

Appendix 11 Body Weight (TK satellite group)

B131138

Sex: Male Bodyweight (g)

10 mg/kg	Day(s) Relative to Start Date						
	1	8	15	21	22	25	28
20201	330.6	334.7	358.6	-	381.6	372.0	-
20202	335.5	358.6	395.9	-	424.8	403.2	-
20203	341.9	361.6	386.2	-	403.8	412.4	-
20204	347.3	361.9	387.0	-	402.6	383.0	-
20205	355.6	388.5	413.6	-	422.0	-	-

Appendix 11 Body Weight (TK satellite group)

B131138

Sex: Male Bodyweight (g)

25 mg/kg	Day(s) Relative to Start Date						
	1	8	15	21	22	25	28
20301	330.1	347.2	374.9	-	354.5	353.2	-
20302	332.6	353.7	387.2	402.3	-	-	-
20303	341.6	364.1	386.1	-	389.9	376.0	-
20304	350.4	389.3	427.3	-	441.6	-	427.8
20305	359.8	380.1	405.5	-	411.6	399.5	-

Appendix 11 Body Weight (TK satellite group)

B131138

Sex: Female Bodyweight (g)

1 mg/kg	Day(s) Relative to Start Date				
	1	8	15	22	25
60101	244.0	258.6	271.5	281.4	279.2
60102	238.0	246.0	255.7	264.0	266.1
60103	254.2	277.9	291.9	299.4	306.9
60104	218.8	239.5	245.4	246.3	251.2
60105	245.0	256.2	271.4	280.9	281.4

Appendix 11 Body Weight (TK satellite group)

B131138

Sex: Female Bodyweight (g)

10 mg/kg	Day(s) Relative to Start Date				
	1	8	15	22	25
60201	237.2	260.7	272.9	287.3	285.4
60202	253.6	272.0	276.3	280.5	279.9
60203	239.2	245.4	286.4	280.8	273.9
60204	237.5	244.5	266.4	257.3	271.8
60205	225.2	247.7	259.7	267.9	261.7

Appendix 11 Body Weight (TK satellite group)

B131138

Sex: Female Bodyweight (g)

25 mg/kg	Day(s) Relative to Start Date				
	1	8	15	22	25
60301	244.6	260.0	272.5	285.0	287.8
60302	243.0	248.9	262.4	258.3	274.2
60303	223.3	238.4	246.9	256.3	249.7
60304	240.4	247.4	261.6	-	-
60305	246.3	260.8	276.2	258.2	277.1

Appendix 12 Hematology (TK satellite group) B131138

Sex: Male Day(s) Relative to Start Date

25 mg/kg	Hematology													
	Red Blood Cell Count (10 ⁶ /μL)	Hemoglobin conc. (g/dL)	Hematocrit (%)	MCV (fL)	MCH (pg)	MCHC (g/dL)	Platelet Count (10 ³ /μL)	Reticulocyte (%)	PT (sec)	APTT (sec)	White Blood Cell Count (10 ³ /μL)	Lymphocyte (%)	Neutrophil (%)	Eosinophil (%)
	29	29	29	29	29	29	29	29	29	29	29	29	29	29
20304	7.26	13.6	38.1	52.5	18.7	35.7	1497	3.66	9.1	12.5	14.32	50.0	47.0	0.4

Appendix 12 Hematology (TK satellite group) B131138

Sex: Male Day(s) Relative to Start Date

25 mg/kg	Hematology						
	Basophil	Monocyte	Lymphocyte	Neutrophil	Eosinophil	Basophil	Monocyte
	(%)	(%)	(10 ³ /μL)				
	29	29	29	29	29	29	29
20304	0.0	2.6	7.16	6.73	0.06	0.00	0.37

Appendix 13

Blood Chemistry (TK satellite group)

B131138

Sex: Male Day(s) Relative to Start Date

25 mg/kg	Blood Chemistry													
	ASAT (U/L)	ALAT (U/L)	LDH (U/L)	Gamma GT (U/L)	ALP (U/L)	Creatine Kinase (U/L)	Total Bilirubin (mg/dL)	Urea Nitrogen (mg/dL)	Creatinine (mg/dL)	Glucose (mg/dL)	Total Cholesterol (mg/dL)	Phospholipid (mg/dL)	Triglyceride (mg/dL)	Total Protein (g/dL)
	29	29	29	29	29	29	29	29	29	29	29	29	29	29
20304	112	33	242	1	533	174	0.1	16.0	0.2	97	49	73	21	5.7

Appendix 13

Blood Chemistry (TK satellite group)

