Diagnostic of allergy diseases

AllergyScreen®/AlleisaScreen®

MEDIWISS
Analytic GmbH

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Content

How allergies work

Allergy is the fifth leading chronic disease in the U.S. and the third most common chronic disease among children under 18 years old.

An allergy is a misguided reaction to foreign substances by the immune system. It is said to be misguided because these foreign substances (called allergens) are generally harmless. A variety of cells play an important role in this type of reaction:

- T-lymphocytes recognize the foreign substances in the body and release chemical cytokines that stimulate the B-lymphocytes
- B-lymphocytes produce immunoglobulin E (IgE) to destroy the substance
- TH1 and TH2 combat the foreign substances
- Mast cells and basophiles (white blood cells) produce mediator chemicals such as histamine and leukotriene

The role of IgE

Class E immunoglobulin (IgE) was first identified in 1964 and plays an important role in Type I allergic reactions. Everyone has IgE antibodies in small amounts to protect the body from parasites. However, allergic persons produce IgE in abnormally elevated quantities.

When stimulated by the appropriate foreign allergen, helper and suppresser cells (sub classes of the T-lymphocytes) stimulate B-lymphocytes to transform into plasma cells. Plasma cells secrete antibodies of various classes which circulate in the blood and are responsible for immunity. If this regulation fails, a B-lymphocyte can also be converted by a normally harmless antigen. These immunoglobulins migrate via the blood stream to the basophiles and mast cells where they are bound to specific receptors within their Fc region. If the organism has further contact with the specific allergen, it migrates directly to the anchored IgE and links two neighbouring molecules with epitopes via the antigen-binding Fc region. This link formation liberates different vasoactive amines from the mast cells, which together with other highly active mediators can lead to the typical symptoms of a Type I allergic reaction.

The most common allergic conditions include hay fever (allergic rhinitis), asthma, allergic conjunctivitis, allergic eczema, hives (urticaria) and allergic shock.

Common allergy triggers

Airborne allergens: pollen, animal dander, mites and mold.

Often pet allergies are triggered by exposure to proteins found in animal skin cells, saliva or urine and are commonly associated with cats, dogs, horses and rodents. Inhaling mold spores can also cause an allergy with incidents typically reported between July and late summer. The most common triggers are Alternaria, Cladosporium, Aspergillus, Penicillium, Mucor and Rhizopus. A wide variety of tree, grass and weed pollen cause an allergic reaction, the intensity of which is influenced by pollen seasons, location, weather and other environmental factors.

- **Foods**

  For adults, the most common triggers of food allergies include shellfish, peanuts, tree nuts, fish and eggs, whereas young children tend to experience allergies to eggs, milk and peanuts. Food intolerance is often confused with food allergy as they share similar symptoms.

- **Insect venoms**

  Insect stings inject chemicals into the body which can cause allergic reactions, in most cases resulting from stings/bites from bees, wasps and fire ants. Mosquitos, flies and fleas can cuase milder reactions.

- **Latex**

  Repeated or prolonged exposure to latex is one of the most common causes of allergic contact dermatitis. Normally harmless, latex is a natural rubber used in a wide range of items: medical supplies (such as gloves and catheters), balloons, children's toys or shoe soles.

- **Medication**

  Some people develop allergies to certain medications, the most common of which include penicillin and related antibiotics. Reactions range from mild localized rashes or hives to life-threatening severe allergic reaction (anaphylaxis).

Changing the testing paradigm

AllergyScreen®/AlleisaScreen®

Allergy diagnostics and the identification of a sensitization against allergens is an interdisciplinary challenge that incorporates knowledge gained through medical science, biochemistry and biology.

Long years of experience and work done with single test systems in allergological labs have shown that only a few key allergens are responsible for the patient's disorders. And so, a question emerged: Why not collect all these key allergens and combine them in one single reaction trough?

AllergyScreen®: Quick and efficient testing of up to 20 allergens per test strip

MEDIWISS Analytic GmbH has vast experience in the extraction of allergens from crude raw material and extensive know-how of western blot protein analysis. This led to the idea of binding high quality, self-extracted, lyophilised allergens to a nitrocellulose membrane with the help of a contact plot printer.

The required antibody and substrate for the visualization of the specific IgE/allergen reaction were available and well known from western blot analysis. It was only necessary to develop a plastic reaction trough in which the test strips could be glued. This resulted in a ready-to-use test for the determination of specific IgE in human serum.

The original contact plot printer used pencils filled with a special protein solution. New sophisticated equipment was developed featuring up to 21 micro dispensing pumps which can be individually programmed according to variable and individual parameters with minimal divergence.

Supportive hardware and software systems were also developed for a camera that photographs the test strips and allows a semi-quantitative analysis of the results: Initially, up to 20 allergens could be measured per test strip.

AlleisaScreen®: Precise testing of up to 30 flexible allergens in a single procedure

The wish for more allergen lines on a single membrane surface led to AlleisaScreen®, a bigger biochip with a maximum capability of 30 allergens on one test strip that is glued in a ready-to-use reaction trough. The fact that these new biochips required a higher camera resolution resulted in the development of a new analysis system.

