

表 8 Ames と *in vivo* TGR の組合せにおける感受性

Ames	TGR			Total
	+	E	-	
+	48	0	8	56
E	1	0	0	1
-	5	0	12	17
Total	54	0	20	74

No. of carcinogens tested in both tests (A): 74

No. (%) of clear positive results in both tests (B): 48 (64.9%)

No. (%) of clear positive results in only 1 of the two tests (C): 14 (18.9%)

Sensitivity (i.e., clearly positive in at least 1 test when both conducted $([B+C]/A)^a$: 83.8%

+, Positive; -, Negative; E, Equivocal

a: If E results are considered positive, the sensitivity is 83.8% (62/74).

表 9 3 試験あるいは 4 試験の組合せにおける感受性

	Test combination			
	Ames + <i>in vitro</i> CA+ <i>in vivo</i> MN	Ames + <i>in vitro</i> CA + TGR	Ames + <i>in vivo</i> MN + TGR	Ames + <i>in vitro</i> CA+ <i>in vivo</i> MN + TGR
No. of carcinogens tested in all three or four test systems	224	64	64	56
No. (%) of clear positive results in all three or four test systems	51/224 (22.8%)	36/64 (56.3%)	31/64 (48.4%)	25/56 (44.6%)
No. (%) of clear positive results in one or two of the three assays	130/224 (58.0%)	21/64 (32.8%)	25/64 (39.1%)	Not applicable
No. (%) of clear positive results in one, two or three of the four assays	Not applicable	Not applicable	Not applicable	25/56 (44.6%)
Sensitivity (i.e., clearly positive in at least one assay when all three or four conducted) ^a	181/224 (80.8%)	57/64 (89.1%)	56/64 (87.5%)	50/56 (89.3%)

a: If equivocal results are considered positive, the sensitivity of the combination of

Ames + *in vitro* CA + *in vivo* MN is 83.0% (186/224). The sensitivities of other test combinations are not changed.

表 10 3 試験あるいは 4 試験の組合せにおける特異性

	Test combination			
	Ames + <i>in vitro</i> CA+ <i>in vivo</i> MN	Ames + <i>in vitro</i> CA + TGR	Ames + <i>in vivo</i> MN + TGR	Ames + <i>in vitro</i> CA+ <i>in vivo</i> MN + TGR
No. of non-carcinogens tested in all three or four test systems (A)	75	4	3	3
No. (%) of clear negative results in all three or four test systems (B)	16	0	1	0
Specificity (B/A) ^a	16/75 (21.3%)	Not calculated	Not calculated	Not calculated

a: If equivocal results are considered negative, the specificity is 29.3% (22/75).

表 11 *In vitro* CA と *in vivo* MN の一貫性

<i>in vitro</i> CA	<i>in vivo</i> MN			Total
	+ (C, NC)	E (C, NC)	- (C, NC)	
+	82 (72, 10)	12 (6, 6)	91 (70, 21)	185
E	3 (1, 2)	0 (0, 0)	12 (7, 5)	15
-	27 (17, 10)	4 (3, 1)	69 (49, 20)	100
Total	112 (90, 22)	16 (9, 7)	172 (126, 46)	300
Concordance ^a	50.3% (151/300)			

+, Positive; -, Negative; E, Equivocal; C, Carcinogens; NC, Non-carcinogens

a: Equivocal (E) results not counted either as positive or negative, but they were included in the total number.

If E results are considered positive, the concordance is 55.3% (166/300).

If E results are considered negative, the concordance is 55.7% (167/300).

