

# Inter-laboratory comparison of semiquantitative allergen-specific Immunoglobulin E test: 7 years of experience in Korea

Hyeyoung Lee<sup>1</sup>  | Ji Hyeong Ryu<sup>2</sup> | Ae-Ran Choi<sup>2</sup> | Yonggoo Kim<sup>2</sup> | Eun-Jee Oh<sup>2</sup> 

<sup>1</sup>Department of Laboratory Medicine, College of Medicine, International St. Mary's Hospital, Catholic Kwandong University, Incheon, Korea

<sup>2</sup>Department of Laboratory Medicine, College of Medicine, Seoul St. Mary's Hospital, The Catholic University of Korea, Seoul, Korea

## Correspondence

Eun-Jee Oh, Department of Laboratory Medicine, College of Medicine, Seoul St. Mary's Hospital, The Catholic University of Korea, 222, Banpo-daero, Seocho-gu, Seoul 06591, Korea.  
Email: ejoh@catholic.ac.kr

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## Abstract

**Introduction:** Multiple allergen simultaneous test (MAST) is widely used as a screening tool for allergic diseases and has the advantage of providing specific IgE (sIgE) results for various allergens in semiquantitative class. We have continuously conducted external quality assessment (EQA) since 2012 for clinical laboratories performing MAST using AdvanSure allergy screen test (LG CHEM, Korea). This study provides an account of the EQA experience.

**Methods:** Samples were prepared using pooled sera collected from patients with suspected allergic disease and sent to each laboratory twice a year. Each round included 4–6 serum samples with sIgE for 10–20 inhaled or food allergens. The acceptable class value was the most frequently reported MAST class  $\pm 1$  titer that exceeded 80% of the total laboratory results.

**Results:** The average number of participating laboratories was 76 (49–90) and the average response rate was 97.3% during the entire survey period. The acceptable rates were consistently high at  $97.7\% \pm 3.7\%$ . Of the total 537 trials, 18 trials (3.4%) were regarded as nonconsensus results, in which acceptable answers did not exceed 80%. For unacceptable results, the false-negative rate ( $1.5\% \pm 2.8\%$ ) was higher than the false-positive rate ( $0.8\% \pm 2.7\%$ ) ( $p < 0.001$ ). MAST class results were correlated with quantitative IgE results by ImmunoCAP (Spearman's correlation coefficient of 0.682 ( $p < 0.001$ ) and gamma index of 0.777 ( $p < 0.001$ ).

**Conclusion:** Although EQA for MAST showed a high level of acceptable answer, some allergen assays require harmonization. Continuous performance of systematic EQA is needed to improve the accuracy of sIgE assays and quality control in clinical laboratories.

## KEYWORDS

allergy, external quality assessment, IgE, multiple allergen simultaneous test, semiquantitative

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## 1 | INTRODUCTION

The incidence of allergic conditions has continuously increased over the past decades.<sup>1</sup> Although in-vivo skin prick test (SPT) is available in clinical practice, some limitations could cause erroneous results in patients taking antihistamines or suffering skin diseases, among others.<sup>2</sup> Therefore, detection of serum allergen-specific Immunoglobulin E (sIgE) is essential for the diagnosis and management of IgE-mediated hypersensitivity reaction and allergic diseases.<sup>3</sup> Commercially available assays using the principles of enzyme immunoassay (EIA) or fluorescent enzyme immunoassay (FEIA) are now widely used.<sup>4</sup> The ImmunoCAP (Thermo Fisher Scientific) based on the FEIA technique is the most popular for the detection of sIgE for individual allergens.<sup>5</sup> However, when testing for multiple allergens is required, the cost is relatively high and labor-intensive compared to multiplex assay.<sup>6</sup> Currently, several multiplex allergen screening tests (MAST) have been developed and are widely used with the advantages of small sample size, short turnaround time, and cost-effectiveness for a various spectrum of sIgE testing.<sup>2</sup> Although MAST showed relatively low sensitivity and accuracy compared to ImmunoCAP assay, it is useful for screening the multiple sIgEs and provides the degree of sIgE measurement with semiquantitative class (from 0 to 6) results.<sup>2,7</sup>

External quality assessment (EQA) is critical to ensure the accuracy and reliability of laboratory results. However, inter-laboratory proficiency testing for sIgE detection was not popular and was only recently introduced into the program of the Korean Association of External Quality Assessment service. The AdvanSure allergy screen test (LG CHEM, Ltd.) is a fully automated line immunoassay for semiquantitative detection of multiple sIgEs developed in Korea.<sup>2,8</sup> Since 2012, we have established local EQA programs for laboratories performing MAST using AdvanSure allergy screen tests. The purpose of this study is to review EQA experience by analyzing semiquantitative data for 7 years and to evaluate the performance of EQA for sIgE test.

## 2 | MATERIALS AND METHODS

### 2.1 | Preparation of serum samples

Leftover sera were collected from patients who visited Seoul St. Mary's hospital and requested the MAST assay in suspicion of allergic diseases. We prepared pooled sera containing sIgE against a wide spectrum of inhalants or food allergens. Pooled sera were homogenized using an agitator at 180 rpm and then filtered using sterile filter paper. Sealed aliquots (each 650  $\mu$ l) were stored at  $-80^{\circ}\text{C}$  until proficiency testing. This study was approved by the Institutional Review Board of Seoul St. Mary's Hospital (KC11SISI0209, KC14SISI0307, KC17SESI0374).

