



FOX FOOD XPLOER INSTRUCTIONS FOR USE

TABLE OF CONTENTS

I.	LANGUAGE DISCLAIMER	2
II.	LIABILITY STATEMENT	2
III.	DESCRIPTION	2
IV.	INTENDED PURPOSE	3
V.	SUMMARY AND EXPLANATION OF THE TEST	3
VI.	PRINCIPLE OF THE PROCEDURE	4
VII.	SHIPMENT AND STORAGE	4
VIII.	WASTE DISPOSAL	4
IX.	GLOSSARY OF SYMBOLS	5
X.	KIT COMPONENTS	6
XI.	REQUIRED EQUIPMENT FOR PROCESSING AND ANALYSING	8
XII.	HANDLING OF ARRAYS	9
XIII.	WARNINGS AND PRECAUTIONS	9
XIV.	ASSAY PROCEDURE	10
XV.	QUALITY CONTROL	15
XVI.	DATA ANALYSIS	15
XVII.	RESULTS	15
XVIII.	LIMITATIONS OF THE PROCEDURE	16
XIX.	EXPECTED VALUES	16
XX.	PERFORMANCE CHARACTERISTICS	17
XXI.	WARRANTY	19
XXII.	ABBREVIATIONS	19



I. LANGUAGE DISCLAIMER

These Instructions for Use (IFU) is provided in multiple languages according to regulation (EU) 2017/746. In the event of any discrepancies or inconsistencies between the English version and any translated version, the English version shall prevail and be considered the authoritative reference.

II. LIABILITY STATEMENT

This IFU has been reviewed for accuracy. The instructions for the FOX Food Xplorer were correct at the time of publication. Subsequent versions of this guide may be updated without prior notice.

The FOX Food Xplorer kit is an in-vitro diagnostic test intended for use by trained laboratory personnel only. The FOX Food Xplorer kit may only be used for its intended purpose in accordance with this IFU. The IFU must be observed without exception. If you are unfamiliar with the use of the FOX Food Xplorer kit, you are obliged to obtain information from MacroArray Diagnostics (MADx) before using it. MADx assumes no liability for improper use of the FOX Food Xplorer kit. MADx shall only be liable for any harm or damage to property directly or indirectly resulting from errors in this IFU in the event of gross negligence or intent, and for personal injury only within the scope of the mandatory statutory provisions.

If any term or provision in this IFU shall be held to be illegal or unenforceable, in whole or in part, under any enactment or rule of law, such term or provision or part shall to that extent be deemed not to form part of this IFU but the enforceability of the remainder of this IFU shall not be affected.

This guide is protected by copyright. No part of it may be duplicated, reproduced, or copied in any electronic or machine-readable format without prior written permission from MADx.

III. DESCRIPTION

The FOX Food Xplorer is an Enzyme-Linked Immunosorbent Assay (ELISA) – based in-vitro diagnostic test for the semi-quantitative measurement of specific immunoglobulin G (IgG). It detects all four IgG subtypes (IgG1-4) and reports a combined total value, without distinguishing between individual subtypes.

Clinical Significance

Elevated IgG levels do not necessarily have to be associated with clinical conditions related to food allergies. The test's ability to produce results associated with food allergy diagnosis is insignificant. The test could generate results about the IgG levels, which could aid in ranking the possibility of a disease but is not the basis to make a diagnosis.



These Instructions for Use are applicable for the following products:

Basic UDI-DI	REF	Product
91201229280KC	80-5001-01	FOX for 50 Analyses
	80-0001-01	FOX for 250 Analyses

IV. INTENDED PURPOSE

The Food Xplorer (FOX) is an Enzyme-Linked Immunosorbent Assay (ELISA) – based in-vitro diagnostic tests for the semi-quantitative measurement of specific immunoglobulin G (IgG) against 286 food antigens. The Food Xplorer is suitable for use with serum or plasma. FOX can be used to support dietary clarification and to monitor dietary compliance. Furthermore, FOX can be used in case of reasonable suspicion of immunologically caused food intolerance. Before starting a diet based on FOX results, it is important to discuss the results with a physician or a dietician. The processing of FOX should always be carried out by professionally trained personnel and/or medical professionals.

V. SUMMARY AND EXPLANATION OF THE TEST

An IgG-mediated food intolerance (also: delayed food hypersensitivity reaction, type III food allergy) can be triggered by any food. The associated symptoms can occur anywhere in the body - but often with a delay (2-72 hours) and range from gastrointestinal complaints to joint pain and migraines. Therefore, the food consumed is usually not directly associated with the reaction and an intolerance often remains undetected.

An IgG-mediated food intolerance usually has its origin in a damaged intestinal barrier, which has increased permeability due to diseases of the digestive tract, inflammation, leaky gut syndrome, the use of medication, etc. Food components can pass undigested or incompletely digested through the intestinal cells and are then recognized by the immune system causing IgG antibody production to be initiated.

Symptom-triggering foods can be identified by detecting food-specific IgG antibodies in human serum. A change in diet and avoidance of the corresponding foods can improve the symptoms.

There is no restriction on the test population. When developing IgG assays, age and sex are typically not considered as critical factors because IgG levels, which are measured in these assays, do not significantly vary based on these demographics.

All food groups are covered by the FOX Food Xplorer. The complete list of FOX food extracts can be found at the end of the instructions for use.

Important information for the user!

For the correct use of FOX, it is necessary for the user to carefully read and follow these instructions for use. The manufacturer assumes no liability for any use of this test system not described in this document or for modifications by the user of the test system.