What started as a simple qualitative visual test strip has been developed into a highly innovative, semi-quantitative nitrocellulose chip system for the determination of allergen specific IgE in human serum with customized, high resolution scanner systems.

Clear advantage over single determination tests

AllergyScreen®/AlleisaScreen®

AllergyScreen®/AlleisaScreen® are two different versions of test kits with many different allergen panels to detect allergen-specific IgE-immmunoglobulins in human serum.

Testing multiple allergens offers a more detailed and extensive analysis

It is extremely important for allergic persons to identify their sensitizations in order to establish an appropriate life plan – even when, from a clinical point of view, not all of these sensitizations are current. Labs can either use single or multiple allergens for the determination of allergic sensitization. In both cases the allergens are extracted in the same way. Single allergen test systems usually test only allergens based on the patient's complaints and clinical history. By contrast, test strips with multiple allergens make it possible to test different allergen groups, thereby determining sensitization with no clinical currency at the time of the test. Since most sensitizations are cross-reactive, key allergens in particular are always present. One trough with several key allergens allows for a rapid detection of all possible antigens in a single lab test. This type of approach is naturally cheaper than single tests, uses less lab materials and less patient's serum. The use of allergen specific test strips with multiple food allergens or test panels with multiple respiratory allergens also lead to a more detailed and extensive patient analysis.

AllergyScreen®

This immunoblot test combined with our evaluation software enables:

- Easy test procedure
- Quick testing and evaluation in just 2.5 hours
- Flexible, customized and country-specific panels
- Testing of 20 allergens per test strip with only 250 µl serum

AlleisaScreen®

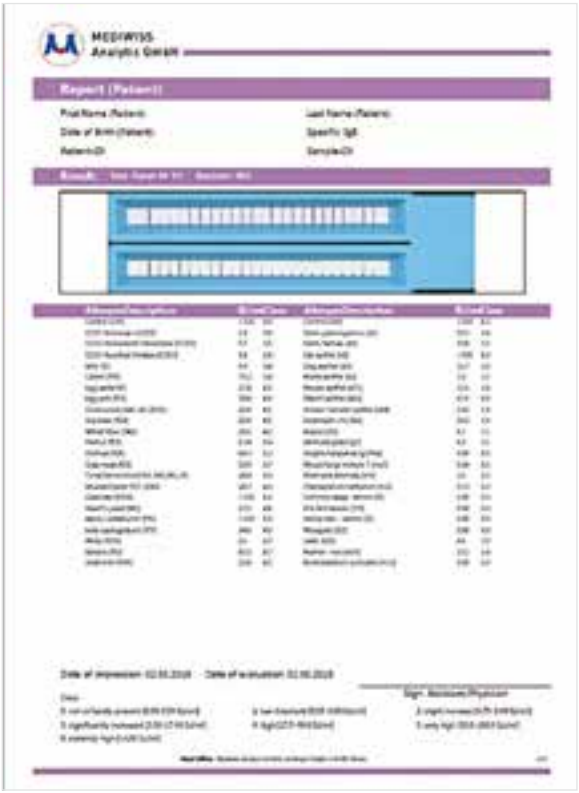
This test offers you all the advantages of our well established AllergyScreen® test, as well as:

