034	sodium salicylate	54-21-7	Solid	Wako Pure	1	STE review
035	ttriton X-100	9002-93-1	Liquid	Sigma-Aldrich	1	STE review
036	citric acid	77-92-9	Solid	Sigma-Aldrich	No data	
037	glycolic acid	79-14-1	Solid	Sigma-Aldrich	2B	NICEATM
038	hexyls cinnamon aldehyde	101-86-0	Liquid	Wako Pure	No data	No data
039	methyl para-Hydroxybenzoate	99-76-3	Solid	Wako Pure	2?	Ohno(1999)
040	potassium sorbate	24634-61-5	Solid	Sigma-Aldrich	No data	No data
041	sodium lauryl sulfate	151-21-3	Solid	Wako Pure	2A?	STE review
042	sucrose fatty acid ester	Non	Solid	TCI	2A?	STE review
043	toluene	108-88-3	Liquid	Wako Pure	2B?	STE review
044	acetone	67-64-1	Liquid	Sigma-Aldrich	2A	STE review
045	(3R,4R)-4-acetoxy-3-[(R)-(tert-butyldimethylsilyl oxy)ethyl]-2-azetidinone	76855-69-1	Solid	Sigma-Aldrich	2A	Glaxo 2
046	2-benzyloxyethanol	622-08-2	Liquid	Wako Pure	2A	STE review
047	ethanol	64-17-5	Liquid	Wako Pure	2A	STE review
048	2-ethyl-1-hexanol	104-76-7	Liquid	Wako Pure	2A	STE review
049	n-hexanol	111-27-3	Liquid	Sigma-Aldrich	2A	STE review
050	isopropyl alcohol	67-63-0	Liquid	Wako Pure	2A	STE review
051	n-lauroylsarcosine sodium salt	137-16-6	Solid	Wako Pure	2B	Kojima (2013)
052	methyl acetate	79-20-9	Liquid	Sigma-Aldrich	2A	STE review
053	methyl cyanoacetate	105-34-0	Liquid	Sigma-Aldrich	2A	STE review
054	methyl ethyl ketone (2-butanone)	78-93-3	Liquid	TCI	2A	STE review
055	myristyl alcohol	112-72-1	Solid	Wako Pure	2A	STE review
056	1-octanol	111-87-5	Liquid	Wako Pure	2A	STE review
057	sodium benzoate	532-32-1	Solid	Sigma-Aldrich	2A	Cosing 18
058	2,4,11,13-tetraazatetra (Chlorohexidine glucocinate)	18472-51-0	Liquid	Wako Pure	2A	NICEATM 2
059	triton X-100 (5%)	9002-93-1	Liquid	Sigma-Aldrich	2B	NICEATM
060	n-butanal	123-72-8	Liquid	Wako Pure	2B	STE review
061	3-chloropropionitrile	542-76-7	Liquid	Wako Pure	2B	ECETOC 58
062	ethyl-2-methylacetoaceta te	609-14-3	Liquid	Sigma	2B	STE review
063	3,3-dithiodipropionic acid	1119-62-6	Solid	Wako Pure	2B	NICEATM
064	3,3-dithiodipropionic acid	1119-62-6	Solid	Wako Pure	2B	NICEATM
065	2-hydroxy-1,4-naphthoq uinone	83-72-7	Solid	Sigma-Aldrich	2B	Cosing 23
066	isopropyl acetoacetate	542-08-5	Liquid	Wako Pure	2B	NICEATM 4
067	2-methyl-1-pentanol	105-30-6	Liquid	Sigma-Aldrich	2B	STE review
068	sodium chloroacetate	3926-62-3	Solid	Sigma-Aldrich	2B	STE review
069	1-bromo-octane	111-83-1	Liquid	Sigma-Aldrich	No	STE review

