表 2.6.5.5-1　白色ラット単回経口投与後の組織中濃度（続）

組織／血漿中濃度比

	Tissue:Plasma Concentration Ratio											
	Sacrifice Time (Hours)											
Tissue	1	SD	3	SD	8	SD	24	SD	72	SD	168	SD
Large intestine	0.926	0.0989	2.90	0.521	7.02	2.10	9.27	4.65	NA	NA	NA	NA
Liver	12.7	1.88	33.5	4.97	25.5	4.66	31.7	2.98	57.6[a]	NA	NA	NA
Lung(s)	6.88	1.16	29.4	5.50	42.0	9.02	25.2	5.29	16.9[b]	NA	NA	NA
Lymph node(s)	1.15	0.259	5.68	1.24	12.4	1.26	15.7	0.390	24.6[a]	NA	NA	NA
Muscle	0.591	0.131	3.53	0.762	4.79	0.346	4.39	0.304	NA	NA	NA	NA
Myocardium	3.18	0.171	9.12	0.554	9.15	1.16	7.56	1.07	8.38[b]	NA	NA	NA
Nasal turbinates	0.349	0.0379	1.25	0.311	2.63	0.622	6.80	1.06	11.8[a]	NA	NA	NA
Pancreas	3.22	0.507	12.2	1.29	15.2	0.714	19.3	2.50	24.8[a]	NA	NA	NA
Pituitary gland	3.19	0.377	13.1	1.81	21.3	1.68	25.8	1.71	31.9[a]	NA	NA	NA
Preputial gland	0.514	0.208	4.34	1.04	12.1	0.833	43.1	14.8	80.3[a]	NA	NA	NA
Prostate gland	0.746	0.129	3.50	0.953	7.53	0.778	7.66	2.63	12.1[a]	NA	NA	NA
Salivary gland(s)	2.46	0.256	11.3	1.21	16.6	1.89	17.1	1.99	15.9[a]	NA	NA	NA
Salivary gland(s), parotid	1.86	0.264	8.52	0.253	12.2	1.90	14.9	0.887	13.1[a]	NA	NA	NA
Seminal vesicle(s)	0.170[b]	NA	0.805	0.378	1.74	0.234	3.28[b]	NA	NA	NA	NA	NA
Skin (nonpigmented)	0.398	0.113	1.66	0.457	3.37	0.606	7.43	2.04	8.50[b]	NA	NA	NA
Small intestine	1.43	0.322	6.70	0.228	9.40	1.45	9.28	1.56	16.5[b]	NA	NA	NA
Spinal cord	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Spleen	5.17	0.828	16.8	2.20	22.9	2.96	24.7	3.61	44.3[a]	NA	NA	NA
Stomach	1.39	0.252	3.58	0.633	5.04	0.544	7.31	1.15	9.02[b]	NA	NA	NA
Stomach mucosa	2.05	0.438	4.46	0.587	5.68	0.379	10.3	1.10	13.1[a]	NA	NA	NA
Stomach wall	0.963	0.0538	2.86	0.429	4.69	0.686	5.90	0.581	10.7[b]	NA	NA	NA
Testis(es)	NA	NA	0.216	0.0273	0.635	0.0532	3.51	0.308	NA	NA	NA	NA
Thymus	0.635	0.103	3.73	0.388	9.53	1.77	12.5	1.85	14.3[b]	NA	NA	NA
Thyroid	4.51	0.377	16.9	1.27	22.4	5.91	23.8	3.84	39.9[a]	NA	NA	NA
Urinary bladder	1.03	0.476	2.18	0.128	3.80	0.634	4.95	0.714	NA	NA	NA	NA

NA: Not applicable. SD: Standard deviation.

[a] Mean is the average of two values.

[b] Mean is based on one value.

