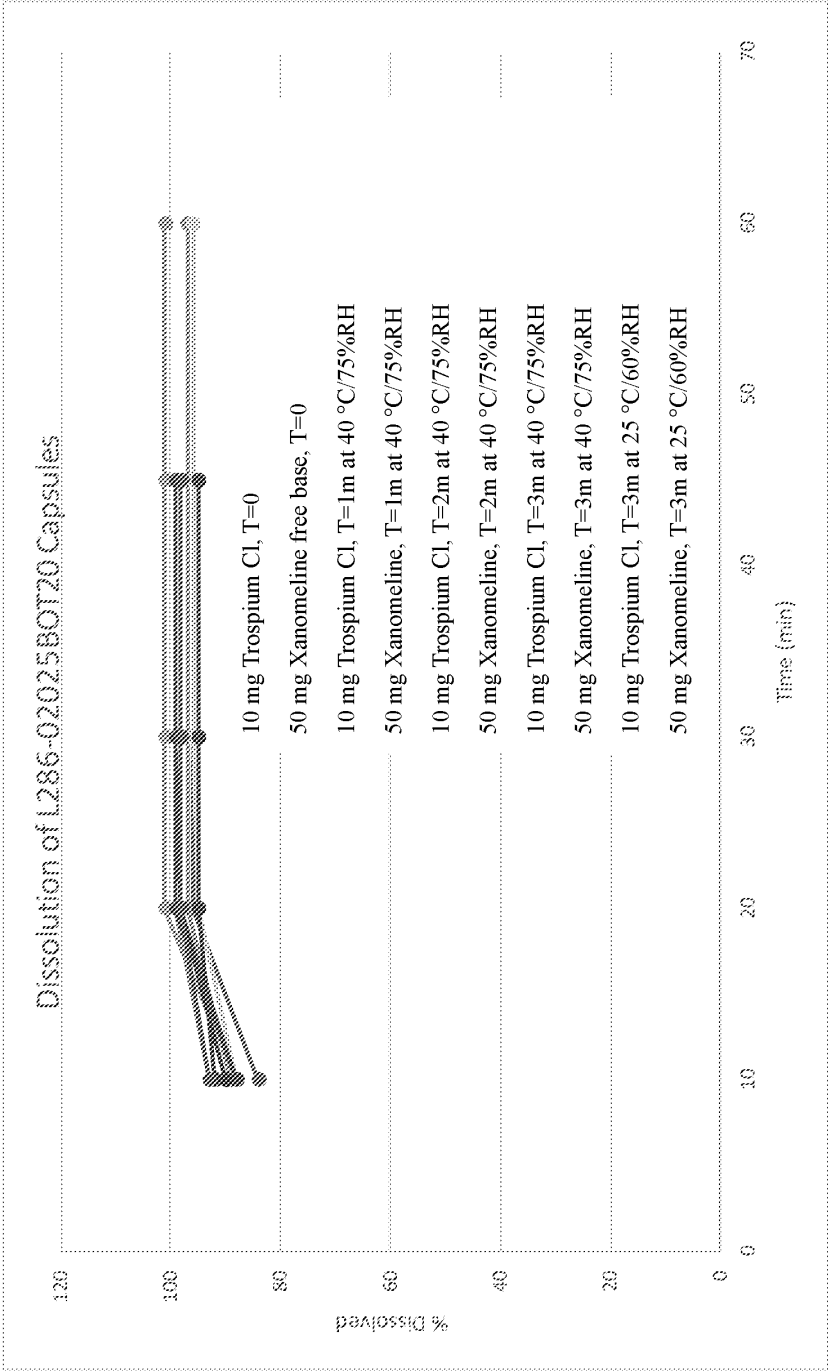


FIG. 5

STORAGE		T = Q		23°C/60%RH		3 Months		6 Months		9 Months	
TEST DESCRIPTION		Release, Rev 01		Stability, Rev 01		Stability, Rev 01		Stability, Rev 01		Stability, Rev 01	
SPECIFICATION used at time of analysis											
Conforms to acceptance criteria (Y/N) Description (Method) Water content by KF (USP <921>, Method 7a) (n=3)	%w/w	Y		Y		Y		Y		Y	
	Off-white opaque hard shell capsule with no markings										
		2.4		2.6		2.5		2.1		2.1	
	% label claim Xanoxaline	104.5 %		99.8		102.3		102.3		102.3	
	mg Xanoxaline/capsule	52.3 %		49.8		51.2		51.2		51.2	
Assay (Concise-28602-AD-01) (n=2)	% label claim Trospium Chloride	97.5 %		97.7		98.6		97.8		97.8	
	mg Trospium Chloride/capsule	9.8 %		9.8		10.0		9.8		9.8	
	Method Revision	0		01		02		03		03	
	Trospium Chloride related compound B	Not detected *		Not detected		Not detected		Not detected		Not detected	
	Trospium Chloride related compound A	Not detected *		<0.1		Not detected		Not detected		Not detected	
Related substances (%LC) * (Concise-28602-AD-01) (n=2)	Unspecified Impurity (Xanoxaline, RRT0.23) %	0.15 %		0.14		0.14		0.14		0.14	
	Unspecified Impurity (Xanoxaline, RRT1.08) %	^		0.18		0.16		0.24		0.24	
	Total Impurities	0.15 %		0.32 %		0.30		0.37		0.37	
	Method Revisions	0		01		02		03		03	

FIG. 6

STORAGE		T=0		30°C/65%RH	
TEST DESCRIPTION		3 Months		6 Months	
SPECIFICATION used at time of analysis		Stability, Rev 01		Stability, Rev 01	
Conforms to acceptance criteria (Y/N)		Y		Y	
Description (Visual)		OR-white opaque hard shell capsule with no markings		No change as compared to Initials	
Water content by KF (USP <921>, Method 1a) (n=3)		2.4		2.5	
Assay (Concise-28622-AD-01) (n=2)	% label claim Xanomeline	104.5 ^c		100.8	
	mg Xanomeline/capsule	52.3 ^c		50.3	
	% label claim Trospium Chloride	97.5 ^c		98.4	
	mg Trospium Chloride/capsule	9.8 ^c		9.8	
	Method Revision	0		01	
Related substances (%LC) ^a (Concise-28622-AD-01) (n=2)	Trospium Chloride related compound B	Not detected ^e		Not detected	
	Trospium Chloride related compound A	Not detected ^e		Not detected	
	Unspecified impurity (Xanomeline, HPLC 2.4) ±1	0.15 ^e		0.14	
	Unspecified impurity (Xanomeline, HPLC 1.05) ±1	-		0.18	
	Total Impurities	0.15 ^e		0.30	
	Method Revision	0		01	

FIG. 7

STORAGE		T=0		40°C/75%RH	
TEST DESCRIPTION		3 Months		6 Months	
SPECIFICATION used at time of analysis		Stability, Rev 01		Stability, Rev 01	
Conforms to acceptance criteria (Y/N)		Y		Y	
Description		OT-white opaque hard shell capsules with no markings		No change as compared to initial	
Water content by KF (USP <921>, Method 1a)		2.4		2.5	
Assay (Corralle 28602-AD-01)		104.5 °		101.7	
mg Xanomeline/capsule		52.3 °		50.9	
Assay (Corralle 28602-AD-01)		97.5 °		97.0	
mg Trospium Chloride/capsule		9.8 °		9.7	
Method Revision		0		01	
Trospium Chloride related compound B		Not detected °		Not detected	
Trospium Chloride related compound A		Not detected °		Not detected	
Unspiked impurity (Xanomeline, FHTC24) °		0.13 °		0.14	
Unspiked impurity (Xanomeline, FHT1.09) °		-		0.14	
Total Impurities		0.15 °		0.28	
Method Revision		0		01	

FIG. 8

STORAGE		Y=0		3 Months		6 Months		9 Months	
TEST DESCRIPTION		Release, Rev 2		Stability, Rev 01		Stability, Rev 01		Stability, Rev 01	
SPECIFICATION used at time of analysis		D128		395		395		395	
Conforms to acceptance criteria [Y/N]	Dissolution (NLT) (Concals-28502-B-01) (0-6) (200 mL of 0.1N HCl, paddle at 50 rpm)	Y		Y		Y		Y	
		Xenotestine		Xenotestine		Xenotestine		Xenotestine	
		Time (min)		Time (min)		Time (min)		Time (min)	
		10		10		10		10	
		30		30		30		30	
		60		60		60		60	
		120		120		120		120	
		180		180		180		180	
		240		240		240		240	
		360		360		360		360	
Microbial Limits * LSP=01%, <22>	Total Yeasts and Mould Counts (TYMC): ≤100 cfu/g Total Aerobic Microbial Counts (TAMC): ≤1000 cfu/g Escherichia coli: Absent	Y		Y		Y		Y	
		N/A		N/A		N/A		N/A	
		N/A		N/A		N/A		N/A	
		N/A		N/A		N/A		N/A	
		N/A		N/A		N/A		N/A	
		N/A		N/A		N/A		N/A	
		N/A		N/A		N/A		N/A	
		N/A		N/A		N/A		N/A	
		N/A		N/A		N/A		N/A	
		N/A		N/A		N/A		N/A	

FIG. 9

STORAGE		T=0		30°C/65%RH	
TEST DESCRIPTION		Release, Rev 0		3 Months	
SPECIFICATION used at time of analysis		Release, Rev 0		Stability, Rev 01	
Conforms to acceptance criteria (Y/N)		Y		Y	
Dissolution (%LC) (Concilia 25002-G-01) (n=8) (500 mL of 0.1N HCl, particles at 50 rpm)	Xenoneline Time (min)	%LC	Range	%LC	Range
	10	94	12-99	95	14-99
	20	98	80-102	96	80-98
	(Q=80%) 30	103	102-104	101	99-103
	45	103	103-104	102	103-104
	Tropacolum Chloride Time (min)	%LC	Range	%LC	Range
	10	49	11-93	30	9-54
	20	93	87-98	84	69-93
	(Q=80%) 30	96	94-102	96	94-102
	45	98	94-102	99	95-102
Microbial Limits * USP <61>, <62>	Method Revision	0		01	
	Total Yeasts and Molds Counts (TYMC): ≤100 cfu/g	<50 cfu/g		N/A	
	Total Aerobic Microbial Counts (TAMC): ≤1000 cfu/g	< 500 cfu/g		N/A	
	Escherichia coli: Absent	Absent		N/A	