表 12 In vitro CA (陰性) と in vivo MN (陽性) 間で結果が不一致となった物質

ID	Chemical	Chemical Grouping	CAS	Carcino- genicity	in vitro CA	in vivo MN
C179	Chlorpromazine hydrochloride	Aromatic amine or amide	69-09-0	+	-	+a
C185	C.I. Direct black 38	Aromatic azo compound	1937-37-7	+	-	+
C198	C.I. Solvent yellow 14	Aromatic azo compound	842-07-9	+	-	+
C217	D&C Red 9	Aromatic azo compound	5160-02-1	+	-	+
C226	Decabromodiphenyl oxide	Polyhalogenated aromatic	1163-19-5	+	-	+
C240	Diazepam	Aromatic amine or amide	439-14-5	+	-	+
C277	3,4-Dihydrocoumarin	Glycidyl ether, amine, ester or amide	119-84-6	+	-	+
C305	Dimethylvinyl chloride	Halogenated alkene	513-37-1	+	-	+
C425	Isoprene	Alkene	78-79-5	+	-	+
C645	Procabazine HCl	Mono- or di-alkylhydrazine	366-70-1	+	-	+
C660	Reserpine	Phenol or precursor	50-55-5	+	-	+b
C691	1,1,2,2-Tetrachloroethane	Gem-dihalide	79-34-5	+	-	+
C705	Titanium dioxide	Alkali, alkali earth, metal salt	13463-67-7	+	-	+
C706	Toluene	Benzene	108-88-3	+	-	+
C734	Trimethylphosphate	Alkyl ester of phosphoric or phosphonic acid	512-56-1	+	-*	+
C738	Tris(2-chloroethyl)phosphate	Alkylating agent	115-96-8	+	-	+
C744	Urethane	Alkyl carbamate	51-79-6	+	-*	+
NC8	dl-Amphetamine sulfate	Amine	60-13-9	-	-	+
NC13	l-Ascorbic acid	Carboxylic acid	50-81-7	-	-	+
NC49	Deltamethrin	Halogenated alkene	52918-63-5	-	-	+
NC59	1,1-Dichloroethane	Gem-dihalide	75-34-3	-	-	+
NC119	Methyl parathion	Alkyl ester of phosphoric or phosphonic acid	298-00-0	-	-	+
NC120	Monochloroacetic acid	Alkylating agent	79-11-8	-	-	+
NC133	Oxytetracycline HCl	Substituted vinyl ketone	2058-46-0	-	-	+
NC152	Resorcinol	Resorcinol or precursor	108-46-3	-	-*	+
NC173	Tolbutamide	Aryl sulphonamide	64-77-7	-	-	+
NC178	Triphenyltin hydroxide	Alkali, alkali earth, metal salt	76-87-9	-	-	+

*: positive response at both >10 mM and 2 mg/mL.

a: due to hypothermia

b: mice, due to hypothermia; negative in rat

表 13 Ames と in vivo TGR の一致性

Ames	TGR			Total
	+ (C, NC)	E (C, NC)	- (C, NC)	
+	48 (48, 0)	0 (0, 0)	10 (8, 2)	58
E	1 (1, 0)	0 (0, 0)	0 (0, 0)	1
-	5 (5, 0)	0 (0, 0)	14 (12, 2)	19
Total	54 (54, 0)	0 (0, 0)	24 (12, 2)	78
Concordance ^a	79.5% (62/78)			

+, Positive; -, Negative; E, Equivocal; C, Carcinogens; NC, Non-carcinogens

a: Equivocal (E) results were not counted either as positive or negative, but they were included in the total number.

If E results are considered positive, the concordance is 80.8% (63/78).

If E results are considered negative, the concordance is 79.5% (62/78).