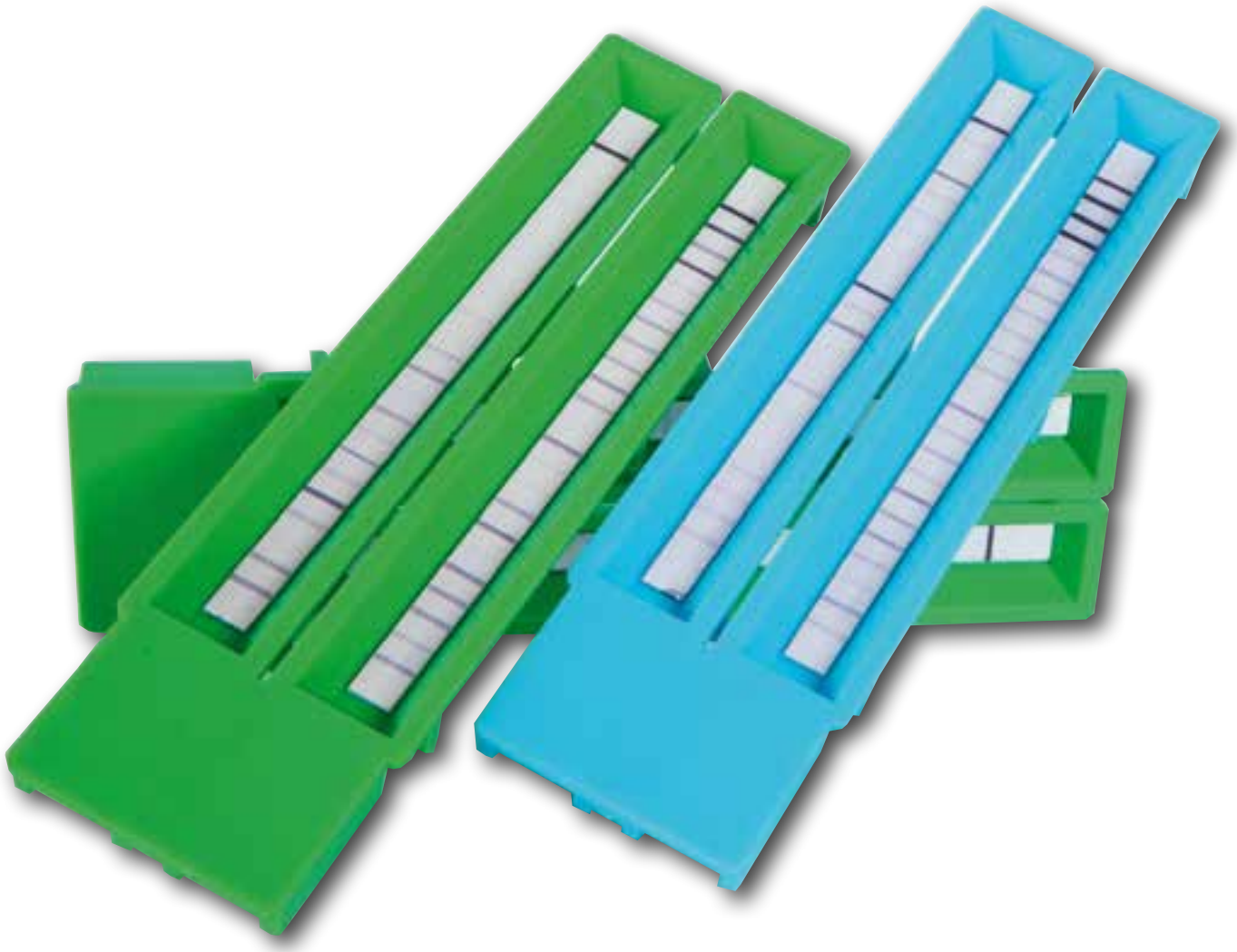
- Testing of 30 allergens per test strip with only 300 µl serum
- An optimized price-allergen ratio of screening systems in allergy diagnostics

MEDIWISS Analytic GmbH produces its own natural crude protein extracts and optimizes them for use on the test strips.

The AlleisaScreen® offers also the possibility to combine up 60 different allergens on one panel. This allows the testing of all key allergens in one determination.

- The testing of 44 – 60 allergens in one run
- Covering of all key allergens with one panel
- Requiring of only 600 µl serum
- An easy evaluation with Improvio scanners
- All allergens clearly shown on one report page





Precise testing methods

AllergyScreen®/AlleisaScreen®

Overview of the AllergyScreen®/AlleisaScreen® processes

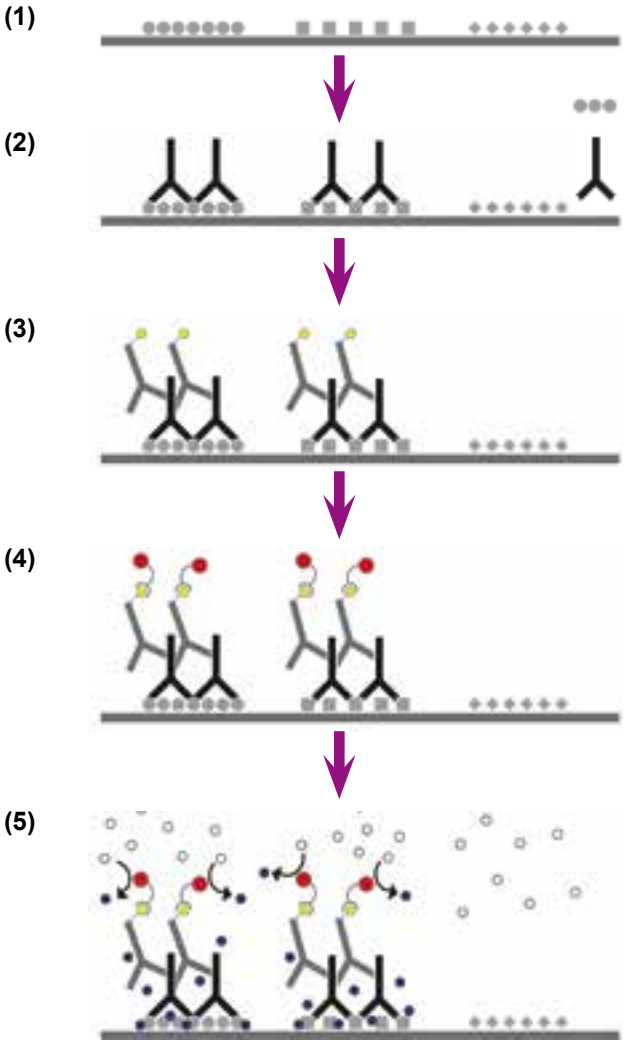
(1) Different crude allergen extracts are bound to a nitrocellulose membrane as lines.