FIG. 10

STORAGE		T=0		43°C/75%RH	
TEST DESCRIPTION		3 Months		6 Months	
SPECIFICATION used at time of analysis		Release, Rev 0		Stability, Rev 01	
Conforms to acceptance criteria (Y/N)		-0136			
Dissolution (%LC) (Consists-28802-0-01) (n=6) 300 mL of 0.1N HCl, paddles at 50rpm	Xanondine Time (min.)	Y	Range	Y	Range
		%LC	Range	%LC	Range
	10	54	12-69	45	6-30
	20	86	50-102	89	30-96
	30	103	102-104	96	93-101
	45	103	103-104	100	98-101
	Tropium Chloride Time (min.)	%LC	Range	%LC	Range
	10	49	11-63	42	3-45
	20	93	87-98	86	74-94
	30	96	94-102	95	87-101
Microbial Limits * USP<61> <62>	Method Revision	0		01	
	Total Yeasts and Molds Counts (TYMC): 5100 cfu/g	<50 cfu/g		N/A	
	Total Aerobic Microbial Counts (TAMC): 51000 cfu/g	< 500 cfu/g		N/A	
	Escherichia coli: Absent	Absent		N/A	
				N/A	

FIG. 11

Xanomeline API Related Substances Profile for Xanomeline/Trospium Cl 50/10 mg Capsules

Stability time point		Initials	T= 3 months	T= 6 months	T= 9 months
Related Substances (%w/w) (n=1) (Concals-28602-AD-01)	Unspecified impurity (RRT 0.23)	0.14	0.14	0.14	0.14
	Unspecified impurity (RRT 1.09)	<0.1	0.16	0.14	0.18
	Method Revision	0	01	02	03

FIG. 12

Trospium Chloride API Related Substances Profile for Xanomeline/Trospium Cl 50/10 mg Capsules

Stability time point		Initials	T= 3 months	T= 6 months	T= 9 months
Related Substances (%w/w) (n=1) (Concals-28602-AD-01)	Unspecified impurity	Not Detected	Not Detected	Not Detected	Not Detected
	Method Revision	0	01	02	03

FIG. 13

Specification for Xanomeline/Trospium Cl 50/10 mg Capsules

TEST DESCRIPTION	ACCEPTANCE CRITERIA	ACCEPTANCE CRITERIA
	Release, Rev 0	Stability, Rev 01
Description (Visual)	White to off-white opaque hard shell capsule with no markings	White to off-white opaque hard shell capsule with no markings
Water Content by KF (USP <921>, Method 1a)	Report result	Report results
Assay (%LC) (Concals-28602-AD)	Xanomeline: 90 - 110% label claim (45 - 55 mg Xanomeline/capsule)	Xanomeline: 90 - 110% label claim (45 - 55 mg Xanomeline/capsule)
	Trospium Chloride: 90 - 110% label claim (9 - 11mg Trospium Chloride/capsule)	Trospium Chloride: 90 - 110% label claim (9 - 11mg Trospium Chloride/capsule)
Related Substances (%LC) ^A (Concals-28602-AD)	Trospium Chloride related compound B: NMT 0.2%LC	Trospium Chloride related compound B: NMT 0.2%LC
	Trospium Chloride related compound A: NMT 0.2%LC	Trospium Chloride related compound A: NMT 0.2%LC
	Any single unspecified impurity: NMT 0.2%LC	Any single unspecified impurity: NMT 0.2%LC
	Total Impurities: NMT 1.5%LC	Total Impurities: NMT 1.5%LC
Dissolution (Concals-28602-B)	Xanomeline: NLT 80% (Q) of labeled amount of Xanomeline is dissolved at 30 minutes. Report profile	Xanomeline: NLT 80% (Q) of labeled amount of Xanomeline is dissolved at 30 minutes. Report profile
	Trospium Chloride: NLT 80% (Q) of labeled amount of Trospium Chloride is dissolved at 30 minutes. Report profile	Trospium Chloride: NLT 80% (Q) of labeled amount of Trospium Chloride is dissolved at 30 minutes. Report profile
Microbial Limits ^B USP <61>, <62>	Total Yeasts and Molds Counts (TYMC): ≤100 cfu/g	Total Yeasts and Molds Counts (TYMC): ≤100 cfu/g
	Total Aerobic Microbial Counts (TAMC): ≤1000 cfu/g	Total Aerobic Microbial Counts (TAMC): ≤1000 cfu/g
	Escherichia coli: Absent	Escherichia coli: Absent

FIG. 14

STORAGE		25°C/60%RH	
TEST DESCRIPTION		3 months	6 months
SPECIFICATION used at time of analysis		Stability, Rev 0	Stability, Rev 0
Conforms to acceptance criteria (Y/N)		Y	Y
	Description	No change as compared to initials	
Water content by KF (USP <921>, Method 1a) (n=3)	%w/w	2.9	2.7
	Oil-white opaque hard shell capsule with no markings	Y	No change as compared to initials
Assay (Corealis-28602-AD-01) (n=2)	% label claim Xanomeline	101.9	102.2
	mg Xanomeline/capsule	50.9	51.1
	% label claim Trospium Chloride	98.3	98.3
	mg Trospium Chloride/capsule	19.7	19.7
	Method Revision	01	03
Related substances (%LC) ^A (Corealis-28602-AD-01) (n=2)	Trospium Chloride related compound B	Not detected	Not detected
	Trospium Chloride related compound A	Not detected	Not detected
	Unspecified Impurity (Xanomeline, PRT0.23) c, b	0.13	0.14
	Unspecified Impurity (Xanomeline, PRT1.09) c, b	0.17	0.14
	Total Impurities	0.30	0.28
	Method Revision	01	03

FIG. 15

STORAGE		T=0		30°C/65%RH
TEST DESCRIPTION		Stability, Rev 0		6 months
SPECIFICATION used at time of analysis		Stability, Rev 0		Stability, Rev 0
Conforms to acceptance criteria (Y/N)		Y	Y	Y
Description (Visual)		Oil-white opaque hard shell capsule with no markings		
Water content by KF (USP <921>, Method 1a) (n=3)	%w/w	2.8		3.0
Assay (Correlis-28602-AD-01) (n=2)	% label claim Xanomeline	101.8		101.5
	mg Xanomeline/capsule	50.9		50.8
	% label claim Trospium Chloride	98.3		96.4
	mg Trospium Chloride/capsule	19.7		19.3
	Method Revision	01		03
Related substances (%LC) ⁴ (Correlis-28602-AD-01) (n=2)	Trospium Chloride related compound B	Not detected		Not detected
	Trospium Chloride related compound A	Not detected		Not detected
	Unspecified impurity (Xanomeline_PRT023) c.o	0.13		0.14
	Unspecified impurity (Xanomeline_PRT109) c.o	0.17		0.23
	Total Impurities	0.30		0.37
	Method Revision	01		03

FIG. 16

STORAGE		40°C/75%RH	
TEST DESCRIPTION		3 months	
SPECIFICATION used at time of analysis		Stability, Rev 0	
Stability, Rev 0		Stability, Rev 0	
Conforms to acceptance criteria (Y/N)		Y	
Description		No change as compared to initials	
Water content by KF (USP <921>, Method 1a) (n=3)		2.9	
Assay (Conals-28502-AD-01) (n=2)		101.8	
		50.9	
		98.1	
		19.6	
		02	
		Not detected	
		<0.1	
		0.14	
		0.20	
		0.33	
		02	
		03	

FIG. 17

STORAGE		T=0		25°C/60%RH	
TEST DESCRIPTION		3 months		6 months	
SPECIFICATION used at time of analysis		Stability, Rev 0		Stability, Rev 0	
Conforms to acceptance criteria (Y/N)		Y		Y	
Dissolution (%LC) (Concals-28602-B-01) (n=6) (500 mL of 0.1N HCl, paddles at 50 rpm)	Xanomeline Time (min.)	%LC	Range	%LC	Range
	10	34	0-66	27	11-46
	20	89	64-97	94	85-101
	(Q=80%) 30	100	88-105	102	99-105
	45	103	99-106	103	99-105
	Trospium Chloride Time (min.)	%LC	Range	%LC	Range
	10	38	0-63	26	11-43
	20	86	70-95	90	83-93
	(Q=80%) 30	97	91-103	96	94-99
	45	100	97-103	97	94-100
Method Revision		01		01	
Microbial Limits ^a USP<61>, <62>	Total Yeasts and Molds Counts (TYMC): ≤100 cfu/g	<50 cfu/g		N/A	
	Total Aerobic Microbial Counts (TAMC): ≤1000 cfu/g	< 500 cfu/g		N/A	
	Escherichia coli: Absent	Absent		N/A	

FIG. 18

STORAGE		T= 0		30°C/65%RH	
TEST DESCRIPTION				6 months	
SPECIFICATION used at time of analysis		Stability, Rev 0		Stability, Rev 0	
Conforms to acceptance criteria (Y/N)		Y		Y	
Dissolution (%LC) (Correlis-28602-B-01) (n=6) (900 mL of 0.1N HCl, paddles at 50 rpm)	Xanomeline				
	Time (min.)				
	10	34	0-66	27	6-48
	20	89	64-97	78	60-99
	(Q=80%) 30	100	88-105	94	85-103
	45	103	98-106	98	91-103
	Trospium Chloride				
	Time (min.)				
	10	30	0-63	29	6-49
	20	86	70-95	80	65-101
Microbial Limits ⁸ USP<61>, <62>	(Q=80%) 30	97	91-103	95	91-103
	45	100	97-103	99	95-103
	Method Revision	01		01	
	Total Yeasts and Molds Counts (TYMC): ≤100 cfu/g			<50 cfu/g	
	Total Aerobic Microbial Counts (TAMC): ≤1000 cfu/g Escherichia coli: Absent			< 500 cfu/g Absent	
				N/A	
				N/A	
				N/A	