### 2.2 | External quality assessment

Twice a year, aliquots were sent to clinical laboratories in Korea where MAST was performed using AdvanSure allergy screen test. In

each round, all participant laboratories received 4–6 serum samples requiring 10–20 sIgEs test results per serum. The laboratories were asked to test sIgE following the same procedure as for routine samples. Results were requested to be submitted in MAST classes. The sIgE classification scales were as follows; class 0: under 0.35 kU/L, class 1: 0.35–0.7 kU/L, class 2: 0.7–3.5 kU/L, class 3: 3.5–17.5 kU/L, class 4: 17.5–50 kU/L, class 5: 50–100 kU/L, class 6: over 100 kU/L. Class  $\geq 1$  was interpreted as positive.

### 2.3 | Data evaluation according to the acceptable class values

We analyzed the results received from individual laboratories, and provided overall results and acceptable class values for each allergen. The acceptable class values were defined the most frequently reported MAST class  $\pm 1$  titer that exceeded 80% of the total laboratories according to the performance evaluation criteria of the Korean Association of External Quality Assessment (KEQAS) for semiquantitative tests.<sup>9</sup> If the sum of the most frequent class and  $\pm 1$  grade was below 80%, the acceptable ranges was not determined and defined as a nonconsensus result. Nonconsensus results were excluded from further analysis. False-negative was when the response result was lower grade than the acceptable range, and false-positive was when the response was in a higher grade than the acceptable answers. For negative sera, any positive result was deemed false. We analyzed subgroups of foodstuff, pollen, mites, mold, and animal epithelia.

### 2.4 | Data comparison with quantitative ImmunoCAP

The concentrations of sIgE with the ImmunoCAP from the 9th round. ImmunoCAP system provided the results using a six-class system, as same as MAST, and values of 0.35 kU/L or more (Class  $\geq 1$ ) were interpreted as positive. The semiquantitative comparisons were performed using the gamma index and Spearman's rank correlation analysis.<sup>10</sup> A Gamma Index closer to 1 indicates a stronger association. Spearman's correlation coefficients were categorized as very high positive (0.9–1.0), high positive (0.7–0.9), moderate positive (0.5–0.7), low positive (0.3–0.5), or negligible ( $< 0.3$ ) correlation.<sup>11</sup> Data were analyzed using MedCalc Statistical Software version 19.1 (MedCalc Software bv).

## 3 | RESULTS

### 3.1 | sIgE EQA program

The average number of the participants was 76 with the maximum number in the 13th round ( $n = 90$ ) and the minimum in the 1st round ( $n = 49$ ). The average response rates increased from 89.8%

to 100% ( $97.3\% \pm 3.1\%$ ) during the survey period (Figure 1). The average accept rates were consistently high ( $97.6\% \pm 1.0\%$ ) over the period. The survey materials consisted of 76 foodstuff, pollen, mites, mold, and animal epithelia allergens with varying intensities from negative to strongly positive (Table 1). During the entire period, the most frequently participated allergens were *D. farinae* (24 trials) and *D. pteronyssinus* (24 trials) including samples with varying results of IgE ranging from negative to class 6. The allergens of animal epithelium consisting cat, dog, and sheep were included in a total of 35 trials. Thirty-eight foodstuffs were included in a total of 206 trials. Six allergens for mites were included in 92 trials. The 5 mold allergens and 24 pollen allergens were included in 42 and 162 trials, respectively.

### 3.2 | Analysis of sIgE EQA results in trials with consensus results

Of the total 537 trials, 18 trials (3.4%) were regarded as nonconsensus results, in which the percentage of acceptable answers did not exceed 80% of the total number of participants. In a total of 519 allergen trials with consensus results, an average of 97.7% of the participants presented acceptable results (Table 2). The average rate of false-negative results ( $1.5\% \pm 2.8\%$ ) was higher than that of false-positive results ( $0.8\% \pm 2.7\%$ ) ( $p < 0.001$ ). Next, we analyzed the participants' results according to allergen subgroups, which included foodstuffs ( $n = 199$ ), pollen ( $n = 160$ ), mites ( $n = 84$ ), mold ( $n = 41$ ), and animal epithelia ( $n = 35$ ). There were no significant differences in acceptable rates in each allergen subgroup, and all allergen groups showed false-negative results more than false-positive results.

Next, to analyze acceptable IgE results reporting rates for specific allergens, we select allergens having at least five trials with consensus results. Total 467 trials for 43 allergens were included.

