

Appendix 1 3 of 3, 2 of 2 および 2 of 3 DA の予測性

1) LLNA との比較

3 of 3	LLNA	
	Non	Sens
Non	10	1
Sens	9	80
Inconclusive	14	53

DA 2of 3	LLNA	
	Non	Sens
Non	22	19
Sens	4	89
Inconclusive	7	27

	3 of 3
(N=100)	
Accuracy (%)	90
Sensitivity (%)	99
Specificity (%)	53
Balanced Accuracy (%)	76

	2 of 3 DA
(N=134)	
Accuracy (%)	83
Sensitivity (%)	82
Specificity (%)	85
Balanced Accuracy (%)	84

2 of 2(1) DPRA and KeratinoSens	LLNA	
	Non	Sens
Non	19	40
Sens	10	78
Inconclusive	4	17

2 of 2(2) h-CLAT and KeratinoSens	LLNA	
	Non	Sens
Non	11	26
Sens	9	59
Inconclusive	13	49

DA performance vs. LLNA data	DPRA and KeratinoSens
(N=147)	
Accuracy (%)	66
Sensitivity (%)	66
Specificity (%)	66
Balanced Accuracy (%)	66

DA performance vs. LLNA data	h-CLAT and KeratinoSens
(N=105)	
Accuracy (%)	67
Sensitivity (%)	69
Specificity (%)	55
Balanced Accuracy (%)	62

2 of 2(3) h-CLAT and DPRA	LLNA	
	Non	Sens
NC	12	24
Sens	9	62
Inconclusive	12	48

DA performance vs. LLNA data	DPRA and h-CLAT
(N=107)	
Accuracy (%)	69
Sensitivity (%)	72

Specificity (%)	57
Balanced Accuracy (%)	65

2) Human skin sensitization との比較

	Human	
	Non	Sens
3 of 3		
Non	2	1
Sens	3	36
Inconclusive	6	16

	Human	
	Non	Sens
2 of 3 DA		
Non	7	5
Sens	1	42
Inconclusive	3	7

	3 of 3
(N=42)	
Accuracy (%)	90
Sensitivity (%)	97
Specificity (%)	40
Balanced Accuracy (%)	69

	2 of 3 DA
(N=55)	
Accuracy (%)	89
Sensitivity (%)	89
Specificity (%)	88
Balanced Accuracy (%)	88

2 of 2(1)	Human	
DPPRA and KeratinoSens	Non	Sens
Non	6	12
Sens	2	34
Inconclusive	3	8

2 of 2(2)	Human	
h-CLAT and KeratinoSens	Non	Sens
Non	3	12
Sens	3	27
Inconclusive	5	15

DA performance vs. Human data	DPPRA and KeratinoSens
(N=54)	
Accuracy (%)	74
Sensitivity (%)	74
Specificity (%)	75
Balanced Accuracy (%)	74

DA performance vs. Human data	h-CLAT and KeratinoSens
(N=45)	
Accuracy (%)	67
Sensitivity (%)	69
Specificity (%)	50
Balanced Accuracy (%)	60

2 of 2(3)	Human	
h-CLAT, DPPRA	NC	Sens
NC	2	10
Sens	4	31
Borderline negative, Borderline positive, Inconclusive, NA	5	12

NA: Not Available

DA performance vs. Human data	DPPRA and h-CLAT

(N=47)	
Accuracy (%)	70
Sensitivity (%)	76
Specificity (%)	33
Balanced Accuracy (%)	54

Appendix 2 2 of 3 DA の偽評価物質

1) LLNA との比較 (偽陰性 19 物質、偽陽性 4 物質)

Sort	Curated Chemical name	CASRN	LLNA. GHS.BIN	LLNA. GHS.SUB	2of3 DA Call.Conf
10	3-Aminophenol	591-27-5	1	1B	0
12	alpha-Amylcinnamic alcohol	101-85-9	1	1B	0
13	Anethole	104-46-1	1	NA	0
15	Anisyl alcohol	105-13-5	1	1B	0
30	Benzyl salicylate	118-58-1	1	1B	0
47	Chlorpromazine	50-53-3	1	NA	0
76	DMSO	67-68-5	1	1B	0
117	p-Isobutyl-alpha-methylhydrocinnamaldehyde	6658-48-6	1	1B	0
120	alpha-Isomethylionone	127-51-5	1	1B	0
122	Isopropyl myristate	110-27-0	1	1B	0
129	Linalool	78-70-6	1	1B	0
141	Methyl pyruvate	600-22-6	1	1B	0
160	OTNE	54464-57-2	1	1B	0
176	Pyridine	110-86-1	1	1B	0
177	Resorcinol	108-46-3	1	1B	0
180	Salicylic acid	69-72-7	1	1B	0
181	Sodium lauryl sulfate	151-21-3	1	1B	0
182	Squaric acid	2892-51-5	1	NA	0
187	2,2,6,6-Tetramethylheptane-3,5-dione	1118-71-4	1	1B	0
111	2-Hydroxypropyl methacrylate	923-26-2	NC	NC	1
114	1-Iodohexane	638-45-9	NC	NC	1
135	Methyl 3-bromopropionate	3395-91-3	NC	NC	1
150	4-Methyl-2-nitroanisole	119-10-8	NC	NC	1