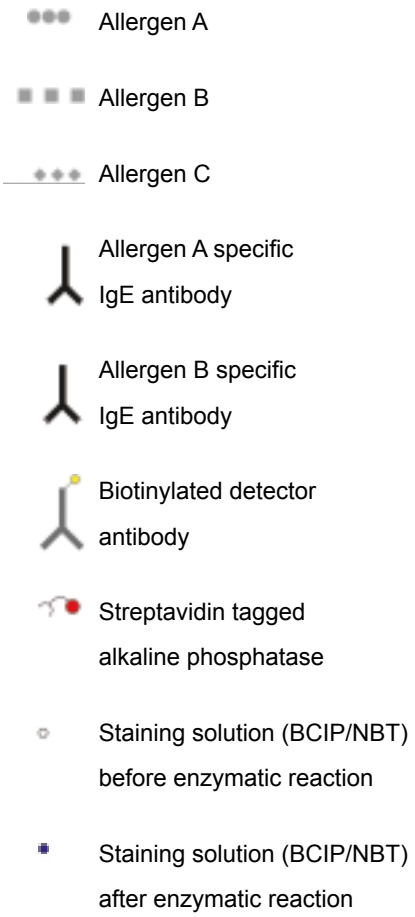
(2) Specific IgE antibodies of the patient serum bind to their respective allergen.

(3) The biotinylated detector antibody, an anti-IgE antibody, binds to the allergen specific IgE human antibodies.

(4) The alkaline phosphatase binds via its streptavidin tag to the biotin group of the detector antibody.

(5) The colorless staining solution (BCIP/NBT) is modified enzymatically, resulting in a blue precipitate.





Key test principles

The AllergyScreen® and the AlleisaScreen® test kits are semi-quantitative *in vitro* systems to determine the presence of allergen-specific IgE antibodies in human serum. A blood sample from the patient is necessary for this test. Liquid allergens, produced for *in vitro* diagnostic purposes, are passively bound as test lines to a nitrocellulose membrane and the membrane strips (called test strips) are glued into the reaction troughs. Customers can select up to 20 allergens using AllergyScreen® and up to 60 different allergens using AlleisaScreen®.

Test principles

1. Different crude allergen extracts are bound as test lines to the surface of a nitrocellulose membrane.
2. To determine allergen-specific IgE antibodies, patients sera (250 µl for AllergyScreen® and 300 µl for AlleisaScreen®) is pipetted into the reaction trough and incubated for 45 minutes at room temperature (20-22 °C). During this time the allergen-specific IgE antibodies bind to the specific allergens on the test strip. Nonbound IgE antibodies are removed by washing.
3. In a next step, polyclonal anti-human IgE detector antibody (AllergyScreen®) or a mix of a monoclonal and a polyclonal anti-human IgE detector antibody (AlleisaScreen®) is pipetted into the reaction trough and incubated for another 45 minutes at room temperature (20-22 °C). These biotin coupled detector antibodies bind to the allergen-specific IgE from the patient serum. Nonbound detector antibodies are removed by washing.
4. The test strip is then incubated with a streptavidin tagged alkaline phosphatase (streptavidin conjugate) for 20 minutes at room temperature (20-22 °C). The streptavidin tag binds to the biotin of the detector antibody. Nonbound streptavidin conjugate is removed by washing.
5. Now the staining solution (color solution) is added to the trough and incubated at room temperature (20-22 °C) for 20 minutes. An enzymatic reaction of the alkaline phosphatase takes place, resulting in a blue band on the respective allergen line. The reaction is stopped by washing. The coloration is directly proportional to the amount of the specific antibody in the serum sample.
6. After thoroughly drying the test strip, an evaluation of the coloration of the allergen lines is carried out by one of Improvio scanners: Improvio C, Improvio M or Improvio L. The concentration of specific IgE in the serum sample is determined and results are given in classes (from 0 to 6) and iU/ml (range 0 to > 100 iU/ml).
7. The calibration of AllergyScreen®/AlleisaScreen® is based on the reactivity of a grass pollen mixture on the test strips of AllergyScreen®/AlleisaScreen® and the results of a suitable reference system which is itself calibrated against the total-IgE WHO preparation 75/502.
8. The used logistic dose-response function: $Y = A_1 + A_2 - A_1/1+10^{(\log x0-x)p}$ and its mathematical parameters were used to create an internal, fixed standard curve for the use in the panel specific set cards for evaluation by the B4C software of BioSciTec scanners, with a semi-quantitative scoring system.

Simplicity combined with quick, precise results

AllergyScreen®/AlleisaScreen®

You will need:

A laboratory washing bottle (500 ml),
a graduated cylinder (500 ml),
a tilt shaker (e.g. ScreenShaker),
a washing retainer (trough holder),
an incubation box,
a 100 µl – 1000 µl pipette,
a timer and some gloves.

