Annex III

Comparative LLNA: DA, Traditional LLNA, Guinea Pig, and Human Skin Sensitization Data

Annex III-1
Comparison of LLNA: DA, Traditional LLNA, Guinea Pig, and Human Results (Alphanumeric Order) C-123

Annex III-2
Comparison of Alternative LLNA: DA Decision Criteria and Traditional LLNA Results (Alphanumeric Order) C-141

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Annex III-1

Comparison of LLNA: DA, Traditional LLNA, Guinea Pig, and Human Results (Alphanumeric Order)

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Table C-III-1-1 Comparative Performance of the LLNA: DA, Traditional LLNA, Guinea Pig, and Human Tests (Alphanumeric Order)

Substance Name	Veh.[1]	LLNA: DA Highest Conc. Tested (%)	LLNA: DA Highest SI[2]	LLNA: DA Reference	Trad. LLNA Result[3]	GP Result[4]	Human Result[5]	Trad. LLNA Reference	GP Reference	Human Reference	Skin Irritation Data	Skin Irritation Reference
Abietic acid	AOO	25	6.26	Idehara et al. 2008	+ (5.2, 25%)	+	+	ICCVAM 1999	ICCVAM 1999	ICCVAM 1999	Nonirritant at 25% (GP)	Basketter et al. 2007b
Abietic acid	AOO	25	4.64	Omori et al. 2008	+ (5.2, 25%)	+	+	ICCVAM 1999	ICCVAM 1999	ICCVAM 1999	Nonirritant at 25% (GP)	Basketter et al. 2007b
Abietic acid	AOO	25	7.96	Omori et al. 2008	+ (5.2, 25%)	+	+	ICCVAM 1999	ICCVAM 1999	ICCVAM 1999	Nonirritant at 25% (GP)	Basketter et al. 2007b
Abietic acid	AOO	25	3.98 at 10%	Omori et al. 2008	+ (5.2, 25%)	+	+	ICCVAM 1999	ICCVAM 1999	ICCVAM 1999	Nonirritant at 25% (GP)	Basketter et al. 2007b
3-Aminophenol	AOO	10	2.83	Omori et al. 2008	+ (5.7, 10%)	NA (+ nonstd)	+	ICCVAM 1999	ICCVAM 1999	ICCVAM 1999	Nonirritant at 5% (GP)	Basketter et al. 2007b
3-Aminophenol	AOO	10	1.76 at 3%	Omori et al. 2008	+ (5.7, 10%)	NA (+ nonstd)	+	ICCVAM 1999	ICCVAM 1999	ICCVAM 1999	Nonirritant at 5% (GP)	Basketter et al. 2007b
3-Aminophenol	AOO	10	2.38	Omori et al. 2008	+ (5.7, 10%)	NA (+ nonstd)	+	ICCVAM 1999	ICCVAM 1999	ICCVAM 1999	Nonirritant at 5% (GP)	Basketter et al. 2007b
Benzalkonium chloride	AOO[6]	2.5	6.68	Idehara et al. 2008	+ (11.1, 2%)[7]	-	+	Gerberick 1992	ICCVAM 1999	ICCVAM 1999	Irritant at 2% in ACE (mice); irritant at 1% in ACE (mice)	Gerberick et al 2002; Manetz and Meade 1999
Benzocaine	**AOO**	**25**	**4.84**	**Idehara et al. 2008**	**+/- (7.6, 20%)[8]**	**+**	**+/-**	**ICCVAM 1999**	**ICCVAM 1999**	**Poole et al. 1970; ICCVAM 1999 (Equivocal data)**	**Negative at ≤ 10% (GP)**	**Basketter and Scholes 1992**

Substance Name	Veh.[1]	LLNA: DA Highest Conc. Tested (%)	LLNA: DA Highest SI[2]	LLNA: DA Reference	Trad. LLNA Result[3]	GP Result[4]	Human Result[5]	Trad. LLNA Reference	GP Reference	Human Reference	Skin Irritation Data	Skin Irritation Reference
p-Benzo-quinone	AOO	0.100	3.79	Idehara unpublished	+ (52.3, 2.5%)	+	+	ICCVAM 1999	ICCVAM 1999	Basketter et al. 1999b	Nonirritant at 2.5% (GP)	Basketter et al. 2007b
1-Bromo-butane	AOO	25	1.65	Idehara et al. 2008	- (1.2, 25%)[9]	NA	NA	ICCVAM 1999	NA	NA	NA	NA
Butyl glycidyl ether	AOO	50	4.59	Idehara unpublished	+ (5.6, 50%)	+	+	ICCVAM 1999	ICCVAM 1999	ICCVAM 1999	Nonirritant at 0.1% (GP)	Wahlberg and Boman 1985
Chlorobenzene	AOO	25	2.44	Idehara et al. 2008	- (1.7, 25%)[9]	-	NA	ICCVAM 1999	ICCVAM 1999	NA	No data. Low irritancy potential assumed based on clinical literature.	Basketter et al. 1998
5-Chloro-2-methyl-4-isothiazolin-3-one	DMF	0.100	7.50	Idehara unpublished	+ (27.7, 0.1%)	+	+	ICCVAM 1999; Gerberick et al. 2005	ICCVAM 1999	ICCVAM 1999	Nonirritant at 0.1% (GP)	Basketter et al. 2007b
Cinnamic alcohol	AOO	90	5.66 at 50%	Idehara unpublished	+ (5.7, 90%)	+	+	Gerberick et al. 2005	Robinson et al. 1990	Jordan and King 1977	Nonirritant at 1% (GP)	Robinson et al. 1990
Cinnamic aldehyde	AOO	15	4.73	Idehara et al. 2008	+ (18.4, 25%)[9]	+	+	ICCVAM 1999	ICCVAM 1999	ICCVAM 1999	Nonirritant at 0.75% (GP); mild irritant at 100% (rabbits)	Basketter et al. 2007b; ECETOC 1995
Citral	AOO	25	4.40	Idehara et al. 2008	+ (20.5, 20%)	+	+	ICCVAM 1999	ICCVAM 1999	ICCVAM 1999	Nonirritant at 0.5% (GP)	Basketter et al. 2007b
Cobalt chloride	DMSO	5	3.64	Idehara et al. 2008	+ (7.2, 5%)	+	+	ICCVAM 1999	ICCVAM 1999	ICCVAM 1999	Negative at ≤ 0.5% (GP)	Basketter and Scholes 1992

Substance Name	Veh.[1]	LLNA: DA Highest Conc. Tested (%)	LLNA: DA Highest SI[2]	LLNA: DA Reference	Trad. LLNA Result[3]	GP Result[4]	Human Result[5]	Trad. LLNA Reference	GP Reference	Human Reference	Skin Irritation Data	Skin Irritation Reference
Cobalt chloride	DMSO	1[10]	2.66	Omori et al. 2008	+ (7.2, 5%)	+	+	ICCVAM 1999	ICCVAM 1999	ICCVAM 1999	Negative at ≤ 0.5% (GP)	Basketter and Scholes 1992
Cobalt chloride	DMSO	3	20.55	Omori et al. 2008	+ (7.2, 5%)	+	+	ICCVAM 1999	ICCVAM 1999	ICCVAM 1999	Negative at ≤ 0.5% (GP)	Basketter and Scholes 1992
Cobalt chloride	DMSO	3	8.07	Omori et al. 2008	+ (7.2, 5%)	+	+	ICCVAM 1999	ICCVAM 1999	ICCVAM 1999	Negative at ≤ 0.5% (GP)	Basketter and Scholes 1992
Cobalt chloride	DMSO	5	2.01	Omori et al. 2008	+ (7.2, 5%)	+	+	ICCVAM 1999	ICCVAM 1999	ICCVAM 1999	Negative at ≤ 0.5% (GP)	Basketter and Scholes 1992
Cobalt chloride	DMSO	5	2.54	Omori et al. 2008	+ (7.2, 5%)	+	+	ICCVAM 1999	ICCVAM 1999	ICCVAM 1999	Negative at ≤ 0.5% (GP)	Basketter and Scholes 1992
Cobalt chloride	DMSO	5	4.25	Omori et al. 2008	+ (7.2, 5%)	+	+	ICCVAM 1999	ICCVAM 1999	ICCVAM 1999	Negative at ≤ 0.5% (GP)	Basketter and Scholes 1992
Cobalt chloride	DMSO	5	5.06	Omori et al. 2008	+ (7.2, 5%)	+	+	ICCVAM 1999	ICCVAM 1999	ICCVAM 1999	Negative at ≤ 0.5% (GP)	Basketter and Scholes 1992
Diethyl maleate	AOO	10.0	3.78	Idehara unpublished	+ (22.6, 100%)[11]	NA	+	Gerberick et al. 2005	NA	Marzulli and Maibach 1980	Nonirritant at 100% (GP)	Basketter et al. 2007b
Diethyl phthalate	AOO	100	1.09	Idehara et al. 2008	- (1.5, 100%)	-	+	Gerberick et al. 2005	Klecak et al. 1977	ICCVAM 1999	Negative at 100% (rabbits)	ECETOC 1995
Dimethyl isophthalate	AOO	25	0.89 at 5%	Idehara unpublished	- (1.0, 25%)	-	-	ICCVAM 1999; Basketter et al. 1999b	ICCVAM 1999; Basketter et al. 1999b	Basketter et al. 1999b	Negative at ≤ 10% (GP)	Basketter and Scholes 1992