表 14 Ames と in vivo TGR 間で結果が不一致となった物質

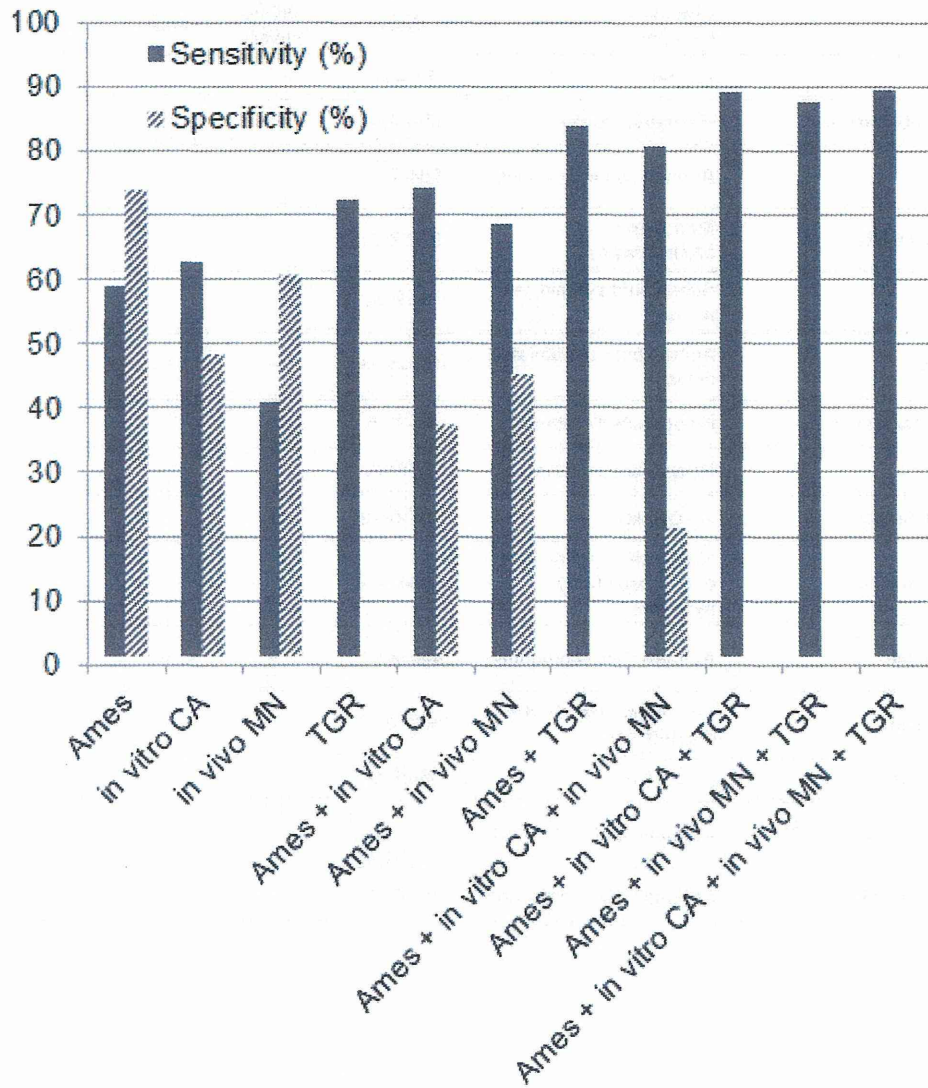
ID	Chemical	Chemical Grouping	CAS	Carcinogenicity	Ames	TGR
C84	Benzene	Benzene	71-43-2	+	-	+
C384	Hexachlorobutadiene	Halogenated alkene	608-73-1	+	-	+
C605	Oxazepam	Aromatic amine or amide	604-75-1	+	-	+
C645	Procarbazine HCl	Mono- or di-alkylhydrazine	366-70-1	+	-	+
C742	Uracil	Substituted pyrimidine or purine	66-22-8	+	-	+
C17	Acrylonitrile	Alpha-, beta-unsaturated nitrile	107-13-1	+	+	-
C137	Carbon tetrachloride	Halogenated methane	56-23-5	+	+	-
C160	Chloroform	Halogenated methane	67-66-3	+	+	-
C257	1,2-Dichloroethane	vic-Dihalide	107-06-2	+	+	-
C395	Hydrazine sulphate	Hydrazine or monoacyl- or monosulphonyl-hydrazine	10034-93-2	+	+	-
C489	Metronidazole	Aromatic nitro compound	443-48-1	+	+	-
C509	Nitrite, sodium	Alkyl nitrite, nitrous acid or nitrite salt	7632-00-0	+	+	-
C622	Phenobarbital	(Thio)urea	50-06-6	+	+	-
NC52	2,6-Diaminotoluene 2HCl	Aromatic amine or amide	15481-70-6	-	+	-
NC126	1-Nitronaphthalene	Aromatic nitro compound	86-59-7	-	+	-

表 15 各試験単独およびそれらの組合せによる感受性および特異性の要約表

Measure	Ames	in vitro CA	in vivo MN	TGR	Ames + in vitro CA	Ames + in vivo MN	Ames + TGR	Ames + in vitro CA + in vivo MN	Ames + in vitro CA + TGR	Ames + in vivo MN + TGR	Ames + in vitro CA + in vivo MN + TGR
Sensitivity (%)	59.0	62.8	41.0	72.4	74.3	68.7	83.8	80.8	89.1	87.5	89.3
Specificity (%)	73.9	48.5	60.5	NC	37.5	45.3	NC	21.3	NC	NC	NC
Concordance (%)	62.6	58.9	45.4	NC	NA	NA	NC	NA	NA	NA	NA

