IVD CAPSULE Aeroallergens

REF P02.00022

English

Intended use

The **IVD CAPSULE Aeroallergens** is a single use, rapid in vitro diagnostic test for the quantitative determination of circulating immunoglobulin E (IgE) specific to the allergen components Phl p 1 + Phl p 5 (combined), Der p 1 + Der p 2 (combined), Alt a 1, Fel d 1 and Can f 1, in human uncoagulated capillary blood sample collected from the patient's fingertip.

The **IVD CAPSULE Aeroallergens** is to be used with the **abioSCOPE 2.0** in vitro diagnostic test system. The system is intended for professional use in clinical laboratory settings or point of care (PoC) locations, including near-patient testing.

The **IVD CAPSULE Aeroallergens** is used to identify sensitization to a given allergen or group of allergens, and, in conjunction with other clinical assessments and laboratory findings, to aid in diagnosing IgE-mediated allergic disorders.

Summary

One-third of the world's population suffers from allergy, and the worldwide prevalence is increasing[1]. Allergy diseases manifest with various symptoms, such as skin rash, rhinitis, itchy throat, nose and ears, and nausea, resulting in impaired quality of life and working capacity[1].

Allergens are molecules which produce an abnormal immune response in allergic patients. Antibodies belonging to the class E of immunoglobulins bound to their cognate allergen trigger the immediate release of active mediators. These mediators, such as histamine and leukotriene, act on the surrounding tissues and cause allergy symptoms[2].

In vitro allergen-specific IgE blood tests allow evaluating a patient's sensitization spectrum without any risk of adverse reactions. The presence of IgE specific for a given allergen is indicative of a potentially clinically relevant sensitization.

Test principle

The blood sample is mixed with a solution containing fluorescently labelled antibodies reactive to human IgE. The blood sample, now containing the IgE-detector antibody complex, is loaded onto the capsule of the kit.

Patient material is drawn through the capsule by capillary action and passes through a built-in separator that excludes cells and particles from the measurement area.

After passing through the separator, the IgE-antibody complex is bound by allergens immobilized on the capsule's read-out area. The concentration of the captured allergen-specific IgE complex is proportional to the fluorescence generated on the sensor surface by the fluorophore conjugated to the signal antibody. Therefore, the measured fluorescence signal is proportional to the concentration of allergen-specific IgE within the sample. The measured fluorescence signal is reported in kU_A/l, according to the radioallergosorbent test (RAST) classes:

IgE conc. [kU_A/l]	Comment
<0.7	Absent, low or undetectable level of allergen specific IgE
0.7 – 3.4	Moderate level of allergen-specific IgE
3.5 – 17	High level of allergen- specific IgE
18 – 49	Very high level of allergen-specific IgE
50 – 100	Ultra-high level of allergen-specific IgE
> 100	Extremely high level of allergen-specific IgE

Table 1 | IgE radioallergosorbent test (RAST) ranges and their signification.

Reagents

The IVD CAPSULE Aeroallergens contains the following IgE serologic assays:

Tests	Interpretation
Phl p 1 + Phl p 5	Major allergens of timothy grass (*Phleum pratense*) pollen
Der p 1 + Der p 2	Major allergens of the house dust mite species *Dermatophagoides pteronyssinus*
Alt a 1	Major allergen of the mold *Alternaria alternata*
Fel d 1	Major allergen of cat dander
Can f 1	Major allergen of dog dander

Table 2| Allergens are purified from either their natural source (Can f 1, Der p 1 and Phl p 1) or are recombinant proteins (Fel d 1, Alt a 1, Phl p 5 and Der p 2).

Each kit contains one vial filled with 50 µl of the **abioMIX** reagent. The **abioMIX** reagent is composed of the fluorescently labeled anti-human IgE antibody, dissolved in a Tris-buffered saline solution supplemented with Tween-20. The **abioMIX** reagent contains a preservative (Table 3).