Substance Name	Veh.[1]	LLNA: DA Highest Conc. Tested (%)	LLNA: DA Highest SI[2]	LLNA: DA Reference	Trad. LLNA Result[3]	GP Result[4]	Human Result[5]	Trad. LLNA Reference	GP Reference	Human Reference	Skin Irritation Data	Skin Irritation Reference
Dimethyl isophthalate	AOO	25	1.34 at 5%	Omori et al. 2008	- (1.0, 25%)	-	-	ICCVAM 1999; Basketter et al. 1999b	ICCVAM 1999; Basketter et al. 1999b	Basketter et al. 1999b	Negative at ≤ 10% (GP)	Basketter and Scholes 1992
Dimethyl isophthalate	AOO	25	1.00 at 5%	Omori et al. 2008	- (1.0, 25%)	-	-	ICCVAM 1999; Basketter et al. 1999b	ICCVAM 1999; Basketter et al. 1999b	Basketter et al. 1999b	Negative at ≤ 10% (GP)	Basketter and Scholes 1992
Dimethyl isophthalate	AOO	25	1.26 at 5%	Omori et al. 2008	- (1.0, 25%)	-	-	ICCVAM 1999; Basketter et al. 1999b	ICCVAM 1999; Basketter et al. 1999b	Basketter et al. 1999b	Negative at ≤ 10% (GP)	Basketter and Scholes 1992
2,4-Dinitrochloro-benzene	AOO	1	7.10	Idehara et al. 2008	+ (43.9, 0.25%)	+	+	ICCVAM 1999	ICCVAM 1999	ICCVAM 1999; Schneider and Akkan 2004	Nonirritant at 0.1% (GP)	Basketter et al. 2007b
2,4-Dinitrochloro-benzene	AOO	0.30	11.97	Omori et al. 2008	+ (43.9, 0.25%)	+	+	ICCVAM 1999	ICCVAM 1999	ICCVAM 1999; Schneider and Akkan 2004	Nonirritant at 0.1% (GP)	Basketter et al. 2007b
2,4-Dinitrochloro-benzene	AOO	0.30	9.23	Omori et al. 2008	+ (43.9, 0.25%)	+	+	ICCVAM 1999	ICCVAM 1999	ICCVAM 1999; Schneider and Akkan 2004	Nonirritant at 0.1% (GP)	Basketter et al. 2007b
2,4-Dinitrochloro-benzene	AOO	0.30	9.96	Omori et al. 2008	+ (43.9, 0.25%)	+	+	ICCVAM 1999	ICCVAM 1999	ICCVAM 1999; Schneider and Akkan 2004	Nonirritant at 0.1% (GP)	Basketter et al. 2007b
2,4-Dinitrochloro-benzene	AOO	0.30	8.53	Omori et al. 2008	+ (43.9, 0.25%)	+	+	ICCVAM 1999	ICCVAM 1999	ICCVAM 1999; Schneider and Akkan 2004	Nonirritant at 0.1% (GP)	Basketter et al. 2007b

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2,4-Dinitrochloro-benzene	AOO	0.30	7.86	Omori et al. 2008	+ (43.9, 0.25%)	+	+	ICCVAM 1999	ICCVAM 1999	ICCVAM 1999; Schneider and Akkan 2004	Nonirritant at 0.1% (GP)	Basketter et al. 2007b
2,4-Dinitrochloro-benzene	AOO	0.30	15.14	Omori et al. 2008	+ (43.9, 0.25%)	+	+	ICCVAM 1999	ICCVAM 1999	ICCVAM 1999; Schneider and Akkan 2004	Nonirritant at 0.1% (GP)	Basketter et al. 2007b
2,4-Dinitrochloro-benzene	AOO	0.30	13.18	Omori et al. 2008	+ (43.9, 0.25%)	+	+	ICCVAM 1999	ICCVAM 1999	ICCVAM 1999; Schneider and Akkan 2004	Nonirritant at 0.1% (GP)	Basketter et al. 2007b
2,4-Dinitrochloro-benzene	AOO	0.30	12.60	Omori et al. 2008	+ (43.9, 0.25%)	+	+	ICCVAM 1999	ICCVAM 1999	ICCVAM 1999; Schneider and Akkan 2004	Nonirritant at 0.1% (GP)	Basketter et al. 2007b
2,4-Dinitrochloro-benzene	AOO	0.30	10.89	Omori et al. 2008	+ (43.9, 0.25%)	+	+	ICCVAM 1999	ICCVAM 1999	ICCVAM 1999; Schneider and Akkan 2004	Nonirritant at 0.1% (GP)	Basketter et al. 2007b
2,4-Dinitrochloro-benzene	AOO	0.30	4.71	Omori et al. 2008	+ (43.9, 0.25%)	+	+	ICCVAM 1999	ICCVAM 1999	ICCVAM 1999; Schneider and Akkan 2004	Nonirritant at 0.1% (GP)	Basketter et al. 2007b
Ethyl acrylate	AOO	50	4.29 at 25%	Idehara unpublished	+ (4, 50%)	-	+	Gerberick et al. 2005	Van der Walle et al. 1982	Marzulli and Maibach 1974	Nonirritant at 0.3 M (GP)	Van der Walle et al. 1982
Ethylene glycol dimethacrylate	MEK	50	4.45	Idehara unpublished	+ (7, 50%)	-	+	ICCVAM 1999	ICCVAM 1999; Gerberick et al.1992	ICCVAM 1999; Basketter et al. 1999b	Nonirritant at 1% (GP)	Wahlberg and Boman 1985
Eugenol	AOO	25	7.07	Idehara et al. 2008	+ (17, 50%)	+	+	ICCVAM 1999	ICCVAM 1999	ICCVAM 1999	Nonirritant at 25% (GP); mild irritant at 100% (rabbits)	Basketter et al. 2007b; ECETOC 1995

Substance Name	Veh.[1]	LLNA: DA Highest Conc. Tested (%)	LLNA: DA Highest SI[2]	LLNA: DA Reference	Trad. LLNA Result[3]	GP Result[4]	Human Result[5]	Trad. LLNA Reference	GP Reference	Human Reference	Skin Irritation Data	Skin Irritation Reference
Formaldehyde	ACE	2.50	5.10	Idehara et al. 2008	+ (4, 1.85%)	+	+	Gerberick et al. 2005; Hilton et al. 1998	ICCVAM 1999	ICCVAM 1999; Kwon et al. 2003	Nonirritant at 2% (GP)	Basketter et al. 2007b
Formaldehyde	ACE	5.0	4.84	Omori et al. 2008	+ (4, 1.85%)	+	+	Gerberick et al. 2005; Hilton et al. 1998	ICCVAM 1999	ICCVAM 1999; Kwon et al. 2003	Nonirritant at 2% (GP)	Basketter et al. 2007b
Formaldehyde	ACE	5.0	3.18	Omori et al. 2008	+ (4, 1.85%)	+	+	Gerberick et al. 2005; Hilton et al. 1998	ICCVAM 1999	ICCVAM 1999; Kwon et al. 2003	Nonirritant at 2% (GP)	Basketter et al. 2007b
Formaldehyde	ACE	5.0	2.69	Omori et al. 2008	+ (4, 1.85%)	+	+	Gerberick et al. 2005; Hilton et al. 1998	ICCVAM 1999	ICCVAM 1999; Kwon et al. 2003	Nonirritant at 2% (GP)	Basketter et al. 2007b
Glutaraldehyde	ACE	0.25	6.45	Idehara et al. 2008	+ (18, 2.5%)	+	+	Basketter et al. 2005; Hilton et al. 1998	Gad et al. 1986	Marzulli and Maibach 1974; Schneider and Akkan 2004	NA	NA
Glutaraldehyde	ACE	0.50	5.00	Omori et al. 2008	+ (18, 2.5%)	+	+	Basketter et al. 2005; Hilton et al. 1998	Gad et al. 1986	Marzulli and Maibach 1974; Schneider and Akkan 2004	NA	NA
Glutaraldehyde	ACE	0.50	3.39	Omori et al. 2008	+ (18, 2.5%)	+	+	Basketter et al. 2005; Hilton et al. 1998	Gad et al. 1986	Marzulli and Maibach 1974; Schneider and Akkan 2004	NA	NA
Glutaraldehyde	ACE	0.50	2.57	Omori et al. 2008	+ (18, 2.5%)	+	+	Basketter et al. 2005; Hilton et al. 1998	Gad et al. 1986	Marzulli and Maibach 1974; Schneider and Akkan 2004	NA	NA

