

Table R-4.3.5. Eye irritation potential of test substances in the SIRC-CVS:TEA validation phase III study

Chemical code	Laboratory	Name of test substance	Run 1	Run 2	Final Evaluation
P3-001	B	2-ethoxyethyl methacrylate	P	P	P
P3-002	C	iso-octylthioglycolate	N	N	N
P3-003	A/B/C	dipropyl disulfide	P/P/N	P/P/N	P
P3-004	C	1-bromo-octane	P	P	P
P3-005	A/B/C	2-(2-ethoxyethoxy)ethanol	N/N/N	N/N/N	N
P3-006	C	dioctyl ether	P	P	P
P3-007	C	3-phenoxybenzyl alcohol	P	P	P
P3-008	B	glycidyl methacrylate	P	P	P
P3-009	C	2-ethylhexylthioglycolate	N	N	N
P3-010	A/B/C	n,n-dimethylguanidine sulfate	N/P/N	N/P/N	N
P3-011	C	6-hydroxy-2,4,5-triaminopyrimidine Sulfate	P	P	P
P3-012	A/B/C	polyethylene hydrogenated castor oil (40E.O.)	N/P/N	N/P/N	N
P3-013	C	2,2'-methylene-bis-(6-(2Hbenzotriazol-2-yl)-4-(1,1,3,3-tetramethylbutyl)phenol)	N	N	N
P3-014	C	cellulose 2-(2-hydroxy-3-(trimethylammonio)propoxy ethyl ether chloride	N	N	N
P3-015	C	3,4-dimethoxy benzaldehyde	P	P	P
P3-016	C	3-chloropropionitrile	P	P	P
P3-017	C	2-methyl-1-pentanol	N	N	N
P3-018	C	ethyl-2-methylacetoacetate	N	N	N
P3-019	A/B/C	diethyl toluamide	P/P/P	P/P/P	P
P3-020	A/B/C	4-nitrobenzoic acid	N/N/N	N/N/N	N
P3-021	C	sodium chloroacetate	P	P	P
P3-022	A	2,4,11,13-tetraazatetra (Chlorohexidine glucocinate)	P	P	P
P3-023	C	-	-	-	-
P3-024	A/B/C	2-amino-3-hydroxy pyridine	P/P/P	P/P/P	P
P3-025	C	sodium benzoate	N	N	N
P3-026	C	methylthioglycolate	P	P	P
P3-027	A	3-(2-aminoethylamino)propyl]trimethoxysilane	P	P	P
P3-028	A/B/C	tetraethylene glycol	P/P/P	P/P/P	P
P3-029	A/B/C	dodecanoic acid	P/P/P	P/P/P	P
P3-030	C	1,2-benzisothiazol-3(2H)-one	P	P	P
P3-031	C	2-hydroxy-1,4-naphthoquinone	P	P	P
P3-032	C	disodium 4,4'-bis(2-sulfonatostyryl)biphenyl	P	P	P
P3-033	A/B/C	gamma-butyrolactone	N/N/N	N/N/N	N
P3-034	C	1-methylpropyl benzene	N	N	N
P3-035	C	4-(methylmercapto)benzaldehyde	P	P	P
P3-036	C	1,9-decaine	P	P	P
P3-037	C	2,4-dimethyl-3-pentanol	N	N	N
P3-038	C	1-ethyl-3-methylimidazolium ethylsulfate	N	N	N
P3-039	C	1,2,4-triazole,sodium salt	P	P	P
P3-040	C	4,4'-(4,5,6,7-tetrabromo-1,1-dioxido-3H-2,1-benzoxathiole-3,3-diyl) bis [2,6-dibromophenol]	P	P	P
P3-041	C	benzenamine,4,4'-(4-aimino-3-methylphenyl)(4-imino-3-methyl-2,5-cyclohexadien-1-ylidene)methyl-2-methy HCl	P	P	P
P3-042	A	1-(9H-carbozol-4-yloxy)-3-[[2-(2-methoxy phenoxy)ethyl] amino]-2-propanol	P	P	P
P3-043	B	3-methyl-1,5-di(2,4-xylyl)-1,3,5-Triazapenta-1,4-dien	P	P	P
P3-044	C	isopropyl acetoacetate	N	N	N
P3-045	A	(3R,4R)-4-acetoxy-3-[(R)-(tert-butyl)dimethylsilyloxy)ethyl]-2-azetidinone	P	P	P
P3-046	B	1-octanol	P	P	P
P3-047	B	2-benzyloxyethanol	N	N	N
P3-048	B	butanol	N	N	N
P3-049	B	isobutyl alcohol	P	P	P
P3-050	B	isopropyl alcohol	N	N	N