Material	Conc.
Fluorescently labelled anti-IgE antibody	2.50 µg/ml
Tween 20 (CAS number 005-64-5)	1.0% (v/v)
Tris(hydroxymethyl)aminomethane (CAS number 77-86-1)	24.8 mM
Sodium Chloride (CAS number 7647-14-5)	137mM
Potassium Chloride (CAS number 7447-40-7)	2.7 mM
Tripotassium-Ethylenediaminetetra acetic acid (CAS number 65501-24-8)	7.23 mM
ProClin300 (CAS number 55965-84-9)	0.04% (v/v)

Table 3| Composition of the **abioMIX** reagent.

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Materials included

- 1x capsule with a panel of IgE serologic assays
- 1x vial of **abioMIX** reagent
- 1x capillary blood collector (**abioPIPETTE**)
- 1x desiccant bag

Test procedures

1. Use the provided **abioPIPETTE** to collect 50 µl of whole blood from the patient's fingertip.
2. Pick up the **abioMIX** vial and flick it to move the **abioMIX** down to the bottom before use. Pierce the cap with the filled **abioPIPETTE**, and completely insert it into the vial without pushing the plunger. Once fully inserted, turn the plunger one-quarter turn clockwise and push on the **abioPIPETTE**'s plunger to dispense the entire blood sample into the **abioMIX** reagent vial. Hold the pressure on the plunger of the **abioPIPETTE** then remove the **abioPIPETTE** and release the plunger outside of the vial.
3. Tap the vial at least 10 times on a hard surface to mix thoroughly the blood-**abioMIX** solution. A mixed sample will have a homogenous color. **Incubate the blood sample mixed with the abioMIX reagent for 5 minutes** before loading it onto the capsule.
4. Outside the vial, push down the plunger completely and hold the pressure. Insert the **abioPIPETTE** in the vial. Release the plunger to completely fill the **abioPIPETTE** with the mix and remove the **abioPIPETTE**. Press the plunger gently to deposit the mixture evenly on the entire surface of the membrane (white area) in the center of the capsule. The mixture should be dispensed slowly to allow solution to wick into the capsule. Be careful not to scrape against the membrane with the pipette tip. The filled capsule should be measured immediately.
5. Fold the lid over to close the capsule. Hold the capsule only by the edges. Be careful not to touch the bottom side of the capsule.
6. To start the measurement, touch the button "measure" on the reader. The tray will open automatically.
7. Place the capsule onto the tray according to the guided capsule position on the screen, then touch the button "close tray".

To measure the sample, refer to the **abioSCOPE 2.0** User Manual.

Storage and stability

Store the **IVD CAPSULE Aeroallergens** at 2-8 °C until use. The kit is stable until the expiration date printed on the label. The **abioMIX** reagent is ready-to-use. Allow the **abioMIX** reagent to warm up to room temperature before use. Use the **abioMIX** reagent within 4 hours of warming.

Traceability and calibration

The **IVD CAPSULE Aeroallergens** is calibrated by the manufacturer using, for each test of the panel, a pool of well characterized clinical samples with a defined sIgE concentration in a whole blood matrix. The IgE calibrators are traceable to the 3rd International Reference Preparation (11/234) of Human Serum Immunoglobulin E from World Health Organisation (WHO)[3]. Each lot of **IVD CAPSULE Aeroallergens** is calibrated using a weighted 5-parameter logistic curve fit data reduction method. The instrument automatically calculates the concentration of each sample and displays it on the instrument screen. The instrument automatically reads in the lot-specific calibration data that are embedded within the capsule chip, eliminating the need for calibration by the user. Allergen-specific IgE values assigned to controls and calibration materials are directly traceable to a master lot of calibrator.

Quality control

For quality control, use the **IVD CAPSULE IgE Control** (not provided)**.** Follow the applicable local regulations and guidelines for quality control.

The control intervals must be adapted to each laboratory's individual requirements. Values obtained should fall within the defined target range. Each laboratory should establish corrective measures to be taken if values fall outside of the defined ranges.

Warnings and precautions

- For in vitro diagnostic use.
- The **IVD CAPSULE Aeroallergens** must be kept refrigerated until use.
- Do not freeze.
- Allow the **abioMIX** reagent vial to reach room temperature before use.
- The **IVD CAPSULE Aeroallergens** should be used within 4 hours after being removed from refrigeration.
- This product requires the handling of human specimens. It is recommended that all human-sourced material should be considered potentially infectious. Universal precautions that apply to your facility should be used for handling and disposal of materials during and after testing[4].