070	1-(9H-carbozol-4-yloxy)-3-[[2-(2-methoxy peony)ethyl] amino]-2-propanol	72956-09-3	Solid	LKT.Labs,Inc	No	Glaxo 14
071	cyclohexanone	108-94-1	Liquid	Sigma-Aldrich	No	STE review
072	1,9-decaine	1647-16-1	Liquid	Sigma-Aldrich	No	STE review
073	3,3-dimethylpentane	562-49-2	Liquid	Sigma-Aldrich	No	STE review
074	2,4-dimethyl-3-pentanol	3970-62-5	Liquid	Sigma-Aldrich	No	STE review
075	3,4-dimethoxy benzaldehyde	120-14-9	Solid	Sigma-Aldrich	No	NICEATM 16
076	dioctyl ether	629-82-3	Liquid	Sigma-Aldrich	No	Cognisa 14
077	2-ethoxyethyl methacrylate	2370-63-0	Liquid	Sigma-Aldrich	No	ECETOC 31
078	ethyl acetate	141-78-6	Liquid	Sigma-Aldrich	No	STE review
079	2-ethylhexyl p-diethyl-amino benzoate	21245-02-3	Liquid	Wako Pure	No	STE review
080	2-ethylhexylthioglycolate	7659-86-1	Liquid	Sigma-Aldrich	No	ECETOC 52
081	1-ethyl-3-methylimidazolium ethylsulfate	342573-75-5	Liquid	AlfaAesar	No	Envoi 5
082	gluconolactone	90-80-2	Solid	Wako Pure	No	NICEATM
083	glycidyl methacrylate	106-91-2	Liquid	Sigma-Aldrich	No	STE review
084	glycerol	56-81-5	Liquid	Wako Pure	No	STE review
085	6-hydroxy-2,4,5-triamino pyrimidine Sulfate	1603-02-7	Solid	Wako Pure	No	Cosing 32
086	2-(2-hydroxy-3-(trimethylammonio)prosody) ethyl ether chloride	68610-92-4	Solid	Sigma-Aldrich	No	J&J 2
087	isopropyl bromide	75-26-3	Liquid	Wako Pure	No	STE review
088	isopropyl myristate	110-27-0	Liquid	Wako Pure	No	STE review
089	methyl cyclopentane	96-37-7	Liquid	TCI	No	STE review
090	3-methyl-1,5-di(2,4-xylyl)-1,3,5-Triazapenta-1,4-dien	33089-61-1	Solid	LKT.Labs,Inc	No	US-EPA 17
091	2,2'-methylene-bis-(6-(2 Hbenzotriazol-2-yl)-4-(1,1,3,3-tetramethylbutyl)phenol)	103597-45-1	Solid	Sigma-Aldrich	No	Ciba 7
092	4-(methylmercapto)benzaldehyde	3446-89-7	Liquid	Sigma-Aldrich	No	ECETOX 38
093	1-methylpropyl benzene	135-98-8	Liquid	Wako Pure	No	STE review
094	3-methoxy-1.2-propanediol	623-39-2	Liquid	TCI	No	STE review
095	methyl amyl ketone (2-heptanol)	110-43-0	Liquid	Wako Pure	No	STE review
096	methyl isobutyl ketone(4-methyl 2-pentanol)	108-10-1	Liquid	Sigma-Aldrich	No	STE review
097	iso-octylthioglycolate	25103-09-7	Liquid	Wako Pure	No	ECETOX 32
098	3-phenoxybenzyl alcohol	13826-35-2	Liquid	Sigma-Aldrich	No	NICEATM 11
099	silica acid	7699-41-4	Solid	Wako Pure	No	Ohio(1999)
100	tween20	9005-64-5	Liquid	Sigma-Aldrich	No	STE review

1) Phase III Test Substance Nos. 036, 038, and 040 were excluded from the analysis due to a lack of in vivo data with individual score were not found.
2) Phase III Test Substance No. 064 was excluded from the analysis due to duplication.

Table 7. Cut-off values and their rational for selection as a criteria of the applicability domain

Property of interest	Inclusion criteria	Rationale for selection	References
Physical state	Solids and liquids only		
Molecular weight	≥180 or ≥220	The criteria were considered the reasonable by the VMT.	Appendix 8.5
Purity	≥95%		
Water solubility	<1.0 g/L 1.0–10.0 g/L 10.0–100.0 g/L 100.0 g/L<	Poorly soluble Somewhat soluble Soluble Highly soluble	SciFinder
Log D	≤2.88 ≤1.70	generally less than 3.0	
Vapor pressure	≤6.0 kPa	Criteria used in SIRC-STE	ENV/JM/TG/RD(2013)19

Table 8.1. Means and standard deviations of IC_{50}s for the relative controls and positive controls in phase I of the SIRC-CVS:TEA

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

*N: Number of relative controls and positive controls

*IC_{50} in μg/mL.

Table 8.2. Means and standard deviations of IC_{50}s for relative controls and positive controls in the SIRC-CVS:TEA validation phase II study

	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

* IC_{50} in μg/mL

Table 8.3. Mean and standard deviation of IC_{50}s for relative controls and positive controls in the SIRC-CVS:TEA validation phase III study

	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 μg/mL.