NC: Not calculated
NA: Not applicable

図1 各試験単独およびそれらの組合せによる感受性および特異性の要約図



Appendix 1: Genotoxicity test results with rodent carcinogens								
ID	Chemical	CAS No.	Amees	<i>in vitro</i> CA	<i>in vivo</i> MN	<i>in vivo</i> MN Ref.	TGR	TGR Ref.
C1	Acetaldehyde	75-07-0	-	+	+	[11]		
C2	Acetaldehyde methylformylhydrazone	16568-02-8	-					
C3	Acetamide	60-35-5	-		-	[11]~		
C4	Acetaminophen	103-90-2	-	+	-	[64]	-	[16]~
C5	Acetone[4-(5-nitro-2-furyl)-2-thiazolyl]hydrazone	18523-69-8						
C6	Acetoxime	127-06-0	-					
C7	N-Acetoxy-2-acetylamino fluorene	6098-44-8	+	+				
C8	1-Acetoxy safrole	34627-78-6	+					
C9	4-Acetylamino biphenyl	4075-79-0						
C10	2-Acetylamino fluorene	53-96-3	+	+	+	[30]	+	[16]
C11	N'-Acetyl-4-(hydroxymethyl)phenylhydrazine	65734-36-5						
C12	1-Acetyl-2-isonicotinoylhydrazine	1078-38-2						
C13	1-Acetyl-2-phenylhydrazine	114-83-0	+					
C14	Acitofurfen	50594-66-6						
C15	Acronyone	7008-42-5						
C16	Acrylamide	79-06-1	E	+	+	[65, 66]	+	[16, 67]
C17	Acrylonitrile	107-13-1	+	+	-3	[11, 41]	-3	[16]~
C18	Actinomycin D	50-76-0	-	+	+	[60]		
C19	Afatoxicol	29611-03-8	+					
C20	Afatoxin B1	1162-65-8	+	+	+	[30]	+	[16]
C21	Afatoxin, crude	-						
C22	Aldrin	309-00-2	-	+	-	[68]		
C23	Allyl glycidyl ether	106-92-3	+	+	+	[69]		
C24	Allyl isothiocyanate	57-06-7	E	+	-	[34]		
C25	Allyl isovalerate	2635-39-4	-	+				
C26	1-Allyl-1-nitrosourea	760-56-5						
C27	Allylhydrazine HCl	62207-83-7						
C28	2-Aminoanthracene	613-13-6	+	E				
C29	2-Aminoanthraquinone	117-79-3	+					
C30	4-Aminoazobenzene	60-09-3	+		+	[11]		
C31	4-Aminobiphenyl	92-67-1	+	+	+	[11]	+	[16]
C32	4-Aminobiphenyl HCl	2113-61-3	+		+	[70]		
C33	1-Amino-2,4-dibromanthraquinone	81-49-2	+	-				
C34	2-Amino-3,4-dimethylimidazo[4,5-f]quinoline (MeIQ)	77094-11-2	+	+			+	[16]
C35	2-Amino-3,8-dimethylimidazo[4,5-f]quinoxaline (MeIQx)	77500-04-0	+		+	[71]	+	[16]
C36	3-Amino-1,4-dimethyl-5H-pyrido[4,3-b]indole acetate (Trp-P-1 acetate)	68808-54-8	+	+				
C37	2-Aminodiphenylene oxide	3693-22-9						
C38	2-Aminodipyrido[1,2-a:3',2'-d]imidazole (Glu-P-2)	67730-10-3	+	+				