Reagent deterioration

The following observations indicate reagent deterioration:

- Presence of turbidity in the **abioMIX** vial.
- Consistently high or low values from assay kits from the same batch.

Limitations

- Test results should be interpreted within the complete clinical picture. Definitive diagnosis and/or clinical decision should not be based solely on the results of any single diagnostic test, but made after all clinical and laboratory findings are evaluated.
- All assay materials are single-use and cannot be re-used.
- This assay uses antibodies of murine (mouse) origin. Patient material reactive to mouse proteins may give anomalous results. Heterophilic antibodies in human blood can interfere with in vitro immunoassays. Patients routinely exposed to animals or to animal blood products can be prone to this interference. The impact of heterophilic antibodies, human rheumatoid factors (RF) and of human anti-mouse antibodies (HAMA) on measurements have not been assessed.
- Low level of allergen-specific IgE should be evaluated with caution when total IgE values are above 1500 kU/l, as clinically elevated total IgE level may result in the overestimation of the level of allergen-specific IgE.
- The **IVD CAPSULE Aeroallergens** contains allergen components. Discrepancies with extract based IgE serologic assays or skin prick tests may be caused by the fact that allergen components may be present in very low amount in natural extract, or that that patient is sensitized to allergen components present in the natural extract and not in the **IVD CAPSULE Aeroallergens**.

Expected values

Non-allergic blood donors have IgE against the panel of allergens of the IVD CAPSULE Aeroallergens that are below 0.7 kU_A/l. Good laboratory practices recommend that each laboratory establishes its own expected reference range for the population it serves.

Values above 0.7 kU_A/l indicates specific IgE antibodies to an allergen, or a group of allergens, detected by the test system. Values below 0.7 kU_A/l indicates undetectable level or the absence of allergen-specific IgE.

Measuring range : 0.70 - 100 kU_A/l

Precision

Between-run and between-day variance components

The between-run and between-day variance components of the different assays of the panel of the **IVD CAPSULE Aeroallergens** on the **abioSCOPE 2.0** have been determined in a study designed according to the CLSI guideline EP05-A3[5]. Three samples with allergen-specific IgE values in the low to moderate range of each assay were measured during 10 days, with two runs of duplicates per day. Study results are depicted in Table 4.

sIgE test	Mean [kU_A/l]	Between-run CV [%]	Between-day CV [%
Phl p 1 + Phl p 5	10.1	<1	10
	8.2	<1	14
	45.0	9	<1
Der p 1 + Der p 2	4.5	16	<1
	5.9	<1	5
	16.4	7	19
Alt a 1	5.4	2	15
	4.8	<1	8
	17.0	7	4
Fel d 1	2.4	20	20
	6.1	4	<1
	20.1	10	<1
Can f 1	5.6	< 1	25
	5.3	16	16
	19.5	< 1	20

Table 4| Precision values of the between-run and between-day precision study. CV: Coefficient of variation.

User-to-user, lot-to-lot, device-to-device precision variance components

A study was conducted following the 3X3X5 design[5], where "3" was either the User, lot or devices, and the "5" were the days and the replicate measurements per day. Two samples were evaluated for each allergen-specific IgE test, one in the low range ($\leqslant$ 5.0 kU_A/l) and one in the high range ($\geqslant$ 20 kU_A/l). For the user-to-user precision variance component, the mean imprecision (coefficient of variation, CV) was 8.5% (standard deviation (SD): 6.4; range: 2.0 to 23%). For the lot-to-lot precision variance component, the mean imprecision was 13.5% (SD: 5.1; range: <1.0 to 18%). For the device-to-device precision variance component, the mean imprecision was 10.7% (SD: 7.1; range: <1.0 to 19%).

Analytical selectivity

The impact of common potential interfering substances was evaluated as per the CLSI guideline EP07[6]. The study was conducted on the Fel d 1 IgE serologic assay with two samples, one in the low range (4.0 kU_A/l) and one in the high range (40 kU_A/l) of the assay. No relevant bias was found up to the following concentrations:

- Triglycerides: 500 mg/dl *
- Free bilirubin: 40 mg/dl §
- Conjugated bilirubin: 40 mg/dl §
- Hemoglobin: 1.0 g/dl §

* An negative bias of more than 20% was found at 1500 mg/dl; § highest tested doses.