10)Appendix 8.6(R) Analysis for prediction

P3-051	B	myristyl alcohol	P	P	P
P3-052	B	hexyl cinnamic aldehyde	P	P	P
P3-053	B	n-butanal	P	P	P
P3-054	B	monoethanolamine	P	P	P
P3-055	B	m-phenylenediamine	P	P	P
P3-056	B	ethyl acetate	N	N	N
P3-057	B	isopropyl myristate	N	N	N
P3-058	B	methoxyethyl acrylate	P	P	P
P3-059	B	methyl acetate	N	N	N
P3-060	B	methyl cyanoacetate	N	N	N
P3-061	B	imidazole	P	P	P
P3-062	B	pyridine	N	N	N
P3-063	B	isopropyl bromide	N	N	N
P3-064	B	cyclohexanone	N	N	N
P3-065	B	2-methylbutyric acid	N	N	N
P3-066	B	calcium thioglycolate trihydrate	-	-	-
P3-067	B	citric acid	P	P	P
P3-068	B	potassium sorbate	N	N	N
P3-069	B	sodium salicylate	N	N	N
P3-070	B	distearyldimethylammonium chloride	P	P	P
P3-071	B	n-lauroylsarcosine sodium salt	P	P	P
P3-072	B	sodium lauryl sulfate	P	P	P
P3-073	A	triton X-100 (5%)	P	P	P
P3-074	A	2-ethylhexyl p-dimethyl-amino benzoate	P	P	P
P3-075	A	promethazine hydrochloride	P	P	P
P3-076	A	2-ethyl-1-hexanol	P	P	P
P3-077	A	3-methoxy-1,2-propanediol	N	N	N
P3-078	A	cyclohexanol	N	N	N
P3-079	A	ethanol	N	N	N
P3-080	A	n-hexanol	N	N	N
P3-081	A	3,3-dimethylpentane	P	P	P
P3-082	A	methyl cyclopentane	P	P	P
P3-083	A	toluene	N	N	N
P3-084	A	acetone	N	N	N
P3-085	A	gluconolactone	N	N	N
P3-086	A	methyl amyl ketone (2-heptanol)	N	N	N
P3-087	A	methyl ethyl ketone (2-butanone)	N	N	N
P3-088	A	methyl isobutyl ketone(4-methyl 2-pentanol)	N	N	N
P3-089	A	glycerol	N	N	N
P3-090	A	cetylpyridinium bromide	P	P	P
P3-091	C	triton X-100	P	P	P
P3-092	C	tween20	P	P	P
P3-093	A	sodium hydroxide	P	P	P
P3-094	A	glycolic acid	N	N	N
P3-095	A	3,3-dithiodipropionic acid	N	N	N
P3-096	A	sucrose fatty acid ester	P	P	P
P3-097	A	methyl para-Hydroxybenzoate	P	P	P
P3-098	A	silic acid	P	P	P
P3-099	A	benzyl alcohol	N	N	N
P3-100	A	lactic acid	N	N	N

*1: N; Negative, P; Positive

*2: Eye irritation potential of common test substances were expressed as a representative of three laboratories.

*3: -, Inapplicable

10)Appendix 8.6(R) Analysis for prediction

Table R-4.1.1. Means and standard deviations of IC50s for test substances, relative controls and positive controls in the SIRC-CVS:TEA validation phase I study

Chemical No.	Name of test substance		Laboratory A			Laboratory A (Retest)			Laboratory B			Laboratory C		
			IC50 ug/mL			IC50 ug/mL			IC50 ug/mL			IC50 ug/mL		
			Test Substance	Relative Control	Positive Control	Test Substance	Relative Control	Positive Control	Test Substance	Relative Control	Positive Control	Test Substance	Relative Control	Positive Control
C01	acetoacetate	N	3	3	3	3	3	3	3	3	3	3	3	3
		Mean	>5000	1677.70	172.07	3296.53	1234.47	83.17	3642.03	1551.63	87.20	>5000	1349.47	82.57
		SD	-	133.12	10.33	292.34	306.25	3.27	142.30	376.15	4.22	-	62.42	1.36
C02	Safflower oil	N	3	3	3	3	3	3	3	3	3	3	3	3
		Mean	>5000	1613.37	170.33	>5000	1264.97	86.60	>5000	1579.80	84.67	>5000	1365.47	80.23
		SD	-	426.35	6.12	-	175.77	4.04	-	31.82	4.84	-	23.28	0.06
C03	3-Chloropropionitrile	N	3	3	3	3	3	3	3	3	3	3	3	3
		Mean	60.60	2386.13	179.70	45.57	1370.83	84.40	38.93	1339.37	88.60	48.53	1390.33	86.70
		SD	10.12	965.97	5.99	6.25	176.47	8.34	6.92	285.34	1.30	1.07	51.83	7.35
C04	Sodium dehydroacetate	N	3	3	3	3	3	3	3	3	3	3	3	3
		Mean	2024.17	1915.33	161.63	854.27	1252.77	84.07	720.77	1646.50	87.50	1026.60	1425.80	78.50
		SD	485.58	314.52	38.54	100.83	188.79	3.50	235.31	75.72	2.78	46.42	33.36	0.44

* N; Number of runs

Table R-4.1.2. Means and standard deviations of IC50s for relative controls and positive controls

	Laboratory A		Laboratory A (Retest)		Laboratory B		Laboratory C	
	Relative Control	Positive Control	Relative Control	Positive Control	Relative Control	Positive Control	Relative Control	Positive Control
N	4	4	4	4	4	4	4	4
Mean	1898.13	170.93	1280.76	84.56	1529.33	86.99	1382.77	82.00
SD	350.30	7.42	61.34	1.46	132.74	1.66	33.25	3.55

* N; Number of relative controls and positive controls

* IC50 was expressed as ug/mL.

Table R-4.1.3. Eye irritation potential of test substances in the SIRC-CVS:TEA validation phase I study

Chemical No.	Name of test substances	Laboratory A			Laboratory A (Retest)			Laboratory B			Laboratory C			Lead laboratory
		Run 1	Run 2	Run 3	Run 1	Run 2	Run 3	Run 1	Run 2	Run 3	Run 1	Run 2	Run 3	
C01	acetoacetate	N	N	N	N	N	N	N	N	N	N	N	N	N
C02	Safflower oil	N	N	N	N	N	N	N	N	N	N	N	N	N
C03	3-Chloropropionitrile	P	P	P	P	P	P	P	P	P	P	P	P	P
C04	Sodium dehydroacetate	N	N	N	P	P	P	P	P	P	P	P	P	P