Precautions:

Sera and all solutions must be at ambient temperature (20-22°C). Dilute the washing buffer concentrate (1:25).

1. Wet the test strips with washing buffer. Remove the washing buffer by gently tapping the troughs on a paper towel. The test strips should be wet but with no surplus buffer on its surface.

2. Pipette 250 µl serum (AllergyScreen®) or 300 µl serum (AlleisaScreen®) into the troughs, taking care that the test strips are completely covered. Carefully slide the washing retainer into the incubation box. Place the incubation box onto the ScreenShaker. Incubate for 45 minutes at room temperature (20-22 °C).

3. Carefully take the washing retainer out of the box. Remove the sera by rinsing the troughs with the washing buffer. Rinse each test strip with washing buffer, thereby shake the washing buffer in the troughs for 10 seconds. Repeat this 6-7 times. Remove the surplus by gently tapping the troughs on paper towels.

4. Pipette 250 µl (AllergyScreen®) or 300 µl (AlleisaScreen®) detector antibody in each trough. Slide the washing retainer into the incubation box and incubate for another 45 minutes on the ScreenShaker at room temperature (20-22 °C).

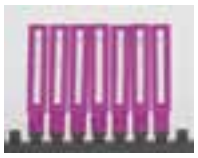
5. Wash the test strips as described in step 3.

6. Pipette 250 µl (AllergyScreen®) or 300 µl (AlleisaScreen®) of the streptavidin conjugate into each reaction trough. Replace the washing retainer into the incubation box and incubate for exactly 20 minutes on the ScreenShaker at room temperature (20-22 °C).

7. Wash the test strips as described in step 3, but this time rinse each test strips 9-10 times.

8. Pipette 250 µl (AllergyScreen®) or 300 µl (AlleisaScreen®) of the staining solution into each reaction trough. Slide the washing retainer into the incubation box and replace it on the ScreenShaker. Incubate for exactly 20 minutes at room temperature on the ScreenShaker at room temperature (20-22 °C).

9. Rinse each test strip several times under running water. Remove the water by gently tapping the trough on a paper towel. Leave the test strips to air dry or use a conventional hair dryer. The background of the test strips will turn white, while the control line and positive tested allergens will stay purple.



Test processing video is available at MEDIWISS Analytic GmbH.
Only for qualified, trained professionals. Not for self-testing.

Standard and customized panels worldwide

MEDIWISS Analytics GmbH provides our customers worldwide with a wide range of test panels with crude allergens and allergen mixtures for diagnostic testing. In order to obtain exceptional results, our own allergens are manufactured from certificated crude raw materials to gain the highest quality standards. The allergens are controlled at every stage of production and standardized against previous extracted lots and our in-house references.

Standard and highly customized allergen-specific panels are available for the testing of multiple allergen combinations.

If you have any questions about our allergens or about how we support our customers with specific allergen combinations, please contact us.

Examples of test panels

Multiple combinations of allergens

Worldwide customized panels

Panel 5 (20 allergens)
Control (Ctrl)
Derm. pteronyssinus (D1)
Derm. farinae (D2)
Alder (T2)
Birch (T3)
Hazel (T4)
Mixed grasses (GX)
Rye (pollen) (G12)
Mugwort (W6)
Plantain (W9)
Cat epithel (E1)
Horse Epithel (E3)
Dog Epithel (E5)
Guinea pig epithel (E6)
Honey bee - venom (I1)
Common wasp - venom (I3)
Ragweed (W1)
Penicillium notatum (M1)
Cladosporium herbarum (M2)
Aspergillus fumigatus (M3)
Alternaria alternate (M6)

Panel 30 Pedi_A (30 allergens)
Control (Ctrl)
Derm. pteron. (D1)
Derm. farinae (D2)
Tree pollen (Tx)
Mixed grasses (GX)
Ragweed (W1)
Mugwort (W6)
Cat epithel (E1)
Dog epithel (E5)
Alternaria alternata (M6)
Latex (K82)
alpha-Lactalbumin (F76)
beta-Lactoglobulin (F77)
Casein (F78)
Lactoferrin (F334)
Milk (F2)
Egg white (F1)
Egg yolk (F75)
Hazelnut (F17)
Peanut (F13)
Chicken (F83)
Mussel mix (Fx207)
Seafish mix (Fx24)
Banana (F92)
Soy bean (F14)
Carrot (F31)
Wheat flour (F4)
Rye flour (F5)
Oat flour (F7)
Camomile (F462)
CCD Mixture (CCDx)

An improvement in *in vitro* allergy diagnosis

CCD-blocking solution

Many allergens are glycoproteins, which consist of a protein part and one or more glycan chains. Glycan chains are composed of different sugars linked together and are bound via an amino-group (N-glycane) or a hydroxyl-group (O-glycane) to the protein part. N-glycanes are particularly immunogen and can induce the production of IgE (anti-CCD IgE).