Figure 2 illustrates the overall acceptable result reporting rates for specific allergens individually. Excluding Japanese hop (90.1%), the rate of correct answers was above 95.0%, which was generally satisfactory. For animal epithelia, high rate of acceptable answers (97.5%) were detected in both cats and dogs. Among foodstuffs, the acceptable answer reporting rate was higher in milk ( $99.9\% \pm 0.4\%$ ) and cheddar cheese ( $99.5\% \pm 0.9\%$ ). The lower acceptable answer reporting rate was observed for tuna ( $95.5\% \pm 5.5\%$ ), rice ( $95.4\% \pm 2.7\%$ ), and onion ( $95.1\% \pm 4.8\%$ ). Among the mites, house dust mite ( $99.0\% \pm 1.4\%$ ) showed higher acceptable answer rate while *D. pteronyssinus* ( $96.0\% \pm 4.2\%$ ) showed lower acceptable answer rate. *Aspergillus fumigatus* ( $99.7\% \pm 0.6\%$ ) in molds, and Japanese cedar ( $99.8 \pm 0.5\%$ ), pigweed ( $99.6\% \pm 0.9\%$ ), and mugwort ( $99.5\% \pm 0.7\%$ ) in pollen showed high acceptable answer rate. For Japanese hop ( $90.1\% \pm 5.5\%$ ), acceptable answer rate was low. Broad acceptable answer reporting rates of  $>5\%$  standard deviation (SD) were found for shrimp (5.3%), tuna (5.5%), Japanese hop (5.5%), and Russian thistle (5.9%). Figure 3 shows the reporting rate of unacceptable results for each allergen by dividing it into false positive and false negative. Among food allergens, mackerel, salmon, and tuna showed only false positive answers.

### 3.3 | Analysis of sIgE EQA results for allergens with nonconsensus results

The distribution of reporting results for allergens with nonconsensus result are shown in Table 3. EQA results for house dust mite ( $n = 6$ ), tomato ( $n = 4$ ), garlic ( $n = 3$ ), *Alternaria alternata* ( $n = 1$ ), cockroach ( $n = 1$ ), *D. pteronyssinus* ( $n = 1$ ), Russian thistle ( $n = 1$ ), and rye pollen ( $n = 1$ ) revealed one or more nonconsensus results. House dust mite allergens showed nonconsensus results over 6 times after 10 rounds. Most of them were found in recent rounds.

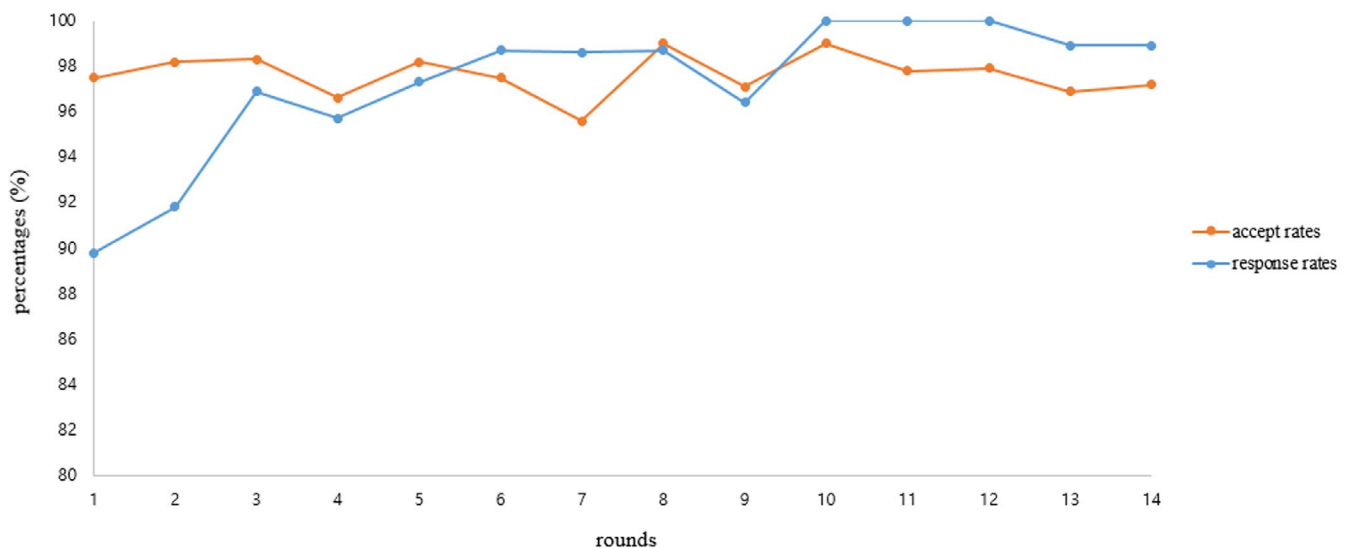


FIGURE 1 External quality assessment program for allergen-specific Immunoglobulin E test from 2012 to 2018. For each round, blue indicates response rates and orange indicates accept rates

TABLE 1 Distribution of allergen specificities in 14 rounds of external quality assessments for allergen-specific Immunoglobulin E test