All further product information can be found in the corresponding instructions for use: <https://www.madx.com/extras>.

VI. PRINCIPLE OF THE PROCEDURE

FOX is a solid-phase immunoassay based on Enzyme-Linked Immunosorbent Assay (ELISA). Food extracts, which are coupled to nanoparticles, are deposited in a systematic fashion onto a solid phase forming a macroscopic array. First, the particle-bound proteins react with specific IgG that is present in the patient's sample. After incubation, non-specific IgG is washed off. The procedure continues by adding an enzyme-labelled anti-human IgG detection antibody which forms a complex with the antigen bound specific IgG. After a second washing step, substrate is added, which is converted to an insoluble, colored precipitate by the antibody-bound enzyme. Finally, the enzyme-substrate reaction is stopped by adding a blocking reagent. The amount of precipitate is proportional to the reactivity of specific IgG in the patient sample. The lab test procedure is followed by image acquisition and analysis using the manual system (ImageXplorer) or the automated system (MAX 9k or MAX 45k). The test results are analyzed with RAPTOR SERVER Analysis Software and reported in IgG classes. RAPTOR SERVER is available in version 1, for the full four-digit version number please refer to the RAPTOR SERVER imprint available at www.raptor-server.com/imprint.

VII. SHIPMENT AND STORAGE

The shipment of FOX takes place at ambient temperature conditions. Nevertheless, the kit must be stored immediately upon delivery at 2-8 °C. Stored correctly, FOX and its components can be used until the indicated expiration date.



Kit reagents are stable for 6 months after opening (at the indicated storage conditions).

VIII. WASTE DISPOSAL

Dispose the used FOX cartridge and unused kit components with laboratory chemical waste. Follow all national, state, and local regulations regarding disposal.



IX. GLOSSARY OF SYMBOLS

	Warning (GHS pictogram) Consult the Safety Data Sheet for more information.
	Catalogue number
	Sufficient for <n> tests
	Do not use if packaging is damaged
	In-vitro diagnostic medical device
	CE mark
	Lot code
	Consult instructions for use
	Manufacturer
	Date of manufacture
	Do not re-use



	Cartridge
	Use-by date
	Temperature limit
	Caution
	Unique device identifier
	MacroArray Diagnostics (MADx)

X. KIT COMPONENTS

New Nomenclature for Reagent Lots

Attention: We are introducing a new lot nomenclature for all MADx reagents (the nomenclature for the cartridges is not affected).

FOX kits with lot number 80DAA01 and subsequently produced lots will be affected by this change.

Key Details:

- **No change for cartridge labels**
- The specific reagents of one reagent lot will show the same label nomenclature and can be combined with different cartridge lots.

We will only vary **position 1 and 2** of our **three-letter code** for the reagents. For instance:

- Reagents with labels **DAA** can be combined with the cartridge lots **DAA, DAB, DAC, DAD,... up to DAT**.
- Reagents with labels **DBA** can be combined with the cartridge lots **DBA, DBB, DBC, DBD,... up to DBT**.



- The RAPTOR SERVER Analysis Software has already been updated to reflect these changes. **No action is required from customers.**

The RAPTOR SERVER will recognize and combine the correct cartridges with the corresponding reagents.

Each component (reagent) is stable until the date stated on each individual component's label. Do not combine or mix reagents from different reagent lots (different first two letters). For a list of antigen extracts and molecular antigens immobilized on the FOX array, please contact pm@macroarraydx.com.

Kit Components REF 80-5001-01	Content	Properties
FOX Cartridge	5 Blisters à 10 FOX for 50 analyses in total	Ready for use. Store at 2-8°C until expiry date. Opened blister is stable for 6 months at 2-8°C.
FOX Sample Diluent	1 bottle à 30 ml	Ready for use. Store at 2-8°C until expiry date. Allow reagent to reach room temperature before use. Opened reagent is stable for 6 months at 2-8°C.
Washing Solution	4 x conc. 1 bottle à 250 ml	Store at 2-8°C until expiry date. Dilute 1:4 with demineralized water before use (250 ml Washing Solution 4x conc. + 750 ml demineralized water). Allow reagent to reach room temperature before use. Opened reagent is stable for 6 months at 2-8°C.
FOX Detection Antibody	1 bottle à 30 ml	Ready for use. Store at 2-8°C until expiry date. Allow reagent to reach room temperature before use. Opened reagent is stable for 6 months at 2- 8°C.
FOX Substrate Solution	1 bottle à 30 ml	Ready for use. Store at 2-8°C until expiry date. Allow reagent to reach room temperature before use. Opened reagent is stable for 6 months at 2- 8°C.
(FOX) Stop Solution	1 bottle à 10 ml	Ready for use. Store at 2-8°C until expiry date. Allow reagent to reach room temperature before use. Opened reagent is stable for 6 months at 2-8°C. May appear as a turbid solution after prolonged storage. This has no effect on results.



