

APPENDIX D

**Performance Characteristics for Use of LLNA EC3 Values to Predict Draft GHS
Categories of Human and Guinea Pig Skin Sensitization Potency**

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Appendix D-1 Performance Characteristics for Use of LLNA EC3 (%) Values to Classify 81 Human Sensitizers into Strong ($\leq 250 \mu\text{g}/\text{cm}^2$) and Weak Sensitizer ($>250 \mu\text{g}/\text{cm}^2$) Categories¹

EC3 Cutoff Values (%)	Substances Correctly Identified as Strong Human Sensitizers ²	Weak Sensitizers Incorrectly Identified as Strong Human Sensitizers ²	Strong Sensitizers Incorrectly Identified as Weak Human Sensitizers ²	Substances Correctly Identified as Weak Human Sensitizers ²	Correct Classification (%)	Over-classification Rate (%)	Under-classification Rate (%)
0.02	1	0	44	36	46%	0%	98%
0.04	2	0	43	36	47%	0%	96%
0.04	3	0	42	36	48%	0%	93%
0.08	4	0	41	36	49%	0%	91%
0.12	5	0	40	36	51%	0%	89%
0.16	7	0	38	36	53%	0%	84%
0.25	9	0	36	36	56%	0%	80%
0.35	10	0	35	36	57%	0%	78%
0.45	11	0	34	36	58%	0%	76%
0.60	12	0	33	36	59%	0%	73%
0.77	13	0	32	36	60%	0%	71%
1.02	14	0	31	36	62%	0%	69%
1.25	15	0	30	36	63%	0%	67%
1.35	16	0	29	36	64%	0%	64%
1.50	17	0	28	36	65%	0%	62%
1.65	18	0	27	36	67%	0%	60%
1.75	19	0	26	36	68%	0%	58%
2.00	20	0	25	36	69%	0%	56%
2.35	22	0	23	36	72%	0%	51%
2.70	23	1	22	35	72%	3%	49%
3.00	23	2	22	34	70%	6%	49%
3.20	25	3	20	33	72%	8%	44%
3.40	25	4	20	32	70%	11%	44%
3.60	26	4	19	32	72%	11%	42%
3.79	27	4	18	32	73%	11%	40%
4.09	27	5	18	31	72%	14%	40%

EC3 Cutoff Values (%)	Substances Correctly Identified as Strong Human Sensitizers ²	Weak Sensitizers Incorrectly Identified as Strong Human Sensitizers ²	Strong Sensitizers Incorrectly Identified as Weak Human Sensitizers ²	Substances Correctly Identified as Weak Human Sensitizers ²	Correct Classification (%)	Over-classification Rate (%)	Under-classification Rate (%)
4.40	28	5	17	31	73%	14%	38%
4.65	29	5	16	31	74%	14%	36%
5.15	30	6	15	30	74%	17%	33%
5.70	31	6	14	30	75%	17%	31%
5.95	31	8	14	28	73%	22%	31%
6.15	32	8	13	28	74%	22%	29%
6.40	33	9	12	27	74%	25%	27%
6.80	34	10	11	26	74%	28%	24%
7.45	34	11	11	25	73%	31%	24%
8.05	35	11	10	25	74%	31%	22%
8.35	35	12	10	24	73%	33%	22%
8.45	35	13	10	23	72%	36%	22%
8.85	36	13	9	23	73%	36%	20%
9.35	37	13	8	23	74%	36%	18%
9.55	37	14	8	22	73%	39%	18%
10.30	37	15	8	21	72%	42%	18%
11.25	37	16	8	20	70%	44%	18%
13.25	37	17	8	19	69%	47%	18%
16.00	37	18	8	18	68%	50%	18%
17.05	37	19	8	17	67%	53%	18%
17.40	37	21	8	15	64%	58%	18%
18.05	37	22	8	14	63%	61%	18%
19.20	37	23	8	13	62%	64%	18%
20.40	38	23	7	13	63%	64%	16%
21.25	38	24	7	12	62%	67%	16%
21.75	39	24	6	12	63%	67%	13%
21.95	39	25	6	11	62%	69%	13%
22.55	39	26	6	10	60%	72%	13%
23.60	39	27	6	9	59%	75%	13%
24.70	40	27	5	9	60%	75%	11%

EC3 Cutoff Values (%)	Substances Correctly Identified as Strong Human Sensitizers ²	Weak Sensitizers Incorrectly Identified as Strong Human Sensitizers ²	Strong Sensitizers Incorrectly Identified as Weak Human Sensitizers ²	Substances Correctly Identified as Weak Human Sensitizers ²	Correct Classification (%)	Over-classification Rate (%)	Under-classification Rate (%)
25.50	40	28	5	8	59%	78%	11%
25.90	40	29	5	7	58%	81%	11%
26.50	40	30	5	6	57%	83%	11%
28.30	41	30	4	6	58%	83%	9%
30.25	41	31	4	5	57%	86%	9%
30.95	42	31	3	5	58%	86%	7%
31.15	43	31	2	5	59%	86%	4%
35.15	44	31	1	5	60%	86%	2%
41.25	44	32	1	4	59%	89%	2%
43.75	44	33	1	3	58%	92%	2%
44.20	44	34	1	2	57%	94%	2%
48.70	45	34	0	2	58%	94%	0%
62.45	45	35	0	1	57%	97%	0%

Abbreviations: EC3 = Estimated concentration needed to produce stimulation index = 3; LLNA = Murine local lymph node assay.

¹Human sensitizers were categorized into strong and weak sensitizer categories based on the threshold dose for human sensitization. There were 45 strong sensitizers with human threshold doses $\leq 250 \mu\text{g}/\text{cm}^2$ and 36 sensitizers (threshold dose $>250 \mu\text{g}/\text{cm}^2$). Geometric mean EC3 (%) values (for substances with multiple results) from LLNA tests were used to predict human sensitization category.

²Number of substances.

Appendix D-2 Performance Characteristics for Use of LLNA EC3 (%) Values to Classify 112 Substances Tested in Human and LLNA Skin Sensitization Tests into Strong ($\leq 250 \mu\text{g}/\text{cm}^2$) and Weak Sensitizer ($>250 \mu\text{g}/\text{cm}^2$) Categories¹

EC3 Cutoff Values (%)	Substances Correctly Identified as Strong Human Sensitizers ²	Weak Sensitizers Incorrectly Identified as Strong Human Sensitizers ²	Strong Sensitizers Incorrectly Identified as Weak Human Sensitizers ²	Substances Correctly Identified as Weak Human Sensitizers ²	Correct Classification (%)	Over-classification Rate (%)	Under-classification Rate (%)
0.02	1	5	60	46	42%	10%	98%
0.04	2	5	59	46	43%	10%	97%
0.04	3	5	58	46	44%	10%	95%
0.08	4	5	57	46	45%	10%	93%
0.12	5	5	56	46	46%	10%	92%
0.16	7	5	54	46	47%	10%	89%
0.25	9	5	52	46	49%	10%	85%
0.35	10	5	51	46	50%	10%	84%
0.45	11	5	50	46	51%	10%	82%
0.60	12	5	49	46	52%	10%	80%
0.77	13	5	48	46	53%	10%	79%
1.02	14	5	47	46	54%	10%	77%
1.25	15	5	46	46	54%	10%	75%
1.35	16	5	45	46	55%	10%	74%
1.50	17	5	44	46	56%	10%	72%
1.65	18	5	43	46	57%	10%	70%
1.75	19	5	42	46	58%	10%	69%
2.00	20	5	41	46	59%	10%	67%
2.35	22	5	39	46	61%	10%	64%
2.70	23	6	38	45	61%	12%	62%
3.00	23	7	38	44	60%	14%	62%
3.20	25	8	36	43	61%	16%	59%
3.40	25	9	36	42	60%	18%	59%
3.60	26	9	35	42	61%	18%	57%
3.79	27	9	34	42	62%	18%	56%

