Honey bee venom (i1)

25 tests | Cat. No. **ED7446**

IVD CE

Instructions for Use (EN)

Version: ED7446_IFU_v1_EN

Date of Issue: 08-01-2026

Symbols used in the device labeling

IVD	In Vitro diagnostic medical device		Temperature limit
CE	CE marking of conformity		Keep away from sunlight
	Manufacturer		Keep Dry Keep away from rain
UDI	Unique Device Identifier		Caution
	Consult instructions for use		Do not re-use
	Contains sufficient for 25 tests	TUBE	Contains 25 tubes for single use test
REF	Catalogue number	CONTENTS	Contents
LOT	Batch code	UK CA	UKCA mark
	Use by date	CH REP	Indicates the authorised representative in Switzerland

1. Intended Purpose

The reagent is intended for in vitro stimulation of basophilic granulocytes in human whole blood. The reagent is intended for professional laboratory use only, not for near-patient testing or self-testing.

What is detected and/or measured

The reagent is intended for in vitro stimulation of basophilic granulocytes and does not provide a detecting or measuring function.

Device function

The reagent is intended for in vitro stimulation of basophilic granulocytes.

Context of a physiological or pathological state

Not applicable. The context of a physiological or pathological state is associated with an analyte that is a measurable marker of the patient's condition. The reagent is an allergen and does not detect or measure any analyte.

Type of assay

Not automated

The reagent does not provide qualitative, semi-quantitative or quantitative results. The reagent is intended for in vitro stimulation of basophilic granulocytes and does not provide a detecting or measuring function.

Type of specimen required

Human heparin and EDTA anticoagulated whole blood

Testing population

For use in patients suspected of having an allergy.

2. Intended user

The reagent is intended for professional laboratory use only, not for near-patient testing or self-testing.

Requirements for qualification

Intended user shall have a state-of-the-art expertise in flow cytometry analysis of human cells, standard laboratory techniques, including pipetting skills, and safe and proper handling of specimens derived from the human body.

Intended user shall be compliant with standard EN ISO 15189 or other national standards, where applicable.

3. Test principle

The surface of basophil cells contains a high-affinity FcεRI receptor to which IgE binds. Allergen molecules that have a high affinity for the FcεRI receptor bind to the receptors, forming cross-links with them, leading to the complete activation of basophils. As a result, cytoplasmic granules containing the transmembrane protein CD63 fuse with the plasma membrane and release inflammatory mediators and expose CD63 markers. The exposed CD63 antigen is a marker of basophil activation (degranulation) and is available for surface detection by a fluorescently labelled monoclonal antibody. Allergen-stimulated basophils also overexpress CD203c antigen on their surface.

4. Reagent(s) provided

Contents

The reagent Honey bee venom (i3) is provided as a lyophilized mixture of allergen extract and protective excipients in a single-use test tube, sufficient for 25 tests. The reagent is a filtered and lyophilized allergen in the presence of salts and protective excipients at an optimum amount suitable for basophil activation.

Composition

Table 1 Description of active components

Main component	Allergen name	Allergen source	Allergen code*	Amount (ng)
Honey bee venom	Api m (venom)	*Apis mellifera*	i1	77

*Allergen common names refer to allergen nomenclature described on the Allergome website. http://allergome.org/

5. Materials required but not provided

BasoFlowEx Kit (ED7043) or other basophil activation assay

6. Equipment required

Centrifuge with appropriate rotor adaptors for 12 x 75 mm round-bottom tubes

Automatic pipette with disposable tips (100 µl) for pipetting specimens

7. Storage and handling

Store at 20 - 30 °C.
Avoid prolonged exposure to light.
Keep dry.

CAUTION: Moisture-sensitive product. Do not open the foil pouch until you are ready to use it for the first time. After opening, reseal the foil pouch tightly with the zip-lock to store any remaining unused tubes. Use the remaining

allergen tubes within 12 months after the first opening.

See Section 10 Procedure (Reagent Preparation) for information about In-Use stability and shelf-life following the first opening.

8. Warnings, precautions and limitations of use

GHS Hazard Classification

Consult Safety Data Sheet (SDS) available on the product page at www.exbio.cz for the full information on the risks posed by chemical substances and mixtures contained in the Product and how they should be handled and disposed.

Biological Hazard

Human biological samples and blood specimens, and any materials coming into contact with them, are always considered infectious materials.

Use personal protective and safety equipment to avoid contact with skin, eyes, and mucous membranes.

Follow all applicable laws, regulations, and procedures for handling and disposing of infectious materials.

Evidence of deterioration

The normal appearance of the reagent provided is a dried white lentil pellet at the bottom of the tube. Do not use the reagent if you observe any change in appearance, for example, the presence of moisture inside the tube.

Limitations of use

Do not use after the expiry date stated on the product labels.

Do not reuse test tubes.

9. Specimen

Use venous peripheral blood collected into a specimen receptacle classified as a medical device, with the anticoagulant EDTA or Heparin.

Process the blood specimen no later than 48 hours after collection.