2) Human skin sensitisation との比較(偽陰性 5 物質、偽陽性 1 物質)

Sort	Curated Chemical name	CASRN	HU. GHS.BIN	2 of 3 DA Call.Conf
47	Chlorpromazine	50-53-3	1B	0
176	Pyridine	110-86-1	1B	0
25	Benzyl alcohol	100-51-6	1B	0
123	Kanamycin	59-01-8	1B	0
183	Sulfanilamide	63-74-1	1B	0
106	Hydrocortisone	50-23-7	NC	1

Note: Chemicals highlighted in light green have false negatives and those highlighted in yellow have false positives.

LLNA.GHS.BIN: LLNA Binary hazard reference classification

LLNA.GHS.SUB: LLNA Potency reference subcategorisation

2 of 3 DA Call.Conf: 2 of 3 DA Hazard prediction considering confidence workflow

HU.GHS.BIN: Human Binary hazard reference classification

Appendix 3 ITS DA の予測性

1)ITSv1 DA

ITSv1 DA in comparison to LLNA
(GL497 と同じ)

ITSv1 DA	LLNA		
	NC	1B	1A
NC	21	11	0
1B	9	55	10
1A	0	12	28
Inconclusive	3	7	0

71% correct classification overall for potency
80% balanced accuracy overall for hazard
(Sensitivity 91% Specificity 70%)

ITSv1 DA in comparison to Human
(GL497 と同じ)

ITSv1 DA	Human		
	NC	1B	1A
NC	4	4	0
1B	5	24	7
1A	0	3	13
Inconclusive	2	0	1

68% correct classification overall for potency
68% balanced accuracy overall for hazard
(Sensitivity 92% Specificity 44%)

2) ITSv2 DA

ITSv2 DA in comparison to LLNA
(GL497 と同じ)

ITSv2 DA	LLNA		
	NC	1B	1A
NC	20	9	0
1B	10	54	10
1A	0	12	26
Inconclusive	3	10	2

71% correct classification overall for potency
79% balanced accuracy overall for hazard
(Sensitivity 92% Specificity 67%)

ITSv1 DA Score h-CLAT and DPRA in
comparison to LLNA (*in silico* を含まず、
Borderline 未使用)

h-CLAT, DPRA	LLNA		
	NC	1B	1A
NC	22	17	0
1B	8	55	20
1A	0	6	18

65% correct classification overall for potency
79% balanced accuracy overall for hazard
(Sensitivity 85% Specificity 73%)

ITSv1 DA Score h-CLAT and DPRA in
comparison to Human (*in silico* を含まず、
Borderline 未使用)

h-CLAT, DPRA	Human		
	NC	1B	1A
NC	4	7	2
1B	5	22	12
1A	0	1	6

54% correct classification overall for potency
63% balanced accuracy overall for hazard
(Sensitivity 82% Specificity 44%)

ITSv2 DA Score h-CLAT and DPRA in
comparison to LLNA (*in silico* を含まず、
Borderline 未使用)

h-CLAT, DPRA	LLNA (n=141)		
	NC	1B	1A
NC	22	14	0
1B	8	55	18
1A	0	6	18

67% correct classification overall for potency
80% balanced accuracy overall for hazard
(Sensitivity 87% Specificity 73%)

ITSv2 DA in comparison to Human
(GL497 と同じ)

ITSv2 DA	Human		
	NC	1B	1A
NC	4	3	0
1B	5	24	6
1A	0	3	12
Inconclusive	2	1	3

70% correct classification overall for potency
69% balanced accuracy overall for hazard
(Sensitivity 94% Specificity 44%)

ITSv2 DA Score h-CLAT and DPRA in
comparison to Human (*in silico* を含まず、
Borderline 未使用)

h-CLAT, DPRA	Human		
	NC	1B	1A
NC	4	6	1
1B	5	22	11
1A	0	1	6

57% correct classification overall for potency
65% balanced accuracy overall for hazard
(Sensitivity 85% Specificity 44%)

Appendix 4 ITS v 1 DA 偽評価物質

1)LLNA との比較(偽陰性 11 物質、偽陽性 9 物質)