Subgroups	Allergen	No. of trials (n = 537)	Class of the most frequent result in each trial, n (%)						
			Negative (n = 112)	1 (n = 1)	2 (n = 70)	3 (n = 177)	4 (n = 70)	5 (n = 18)	6 (n = 89)
Animal epithelia	Cat	19	1 (5.3)*		1 (5.3)	3 (15.8)	6 (31.6)	2 (10.5)	6 (31.6)
	Dog	15	1 (6.7)			4	7 (46.7)	1 (6.7)	2 (13.3)
	Sheep	1	1 (100.0)						
Foodstuffs	Anchovy	1	1 (100.0)						
	Apple	2		1 (50.0)			1 (50.0)		
	Barley meal	7		3 (42.9)		3 (42.9)	1 (14.3)		
	Beef	2			1 (50.0)		1 (50.0)		
	Buck-wheat	2	2 (100.0)						
	Cacao	1	1 (100.0)						
	CCD	1	1 (100.0)						
	Cheddar cheese	10	5 (50.0)			3 (30.0)	1 (10.0)		1 (10.0)
	Chicken	7	3 (42.9)			4 (57.1)			
	Citrus mix	3	1 (33.3)			2 (66.7)			1 (25.0)
	Codfish	4	3 (75.0)						
	Crab	10	2 (20.0)			4 (40.0)	4 (40.0)		
	Cucumber	1			1 (100.0)				
	Egg White	12	3 (25.0)		3 (25.0)		2 (16.7)	2 (16.7)	2 (16.7)
	Garlic	13	1 (7.7)		3 (23.1)	6 (46.2)	1 (7.7)		2 (15.4)
	Hazel nut	1		1 (100.0)					
	Honey bee	1		1 (100.0)					
	Mackerel	8	7 (87.5)				1 (12.5)		
	Maize	1			1 (100.0)				
	Milk	13	4 (30.8)			6 (46.2)	1 (7.7)		2 (15.4)
	Mushroom	1	1 (100.0)						
	Mussel	1				1 (100.0)			
	Onion	6		1 (16.7)		4 (66.7)		1 (16.7)	
Peach	13		3 (23.1)		5 (38.5)	3 (23.1)	1 (7.7)	1 (7.7)	
Peanut	10				1 (10.0)	1 (10.0)		9 (90.0)	

TABLE 1 (Continued)

Subgroups	Allergen	No. of trials (n = 537)	Class of the most frequent result in each trial, n (%)						
			Negative (n = 112)	1 (n = 1)	2 (n = 70)	3 (n = 177)	4 (n = 70)	5 (n = 18)	6 (n = 89)
	Pork	8	1 (12.5)		3 (37.5)	2 (25.0)	2 (25.0)		
	Potato	2			1 (50.0)	1 (50.0)			
	Pupa, silk cocoon	1	1 (100.0)						
	Rice	7	1 (14.3)		2 (28.6)	3 (42.9)	1 (14.3)		
	Salmon	7	5 (71.4)			1 (14.3)	1 (14.3)		
	Shrimp	11	2 (18.2)			7 (63.6)	2 (18.2)		
	Soy bean	11	5 (45.5)		3 (27.3)	1 (9.1)	1 (9.1)	1 (9.1)	
	Squid	1				1 (100.0)			
	Tomato	7	1 (14.3)		1 (14.3)	3 (42.9)	1 (14.3)		1 (14.3)
	Tuna	6	5 (83.3)			1 (16.7)			
	Walnut	2				1 (50.0)			1 (50.0)
	Wheat flour	10			3 (30.0)	5 (50.0)	1 (10.0)		1 (10.0)
	Yeast, bakers	2	1 (50.0)			1 (50.0)			
Mites	Acarus siro	11	1 (9.1)			8 (72.7)	1 (9.1)		1 (9.1)
	Cockroach	8	2 (25.0)		1 (12.5)	2 (25.0)	2 (25.0)		1 (12.5)
	<i>D. farinae</i>	24	1 (4.2)			3 (12.5)	2 (8.3)		18 (75.0)
	<i>D. pteronyssinus</i>	24	1 (4.2)			3 (12.5)	4 (16.7)		16 (66.7)
	House dust mite	21				11 (52.4)	1 (4.8)	4 (19.0)	5 (23.8)
	Storage mite	4				4 (100.0)			
Mold	<i>Alternaria alternata</i>	12	1 (8.3)		4 (33.3)	5 (41.7)	1 (8.3)		1 (8.3)
	<i>Aspergillus fumigatus</i>	8	7 (87.5)			1 (12.5)			
	<i>Candida albicans</i>	7			2 (28.6)	3 (42.9)	1 (14.3)		1 (14.3)
	<i>Cladosporium herbarum</i>	11	7 (63.6)			2 (18.2)	2 (18.2)		
	<i>Penicillium notatum</i>	4	2 (50.0)		2 (50.0)				

(Continues)

TABLE 1 (Continued)