EC3 Cutoff Values (%)	Substances Correctly Identified as Strong Human Sensitizers ²	Weak Sensitizers Incorrectly Identified as Strong Human Sensitizers ²	Strong Sensitizers Incorrectly Identified as Weak Human Sensitizers ²	Substances Correctly Identified as Weak Human Sensitizers ²	Correct Classification (%)	Over-classification Rate (%)	Under-classification Rate (%)
4.09	27	10	34	41	61%	20%	56%
4.40	28	10	33	41	62%	20%	54%
4.65	29	10	32	41	62%	20%	52%
5.15	30	11	31	40	63%	22%	51%
5.70	31	11	30	40	63%	22%	49%
5.95	31	13	30	38	62%	25%	49%
6.15	32	13	29	38	63%	25%	48%
6.40	33	14	28	37	62%	27%	46%
6.80	34	15	27	36	63%	29%	44%
7.45	34	16	27	35	62%	31%	44%
8.05	35	16	26	35	62%	31%	43%
8.35	35	17	26	34	62%	33%	43%
8.45	35	18	26	33	61%	35%	43%
8.85	36	18	25	33	62%	35%	41%
9.35	37	18	24	33	62%	35%	39%
9.55	37	19	24	32	62%	37%	39%
10.30	37	20	24	31	61%	39%	39%
11.25	37	21	24	30	60%	41%	39%
13.25	37	22	24	29	59%	43%	39%
16.00	37	23	24	28	58%	45%	39%
17.05	37	24	24	27	57%	47%	39%
17.40	37	26	24	25	55%	51%	39%
18.05	37	27	24	24	54%	53%	39%
19.20	37	28	24	23	54%	55%	39%
20.40	38	28	23	23	54%	55%	38%
21.25	38	29	23	22	54%	57%	38%
21.75	39	29	22	22	54%	57%	36%
21.95	39	30	22	21	54%	59%	36%
22.55	39	31	22	20	53%	61%	36%
23.60	39	32	22	19	52%	63%	36%

EC3 Cutoff Values (%)	Substances Correctly Identified as Strong Human Sensitizers ²	Weak Sensitizers Incorrectly Identified as Strong Human Sensitizers ²	Strong Sensitizers Incorrectly Identified as Weak Human Sensitizers ²	Substances Correctly Identified as Weak Human Sensitizers ²	Correct Classification (%)	Over-classification Rate (%)	Under-classification Rate (%)
24.70	40	32	21	19	53%	63%	34%
25.50	40	33	21	18	52%	65%	34%
25.90	40	34	21	17	51%	67%	34%
26.50	40	35	21	16	50%	69%	34%
28.30	41	35	20	16	51%	69%	33%
30.25	41	36	20	15	50%	71%	33%
30.95	42	36	19	15	51%	71%	31%
31.15	43	36	18	15	52%	71%	30%
35.15	44	36	17	15	53%	71%	28%
41.25	44	37	17	14	52%	73%	28%
43.75	44	38	17	13	51%	75%	28%
44.20	44	39	17	12	50%	76%	28%
48.70	45	39	16	12	51%	76%	26%
62.45	45	40	16	11	50%	78%	26%

Abbreviations: EC3 = Estimated concentration needed to produce stimulation index =3; LLNA = Murine local lymph node assay.

¹Human sensitizers were categorized into strong and weak sensitizer categories based on the threshold dose for human sensitization. The 16 substances that were false negative in the LLNA were added to the 45 substances categorized as strong human sensitizers (human threshold doses $\leq 250 \mu\text{g}/\text{cm}^2$) for a total of 61 strong human sensitizers. The five substances that were false positive in the LLNA and the 10 LLNA negative/human negative were added to the 36 weak human sensitizers (threshold dose $>250 \mu\text{g}/\text{cm}^2$) for a total of 51 weak human sensitizers. Geometric mean EC3 (%) values (for substances with multiple results) from LLNA tests were used to predict human sensitization category.

²Number of substances.

Appendix D-3 Performance Characteristics for Use of LLNA EC3 (%) Values to Classify 81 Human Sensitizers into Strong ($\leq 500 \mu\text{g}/\text{cm}^2$) and Weak Sensitizer ($>500 \mu\text{g}/\text{cm}^2$) Categories¹

EC3 Cutoff Values (%)	Substances Correctly Identified as Strong Human Sensitizers ²	Weak Sensitizers Incorrectly Identified as Strong Human Sensitizers ²	Strong Sensitizers Incorrectly Identified as Weak Human Sensitizers ²	Substances Correctly Identified as Weak Human Sensitizers ²	Correct Classification (%)	Over-classification Rate (%)	Under-classification Rate (%)
0.02	1	0	51	29	37%	0%	97
0.04	2	0	50	29	38%	0%	94
0.04	3	0	49	29	40%	0%	91
0.08	4	0	48	29	41%	0%	88
0.12	5	0	47	29	42%	0%	85
0.16	7	0	45	29	44%	0%	82
0.25	9	0	43	29	47%	0%	79
0.35	10	0	42	29	48%	0%	76
0.45	11	0	41	29	49%	0%	76
0.60	12	0	40	29	51%	0%	74
0.77	13	0	39	29	52%	0%	74
1.02	14	0	38	29	53%	0%	74
1.25	15	0	37	29	54%	0%	71
1.35	16	0	36	29	56%	0%	68
1.50	17	0	35	29	57%	0%	68
1.65	18	0	34	29	58%	0%	62
1.75	19	0	33	29	59%	0%	53
2.00	20	0	32	29	60%	0%	50
2.35	22	0	30	29	63%	0%	50
2.70	23	1	29	28	63%	3%	47
3.00	23	2	29	27	62%	7%	47
3.20	26	2	26	27	65%	7%	47
3.40	27	2	25	27	67%	7%	44
3.60	28	2	24	27	68%	7%	41
3.79	29	2	23	27	69%	7%	38
4.09	29	3	23	26	68%	10%	38

EC3 Cutoff Values (%)	Substances Correctly Identified as Strong Human Sensitizers ²	Weak Sensitizers Incorrectly Identified as Strong Human Sensitizers ²	Strong Sensitizers Incorrectly Identified as Weak Human Sensitizers ²	Substances Correctly Identified as Weak Human Sensitizers ²	Correct Classification (%)	Over-classification Rate (%)	Under-classification Rate (%)
4.40	30	3	22	26	69%	10%	35
4.65	31	3	21	26	70%	10%	29
5.15	32	4	20	25	70%	14%	29
5.70	33	4	19	25	72%	14%	26
5.95	33	6	19	23	69%	21%	26
6.15	34	6	18	23	70%	21%	26
6.40	35	7	17	22	70%	24%	26
6.80	36	8	16	21	70%	28%	26
7.45	36	9	16	20	69%	31%	24
8.05	37	9	15	20	70%	31%	24
8.35	37	10	15	19	69%	34%	21
8.45	37	11	15	18	68%	38%	18
8.85	38	11	14	18	69%	38%	18
9.35	39	11	13	18	70%	38%	18
9.55	39	12	13	17	69%	41%	18
10.30	39	13	13	16	68%	45%	18
11.25	39	14	13	15	67%	48%	18
13.25	39	15	13	14	65%	52%	18
16.00	39	16	13	13	64%	55%	15
17.05	39	17	13	12	63%	59%	15
17.40	40	18	12	11	63%	62%	15
18.05	40	19	12	10	62%	66%	15
19.20	40	20	12	9	60%	69%	12
20.40	41	20	11	9	62%	69%	12
21.25	42	20	10	9	63%	69%	12
21.75	43	20	9	9	64%	69%	9
21.95	43	21	9	8	63%	72%	9
22.55	44	21	8	8	64%	72%	9
23.60	44	22	8	7	63%	76%	9
24.70	45	22	7	7	64%	76%	9