* N; Negative, P; Positive,

10)Appendix 8.6(R) Analysis for prediction

P2-011	1	239.43	1427.67	85.70	109.83	1160.10	89.67	227.00	1755.53	93.23
	2	123.70	1298.27	83.53	121.50	1094.97	91.40	243.67	1543.40	97.40
	3	130.17	1322.27	86.03	115.00	1222.50	93.93	176.37	1449.23	86.73
	Mean	164.43	1349.40	85.09	115.44	1159.19	91.67	215.68	1582.72	92.46
P2-012	1	3575.53	1372.63	84.27	3615.73	1188.53	87.27	4386.23	1652.83	107.63
	2	3630.43	1268.97	82.40	3721.63	1256.27	91.40	4246.53	1738.87	95.70
	3	2965.90	1298.63	82.43	4259.13	1049.27	94.17	4589.23	1455.00	87.20
	Mean	3390.62	1313.41	83.03	3865.50	1164.69	90.94	4407.33	1615.57	96.84
P2-013	1	434.83	1470.87	87.40	398.80	1197.70	88.63	352.80	1670.07	95.80
	2	1055.60	1329.70	85.57	544.13	1339.73	92.37	298.50	1600.60	95.03
	3	703.80	1127.00	82.33	336.27	1090.73	91.73	177.87	1326.67	89.80
	Mean	731.41	1309.19	85.10	426.40	1209.39	90.91	276.39	1532.44	93.54
P2-014	1	91.93	1434.87	84.70	<45.1	1135.30	90.93	55.20	1639.87	91.10
	2	82.47	1247.37	84.90	64.77	1248.77	91.00	70.30	1683.13	90.50
	3	115.20	1471.33	80.77	<44.4	1190.53	91.20	100.67	1803.03	91.07
	Mean	96.53	1384.52	83.46	<64.77	1191.53	91.04	75.39	1708.68	90.89
P2-015	1	664.00	1473.57	81.47	452.27	1142.77	82.47	1288.70	1553.47	89.97
	2	1152.17	1172.77	83.87	395.00	1203.53	93.83	1054.47	1495.20	94.37
	3	809.23	1232.50	82.27	283.93	1180.93	94.23	1279.93	1754.03	87.53
	Mean	875.13	1292.94	82.53	377.07	1175.74	90.18	1207.70	1600.90	90.62
P2-016	1	796.67	1300.10	82.53	618.03	1203.53	88.97	1419.93	1669.03	95.47
	2	715.13	1364.63	87.13	632.63	1168.57	87.80	1191.07	1850.53	96.93
	3	605.57	1385.97	82.33	629.70	1149.63	92.83	1311.20	1853.70	92.63
	Mean	705.79	1350.23	84.00	626.79	1173.91	89.87	1307.40	1791.09	95.01
P2-017	1	57.67	1298.20	86.83	68.53	1282.07	90.20	49.43	1699.50	97.00
	2	92.73	1332.43	83.87	44.03	1177.10	92.10	90.17	1487.10	94.13
	3	66.53	1260.83	83.23	43.67	1202.43	91.50	<39.1	1589.73	90.93
	Mean	72.31	1297.16	84.64	52.08	1220.53	91.27	<90.17	1592.11	94.02
P2-018	1	<46.4	1226.20	86.13	<39.1	1305.83	93.77	<39.1	1606.07	94.53
	2	69.93	1372.13	82.80	<39.1	1145.77	88.13	<39.1	1644.93	92.83
	3	<65.0	1416.70	84.97	<39.1	1150.93	93.90	<39.1	1477.17	100.90
	Mean	<69.93	1338.34	84.63	<39.1	1200.84	91.93	<39.1	1576.06	96.09
P2-019	1	359.37	1272.43	84.77	385.97	1387.10	89.87	1471.77	1679.23	98.20
	2	567.03	1301.33	85.80	94.77	1311.97	88.73	1268.13	1676.53	89.30
	3	397.97	1254.83	79.63	418.47	1198.10	93.30	1208.87	1720.37	90.50
	Mean	441.46	1276.20	83.40	299.73	1299.06	90.63	1316.26	1692.04	92.67
P2-020	1	3074.00	1232.70	87.07	1729.57	1392.87	88.00	4013.20	1721.57	94.60
	2	2633.47	1331.47	86.57	2187.27	1228.00	90.53	3593.00	1851.43	95.83
	3	3002.77	1364.20	80.87	2109.37	1196.90	92.03	3504.93	1749.60	94.63
	Mean	2903.41	1309.46	84.83	2008.73	1272.59	90.19	3703.71	1774.20	95.02

*; Each IC50 for test substances, relative controls and positive controls was expressed as an average every set.

Table R-4.2.2. Means and standard deviations of IC50s for relative controls and

	Laboratory A		Laboratory B		Laboratory C	
	Relative Control	Positive Control	Relative Control	Positive Control	Relative Control	Positive Control
N	60	60	60	60	60	60
Mean	1355.51	85.01	1232.08	90.82	1605.07	91.98
SD	106.68	2.69	84.18	2.68	154.61	4.57

* N; Numbers of each test substances, relative controls and positive controls

* IC50 was expressed as ug/mL.

Table R-4.2.3. Eye irritation potential of test substances in the SIRC-CVS:TEA validation phase II study