Table 9.1. The IC_{50}s for test substances, relative controls and positive controls in the SIRC-CVS:TEA validation phase I study

No.	Name of test substance		Laboratory A			Laboratory B			Laboratory C			Laboratory C (Retest)		
			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 Sbstance	Relative Control	Positive Control	Test Substance	Relative Control	Positive Control
C01	Ethyl-2-methyl acetoacetate	N	3	3	3	3	3	3	3	3	3	3	3	3
		Mean	>5000	1349.47	82.57	3642.03	1551.63	87.20	>5000	1677.70	172.07	3296.53	1234.47	83.17
		SD	-	62.42	1.36	142.30	376.15	4.22	-	133.12	10.33	292.34	306.25	3.27
C02	Safflower oil	N	3	3	3	3	3	3	3	3	3	3	3	3
		Mean	>5000	1365.47	80.23	>5000	1579.80	84.67	>5000	1613.37	170.33	>5000	1264.97	86.60
		SD	-	23.28	0.06	-	31.82	4.84	-	426.35	6.12	-	175.77	4.04
C03	3-Chloro-propionitrile	N	3	3	3	3	3	3	3	3	3	3	3	3
		Mean	48.53	1390.33	86.70	38.93	1339.37	88.60	60.60	2386.13	179.70	45.57	1370.83	84.40
		SD	1.07	51.83	7.35	6.92	285.34	1.30	10.12	965.97	5.99	6.25	176.47	8.34
C04	Sodium dehydroacetate	N	3	3	3	3	3	3	3	3	3	3	3	3
		Mean	1026.60	1425.80	78.50	720.77	1646.50	87.50	2024.17	1915.33	161.63	854.27	1252.77	84.07
		SD	46.42	33.36	0.44	235.31	75.72	2.78	485.58	314.52	38.54	100.83	188.79	3.50

* N; Number of runs

Table 9.2. Eye irritation potential of test substances in the SIRC-CVS:TEA validation phase I study

Chemical No.	Name of test substances	Laboratory A			Laboratory B			Laboratory C			Laboratory (Retest)			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	Ethyl-2-methyl 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	P	P	P	P	P	P	P	N	N	P	P	P	P

* N; Negative, P; Positive

Table 9.3. Transferability of the SIRC-CVS:TEA method using the phase I study

Chemical No.	Name of test substances	Laboratory A	Laboratory B	Laboratory (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 10.1. The IC_{50}s for test substances, relative controls and positive controls in the SIRC-CVS:TEA validation phase II study

Chemical code	Set	Laboratory A			Laboratory B			Laboratory C		
		IC50 ug/mL			IC50 ug/mL			IC50 ug/mL		
		Test Substance	Relative Control	Positive Control	Test Substance	Relative Control	Positive Control	Test Sbstance	Relative Control	Positive Control
Phase II-A										
P2-001	1	141.00	1478.77	85.83	288.07	1295.93	88.77	298.30	1512.17	84.57
	2	71.73	1235.60	88.27	260.17	1327.03	93.77	266.57	1453.57	88.40
	3	101.80	1589.07	87.90	452.27	1177.97	91.83	282.87	1304.20	84.83
	Mean	104.84	1434.48	87.33	333.50	1266.98	91.46	282.58	1423.31	85.93
P2-002	1	>5000	1602.33	84.53	>5000	1402.37	89.93	>5000	1755.00	93.67
	2	>5000	1281.53	89.30	>3989.1	1330.83	96.23	>5000	1198.70	92.47
	3	>5000	1384.27	88.20	>5000	1274.03	92.30	>5000	1525.30	89.47
	Mean	>5000	1422.71	87.34	>3989.1	1335.74	92.82	>5000	1493.00	91.87
P2-003	1	4130.03	1517.03	86.20	3188.87	1320.57	90.90	>4673.4	1808.87	90.63
	2	3899.03	1452.13	88.73	3654.77	1357.83	93.17	>5000	1348.53	89.73
	3	3931.70	1513.40	88.67	3025.03	1290.27	92.37	>5000	1338.87	86.60
	Mean	3986.92	1494.19	87.87	3289.56	1322.89	92.14	>4673.4	1498.76	88.99
P2-004	1	1342.27	1518.23	89.37	1147.50	1413.97	93.20	1409.60	1525.10	80.33
	2	925.50	1352.43	90.73	778.47	1184.47	92.53	1216.40	1531.50	85.33
	3	1151.90	1440.13	86.43	1061.47	1295.83	90.80	1099.60	1508.13	86.57
	Mean	1139.89	1436.93	88.84	995.81	1298.09	92.18	1241.87	1521.58	84.08
P2-005	1	1791.60	1362.47	84.63	1949.60	1273.83	88.43	>5000	1837.10	95.87
	2	1783.17	1288.30	88.20	3630.77	1379.60	88.43	>5000	1532.13	90.93
	3	1868.60	1341.87	85.50	>3506.9	1256.43	90.27	>4952.0	1264.60	91.33
	Mean	1814.46	1330.88	86.11	>1949.6	1303.29	89.04	>4952.0	1544.61	92.71