Subgroups	Allergen	No. of trials (n = 537)	Class of the most frequent result in each trial, n (%)							
			Negative (n = 112)	1 (n = 1)	2 (n = 70)	3 (n = 177)	4 (n = 70)	5 (n = 18)	6 (n = 89)	
Pollen	Acacia	2	2 (100.0)							
	Ash mix	2			2 (100.0)					
	Bermuda grass	11	2 (18.2)		4 (36.4)	3 (27.3)	2 (18.2)			
	Birch	1				1 (100.0)				
	Birch-Alder mix	2			1 (50.0)	1 (50.0)				
	Dandelion	2	1 (50.0)		1 (50.0)					
	Goldenrod	6	1 (16.7)		3 (50.0)	1 (16.7)	1 (16.7)		1 (16.7)	
	Japanese cedar	6	5 (83.3)			1 (16.7)				
	Japanese hop	5			2 (40.0)	1 (20.0)	1 (20.0)	1 (20.0)		1 (20.0)
	Mugwort	8			1 (12.5)	6 (75.0)				1 (12.5)
	Oak white	4	2 (50.0)			2 (50.0)				
	Orchard grass	14	1 (7.1)			6 (42.9)	6 (42.9)			1 (7.1)
	Oxeye daisy	3			2 (66.7)	1 (33.3)				
	Pigweed	7	2 (28.6)		3 (42.9)	1 (14.3)	1 (14.3)			
	Pine	2	2 (100.0)							
	Poplar mix	7	6 (85.7)							
	Ragweed, short	8		1 (12.5)	1 (12.5)	4 (50.0)	2 (25.0)			
	Reed	12	1 (8.3)		1 (8.3)	7 (58.3)	1 (8.3)	1 (8.3)		1 (8.3)
	Russian thistle	10			4 (40.0)	3 (30.0)		1 (10.0)		2 (20.0)
	Rye pollens	18			2 (11.1)	8 (44.4)				8 (44.4)
	Sallow willow	3				3 (100.0)				
	Sweet vernal grass	12	1 (8.3)		1 (8.3)	8 (66.7)	1 (8.3)			1 (8.3)
	Sycamore mix	4	3 (75.0)			1 (25.0)				
	Timothy grass	13	1 (7.7)			5 (38.5)	4 (30.8)	2 (15.4)		1 (7.7)

Note: \*Number of trials (%).

TABLE 2 sIgE EQA results in 519 allergen trials with consensus results

Allergen	No. of trials	Frequency (%) of participants' results in each trial					
		Acceptable results		False negative results		False positive results	
		Mean (%)	SD (%)	Mean (%)	SD (%)	Mean (%)	SD (%)
Animal epithelia	35	97.6	3.1	1.8	2.7	0.6	2.2
Foodstuffs	199	97.7	3.6	1.4	2.7	0.9	2.6
Mites	84	97.4	4.0	1.9	3.1	0.7	3.1
Mold	41	97.7	3.6	1.4	2.3	0.9	3.0
Pollen	160	97.8	3.8	1.4	3.0	0.7	2.6
Total	519	97.7	3.7	1.5	2.8	0.8	2.7

### 3.4 | Comparison of sIgE EQA results with ImmunoCAP results

Semiquantitative comparisons between ImmunoCAP and MAST are shown in Table 4. Within the total allergens available for comparison, spearman's correlation coefficient was 0.682 ( $p < 0.001$ ) and the gamma index was 0.777 ( $p < 0.001$ ). In allergen subgroups, foodstuffs (high positive), mites (moderate positive), mold (moderately positive), and pollen showed significant associations between the IgE class results of MAST and ImmunoCAP.

## 4 | DISCUSSION

Until participating in KEQAS in 2020, there was no EQA program for sIgE assay in Korea. In this study, we reviewed EQA experience with interlaboratory comparisons of allergen-specific IgE assays conducted by a single institution since 2012. During the entire survey program across 14 round, relatively high rates of acceptable answer reporting were found. However, some allergens showed differences in IgE results, making it impossible to determine the consensus even using the same reagents. Therefore, we confirmed the need for a systematic EQA to improve the accuracy of assay and the quality control of clinical laboratories.

The performance evaluation criteria for semiquantitative and qualitative IgE tests have not yet been standardized.<sup>12</sup> In this study, EQA for semiquantitative IgE results was analyzed by applying the performance evaluation criteria of KEQAS.<sup>9</sup> Koch and Aberer analyzed the EQA of the Austrian allergy test for 25 years with an acceptable range of  $\pm 1$  or 2 of the most frequent values. Also, for a positive sample, a case where the answer was higher than the acceptable answer by grade 2 or negative, and for a negative sample reported as positive was defined as unacceptable.<sup>13</sup> We analyzed the results using the KEQAS standard to ensure consistency of sIgE EQA program. KEQAS standard define acceptable class values as the most frequently reported MAST class  $\pm 1$  titer that exceeded 80% of the total laboratories.