Chemical code	Name of test substance	Set	Laboratory A			Laboratory B			Laboratory C			Final Evaluation
			Run 1	Run 2	Run 3	Run 1	Run 2	Run 3	Run 1	Run 2	Run 3	
P2-001	piperonylbutoxide	1	P	P	P	P	P	P	P	P	P	P
		2	P	P	P	P	P	P	P	P	P	
		3	P	P	P	P	P	P	P	P	P	
P2-002	2,5-dimethylhexaediol	1	N	N	N	N	N	N	N	N	N	N
		2	N	N	N	N	N	N	N	N	N	
		3	N	N	N	N	N	N	N	N	N	
P2-003	1-(2-propoxy-1-methylethoxy)-2-propanol	1	N	N	N	N	N	N	N	N	N	N
		2	N	N	N	N	N	N	N	N	N	
		3	N	N	N	N	N	N	N	N	N	
P2-004	ammonium nitrate	1	P	P	P	P	P	P	P	P	P	P
		2	P	P	P	P	P	P	P	P	P	
		3	P	P	P	P	P	P	P	P	P	
P2-005	potassium tetrafluoroborate	1	N	N	N	N	N	N	N	N	N	N
		2	N	N	N	N	N	N	N	N	N	
		3	N	N	N	N	N	N	N	N	N	
P2-006	3,4,4'-trichlorocarbanilide	1	P	P	P	P	P	P	P	P	P	P
		2	P	P	P	P	P	P	P	P	P	
		3	P	P	P	P	P	P	P	P	P	
P2-007	1-bromohexane	1	P	P	P	P	P	P	P	P	P	P
		2	P	P	P	P	P	P	P	P	P	
		3	P	P	P	P	P	P	P	P	P	
P2-008	4,4'-methylenebis(2,6-di-tert-butylphenol)	1	N	N	N	N	N	N	N	N	N	N
		2	N	N	N	N	N	N	N	N	N	
		3	N	N	N	N	N	N	N	N	N	
P2-009	propylene glycol propyl ether	1	N	N	N	N	N	N	N	N	N	N
		2	N	N	N	N	N	N	N	N	N	
		3	N	N	N	N	N	N	N	N	N	
P2-010	ethyl thioglycolate	1	P	P	P	P	P	P	P	P	P	P
		2	P	P	P	P	P	P	P	P	P	
		3	P	P	P	P	P	P	P	P	P	
P2-011	sodium oxalate	1	P	P	P	P	P	P	P	P	P	P
		2	P	P	P	P	P	P	P	P	P	
		3	P	P	P	P	P	P	P	P	P	
P2-012	2-phospho-L-ascorbic acid trisodium salt	1	N	N	N	N	N	N	N	N	N	N
		2	N	N	N	N	N	N	N	N	N	
		3	N	N	N	N	N	N	N	N	N	
P2-013	1-bromo-4-chlorobutane	1	P	P	P	P	P	P	P	P	P	P
		2	P	P	P	P	P	P	P	P	P	
		3	P	P	P	P	P	P	P	P	P	
P2-014	sodium hydrogensulfite	1	P	P	P	P	P	P	P	P	P	P
		2	P	P	P	P	P	P	P	P	P	
		3	P	P	P	P	P	P	P	P	P	
P2-015	isobutyraldehyde	1	P	P	P	P	P	P	P	P	P	P
		2	P	P	P	P	P	P	P	P	P	
		3	P	P	P	P	P	P	P	P	P	
P2-016	1-naphthaleneacetic acid	1	P	P	P	P	P	P	P	P	P	P
		2	P	P	P	P	P	P	P	P	P	
		3	P	P	P	P	P	P	P	P	P	
P2-017	propyl 4-hydroxybenzoate	1	P	P	P	P	P	P	P	P	P	P
		2	P	P	P	P	P	P	P	P	P	
		3	P	P	P	P	P	P	P	P	P	
P2-018	ethyl 2,6-dichloro-5-fluoro-beta-oxo-3-pyridinepro	1	P	P	P	P	P	P	P	P	P	P
		2	P	P	P	P	P	P	P	P	P	
		3	P	P	P	P	P	P	P	P	P	
P2-019	camphene	1	P	P	P	P	P	P	P	P	P	P
		2	P	P	P	P	P	P	P	P	P	
		3	P	P	P	P	P	P	P	P	P	
P2-020	cyclopentanol	1	N	N	N	N	N	N	N	N	N	N
		2	N	N	N	N	N	N	N	N	N	
		3	N	N	N	N	N	N	N	N	N	

*N; Negative, P; Positive

10)Appendix 8.6(R) Analysis for prediction

Table R-4.3.1. The IC50s for test substances, relative controls and positive controls at laboratory A in the SIRC-CVS:TEA validation phase III study

Chemical Code	Chemical Codei in Laboratory A	Test Substance (IC50 ug/mL)			Relative Control (IC50 ug/mL)			Positive Control (IC50 ug/mL)		
		Run 1	Run 2	Mean	Run 1	Run 2	Mean	Run 1	Run 2	Mean
P3-003 ^{*2}	SA82	212.80	259.20	236.00	1069.30	1081.90	1075.60	93.70	90.20	91.95
P3-005 ^{*2}	SA89	>5000	>5000	>5000	1057.70	1275.50	1166.60	86.70	95.50	91.10
P3-010 ^{*2}	SA90	1323.30	1653.30	1488.30	1040.30	1053.70	1047.00	88.30	91.40	89.85
P3-012 ^{*2}	SA84	1460.90	1541.20	1501.05	1040.10	1088.50	1064.30	87.30	93.80	90.55
P3-019 ^{*2}	SA88	155.80	202.50	179.15	1096.70	1219.70	1158.20	86.30	90.60	88.45
P3-020 ^{*2}	SA83	1347.40	1588.50	1467.95	1076.00	1044.60	1060.30	85.60	94.40	90.00
P3-022	SA61	<39.1	42.40	<42.4	1095.40	1159.10	1127.25	86.90	90.80	88.85
P3-024 ^{*2}	SA86	151.80	182.90	167.35	1039.00	1095.20	1067.10	89.20	91.40	90.30
P3-027	SA96	484.90	869.10	677.00	1040.50	1417.70	1229.10	86.70	91.20	88.95
P3-028 ^{*2}	SA85	<39.1	<39.1	<39.1	1037.20	1101.00	1069.10	89.90	90.50	90.20
P3-029 ^{*2}	SA87	42.20	46.00	44.10	1073.70	1082.10	1077.90	89.80	91.50	90.65
P3-033 ^{*2}	SA81	>5000	>5000	>5000	1010.50	1257.20	1133.85	94.00	85.90	89.95
P3-042	SA62	<39.1	<39.1	<39.1	1206.60	1133.10	1169.85	83.70	92.20	87.95
P3-045	SA63	117.70	128.70	123.20	1031.80	1121.70	1076.75	78.10	91.90	85.00
P3-073	SA65	444.10	470.60	457.35	1085.60	1084.00	1084.80	80.30	90.70	85.50
P3-074	SA76	52.10	47.50	49.80	1056.30	1063.60	1059.95	88.20	85.20	86.70
P3-075	SA64	<39.1	<39.1	<39.1	1203.10	1010.60	1106.85	85.20	87.00	89.10
P3-076	SA67	946.30	761.90	854.10	1038.10	1054.50	1046.30	94.20	80.60	87.40
P3-077	SA80	>5000	>5000	>5000	1194.40	1253.60	1224.00	91.50	92.00	91.75
P3-078	SA70	1941.10	2253.70	2097.40	1068.90	1138.00	1103.45	96.80	91.60	94.20
P3-079	SA91	>5000	>5000	>5000	1033.50	1412.30	1222.90	84.20	92.70	88.45
P3-080	SA72	1082.20	1666.50	1374.35	1010.20	1030.00	1020.10	90.90	85.80	88.35
P3-081	SA78	84.60	352.00	218.30	1114.00	1130.40	1122.20	90.80	91.20	91.00
P3-082	SA98	777.30	857.30	817.30	1152.50	1335.80	1244.15	85.70	91.70	88.70
P3-083	SA69	>5000	>5000	>5000	1090.90	1168.30	1129.60	92.10	93.30	92.70
P3-084	SA92	4903.10	>5000	>4903.1	1073.70	1446.40	1260.05	87.30	89.70	88.50
P3-085	SA97	3331.80	3672.40	3502.10	1036.10	1149.10	1092.60	84.40	92.80	88.60
P3-086	SA71	2243.50	3624.50	2934.00	1119.60	1151.00	1135.30	92.80	92.30	92.55
P3-087	SA94	>5000	3648.00	>3648	1032.80	1408.90	1220.85	87.60	88.00	87.80
P3-088	SA68	>5000	>5000	>5000	1085.90	1201.10	1143.50	86.60	90.20	88.40
P3-089	SA79	>5000	>5000	>5000	1059.50	1076.60	1068.05	90.70	93.20	91.95
P3-090	SA75	<39.1	<39.1	<39.1	1172.00	1186.00	1179.00	89.10	90.80	89.95
P3-093	SA74	682.60	866.20	774.40	1053.80	1186.70	1120.25	93.00	93.10	93.05
P3-094	SA95	1429.50	1504.20	1466.85	1043.00	1277.70	1160.35	87.20	95.80	91.50