FIG. 19

STORAGE		T=0		40°C/75%RH	
TEST DESCRIPTION		3 months		6 months	
SPECIFICATION used at time of analysis		Stability, Rev 0		Stability, Rev 0	
Conforms to acceptance criteria (Y/N) Dissolution (%LC) (Coreale-28602-B-01) (n=6) (900 mL of 0.1N HCl, paddles at 50 rpm)	Xanomeline	Y		Y	
	Time (min.)	Range		Range	
	10	%LC	34	%LC	32
	20	Range	0-66	Range	3-58
	(Q=80%)	%LC	89	%LC	89
	30	Range	64-97	Range	70-98
	45	%LC	100	%LC	99
	Trospium Chloride	Range	88-105	Range	87-103
	Time (min.)	%LC	103	%LC	99
	10	Range	90-106	Range	95-103
Microbial Limits ^a USP<61>, <62>	Trospium Chloride	Y		Y	
	Time (min.)	Range		Range	
	10	%LC	30	%LC	26
	20	Range	0-63	Range	2-59
	(Q=80%)	%LC	86	%LC	86
	30	Range	70-85	Range	75-96
	45	%LC	97	%LC	94
	Method Revision	Range	91-103	Range	87-98
	Total Yeasts and Molds Counts (TYMC): ≤100 cfu/g	%LC	100	%LC	96
	Total Aerobic Microbial Counts (TAMC): ≤1000 cfu/g	Range	97-103	Range	92-98
Escherichia coli: Absent		01		01	
		<50 cfu/g		N/A	
		< 500 cfu/g		N/A	
		Absent		N/A	

FIG. 20

Xanomeline API Related Substances Profile for Xanomeline/Trospium Cl 50/20 mg Capsules

Stability time point		Initials	T= 3 months	T= 6 months
Related Substances (%w/w) (n=1) (Corealis-28602-AD-01)	Unspecified impurity (RRT 0.24)	0.14	0.14	0.14
	Unspecified impurity (RRT 1.09)	0.20	0.14	0.18
	Method Revision	01	02	03

FIG. 21

Trospium Chloride API Related Substances Profile for Xanomeline/Trospium Cl 50/20 mg Capsules

Stability time point		Initials	T= 3 months	T= 6 months
Related Substances (%w/w) (n=1) (Corealis-28602-AD-01)	Unspecified impurity	Not Detected	Not Detected	Not Detected
	Method Revision	01	02	03

FIG. 22

Specification for Xanomeline/Trospium Cl 50/20 mg Capsules

TEST DESCRIPTION	ACCEPTANCE CRITERIA
	Stability, Rev D
Description (Visual)	White to off-white opaque hard shell capsule with no markings
Water Content by KF (USP <921>, Method 1a)	Report result
Assay (%LC) (Corealis-28602-AD)	Xanomeline: 90 - 110% label claim (45 - 55 mg Xanomeline/capsule)
	Trospium Chloride: 90 - 110% label claim (18 - 22mg Trospium Chloride/capsule)
Related Substances (%LC)* (Corealis-28602-AD)	Trospium Chloride related compound B: NMT 0.2%LC
	Trospium Chloride related compound A: NMT 0.2%LC
	Any single unspecified impurity: NMT 0.2%LC
Dissolution (Corealis-28602-B)	Total Impurities: NMT 1.5%LC
	Xanomeline: NLT 80% (Q) of labeled amount of Xanomeline is dissolved at 30 minutes. Report profile
	Trospium Chloride: NLT 80% (Q) of labeled amount of Trospium Chloride is dissolved at 30 minutes. Report profile
Microbial Limits* USP <61>, <62>	Total Yeasts and Molds Counts (TYMC): ≤100 cfu/g
	Total Aerobic Microbial Counts (TAMC): ≤1000 cfu/g
	Escherichia coli: Absent

FIG. 23

STORAGE		T= 0		30°C/65%RH
TEST DESCRIPTION		Stability, Rev 0		6 months
SPECIFICATION used at time of analysis		Stability, Rev 0		Stability, Rev 0
Conforms to acceptance criteria (Y/N)		Y		Y
Description (Visual)		Off-white opaque hard shell capsule with no markings		No change as compared to initials
Water content by KF (USP <921>, Method 1a) (n=3)	%w/w	2.4		2.2
Assay (Concals-28602-AD-01) (n=2)	% label claim Xanomeline	102.0		102.8
	mg Xanomeline/capsule	76.5		77.1
	% label claim Trospium Chloride	95.9		96.0
	mg Trospium Chloride/capsule	9.6		9.6
Related substances (%LC) ^a (Concals-28602-AD-01) (n=2)	Method Revision	01		03
	Trospium Chloride related compound B	Not detected		Not detected
	Trospium Chloride related compound A	Not detected		Not detected
	Unspecified Impurity (Xanomeline_RRT0.24) c, b	0.15		0.14
	Unspecified Impurity (Xanomeline_RRT 1.10) c, b	0.15		0.24
	Total Impurities	0.30		0.38
	Method Revision	01		03

FIG. 25

STORAGE		40°C/75%RH	
TEST DESCRIPTION		3 months	6 months
SPECIFICATION used at time of analysis		Stability, Rev 0	Stability, Rev 0
Conforms to acceptance criteria (Y/N)		Y	N
Description (Visual)		Off-white opaque hard shell capsule with no markings	No change as compared to initials as compared to initials
Water content by KF (USP <921>, Method 1a) (n=3)	%w/w	2.4	2.3
Assay (Coreals-28602-AD-01) (n=2)	% label claim Xanomeline	102.0	103.3 ^E
	mg Xanomeline/capsule	76.5	77.5 ^F
	% label claim Trospium Chloride	95.9	98.7 ^F
	mg Trospium Chloride/capsule	9.6	9.9 ^F
	Method Revision	01	02
Related substances (%LC) ^A (Coreals-28602-AD-01) (n=2)	Trospium Chloride related compound B	Not detected	Not detected
	Trospium Chloride related compound A	Not detected	<0.1
	Unspecified Impurity (Xanomeline_RRT0.24) ^{C, E}	0.15	0.14
	Unspecified Impurity (Xanomeline_RRT1.10) ^{C, E}	0.15	0.20
	Total Impurities	0.30	0.34
	Method Revision	01	02
			03

FIG. 26

STORAGE		T = 0		25°C/60%RH	
TEST DESCRIPTION		3 months		6 months	
SPECIFICATION used at time of analysis		Stability, Rev 0		Stability, Rev 0	
Conforms to acceptance criteria (Y/N)		Y		Y	
Dissolution (%LC) (Corasis-28502-B-01) (n=6) (900 mL of 0.1N HCl, paddles at 50 rpm)	Xanomeline	Range		Range	
	Time (min.)	Time (min.)		Time (min.)	
	10	11-53		2-73	
	20	79-98		83-103	
	(Q=80%) 30	99-103		95-107	
	45	103-105		98-107	
	Trospium Chloride	Range		Range	
	Time (min.)	Time (min.)		Time (min.)	
	10	12-47		2-64	
	20	74-91		70-100	
Microbial Limits ^a USP <61>, <62>	(Q=80%) 30	93-103		89-104	
	45	95-105		91-104	
	Method Revision	01		01	
	Total Yeasts and Molds	<50 cfu/g		N/A	
	Counts (TYMC):	≤100 cfu/g		N/A	
	Total Aerobic Microbial	< 500 cfu/g		N/A	
	Counts (TAMC):	≤1000 cfu/g		N/A	
	Escherichia coli: Absent	Absent		N/A	

FIG. 27

STORAGE		T=0		30°C/65%RH	
TEST DESCRIPTION		Stability, Rev 0		6 months	
SPECIFICATION used at time of analysis		Stability, Rev 0		Stability, Rev 0	
Disolution (%LC) (Cereals-28502-B-01) (n=6) (900 mL of 0.1N HCl, paddles at 50 rpm)	Conforms to acceptance criteria (Y/N)	Y		Y	
	Xanomeline	Range		Range	
	Time (min.)	%LC	Range	%LC	Range
	10	30	11-53	24	0-48
	20	87	79-98	93	86-101
	(Q=80%) 30	101	99-103	102	101-103
	45	104	103-105	103	102-104
	Trospium Chloride	Range		Range	
	Time (min.)	%LC	Range	%LC	Range
	10	26	12-47	23	0-44
Microbial Limits ^a USP<61>, <62>	20	84	74-91	91	87-94
	(Q=80%) 30	98	93-103	99	96-106
	45	102	95-105	99	96-107
	Method Revision	01		01	
	Total Yeasts and Molds Counts (TYMC): ≤100 cfu/g	<50 cfu/g		N/A	
	Total Aerobic Microbial Counts (TAMC): ≤1000 cfu/g	< 500 cfu/g		N/A	
	Escherichia coli: Absent	Absent		N/A	

FIG. 28

STORAGE		T = 0		40°C/75%RH	
TEST DESCRIPTION		Stability, Rev 0		Stability, Rev 0	
SPECIFICATION used at time of analysis		3 months		6 months	
Conforms to acceptance criteria (Y/N)		Y		N	
Dissolution (%LC) (Correlis-28602-B-01) (n=6) (900 mL of 0.1N HCl, paddles at 50 rpm)	Xanomeline	%LC	Range	%LC	Range ^f
	Time (min.)				
	10	30	11-53	39	26
	20	87	79-98	95	85
	(Q=80%) 30	101	99-103	103	97
	45	104	103-105	104	100
	Trospium Chloride	%LC	Range	%LC	Range ^f
	Time (min.)				
	10	26	12-47	36	24
	20	84	74-91	91	83
Microbial Limits ^a USP<61>, <62>	(Q=80%) 30	98	93-103	98	94
	45	102	95-105	99	97
	Method Revision	01		01	
	Total Yeasts and Molds Counts (TYMC): ≤100 cfu/g	<50 cfu/g		N/A	
	Total Aerobic Microbial Counts (TAMC): ≤1000 cfu/g Escherichia coli: Absent	< 500 cfu/g Absent		N/A N/A	