It is well known that the causes of the discrepancy in the sIgE assays is the difference in allergens contained in the reagents, the difference in extraction methods, and the difference in allergen attachment methods.<sup>3</sup> Standardization of allergy tests and implementation of EQA have not been easily achieved to date, and there are many challenges to be solved. There is no internationally recognized reference preparation for sIgE. Standard curves for every allergen are unavailable and a total IgE calibration curve is used to obtain sIgE concentrations by heterologous interpolation.<sup>3</sup> Total IgE reagents react with the constant region of the IgE, such as fragment crystallizable region. However, specific IgE reagents react with the active binding site, such as fragment antibody binding region which epitope specificity, affinity/avidity differs from patient to patient. This might have affected the amount of specific IgE in a given system.<sup>14</sup>

When we analyzed reporting results according to allergen subgroup or individual allergen, there was no significant difference in

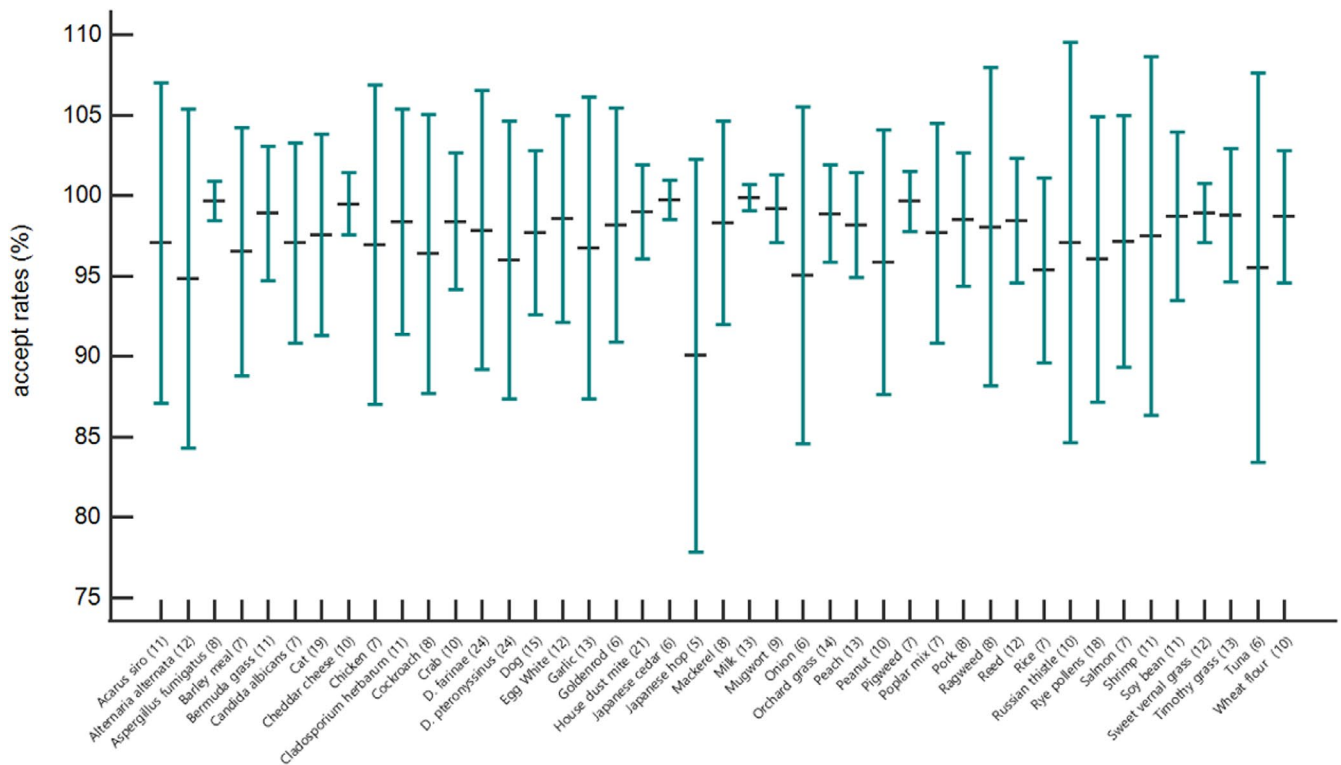


FIGURE 2 Acceptable IgE results reporting rates for specific allergens across the entire EQA program. \*Allergens with at least 5 trials with consensus results were included in this figure. Results (%) present the average  $\pm$  2 standard deviation