EC3 Cutoff Values (%)	Substances Correctly Identified as Strong Human Sensitizers ²	Weak Sensitizers Incorrectly Identified as Strong Human Sensitizers ²	Strong Sensitizers Incorrectly Identified as Weak Human Sensitizers ²	Substances Correctly Identified as Weak Human Sensitizers ²	Correct Classification (%)	Over-classification Rate (%)	Under-classification Rate (%)
25.50	46	22	6	7	65%	76%	9
25.90	47	22	5	7	67%	76%	9
26.50	47	23	5	6	65%	79%	9
28.30	48	23	4	6	67%	79%	9
30.25	48	24	4	5	65%	83%	9
30.95	49	24	3	5	67%	83%	9
31.15	50	24	2	5	68%	83%	9
35.15	51	24	1	5	69%	83%	9
41.25	51	25	1	4	68%	86%	6
43.75	51	26	1	3	67%	90%	6
44.20	51	27	1	2	65%	93%	3
48.70	52	27	0	2	67%	93%	3
62.45	52	28	0	1	65%	97%	0

Abbreviations: EC3 = Estimated concentration needed to produce stimulation index = 3; LLNA = Murine local lymph node assay.

¹Human sensitizers were categorized into strong and weak sensitizer categories based on the threshold dose for human sensitization. There were 52 strong human sensitizers (human threshold doses $\leq 500 \mu\text{g}/\text{cm}^2$) and 29 weak human sensitizers (threshold dose $> 500 \mu\text{g}/\text{cm}^2$). Geometric EC3 (%) values (for substances with multiple results) from LLNA tests were used to predict human sensitization category.

²Number of substances.

Appendix D-4 Performance Characteristics for Use of LLNA EC3 (%) Values to Classify 112 Substances Tested in Human and LLNA Skin Sensitization Tests into Strong ($\leq 500 \mu\text{g}/\text{cm}^2$) and Weak Sensitizer ($>500 \mu\text{g}/\text{cm}^2$) Categories¹

EC3 Cutoff Values (%)	Substances Correctly Identified as Strong Human Sensitizers ²	Weak Sensitizers Incorrectly Identified as Strong Human Sensitizers ²	Strong Sensitizers Incorrectly Identified as Weak Human Sensitizers ²	Substances Correctly Identified as Weak Human Sensitizers ²	Correct Classification (%)	Over-classification Rate (%)	Under-classification Rate (%)
0.02	1	5	67	39	36%	11%	99%
0.04	2	5	66	39	37%	11%	97%
0.04	3	5	65	39	37%	11%	96%
0.08	4	5	64	39	38%	11%	94%
0.12	5	5	63	39	39%	11%	93%
0.16	7	5	61	39	41%	11%	90%
0.25	9	5	59	39	43%	11%	87%
0.35	10	5	58	39	44%	11%	85%
0.45	11	5	57	39	45%	11%	84%
0.60	12	5	56	39	46%	11%	82%
0.77	13	5	55	39	46%	11%	81%
1.02	14	5	54	39	47%	11%	79%
1.25	15	5	53	39	48%	11%	78%
1.35	16	5	52	39	49%	11%	76%
1.50	17	5	51	39	50%	11%	75%
1.65	18	5	50	39	51%	11%	74%
1.75	19	5	49	39	52%	11%	72%
2.00	20	5	48	39	53%	11%	71%
2.35	22	5	46	39	54%	11%	68%
2.70	23	6	45	38	54%	14%	66%
3.00	23	7	45	37	54%	16%	66%
3.20	26	7	42	37	56%	16%	62%
3.40	27	7	41	37	57%	16%	60%
3.60	28	7	40	37	58%	16%	59%

EC3 Cutoff Values (%)	Substances Correctly Identified as Strong Human Sensitizers ²	Weak Sensitizers Incorrectly Identified as Strong Human Sensitizers ²	Strong Sensitizers Incorrectly Identified as Weak Human Sensitizers ²	Substances Correctly Identified as Weak Human Sensitizers ²	Correct Classification (%)	Over-classification Rate (%)	Under-classification Rate (%)
3.79	29	7	39	37	59%	16%	57%
4.09	29	8	39	36	58%	18%	57%
4.40	30	8	38	36	59%	18%	56%
4.65	31	8	37	36	60%	18%	54%
5.15	32	9	36	35	60%	20%	53%
5.70	33	9	35	35	61%	20%	51%
5.95	33	11	35	33	59%	25%	51%
6.15	34	11	34	33	60%	25%	50%
6.40	35	12	33	32	60%	27%	49%
6.80	36	13	32	31	60%	30%	47%
7.45	36	14	32	30	59%	32%	47%
8.05	37	14	31	30	60%	32%	46%
8.35	37	15	31	29	59%	34%	46%
8.45	37	16	31	28	58%	36%	46%
8.85	38	16	30	28	59%	36%	44%
9.35	39	16	29	28	60%	36%	43%
9.55	39	17	29	27	59%	39%	43%
10.30	39	18	29	26	58%	41%	43%
11.25	39	19	29	25	57%	43%	43%
13.25	39	20	29	24	56%	45%	43%
16.00	39	21	29	23	55%	48%	43%
17.05	39	22	29	22	54%	50%	43%
17.40	40	23	28	21	54%	52%	41%
18.05	40	24	28	20	54%	55%	41%
19.20	40	25	28	19	53%	57%	41%
20.40	41	25	27	19	54%	57%	40%
21.25	42	25	26	19	54%	57%	38%
21.75	43	25	25	19	55%	57%	37%

EC3 Cutoff Values (%)	Substances Correctly Identified as Strong Human Sensitizers ²	Weak Sensitizers Incorrectly Identified as Strong Human Sensitizers ²	Strong Sensitizers Incorrectly Identified as Weak Human Sensitizers ²	Substances Correctly Identified as Weak Human Sensitizers ²	Correct Classification (%)	Over-classification Rate (%)	Under-classification Rate (%)
21.95	43	26	25	18	54%	59%	37%
22.55	44	26	24	18	55%	59%	35%
23.60	44	27	24	17	54%	61%	35%
24.70	45	27	23	17	55%	61%	34%
25.50	46	27	22	17	56%	61%	32%
25.90	47	27	21	17	57%	61%	31%
26.50	47	28	21	16	56%	64%	31%
28.30	48	28	20	16	57%	64%	29%
30.25	48	29	20	15	56%	66%	29%
30.95	49	29	19	15	57%	66%	28%
31.15	50	29	18	15	58%	66%	26%
35.15	51	29	17	15	59%	66%	25%
41.25	51	30	17	14	58%	68%	25%
43.75	51	31	17	13	57%	70%	25%
44.20	51	32	17	12	56%	73%	25%
48.70	52	32	16	12	57%	73%	24%
62.45	52	33	16	11	56%	75%	24%

Abbreviations: EC3 = Estimated concentration needed to produce stimulation index =3; LLNA = Murine local lymph node assay.

¹Human sensitizers were categorized into strong and weak sensitizer categories based on the threshold dose for human sensitization. The 16 substances that were false negative in the LLNA were added to the 52 substances categorized as strong human sensitizers (human threshold doses $\leq 500 \mu\text{g}/\text{cm}^2$) for a total of 68 strong human sensitizers. The five substances that were false positive in the LLNA and the 10 substances that were LLNA negative/human negative were added to the 29 weak human sensitizers (threshold dose $> 500 \mu\text{g}/\text{cm}^2$) for a total of 44 weak human sensitizers. Geometric mean EC3 (%) values (for substances with multiple results) from LLNA tests were used to predict human sensitization category.

²Number of substances.