10)Appendix 8.6(R) Analysis for prediction

P3-095	SA73	1864.40	1696.90	1780.65	1149.40	1065.10	1107.25	91.40	92.40	91.90
P3-096	SA100	94.30	67.00	80.65	1058.70	1040.70	1049.70	88.10	89.50	88.80
P3-097	SA99	132.40	274.50	203.45	1085.70	1103.20	1094.45	88.70	84.60	86.65
P3-098	SA93	190.00	168.80	179.40	1146.30	1024.90	1085.60	87.10	89.40	88.25
P3-099	SA66	1133.60	1574.30	1353.95	1016.00	1209.40	1112.70	86.80	92.30	89.55
P3-100	SA77	2043.90	2606.80	2325.35	1031.60	1100.90	1066.25	91.00	91.00	91.00

*1; Each IC50 for test substances, relative controls and positive controls was expressed as an average every set.

*2; Ten test substances were shared in Laboratory A, B and C.

10)Appendix 8.6(R) Analysis for prediction

Table R-4.3.2. The IC50s for test substances, relative controls and positive controls at laboratory B in the SIRC-CVS:TEA validation phase III study

Chemical Code	Chemical Code in Laboratory B	Test Substance (IC50 ug/mL)			Relative Control (IC50 ug/mL)			Positive Control (IC50 ug/mL)		
		Run 1	Run 2	Mean	Run 1	Run 2	Mean	Run 1	Run 2	Mean
P3-001	SB62	119.60	122.60	121.10	1673.80	1571.90	1622.85	89.80	90.40	90.10
P3-003 ^{*2}	SB79	695.20	672.80	684.00	1352.70	1038.20	1195.45	93.90	91.40	92.65
P3-005 ^{*2}	SB72	>5000	>5000	>5000	1077.80	1260.80	1169.30	87.30	86.80	87.05
P3-008	SB63	17.70	22.80	20.25	1186.90	1573.00	1379.95	91.60	95.40	93.50
P3-010 ^{*2}	SB71	626.80	535.20	581.00	1394.20	1488.50	1441.35	91.80	91.40	91.60
P3-012 ^{*2}	SB77	814.20	768.80	791.50	1089.70	1433.60	1261.65	89.40	86.90	88.15
P3-019 ^{*2}	SB73	265.50	187.40	226.45	1193.40	1296.80	1245.10	92.30	87.10	89.70
P3-020 ^{*2}	SB78	2923.40	2017.90	2470.65	1026.60	1305.70	1166.15	79.60	85.80	82.70
P3-024 ^{*2}	SB75	71.70	63.10	67.40	1155.30	1095.60	1125.45	92.40	89.70	91.05
P3-028 ^{*2}	SB76	6.90	11.70	9.30	1455.30	1580.90	1518.10	86.80	93.50	90.15
P3-029 ^{*2}	SB74	<39.1	<39.1	<39.1	1141.60	1274.10	1207.85	80.80	88.60	84.70
P3-033 ^{*2}	SB80	4864.90	4126.60	4495.75	1120.40	1081.20	1100.80	92.10	85.30	88.70
P3-043	SB61	163.30	191.90	177.60	1572.90	1387.20	1480.05	78.10	91.50	84.80
P3-046	SB64	783.50	346.30	564.90	1281.80	1239.30	1260.55	92.80	91.30	92.05
P3-047	SB65	1599.20	1570.60	1584.90	1282.40	1430.40	1356.40	91.90	89.30	90.60
P3-048	SB66	2203.10	2105.00	2154.05	1298.60	1277.30	1287.95	91.90	92.60	92.25
P3-049	SB67	772.60	414.80	593.70	1668.10	1571.90	1620.00	78.40	89.70	84.05
P3-050	SB68	>5000	>5000	>5000	1275.10	1154.20	1214.65	92.10	86.70	89.40
P3-051	SB69	128.70	312.50	220.60	1334.10	1571.00	1452.55	94.90	93.10	94.00
P3-052	SB70	92.10	98.30	95.20	1302.20	1534.70	1418.45	94.40	89.00	91.70
P3-053	SB81	720.40	213.40	466.90	1068.60	1704.30	1386.45	81.60	92.80	87.20
P3-054	SB82	195.50	169.90	182.70	1319.00	1133.40	1226.20	89.00	91.10	90.05
P3-055	SB83	17.30	20.60	18.95	1071.60	1527.10	1299.35	89.90	89.80	89.85
P3-056	SB84	>5000	>5000	>5000	1359.10	1262.40	1310.75	87.00	84.80	85.90
P3-057	SB85	>5000	>5000	>5000	1173.10	1365.70	1269.40	92.30	92.50	92.40
P3-058	SB86	11.30	13.90	12.60	1188.30	1569.80	1379.05	87.30	88.70	88.00
P3-059	SB87	>5000	>5000	>5000	1101.00	1408.10	1254.55	88.90	89.50	89.20
P3-060	SB88	1343.60	1473.80	1408.70	1103.50	1431.30	1267.40	78.40	87.00	82.70
P3-061	SB89	620.50	604.40	612.45	1084.00	1028.60	1056.30	89.50	82.70	86.10
P3-062	SB90	1729.40	1824.40	1776.90	1291.70	1472.40	1382.05	92.50	89.70	91.10
P3-063	SB91	>2500	>2500	>2500	1251.80	1457.50	1354.65	88.90	90.20	89.55
P3-064	SB92	1619.00	1403.10	1511.05	1262.80	1329.40	1296.10	89.90	90.00	89.95
P3-065	SB93	1604.10	1429.40	1516.75	1396.40	1067.30	1231.85	88.50	88.70	88.60
P3-066	SB94	-	-	-	-	-	-	-	-	-