Substance Name	Veh.[1]	LLNA: DA Highest Conc. Tested (%)	LLNA: DA Highest SI[2]	LLNA: DA Reference	Trad. LLNA Result[3]	GP Result[4]	Human Result[5]	Trad. LLNA Reference	GP Reference	Human Reference	Skin Irritation Data	Skin Irritation Reference
Hexane	AOO	100	2.31	Idehara et al. 2008	- (2.2, 100%)	NA	-	ICCVAM 1999	NA	ICCVAM 1999	Irritant at 100% (humans)	Kligman 1966c
Hexyl cinnamic aldehyde	AOO	25	6.47	Idehara et al. 2008	+ (20, 50%)	+	+	ICCVAM 1999	ICCVAM 1999	Basketter et al. 1999b	Nonirritant at ≤10% (GP); mild irritant at 100% (rabbits)	Basketter et al. 2007b; ECETOC 1995
Hexyl cinnamic aldehyde	AOO	25	5.78	Omori et al. 2008	+ (20, 50%)	+	+	ICCVAM 1999	ICCVAM 1999	Basketter et al. 1999b	Nonirritant at ≤10% (GP); mild irritant at 100% (rabbits)	Basketter et al. 2007b; ECETOC 1995
Hexyl cinnamic aldehyde	AOO	25	4.82	Omori et al. 2008	+ (20, 50%)	+	+	ICCVAM 1999	ICCVAM 1999	Basketter et al. 1999b	Nonirritant at ≤10% (GP); mild irritant at 100% (rabbits)	Basketter et al. 2007b; ECETOC 1995
Hexyl cinnamic aldehyde	AOO	25	4.44	Omori et al. 2008	+ (20, 50%)	+	+	ICCVAM 1999	ICCVAM 1999	Basketter et al. 1999b	Nonirritant at ≤10% (GP); mild irritant at 100% (rabbits)	Basketter et al. 2007b; ECETOC 1995
Hexyl cinnamic aldehyde	AOO	25	5.11	Omori et al. 2008	+ (20, 50%)	+	+	ICCVAM 1999	ICCVAM 1999	Basketter et al. 1999b	Nonirritant at ≤10% (GP); mild irritant at 100% (rabbits)	Basketter et al. 2007b; ECETOC 1995
Hexyl cinnamic aldehyde	AOO	25	3.97	Omori et al. 2008	+ (20, 50%)	+	+	ICCVAM 1999	ICCVAM 1999	Basketter et al. 1999b	Nonirritant at ≤10% (GP); mild irritant at 100% (rabbits)	Basketter et al. 2007b; ECETOC 1995
Hexyl cinnamic aldehyde	AOO	25	5.50	Omori et al. 2008	+ (20, 50%)	+	+	ICCVAM 1999	ICCVAM 1999	Basketter et al. 1999b	Nonirritant at ≤10% (GP); mild irritant at 100% (rabbits)	Basketter et al. 2007b; ECETOC 1995
Hexyl cinnamic aldehyde	AOO	25	7.09	Omori et al. 2008	+ (20, 50%)	+	+	ICCVAM 1999	ICCVAM 1999	Basketter et al. 1999b	Nonirritant at ≤10% (GP); mild irritant at 100% (rabbits)	Basketter et al. 2007b; ECETOC 1995

Substance Name	Veh.[1]	LLNA: DA Highest Conc. Tested (%)	LLNA: DA Highest SI[2]	LLNA: DA Reference	Trad. LLNA Result[3]	GP Result[4]	Human Result[5]	Trad. LLNA Reference	GP Reference	Human Reference	Skin Irritation Data	Skin Irritation Reference
Hexyl cinnamic aldehyde	AOO	25	10.22	Omori et al. 2008	+ (20, 50%)	+	+	ICCVAM 1999	ICCVAM 1999	Basketter et al. 1999b	Nonirritant at ≤10% (GP); mild irritant at 100% (rabbits)	Basketter et al. 2007b; ECETOC 1995
Hexyl cinnamic aldehyde	AOO	25	3.88	Omori et al. 2008	+ (20, 50%)	+	+	ICCVAM 1999	ICCVAM 1999	Basketter et al. 1999b	Nonirritant at ≤10% (GP); mild irritant at 100% (rabbits)	Basketter et al. 2007b; ECETOC 1995
Hexyl cinnamic aldehyde	AOO	25	3.51	Omori et al. 2008	+ (20, 50%)	+	+	ICCVAM 1999	ICCVAM 1999	Basketter et al. 1999b	Nonirritant at ≤10% (GP); mild irritant at 100% (rabbits)	Basketter et al. 2007b; ECETOC 1995
Hexyl cinnamic aldehyde	AOO	25	4.47	Omori et al. 2008	+ (20, 50%)	+	+	ICCVAM 1999	ICCVAM 1999	Basketter et al. 1999b	Nonirritant at ≤10% (GP); mild irritant at 100% (rabbits)	Basketter et al. 2007b; ECETOC 1995
Hexyl cinnamic aldehyde	AOO	25	5.71	Omori et al. 2008	+ (20, 50%)	+	+	ICCVAM 1999	ICCVAM 1999	Basketter et al. 1999b	Nonirritant at ≤10% (GP); mild irritant at 100% (rabbits)	Basketter et al. 2007b; ECETOC 1995
Hexyl cinnamic aldehyde	AOO	25	5.41	Omori et al. 2008	+ (20, 50%)	+	+	ICCVAM 1999	ICCVAM 1999	Basketter et al. 1999b	Nonirritant at ≤10% (GP); mild irritant at 100% (rabbits)	Basketter et al. 2007b; ECETOC 1995
Hexyl cinnamic aldehyde	AOO	25	7.60	Omori et al. 2008	+ (20, 50%)	+	+	ICCVAM 1999	ICCVAM 1999	Basketter et al. 1999b	Nonirritant at ≤10% (GP); mild irritant at 100% (rabbits)	Basketter et al. 2007b; ECETOC 1995
Hexyl cinnamic aldehyde	AOO	25	3.92	Omori et al. 2008	+ (20, 50%)	+	+	ICCVAM 1999	ICCVAM 1999	Basketter et al. 1999b	Nonirritant at ≤10% (GP); mild irritant at 100% (rabbits)	Basketter et al. 2007b; ECETOC 1995
Hexyl cinnamic aldehyde	AOO	25	8.42	Omori et al. 2008	+ (20, 50%)	+	+	ICCVAM 1999	ICCVAM 1999	Basketter et al. 1999b	Nonirritant at ≤10% (GP); mild irritant at 100% (rabbits)	Basketter et al. 2007b; ECETOC 1995