Appendix D-5 Performance Characteristics for Use of LLNA EC3 (%) Values to Predict GHS Categories (Based on the Most Conservative Result) for Strong and Weak Guinea Pig Skin Sensitizers for 53 Substances (31 Category 1 and 22 Category 2 Sensitizers)¹

EC3 Cutoff Values (%)	Substances Correctly Identified as Strong Guinea Pig Sensitizers ²	Weak Sensitizers Incorrectly Identified as Strong Guinea Pig Sensitizers ²	Strong Sensitizers Incorrectly Identified as Weak Guinea Pig Sensitizers ²	Substances Correctly Identified as Weak Guinea Pig Sensitizers ²	Accuracy (%)	Over-classification Rate (%)	Under-classification Rate (%)
0.0009	1	0	30	22	43%	0%	97%
0.0015	2	0	29	22	45%	0%	94%
0.0024	3	0	28	22	47%	0%	90%
0.0064	4	0	27	22	49%	0%	87%
0.010	5	0	26	22	51%	0%	84%
0.011	6	0	25	22	53%	0%	81%
0.021	7	0	24	22	55%	0%	77%
0.033	8	0	23	22	57%	0%	74%
0.038	9	0	22	22	58%	0%	71%
0.045	10	0	21	22	60%	0%	68%
0.065	11	0	20	22	62%	0%	65%
0.095	11	1	20	21	60%	5%	65%
0.135	12	1	19	21	62%	5%	61%
0.180	12	2	19	20	60%	9%	61%
0.21	13	2	18	20	62%	9%	58%
0.27	14	2	17	20	64%	9%	55%
0.34	15	2	16	20	66%	9%	52%
0.38	16	2	15	20	68%	9%	48%
0.45	19	2	12	20	74%	9%	39%
0.53	20	2	11	20	75%	9%	35%
0.68	20	3	11	19	74%	14%	35%
0.90	21	4	10	18	74%	18%	32%
1.20	22	4	9	18	75%	18%	29%
1.75	23	4	8	18	77%	18%	26%
2.15	24	4	7	18	79%	18%	23%

EC3 Cutoff Values (%)	Substances Correctly Identified as Strong Guinea Pig Sensitizers ²	Weak Sensitizers Incorrectly Identified as Strong Guinea Pig Sensitizers ²	Strong Sensitizers Incorrectly Identified as Weak Guinea Pig Sensitizers ²	Substances Correctly Identified as Weak Guinea Pig Sensitizers ²	Accuracy (%)	Over-classification Rate (%)	Under-classification Rate (%)
2.75	25	4	6	18	81%	18%	19%
3.40	25	5	6	17	79%	23%	19%
4.20	26	5	5	17	81%	23%	16%
5.20	27	5	4	17	83%	23%	13%
5.58	27	6	4	16	81%	27%	13%
5.83	27	7	4	15	79%	32%	13%
6.25	28	7	3	15	81%	32%	10%
7.40	28	8	3	14	79%	36%	10%
9.05	28	9	3	13	77%	41%	10%
10.20	28	10	3	12	75%	45%	10%
10.80	28	11	3	11	74%	50%	10%
11.20	28	12	3	10	72%	55%	10%
12.40	29	12	2	10	74%	55%	6%
15.05	29	13	2	9	72%	59%	6%
17.35	30	13	1	9	74%	59%	3%
18.20	31	13	0	9	75%	59%	0%
18.90	31	14	0	8	74%	64%	0%
20.00	31	15	0	7	72%	68%	0%
22.25	31	16	0	6	70%	73%	0%
25.25	31	17	0	5	68%	77%	0%
26.80	31	18	0	4	66%	82%	0%
28.95	31	19	0	3	64%	86%	0%
35.6	31	20	0	2	62%	91%	0%

Abbreviations: BT = Buehler test; EC3 = Estimated concentration needed to produce stimulation index =3; GHS = United Nations Globally Harmonized System for the Classification and Labelling of Chemicals; GPMT = Guinea pig maximization test; LLNA = Murine local lymph node assay.

¹Guinea pig skin sensitizers were categorized into GHS Category 1 and Category 2 sensitizers based on the most conservative results (if multiple tests were available) of the GPMT or BT. For the GPMT, substances producing a response rate of 60% with an intradermal induction dose >0.1% to ≤1%, or a 30-60% response rate with an intradermal induction dose of ≤0.1%, were classified as Category 1 sensitizers. For the BT, substances producing a response rate ≥60% with a topical induction dose of >0.2% to ≤20%, or a ≥15% response rate with a topical induction dose of ≤0.2%, were classified as Category 1 sensitizers. For the GPMT, substances producing a response rate >30% with an intradermal induction dose >1.0%, or a 30-60% response rate with an intradermal induction dose of >0.1% to ≤1.0% were classified as Category 2 sensitizers. For the BT, substances producing a response rate ≥15% to 60% with a topical induction dose of >0.2% to 20%, or a response rate ≥15% with a topical induction dose of >20% were classified

as Category 2 sensitizers. Of the 53 substances used for this analysis, 31 were Category 1 sensitizers and 22 were Category 2 sensitizers. The most conservative EC3 (%) values (if multiple values were available) from LLNA tests were used to predict guinea pig GHS sensitization category.

²Number of substances.

Appendix D-6 Performance Characteristics for Use of LLNA EC3 (%) Values to Predict GHS Categories for Strong and Weak Guinea Pig Skin Sensitizers for 105 Substances (31 Category 1¹ and 22 Category 2² Sensitizers, 4 LLNA False Negative, and 29 LLNA False Positive, and 19 LLNA Correct Negative Substances)¹

EC3 Cutoff Values (%)	Substances Correctly Identified as Strong Guinea Pig Sensitizers ²	Weak Sensitizers Incorrectly Identified as Strong Guinea Pig Sensitizers ²	Strong Sensitizers Incorrectly Identified as Weak Guinea Pig Sensitizers ²	Substances Correctly Identified as Weak Guinea Pig Sensitizers ²	Accuracy (%)	Over-classification Rate (%)	Under-classification Rate (%)
0.0009	1	29	34	41	40%	41%	97%
0.0015	2	29	33	41	41%	41%	94%
0.0024	3	29	32	41	42%	41%	91%
0.0064	4	29	31	41	43%	41%	89%
0.010	5	29	30	41	44%	41%	86%
0.011	6	29	29	41	45%	41%	83%
0.021	7	29	28	41	46%	41%	80%
0.033	8	29	27	41	47%	41%	77%
0.038	9	29	26	41	48%	41%	74%
0.045	10	29	25	41	49%	41%	71%
0.065	11	29	24	41	50%	41%	69%
0.095	11	30	24	40	49%	43%	69%
0.135	12	30	23	40	50%	43%	66%
0.180	12	31	23	39	49%	44%	66%
0.21	13	31	22	39	50%	44%	63%
0.27	14	31	21	39	50%	44%	60%
0.34	15	31	20	39	51%	44%	57%
0.38	16	31	19	39	52%	44%	54%
0.45	19	31	16	39	55%	44%	46%
0.53	20	31	15	39	56%	44%	43%
0.68	20	32	15	38	55%	46%	43%
0.90	21	33	14	37	55%	47%	40%
1.20	22	33	13	37	56%	47%	37%
1.75	23	33	12	37	57%	47%	34%
2.15	24	33	11	37	58%	47%	31%