FIG. 29

Xanomeline API Related Substances Profile for Xanomeline/Trospium Cl 75/10 mg Capsules

Stability time point		Initials	T= 3 months	T= 6 months
Related Substances (%w/w) (n=1) (Corealis-28602-AD-01)	Unspecified impurity (RRT 0.23)	0.14	0.14	0.14
	Unspecified impurity (RRT 1.09)	0.20	0.14	0.21
	Method Revision	01	02	03

FIG. 30

Trospium Chloride API Related Substances Profile for Xanomeline/Trospium Cl 75/10 mg Capsules

Stability time point		Initials	T= 3 months	T= 6 months
Related Substances (%w/w) (n=1) (Corealis-28602-AD-01)	Unspecified impurity	Not Detected	Not Detected	Not Detected
	Method Revision	01	02	03

FIG. 31

Specification for Xanomeline/Trospium Cl 75/10 mg Capsules

TEST DESCRIPTION	ACCEPTANCE CRITERIA
	Stability, Rev 0
Description (Visual)	White to off-white opaque hard shell capsule with no markings
Water Content by KF (USP <921>, Method 1a)	Report result
Assay (%LC) (Corealis-28602-AD)	Xanomeline: 90 – 110% label claim (68 – 83 mg Xanomeline/capsule)
	Trospium Chloride: 90 – 110% label claim (9 – 11 mg Trospium Chloride/capsule)
Related Substances (%LC) ^A (Corealis-28602-AD)	Trospium Chloride related compound B: NMT 0.2%LC
	Trospium Chloride related compound A: NMT 0.2%LC
	Any single unspecified Impurity: NMT 0.2%LC
Dissolution (Corealis-28602-B)	Total Impurities: NMT 1.5%LC
	Xanomeline: NLT 80% (Q) of labeled amount of Xanomeline is dissolved at 30 minutes. Report profile
	Trospium Chloride: NLT 80% (Q) of labeled amount of Trospium Chloride is dissolved at 30 minutes. Report profile
Microbial Limits ^B USP<61>, <62>	Total Yeasts and Molds Counts (TYMC): ≤100 cfu/g
	Total Aerobic Microbial Counts (TAMC): ≤1000 cfu/g
	Escherichia coli: Absent

FIG. 32

STORAGE		T= 0		25°C/60%RH	
TEST DESCRIPTION		3 Months		6 Months	
SPECIFICATION used at time of analysis		Stability, Rev 0		Stability, Rev 0	
Conforms to acceptance criteria (Y/N)		Y		Y	
Dissolution (%LC) (Coraleis-28602 6-01) (n=6) (500 mL of 0.1N HCl, paddles at 50 rpm)	Xanomeline	Y		Y	
	Time (min.)	Range		Range	
	10	%LC	27	%LC	41
	20	Range	7-93	Range	7-94
	(Q=80%) 30	%LC	86	%LC	98
	45	Range	74-93	Range	94-105
	Trospium Chloride	%LC	98	%LC	103
	Time (min.)	Range	86-104	Range	101-105
	10	%LC	101	%LC	103
	20	Range	91-105	Range	102-105
Microbial Limits * USP<61>, <62>	Method Revision	01		01	
	Total Yeasts and Molds Counts (TYMC): ≤100 cfu/g	<50 cfu/g		N/A	
	Total Aerobic Microbial Counts (TAMC): ≤1000 cfu/g	< 500 cfu/g		N/A	
	Escherichia coli: Absent	Absent		N/A	

FIG. 33

STORAGE		T= 0		30°C/65%RH	
TEST DESCRIPTION		Stability, Rev 0		6 Months	
SPECIFICATION used at time of analysis		Stability, Rev 0		Stability, Rev 0	
Conforms to acceptance criteria (Y/N)		Y		Y	
Dissolution (%LC) (Correlis-28602-B-01) (n=6) (900 mL of 0.1N HCl, paddles at 50 rpm)	Xanomeline	Range		Range	
	Time (min.)	%LC		%LC	
	10	27		18	
	20	88		85	
	(Q=80%) 30	98		99	
	45	101		103	
	Trospium Chloride	Range		Range	
	Time (min.)	%LC		%LC	
	10	26		12	
	20	84		81	
Microbial Limits ^a USP<61>, <62>	(Q=80%) 30	96		94	
	45	99		97	
	Method Revision	01		01	
	Total Yeasts and Molds Counts (TYMC): ≤100 cfu/g	<50 cfu/g		N/A	
	Total Aerobic Microbial Counts (TAMC): ≤1000 cfu/g	< 500 cfu/g		N/A	
Escherichia coli: Absent		Absent		N/A	

FIG. 34

STORAGE		40°C/75%RH	
TEST DESCRIPTION		6 Months	
SPECIFICATION used at time of analysis		Stability, Rev 0	
Conforms to acceptance criteria (Y/N)		Stability, Rev 0	
Description (Visual)		Stability, Rev 0	
Water content by KF (USP <921>, Method 1a) (n=3)		Stability, Rev 0	
Assay (Coreals-28602-AD-01) (n=2)	% label claim Xanomeline	Y	No change as compared to Initials
	mg Xanomeline/capsule	Y	No change as compared to Initials
	% label claim Trospium Chloride	Y	No change as compared to Initials
	mg Trospium Chloride/capsule	Y	No change as compared to Initials
	Method Revision	01	02
Related substances (%LC) ^a (Coreals-28602-AD-01) (n=2)	Trospium Chloride related compound B	Not detected	Not detected
	Trospium Chloride related compound A	Not detected	<0.1
	Unspecified impurity (Xanomeline, RRT 0.24) ± 5	0.15	0.14
	Unspecified impurity (Xanomeline, RRT 1.10) ± 5	0.18	0.21
	Total Impurities	0.32	0.35
Method Revision		01	02

FIG. 35

STORAGE		T= 0		25°C/60%RH			
TEST DESCRIPTION				3 Months		6 Months	
SPECIFICATION used at time of analysis		Stability, Rev 0		Stability, Rev 0		Stability, Rev 0	
Conforms to acceptance criteria (Y/N)		Y		Y		Y	
Dissolution (%LC) (Corals: 28602-B-01) (n=6) (900 mL of 0.1N HCl, paddles at 50 rpm)	Xanomeline						
	Time (min.)	%LC	Range	%LC	Range	%LC	Range
	10	27	7-39	41	7-94	26	10-48
	20	86	74-99	98	84-105	95	89-101
	(Q=80%) 30	98	86-104	103	101-105	105	105-107
	45	101	91-105	103	102-105	106	105-108
	Trospium Chloride	%LC	Range	%LC	Range	%LC	Range
	Time (min.)						
	10	26	7-65	35	5-82	22	9-39
	20	84	75-93	92	86-97	91	87-93
Microbial Limits * USP <61>, <62>	(Q=80%) 30	96	89-101	96	92-100	100	97-103
	45	99	93-102	96	93-100	101	97-104
	Method Revision	01		01		01	
	Total Yeasts and Molds Counts (TYMC): ≤100 cfu/g	<50 cfu/g		N/A		N/A	
Microbial Limits * USP <61>, <62>	Total Aerobic Microbial Counts (TAMC): ≤1000 cfu/g	< 500 cfu/g		N/A		N/A	
	Escherichia coli: Absent	Absent		N/A		N/A	

FIG. 36

STORAGE		T= 0		30°C/65%RH	
TEST DESCRIPTION				8 Months	
SPECIFICATION used at time of analysis		Stability, Rev 0		Stability, Rev 0	
Conforms to acceptance criteria (Y/N)		Y		Y	
Dissolution (%LC) (Corals-29602-B-01) (n=6) (900 mL of 0.1N HCl, paddles at 50 rpm)	Xanomeline				
	Time (min.)				
	10	27	7-59	16	5-45
	20	86	74-99	85	76-89
	(Q=80%) 30	98	86-104	99	86-101
	45	101	91-105	103	99-105
	Trospium Chloride				
	Time (min.)				
	10	26	7-85	12	5-34
	20	84	75-93	81	77-85
Microbial Limits * USP<61>, <62>	(Q=80%) 30	96	89-101	94	92-96
	45	98	93-102	97	95-100
	Method Revision	01		01	
	Total Yeasts and Molds Counts (TYMC): ≤100 cfu/g			<50 cfu/g	
	Total Aerobic Microbial Counts (TAMC): ≤1000 cfu/g			< 500 cfu/g	
	Escherichia coli: Absent			Absent	

FIG. 37

STORAGE		T= 0		40°C/75%RH		
TEST DESCRIPTION		Stability, Rev 0		Stability, Rev 0		
SPECIFICATION used at time of analysis		Stability, Rev 0		Stability, Rev 0		
Conforms to acceptance criteria (YN)		Y		Y		
Dissolution (%LC) (Corasil-28602-B-01) (n=6) (900 mL of 0.1N HCl, paddles at 50 rpm)	Xanomeline	%LC	Range	%LC ^a	Range ^a	
	Time (min.)					
	10	27	7-69	43	22-64	
	20	86	74-99	91	71-100	
	(Q=80%) 30	98	86-104	99	83-103	
	45	101	91-105	100	84-103	
	Trospium Chloride	%LC	Range	%LC ^a	Range	
	Time (min.)					
	10	26	7-65	39	18-67	
	20	84	75-93	89	73-100	
Microbial Limits ^a USP<61>, <62>	(Q=80%) 30	96	89-101	96	90-105	
	45	99	93-102	97	93-106	
	Method Revision		01		01	
	Total Yeasts and Molds Counts (TYMC): ≤100 cfu/g	<50 cfu/g		N/A		
	Total Aerobic Microbial Counts (TAMC): ≤1000 cfu/g	< 500 cfu/g		N/A		
	Escherichia coli: Absent	Absent		N/A		