The IgE antibodies are highly cross-reactive for glycoproteins of plants, insects and molluscs. Therefore, glycan chains are named “cross-reactive carbohydrate determinants” (CCDs).

CCDs have been found in allergen extracts of plant or animal origins like tree, weed and grass pollen, vegetables, fruits, seeds and nuts, latex, insect venoms, snails and parasites.

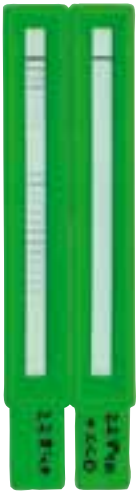
Approximately 25% of allergic patients produce anti-CCD IgE. The sensitization of patients against CCDs results probably from pollen allergens or insect stings. While the occurrence of CCDs in allergen extracts induce usually no positive results in skin tests, they can lead to “false-positive” results or increase a positive result in *in vitro* tests. For this reason, especially in *in vitro* tests for the detection of allergen specific IgE, the possible occurrence of specific anti-CCD IgE must be considered.

The CCD-blocking solution is a mixture of three important plant glycoproteins with different N- and O-glycan chains:

- Bromelain (from pineapple)
- Peroxidase (from horseradish)
- Ascorbat Oxidase (from courgette)

To exclude “false-positive“ or increased positive results in the AlleryScreen®/AlleisaScreen® tests, a patient serum can be mixed with the CCD-blocking solution, which leads to an inhibition of such glycan-specific IgE and is an improvement in *in* vitro allergy diagnosis.
Before testing it in our AlleryScreen®/AlleisaScreen® or other tests the patient serum is mixed thoroughly with 10% CCD-blocking solution (e.g. 270 µl serum + 30 µl CCD-blocking solution) and incubated at room temperature (20-22 °C) for 30 minutes.

After incubation the CCD-serum mix can be directly used in the AllergyScreen® (250 µl) or AlleisaScreen® (300 µl) assay or other tests.



The trough on the left side shows Panel 30 Food A (food allergens) worked off with a serum without CCD-blocking solution and the trough of the right side shows the same serum after preincubation with 10% CCD-blocking solution. The CCD-inhibition shows that the patient was not sensitized against any of the tested allergens.

The reduction of positive allergen lines after inhibition of a serum with CCD-blocking solution indicates that the positive response is completely or partly due to a reaction of anti-CCD IgE in patients sera with glycoproteins in allergens.

The use of the CCD-blocking solution makes it now possible to distinguish between a “false” glycan-based sensitization against CCDs or a “true” protein-based sensitization.

Quality controlled from beginning to end

Professional production acc. ISO 13485:2016

MEDIWISS Analytic GmbH manufactures high quality crude protein raw allergen extracts from certificated raw materials. About 500 different allergens are available for manifold combinations on our AllergyScreen®/AlleisaScreen® test strips.

The production of each allergen extract adheres to the following procedures:

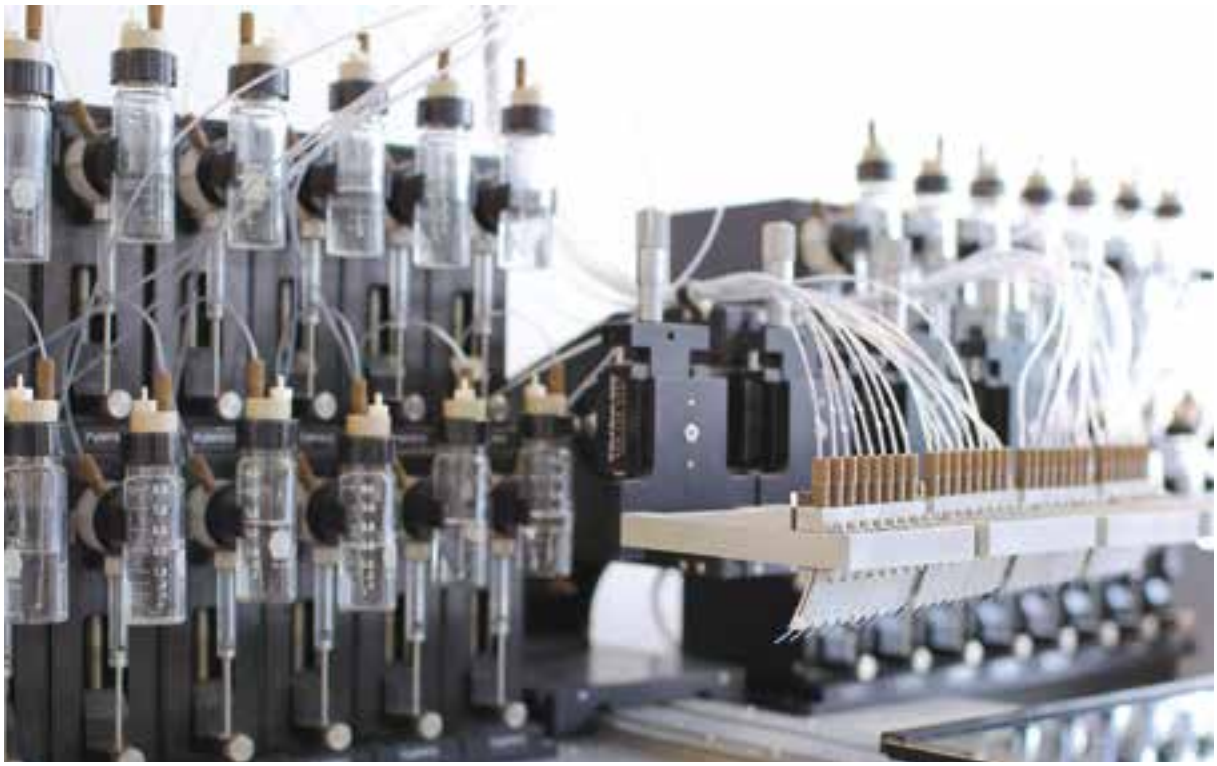
- Homogenization of raw material in special buffers
- Purification by dialysation
- Centrifugation and filtration
- Lyophilisation of the extract for long term storage.