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Hexyl cinnamic aldehyde	AOO	25	6.45	Omori et al. 2008	+ (20, 50%)	+	+	ICCVAM 1999	ICCVAM 1999	Basketter et al. 1999b	Nonirritant at ≤10% (GP); mild irritant at 100% (rabbits)	Basketter et al. 2007b; ECETOC 1995
Hydroxy-citronellal	AOO	50	5.69	Idehara et al. 2008	+ (8.5, 100%)	+	+	ICCVAM 1999	ICCVAM 1999	ICCVAM 1999	Nonirritant at 50% (GP); negative at 100% (rabbits)	Basketter et al. 2007b; ECETOC 1995
Imidazolidinyl urea	DMF	50	4.67	Idehara et al. 2008	+ (5.5, 50%)	+	+	Gerberick et al. 2005	ICCVAM 1999	ICCVAM 1999	Negative at ≤75% (GP)	Basketter and Scholes 1992
Isoeugenol	AOO	50	12.36 at 25%	Idehara et al. 2008	+ (31, 5%)	+	+	ICCVAM 1999	ICCVAM 1999	ICCVAM 1999	Nonirritant at 5% (GP)	Basketter et al. 2007b
Isoeugenol	AOO	10	6.11	Omori et al. 2008	+ (31, 5%)	+	+	ICCVAM 1999	ICCVAM 1999	ICCVAM 1999	Nonirritant at 5% (GP)	Basketter et al. 2007b
Isoeugenol	AOO	10	5.54	Omori et al. 2008	+ (31, 5%)	+	+	ICCVAM 1999	ICCVAM 1999	ICCVAM 1999	Nonirritant at 5% (GP)	Basketter et al. 2007b
Isoeugenol	AOO	10	7.09	Omori et al. 2008	+ (31, 5%)	+	+	ICCVAM 1999	ICCVAM 1999	ICCVAM 1999	Nonirritant at 5% (GP)	Basketter et al. 2007b
Isopropanol	AOO	50	1.08 at 25%	Idehara et al. 2008	- (1.7, 50%)[9]	-	+	ICCVAM 1999	ICCVAM 1999	Kwon et al. 2003	Negative at 100% (rabbits)	ECETOC 1995
Isopropanol	AOO	50	1.54 at 10%	Omori et al. 2008	- (1.7, 50%)[9]	-	+	ICCVAM 1999	ICCVAM 1999	Kwon et al. 2003	Negative at 100% (rabbits)	ECETOC 1995
Isopropanol	AOO	50	0.91 at 10%	Omori et al. 2008	- (1.7, 50%)[9]	-	+	ICCVAM 1999	ICCVAM 1999	Kwon et al. 2003	Negative at 100% (rabbits)	ECETOC 1995
Isopropanol	AOO	50	1.01 at 10%	Omori et al. 2008	- (1.7, 50%)[9]	-	+	ICCVAM 1999	ICCVAM 1999	Kwon et al. 2003	Negative at 100% (rabbits)	ECETOC 1995

Substance Name	Veh.[1]	LLNA: DA Highest Conc. Tested (%)	LLNA: DA Highest SI[2]	LLNA: DA Reference	Trad. LLNA Result[3]	GP Result[4]	Human Result[5]	Trad. LLNA Reference	GP Reference	Human Reference	Skin Irritation Data	Skin Irritation Reference
Isopropanol	AOO	50	1.57 at 10%	Omori et al. 2008	- (1.7, 50%)[9]	-	+	ICCVAM 1999	ICCVAM 1999	Kwon et al. 2003	Negative at 100% (rabbits)	ECETOC 1995
Isopropanol	AOO	50	0.76 at 25%	Omori et al. 2008	- (1.7, 50%)[9]	-	+	ICCVAM 1999	ICCVAM 1999	Kwon et al. 2003	Negative at 100% (rabbits)	ECETOC 1995
Isopropanol	AOO	50	1.97 at 10%	Omori et al. 2008	- (1.7, 50%)[9]	-	+	ICCVAM 1999	ICCVAM 1999	Kwon et al. 2003	Negative at 100% (rabbits)	ECETOC 1995
Isopropanol	AOO	50	1.45 at 10%	Omori et al. 2008	- (1.7, 50%)[9]	-	+	ICCVAM 1999	ICCVAM 1999	Kwon et al. 2003	Negative at 100% (rabbits)	ECETOC 1995
Isopropanol	AOO	50	1.21 at 10%	Omori et al. 2008	- (1.7, 50%)[9]	-	+	ICCVAM 1999	ICCVAM 1999	Kwon et al. 2003	Negative at 100% (rabbits)	ECETOC 1995
Isopropanol	AOO	50	0.70 at 25%	Omori et al. 2008	- (1.7, 50%)[9]	-	+	ICCVAM 1999	ICCVAM 1999	Kwon et al. 2003	Negative at 100% (rabbits)	ECETOC 1995
Isopropanol	AOO	50	1.25	Omori et al. 2008	- (1.7, 50%)[9]	-	+	ICCVAM 1999	ICCVAM 1999	Kwon et al. 2003	Negative at 100% (rabbits)	ECETOC 1995
Lactic acid	DMSO	50	1.06 at 10%	Idehara et al. 2008	- (2.2, 25%)	-	-	ICCVAM 1999	ICCVAM 1999	Basketter et al. 1999b	Slightly irritating at 10% aq. (rabbits)	Cosmetic Ingredient Review Expert Panel 1998
Lactic acid	DMSO	25	0.93 at 5%	Omori et al. 2008	- (2.2, 25%)	-	-	ICCVAM 1999	ICCVAM 1999	Basketter et al. 1999b	Slightly irritating at 10% aq. (rabbits)	Cosmetic Ingredient Review Expert Panel 1998
Lactic acid	DMSO	25	0.99 at 5%	Omori et al. 2008	- (2.2, 25%)	-	-	ICCVAM 1999	ICCVAM 1999	Basketter et al. 1999b	Slightly irritating at 10% aq. (rabbits)	Cosmetic Ingredient Review Expert Panel 1998

Substance Name	Veh.[1]	LLNA: DA Highest Conc. Tested (%)	LLNA: DA Highest SI[2]	LLNA: DA Reference	Trad. LLNA Result[3]	GP Result[4]	Human Result[5]	Trad. LLNA Reference	GP Reference	Human Reference	Skin Irritation Data	Skin Irritation Reference
Lactic acid	DMSO	25	0.97 at 10%	Omori et al. 2008	- (2.2, 25%)	-	-	ICCVAM 1999	ICCVAM 1999	Basketter et al. 1999b	Slightly irritating at 10% aq. (rabbits)	Cosmetic Ingredient Review Expert Panel 1998
Lactic acid	DMSO	25	0.91	Omori et al. 2008	- (2.2, 25%)	-	-	ICCVAM 1999	ICCVAM 1999	Basketter et al. 1999b	Slightly irritating at 10% aq. (rabbits)	Cosmetic Ingredient Review Expert Panel 1998
2-Mercaptobenzo-thiazole	DMF	50	2.00	Idehara et al. 2008	+ (8.6, 10%)	+	+	ICCVAM 1999	ICCVAM 1999	ICCVAM 1999	Nonirritant at 10% (GP); nonirritant at 25% (humans)	Basketter et al. 2007b; Kligman 1966c
Methyl methacrylate	AOO	100	1.81	Idehara unpublished	+ (3.6, 100%)	+	+ (case studies, no exposure concen-tration)	Betts et al. 2006	Van der Walle et al. 1982	Betts et al. 2006	Nonirritant at 3 M (GP)	Van der Walle et al. 1982
Methyl salicylate	AOO	25	1.20	Idehara et al. 2008	- (2.9, 20%)	-	-	ICCVAM 1999	ICCVAM 1999	ICCVAM 1999	Irritant at 10% AOO (mice)	Gerberick et al 2002
Methyl salicylate	AOO	25	1.55	Omori et al. 2008	- (2.9, 20%)	-	-	ICCVAM 1999	ICCVAM 1999	ICCVAM 1999	Irritant at 10% AOO (mice)	Gerberick et al 2002
Methyl salicylate	AOO	25	1.77 at 10%	Omori et al. 2008	- (2.9, 20%)	-	-	ICCVAM 1999	ICCVAM 1999	ICCVAM 1999	Irritant at 10% AOO (mice)	Gerberick et al 2002
Methyl salicylate	AOO	25	0.83	Omori et al. 2008	- (2.9, 20%)	-	-	ICCVAM 1999	ICCVAM 1999	ICCVAM 1999	Irritant at 10% AOO (mice)	Gerberick et al 2002
Nickel (II) chloride	DMSO	10	1.30	Idehara unpublished	- (2.4, 5%)	+	+	ICCVAM 1999	ICCVAM 1999	Vandenberg and Epstein 1963	Negative at ≤ 0.15% (GP)	Basketter and Scholes 1992