FIG. 38

Xanomeline API Related Substances Profile for Xanomeline/Trospium Cl 75/20 mg Capsules

Stability time point		Initials	T= 3 months	T= 6 months
Related Substances (%w/w) (n=1) (Corealis-28602-AD-01)	Unspecified Impurity (RRT 0.23)	0.14	0.14	0.14
	Unspecified Impurity (RRT 1.09)	0.20	0.14	0.21
	Method Revision	01	02	03

FIG. 39

Trospium Chloride API Related Substances Profile for Xanomeline/Trospium Cl 75/20 Capsules

Stability time point		Initials	T= 3 months	T= 6 months
Related Substances (%w/w) (n=1) (Corealis-28602-AD-01)	Unspecified Impurity	Not Detected	Not Detected	Not Detected
	Method Revision	01	02	03

FIG. 40

Specification for Xanomeline/Trospium Cl 75/20 mg Capsules

TEST DESCRIPTION	ACCEPTANCE CRITERIA
	Stability, Rev 0
Description (Visual)	White to off-white opaque hard shell capsule with no markings
Water Content by KF (USP <921>, Method 1a)	Report result
Assay (%LC) (Corealis-28602-AD)	Xanomeline: 90 - 110% label claim (68 - 83 mg Xanomeline/capsule)
	Trospium Chloride: 90 - 110% label claim (18 - 22mg Trospium Chloride/capsule)
Related Substances (%LC) ^a (Corealis-28602-AD)	Trospium Chloride related compound B: NMT 0.2%LC
	Trospium Chloride related compound A: NMT 0.2%LC
	Any single unspecified impurity: NMT 0.2%LC
	Total Impurities: NMT 1.5%LC
Dissolution (Corealis-28602-B)	Xanomeline: NLT 80% (Q) of labeled amount of Xanomeline is dissolved at 30 minutes. Report profile
	Trospium Chloride: NLT 80% (Q) of labeled amount of Trospium Chloride is dissolved at 30 minutes. Report profile
Microbial Limits [®] USP<61>, <62>	Total Yeasts and Molds Counts (TYMC): ≤100 cfu/g
	Total Aerobic Microbial Counts (TAMC): ≤1000 cfu/g
	Escherichia coli: Absent