The potency of each crude allergen extract is determined by a special in-house reference serum and additional positive/negative patient sera.

High qualitative crude allergen extracts are dispensed as lines on a nitrocellulose membrane by a Biodot printing device with high resolution syringe pumps.

After drying and blocking, a Biodot cutting device precisely cuts the nitrocellulose membranes into test strips. The final test strips are glued into reaction troughs and sent to our customers worldwide in test kits for 20-24 determinations.

CM5000 Guillotine Cutter



Biodot, FrontLine HR™ Microliter Contact Dispenser with 32 pumps.
FrontLine HR has a flexible dispense tip that rides on the substrate surface with the dispensed fluid emerging from dragging tip. The fluid flow rate can be synchronized with motion to create a quantitative volume per unit length of reagent on the substrate surface.

The scanning devices:
The Improvio Family

- Scans 1–36 test strips at a time
- Print out and program in several languages available
- Data export via Windows-Excel™, CSV or XML
- Data import via CSV
- Data transfer to LIMS possible
- Integrated self-control of the system by Fuji™ gray scale

	Improvio C	Improvio M	Improvio L
Strips scanned at a time	1–4 strips	1–10 strips	1–36 strips
Dimensions (w x d x h)	30 x 23 x 8 cm	30 x 31 x 8 cm	60 x 38 x 11 cm
Weight	2.3 kg	3.0 kg	17 kg
Casing	2 part plastic casing	2 part plastic casing	3 part metal casing + plastic tray for test strips
Drawer	mechanical drawer	mechanical drawer	mechanical drawer
AllergyScreen®/ AlleisaScreen®	yes	yes	yes
Free position of test strips	yes	yes	no
Easy to clean	yes	yes	yes
Simple Installation	yes	yes	yes
Calibration card	yes	yes	yes
Computer connection	USB 2.0	USB 2.0	USB 2.0
Technology	Color CCD Sensor	Color CCD Sensor	Color CCD Sensor
Resolution (optical)	1200 x 2400 dpi	1200 x 2400 dpi	1200 x 2400 dpi
Lamp	LED	LED	LED
Power supply	1 x external power supply, CE certified	1 x external power supply, CE certified	1 x external power supply, CE certified
Power Consumption	18 W	18 W	18 W
Power Adapter Input	100-240 V AC; 47-63 Hz; 1.35-0.53 A	100-240 V AC; 47-63 Hz; 1.35-0.53 A	100-240 V AC; 47-63 Hz; 1.35-0.53 A
Power Adapter Output	24 V DC; 0.75 A; 50 W max	24 V DC; 0.75 A; 50 W max	24 V DC; 0.75 A; 50 W max
Cable length	150 cm	150 cm	150 cm

ScreenShaker

By using the ScreenShaker a constant moistening of the AllergyScreen®/AlleisaScreen® troughs is ensured during incubation time. This system can be used with a maximum capacity of 2 complete incubation boxes (stacked upon each other). It is important to look for an accurate positioning of the incubation boxes upon the carrier plate of the ScreenShaker. The ScreenShaker must be water leveled to ensure an uniform distribution of the development solutions.