Substance Name	Veh.[1]	LLNA: DA Highest Conc. Tested (%)	LLNA: DA Highest SI[2]	LLNA: DA Reference	Trad. LLNA Result[3]	GP Result[4]	Human Result[5]	Trad. LLNA Reference	GP Reference	Human Reference	Skin Irritation Data	Skin Irritation Reference
Nickel (II) sulfate hexahydrate	DMSO	5.0	2.17 at 2.5%	Idehara et al. 2008	+ (3.1, 5%)	+	+	Ryan et al. 2002	ICCVAM 1999	ICCVAM 1999	Irritant at 10% (humans); nonirritant at 0.15% (GP)	Kligman 1966c; Scholes et al. 1992
Nickel (II) sulfate hexahydrate	DMSO	10	1.52 at 3%	Omori et al. 2008	+ (3.1, 5%)	+	+	Ryan et al. 2002	ICCVAM 1999	ICCVAM 1999	Irritant at 10% (humans); nonirritant at 0.15% (GP)	Kligman 1966c; Scholes et al. 1992
Nickel (II) sulfate hexahydrate	DMSO	10	11.78	Omori et al. 2008	+ (3.1, 5%)	+	+	Ryan et al. 2002	ICCVAM 1999	ICCVAM 1999	Irritant at 10% (humans); nonirritant at 0.15% (GP)	Kligman 1966c; Scholes et al. 1992
Nickel (II) sulfate hexahydrate	DMSO	10	3.49 at 1%	Omori et al. 2008	+ (3.1, 5%)	+	+	Ryan et al. 2002	ICCVAM 1999	ICCVAM 1999	Irritant at 10% (humans); nonirritant at 0.15% (GP)	Kligman 1966c; Scholes et al. 1992
Nickel (II) sulfate hexahydrate	DMSO	10	0.79 at 3%	Omori et al. 2008	+ (3.1, 5%)	+	+	Ryan et al. 2002	ICCVAM 1999	ICCVAM 1999	Irritant at 10% (humans); nonirritant at 0.15% (GP)	Kligman 1966c; Scholes et al. 1992
Nickel (II) sulfate hexahydrate	DMSO	10	1.24 at 3%	Omori et al. 2008	+ (3.1, 5%)	+	+	Ryan et al. 2002	ICCVAM 1999	ICCVAM 1999	Irritant at 10% (humans); nonirritant at 0.15% (GP)	Kligman 1966c; Scholes et al. 1992
Nickel (II) sulfate hexahydrate	DMSO	10	2.13	Omori et al. 2008	+ (3.1, 5%)	+	+	Ryan et al. 2002	ICCVAM 1999	ICCVAM 1999	Irritant at 10% (humans); nonirritant at 0.15% (GP)	Kligman 1966c; Scholes et al. 1992
Nickel (II) sulfate hexahydrate	DMSO	10	1.56 at 3%	Omori et al. 2008	+ (3.1, 5%)	+	+	Ryan et al. 2002	ICCVAM 1999	ICCVAM 1999	Irritant at 10% (humans); nonirritant at 0.15% (GP)	Kligman 1966c; Scholes et al. 1992
Phenyl benzoate	AOO	10	4.24 at 5%	Idehara unpublished	+ (11.1, 25%)	+	+	ICCVAM 1999	ICCVAM 1999	Basketter et al 2005	NA	NA

Substance Name	Veh.[1]	LLNA: DA Highest Conc. Tested (%)	LLNA: DA Highest SI[2]	LLNA: DA Reference	Trad. LLNA Result[3]	GP Result[4]	Human Result[5]	Trad. LLNA Reference	GP Reference	Human Reference	Skin Irritation Data	Skin Irritation Reference
p-Phenylenediamine	AOO	1	5.14 at 0.25%	Idehara et al. 2008	+ (26, 1%)	+	+	ICCVAM 1999	ICCVAM 1999	ICCVAM 1999	Nonirritant at 0.5% (GP)	Basketter et al. 2007b
Phthalic anhydride	AOO	1.0	6.85	Idehara et al. 2008	+ (26.0, 10%)[12]	+	+	ICCVAM 1999	ICCVAM 1999	Basketter et al. 2001	Negative at ≤ 10% (GP)	Basketter and Scholes 1992
Potassium dichromate	DMSO	1.0	5.49	Idehara et al. 2008	+ (33.6, 0.5%)	+	+	ICCVAM 1999	ICCVAM 1999	ICCVAM 1999	Nonirritant at 0.15% (GP)	Basketter et al. 2007b
Potassium dichromate	DMSO	1.0	4.78	Omori et al. 2008	+ (33.6, 0.5%)	+	+	ICCVAM 1999	ICCVAM 1999	ICCVAM 1999	Nonirritant at 0.15% (GP)	Basketter et al. 2007b
Potassium dichromate	DMSO	1.0	4.08	Omori et al. 2008	+ (33.6, 0.5%)	+	+	ICCVAM 1999	ICCVAM 1999	ICCVAM 1999	Nonirritant at 0.15% (GP)	Basketter et al. 2007b
Potassium dichromate	DMSO	1.0	6.01	Omori et al. 2008	+ (33.6, 0.5%)	+	+	ICCVAM 1999	ICCVAM 1999	ICCVAM 1999	Nonirritant at 0.15% (GP)	Basketter et al. 2007b
Potassium dichromate	DMSO	1.0	6.37	Omori et al. 2008	+ (33.6, 0.5%)	+	+	ICCVAM 1999	ICCVAM 1999	ICCVAM 1999	Nonirritant at 0.15% (GP)	Basketter et al. 2007b
Propyl gallate	AOO	2.5	4.95	Idehara unpublished	+ (33.6, 25%)	+	+	ICCVAM 1999	ICCVAM 1999	ICCVAM 1999	Nonirritant at 5% (GP)	Basketter and Scholes 1992
Propylparaben	AOO	25	1.28	Idehara et al. 2008	- (1.4, 25%)[13]	-	+	ICCVAM 1999	ICCVAM 1999	ICCVAM 1999	Nonirritant at 10% (GP)	Basketter and Scholes 1992
Resorcinol	AOO	25	4.33	Idehara et al. 2008	+ (10.4, 50%)	-	+	Basketter et al. 2007a	ICCVAM 1999	ICCVAM 1999; Basketter et al. 2007a	Nonirritant at 15% (humans)	Kligman 1966c
Salicylic acid	AOO	25	2.00	Idehara unpublished	- (2.5, 25%)	-	-	ICCVAM 1999	ICCVAM 1999	ICCVAM 1999	Irritant at 20% aq. (mice)	Gerberick et al. 2002

Substance Name	Veh.[1]	LLNA: DA Highest Conc. Tested (%)	LLNA: DA Highest SI[2]	LLNA: DA Reference	Trad. LLNA Result[3]	GP Result[4]	Human Result[5]	Trad. LLNA Reference	GP Reference	Human Reference	Skin Irritation Data	Skin Irritation Reference
Sodium lauryl sulfate	DMF	10	3.39	Idehara et al. 2008	+ (8.9, 20%)[9]	-	-	ICCVAM 1999	ICCVAM 1999	ICCVAM 1999	Irritant at 20% (humans); Irritant at 20% (rabbits); irritant at 10% in DMF (mice)	Kligman 1966c; ECETOC 1995; Antonopoulos et al. 2008
Sulfanilamide	DMF	50	0.86 at 25%	Idehara unpublished	- (1, 50%)[14]	-	+	ICCVAM 1999	ICCVAM 1999	ICCVAM 1999; Kligman 1966c	Nonirritant at 25% (humans)	Kligman 1966c
Toluene 2,4-diisocyanate	**AOO**	**0.25**	**9.43**	**Idehara et al. 2008**	**+[15] (NA)**	**+**	**+**	**van Och et al. 2001**	**NA**	**Basketter et al. 2001**	**NA**	**NA**
Trimellitic anhydride	AOO	0.50	4.96	Idehara et al. 2008	+ (4.6, 25%)	+	NA	ICCVAM 1999; Basketter and Scholes 1992	ICCVAM 1999; Gad et al. 1986	ICCVAM 1999; Basketter et al. 2001	Negative at ≤ 10% (GP)	Basketter and Scholes 1992

Bold Substances not included in accuracy analyses.

Abbreviations: ACE = acetone; AOO = acetone: olive oil (4:1); aq. = aqueous; CASRN = Chemical Abstracts Service Registry Number; Conc. = concentration; DMF = *N*,*N*-dimethylformamide; DMSO = dimethylsulfoxide; ECETOC = European Centre for Ecotoxicology and Toxicology of Chemicals; GP = guinea pig; LLNA = murine local lymph node assay; LLNA: DA = murine local lymph node assay modified by Daicel Chemical Industries, Ltd., based on ATP content; MEK = methyl ethyl ketone; NA = not available; nonstd = nonstandard; SI = stimulation index; Trad. = traditional; "+" = Sensitizer.

"-" = Nonsensitizer.

[1] Applies to both traditional LLNA and LLNA: DA, unless otherwise noted.

[2] Highest SI occurred at highest concentration tested, unless otherwise noted.

[3] Numbers in parentheses indicate the highest SI and the highest concentration tested. Highest SI occurred at highest concentration tested, unless otherwise footnoted.

[4] GP refers to outcomes obtained by studies conducted using either the guinea pig maximization test or the Buehler test.

[5] Human refers to outcomes obtained by studies conducted using the human maximization test, inclusion of the test substance in a human patch test allergen kit, and/or published clinical case studies/reports.

[6] Vehicle for traditional LLNA was acetone.

[7] Highest SI occurred at 1%.

[8] Equivocal traditional LLNA data (ICCVAM 1999); substance not included in accuracy analyses.

[9] Highest SI occurred at 10%.

[10] Data not reported for the highest dose (i.e., 3%), only for 0.3% and 1%.