表 2.6.5.5-2　有色ラット単回経口投与後の組織中濃度

	Test Article: [^{14}C]entrectinib
	Location in CTD: 4.2.2.3-5
	Study No. SR-[redacted]-003 (1087284)
Species: Rat (Long Evans)	
Gender (M/F)/Number of Animals: 3 M per group per sampling time	
Feeding Condition: Fed	
Vehicle/Formulation: 0.5% methylcellulose and 1% Tween® 80 in reverse osmosis water	
Method of Administration: PO	
Dose (mg/kg): 20	
Radionuclide: ^{14}C	
Specific Activity: 5.49 μCi/mg in dosing formulation (ca.111 μCi/kg)	
Analyte/Assay: Radioactivity/Quantitative whole-body autoradiography (QWBA)	
Sampling Time: l, 3, 8, 24, 72, and 168 h postdose	

表 2.6.5.5-2　有色ラット単回経口投与後の組織中濃度（続）

	Concentration (ng Equivalents [^{14}C]RXDX-101/g)											
	Sacrifice Time (Hours)											
Tissue	1	SD	3	SD	8	SD	24	SD	72	SD	168	SD
Adrenal gland(s)	4990	1590	19200	4020	17300	1990	3720	1100	734	117	453	20.8
Arterial wall	ND	0.00	ND	0.00	ND	0.00	ND	0.00	ND	0.00	ND	0.00
Bile	55400	34400	66200	10300	39300	6350	5380	530	ND	0.00	ND	0.00
Blood	1210	257	2370	96.4	1850	70.6	BLQ	0.00	ND	0.00	ND	0.00
Bone	BLQ	0.00	381	157	410	135	BLQ	0.00	ND	0.00	ND	0.00
Bone marrow	1310	312	6590	1240	10900	1300	1540	183	352	64.0	241	41.6
Brain cerebellum	BLQ	0.00	BLQ	0.00	BLQ	0.00	ND	0.00	ND	0.00	ND	0.00
Brain cerebrum	BLQ	0.00	BLQ	0.00	BLQ	0.00	ND	0.00	ND	0.00	ND	0.00
Brain choroid plexus	1580	159	4160	617	5630	627	1410	144	492	76.3	ND	0.00
Brain medulla	BLQ	0.00	BLQ	0.00	BLQ	0.00	ND	0.00	ND	0.00	ND	0.00
Brain olfactory lobe	BLQ	0.00	BLQ	0.00	BLQ	0.00	ND	0.00	ND	0.00	ND	0.00
Bulbo-urethral gland	1730	447	7410	1070	9170	1010	1900	197	237	41.2	ND	0.00
Cecum	875[a]	NA	4320	1100	9040	3150	986	72.5	BLQ	142	ND	0.00
Diaphragm	1640	585	5040	777	5250	592	667	71.5	BLQ	0.00	ND	0.00
Epididymis	BLQ	0.00	463	10.8	1050	135	768	295	204	177	BLQ	133
Esophagus	896	175	3730	760	4210	606	640	128	BLQ	0.00	ND	0.00
Exorbital lacrimal gland	756	173	5040	1160	10100	1090	4650	505	1770	259	1070	162
Eye lens	BLQ	0.00	BLQ	0.00	BLQ	0.00	BLQ	0.00	BLQ	0.00	BLQ	0.00
Eye uveal tract	1180	73.3	7350	1860	22500	1780	23200	3670	24100	2120	16800	309
Eye(s)	210	27.2	1440	326	3520	1010	4000	486	4160	488	3410	648
Fat (abdominal)	BLQ	181	778	232	959	49.5	BLQ	0.00	ND	0.00	ND	0.00
Fat (brown)	1300	231	4500	581	5120	253	766	151	BLQ	147	BLQ	161
Harderian gland	438	150	3410	1060	11100	570	10400	1470	4530	394	604	182

BLQ: Calculated value is below the limit of quantitation (<179 ng eq/g).　NA: Not applicable.
ND: Not detectable (sample shape not discernable from background or surrounding tissue).　SD: Standard deviation.
[a] Mean is the average of two values.