B131138

Sex: Male Day(s) Relative to Start Date

25 mg/kg	Blood Chemistry													
	A/G Ratio	Albumin (%)	Alpha1 Globulin (%)	Alpha2 Globulin (%)	Beta Globulin (%)	Gamma Globulin (%)	Albumin (g/dL)	Alpha1 Globulin (g/dL)	Alpha2 Globulin (g/dL)	Beta Globulin (g/dL)	Gamma Globulin (g/dL)	Ca (mg/dL)	Inorganic Phosphorus (mg/dL)	Na (mmol/L)
	29	29	29	29	29	29	29	29	29	29	29	29	29	29
20304	0.62	38.3	22.3	11.3	23.1	5.0	2.2	1.3	0.6	1.3	0.3	9.5	8.3	146

Sex: Male Day(s) Relative to Start Date

25 mg/kg	Blood Chemistry	
	K	Cl
	(mmol/L)	(mmol/L)
	29	29
20304	4.6	106

Appendix 14 Organ Weight (TK satellite group) B131138

Sex: Male Day(s) Relative to Start Date

25 mg/kg	Organ Weight (Rat)													
	Final Body Weight (g)	Brain (g)	Brain Ratio (%)	Pituitary (mg)	Pituitary Ratio ($\times 10^{\wedge}3\%$)	Thyroids (mg)	Thyroids Ratio ($\times 10^{\wedge}3\%$)	Thymus (mg)	Thymus Ratio ($\times 10^{\wedge}3\%$)	Submand. GLs (g)	Submand. GLs Ratio (%)	Lungs (g)	Lungs Ratio (%)	Heart (g)
	29	29	29	29	29	29	29	29	29	29	29	29	29	29
20304	412.0	1.97	0.48	15.8	3.8	24.6	6.0	308	74.8	0.69	0.17	1.73	0.42	1.31

Appendix 14 Organ Weight (TK satellite group) B131138

Sex: Male Day(s) Relative to Start Date

25 mg/kg	Organ Weight (Rat)												
	Heart Ratio (%)	Liver (g)	Liver Ratio (%)	Spleen (g)	Spleen Ratio (%)	Kidneys (g)	Kidneys Ratio (%)	Adrenals (mg)	Adrenals Ratio (x10 ⁻³ %)	Testes (g)	Testes Ratio (%)	Prostate (g)	Prostate Ratio (%)
	29	29	29	29	29	29	29	29	29	29	29	29	29
20304	0.32	8.91	2.16	0.85	0.21	3.11	0.75	63.2	15.3	3.72	0.90	0.46	0.11

SEX: MALE

GROUP 5 5 5 5 5 6 6 6 6 7 7 7 7
 REMOVAL REASON F F F F F F F F D F F F F

ANIMAL 2 2 2 2 2 2 2 2 2 2 2 2 2
 NUMBER 0 0 0 0 0 0 0 0 0 0 0 0 0
 1 1 1 1 1 2 2 2 2 3 3 3 3
 0 0 0 0 0 0 0 0 0 0 0 0 0
 1 2 3 4 5 1 2 4 5 1 3 4 5

Necropsy Findings; + + + + + + + + + + + + +
 Present P P P P P P P P P
 Absent P P P P P
 Administered Site; + + + + + + + + + + +
 Nodule P P P . P P P P
 Hematoma P
 Abdominal Cavity; + . + . +
 Increase; abdominal fluid P
 Adhesion; multiple organs; hematoma P
 Adhesion; multiple organs; nodule P . P

-657-

SEX: FEMALE

GROUP 7
REMOVAL REASON D

ANIMAL 6
NUMBER 0
3
0
4

Necropsy Findings; +
Present P

Administered Site; +
Nodule P

Abdominal Cavity; +
Increase; abdominal fluid P
Adhesion; multiple organs; nodule P

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Key Page

Group Code	Description
5	1 mg/kg
6	10 mg/kg
7	25 mg/kg

Removal Reason Code	Description
D	Death
F	Scheduled sacrifice

Tissue Result Code	Description
N	N.V.L
.	Not Recorded
+	Tissue Observation Present
X	Not Examined

Grade Code	Description
.	not recorded
#	duplicate
P	present - no grade or classification

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11. $[^{14}\text{C}]$ P092 マレイン酸塩の合成