[11] Highest SI occurred at 50%.

[12] Highest SI occurred at 2.5%.

[13] Highest SI occurred at 5%.

[14] Highest SI occurred at both 10% and 25%.

[15] Comparable LLNA reference data from modified LLNA test (van Och et al. 2000).

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Annex III-2

Comparison of Alternative LLNA: DA Decision Criteria and Traditional LLNA Results

(Alphanumeric Order)

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Table C-III-2-1 Comparative Performance of Various LLNA: DA SI Values and Traditional LLNA Tests (Alphanumeric Order)

Substance Name	CASRN	Highest Conc. Tested (%)	Highest SI[1]	Stats.[2]	≥95 % CI	≥3 SD	≥2 SD	SI ≥											LLNA: DA Ref.	Trad. LLNA Result	Trad. LLNA Ref.
								5.0	4.5	4.0	3.5	3.0	2.5	2.0	1.8	1.5	1.3	1.0			
Abietic acid	514-10-3	25	6.26	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	Idehara et al. 2008	+	ICCVAM 1999
Abietic acid	514-10-3	25	4.64	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	Omori et al. 2008	+	ICCVAM 1999
Abietic acid	514-10-3	25	7.96	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	Omori et al. 2008	+	ICCVAM 1999
Abietic acid	514-10-3	25	3.98 at 10%	+	+	+	+	-	-	-	+	+	+	+	+	+	+	+	Omori et al. 2008	+	ICCVAM 1999
3-Amino-phenol	591-27-5	10	2.83	+	+	+	+	-	-	-	-	-	+	+	+	+	+	+	Omori et al. 2008	+	ICCVAM 1999
3-Amino-phenol	591-27-5	10	1.76 at 3%	+	+	+	+	-	-	-	-	-	-	-	-	+	+	+	Omori et al. 2008	+	ICCVAM 1999
3-Amino-phenol	591-27-5	10	2.38	+	+	+	+	-	-	-	-	-	-	+	+	+	+	+	Omori et al. 2008	+	ICCVAM 1999
Benzalkonium chloride	8001-54-5	2.5	6.68	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	Idehara et al. 2008	+	Gerberick et al. 1992
Benzocaine	**94-09-7**	**25**	**4.84**	**+**	**+**	**+**	**+**	**-**	**+**	**+**	**+**	**+**	**+**	**+**	**+**	**+**	**+**	**+**	**Idehara et al. 2008**	**+/-[3]**	**ICCVAM 1999**
p-Benzo-quinone	106-51-4	0.100	3.79	+	+	+	+	-	-	-	+	+	+	+	+	+	+	+	Idehara unpublished	+	ICCVAM 1999
1-Bromo-butane	109-65-9	25	1.65	+	+	+	+	-	-	-	-	-	-	-	-	+	+	+	Idehara et al. 2008	-	ICCVAM 1999
Butyl glycidyl ether	2426-08-6	50	4.59	+	+	-	+	-	+	+	+	+	+	+	+	+	+	+	Idehara unpublished	+	ICCVAM 1999
Chlorobenzene	108-90-7	25	2.44	+	+	+	+	-	-	-	-	-	-	+	+	+	+	+	Idehara et al. 2008	-	ICCVAM 1999
5-Chloro-2-methyl-4-isothiazolin-3-one	26172-55-4	0.100	7.50	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	Idehara unpublished	+	ICCVAM 1999; Gerberick et al. 2005

Substance Name	CASRN	Highest Conc. Tested (%)	Highest SI[1]	Stats.[2]	≥95 % CI	≥3 SD	≥2 SD	SI ≥											LLNA: DA Ref.	Trad. LLNA Result	Trad. LLNA Ref.
								5.0	4.5	4.0	3.5	3.0	2.5	2.0	1.8	1.5	1.3	1.0			
Cinnamic alcohol	104-54-1	90	5.66 at 50%	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	Idehara unpublished	+	Gerberick et al. 2005
Cinnamic aldehyde	104-55-2	15	4.73	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	Idehara et al. 2008	+	ICCVAM 1999
Citral	5392-40-5	25	4.40	+	+	+	+	-	-	+	+	+	+	+	+	+	+	+	Idehara et al. 2008	+	ICCVAM 1999
Cobalt chloride	7646-79-9	5	3.64	+	+	+	+	-	-	-	+	+	+	+	+	+	+	+	Idehara et al. 2008	+	ICCVAM 1999
Cobalt chloride	7646-79-9	1[4]	2.66	+	+	+	+	-	-	-	-	-	+	+	+	+	+	+	Omori et al. 2008	+	ICCVAM 1999
Cobalt chloride	7646-79-9	3	20.55	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	Omori et al. 2008	+	ICCVAM 1999
Cobalt chloride	7646-79-9	3	8.07	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	Omori et al. 2008	+	ICCVAM 1999
Cobalt chloride	7646-79-9	5	2.01	+	+	+	+	-	-	-	-	-	-	+	+	+	+	+	Omori et al. 2008	+	ICCVAM 1999
Cobalt chloride	7646-79-9	5	2.54	+	+	+	+	-	-	-	-	-	+	+	+	+	+	+	Omori et al. 2008	+	ICCVAM 1999
Cobalt chloride	7646-79-9	5	4.25	+	+	+	+	-	-	+	+	+	+	+	+	+	+	+	Omori et al. 2008	+	ICCVAM 1999
Cobalt chloride	7646-79-9	5	5.06	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	Omori et al. 2008	+	ICCVAM 1999
Diethyl maleate	141-05-9	10.0	3.78	+	+	+	+	-	-	-	+	+	+	+	+	+	+	+	Idehara unpublished	+	Gerberick et al. 2005
Diethyl phthalate	84-66-2	100	1.09	-	+	-	-	-	-	-	-	-	-	-	-	-	-	+	Idehara et al. 2008	-	Gerberick et al. 2005
Dimethyl isophthalate	1459-93-4	25	0.89 at 5%	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	Idehara unpublished	-	ICCVAM 1999; Basketter et al. 1999b

Substance Name	CASRN	Highest Conc. Tested (%)	Highest SI[1]	Stats.[2]	≥95 % CI	≥3 SD	≥2 SD	SI ≥											LLNA: DA Ref.	Trad. LLNA Result	Trad. LLNA Ref.
								5.0	4.5	4.0	3.5	3.0	2.5	2.0	1.8	1.5	1.3	1.0			
Dimethyl isophthalate	1459-93-4	25	1.34 at 5%	-	+	-	-	-	-	-	-	-	-	-	-	-	+	+	Omori et al. 2008	-	ICCVAM 1999; Basketter et al. 1999b
Dimethyl isophthalate	1459-93-4	25	1.00 at 5%	-	+	-	-	-	-	-	-	-	-	-	-	-	-	+	Omori et al. 2008	-	ICCVAM 1999; Basketter et al. 1999b
Dimethyl isophthalate	1459-93-4	25	1.26 at 5%	-	+	-	-	-	-	-	-	-	-	-	-	-	-	+	Omori et al. 2008	-	ICCVAM 1999; Basketter et al. 1999b
2,4-Dinitrochloro-benzene	97-00-7	1	7.10	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	Idehara et al. 2008	+	ICCVAM 1999
2,4-Dinitrochloro-benzene	97-00-7	0.30	11.97	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	Omori et al. 2008	+	ICCVAM 1999
2,4-Dinitrochloro-benzene	97-00-7	0.30	9.23	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	Omori et al. 2008	+	ICCVAM 1999
2,4-Dinitrochloro-benzene	97-00-7	0.30	9.96	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	Omori et al. 2008	+	ICCVAM 1999
2,4-Dinitrochloro-benzene	97-00-7	0.30	8.53	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	Omori et al. 2008	+	ICCVAM 1999
2,4-Dinitrochloro-benzene	97-00-7	0.30	7.86	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	Omori et al. 2008	+	ICCVAM 1999
2,4-Dinitrochloro-benzene	97-00-7	0.30	15.14	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	Omori et al. 2008	+	ICCVAM 1999
2,4-Dinitrochloro-benzene	97-00-7	0.30	13.18	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	Omori et al. 2008	+	ICCVAM 1999
2,4-Dinitrochloro-benzene	97-00-7	0.30	12.60	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	Omori et al. 2008	+	ICCVAM 1999
2,4-Dinitrochloro-benzene	97-00-7	0.30	10.89	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	Omori et al. 2008	+	ICCVAM 1999