Chemical code	Set	Laboratory A			Laboratory B			Laboratory C		
		IC_{50} ug/mL			IC_{50} ug/mL			IC_{50} ug/mL		
		Test Substance	Relative Control	Positive Control	Test Substance	Relative Control	Positive Control	Test Sbstance	Relative Control	Positive Control
Phase II-B										
P2-006	1	<39.1	1223.40	85.67	<39.1	1323.80	86.00	<39.1	1768.27	91.50
	2	<39.1	1334.50	83.60	<39.1	1122.43	92.80	<39.1	1692.43	98.77
	3	<39.1	1221.33	82.13	<39.1	1256.37	94.83	<39.1	1710.83	87.37
	Mean	<39.1	1259.74	83.80	<39.1	1234.20	91.21	<39.1	1723.84	92.54
P2-007	1	266.20	1452.87	85.27	99.30	1227.27	82.93	519.13	1613.90	90.67
	2	506.50	1312.67	86.23	110.30	1214.47	88.37	421.67	1718.20	92.53
	3	906.33	1373.43	78.30	408.30	1242.57	93.40	421.50	1432.00	85.20
	Mean	559.68	1379.66	83.27	205.97	1228.10	88.23	454.10	1588.03	89.47
P2-008	1	>5000	1417.17	88.13	>2345.6	1221.30	86.53	>5000	1672.70	88.97
	2	3365.35	1356.67	80.43	>5000	1224.97	89.97	>5000	1715.73	93.53
	3	3670.67	1239.17	81.17	>5000	1104.43	90.80	>5000	1510.83	85.27
	Mean	>3365.35	1337.67	83.24	>2345.6	1183.57	89.10	>5000	1633.09	89.26
P2-009	1	>4865.3	1345.63	86.83	3561.93	1227.47	89.87	>5000	1524.27	93.67
	2	>3048.1	1215.83	83.63	3528.17	1248.63	89.30	>5000	1681.47	95.30
	3	>4537.5	1457.47	83.90	3661.80	1166.23	92.73	>5000	1689.60	93.07
	Mean	>3048.1	1339.64	84.79	3583.97	1214.11	90.63	>5000	1631.78	94.01
P2-010	1	<39.1	1618.87	89.40	<51.4	1220.37	89.23	<39.1	1421.63	96.70
	2	<39.1	1333.93	85.30	<39.1	1237.93	90.80	<39.1	1619.03	92.90
	3	<39.1	1407.60	85.90	138.30	1103.27	92.80	<39.1	1691.83	91.17
	Mean	<39.1	1453.47	86.87	<138.3	1187.19	90.94	<39.1	1577.50	93.59
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

Chemical code	Set	Laboratory A			Laboratory B			Laboratory C		
		IC_{50} ug/mL			IC_{50} ug/mL			IC_{50} ug/mL		
		Test Substance	Relative Control	Positive Control	Test Substance	Relative Control	Positive Control	Test Sbstance	Relative Control	Positive Control
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

Chemical code	Set	Laboratory A			Laboratory B			Laboratory C		
		IC_{50} ug/mL			IC_{50} ug/mL			IC_{50} ug/mL		
		Test Substance	Relative Control	Positive Control	Test Substance	Relative Control	Positive Control	Test Sbstance	Relative Control	Positive Control
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 10.2. Intra-laboratory reproducibility of the SIRC-CVS:TEA method using the 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 10.3. Intra-laboratory reproducibility of the SIRC-CVS:TEA method using the phase II study in laboratory B

Chemical code	Name of test substance	LaboratoryB			
		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 10.4. Intra-laboratory reproducibility of the SIRC-CVS:TEA method using the 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 10.5. 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	

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	
P2-010	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	

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	
P2-020	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; Posit

Table 11.1. The IC_{50}s 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 Sbstance (IC_{50} ug/mL)			Relative Control (IC_{50} ug/mL)			Positive Control (IC_{50} 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

Chemical Code	Chemical Codei in Laboratory A	Test Sbstance (IC_{50} ug/mL)			Relative Control (IC_{50} ug/mL)			Positive Control (IC_{50} ug/mL)		
		Run 1	Run 2	Mean	Run 1	Run 2	Mean	Run 1	Run 2	Mean
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
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.

Table 11.2. 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 Sbstance (IC_{50} ug/mL)			Relative Control (IC_{50} ug/mL)			Positive Control (IC_{50} 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

Chemical Code	Chemical Code in Laboratory B	Test Sbstance (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
P3-060	**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**	-	-	-	-	-	-	-	-	-
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