Kit Components REF 80-0001-01	Content	Properties
FOX Cartridge	5 Blisters à 50 FOX for 250 analyses in total.	Ready for use. Store at 2-8°C until expiry date. Opened blister is stable for 6 months at 2-8°C.
FOX Sample Diluent	5 bottles à 30 ml	Ready for use. Store at 2-8°C until expiry date. Allow reagent to reach room temperature before use. Opened reagent is stable for 6 months at 2- 8°C.
Washing Solution	4 x conc. 5 bottles à 250 ml	Store at 2-8°C until expiry date. Dilute 1 to 4 with demineralized water before use (250 ml Washing Solution + 750 ml demineralized water). Allow reagent to reach room temperature before use. Opened reagent is stable for 6 months at 2-8°C.
FOX Detection Antibody	5 bottles à 30 ml	Ready for use. Store at 2-8°C until expiry date. Allow reagent to reach room temperature before use. Opened reagent is stable for 6 months at 2- 8°C.
FOX Substrate Solution	5 bottles à 30 ml	Ready for use. Store at 2-8°C until expiry date. Allow reagent to reach room temperature before use. Opened reagent is stable for 6 months at 2- 8°C.
(FOX) Stop Solution	5 bottles à 10 ml	Ready for use. Store at 2-8°C until expiry date. Allow reagent to reach room temperature before use. Opened reagent is stable for 6 months at 2-8°C. May appear as a turbid solution after prolonged storage. This has no effect on results.

XI. REQUIRED EQUIPMENT FOR PROCESSING AND ANALYSING

Manual Analysis:

- ImageXplorer (REF 11-0000-01)
- Arrayholder (optional)
- Lab Rocker (inclination angle 8°, required speed 8 rpm)
- Incubation chamber (WxDxH – 35x25x2 cm)
- RAPTOR SERVER Analysis Software
- PC/Laptop



Required equipment, not provided by MADx:

- Demineralized water
- Pipettes & tips (100 µl & 100 - 1000 µl)

Automatic Analysis:

- MAX device (MAX 9k or MAX 45k – REF 17-0000-01 or REF 16-0000-01)
- Washing Solution (REF 00-5003-01)
- Stop Solution (REF 00-5007-01)
- RAPTOR SERVER Analysis Software
- PC/Laptop

Maintenance services according to manufacturer's instructions.

XII. HANDLING OF ARRAYS

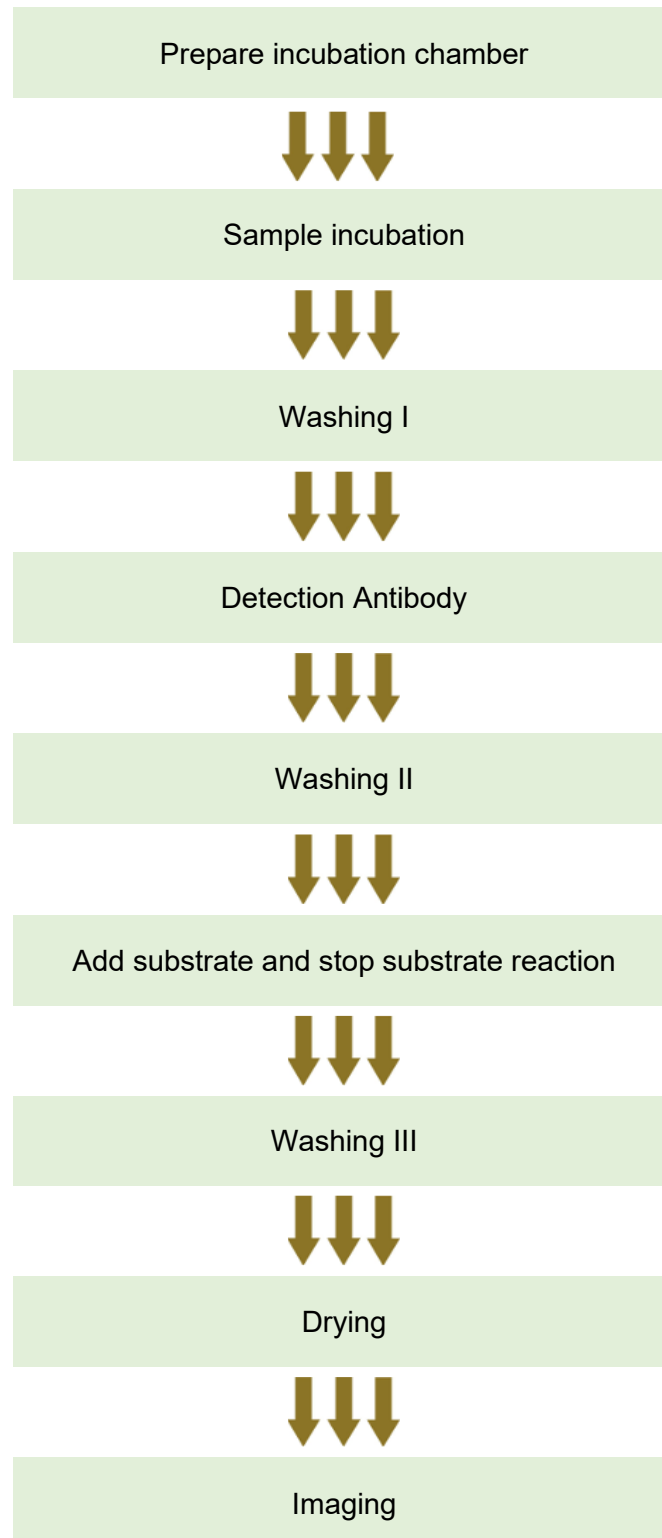
Do not touch the array surface. Any surface defects caused by blunt or sharp objects can interfere with the results. Do not acquire FOX images before array is completely dry (dry at room temperature).