FIG. 41

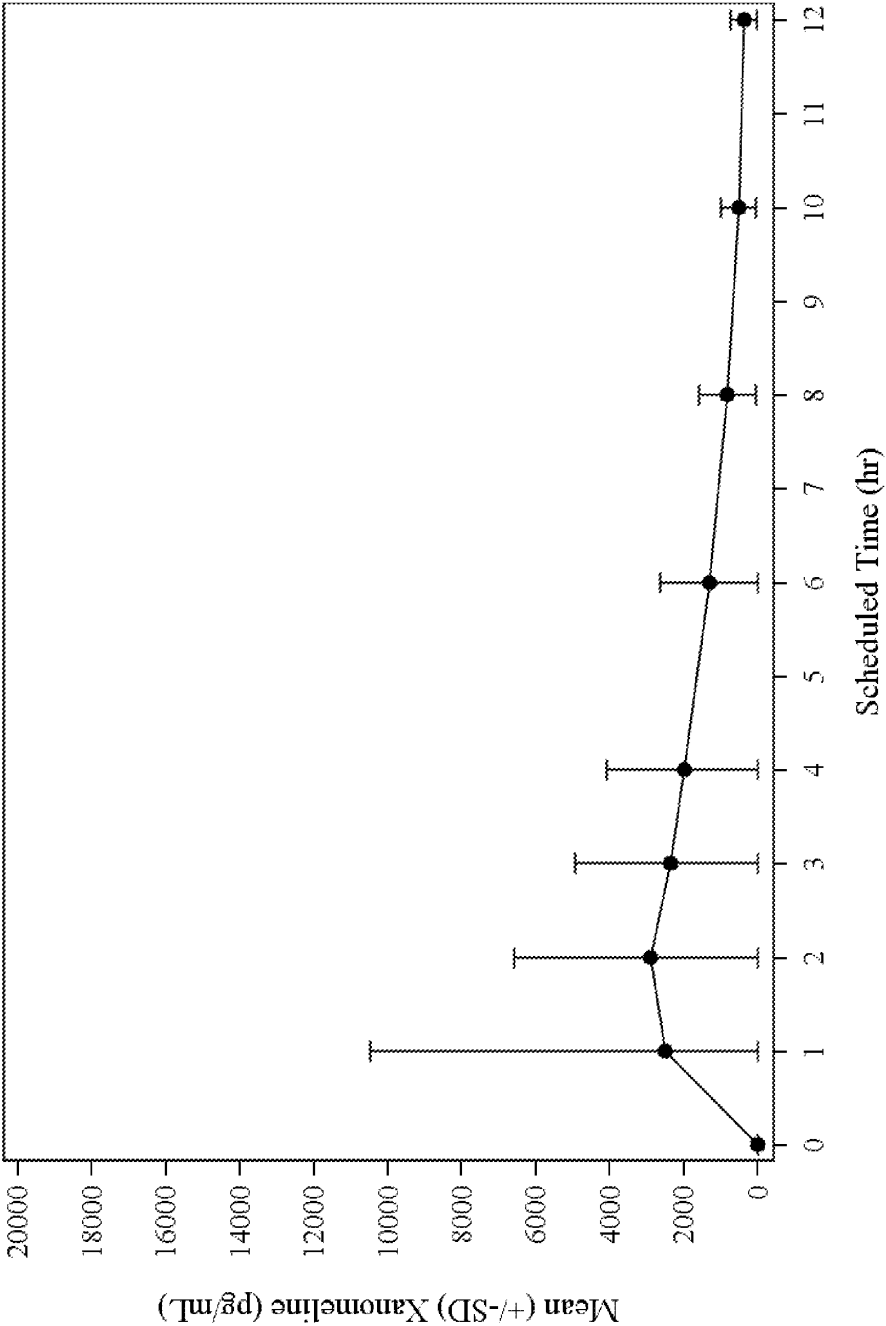


FIG. 42

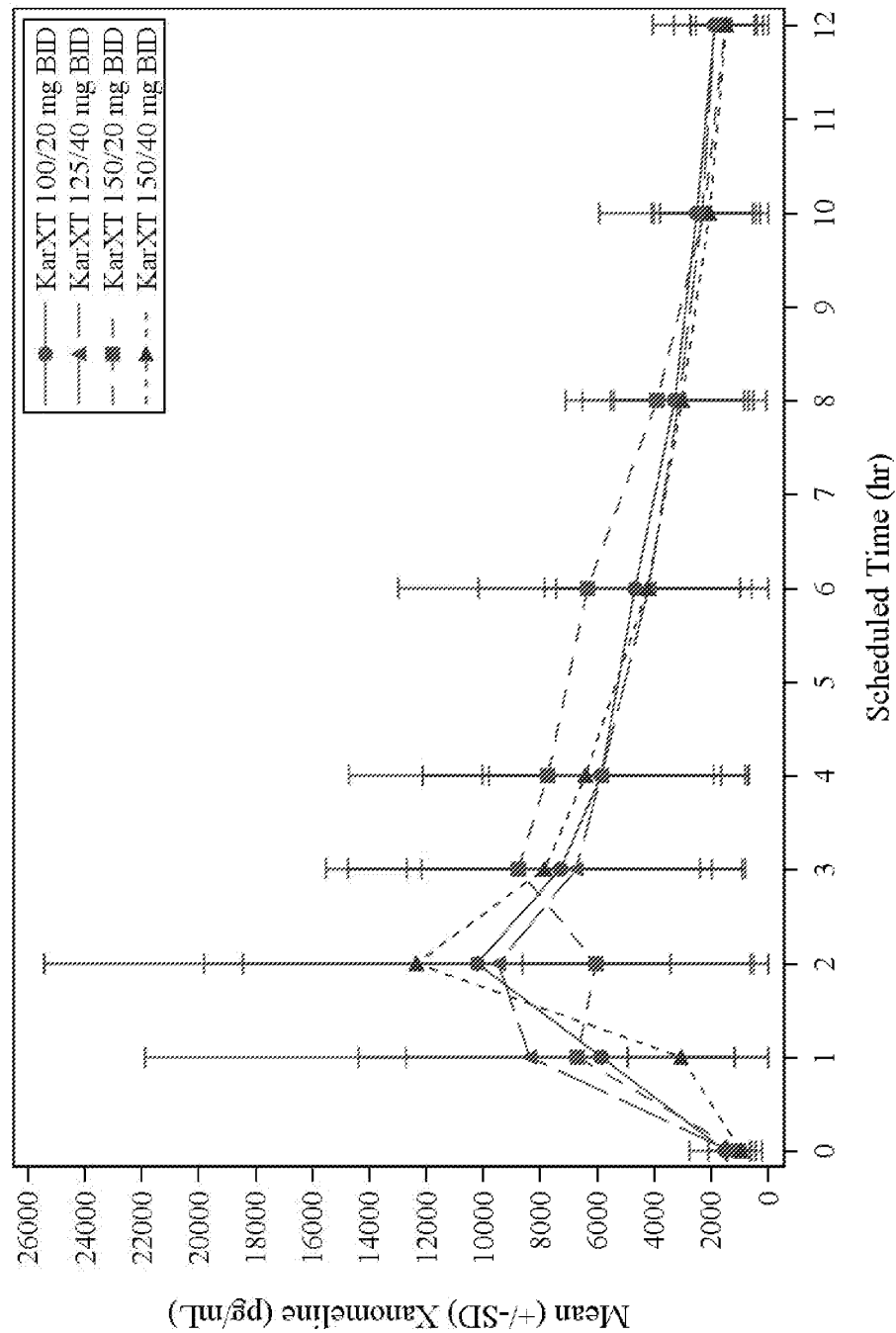


FIG. 43

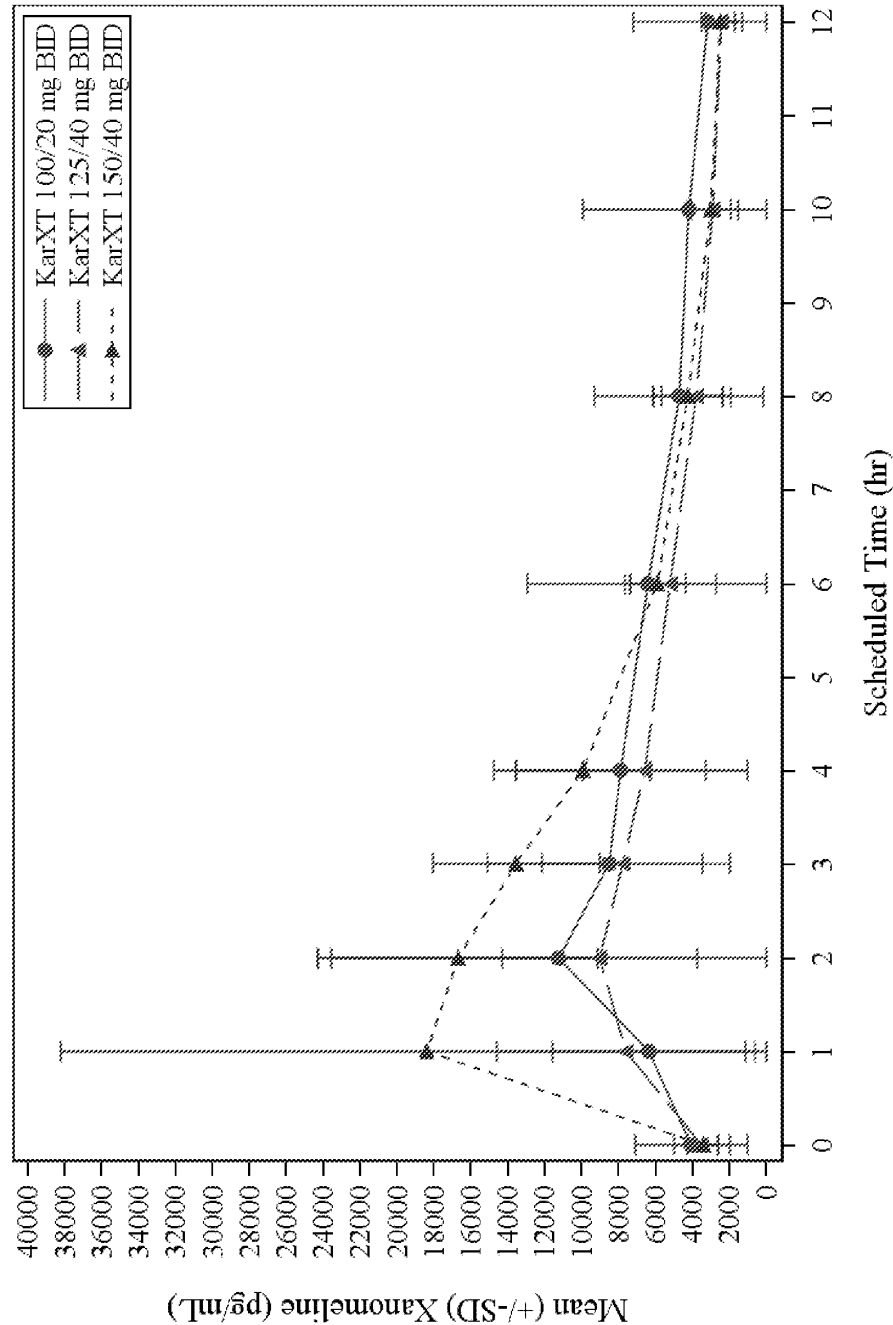


FIG. 44