EC3 Cutoff Values (%)	Substances Correctly Identified as Strong Guinea Pig Sensitizers ²	Weak Sensitizers Incorrectly Identified as Strong Guinea Pig Sensitizers ²	Strong Sensitizers Incorrectly Identified as Weak Guinea Pig Sensitizers ²	Substances Correctly Identified as Weak Guinea Pig Sensitizers ²	Accuracy (%)	Over-classification Rate (%)	Under-classification Rate (%)
2.75	25	33	10	37	59%	47%	29%
3.40	25	34	10	36	58%	49%	29%
4.20	26	34	9	36	59%	49%	26%
5.20	27	34	8	36	60%	49%	23%
5.58	27	35	8	35	59%	50%	23%
5.83	27	36	8	34	58%	51%	23%
6.25	28	36	7	34	59%	51%	20%
7.40	28	37	7	33	58%	53%	20%
9.05	28	38	7	32	57%	54%	20%
10.20	28	39	7	31	56%	56%	20%
10.80	28	40	7	30	55%	57%	20%
11.20	28	41	7	29	54%	59%	20%
12.40	29	41	6	29	55%	59%	17%
15.05	29	42	6	28	54%	60%	17%
17.35	30	42	5	28	55%	60%	14%
18.20	31	42	4	28	56%	60%	11%
18.90	31	43	4	27	55%	61%	11%
20.00	31	44	4	26	54%	63%	11%
22.25	31	45	4	25	53%	64%	11%
25.25	31	46	4	24	52%	66%	11%
26.80	31	47	4	23	51%	67%	11%
28.95	31	48	4	22	50%	69%	11%
35.6	31	49	4	21	50%	70%	11%

Abbreviations: BT = Buehler test; EC3 = Estimated concentration needed to produce stimulation index =3; GHS = United Nations Globally Harmonized System for the Classification and Labelling of Chemicals; GPMT = Guinea pig maximization test; LLNA = Murine local lymph node assay.

¹Guinea pig skin sensitizers were categorized into GHS Category 1 and Category 2 sensitizers based on the results of the most conservative GPMT or BT result. For the GPMT, substances producing a response rate of 60% with an intradermal induction dose >0.1% to ≤1%, or a 30-60% response rate with an intradermal induction dose of ≤0.1%, were classified as Category 1 sensitizers. For the BT, substances producing a response rate ≥60% with a topical induction dose of >0.2% to ≤20%, or a ≥15% response rate with a topical induction dose of ≤0.2%, were classified as Category 1 sensitizers. For the GPMT, substances producing a response rate >30% with an intradermal induction dose >1.0%, or a 30-60% response rate with an intradermal induction dose of >0.1% to ≤1.0% were classified as Category 2 sensitizers. For the BT, substances producing a response rate ≥15% to 60% with a topical induction dose of >0.2% to 20%, or a response rate ≥15% with a topical induction dose of >20% were classified as Category 2 sensitizers. Of the 105

substances used for this analysis, 31 were Category 1 sensitizers, 22 were Category 2 sensitizers, four were false negative in the LLNA, 29 were false positive in the LLNA, and 19 were correct negatives in the LLNA. The most conservative EC3 (%) values from LLNA tests were used to predict guinea pig GHS sensitization category.

²Number of substances.

Appendix D-7 Performance Characteristics for Use of LLNA EC3 (%) Values to Predict GHS Categories (Based on a Weight of Evidence Result) for Strong and Weak Guinea Pig Skin Sensitizers for 52 Substances (23 Category 1 and 29 Category 2 Sensitizers)¹

EC3 Cutoff Values (%)	Substances Correctly Identified as Strong Guinea Pig Sensitizers ²	Weak Sensitizers Incorrectly Identified as Strong Guinea Pig Sensitizers ²	Strong Sensitizers Incorrectly Identified as Weak Guinea Pig Sensitizers ²	Substances Correctly Identified as Weak Guinea Pig Sensitizers ²	Correct Classification (%)	Over-classification Rate (%)	Under-classification Rate (%)
0.0064	1	0	22	29	58%	0%	96%
0.0100	2	0	21	29	60%	0%	91%
0.0250	3	0	20	29	62%	0%	87%
0.0445	3	1	20	28	60%	3%	87%
0.080	4	1	19	28	62%	3%	83%
0.115	5	2	18	27	62%	7%	78%
0.125	6	3	17	26	62%	10%	74%
0.165	6	4	17	25	60%	14%	74%
0.250	6	5	17	24	58%	17%	74%
0.330	7	5	16	24	60%	17%	70%
0.380	8	5	15	24	62%	17%	65%
0.600	11	5	12	24	67%	17%	52%
0.820	12	5	11	24	69%	17%	48%
0.870	12	6	11	23	67%	21%	48%
1.05	13	6	10	23	69%	21%	43%
1.25	13	7	10	22	67%	24%	43%
1.35	14	7	9	22	69%	24%	39%
1.50	16	7	7	22	73%	24%	30%
1.70	17	7	6	22	75%	24%	26%
1.95	17	8	6	21	73%	28%	26%
2.15	18	8	5	21	75%	28%	22%
2.85	19	8	4	21	77%	28%	17%
3.60	20	8	3	21	79%	28%	13%
4.00	20	9	3	20	77%	31%	13%
4.90	20	10	3	19	75%	34%	13%

EC3 Cutoff Values (%)	Substances Correctly Identified as Strong Guinea Pig Sensitizers ²	Weak Sensitizers Incorrectly Identified as Strong Guinea Pig Sensitizers ²	Strong Sensitizers Incorrectly Identified as Weak Guinea Pig Sensitizers ²	Substances Correctly Identified as Weak Guinea Pig Sensitizers ²	Correct Classification (%)	Over-classification Rate (%)	Under-classification Rate (%)
5.75	20	11	3	18	73%	38%	13%
6.15	20	12	3	17	71%	41%	13%
6.40	20	13	3	16	69%	45%	13%
7.85	20	14	3	15	67%	48%	13%
10.10	20	15	3	14	65%	52%	13%
11.25	21	15	2	14	67%	52%	9%
11.55	21	16	2	13	65%	55%	9%
14.00	21	17	2	12	63%	59%	9%
16.75	21	18	2	11	62%	62%	9%
17.75	21	19	2	10	60%	66%	9%
18.90	21	20	2	9	58%	69%	9%
20.10	21	21	2	8	56%	72%	9%
20.85	21	22	2	7	54%	76%	9%
21.30	21	23	2	6	52%	79%	9%
22.35	21	24	2	5	50%	83%	9%
23.60	21	25	2	4	48%	86%	9%
24.70	22	25	1	4	50%	86%	4%
26.10	22	26	1	3	48%	90%	4%
28.95	22	27	1	2	46%	93%	4%
37.65	22	28	1	1	44%	97%	4%
48.55	23	28	0	1	46%	97%	0%

Abbreviations: BT = Buehler test; EC3 = Estimated concentration needed to produce stimulation index =3; GHS = United Nations Globally Harmonized System for the Classification and Labelling of Chemicals; GPMT = Guinea pig maximization test; LLNA = Murine local lymph node assay.

¹Guinea pig skin sensitizers were categorized into GHS Category 1 and Category 2 sensitizers based on a weight of evidence approach (if multiple tests were available) of the GPMT or BT. For the GPMT, substances producing a response rate of 60% with an intradermal induction dose >0.1% to ≤1%, or a 30-60% response rate with an intradermal induction dose of ≤0.1%, were classified as Category 1 sensitizers. For the BT, substances producing a response rate ≥60% with a topical induction dose of >0.2% to ≤20%, or a ≥15% response rate with a topical induction dose of ≤0.2%, were classified as Category 1 sensitizers. For the GPMT, substances producing a response rate >30% with an intradermal induction dose >1.0%, or a 30-60% response rate with an intradermal induction dose of >0.1% to ≤1.0% were classified as Category 2 sensitizers. For the BT, substances producing a response rate ≥15% to 60% with a topical induction dose of >0.2% to 20%, or a response rate ≥15% with a topical induction dose of >20% were classified as Category 2 sensitizers. Of the 52 substances used for this analysis, 23 were Category 1 sensitizers and 29 were Category 2 sensitizers. The geometric mean EC3 (%) values (if multiple values were available) from LLNA tests were used to predict guinea pig GHS sensitization category.