XIII. WARNINGS AND PRECAUTIONS

- It is recommended to wear hand and eye protection as well as lab coats and follow good laboratory practice when preparing and handling reagents and samples.
- In accordance with good laboratory practice, all blood source material (e.g. ingredients in reagents or other components) should be considered potentially infectious and handled with the same precautions as blood samples.
- The FOX Sample Diluent is partially prepared from human blood sources. The product was tested non-reactive for Hepatitis B Surface Antigen (HBsAg), antibodies to Hepatitis C (HCV) and antibodies to HIV-1/HIV-2.
- FOX Sample Diluent and Washing Solution contain sodium azide as a preservative and must be handled with care. Safety data sheet is available upon request.
- The (FOX) Stop Solution contains Ethylenediaminetetraacetic acid (EDTA)-Solution and must be handled with care. Safety data sheet is available upon request.
- For in-vitro diagnostic use only. Not for internal or external use in humans or animals.
- Only personnel trained in laboratory practice should use this kit.
- Upon arrival, check the kit components for damage. If one of the components is damaged (e.g. buffer bottles), contact MADx (support@madx.com) or your local distributor. Do not use damaged kit components, as their use may lead to poor kit performance.
- Do not use reagents beyond their expiry dates.
- Do not mix reagents from different lots.



XIV. ASSAY PROCEDURE





Preparation

Preparation of samples: Serum or plasma (heparin, citrate, EDTA) samples from capillary or venous blood can be used. Blood samples can be collected using standard procedures. Store samples at 2–8 °C for up to one week. Keep serum and plasma samples at -20 °C for prolonged storage. Shipment of serum/plasma samples at room temperature is applicable. Always allow samples to reach room temperature before use.

Preparation of Washing Solution (for REF 80-5001-01 und REF 80-0000-01): Pour the content of 1 vial of Washing Solution into the washing container of the instrument. Fill demineralized water up to the mark and carefully mix the container several times without generating foam. The opened reagent is stable for 6 months at 2-8 °C.

Personnel using the automated procedure of FOX must be trained in handling MAX devices (MAX45k or MAX9k). Instructions on how to run a test are provided in MAX IFU subchapters XVII.7-10 and must be followed.

Automatically processed FOX tests **must be prediluted manually**. Requirements and instructions for dilutions are available in the MAX IFU chapter XXI (Technical Specification).

The current version of the MAX IFU (Systems) can be found here:
<https://www.madx.com/de/extras>

	The minimum sample volume required for FOX test using only Low Volume tubes is 600 µl, which consists of 12 µl serum mixed with 588 µl of Sample Diluent.
--	--

Incubation chamber: Close lid for all assay steps to prevent drop in humidity.

Parameters of manual procedure:

- 10 µl sample + 490 µl FOX Sample Diluent
- 500 µl FOX Detection Antibody
- 500 µl FOX Substrate Solution
- 100 µl (FOX) Stop Solution
- 4500 µl Washing Solution

Assay time is approximately 3 h 30 min (without drying of processed array).

It is not recommended to run more assays than can be pipetted in 8 min. All incubations are performed at room temperature, 20-26 °C.

	All reagents are to be used at room temperature (20-26 °C). The assay must not be performed in direct sunlight.
--	--



Prepare incubation chamber

Open incubation chamber and place paper towels on bottom part. Soak paper towels with demineralized water until no dry parts of the paper towels are visible.

1. Sample incubation

Predilute 10 µl sample with 490 µl FOX Sample Diluent in a separate tube. Take out the needed number of FOX cartridges and place them into the array holder(s). Add 500 µl of the prediluted sample to the cartridges. Ensure that the resulting solution is spread evenly. Place the cartridges in the prepared incubation chamber and put the incubation chamber with the cartridges on the lab rocker so that the cartridges rock along the long side of the cartridge. Start the serum incubation at 8 rpm for 2 hours. Close the incubation chamber before starting the lab rocker. After 2 hours, discharge the patient samples into a collection container and vigorously tap the cartridges on a stack of dry paper towels to remove droplets.



Avoid touching the array surface with the paper towel! Avoid any carry over or cross-contamination of patient samples between individual FOX cartridges!

1a. Washing I

Add 500 µl Washing Solution to each cartridge and incubate on the lab rocker (at 8 rpm) for 5 minutes. Discharge the Washing Solution into a collection container and vigorously tap the cartridges on a stack of dry paper towels.

Repeat this step 2 more times.

2. Add Detection Antibody

Add 500 µl of FOX Detection Antibody to each cartridge.



Make sure that the complete array surface is covered by the FOX Detection Antibody solution.

Place the cartridges into the incubation chamber on the lab rocker and incubate at 8 rpm for 30 minutes. Discharge the Detection Antibody solution into a collection container and vigorously tap the cartridges on a stack of dry paper towels.



2a. Washing II

Add 500 µl Washing Solution to each cartridge and incubate on the lab rocker at 8 rpm for 5 minutes. Discharge the Washing Solution into a collection container and vigorously tap the cartridges on a stack of dry paper towels.

Repeat this step 4 more times.

3+4. Add Substrate Solution and stop substrate reaction

Add 500 µl of FOX Substrate Solution to each cartridge. The timer should be started upon filling the first cartridge, followed by the filling of the remaining cartridges. Make sure that the complete array surface is covered by the Substrate Solution and incubate the arrays for exactly 8 minutes without shaking (**lab rocker at 0 rpm and in horizontal position**).

After exactly 8 minutes, add 100 µl of the (FOX) Stop Solution to all cartridges, starting with the first cartridge to assure that all arrays are incubated for the same time with the Substrate Solution. After the (FOX) Stop Solution has been pipetted onto all arrays, gently agitate the cartridge to ensure even distribution of the solution. Afterwards discharge (FOX) Substrate/Stop Solution from the cartridges and vigorously tap the cartridges on a stack of dry paper towels.



The Lab Rocker must NOT SHAKE during substrate incubation!