ID	Chemical	CAS No.	Ames	in vitro CA	in vivo MN	in vivo MN Ref.	TGR	TGR Ref.
C39	3-Amino-4-ethoxyacetanilide	17026-81-2	+	-				
C40	3-Amino-9-ethylcarbazole HCl	6109-97-3	+	-				
C41	3-Amino-9-ethylcarbazole mixture	Mixture	+					
C42	2-Aminofluorene	153-73-6	+					
C43	2-Amino-6-methylpyrido[1,2-a:3',2'-d]imidazole (Glu-P-1)	67730-11-4	+	+				
C44	2-Amino-3-methylimidazo[4,5-f]quinoline (IQ)	76180-96-6	+		-	[72]	+	[16]
C45	2-Amino-3-methylimidazo[4,5-f]quinoline HCl (IQ.HCl)	-	+				+	[16]
C46	2-Amino-1-methyl-6-phenylimidazo[4,5-b]pyridine hydrochloride (PhIP.HCl)	105660-23-6	+	+	+	[73]	+	[16]
C47	3-Amino-1-methyl-5H-pyrindo[4,3-b]indole acetate (Trp-P-2 acetate)	72264-86-1	+	+				
C48	2-Amino-5-(5-nitro-2-furyl)-1,3,4-oxadiazole	3773-85-1						
C49	2-Amino-5-(5-nitro-2-furyl)-1,3,4-thiadiazole	712-68-6						
C50	2-Amino-4-(5-nitro-2-furyl)thiazole	36514-71-6	+					
C51	trans-6-Amino-3[2-(5-nitro-2-furyl)vinyl]-1,2,4-oxadiazole	28764-66-9						
C52	2-Amino-4-nitrophenol	99-87-0	+	+	-	[50]		
C53	2-Amino-5-nitrophenol	121-83-0	+	+				
C54	4-Amino-2-nitrophenol	119-34-6	+	+				
C55	2-Amino-4-(p-nitrophenyl)thiazole	2104-09-9						
C56	2-Amino-5-nitrothiazole	121-66-4	+	+				
C57	2-Amino-9H-pyrido[2,3-b]indole (A-alpha-C)	26148-86-6	+	+			+	[16]
C58	3-Amino-1,2,4-triazole (Amitrole)	61-82-6	-	-	-	[74]-		
C59	11-Aminoundecanoic acid	2432-99-7	-	-	-	[34]		
C60	1-Amyl-1-nitrosourea	10569-74-9		+				
C61	Amylopectin sulphate	9047-13-6						
C62	Aniline HCl	142-04-1	-	+	+	[75]		
C63	o-Anisidine HCl	134-23-2	+		-	[50]		
C64	Aramite	140-67-8						
C65	Arecoline HCl	61-94-9			+	[30]		
C66	Aristolochic acid	313-67-7	++	+++	-	[76]	+	[16]
C67	Aroclor 1254	27323-16-6	-					
C68	Aroclor 1260	11096-82-6						
C69	Asbestos	12001-29-6	-	+	-	[11]-		
C70	Atrazine	1912-24-9	-	+	+	[77]		
C71	Auramine O	2465-27-2	+	+				
C72	5-Azacytidine	320-67-2	+	+	+	[50]		
C73	Azaserine	115-02-6	+		+	[11]		
C74	Azathioprine	445-86-6	+	+	+	[30]	+	[16]
C75	Azobenzene	103-33-3	+	E	+	[26]		
C76	Azoxymethane	26643-46-2	+					
C77	1-Azoxypropane	17697-55-1						
C78	2-Azoxypropane	17697-53-9						

ID	Chemical	CAS No.	Ames	<i>in vitro</i> CA	<i>in vivo</i> MN	<i>in vivo</i> MN Ref.	TGR	TGR Ref.
C79	Barbital, sodium	144-02-5		+				
C80	Bemtridine	86133-11-3	-					
C81	Benomyi	17804-35-2	-		+	[78]		
C82	Benzaldehyde	100-52-7	-	+				
C83	Benz[a]anthracene	56-56-3	+		+	[11]		
C84	Benzene	71-43-2	-	+	+	[50]	+	[16]
C85	Benzidine	92-67-5	+	+	+	[50]		
C86	Benzidine 2HCl	531-85-1	+	+	+	[50]		
C87	Benzofuran	271-89-6	-	-				
C88	Benzo[a]pyrene	50-32-8	+	+	+	[30]	+	[16]
C89	1,4-Benzoquinone	106-51-4	-		+	[79]		
C90	Benzotrionide	96-07-7	+					
C91	Benzoyl hydrazine	513-94-5						
C92	Benzyl acetate	140-11-4	-	-	-	[34]		
C93	Benzyl chloride	100-44-7	+	+	-	[30]-		
C94	o-Benzyl-p-chlorophenol	120-32-1	-	-				
C95	Benzylhydrazine 2HCl	20570-96-1						
C96	2-Biphenylamine HCl	2185-92-4	+	+	-	[34]		
C97	2,2-Bis(bromomethyl)-1,3-propanediol, technical grade	3296-90-0	+	+	E	[50]		
C98	Bis(2-chloro-1-methylethyl)ether, technical grade	108-60-1	+	+				
C99	Bis-2-chloroethylether	111-44-4	+					
C100	Bis-1,2-(chloromethoxy)ethane	13483-16-6						
C101	Bis-1,4-(chloromethoxy)-p-xylene	56694-91-8						
C102	Bis-(chloromethyl)ether	542-88-1						
C103	Bis(2,3-dibromopropyl)phosphate, magnesium salt	36711-31-6	+	+				
C104	Bis(dimethylamino)benzophenone (Michler's ketone)	90-94-8	+	E				
C105	4-Bis(2-hydroxyethyl)amino-2-(5-nitro-2-trienyl)quinazoline	33372-39-3	TC					
C106	Bis-2-hydroxyethylthiocarbamic acid, potassium	23746-34-1						
C107	Bromate, potassium	7758-01-2	+	+	+	[30]	+	[16]
C108	Bromocriptine mesylate	22260-51-1			-	[80]		
C109	Bromodichloromethane	75-27-4	-	+	-	[50, 61]		
C110	Bromoethane	74-96-4	+	-				
C111	2-Bromoethanol	540-51-2	+					
C112	7-Bromomethyl-12-methylbenz[a]anthracene	16238-56-5	+					
C113	Budesonide	51333-22-3						
C114	1,3-Butadiene	106-99-0	+		+	[30]	+	[16]
C115	tert-Butyl alcohol	75-85-0	-	-	-	[36, 50]		
C116	Butylated hydroxyanisole	25013-16-5	-	+	-	[50]		
C117	Butylated hydroxytoluene	128-37-0	-	-	-	[50]		
C118	Butylbenzyl phthalate	85-86-7	-	-	-	[50]		