²Number of substances.

Appendix D-8 Performance Characteristics for Use of LLNA EC3 (%) Values to Predict GHS Categories (Based on a Weight of Evidence Result) for Strong and Weak Guinea Pig Skin Sensitizers for 105 Substances (23 Category 1¹ and 29 Category 2² Sensitizers, 4 LLNA False Negative, 30 LLNA False Positive, and 19 LLNA Correct Negative Substances)¹

EC3 Cutoff Values (%)	Substances Correctly Identified as Strong Guinea Pig Sensitizers ²	Weak Sensitizers Incorrectly Identified as Strong Guinea Pig Sensitizers ²	Strong Sensitizers Incorrectly Identified as Weak Guinea Pig Sensitizers ²	Substances Correctly Identified as Weak Guinea Pig Sensitizers ²	Correct Classification (%)	Over-classification Rate (%)	Under-classification Rate (%)
0.0064	1	30	26	48	47%	38%	96%
0.0100	2	30	25	48	48%	38%	93%
0.0250	3	30	24	48	49%	38%	89%
0.0445	3	31	24	47	48%	40%	89%
0.080	4	31	23	47	49%	40%	85%
0.115	5	32	22	46	49%	41%	81%
0.125	6	33	21	45	49%	42%	78%
0.165	6	34	21	44	48%	44%	78%
0.250	6	35	21	43	47%	45%	78%
0.330	7	35	20	43	48%	45%	74%
0.380	8	35	19	43	49%	45%	70%
0.600	11	35	16	43	51%	45%	59%
0.820	12	35	15	43	52%	45%	56%
0.870	12	36	15	42	51%	46%	56%
1.05	13	36	14	42	52%	46%	52%
1.25	13	37	14	41	51%	47%	52%
1.35	14	37	13	41	52%	47%	48%
1.50	16	37	11	41	54%	47%	41%
1.70	17	37	10	41	55%	47%	37%
1.95	17	38	10	40	54%	49%	37%
2.15	18	38	9	40	55%	49%	33%
2.85	19	38	8	40	56%	49%	30%
3.60	20	38	7	40	57%	49%	26%
4.00	20	39	7	39	56%	50%	26%

EC3 Cutoff Values (%)	Substances Correctly Identified as Strong Guinea Pig Sensitizers ²	Weak Sensitizers Incorrectly Identified as Strong Guinea Pig Sensitizers ²	Strong Sensitizers Incorrectly Identified as Weak Guinea Pig Sensitizers ²	Substances Correctly Identified as Weak Guinea Pig Sensitizers ²	Correct Classification (%)	Over-classification Rate (%)	Under-classification Rate (%)
4.90	20	40	7	38	55%	51%	26%
5.75	20	41	7	37	54%	53%	26%
6.15	20	42	7	36	53%	54%	26%
6.40	20	43	7	35	52%	55%	26%
7.85	20	44	7	34	51%	56%	26%
10.10	20	45	7	33	50%	58%	26%
11.25	21	45	6	33	51%	58%	22%
11.55	21	46	6	32	50%	59%	22%
14.00	21	47	6	31	50%	60%	22%
16.75	21	48	6	30	49%	62%	22%
17.75	21	49	6	29	48%	63%	22%
18.90	21	50	6	28	47%	64%	22%
20.10	21	51	6	27	46%	65%	22%
20.85	21	52	6	26	45%	67%	22%
21.30	21	53	6	25	44%	68%	22%
22.35	21	54	6	24	43%	69%	22%
23.60	21	55	6	23	42%	71%	22%
24.70	22	55	5	23	43%	71%	19%
26.10	22	56	5	22	42%	72%	19%
28.95	22	57	5	21	41%	73%	19%
37.65	22	58	5	20	40%	74%	19%
48.55	23	58	4	20	41%	74%	15%

Abbreviations: BT = Buehler test; EC3 = Estimated concentration needed to produce stimulation index =3; GHS = United Nations Globally Harmonized System for the Classification and Labelling of Chemicals; GPMT = Guinea pig maximization test; LLNA = Murine local lymph node assay.

¹Guinea pig skin sensitizers were categorized into GHS Category 1 and Category 2 sensitizers using a weight of evidence approach (if multiple test results were available) based on the results of the GPMT or BT. For the GPMT, substances producing a response rate of 60% with an intradermal induction dose >0.1% to ≤1%, or a 30-60% response rate with an intradermal induction dose of ≤0.1%, were classified as Category 1 sensitizers. For the BT, substances producing a response rate ≥60% with a topical induction dose of >0.2% to ≤20%, or a ≥15% response rate with a topical induction dose of ≤0.2%, were classified as Category 1 sensitizers. For the GPMT, substances producing a response rate >30% with an intradermal induction dose >1.0%, or a 30-60% response rate with an intradermal induction dose of >0.1% to ≤1.0% were classified as Category 2 sensitizers. For the BT, substances producing a response rate ≥15% to 60% with a topical induction dose of >0.2% to 20%, or a response rate ≥15% with a topical induction dose of >20% were classified as Category 2 sensitizers. Of the 105 substances used for this analysis, 23 were Category 1 sensitizers, 29 were Category 2 sensitizers, four were false negative in the LLNA, 30

were false positive in the LLNA, and 19 were correct negatives in the LLNA. The geometric mean EC3 (%) values (if multiple results were available) from LLNA tests were used to predict guinea pig GHS sensitization category.

²Number of substances.

Appendix D-9 Performance Characteristics for Use of LLNA EC3 (%) Values to Predict GHS Categories (Based on the Most Conservative Result) for Strong and Weak Guinea Pig Skin Sensitizers for 32 Substances with Guinea Pig, LLNA, and Human Data (19 Category 1 and 13 Category 2 Sensitizers)¹

EC3 Cutoff Values (%)	Substances Correctly Identified as Strong Guinea Pig Sensitizers ²	Weak Sensitizers Incorrectly Identified as Strong Guinea Pig Sensitizers ²	Strong Sensitizers Incorrectly Identified as Weak Guinea Pig Sensitizers ²	Substances Correctly Identified as Weak Guinea Pig Sensitizers ²	Correct Classification (%)	Over-classification Rate (%)	Under-classification Rate (%)
0.0015	1	0	18	13	44%	0%	95%
0.0024	2	0	17	13	47%	0%	89%
0.0064	3	0	16	13	50%	0%	84%
0.011	4	0	15	13	53%	0%	79%
0.021	5	0	14	13	56%	0%	74%
0.0325	6	0	13	13	59%	0%	68%
0.0375	7	0	12	13	62%	0%	63%
0.045	8	0	11	13	66%	0%	58%
0.105	9	0	10	13	69%	0%	53%
0.28	9	1	10	12	66%	8%	53%
0.45	10	1	9	12	69%	8%	47%
0.53	11	1	8	12	72%	8%	42%
0.78	11	2	8	11	69%	15%	42%
1.6	12	2	7	11	72%	15%	37%
2.75	13	2	6	11	75%	15%	32%
3.4	13	3	6	10	72%	23%	32%
4.2	14	3	5	10	75%	23%	26%
5.28	15	3	4	10	78%	23%	21%
5.83	15	4	4	9	75%	31%	21%
8.3	16	4	3	9	78%	31%	16%
11	16	5	3	8	75%	38%	16%
12.4	17	5	2	8	78%	38%	11%
15.05	17	6	2	7	75%	46%	11%
17.35	18	6	1	7	78%	46%	5%
18.2	19	6	0	7	81%	46%	0%

EC3 Cutoff Values (%)	Substances Correctly Identified as Strong Guinea Pig Sensitizers ²	Weak Sensitizers Incorrectly Identified as Strong Guinea Pig Sensitizers ²	Strong Sensitizers Incorrectly Identified as Weak Guinea Pig Sensitizers ²	Substances Correctly Identified as Weak Guinea Pig Sensitizers ²	Correct Classification (%)	Over-classification Rate (%)	Under-classification Rate (%)
19.5	19	7	0	6	78%	54%	0%
22.25	19	8	0	5	75%	62%	0%
25.25	19	9	0	4	72%	69%	0%
26.8	19	10	0	3	69%	77%	0%
28.95	19	11	0	2	66%	85%	0%
35.6	19	12	0	1	62%	92%	0%

Abbreviations: BT = Buehler test; EC3 = Estimated concentration needed to produce stimulation index =3; GHS = United Nations Globally Harmonized System for the Classification and Labelling of Chemicals; GPMT = Guinea pig maximization test; LLNA = Murine local lymph node assay.