10)Appendix 8.6(R) Analysis for prediction

P3-067	SB95	875.30	807.70	841.50	1257.50	1405.50	1331.50	78.10	92.00	85.05
P3-068	SB96	1584.60	1468.40	1526.50	1176.90	1395.80	1286.35	93.30	87.90	90.60
P3-069	SB97	1276.00	1587.50	1431.75	1112.00	1368.80	1240.40	93.80	90.60	92.20
P3-070	SB98	3.60	14.00	8.80	1553.30	1683.60	1618.45	80.30	91.10	85.70
P3-071	SB99	97.50	70.70	84.10	1445.10	1194.80	1319.95	95.50	90.00	92.75
P3-072	SB100	57.20	60.10	58.65	1076.20	1605.60	1340.90	93.40	91.40	92.40

*1; Each IC50 of test substances, relative controls and positive controls was expressed as an average every set.

*2; Ten test substances were shared in Laboratory A, B and C.

*3: -; Inapplicable

10)Appendix 8.6(R) Analysis for prediction

Table R-4.3.3. The IC50s for test substances, relative controls and positive controls at laboratory C in the SIRC-CVS:TEA validation phase III study

Chemical Code	Chemical Code in Laboratory C	Test Substance (IC50 ug/mL)			Relative Control (IC50 ug/mL)			Positive Control (IC50 ug/mL)		
		Run 1	Run 2	Mean	Run 1	Run 2	Mean	Run 1	Run 2	Mean
P3-002	SC72	>2500	>2500	>2500	1628.00	1753.10	1690.55	126.10	123.50	124.80
P3-003 ^{*2}	SC61	>2500	>2500	>2500	1177.80	1413.70	1295.75	87.50	102.00	94.75
P3-004	SC74	105.80	244.30	175.05	1085.20	1618.10	1351.65	123.80	126.50	125.15
P3-005 ^{*2}	SC62	>5000	>5000	>5000	1256.90	1375.10	1316.00	109.00	119.60	114.30
P3-006	SC77	845.80	1302.60	1074.20	1248.60	1555.90	1402.25	129.50	126.00	127.75
P3-007	SC79	77.40	35.40	56.40	1181.10	1747.40	1464.25	136.50	129.90	133.20
P3-009	SC80	>2500	>2500	>2500	1256.90	1665.80	1461.35	109.00	111.90	110.45
P3-010 ^{*2}	SC63	3464.60	2748.70	3106.65	1831.10	1108.60	1469.85	120.60	87.50	104.05
P3-011	SC81	<39.1	<39.1	<39.1	1285.60	1418.20	1351.90	180.80	137.30	159.05
P3-012 ^{*2}	SC64	3210.00	2765.90	2987.95	1851.80	1415.30	1633.55	117.10	119.50	118.30
P3-013	SC82	>5000	>5000	>5000	1186.40	1123.90	1155.15	125.70	140.60	133.15
P3-014	SC83	>5000	>5000	>5000	1400.10	1064.40	1232.25	114.80	133.40	124.10
P3-015	SC84	328.00	218.10	273.05	1071.90	1250.00	1160.95	141.60	133.20	137.40
P3-016	SC85	<39.1	40.40	<40.4	1017.50	1013.80	1015.65	140.10	130.60	135.35
P3-017	SC87	>2500	>2500	>2500	1353.90	1365.50	1359.70	123.70	138.30	131.00
P3-018	SC88	>5000	>5000	>5000	1154.10	1269.40	1211.75	116.70	121.10	118.90
P3-019 ^{*2}	SC65	285.10	246.00	265.55	1159.40	1913.30	1536.35	121.20	118.80	120.00
P3-020 ^{*2}	SC66	1946.00	2991.20	2468.60	1864.20	1573.00	1718.60	129.60	113.20	121.40
P3-021	SC90	<39.1	39.80	<39.8	1115.00	1166.50	1140.75	120.20	143.20	131.70
P3-023	SC91	-	-	-	-	-	-	-	-	-
P3-024 ^{*2}	SC68	172.90	55.30	114.10	1182.30	1678.20	1430.25	136.10	90.90	113.50
P3-025	SC92	>5000	>5000	>5000	1017.10	1112.30	1064.70	137.20	124.90	131.05
P3-026	SC93	<39.1	<39.1	<39.1	1674.10	1106.50	1390.30	120.20	129.00	124.60
P3-028 ^{*2}	SC69	<39.1	<39.1	<39.1	1822.50	1787.80	1805.15	116.70	82.60	99.65
P3-029 ^{*2}	SC70	55.70	33.20	44.45	1786.40	1433.90	1610.15	128.00	113.90	120.95
P3-030	SC97	<19.5	<19.5	<19.5	1061.00	1169.40	1115.20	124.90	136.40	130.65
P3-031	SC89	85.90	86.50	86.20	1259.60	1112.60	1186.10	111.50	123.10	117.30
P3-032	SC98	41.70	55.90	48.80	1279.50	1369.20	1324.35	123.90	129.10	126.50
P3-033 ^{*2}	SC67	>5000	>5000	>5000	1133.00	1794.70	1463.85	114.70	83.90	99.30
P3-034	SC71	>2500	>2500	>2500	1244.80	1743.90	1494.35	141.30	98.90	120.10
P3-035	SC73	103.30	184.50	143.90	1269.40	1754.20	1511.80	105.90	109.20	107.55
P3-036	SC75	931.40	940.20	935.80	1418.20	1676.30	1547.25	148.00	119.40	133.70
P3-037	SC76	>2500	>2500	>2500	1389.20	1181.20	1285.20	114.00	122.70	118.35
P3-038	SC78	1786.60	2253.10	2019.85	1070.70	1288.20	1179.45	121.60	119.00	120.30