ID	Chemical	CAS No.	Ames	<i>in vitro</i> CA	<i>in vivo</i> MN	<i>in vivo</i> MN Ref.	TGR	TGR Ref.
C119	N-n-Butyl-N-formylhydrazine	16120-70-0						
C120	N-Butylhydrazine HCl	56795-55-4						
C121	N-Butyl-N-(4-hydroxybutyl)nitrosamine	3817-11-6	+					
C122	N-n-Butyl-N-nitrosourea	869-01-2	+	+				
C123	beta-Butyrolactone	3058-88-0	+		+	[11]		
C124	Cadmium chloride	10106-54-2	+	+	+	[62]		
C125	Cadmium sulphate	10124-36-4	-	+				
C126	Caffeic acid	331-39-5	-	+	-	[50]~		
C127	Calciferol	80-14-6		TC				
C128	Calcium chromate	13765-19-0	+	+	-	[63]		
C129	Calcium valproate	33433-82-8						
C130	Capsaicin	404-86-4	+	-*	-	[22, 23]		
C131	Captadol	2425-06-1	+	+				
C132	Captaf	133-06-2	+	+	+	[30]		
C133	Carbamyl hydrazine HCl	563-41-7	-		-	[64]		
C134	1-Carbamyl-2-phenylhydrazine	103-03-7						
C135	Carbaryl	53-25-2	+	+	+	[69]		
C136	Carbazole	66-74-8	-					
C137	Carbon tetrachloride	56-23-5	+	-	-	[11]	-	[16]~
C138	Carboxymethylnitrosourea	60391-92-6	-	+				
C139	Carrageenan, acid-degraded	9000-07-1						
C140	Catechol	120-80-9	-	+	+	[65]		
C141	Chloral hydrate	302-17-0	+	+	+	[60]		
C142	Chloramben	133-90-4	+	+				
C143	Chlorambucil	305-03-3	+	+	+	[11]	+	[16]
C144	Chlordane, technical grade	12769-03-6	+					
C145	Chlordane, analytical grade	57-74-9	-	-				
C146	Chlorogenic acid	115-25-6	-	+				
C147	Chlorinated paraffins: C12	108171-28-2	-	+				
C148	Chlorinated paraffins: C23	63449-39-8	-					
C149	Chlormaphazine	494-03-1	+		+	[66]		
C150	Chloroacetaldehyde	107-20-0	+					
C151	4-Chloro-4'-aminodiphenylether	101-73-1						
C152	p-Chloroaniline HCl	20266-96-7	+		+	[60]		
C153	Chlorobenzene	108-90-7	-	+	-	[34]		
C154	Chlorobenzilate	510-15-6	-	-				
C155	Chlorodibromomethane	124-48-1	+	+	-	[60]		
C156	2-Chloro-5-(3,5-dimethylpipendinosulphonyl)benzoic acid	37067-94-6						
C157	Chloroethane	75-00-3	+		-	[67]		
C158	1-Chloroethylnitroso-3-(2-hydroxypropyl)urea	-						