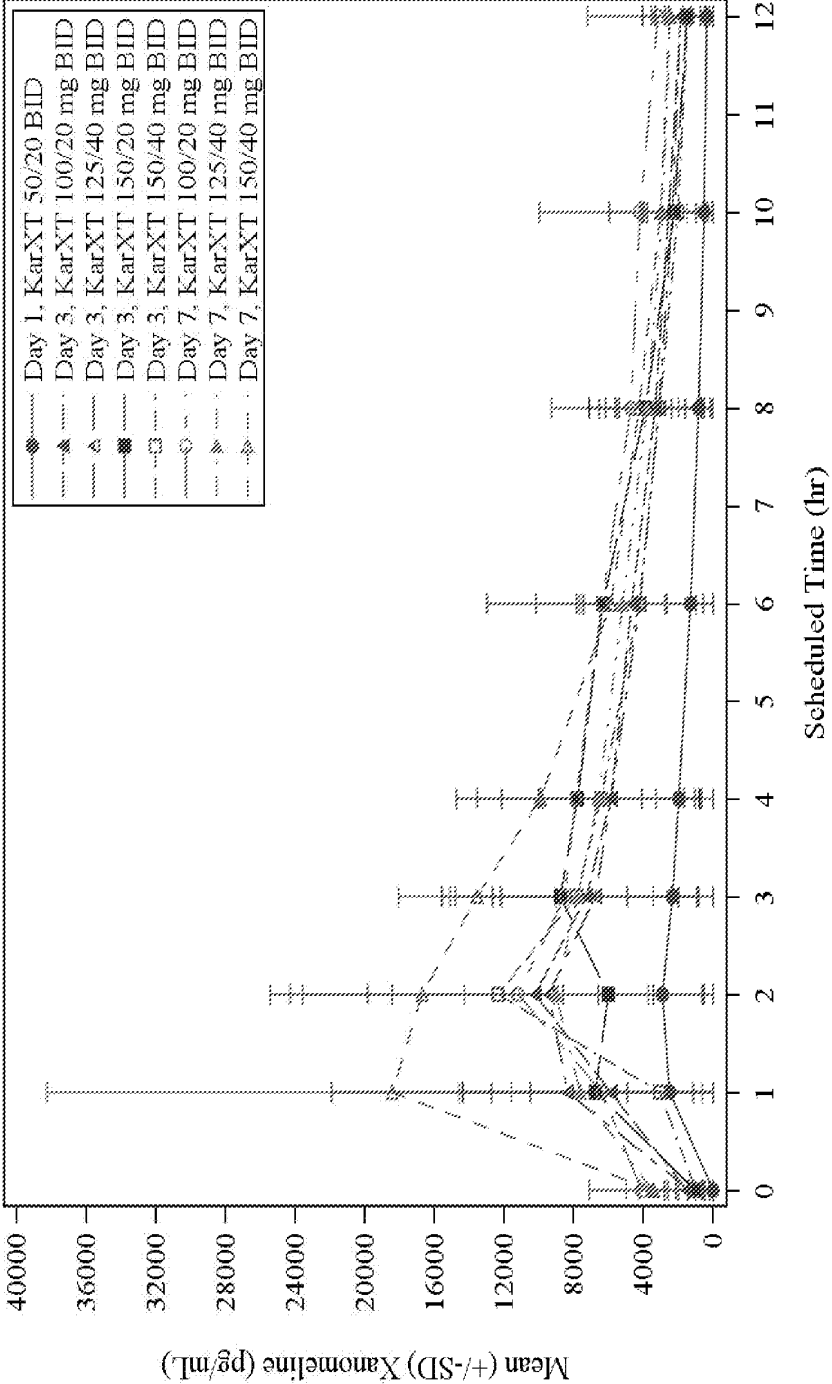


FIG. 45

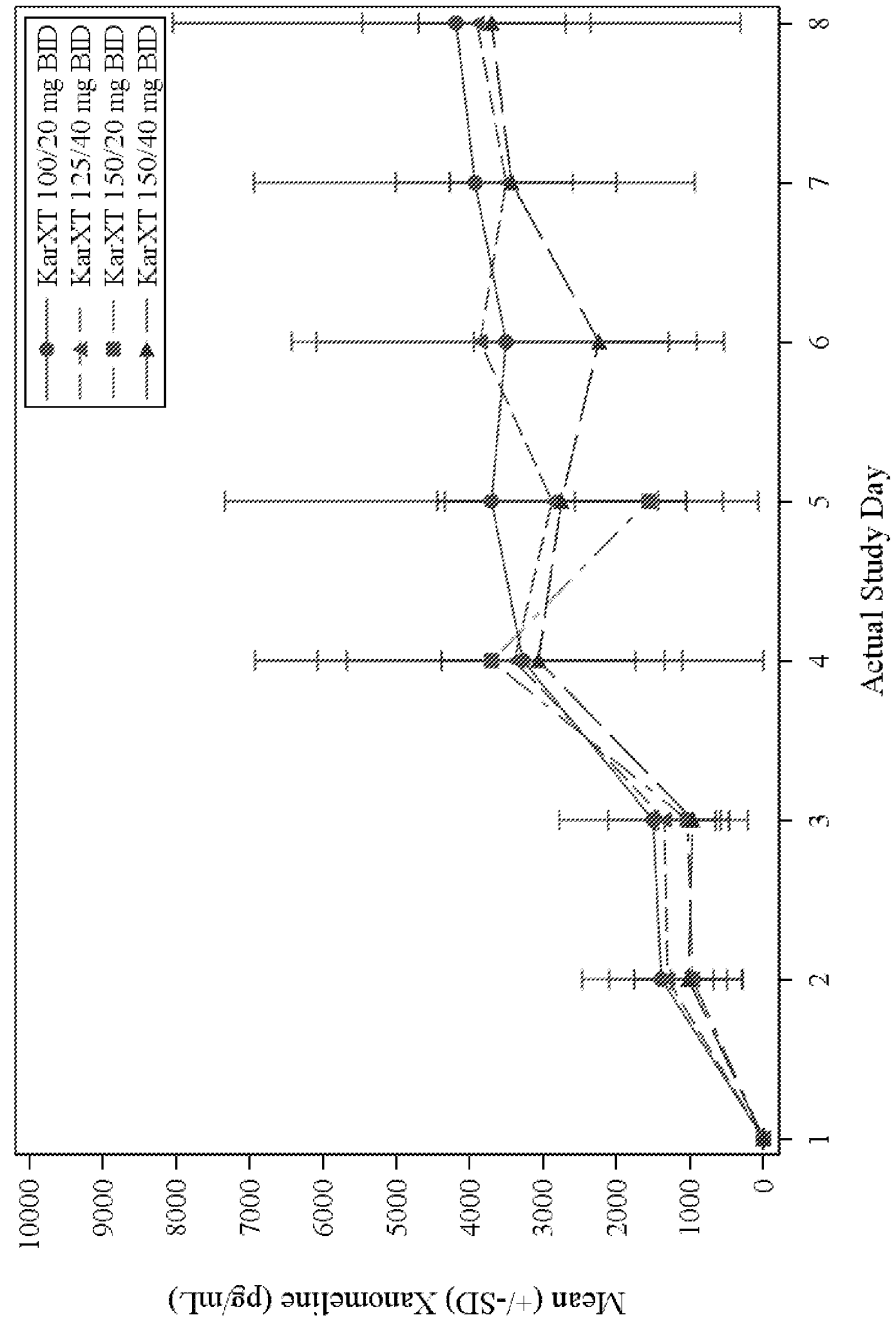


FIG. 46

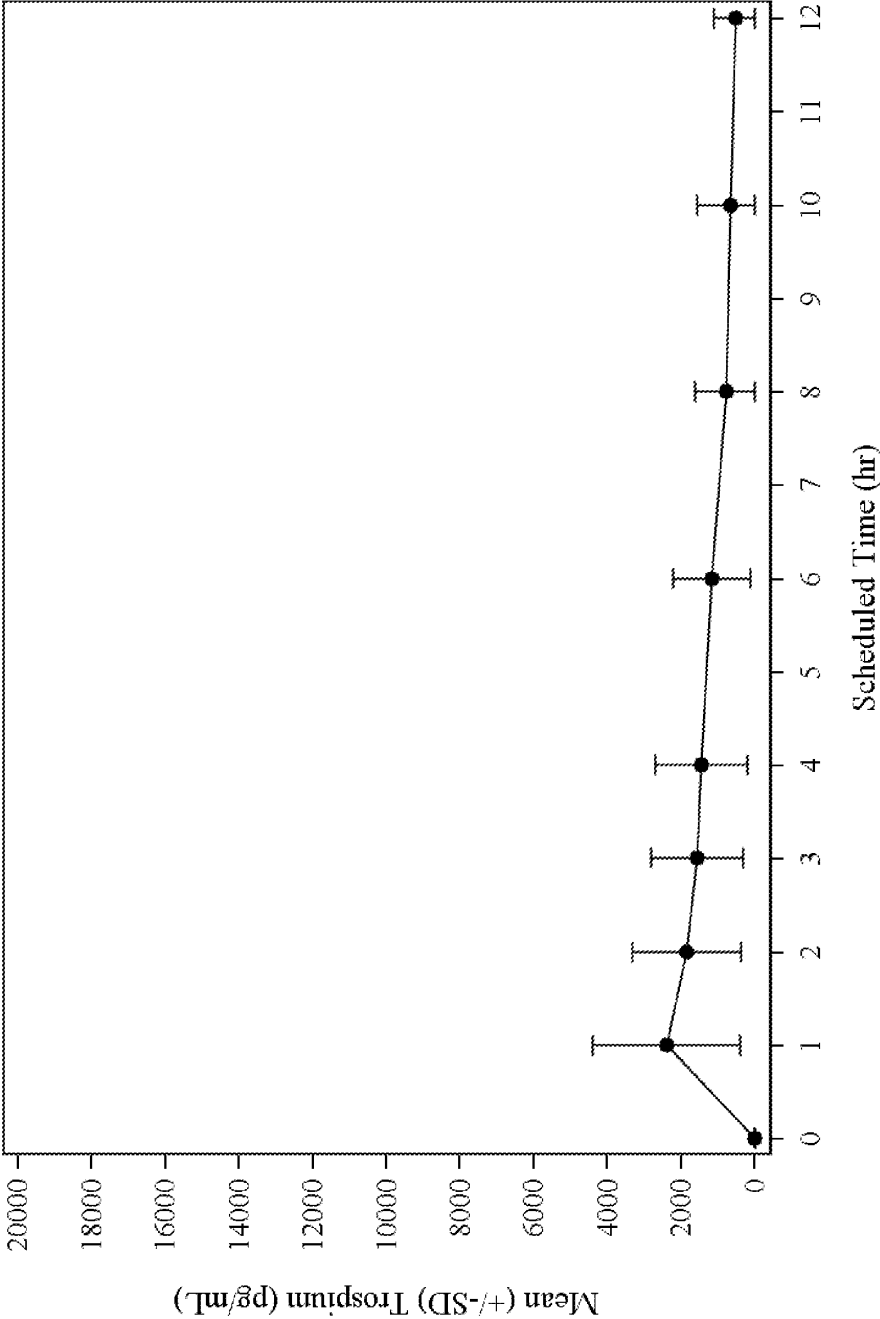


FIG. 47

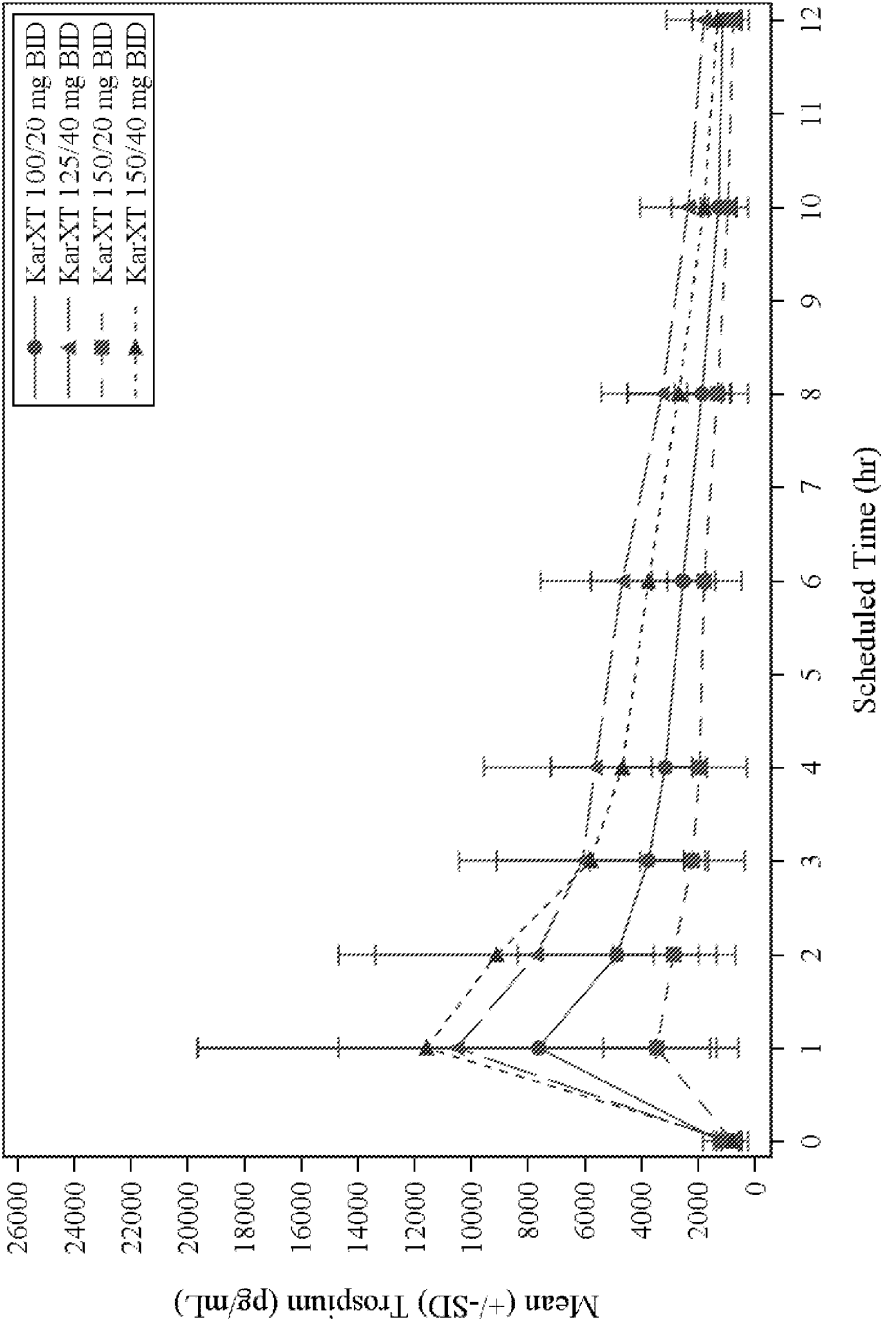