Sort	Curated Chemical name	CASRN	LLNA. GHS.SUB	ITSv1 DA Score	ITSv1 DA Call Conf
18	BADGE	1675-54-3	1A	4	1B
60	Dibenzoyl peroxide	94-36-0	1A	4	1B
77	DNBS, sodium salt	885-62-1	1A	5	1B
96	Glyoxal	107-22-2	1A	5	1B
104	HHPA	85-42-7	1A	3	1B
119	Isoeugenol	97-54-1	1A	4	1B
130	Maleic anhydride	108-31-6	1A	5	1B
154	1-Naphthol	90-15-3	1A	4	1B
157	2-Nitro-p-phenylenediamine	5307-14-2	1A	5	1B
171	Phthalic anhydride	85-44-9	1A	3	1B
8	5-Amino-o-cresol	2835-95-2	1B	6	1A
21	1,2-Benzisothiazol-3(2H)-one	2634-33-5	1B	7	1A
51	Citral	5392-40-5	1B	7	1A
58	Diacetyl	431-03-8	1B	6	1A
65	Diethyl maleate	141-05-9	1B	6	1A
80	Ethyl acrylate	140-88-5	1B	6	1A
86	2-Ethylhexyl acrylate	103-11-7	1B	6	1A
98	Hepta-2,4-dienal	5910-85-0	1B	7	1A
100	trans-Hex-2-enal	6728-26-3	1B	7	1A
134	Methyl acrylate	96-33-3	1B	7	1A
179	Safranal	116-26-7	1B	6	1A
189	Thiram	137-26-8	1B	7	1A
5	Allyl phenoxyacetate	7493-74-5	1B	0	NC
15	Anisyl alcohol	105-13-5	1B	1	NC
30	Benzyl salicylate	118-58-1	1B	1	NC
70	Dihydroeugenol	2785-87-7	1B	1	NC
76	DMSO	67-68-5	1B	1	NC
122	Isopropyl myristate	110-27-0	1B	1	NC
141	Methyl pyruvate	600-22-6	1B	1	NC
161	Oxalic acid	144-62-7	1B	1	NC
176	Pyridine	110-86-1	1B	1	NC
180	Salicylic acid	69-72-7	1B	1	NC
181	Sodium lauryl sulfate	151-21-3	1B	0	NC
17	Appleide	478695-70-4	NC	2	1B
44	3-Chloro-p-anisaldehyde	4903-09-7	NC	3	1B
111	2-Hydroxypropyl methacrylate	923-26-2	NC	3	1B
114	1-Iodohexane	638-45-9	NC	4	1B
123	Kanamycin	59-01-8	NC	2	1B
135	Methyl 3-bromopropionate	3395-91-3	NC	3	1B
146	2-Methyldecanenitrile	69300-15-8	NC	2	1B
150	4-Methyl-2-nitroanisole	119-10-8	NC	2	1B
166	3-Phenoxypropanenitrile	3055-86-5	NC	2	1B

2) Human skin sensitisation との比較(偽陰性 4 物質、偽陽性 5 物質)

Sort	Curated Chemical name	CASRN	HU. GHS.SUB	ITSv1 DA Score	ITSv1 DA Call.Conf
32	BGE	2426-08-6	1A	3	1B
96	Glyoxal	107-22-2	1A	5	1B
133	1-(4-Methoxyphenyl)pent-1-en-3-one	104-27-8	1A	4	1B
168	Phenylacetaldehyde	122-78-1	1A	5	1B
147	6-Methylhepta-3,5-dien-2-one	1604-28-0	1A	4	1B
68	Diethylenetriamine	111-40-0	1A	2	1B
20	Benzaldehyde	100-52-7	1A	2	1B
189	Thiram	137-26-8	1B	7	1A
80	Ethyl acrylate	140-88-5	1B	6	1A
131	2-Mercaptobenzothiazole	149-30-4	1B	6	1A
176	Pyridine	110-86-1	1B	1	NC
25	Benzyl alcohol	100-51-6	1B	1	NC
183	Sulfanilamide	63-74-1	1B	1	NC
54	Coumarin	91-64-5	1B	1	NC
52	Citronellol	106-22-9	NC	4	1B
101	Hexyl salicylate	6259-76-3	NC	2	1B
120	alpha-Isomethylionone	127-51-5	NC	3	1B
160	OTNE	54464-57-2	NC	3	1B
106	Hydrocortisone	50-23-7	NC	4	1B

Note: Note: Chemicals highlighted in light green have misclassification and those highlighted in yellow have false positives.