Inter-method comparability and agreement

The comparability of test results between the **IVD CAPSULE Aeroallergens** on the **abioSCOPE 2.0** device and the laboratory reference method Phadia Laboratory System "ImmunoCAP" (ThermoFisher Scientific, Uppsala, Sweden) was assessed in a study designed according to the CLSI guideline EP09c[7]. All clinical samples were assessed as venous whole blood on the **abioSCOPE 2.0** and venous plasma on the Phadia Laboratory System (ThermoFisher Scientific). A non-Weighted Deming linear regression was used to determine the slope and intercept in the range 0.7 to 100 kU_A/l (Table 5). The extend of linear correlation was assessed with the Simple Pearson coefficient *r* and its squared value (R^2).

sIgE test	Slope (95% CI)	Intercept (95% CI)	*r*; R^2
Phl p 1 + Phl p 5	0.6 (0.3 to 0.8)	2.4 (-2.1 to 7.0)	0.93; 0.86
Der p 1 + Der p 2	0.9 (0.8 to 1.1)	1.7 (-0.6 to 4.0)	0.96; 093
Alt a 1	1.5 (0.6 to 2.4)	-8.2 (-19.3 to 2.8)	0.92; 0.85
Fel d 1	1.0 (0.7 to 1.3)	-7.4 (-14.7 to 0.0)	0.94; 0.88
Can f 1	1.0 (-0.8 to 1.2)	-3.8 (-9.1 to 1.5)	0.88; 0.77

Table 5| Slope and intercepts with their 95% CI determined by non-Weighted Deming regression, and the Simple Pearson coefficient (*r*) and its squared value (R^2) determined by least square regression. * Due to the low number of positive samples, the linear regression was performed using the least square regression statistics and covered the range 0.0 to 100 kU_A/l. CI: confidence interval.

Expressed as inter-class agreements (semi-quantitative analysis), the pooled test results were divided between the different RAST classes (Table 6).

		ImmunoCAP RAST Class scoring					
		0-1	2	3	4	5	6
IgE assay on abioSCOPE 2.0	0-1	38	11	7			
	2	13	13	4	1		
	3		3	16	7		
	4			1	19	5	
	5				1	8	1
	6					1	1

Table 6| Inter-class division of test results between the two methods (all test results pooled).

Each test's agreement with the reference laboratory method has also been computed as binary classification, i.e., a test results < 0.7 kU_A/l was counted as "negative" and a test result ≥ 0.7 kU_A/l was counted as "positive" (qualitative assessment) (Table 7).

sIgE test	PPA (%)	NPA (%)	OPA (%)
Phl p 1 + Phl p 5	100	45	80
Der p 1 + Der p 2	100	80	93
Alt a 1	90	70	83
Fel d 1	80	80	80
Can f 1	40	100	60
All	82	75	79

Table 7| Inter-method agreement expressed in percent. For each IgE serologic assay, 30 samples were assessed on both methods. PPA: positive percent agreement, NPA: negative percent agreement, OPA: overall percent agreement.

References

1. Global Atlas of Allergy; published by the European Academy of Allergy and Clinical Immunology (EAACI), 2014
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5. Clinical and Laboratory Standards Institute (CLSI), "Evaluation of Precision of Quantitative Measurement Procedures; Approved Guideline – Third Edition." CLSI Document EP05-A3. Wayne, PA: CLSI; 2014.
6. Clinical and Laboratory Standards Institute (CLSI), "Interference Testing in Clinical Chemistry. Third Edition." CLSI Document EP07. Wayne, PA: CLSI; 2018.
7. Clinical and Laboratory Standards Institute (CLSI), "Measurement Procedure Comparison and Bias Estimation Using Patient Samples - Third Edition." CLSI Document EP09c. Wayne, PA: CLSI; 2018.

CE marking

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Use with plain (uncoagulated) capillary blood.