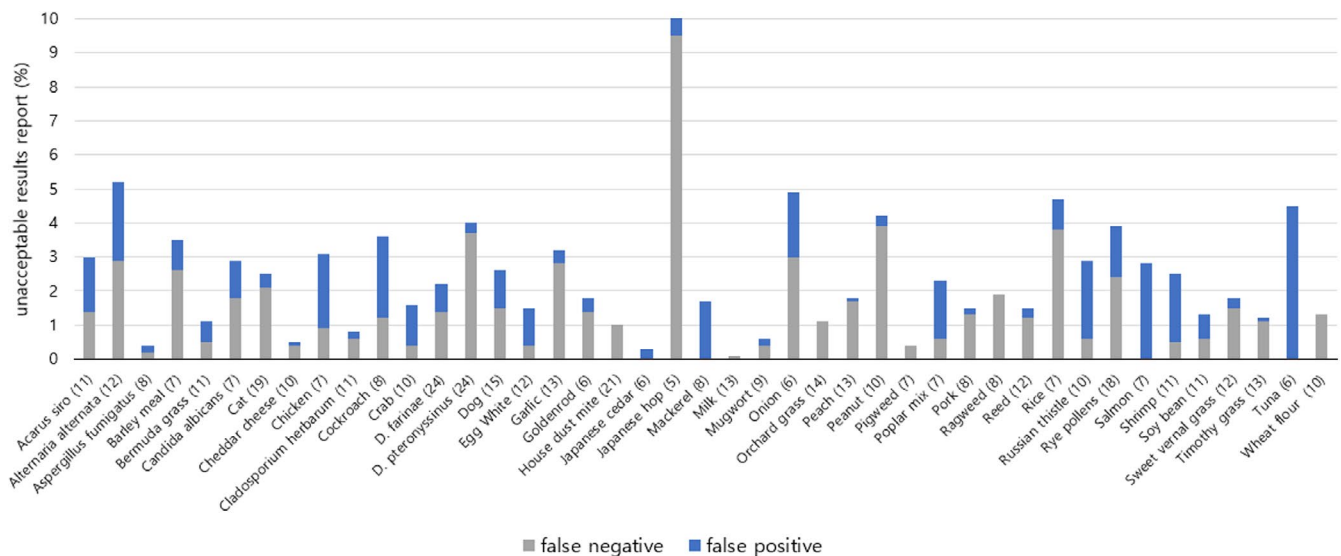


FIGURE 3 Unacceptable IgE results (false negative and false positive answers) reporting rates for specific allergens across the entire EQA programs. \*Allergens with at least 5 trials with consensus results were included in this figure

acceptable rates in each allergen subgroup, and all allergen groups showed false negative results more than false positives. Among allergens having consensus results for acceptable range, broad acceptable answer reporting rates of  $>5\%$  SD were found for shrimp (5.3%), tuna (5.5%), Japanese hop (5.5%), and Russian thistle (5.9%).

This study is meaningful as the EQA program was conducted for domestically developed reagent. Due to the significant differences in the prevalence of allergic disease by age, gender, and ethnicity, the allergen panels should be modified following the geographical region and target population.<sup>15-17</sup> The changes in environmental materials in modern society must be taken into



TABLE 3 Distribution of reporting results for allergens with one or more nonconsensus results across all EQA program

(A) House dust mite																				
Round (No. of participants)																				
IgE results (class)	1 (44)	1 (44)	2 (56)	2 (56)	3 (62)	3 (63)	4 (66)	5 (71)	5 (70)	6 (78)	8 (74)	8 (74)	9 (80)	10* (81)	11* (88)	12* (87)	13* (88)	13* (89)	14* (87)	14* (88)
Negative	0	0	0	0	2	0	0	0	0	0	1	0	0	0	0	1	0	0	0	0
1	0	2	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
2	9	11	14	0	0	0	0	0	0	0	30	0	0	0	0	0	0	0	0	0
3	68	89	75	86	0	0	0	1	0	3	69	24	26	51	66	71	76	76	63	63
4	27	2	11	0	3	63	17	14	0	21	0	15	3	1	0	2	0	0	15	15
5	0	0	0	0	5	16	42	51	0	46	0	49	4	6	1	2	0	0	0	0
6	0	0	0	100	95	79	41	34	100	31	0	12	68	42	33	23	24	24	23	23
(B) Tomato																				
Round (No. of participants)																				
IgE results (class)	1 (44)	5 (70)	7 (68)	9* (80)	11* (88)	12* (86)	14* (87)													
Negative	2	100	4	0	0	1	1													
1	2	0	7	0	0	0	0													
2	0	0	76	0	0	0	3													
3	18	0	12	26	66	69	74													
4	61	0	0	3	0	7	0													
5	16	0	0	1	0	0	0													
6	0	0	0	70	34	23	22													
(C) Garlic																				
Round (No. of participants)																				
IgE results (class)	1 (44)	2 (55)	3 (63)	5 (70)	5 (70)	6 (78)	8 (74)	9 (80)	10 (81)	11* (88)	12* (86)	14* (87)								
Negative	2	0	2	0	0	0	1	3	0	0	0	1								
1	0	0	2	0	0	1	11	3	2	0	0	0								
2	0	2	2	0	0	13	81	36	57	0	1	68								
3	0	73	5	16	0	82	7	58	41	65	57	8								
4	0	25	6	79	0	4	0	1	0	1	17	1								
5	0	0	27	4	0	0	0	0	0	0	1	0								
6	98	0	57	1	0	0	0	0	0	34	23	22								

(Continues)



TABLE 3 (Continued)