¹Guinea pig skin sensitizers were categorized into GHS Category 1 and Category 2 sensitizers based on the most conservative results (if multiple tests were available) of the GPMT or BT. For the GPMT, substances producing a response rate of 60% with an intradermal induction dose >0.1% to ≤1%, or a 30-60% response rate with an intradermal induction dose of ≤0.1%, were classified as Category 1 sensitizers. For the BT, substances producing a response rate ≥60% with a topical induction dose of >0.2% to ≤20%, or a ≥15% response rate with a topical induction dose of ≤0.2%, were classified as Category 1 sensitizers. For the GPMT, substances producing a response rate >30% with an intradermal induction dose >1.0%, or a 30-60% response rate with an intradermal induction dose of >0.1% to ≤1.0% were classified as Category 2 sensitizers. For the BT, substances producing a response rate ≥15% to 60% with a topical induction dose of >0.2% to 20%, or a response rate ≥15% with a topical induction dose of >20% were classified as Category 2 sensitizers. Of the 32 substances used for this analysis, 19 were Category 1 sensitizers and 13 were Category 2 sensitizers. The most conservative EC3 (%) values (if multiple values were available) from LLNA tests were used to predict guinea pig GHS sensitization category.

²Number of substances.

Appendix D-10 Performance Characteristics for Use of LLNA EC3 (%) Values to Predict GHS Categories (Based on the Most Conservative Result) for Strong and Weak Guinea Pig Skin Sensitizers for 47 Substances with Guinea Pig, LLNA, and Human Data (19 Category 1¹ and 13 Category 2² Sensitizers, 2 LLNA False Negative, 6 LLNA False Positive, and 7 LLNA Correct Negative Substances)¹

EC3 Cutoff Values (%)	Substances Correctly Identified as Strong Guinea Pig Sensitizers ²	Weak Sensitizers Incorrectly Identified as Strong Guinea Pig Sensitizers ²	Strong Sensitizers Incorrectly Identified as Weak Guinea Pig Sensitizers ²	Substances Correctly Identified as Weak Guinea Pig Sensitizers ²	Correct Classification (%)	Over-classification Rate (%)	Under-classification Rate (%)
0.0015	1	1	20	20	45%	23%	95%
0.0024	2	6	19	20	47%	23%	90%
0.0064	3	6	18	20	49%	23%	86%
0.011	4	6	17	20	51%	23%	81%
0.021	5	6	16	20	53%	23%	76%
0.0325	6	6	15	20	55%	23%	71%
0.0375	7	6	14	20	57%	23%	67%
0.045	8	6	13	20	60%	23%	62%
0.105	9	6	12	20	62%	23%	57%
0.28	9	7	12	19	60%	27%	57%
0.45	10	7	11	19	62%	27%	52%
0.53	11	7	10	19	64%	27%	48%
0.78	11	8	10	18	62%	31%	48%
1.6	12	8	9	18	64%	31%	43%
2.75	13	8	8	18	66%	31%	38%
3.4	13	9	8	17	64%	35%	38%
4.2	14	9	7	17	66%	35%	33%
5.28	15	9	6	17	68%	35%	29%
5.83	15	10	6	16	66%	38%	29%
8.3	16	10	5	16	68%	38%	24%
11	16	11	5	15	66%	42%	24%
12.4	17	11	4	15	68%	42%	19%
15.05	17	12	4	14	66%	46%	19%
17.35	18	12	3	14	68%	46%	14%

EC3 Cutoff Values (%)	Substances Correctly Identified as Strong Guinea Pig Sensitizers ²	Weak Sensitizers Incorrectly Identified as Strong Guinea Pig Sensitizers ²	Strong Sensitizers Incorrectly Identified as Weak Guinea Pig Sensitizers ²	Substances Correctly Identified as Weak Guinea Pig Sensitizers ²	Correct Classification (%)	Over-classification Rate (%)	Under-classification Rate (%)
18.2	19	12	2	14	70%	46%	10%
19.5	19	13	2	13	68%	50%	10%
22.25	19	14	2	12	66%	54%	10%
25.25	19	15	2	11	64%	58%	10%
26.8	19	16	2	10	62%	62%	10%
28.95	19	17	2	9	60%	65%	10%
35.6	19	18	2	8	57%	69%	10%

Abbreviations: BT = Buehler test; EC3 = Estimated concentration needed to produce stimulation index =3; GHS = United Nations Globally Harmonized System for the Classification and Labelling of Chemicals; GPMT = Guinea pig maximization test; LLNA = Murine local lymph node assay.

¹Guinea pig skin sensitizers were categorized into GHS Category 1 and Category 2 sensitizers based on the most conservative result (if multiple test results were available) of the GPMT or BT. For the GPMT, substances producing a response rate of 60% with an intradermal induction dose >0.1% to ≤1%, or a 30-60% response rate with an intradermal induction dose of ≤0.1%, were classified as Category 1 sensitizers. For the BT, substances producing a response rate ≥60% with a topical induction dose of >0.2% to ≤20%, or a ≥15% response rate with a topical induction dose of ≤0.2%, were classified as Category 1 sensitizers. For the GPMT, substances producing a response rate >30% with an intradermal induction dose >1.0%, or a 30-60% response rate with an intradermal induction dose of >0.1% to ≤1.0% were classified as Category 2 sensitizers. For the BT, substances producing a response rate ≥15% to 60% with a topical induction dose of >0.2% to 20%, or a response rate ≥15% with a topical induction dose of >20% were classified as Category 2 sensitizers. Of the 47 substances used for this analysis, 19 were Category 1 sensitizers, 13 were Category 2 sensitizers, two were false negative in the LLNA, six were false positive in the LLNA, and seven were correct negatives in the LLNA. The most conservative EC3 (%) value (if multiple results were available) from LLNA tests were used to predict guinea pig GHS sensitization category.

²Number of substances.