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P3-039	SC95	919.10	922.50	920.80	1286.30	1143.10	1214.70	126.80	131.70	129.25
P3-040	SC96	62.50	56.20	59.35	1173.40	1116.60	1145.00	134.00	123.10	128.55
P3-041	SC99	<39.1	<39.1	<39.1	1456.50	1159.60	1308.05	138.80	146.30	142.55
P3-044	SC86	3114.80	2076.00	2595.40	1801.20	1154.50	1477.85	118.40	127.20	122.80
P3-091	SC94	<39.1	<39.1	<39.1	1356.10	1241.50	1298.80	129.10	135.60	132.35
P3-092	SC100	149.60	443.10	296.35	1193.80	1143.70	1168.75	119.00	121.40	120.20

*1; Each IC50 of test substances, relative controls and positive controls was expressed as an average every set.

*2; Ten test substances were shared in Laboratory A, B and C.

*3: -; Inapplicable

Table R-4.3.4. Mean and standard deviation of IC50s for relative controls and positive controls of Phase III in the SIRC-CVS:TEA validation

	Laboratory A		Laboratory B		Laboratory C	
	Relative Control	Positive Control	Relative Control	Positive Control	Relative Control	Positive Control
N	40	40	39	39	39	39
Mean	1119.58	89.65	1317.34	89.19	1358.71	123.18
SD	61.58	2.05	134.27	3.04	189.60	12.34

* N; Numbers of each test substances, relative controls and positive controls

* IC50 was expressed as ug/mL.

Table R-4.4. Transferability of the SIRC-CVS:TEA method using Phase I study

Chemical No.	Name of test substances	Laboratory A	Laboratory B	Laboratory C (Retest)	Transferability
C01	Ethyl-2-methyl acetoacetate	N	N	N	Good
C02	Safflower oil	N	N	N	Good
C03	3-Chloropropionitrile	P	P	P	Good
C04	Sodium dehydroacetate	P	P	P	Good

* N; Negative, P; Positive,

Table R-4.5.1.1. Intra-laboratory reproducibility of the SIRC-CVS:TEA method
using Phase II study in laboratory A

Chemical code	Name of test substance	Laboratory A			
		Set 1	Set 2	Set 3	Intra-laboratory reproducibility
P2-001	piperonylbutoxide	P	P	P	1
P2-002	2,5-dimethylhexaediol	N	N	N	1
P2-003	1-(2-propoxy-1-methylethoxy)-2-propanol	N	N	N	1
P2-004	ammonium nitrate	P	P	P	1
P2-005	potassium tetrafluoroborate	N	N	N	1
P2-006	3,4,4'-trichlorocarbanilide	P	P	P	1
P2-007	1-bromohexane	P	P	P	1
P2-008	4,4'-methylenebis(2,6-di-tert-butylphenol)	N	N	N	1
P2-009	propylene glycol propyl ether	N	N	N	1
P2-010	ethyl thioglycolate	P	P	P	1
P2-011	sodium oxalate	P	P	P	1
P2-012	2-phospho-L-ascorbic acid trisodium salt	N	N	N	1
P2-013	1-bromo-4-chlorobutane	P	P	P	1
P2-014	sodium hydrogensulfite	P	P	P	1
P2-015	isobutyraldehyde	P	P	P	1
P2-016	1-naphthaleneacetic acid	P	P	P	1
P2-017	propyl 4-hydroxybenzoate	P	P	P	1
P2-018	ethyl 2,6-dichloro-5-fluoro-beta-oxo-3-pyridinepro	P	P	P	1
P2-019	camphene	P	P	P	1
P2-020	cyclopentanol	N	N	N	1

*1: N; Negative, P; Positive

*2: 1; All sets' judge agreed.