(F) D. pteronyssinus																								
IgE results (class)	Round (No. of participants)																							
	1 (44)	1 (44)	1 (44)	1 (44)	1 (44)	2 (56)	2 (56)	3 (62)	3 (63)	5 (71)	5 (70)	6 (78)	6 (78)	7 (68)	7 (68)	8 (74)	9 (80)	10 (81)	10* (81)	11 (88)	12 (87)	13 (89)	14 (88)	
5	0	0	25	0	2	35	0	0	0	35	34	3	15	15	4	12	0	33	5	19	0	0	2	33
6	0	100	66	0	95	51	100	0	98	59	38	97	79	44	81	76	4	43	43	49	34	24	1	23
(G) Russian thistle																								
IgE results (class)	Round (No. of participants)																							
	1 (44)	1 (44)	1 (44)	4 (66)	4 (66)	5 (71)	5 (71)	6 (78)	6 (78)	9 (80)	9 (80)	10 (81)	10 (81)	11 (88)	11 (88)	14*								
Negative	0	0	0	2	0	0	1	0	1	1	0	0	0	0	0	0								
1	0	0	7	0	0	0	0	0	0	1	1	1	0	0	0	0								
2	0	82	89	0	0	0	49	29	64	66	66	64	66	66	17									
3	0	18	5	0	0	1	50	68	35	15	15	35	60	60	60									
4	0	0	0	0	0	41	0	1	0	19	0	0	0	0	0									
5	0	0	0	17	51	51	0	0	0	0	0	0	0	0	1									
6	100	0	0	82	7	7	0	0	0	0	0	0	0	0	22									
(H) Rye pollens																								
IgE results (class)	Round (No. of participants)																							
	1 (44)	1 (44)	2 (56)	2 (55)	4 (66)	4 (66)	5 (71)	5 (70)	6 (78)	6 (78)	9 (80)	9 (80)	10 (81)	10 (81)	11 (88)	12 (87)	13 (88)							
Negative	2	0	0	0	6	0	0	1	3	0	4	0	1	0	0	1	0							
1	0	0	0	0	0	0	16	0	0	0	0	0	1	0	0	0	0							
2	2	0	0	0	0	0	76	6	47	21	3	2	38	1	0	0	0							
3	0	0	2	0	0	0	7	77	51	69	25	89	51	69	79	77	77							
4	0	0	0	0	0	0	0	14	1	6	0	6	11	18	17	10	10							
5	5	0	0	0	2	38	4	0	0	0	0	0	0	11	2	9	9							
6	91	100	0	98	100	92	48	94	0	0	73	0	0	0	0	3	3							

Note: \*EQA round with nonconsensus results. \*\*percentages of laboratories reporting that class in each round. Bold type indicates acceptable class values as most frequently reported MAST class  $\pm 1$  titer that exceeded 80% of the total laboratories. Class results that contain more than 80% of the sum of all results are shown in dark red.

TABLE 4 Comparison analysis of semiquantitative results between MAST and ImmunoCAP

Allergens	Spearman's correlation coefficient		Gamma index	
	95% CI	p-Value	95% CI	p-Value
Total	(0.600–0.750)	<0.001	0.777	<0.001
Foodstuffs	(0.638–0.831)	<0.001	0.786	<0.001
Pollen	(0.264–0.661)	<0.001	0.702	<0.001
Mites	(0.232–0.776)	0.002	0.686	<0.001
Mold	(0.283–0.890)	0.004	0.191	0.002
Animal epithelia	(–0.183–0.784)	0.165	0.778	0.197

Note: Abbreviation: CI, confidence interval.

account for the progressive development of the MAST assay.<sup>18</sup> Also, the strength of this EQA program is its voluntary participation in laboratories using the same products and continuously collecting national data for 7 years. As expected of high comparability, the observed acceptable rates exceeded 95% over the entire period. Nevertheless, some laboratories reported unacceptable results. There can be various causes for unacceptable result reporting in EQA. In a previous study, considerable differences have been reported in laboratories using the same assay as well as different sIgE assays, suggesting performance error observed.<sup>3</sup> It is necessary to check the calibration regularly to make sure that the devices are properly performed. Another reason may be differences in reagent lot number. It is necessary to check whether there are any changes or errors in antigen production or reagent preparation by the manufacturer. There is also the possibility of clerical errors such as data entry errors, use of different encodings, or different samples. In this study, the EQA for house dust, tomato, and garlic allergen-specific IgE showed continuously nonconsensus results. Laboratory directors should be aware of these errors and be careful when interpreting the EQA results.

When comparing the results of EQA's response and Immucap, a spearman's correlation coefficient of 0.682 and a gamma index of 0.777 were observed. A previous study comparing AdvanSure with Immucap reported gamma index ranged from 0.819 to 0.990,<sup>10</sup> while about 60% of the total agreement was observed in another study.<sup>8</sup> The relatively good correlation in our study suggested that MAST assay may be used as a supplementary means of the quantitative measurement for sIgE.

This study has limitations. Although this study analyzed EQA results from MAST assays compared to highly validated ImmunoCAP results, they may not correlate with class values from semiquantitative sIgE assays. False negativity and false positivity of the results were determined by consensus result, not clinical symptoms or SPT results. Since external quality assessment is highly dependent on policies and management models, this study can hardly be guiding outside of Korea. However, it is meaningful in suggesting the concordance rate of semiquantitative results for various allergens. It is difficult to standardize serum sIgE testing. Therefore, laboratories performing sIgE assay require regular calibration and internal/external quality control, or interlaboratory comparison.

In this study, 7 years of IgE EQA experience was reviewed and the reported results were analyzed. Our experience in sample manufacturing, shipping, and reporting results analysis is expected to assist in the successful implementation of other IgE EQA programs. Agreed regional or national consensus may help harmonize laboratory diagnostic strategies and explain the need for EQA along with strengthening education on their use.

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## DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

## ORCID

Hyeyoung Lee  <https://orcid.org/0000-0001-8871-5091>

Eun-Jee Oh  <https://orcid.org/0000-0001-5870-915X>

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