Substance Name	CASRN	Highest Conc. Tested (%)	Highest SI[1]	Stats.[2]	≥95 % CI	≥3 SD	≥2 SD	SI ≥											LLNA: DA Ref.	Trad. LLNA Result	Trad. LLNA Ref.
								5.0	4.5	4.0	3.5	3.0	2.5	2.0	1.8	1.5	1.3	1.0			
2,4-Dinitrochloro-benzene	97-00-7	0.30	4.71	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	Omori et al. 2008	+	ICCVAM 1999
Ethyl acrylate	140-88-5	50	4.29 at 25%	+	+	-	-	-	-	+	+	+	+	+	+	+	+	+	Idehara unpublished	+	Gerberick et al. 2005
Ethylene glycol dimethacrylate	97-90-5	50	4.45	+	+	+	+	-	-	+	+	+	+	+	+	+	+	+	Idehara unpublished	+	ICCVAM 1999
Eugenol	97-53-0	25	7.07	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	Idehara et al. 2008	+	ICCVAM 1999
Formaldehyde	50-00-0	2.50	5.10	+	+	+	+	+	-	-	-	-	-	-	-	-	-	-	Idehara et al. 2008	+	Gerberick et al. 2005; Hilton et al. 1998
Formaldehyde	50-00-0	5.0	4.84	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	Omori et al. 2008	+	Gerberick et al. 2005; Hilton et al. 1998
Formaldehyde	50-00-0	5.0	3.18	+	+	+	+	-	-	-	-	+	+	+	+	+	+	+	Omori et al. 2008	+	Gerberick et al. 2005; Hilton et al. 1998
Formaldehyde	50-00-0	5.0	2.69	+	+	+	+	-	-	-	-	-	+	+	+	+	+	+	Omori et al. 2008	+	Gerberick et al. 2005; Hilton et al. 1998
Glutaraldehyde	111-30-8	0.25	6.45	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	Idehara et al. 2008	+	Basketter et al. 2005; Hilton et al. 1998
Glutaraldehyde	111-30-8	0.50	5.00	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	Omori et al. 2008	+	Basketter et al. 2005; Hilton et al. 1998
Glutaraldehyde	111-30-8	0.50	3.39	+	+	+	+	-	-	-	-	+	+	+	+	+	+	+	Omori et al. 2008	+	Basketter et al. 2005; Hilton et al. 1998
Glutaraldehyde	111-30-8	0.50	2.57	+	+	+	+	-	-	-	-	-	+	+	+	+	+	+	Omori et al. 2008	+	Basketter et al. 2005; Hilton et al. 1998

Substance Name	CASRN	Highest Conc. Tested (%)	Highest SI[1]	Stats.[2]	≥95 % CI	≥3 SD	≥2 SD	SI ≥											LLNA: DA Ref.	Trad. LLNA Result	Trad. LLNA Ref.
								5.0	4.5	4.0	3.5	3.0	2.5	2.0	1.8	1.5	1.3	1.0			
Hexane	110-54-3	100	2.31	+	+	+	+	-	-	-	-	-	-	+	+	+	+	+	Idehara et al. 2008	-	ICCVAM 1999
Hexyl cinnamic aldehyde	101-86-0	25	6.47	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	Idehara et al. 2008	+	ICCVAM 1999
Hexyl cinnamic aldehyde	101-86-0	25	5.78	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	Omori et al. 2008	+	ICCVAM 1999
Hexyl cinnamic aldehyde	101-86-0	25	4.82	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	Omori et al. 2008	+	ICCVAM 1999
Hexyl cinnamic aldehyde	101-86-0	25	4.44	+	+	+	+	-	-	+	+	+	+	+	+	+	+	+	Omori et al. 2008	+	ICCVAM 1999
Hexyl cinnamic aldehyde	101-86-0	25	5.11	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	Omori et al. 2008	+	ICCVAM 1999
Hexyl cinnamic aldehyde	101-86-0	25	3.97	+	+	+	+	-	-	-	+	+	+	+	+	+	+	+	Omori et al. 2008	+	ICCVAM 1999
Hexyl cinnamic aldehyde	101-86-0	25	5.50	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	Omori et al. 2008	+	ICCVAM 1999
Hexyl cinnamic aldehyde	101-86-0	25	7.09	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	Omori et al. 2008	+	ICCVAM 1999
Hexyl cinnamic aldehyde	101-86-0	25	10.22	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	Omori et al. 2008	+	ICCVAM 1999
Hexyl cinnamic aldehyde	101-86-0	25	3.88	+	+	+	+	-	-	-	+	+	+	+	+	+	+	+	Omori et al. 2008	+	ICCVAM 1999
Hexyl cinnamic aldehyde	101-86-0	25	3.51	+	+	+	+	-	-	-	+	+	+	+	+	+	+	+	Omori et al. 2008	+	ICCVAM 1999
Hexyl cinnamic aldehyde	101-86-0	25	4.47	+	+	+	+	-	-	+	+	+	+	+	+	+	+	+	Omori et al. 2008	+	ICCVAM 1999
Hexyl cinnamic aldehyde	101-86-0	25	5.71	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	Omori et al. 2008	+	ICCVAM 1999
Hexyl cinnamic aldehyde	101-86-0	25	5.41	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	Omori et al. 2008	+	ICCVAM 1999

Substance Name	CASRN	Highest Conc. Tested (%)	Highest SI[1]	Stats.[2]	≥95 % CI	≥3 SD	≥2 SD	SI ≥											LLNA: DA Ref.	Trad. LLNA Result	Trad. LLNA Ref.
								5.0	4.5	4.0	3.5	3.0	2.5	2.0	1.8	1.5	1.3	1.0			
Hexyl cinnamic aldehyde	101-86-0	25	7.60	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	Omori et al. 2008	+	ICCVAM 1999
Hexyl cinnamic aldehyde	101-86-0	25	3.92	+	+	+	+	-	-	-	+	+	+	+	+	+	+	+	Omori et al. 2008	+	ICCVAM 1999
Hexyl cinnamic aldehyde	101-86-0	25	8.42	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	Omori et al. 2008	+	ICCVAM 1999
Hexyl cinnamic aldehyde	101-86-0	25	6.45	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	Omori et al. 2008	+	ICCVAM 1999
Hydroxycitronellal	107-75-5	50	5.69	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	Idehara et al. 2008	+	ICCVAM 1999
Imidazolidinyl urea	39236-46-9	50	4.67	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	Idehara et al. 2008	+	Gerberick et al. 2005
Isoeugenol	97-54-1	50	12.36 at 25%	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	Idehara et al. 2008	+	ICCVAM 1999
Isoeugenol	97-54-1	10	6.11	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	Omori et al. 2008	+	ICCVAM 1999
Isoeugenol	97-54-1	10	5.54	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	Omori et al. 2008	+	ICCVAM 1999
Isoeugenol	97-54-1	10	7.09	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	Omori et al. 2008	+	ICCVAM 1999
Isopropanol	67-63-0	50	1.08 at 25%	-	+	-	-	-	-	-	-	-	-	-	-	-	-	+	Idehara et al. 2008	-	ICCVAM 1999
Isopropanol	67-63-0	50	1.54 at 10%	-	+	-	+	-	-	-	-	-	-	-	-	+	+	+	Omori et al. 2008	-	ICCVAM 1999
Isopropanol	67-63-0	50	0.91 at 10%	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	Omori et al. 2008	-	ICCVAM 1999
Isopropanol	67-63-0	50	1.01 at 10%	-	-	-	-	-	-	-	-	-	-	-	-	-	-	+	Omori et al. 2008	-	ICCVAM 1999
Isopropanol	67-63-0	50	1.57 at 10%	+	+	-	+	-	-	-	-	-	-	-	-	+	+	+	Omori et al. 2008	-	ICCVAM 1999