4a. Washing III

Add 500 µl Washing Solution to each cartridge and incubate on the lab rocker at 8 rpm for 30 seconds. Discharge the Washing Solution into a collection container and vigorously tap the cartridges on a stack of dry paper towels.

5. Image analysis

After finishing the assay procedure, air dry the arrays at room temperature until they are completely dry (can take up to 45 min). If the arrays require an extended drying period, they should be stored in a light-protected environment until analysis.



The complete drying is essential for the sensitivity of the test. Only completely dried arrays provide an optimal signal-to-noise ratio.



Finally, the dried arrays are scanned with the ImageXplorer or a MAX device and analyzed with RAPTOR SERVER Analysis Software (see details in the RAPTOR SERVER software handbook). The RAPTOR SERVER Analysis Software is only verified in combination with the ImageXplorer instrument or the MAX devices, therefore MADx does not take any responsibilities for results which have been obtained with any other image capture device (like scanners).

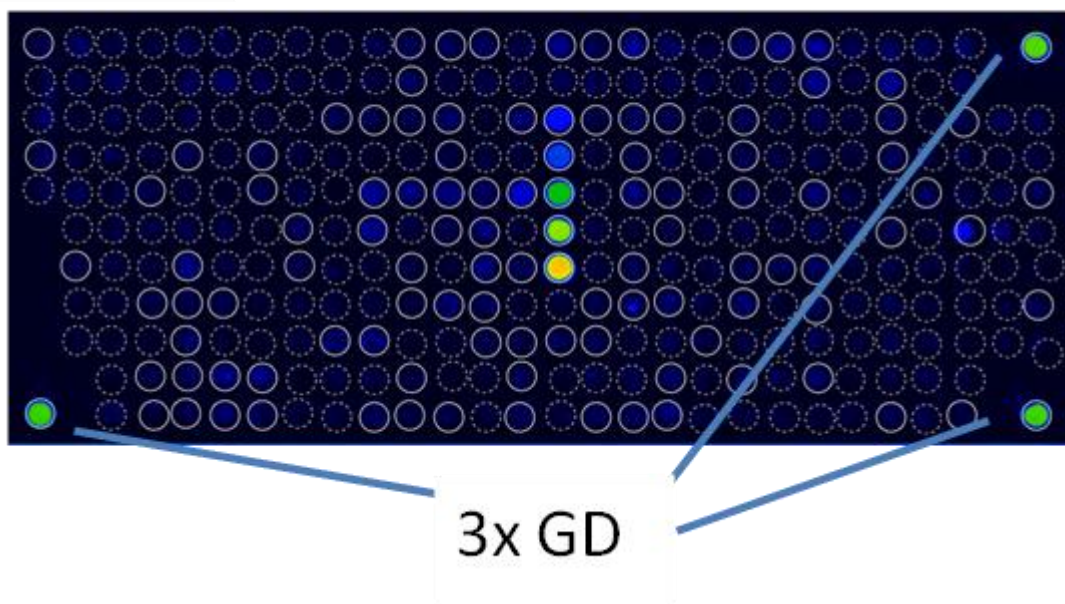
The array with the grid is displayed in the analytical image area. The software automatically locates the array by detecting the Guide Dots (GD). FOX contains three Guide Dots for this purpose.

After processing, the Guide Dots have to be easily visible with the naked eye. Please also verify their correct orientation as shown in the image for FOX below. If they are not visible, please contact your local distributor or MADx support on how to proceed. In case the Guide Dots are visible, the cartridge can be further analyzed.

During the image acquisition of an FOX cartridge, RAPTOR SERVER evaluates the signal of all Guide Dots as well as the background signal of the membrane surface. If all quality criteria are fulfilled, the “automatic QC” field under the image is set to “OK”.

In order to exclude the influence of artifacts in the automated image analysis (satellite spots, sample contaminations, dust, smeared spots, ...), the images must be checked by a trained operator before the results are approved in order to exclude false results. In case of discrepancies between the processed array and the image acquired by the RAPTOR SERVER please consult your local distributor or MADx Support.

FOX





Assay Calibration

Semi-quantitative evaluation of the test results is based on a heterologous calibration against an IgG reference curve. Curve parameters are determined from the standard features of the test panel. A curve fit is calculated, and the resulting equation applied to transform arbitrary intensity units into quantitative units. The standard curve for each lot is adjusted by in-house reference testing against serum samples tested on a reference test system for specific IgG against several antigens. Lot specific calibration parameters are provided by the RAPTOR SERVER Analysis Software and selected according to the lot-specific QR codes. FOX sIgG test results are expressed as µg/ml.

Measuring Range

Specific IgG 5.0 - 50.0 µg/ml

XV. QUALITY CONTROL

Record keeping for each assay

According to good laboratory practice it is recommended to record the lot numbers of all reagents used.

Control Specimens

According to good laboratory practice it is recommended that quality control samples are included within defined intervals.

XVI. DATA ANALYSIS

For the image analysis of processed arrays, the ImageXplorer or a MAX device has to be used. FOX images are automatically analyzed using RAPTOR SERVER Analysis Software and a report is generated summarizing the results for the user.

XVII. RESULTS

FOX is a semi-quantitative ELISA method for specific IgG. Specific IgG antibodies are expressed as IgG response units (µg/ml). RAPTOR SERVER Analysis Software automatically calculates and reports sIgG results semi-quantitatively as classes (negative, low, intermediate and highly elevated).



XVIII. LIMITATIONS OF THE PROCEDURE

The IgG reactivity determined with the FOX test system shows the degree of sensitization of the patient to the food antigens investigated. A correlation between the level of the determined IgG reactivity and the occurrence or severity of clinical symptoms cannot be deduced.