LLNA.GHS.SUB: LLNA Potency reference subcategorization

ITSv1 DA Score: ITSv1 DA total score

ITSv1 DA Call.Conf: ITSv1 DA Hazard prediction considering confidence workflow

HU.GHS.BIN: Human Binary hazard reference classification

Appendix5 1TSv2 DA 評価物質

1)LLNA との比較(偽陰性 9 物質、偽陽性 10 物質)

Sort	Curated Chemical name	CASRN	LLNA. GHS.SUB	ITSv2 DA Score	ITSv2 DA Call.Conf
18	BADGE	1675-54-3	1A	4	1B
60	Dibenzoyl peroxide	94-36-0	1A	4	1B
77	DNBS, sodium salt	885-62-1	1A	5	1B
96	Glyoxal	107-22-2	1A	5	1B
104	HHPA	85-42-7	1A	3	1B
119	Isoeugenol	97-54-1	1A	4	1B
130	Maleic anhydride	108-31-6	1A	5	1B
154	1-Naphthol	90-15-3	1A	4	1B
157	2-Nitro-p-phenylenediamine	5307-14-2	1A	5	1B
171	Phthalic anhydride	85-44-9	1A	3	1B
8	5-Amino-o-cresol	2835-95-2	1B	6	1A
21	1,2-Benzisothiazol-3(2H)-one	2634-33-5	1B	7	1A
51	Citral	5392-40-5	1B	7	1A
58	Diacetyl	431-03-8	1B	6	1A
65	Diethyl maleate	141-05-9	1B	6	1A
80	Ethyl acrylate	140-88-5	1B	6	1A
86	2-Ethylhexyl acrylate	103-11-7	1B	6	1A
98	Hepta-2,4-dienal	5910-85-0	1B	7	1A
100	trans-Hex-2-enal	6728-26-3	1B	7	1A
134	Methyl acrylate	96-33-3	1B	7	1A
179	Safranal	116-26-7	1B	6	1A
189	Thiram	137-26-8	1B	6	1A
5	Allyl phenoxyacetate	7493-74-5	1B	1	NC
30	Benzyl salicylate	118-58-1	1B	1	NC
70	Dihydroeugenol	2785-87-7	1B	1	NC
76	DMSO	67-68-5	1B	1	NC
122	Isopropyl myristate	110-27-0	1B	1	NC
141	Methyl pyruvate	600-22-6	1B	1	NC
161	Oxalic acid	144-62-7	1B	1	NC
176	Pyridine	110-86-1	1B	1	NC
181	Sodium lauryl sulfates	151-21-3	1B	0	NC
17	Applelde	478695-70-4	NC	2	1B
25	Benzyl alcohol	100-51-6	NC	2	1B
44	3-Chloro-p-anisaldehyde	4903-09-7	NC	3	1B
111	2-Hydroxypropyl methacrylate	923-26-2	NC	2	1B
114	1-Iodohexane	638-45-9	NC	3	1B
123	Kanamycin	59-01-8	NC	2	1B
135	Methyl 3-bromopropionate	3395-91-3	NC	3	1B
146	2-Methyldecanenitrile	69300-15-8	NC	2	1B
150	4-Methyl-2-nitroanisole	119-10-8	NC	2	1B
166	3-Phenoxypropanenitrile	3055-86-5	NC	2	1B

2) Human skin sensitisation との比較(偽陰性 3 物質、偽陽性 5 物質)

Sort	Curated Chemical name	CASRN	HU. GHS.SUB	ITSv2 DA Score	ITSv2 DA Call.Conf
32	BGE	2426-08-6	1A	3	1B
96	Glyoxal	107-22-2	1A	5	1B
133	1-(4-Methoxyphenyl)pent-1-en-3-one	104-27-8	1A	4	1B
168	Phenylacetaldehyde	122-78-1	1A	5	1B
147	6-Methylhepta-3,5-dien-2-one	1604-28-0	1A	4	1B
68	Diethylenetriamine	111-40-0	1A	2	1B
189	Thiram	137-26-8	1B	6	1A
80	Ethyl acrylate	140-88-5	1B	6	1A
131	2-Mercaptobenzothiazole	149-30-4	1B	6	1A
176	Pyridine	110-86-1	1B	1	NC
183	Sulfanilamide	63-74-1	1B	0	NC
54	Coumarin	91-64-5	1B	0	NC
52	Citronellol	106-22-9	NC	4	1B
101	Hexyl salicylate	6259-76-3	NC	2	1B
120	alpha-Isomethylionone	127-51-5	NC	3	1B
160	OTNE	54464-57-2	NC	3	1B
106	Hydrocortisone	50-23-7	NC	3	1B

Note: Note: Chemicals highlighted in light green have misclassification and those highlighted in yellow have false positives.

LLNA.GHS.SUB: LLNA Potency reference subcategorization

ITSv2 DA Score: ITSv2 DA total score

ITSv2 DA Call.Conf: ITSv2 DA Hazard prediction considering confidence workflow

HU.GHS.BIN: Human Binary hazard reference classification