Substance Name	CASRN	Highest Conc. Tested (%)	Highest SI[1]	Stats.[2]	≥95 % CI	≥3 SD	≥2 SD	SI ≥											LLNA: DA Ref.	Trad. LLNA Result	Trad. LLNA Ref.
								5.0	4.5	4.0	3.5	3.0	2.5	2.0	1.8	1.5	1.3	1.0			
Isopropanol	67-63-0	50	0.76 at 25%	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	Omori et al. 2008	-	ICCVAM 1999
Isopropanol	67-63-0	50	1.97 at 10%	-	+	+	+	-	-	-	-	-	-	-	+	+	+	+	Omori et al. 2008	-	ICCVAM 1999
Isopropanol	67-63-0	50	1.45 at 10%	-	+	-	+	-	-	-	-	-	-	-	-	-	+	+	Omori et al. 2008	-	ICCVAM 1999
Isopropanol	67-63-0	50	1.21 at 10%	-	+	-	-	-	-	-	-	-	-	-	-	-	-	+	Omori et al. 2008	-	ICCVAM 1999
Isopropanol	67-63-0	50	0.70 at 25%	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	Omori et al. 2008	-	ICCVAM 1999
Isopropanol	67-63-0	50	1.25	-	+	-	+	-	-	-	-	-	-	-	-	-	-	+	Omori et al. 2008	-	ICCVAM 1999
Lactic acid	50-21-5	50	1.06 at 10%	-	+	-	-	-	-	-	-	-	-	-	-	-	-	+	Idehara et al. 2008	-	ICCVAM 1999
Lactic acid	50-21-5	25	0.93 at 5%	-	+	-	-	-	-	-	-	-	-	-	-	-	-	-	Omori et al. 2008	-	ICCVAM 1999
Lactic acid	50-21-5	25	0.99 at 5%	+	+	-	-	-	-	-	-	-	-	-	-	-	-	-	Omori et al. 2008	-	ICCVAM 1999
Lactic acid	50-21-5	25	0.97 at 10%	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	Omori et al. 2008	-	ICCVAM 1999
Lactic acid	50-21-5	25	0.91	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	Omori et al. 2008	-	ICCVAM 1999
2-Mercapto-benzothiazole	149-30-4	50	2.00	-	+	+	+	-	-	-	-	-	-	+	+	+	+	+	Idehara et al. 2008	+	ICCVAM 1999
Methyl methacrylate	80-62-6	100	1.81	-	+	-	-	-	-	-	-	-	-	-	+	+	+	+	Idehara unpublished	+	Betts et al. 2006
Methyl salicylate	119-36-8	25	1.20	-	+	-	+	-	-	-	-	-	-	-	-	-	-	+	Idehara et al. 2008	-	ICCVAM 1999
Methyl salicylate	119-36-8	25	1.55	-	+	+	+	-	-	-	-	-	-	-	-	+	+	+	Omori et al. 2008	-	ICCVAM 1999

Substance Name	CASRN	Highest Conc. Tested (%)	Highest SI[1]	Stats.[2]	≥95 % CI	≥3 SD	≥2 SD	SI ≥											LLNA: DA Ref.	Trad. LLNA Result	Trad. LLNA Ref.
								5.0	4.5	4.0	3.5	3.0	2.5	2.0	1.8	1.5	1.3	1.0			
Methyl salicylate	119-36-8	25	1.77 at 10%	-	+	-	-	-	-	-	-	-	-	-	-	+	+	+	Omori et al. 2008	-	ICCVAM 1999
Methyl salicylate	119-36-8	25	0.83	-	-	-	-	-	-	-	-	-	-	+	-	-	-	-	Omori et al. 2008	-	ICCVAM 1999
Nickel (II) chloride	7718-54-9	10	1.30	-	+	+	+	-	-	-	-	-	-	-	-	-	+	+	Idehara unpublished	-	ICCVAM 1999
Nickel (II) sulfate hexahydrate	10101-97-0	5.0	2.17 at 2.5%	+	+	+	+	-	-	-	-	-	-	+	+	+	+	+	Idehara et al. 2008	+	Ryan et al. 2002
Nickel (II) sulfate hexahydrate	10101-97-0	10	1.52 at 3%	-	+	-	-	-	-	-	-	-	-	-	-	+	+	+	Omori et al. 2008	+	Ryan et al. 2002
Nickel (II) sulfate hexahydrate	10101-97-0	10	11.78	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	Omori et al. 2008	+	Ryan et al. 2002
Nickel (II) sulfate hexahydrate	10101-97-0	10	3.49 at 1%	+	+	+	+	-	-	-	-	+	+	+	+	+	+	+	Omori et al. 2008	+	Ryan et al. 2002
Nickel (II) sulfate hexahydrate	10101-97-0	10	0.79 at 3%	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	Omori et al. 2008	+	Ryan et al. 2002
Nickel (II) sulfate hexahydrate	10101-97-0	10	1.24 at 3%	-	+	+	+	-	-	-	-	-	-	-	-	-	-	+	Omori et al. 2008	+	Ryan et al. 2002
Nickel (II) sulfate hexahydrate	10101-97-0	10	2.13	+	+	+	+	-	-	-	-	-	-	+	+	+	+	+	Omori et al. 2008	+	Ryan et al. 2002
Nickel (II) sulfate hexahydrate	10101-97-0	10	1.56 at 3%	-	+	-	-	-	-	-	-	-	-	-	-	+	+	+	Omori et al. 2008	+	Ryan et al. 2002
Phenyl benzoate	93-99-2	10.0	4.24 at 5%	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	Idehara unpublished	+	ICCVAM 1999
p-Phenylene-diamine	106-50-3	1	5.14 at 0.25%	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	Idehara et al. 2008	+	ICCVAM 1999
Phthalic anhydride	85-44-9	1.0	6.85	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	Idehara et al. 2008	+	ICCVAM 1999

Substance Name	CASRN	Highest Conc. Tested (%)	Highest SI[1]	Stats.[2]	≥95 % CI	≥3 SD	≥2 SD	SI ≥											LLNA: DA Ref.	Trad. LLNA Result	Trad. LLNA Ref.
								5.0	4.5	4.0	3.5	3.0	2.5	2.0	1.8	1.5	1.3	1.0			
Potassium dichromate	7778-50-9	1.0	5.49	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	Idehara et al. 2008	+	ICCVAM 1999
Potassium dichromate	7778-50-9	1.0	4.78	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	Omori et al. 2008	+	ICCVAM 1999
Potassium dichromate	7778-50-9	1.0	4.08	+	+	+	+	-	-	+	+	+	+	+	+	+	+	+	Omori et al. 2008	+	ICCVAM 1999
Potassium dichromate	7778-50-9	1.0	6.01	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	Omori et al. 2008	+	ICCVAM 1999
Potassium dichromate	7778-50-9	1.0	6.37	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	Omori et al. 2008	+	ICCVAM 1999
Propyl gallate	121-79-9	2.5	4.95	+	+	-	-	-	+	+	+	+	+	+	+	+	+	+	Idehara unpublished	+	ICCVAM 1999
Propylparaben	94-13-3	25	1.28	-	+	+	+	-	-	-	-	-	-	-	-	-	-	+	Idehara et al. 2008	-	ICCVAM 1999
Resorcinol	108-46-3	25	4.33	+	+	+	+	-	-	+	+	+	+	+	+	+	+	+	Idehara et al. 2008	+	Basketter et al. 2007a
Salicylic acid	69-72-7	25	2.00	+	+	-	+	-	-	-	-	-	-	+	+	+	+	+	Idehara unpublished	-	ICCVAM 1999
Sodium lauryl sulfate	151-21-3	10	3.39	+	+	+	+	-	-	-	-	+	+	+	+	+	+	+	Idehara et al. 2008	+	ICCVAM 1999
Sulfanilamide	63-74-1	50	0.86 at 25%	+	-	-	-	-	-	-	-	-	-	-	-	-	-	-	Idehara unpublished	-	ICCVAM 1999
Toluene 2,4-diisocyanate	**584-84-9**	**0.25**	**9.43**	**+**	**+**	**+**	**+**	**+**	**+**	**+**	**+**	**+**	**+**	**+**	**+**	**+**	**+**	**+**	**Idehara et al. 2008**	**+[5]**	**Van Och et al. 2001**
Trimellitic anhydride	552-30-7	0.50	4.96	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	Idehara et al. 2008	+	ICCVAM 1999; Basketter and Scholes 1992

Entries in boldface indicate substances not included in accuracy analyses.

Abbreviations: CASRN = Chemical Abstracts Service Registry Number; CI = confidence interval (mean ATP measurement of any treatment group is greater than 95% CI of mean ATP measurement for vehicle control group); Conc. = concentration; LLNA = murine local lymph node assay; LLNA: DA = murine local lymph node assay modified by Daicel Chemical Industries, Ltd., based on ATP

content; Ref. = reference; SD = standard deviation (mean ATP measurement of any treatment group is greater than two or three SD for vehicle control group); SI = stimulation index; stats. = statistics (analysis of variance for multiple dose groups or *t*-test to compare one treatment group to the vehicle control group); Trad. = traditional.

"+" = Sensitizer.

"-" = Nonsensitizer.

[1] Highest SI occurred at highest concentration tested, unless otherwise noted.

[2] The ATP data were log-transformed prior to statistical analyses. For analysis of variance, significance at $p < 0.05$ was further tested by Dunnett's test.

[3] Equivocal (i.e., results that were not reproducible) traditional LLNA data (ICCVAM 1999). Substance not included in accuracy analyses.

[4] Data not reported for the highest dose (i.e., 3%), only for 0.3% and 1%.

[5] LLNA reference data from modified LLNA test (van Och et al. 2000). Substance not included in accuracy analyses.