The results obtained must always be interpreted in combination with the full clinical symptoms. A definitive clinical diagnosis should only be made in conjunction with all available clinical findings by medical professionals and shall not be based on results of a single diagnostic method only.

False-positive test results may occur due to cross-reactivity of the tested antigen with epitopes of other antigens. Antigenic epitopes may be lost during the production of food extracts, which may lead to false-negative results. IgG antibodies to food antigens that occur only during industrial preparation, food preparation, or digestion may not be detectable in the patient sample.

Attention:

- The test result does not diagnose food allergies as these are IgE-mediated allergic disorders.
- The test result does not diagnose food intolerance (e.g. lactose or fructose intolerance).
- The test result does not diagnose coeliac disease.

XIX. EXPECTED VALUES

The close association between antigen-specific IgG antibody levels and type III food allergy symptoms is well known and is described in literature (see section "References" below). Each patient will show an individual IgG profile when tested with FOX. The IgG response with samples from healthy individuals will be below 10.0 µg/ml for single food antigens when tested with FOX. Good laboratory practice recommends that each laboratory establishes its own range of expected values.



XX. PERFORMANCE CHARACTERISTICS

1. Precision (lot-to-lot variation) with ImageXplorer

The lot-to-lot variation was determined on three cartridge lots in three separate runs. Multi-sensitized samples were included in the study. The study comprised 867 antigen/sample combinations covering 121 individual antigens over the entire measuring range.

	10.0 - 19.9 µg/ml	≥ 10.0 µg/ml	≥ 20.0 µg/ml
Total CV%	9.1	6.3	4.3

2. Precision with MAX devices

The variation between different MAX devices in the FOX assay was determined on three MAX 9k devices in three separate runs (same FOX lot). Three selected multi-sensitized samples were tested covering the majority of priority antigens. For the selected antigens, the CV (in %) was calculated between runs and between instruments (= total CV).

	10.0 - 19.9 µg/ml	≥ 10.0 µg/ml	≥ 20.0 µg/ml
Total CV% MAX 9k	8.8	6.2	5.0

3. Repeatability (within-run precision) with ImageXplorer

In the repeatability study, multi-sensitized samples were tested 10 times by the same operator on different days. The study comprised 862 antigen/sample combinations covering 115 individual antigens over the entire measuring range.

	10.0 - 19.9 µg/ml	≥ 10.0 µg/ml	≥ 20.0 µg/ml
Total CV%	11.3	7.2	5.4

4. Homogeneity with MAX devices

The homogeneity of the FOX results within a MAX 9k test run was tested on three separate MAX 9k devices. A single multi-sensitized positive test sample was tested at all positions of the cartridge carousel.

	10.0 - 19.9 µg/ml	≥ 10.0 µg/ml	≥ 20.0 µg/ml
Total CV%	8.3	6.3	5.6



5. Analytical sensitivity

Analytical sensitivity is a measurement of the accuracy of a test at low concentrations of the analyte. The Limit of Detection (LOD) of the FOX test is 5.0 µg/ml for all food extracts.

6. Analytical specificity

To determine the analytical specificity, different immunoglobulins were printed on the cartridge using the same protocol as for the IgG guide dots (spotting on nitrocellulose at 0.125 und 0.25 mg/ml, respectively). The specificity of the detection antibody was then measured as positive signal on each immunoglobulin spot. The following signals were detected for each Ig subtype:

	IgE	IgM	IgA
Signal - Noise value	0.83 µg/ml	0.28 µg/ml	6.9 µg/ml

All values were below the claimed specification of < 8 µg/ml. IgD was not tested, as it is typically present at much lower concentrations than other immunoglobulins. In summary, no detectable cross-reactivity with other human immunoglobulins is observed at normal physiological concentrations.

7. Interference

There is no detectable interference with bilirubin (10 µg/ml), triglycerides (5 mg/ml) and hemoglobin (0.2 g/ml) at normal physiological concentrations.

8. Sample type

Four different types of samples have been tested: serum, heparin plasma, EDTA and citrate plasma. The different sample types were collected from 3 blood donors covering the most important antigens.

The serum values serve as reference values. All other samples are assessed relative to serum. Specification: 90% of the values for the other samples must fall within ±25% of serum values.

The results show that the different sample types do not interfere with the results.

Parameter	Heparin	Citrate	EDTA
% within ± 25%	100.0	99.1	100.0
Mean quotient against serum	1.03	1.0	1.0



9. Information on clinical performance

The clinical performance and clinical evidence evaluation is covered with the correlation study. In the correlation study, around 20 positive samples covering ≥ 50 positive responses (covering the measuring range for the priority foods) have been tested with FOX and with a reference test (RIDA Chip Foodguide by R-Biopharm). The correlation of the different test systems was evaluated. All tested priority food extracts displayed a qualitative agreement with the reference test system of $> 50\%$. The mean qualitative agreement with the reference test system was 81.2 % for the majority of the priority food extracts.

Additionally, for the comparison of the two FOX methods (manual vs. automated assay) 27 plasma and/or serum samples were tested and the IgG level (in $\mu\text{g/ml}$) for each food extract/sample combination was compared between the two FOX methods. The results between the manual and the automated system were comparable and R^2 was 0.98.

XXI. WARRANTY

The performance data presented were obtained using the procedure outlined in these Instructions for Use. Any change or modification in the procedure may affect the results and MacroArray Diagnostics disclaims all warranties expressed (including the implied warranty of merchantability and fitness for use) in such an event. Consequently, MacroArray Diagnostics and its local distributors shall not be liable for damages indirect or consequential in such an event.