Appendix D-11 Performance Characteristics for Use of LLNA EC3 (%) Values to Predict GHS Categories (Based on a Weight of Evidence Approach) for Strong and Weak Guinea Pig Skin Sensitizers for 32 Substances with Guinea Pig, LLNA, and Human Data (12 Category 1 and 20 Category 2 Sensitizers)¹

EC3 Cutoff Values (%)	Substances Correctly Identified as Strong Guinea Pig Sensitizers ²	Weak Sensitizers Incorrectly Identified as Strong Guinea Pig Sensitizers ²	Strong Sensitizers Incorrectly Identified as Weak Guinea Pig Sensitizers ²	Substances Correctly Identified as Weak Guinea Pig Sensitizers ²	Correct Classification (%)	Over-classification Rate (%)	Under-classification Rate (%)
0.025	1	0	11	20	66%	0%	92%
0.0445	1	1	11	19	62%	5%	92%
0.0795	2	1	10	19	66%	5%	83%
0.115	3	1	9	19	69%	5%	75%
0.16	4	2	8	18	69%	10%	67%
0.3	4	3	8	17	66%	15%	67%
0.62	5	3	7	17	69%	15%	58%
1.07	5	4	7	16	66%	20%	58%
1.45	6	4	6	16	69%	20%	50%
1.70	7	4	5	16	72%	20%	42%
2.00	7	5	5	15	69%	25%	42%
2.85	8	5	4	15	72%	25%	33%
3.6	9	5	3	15	75%	25%	25%
4.00	9	6	3	14	72%	30%	25%
5.15	9	7	3	13	69%	35%	25%
6.15	9	8	3	12	66%	40%	25%
7.75	9	9	3	11	63%	45%	25%
10.1	9	10	3	10	59%	50%	25%
11.25	10	10	2	10	62%	50%	17%
14.3	10	11	2	9	59%	55%	17%
17.75	10	12	2	8	56%	60%	17%
19.60	10	13	2	7	53%	65%	17%
21.25	10	14	2	6	50%	70%	17%
22.35	10	15	2	5	47%	75%	17%
23.60	10	16	2	4	44%	80%	17%

EC3 Cutoff Values (%)	Substances Correctly Identified as Strong Guinea Pig Sensitizers ²	Weak Sensitizers Incorrectly Identified as Strong Guinea Pig Sensitizers ²	Strong Sensitizers Incorrectly Identified as Weak Guinea Pig Sensitizers ²	Substances Correctly Identified as Weak Guinea Pig Sensitizers ²	Correct Classification (%)	Over-classification Rate (%)	Under-classification Rate (%)
24.7	11	16	1	4	47%	80%	8%
26.1	11	17	1	3	44%	85%	8%
28.95	11	18	1	2	41%	90%	8%
37.65	11	19	1	1	38%	95%	8%
48.55	12	19	0	1	41%	95%	0%

Abbreviations: BT = Buehler test; EC3 = Estimated concentration needed to produce stimulation index =3; GHS = United Nations Globally Harmonized System for the Classification and Labelling of Chemicals; GPMT = Guinea pig maximization test; LLNA = Murine local lymph node assay.

¹Guinea pig skin sensitizers were categorized into GHS Category 1 and Category 2 sensitizers based on a weight of evidence approach (if multiple tests were available) of the GPMT or BT. For the GPMT, substances producing a response rate of 60% with an intradermal induction dose >0.1% to ≤1%, or a 30-60% response rate with an intradermal induction dose of ≤0.1%, were classified as Category 1 sensitizers. For the BT, substances producing a response rate ≥60% with a topical induction dose of >0.2% to ≤20%, or a ≥15% response rate with a topical induction dose of ≤0.2%, were classified as Category 1 sensitizers. For the GPMT, substances producing a response rate >30% with an intradermal induction dose >1.0%, or a 30-60% response rate with an intradermal induction dose of >0.1% to ≤1.0% were classified as Category 2 sensitizers. For the BT, substances producing a response rate ≥15% to 60% with a topical induction dose of >0.2% to 20%, or a response rate ≥15% with a topical induction dose of >20% were classified as Category 2 sensitizers. Of the 32 substances used for this analysis, 12 were Category 1 sensitizers and 20 were Category 2 sensitizers. The geometric mean EC3 (%) values (if multiple values were available) from LLNA tests were used to predict guinea pig GHS sensitization category.

²Number of substances.

Appendix D-12 Performance Characteristics for Use of LLNA EC3 (%) Values to Predict GHS Categories (Based on a Weight of Evidence Approach) for Strong and Weak Guinea Pig Skin Sensitizers for 47 Substances with Guinea Pig, LLNA, and Human Data (12 Category 1¹ and 20 Category 2² Sensitizers, 2 LLNA False Negative, 6 LLNA False Positive, and 7 LLNA Correct Negative Substances)¹

EC3 Cutoff Values (%)	Substances Correctly Identified as Strong Guinea Pig Sensitizers ²	Weak Sensitizers Incorrectly Identified as Strong Guinea Pig Sensitizers ²	Strong Sensitizers Incorrectly Identified as Weak Guinea Pig Sensitizers ²	Substances Correctly Identified as Weak Guinea Pig Sensitizers ²	Correct Classification (%)	Over-classification Rate (%)	Under-classification Rate (%)
0.025	1	6	13	27	60%	18%	93%
0.0445	1	7	13	26	57%	21%	93%
0.0795	2	7	12	26	60%	21%	86%
0.115	3	7	11	26	62%	21%	79%
0.16	4	8	10	25	62%	24%	71%
0.30	4	9	10	24	60%	27%	71%
0.62	5	9	9	24	62%	27%	64%
1.07	5	10	9	23	60%	30%	64%
1.45	6	10	8	23	62%	30%	57%
1.70	7	10	7	23	64%	30%	50%
2.00	7	11	7	22	62%	33%	50%
2.85	8	11	6	22	64%	33%	43%
3.60	9	11	5	22	66%	33%	36%
4.00	9	12	5	21	64%	36%	36%
5.15	9	13	5	20	62%	39%	36%
6.15	9	14	5	19	60%	42%	36%
7.75	9	15	5	18	57%	45%	36%
10.10	9	16	5	17	55%	48%	36%
11.25	10	16	4	17	57%	48%	29%
14.30	10	17	4	16	55%	52%	29%
17.75	10	18	4	15	53%	55%	29%
19.60	10	19	4	14	51%	58%	29%
21.25	10	20	4	13	49%	61%	29%
22.35	10	21	4	12	47%	64%	29%

EC3 Cutoff Values (%)	Substances Correctly Identified as Strong Guinea Pig Sensitizers ²	Weak Sensitizers Incorrectly Identified as Strong Guinea Pig Sensitizers ²	Strong Sensitizers Incorrectly Identified as Weak Guinea Pig Sensitizers ²	Substances Correctly Identified as Weak Guinea Pig Sensitizers ²	Correct Classification (%)	Over-classification Rate (%)	Under-classification Rate (%)
23.60	10	22	4	11	45%	67%	29%
24.70	11	22	3	11	47%	67%	21%
26.10	11	23	3	10	45%	70%	21%
28.95	11	24	3	9	43%	73%	21%
37.65	11	25	3	8	40%	76%	21%
48.55	12	25	2	8	43%	76%	14%

Abbreviations: BT = Buehler test; EC3 = Estimated concentration needed to produce stimulation index =3; GHS = United Nations Globally Harmonized System for the Classification and Labelling of Chemicals; GPMT = Guinea pig maximization test; LLNA = Murine local lymph node assay.

¹Guinea pig skin sensitizers were categorized into GHS Category 1 and Category 2 sensitizers based on a weight of evidence approach (if multiple test results were available) of the GPMT or BT. For the GPMT, substances producing a response rate of 60% with an intradermal induction dose >0.1% to ≤1%, or a 30-60% response rate with an intradermal induction dose of ≤0.1%, were classified as Category 1 sensitizers. For the BT, substances producing a response rate ≥60% with a topical induction dose of >0.2% to ≤20%, or a ≥15% response rate with a topical induction dose of ≤0.2%, were classified as Category 1 sensitizers. For the GPMT, substances producing a response rate >30% with an intradermal induction dose >1.0%, or a 30-60% response rate with an intradermal induction dose of >0.1% to ≤1.0% were classified as Category 2 sensitizers. For the BT, substances producing a response rate ≥15% to 60% with a topical induction dose of >0.2% to 20%, or a response rate ≥15% with a topical induction dose of >20% were classified as Category 2 sensitizers. Of the 47 substances used for this analysis, 19 were Category 1 sensitizers, 13 were Category 2 sensitizers, two were false negative in the LLNA, six were false positive in the LLNA, and seven were correct negatives in the LLNA. The geometric mean EC3 (%) value (if multiple results were available) from LLNA tests were used to predict guinea pig GHS sensitization category.

²Number of substances.