Table R-4.5.1.2. Intra-laboratory reproducibility of the SIRC-CVS:TEA method
using Phase II study in laboratory B

Chemical code	Name of test substance	Laboratory B			
		Set 1	Set 2	Set 3	Intra-laboratory reproducibility
P2-001	piperonylbutoxide	P	P	P	1
P2-002	2,5-dimethylhexaediol	N	N	N	1
P2-003	1-(2-propoxy-1-methylethoxy)-2-propanol	N	N	N	1
P2-004	ammonium nitrate	P	P	P	1
P2-005	potassium tetrafluoroborate	N	N	N	1
P2-006	3,4,4'-trichlorocarbanilide	P	P	P	1
P2-007	1-bromohexane	P	P	P	1
P2-008	4,4'-methylenebis(2,6-di-tert-butylphenol)	N	N	N	1
P2-009	propylene glycol propyl ether	N	N	N	1
P2-010	ethyl thioglycolate	P	P	P	1
P2-011	sodium oxalate	P	P	P	1
P2-012	2-phospho-L-ascorbic acid trisodium salt	N	N	N	1
P2-013	1-bromo-4-chlorobutane	P	P	P	1
P2-014	sodium hydrogensulfite	P	P	P	1
P2-015	isobutyraldehyde	P	P	P	1
P2-016	1-naphthaleneacetic acid	P	P	P	1
P2-017	propyl 4-hydroxybenzoate	P	P	P	1
P2-018	ethyl 2,6-dichloro-5-fluoro-beta-oxo-3-pyridinepro	P	P	P	1
P2-019	camphene	P	P	P	1
P2-020	cyclopentanol	N	N	N	1

*1: N; Negative, P; Positive

*2: 1; All sets' judge agreed.

Table R-4.5.1.3. Intra-laboratory reproducibility of the SIRC-CVS:TEA method
using Phase II study in laboratory C

Chemical code	Name of test substance	Laboratory C			
		Set 1	Set 2	Set 3	Intra-laboratory reproducibility
P2-001	piperonylbutoxide	P	P	P	1
P2-002	2,5-dimethylhexaediol	N	N	N	1
P2-003	1-(2-propoxy-1-methylethoxy)-2-propanol	N	N	N	1
P2-004	ammonium nitrate	P	P	P	1
P2-005	potassium tetrafluoroborate	N	N	N	1
P2-006	3,4,4'-trichlorocarbanilide	P	P	P	1
P2-007	1-bromohexane	P	P	P	1
P2-008	4,4'-methylenebis(2,6-di-tert-butylphenol)	N	N	N	1
P2-009	propylene glycol propyl ether	N	N	N	1
P2-010	ethyl thioglycolate	P	P	P	1
P2-011	sodium oxalate	P	P	P	1
P2-012	2-phospho-L-ascorbic acid trisodium salt	N	N	N	1
P2-013	1-bromo-4-chlorobutane	P	P	P	1
P2-014	sodium hydrogensulfite	P	P	P	1
P2-015	isobutyraldehyde	P	P	P	1
P2-016	1-naphthaleneacetic acid	P	P	P	1
P2-017	propyl 4-hydroxybenzoate	P	P	P	1
P2-018	ethyl 2,6-dichloro-5-fluoro-beta-oxo-3-pyridinepro	P	P	P	1
P2-019	camphene	P	P	P	1
P2-020	cyclopentanol	N	N	N	1

*1: N; Negative, P; Positive

*2: 1; All sets' judge agreed.

Table R-4.5.2.1. Inter-laboratory reproducibility of the SIRC-CVS:TEA method in Phase II study

Chemical code	Name of test substance	Laboratory A	Laboratory B	Laboratory C	Inter-laboratory reproducibility
P2-001	piperonylbutoxide	P	P	P	1
P2-002	2,5-dimethylhexaediol	N	N	N	1
P2-003	1-(2-propoxy-1-methylethoxy)-2-propanol	N	N	N	1
P2-004	ammonium nitrate	P	P	P	1
P2-005	potassium tetrafluoroborate	N	N	N	1
P2-006	3,4,4'-trichlorocarbanilide	P	P	P	1
P2-007	1-bromohexane	P	P	P	1
P2-008	4,4'-methylenebis(2,6-di-tert-butylphenol)	N	N	N	1
P2-009	propylene glycol propyl ether	N	N	N	1
P2-010	ethyl thioglycolate	P	P	P	1
P2-011	sodium oxalate	P	P	P	1
P2-012	2-phospho-L-ascorbic acid trisodium salt	N	N	N	1
P2-013	1-bromo-4-chlorobutane	P	P	P	1
P2-014	sodium hydrogensulfite	P	P	P	1
P2-015	isobutyraldehyde	P	P	P	1
P2-016	1-naphthaleneacetic acid	P	P	P	1
P2-017	propyl 4-hydroxybenzoate	P	P	P	1
P2-018	ethyl 2,6-dichloro-5-fluoro-beta-oxo-3-pyridinepro	P	P	P	1
P2-019	camphene	P	P	P	1
P2-020	cyclopentanol	N	N	N	1

*1: N; Negative, P; Positive

*2: 1; All laboratories' judge agreed.

Table R-4.5.2.2. Inter-laboratory reproducibility of the SIRC-CVS:TEA method
in Phase III study

Chemical code	Name of test substance	Laboratory A	Laboratory B	Laboratory C	Inter-laboratory reproducibility
P3-003	dipropyl disulfide	P	P	N	0
P3-005	2-(2-ethoxyethoxy)ethanol	N	N	N	1
P3-010	n,n-dimethylguanidine sulfate	N	P	N	0
P3-012	polyethylene hydrogenated caster oil (40E.O.)	N	P	N	0
P3-019	diethyl toluamide	P	P	P	1
P3-020	4-nitrobenzoic acid	N	N	N	1
P3-024	2-amino-3-hydroxy pyridine	P	P	P	1
P3-028	tetraethylene glycol	P	P	P	1
P3-029	dodecanoic acid	P	P	P	1
P3-033	gamma-butyrolactone	N	N	N	1

*1: N; Negative, P; Positive

*2: 1; All laboratories' judge agreed, 0; Only two laboratories' judge agreed.