FIG. 48

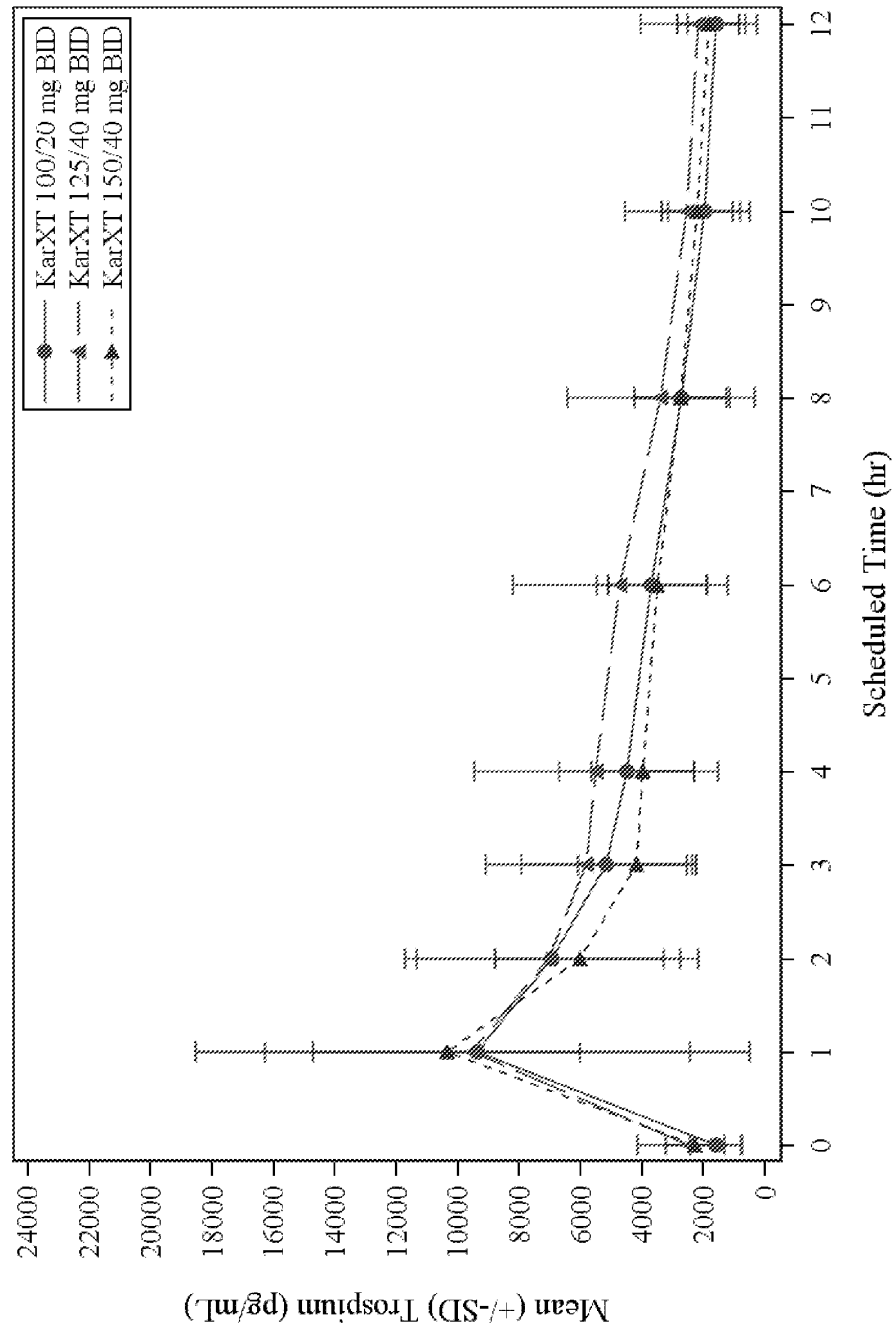


FIG. 49

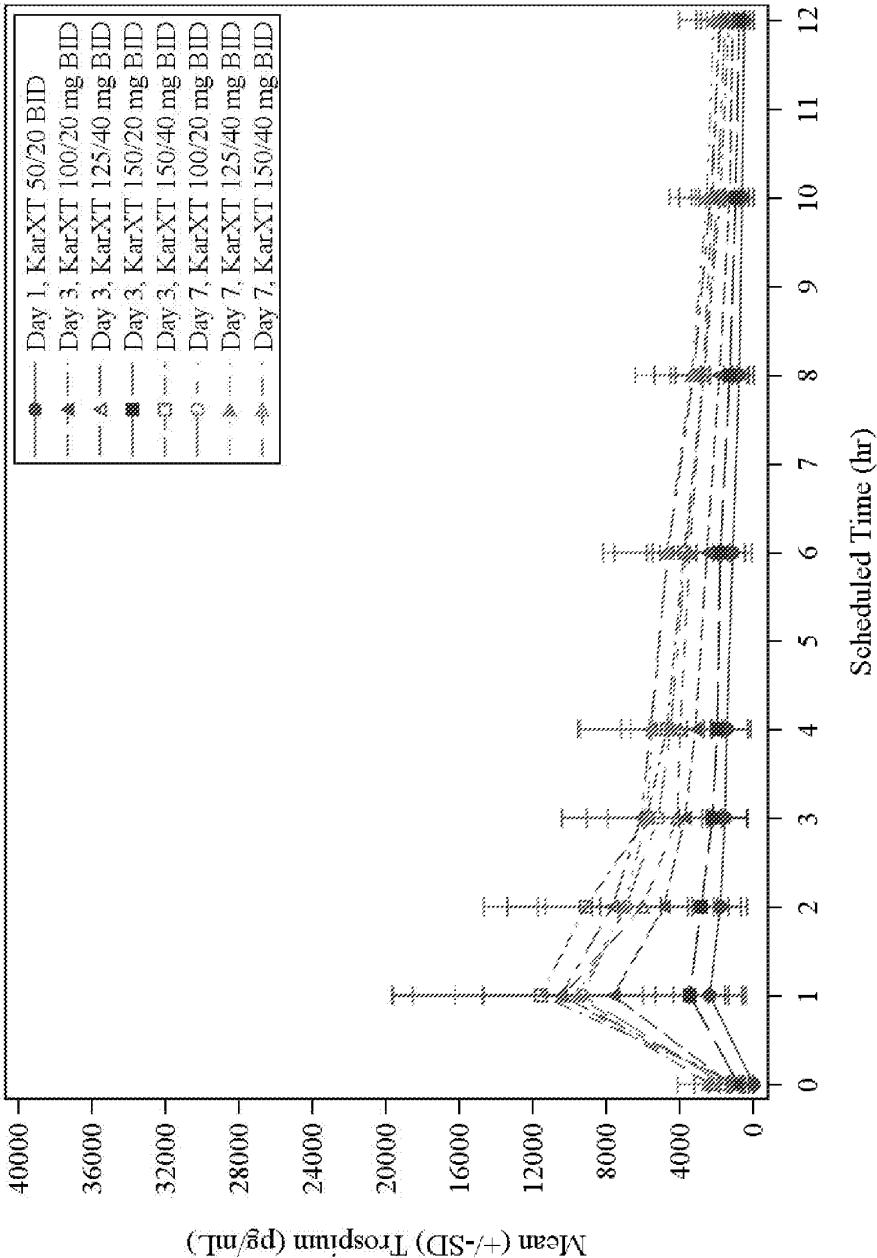


FIG. 50

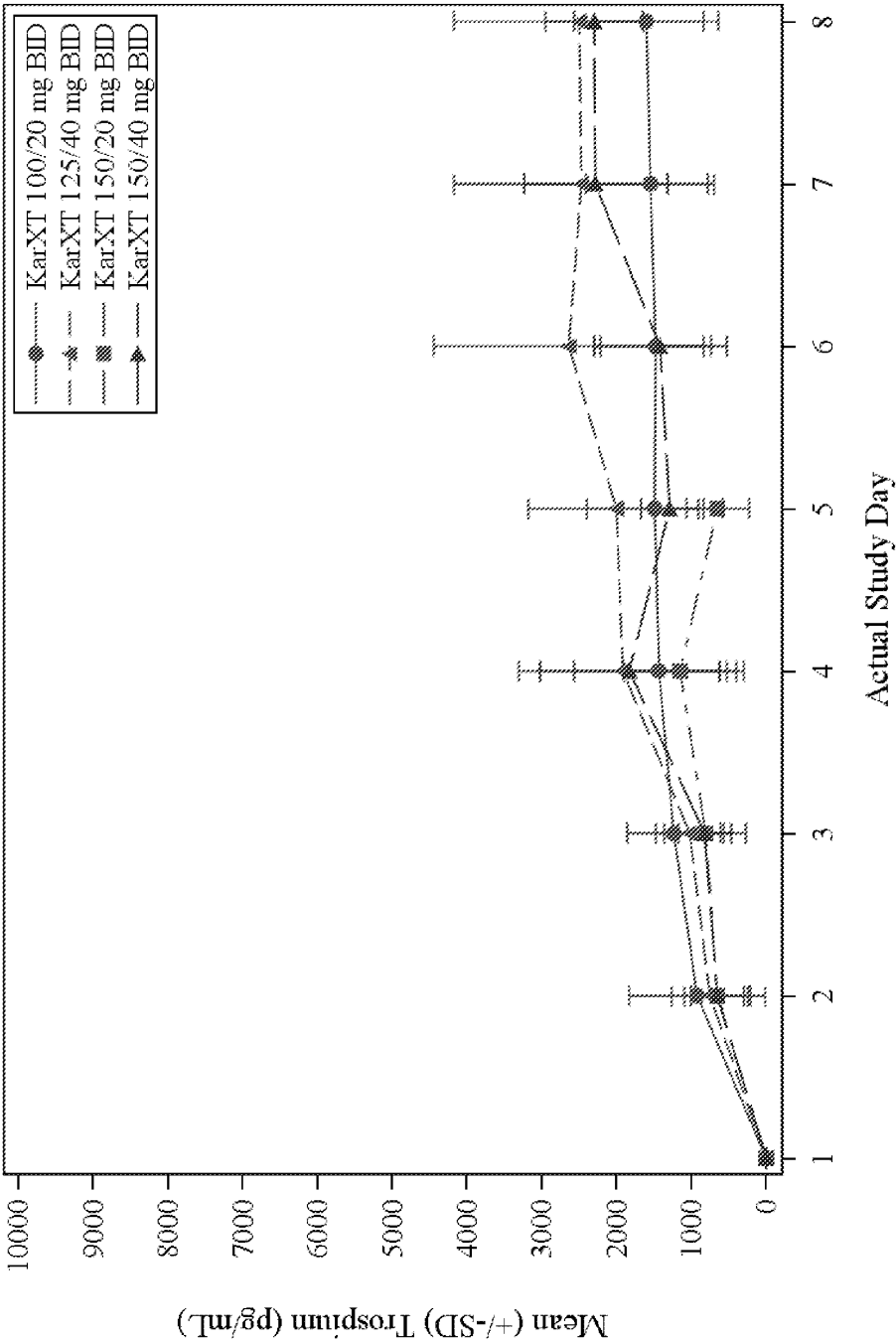


FIG. 51