ScreenShaker with incubation box during test processing

Excellent results at a greatly reduced cost

Comparative Studies

AllergyScreen® in comparison with a single allergen determination system (in-house studies)

Latex

Sensitivity:	92.9 %
Specificity:	100.0 %
Accuracy:	92.9 %

Bee

Sensitivity:	93.8 %
Specificity:	100.0 %
Accuracy:	97.2 %

Wasp

Sensitivity:	95.7 %
Specificity:	78.6 %
Accuracy:	89.2 %

Food

Sensitivity:	76.8 %
Specificity:	77.5 %
Accuracy:	77.1 %

Comparison of a single allergen determination system (SADS), skin-prick test and AllergyScreen® (Inhalative allergens)

Sensitivity

Prick-test/AllergyScreen®:	95.1 %
Prick-test/SADS:	95.8 %
SADS /AllergyScreen®:	84.3 %

Specificity

Prick-test/AllergyScreen®:	80.2 %
Prick-test/SADS:	76.1 %
SADS/AllergyScreen®:	95.0 %

Accuracy

Prick-test/AllergyScreen®:	88.3 %
Prick-test/SADS:	87.5 %
SADS/AllergyScreen®:	90.6 %

A comparison with an established single allergen determination system (SADS) and skin test has shown that the AllergyScreen® system offers a highly effective method for determining a patient's comprehensive specific sensitization pattern. The sensitivity and specificity of the system is very similar to skin testing, and corresponds to a conventional single allergen system.

What's more, the Allergy-/AlleisaScreen® systems achieve precise results at a low cost and with a minimum material expenditure.

A complete study overview is available on our website: www.mediwiss-analytic.de. Simply register and you will be provided with a login-password. You are also welcome to contact us directly for further information.

Kersten, W. (2002). Allergologie, Band 25(4): 203-208.

Intra-assay and Inter-assay for AllergyScreen® and AlleisaScreen®

Intra-assay and Inter-assay for AllergyScreen®

Intra-assay variation: mean value	3.1 %
Inter-assay variation: mean value	4.5 %

Intra-assay and Inter-assay for AlleisaScreen®

Intra-assay variation: mean value	3.3 %
Inter-assay variation: mean value	3.5 %

(In-house study, 2019)

Excellent results at a greatly reduced cost

Comparative Studies

Comparison of the AllergyScreen®/AlleisaScreen® results with the target values of a reference in an international ring trial

Introduction

The company MEDIWISS Analytic GmbH was taking part in a ring trail from 2002 until 2018. Most of the other participants used a single allergen determination system from a competitor for specific IgE.

Each quarter serum samples from patients with a clinical relevant sensitisation were sent to all participants. These samples were processed according to the standard procedure of the laboratory. The findings of the tests were reported back to the institute of the University hospital in Graz, Austria. After all participants had submitted the results of their testing, all findings were summarised in a table and sent back to the participants. The most frequently determined "RAST" class was rated as definitely correct [1]. These values were used as reference values in this study.

Results

Comparison of the results for all allergens obtained with the AllergyScreen®/AlleisaScreen® test systems and the reference system. The results were used for calculating the sensitivity, specificity and concordance of the AllergyScreen®/AlleisaScreen® test, respectively.

All allergens		Reference		
		negative	positive	total
AllergyScreen®/ AlleisaScreen®	negative	**53**	**117**	170
	positive	**4**	**1161**	1165
	total	57	1278	1335

Sensitivity: 90.85 %

Specificity: 92.98 %

Concordance: 90.94 %

Cross-tabulation of the results of all allergens. The results obtained with the AllergyScreen®/ AlleisaScreen® test system and the reference system are given in "RAST" classes, respectively.

All allergens	Reference-System								
AllergyScreen®/ AlleisaScreen®	**Classes**	**0**	**1**	**2**	**3**	**4**	**5**	**6**	**total**
	0	**53**	14	71	27	5	0	0	170
	1	0	**8**	53	28	1	0	0	90
	2	2	9	**146**	106	20	0	0	283
	3	2	3	87	**220**	70	20	7	409
	4	0	0	16	86	**75**	20	5	202
	5	0	0	3	28	21	**13**	3	68
	6	0	0	0	23	44	24	**22**	113
	total	57	34	376	518	236	77	37	**1335**

Internal study MEDIWISS Analytic GmbH, Germany "2019-03 Comparison of the AllergyScreen®/ AlleisaScreen® results with the target values of an international ring trial".

[1] Comparability and quality of IgE-based in vitro allergy diagnosis: 25 years of external quality assessment; Lukas Koch, Werner Aberer; Wien Klin Wochenschr (2014) **126**:631-641

There are several other published studies about analytical and clinical performance of AllergyScreen®/ AlleisaScreen® tests which can be requested from the manufacturer.

MEDIWISS Analytic GmbH

MEDIWISS Analytic GmbH has been developing, manufacturing and selling their own medical products since the foundation in 1999 in Moers, Germany. Our experience in allergologic *in vitro* diagnostics, developments and technologies have transformed us into a worldwide company that plays an important role in allergy screening diagnostics.

Our guiding objective is to provide a complete system for the allergy screening of specific IgE antibodies with test panels, hardware, software and customer support. Team members are certified biologists and are regularly trained in the latest medical requirements in the field of allergy and immunology.

Our aim is to simplify professional allergy diagnostics with concomitant sensitivity and specificity. To this end, our products are developed and manufactured to meet the highest standards. Customer suggestions and requirements are taken into consideration since their input ensures the optimal support of customers and distributors around the world.

Our pursuit of quality is demonstrated by our certification according to ISO 13485:2016.

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