XXII. ABBREVIATIONS

FOX	Food Xplorer
EDTA	Ethylenediaminetetraacetic acid
ELISA	Enzyme-Linked Immunosorbent Assay
IgG	Immunoglobulin G
IVD	In-vitro diagnostic
MADx	MacroArray Diagnostics
REF	Reference number
rpm	Rounds per minute
slgG	Specific IgG
μl	Microliter



ANTIGEN LIST FOX

Vegetables: Artichoke, Arugula, Avocado, Bamboo sprouts, Broccoli, Brussels sprouts, Cabbage, Caper, Carrot, Cauliflower, Celery bulb, Celery stalk, Chard, Chicorée, Chinese cabbage, Chives, Cucumber, Eggplant, Endive, Fennel (bulb), Garlic, Green cabbage, Horseradish, Kiwano, Kohlrabi, Lamb's lettuce, Leek, Nettle leaves, Olive, Onion, Parsnip, Pok-Choi, Potato, Pumpkin (butternut), Pumpkin (hokkaido), Radicchio, Radish, Red beet, Red cabbage, Romanesco, Savoy, Shallot, Spinach, Sweet potato, Tomato, Turnip, Watercress, White Asparagus, White cabbage, Wild garlic, Zucchini

Fish & Seafood: Abalone, Atlantic cod, Atlantic herring, Atlantic redfish, Carp, Caviar, Cockle, Common mussel, Crab, Eel, European anchovy, European pilchard, European plaice, Gilt-head bream, Haddock, Hake, Lobster, Mackerel, Monkfish, Noble crayfish, Northern pike, Northern prawn, Octopus, Oyster, Razor shell, Salmon, Scallop, Sepia, Shrimp mix, Sole, Squid, Swordfish, Thornback Ray, Trout, Tuna, Turbot, Venus clam

Fruits: Apple, Apricot, Banana, Blackberry, Blueberry, Cherry, Cranberry, Date, Elderberry, Fig, Gooseberry, Grape, Grapefruit, Kiwi, Lemon, Lime, Lychee, Mango, Melon, Mulberry, Nectarine, Orange, Papaya, Passion fruit, Peach, Pear, Physalis, Pineapple, Plum, Pomegranate, Raisin, Raspberry, Red currant, Strawberry, Tangerine, Watermelon

Spices: Anise, Basil, Bay leaf, Caraway, Cardamom, Cayenne pepper, Chili (red), Cinnamon, Clove, Coriander, Cumin, Curry, Dill, Fenugreek, Ginger, Juniper berry, Lemongrass, Marjoram, Mint, Mustard, Nutmeg, Oregano, Paprika, Parsley, Pepper (black/white/green/red/yellow), Rosemary, Sage, Tarragon, Thyme, Turmeric, Vanilla

Cereals & Seeds: Amaranth, Barley, Buckwheat, Chickpea, Corn, Durum, Einkorn, Emmer, Gluten, Hempseed, Linseed, Lupine seed, Malt (barley), Millet, Oat, Pine nut, Polish wheat, Poppy seed, Pumpkin seed, Quinoa, Rapeseed, Rice, Rye, Sesame, Spelt, Sunflower, Wheat, Wheat bran, Wheat gliadin, Wheatgrass

Novel Foods: Almond milk, Aloe, Aronia, Baobab, Chia seed, Chlorella, Dandelion root, Ginkgo, Ginseng, Greater burdock root, Guarana, House cricket, Maca root, Mealworm, Migratory locust, Nori, Safflower oil, Spirulina, Tapioca, Wakame, Yacón root

Egg & Milk: Buffalo milk, Buttermilk, Camel milk, Camembert, Cottage cheese, Cow milk, Egg white, Egg yolk, Emmental, Goat cheese, Goat milk, Gouda, Mozzarella, Parmesan, Quail egg, Sheep cheese, Sheep milk

Meat: Beef, Boar, Chicken, Duck, Goat, Horse, Lamb, Ostrich, Pork, Rabbit, Stag, Turkey, Veal, Venison

Nuts: Almond, Brazil nut, Cashew, Coconut, Coconut milk, Hazelnut, Kola nut, Macadamia, Pecan nut, Pistachio, Sweet chestnut, Tigernut, Walnut

Coffee & Tea: Chamomile, Cocoa, Coffee, Hibiscus, Jasmine, Moringa, Peppermint, Tee (black), Tee (green)



Legumes: Green bean, Lentil, Mung bean, Pea, Peanut, Soy, Sugar pea, Tamarind, White bean

Edible Mushrooms: Boletus, Chanterelle, Enoki, French horn mushroom, Oyster mushroom, White mushroom

Other: Agar agar, Aspergillus niger, Baker's yeast, Brewer's yeast, Elderflower, Honey, Hops, M-Transglutaminase (meat glue), Cane sugar, Cross-reactive Carbohydrate Determinants