Synthesis of [¹⁴C]P092 maleate

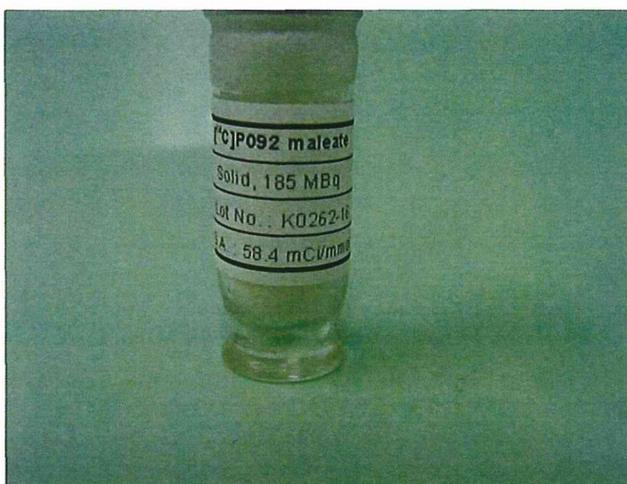
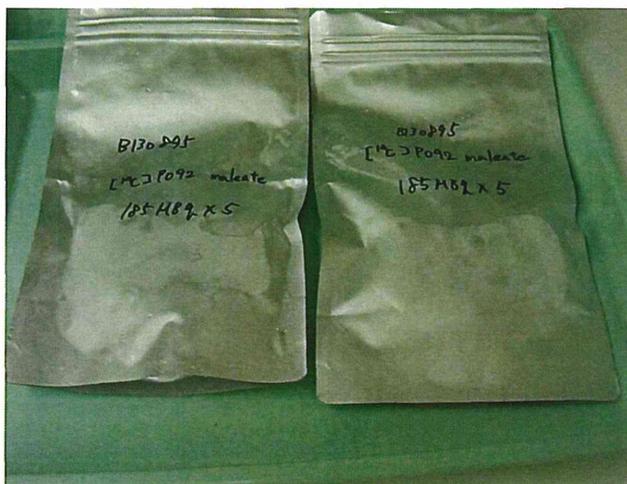
(Study No.:B130895)

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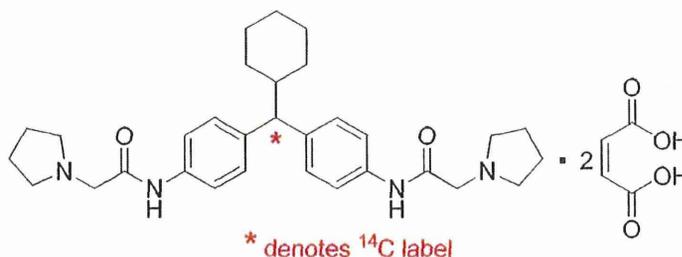
Pictures: [¹⁴C]P092 maleate



CERTIFICATE OF ANALYSIS

(non-GMP, For Research Use Only)

Project No. C-0188



PRODUCT NAME	: [¹⁴ C]P092 maleate
MOLECULAR FORMULA	: ¹⁴ C ₁ C ₃₈ H ₅₀ N ₄ O ₁₀
MOLECULAR WEIGHT	: 736.70 (at this specific activity)
LOT NUMBER	: K0262-16
DATE OF ANALYSIS	: February 21, 2014
SPECIFIC ACTIVITY	: 58.4 mCi/mmol by LSC
CHEMICAL PURITY	: 98.2% by UV-HPLC
RADIOCHEMICAL PURITY	: 98.5% by HPLC on-line β-RAM & Laura 4
PHYSICAL DESCRIPTION	: White Solid
PACKAGING	: 1850 MBq (50 mCi) in screw-capped 10 vials : (185 MBq x 10 vials)
STORAGE	: Store at -80 °C in the absence of moisture, light and air

SPECTROSCOPIC DATA:

¹H Nuclear Magnetic Resonance Spectroscopy

Instrument : Varian 400 MHz

Solvent : D₂O

APCI Mass Spectroscopy

Instrument : Thermo LCQ-Fleet

CHROMATOGRAPHIC DATA:

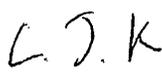
High Performance Liquid Chromatography

Instrument : Agilent 1200
Column : Inertsil ODS-2 (4.6 × 250 mm, 5 μm)
Mobile phase : A = 0.2% TFA Water
 B = Acetonitrile
Gradient : Time 0 20 50 50.1 60
 %B 20 60 60 20 20
Column Temperature : 40 °C
Flow rate : 1.0 mL/min
UV detection : 254 nm
Radiodetector : Lab Logic system, β-RAM 4
Radio detection : β-RAM
Integrator : Laura 4
Splitter : 0 % (off)
Flow Cell Volume : 500 μL
Scint flow : 3.0 mL/min
Cocktail : ULTIMA-FLO™ AP

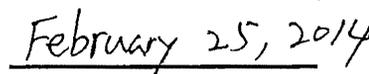
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LAB Manager



QC Manager



Date