表 2.6.5.5-2　有色ラット単回経口投与後の組織中濃度（続）

	Concentration (ng Equivalents [^{14}C]RXDX-101/g)											
	Sacrifice Time (Hours)											
Tissue	1	SD	3	SD	8	SD	24	SD	72	SD	168	SD
Intra-orbital lacrimal gland	729	229	4400	1270	9220	393	5150	1010	2080	288	1290	302
Kidney cortex	4020	1030	15600	2550	13600	1490	2160	372	740	90.5	407	75.6
Kidney medulla	3630	814	14000	2510	15300	2460	2880	532	939	83.2	417	63.1
Kidney(s)	3790	913	14800	2680	14500	1920	2530	425	836	83.6	410	69.3
Large intestine	748	184	3650	294	3870	463	1570	914	BLQ	149	BLQ	0.00
Liver	9710	1850	29800	4570	21100	3550	3230	412	987	12.0	319	113
Lung(s)	4490	705	24100	843	44900	3950	2820	428	250	53.1	BLQ	115
Lymph node(s)	882	210	4830	953	10400	2010	1710	339	507	37.5	326	68.7
Muscle	590	157	2680	692	3380	303	431	70.5	BLQ	0.00	ND	0.00
Myocardium	2360	516	7330	1070	6290	480	686	29.8	BLQ	0.00	ND	0.00
Nasal turbinates	284	49.6	889	47.4	1800	576	728	223	224	30.2	ND	0.00
Pancreas	2390	768	9560	1540	10900	1080	1730	122	395	17.1	205	18.8
Pituitary gland	2310	681	15500	3720	31500	10100	5650	3210	2210	846	1140	566
Preputial gland	557	232	2020	551	4080	2240	4100	1330	2730	117	3160	2580
Prostate gland	484	158	2100	458	4110	1160	667	92.4	BLQ	0.00	ND	0.00
Salivary gland(s)	1740	453	8380	1250	12100	1170	1690	334	290	40.5	BLQ	104
Salivary gland(s), parotid	1310	385	6390	922	8170	857	1500	251	305	63.0	BLQ	0.00
Seminal vesicle(s)	BLQ	128	799	166	1130	329	210	184	BLQ	0.00	ND	0.00
Skin (nonpigmented)	240	51.5	1040	250	1840	72.3	544	87.0	BLQ	0.00	BLQ	0.00
Skin (pigmented)	259	70.2	1160	164	2120	333	990	367	525	103	BLQ	167
Small intestine	2590	2350	5960	1300	6980	298	1040	554	BLQ	132	BLQ	137
Spinal cord	BLQ	0.00	BLQ	0.00	BLQ	0.00	ND	0.00	ND	0.00	ND	0.00
Spleen	3840	927	13000	2120	16500	2740	2440	476	797	100	514	45.3

BLQ: Calculated value is below the limit of quantitation (<179 ng eq/g).
ND: Not detectable (sample shape not discernable from background or surrounding tissue).　SD: Standard deviation.

表 2.6.5.5-2　有色ラット単回経口投与後の組織中濃度（続）

	Concentration (ng Equivalents [^{14}C]RXDX-101/g)											
	Sacrifice Time (Hours)											
Tissue	1	SD	3	SD	8	SD	24	SD	72	SD	168	SD
Stomach	891	155	2760	383	3270	166	719	52.3	BLQ	132	ND	0.00
Stomach mucosa	1110	130	3930	558	3540	780	860	151	232	37.9	BLQ	150
Stomach wall	768	92.9	2320	472	4050	580	491	54.2	BLQ	0.00	ND	0.00
Testis(es)	BLQ	0.00	222	31.7	519	117	423	62.2	BLQ	0.00	ND	0.00
Thymus	497	93.3	3070	391	6230	77.0	1230	301	257	44.6	BLQ	0.00
Thyroid	3370	764	11700	310	12700	2510	2630	73.9	693	47.0	458	131
Urinary bladder	406	108	4120[a]	NA	3160	248	1170[a]	NA	BLQ	0.00	ND	0.00
Urine	825	254	4240	2320	6820	4030	1010	280	BLQ	0.00	ND	0.00

BLQ: Calculated value is below the limit of quantitation (<179 ng eq/g).　NA: Not applicable.
ND: Not detectable (sample shape not discernable from background or surrounding tissue).　SD: Standard deviation.
[a] Mean is the average of two values