Molecular antigens: Bos d 4, Bos d 5, Bos d 8



REFERENCES

1. Clinical relevance of IgG antibodies against food antigens in Crohn's disease: a double-blind cross-over diet intervention study. Bentz, S et al. 2010; Zurich Open Repository and Archive
2. Food Exclusion Based on IgG Antibodies Alleviates Symptoms in Ulcerative Colitis: A Prospective Study. L Jian et al. 2018; Inflammatory Bowel Diseases
3. Serological investigation of IgG and IgE antibodies against food antigens in patients with inflammatory bowel disease. HY Wang et al. 2019; World Journal of Clinical Cases
4. The Value of Eliminating Foods According to Food-specific Immunoglobulin G Antibodies in Irritable Bowel Syndrome with Diarrhoea. H Guo et al. 2012; The Journal of International Medical Research
5. Prevalence of IgG-mediated food intolerance among patients with allergic symptoms. Shakoor et al. 2016; Annals of Saudi medicine
6. The Clinical Application Value of Multiple Combination Food Intolerance Testing. S Lin et al. 2018; Iranian Journal of Public Health
7. Chronic Food Antigen-specific IgG-mediated Hypersensitivity Reaction as A Risk Factor for Adolescent Depressive Disorder. R Tao et al. 2019; Genomics, Proteomics & Bioinformatics
8. Diet restriction in migraine, based on IgG against foods: A clinical double-blind, randomised, cross-over trial. Alpay et al. 2010; Cephalalgia

The connection between food intake, elevated IgG levels and chronic disorders has been described in peer reviewed publications and case studies. Nonetheless, this connection is still debated in the scientific community and a consensus has not been reached so far.

CHANGE HISTORY

Version	Description	Replaces
8.1	Typos were corrected throughout the manuscript	08



© Copyright by MacroArray Diagnostics

MacroArray Diagnostics (MADx)

Lemböckgasse 59, Top 4

1230 Vienna, Austria

+43 (0)1 865 2573

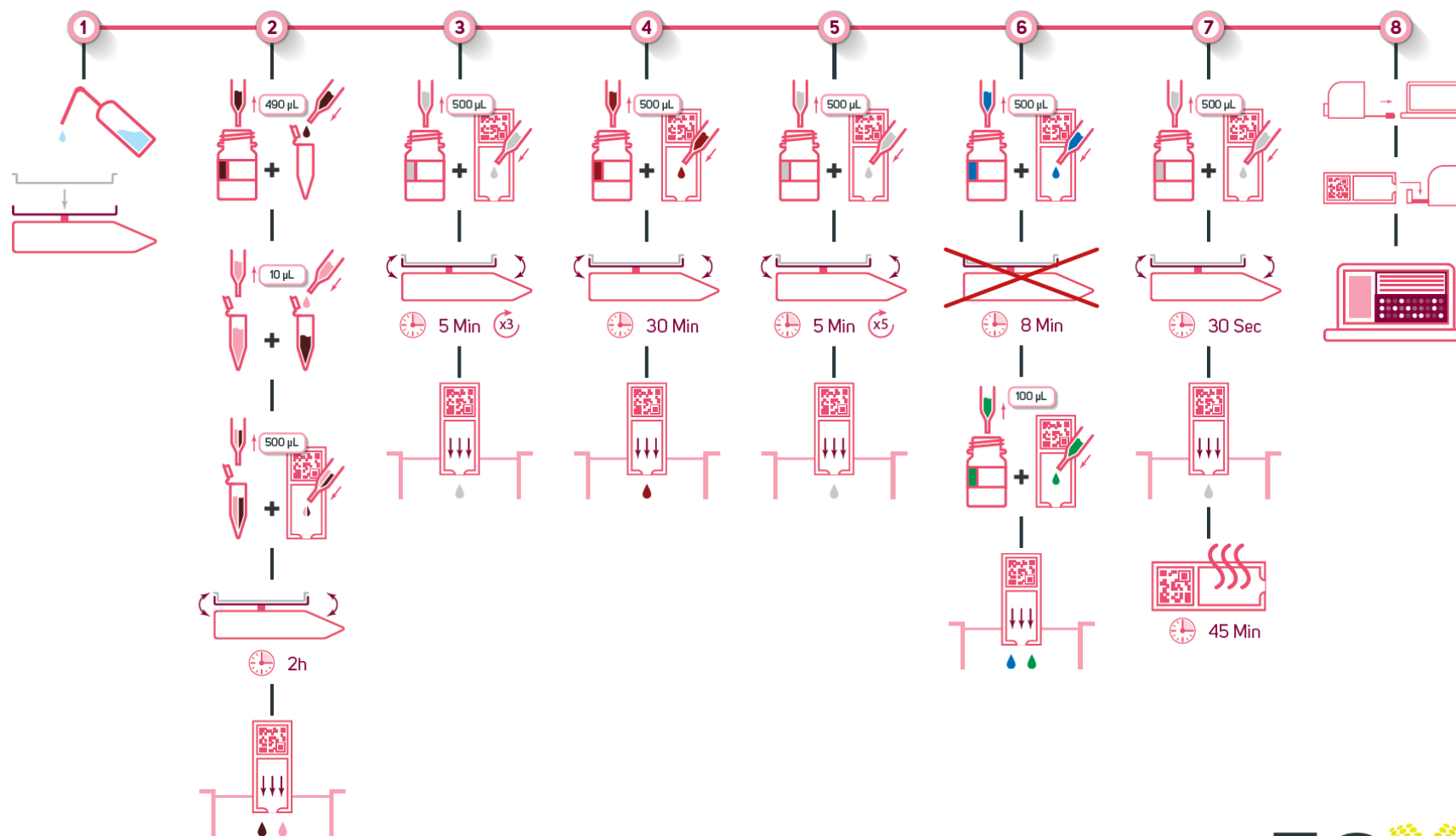
<https://www.madx.com>

Version number: 80-IFU-01-EN-8.1

Released: 09-2025



Quick Guide



● FOX Sample Diluent

● Patient Sample

● FOX Washing Solution

● FOX Detection Antibody

● FOX Substrate Solution

● FOX Stop Solution