Endogenous Interference

Based on scientific literature research and CLSI-EP07, endogenous interference sources are identified in Table 2.

Table 2 Endogenous Interference of the reagent

Endogenous interference	Impact	Reference
Triglycerides	Elevated triglyceride levels corresponded to higher monocyte and basophil counts.	1

Erythrocytes	Insufficient lysis, with red blood cells present in the sample, may affect cell counting.	2
Hemoglobin	Hemolyzed samples may produce unreliable results.	3
Bilirubin	Bilirubin increases the fluorescence background of cells due to its high autofluorescence.	4
Lipemia	High circulating levels of lipids may impact the flow cytometry analysis of specific blood cell populations.	5

Exogenous Interference

Specimens older than 48 hours may yield erroneous results.

10. Procedure

Preparation of reagent(s) provided

No reagent preparation is necessary.

Keep the device's primary container dry.

Use the reagent directly from its original primary container. Time, for which the reagent is in use (exposed to light and elevated temperature), shall not exceed 4 hours per day.

Following the first opening, the reagent retains its performance characteristics until the expiry date when stored under the stated conditions in its original primary container.

Preparation of materials required but not provided

N/A. There is no need to prepare any additional materials.

Quality control

N/A. Reagent is an allergen.

Specimen staining

1. Take the labeled single-use test tube with the appropriate allergen from the bag. Thoroughly reseal the foil pouch with the zip-lock for storage of the remaining unused tubes.
2. Centrifuge the allergen single-use test tube for 1 min. at 200×g.

   CAUTION: The allergen may be released from the bottom of the tube due to harsh shipping conditions.
3. Then follow the procedure described in the IFU of the device intended for basophil activation examination (BAT test).

11. Performance characteristics

Cut-off for basophil activation using the allergen reagent Honey bee venom (i1) in 10 blood samples of non-sensitized donors, analyzed on two flow cytometers (BD FACSLyric™ and BC DxFLEX), is provided in Table 3. Based on the results, a technical cut-off of 5% stimulation of basophils has been established.

A percentage of activated basophils above the 5 % cut-off value indicates the donor may be sensitized.

Cut-off values, which differentiate between sensitized and non-sensitized responses, are specific to each allergen.

Table 3 Cut-off value basophil activation on two platforms

Parameter	Cytometer	n	Mean + 3SD [%]
Activated basophils of reagent ED7446 in non-sensitized donors	BD FACS Lyric™	10	1.1
	BD DxFLEX	10	3.3

12. Limitations

Honey bee venom (i1) reagent has not been validated for use in specimens collected with acid citrate dextrose (ACD) anticoagulants.
Honey bee venom (i1) reagent has not been validated with devices other than the BasoFlowEx Kit (EXBIO, cat. no. ED7043).

In 10–15% of patients (non-responders), results are uninterpretable because their basophils do not respond to allergens or controls due to differences in the intracellular signaling pathway of anti-IgE and/or anti-FcεRI, particularly in the expression of Syk[6].

13. References

1) Andersen, CJ & Vance, TM Gender Dictates the Relationship between Serum Lipids and Leukocyte Counts in the National Health and Nutrition examination Survey 1999-2004. J Clin Med. 2019;*8*(3):365. doi:10.3390/jcm8030365.
2) Lecoeur, H et al. Comparative analysis of flow cytometric methods for apoptosis quantitation in murine thymocytes and human peripheral lymphocytes from controls and HIV-infected persons Evidence for interference by granulocytes and erythrocytes, J Immunol Methods. 1996;198(1):87-99. doi:10.1016/0022-1759(96)00148-2.
3) de Jonge, G et al. Interference of in vitro hemolysis complete blood count. J Clin Lab Anal. 2018 Jun;32(5): e22396. doi: 10.1002/jcla.22396.

4) Haga, Y et al. Flow cytometric measurement of intracellular bilirubin in human peripheral blood mononuclear cells exposed to unconjugated bilirubin. Clin Biochem. 1992 Aug;25(4):277-83. doi: 10.1016/0009-9120(92)80033-d.
5) van Ierssel, SH et al. Endothelial Microparticles (EMP) for the Assessment of Endothelial Function: An In Vitro and In Vivo Study on Possible Interference of Plasma Lipids. PLoS One. 2012;7(2):e31496. doi:10.1371/journal.pone.0031496.
6) Eberlein B, et al. Basophil activation test in Hymenoptera venom allergy. Allergol Select. 2024 Aug 19;8:293-298. doi: 10.5414/ALX02522E.

14. Use of Third Party Trademarks

BD FACSLyric™ and FlowJo™ are registered trademarks of Becton, Dickinson and Company, DxFLEX is a registered trademark of Beckman Coulter, Inc., VenturiOne® is a registered trademark of Applied Cytometry, Infinicyt™ is a registered trademark of Cytognos S.L..

15. Revision History

Version 1, ED7446_IFU_v1

Initial release according to IVDR 2017/746 requirements.

16. Manufacturer

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17. Authorized Representatives

N/A

NOTICE: Any serious incident that has occurred in relation to the device shall be reported to the manufacturer and the local competent authority.