Symbol	EN	FR	ES	IT	DE	PT	HR	SV	NL
	Sufficient for <n> tests	Suffisant pour <n> tests	Suficiente para <n> pruebas	Sufficiente per <n> analisi	Inhalt ausreichend für <n> Prüfungen	Suficiente para <n> testes	Dostatno za <n> testova	Räcker till <n> tester	Voldoende voor <n> tests
	Read instruction for use	Veuillez lire les Instructions d'utilisation	Lea las instrucciones de uso	Leggere le istruzioni per l'uso	Gebrauchsanweisung beachten	Leia as instruções de uso	Pročitati upute za uporabu	Läs bruksanvisningen	Lees de gebruiksaanwijzing
	Use by Date	Date de péremption	Fecha de caducidad	Usare entro	Verwendbar bis	Validade	Upotrijebiti do datuma	Används senast datum	Gebruik voor Datum
	Batch code	Code du lot	Código de lote	Codice lotto	Chargenbezeichnung	Código de lote	Šifra serije	Lotnummer	Lotnummer
	Catalog number	Numéro de catalogue	Número de catálogo	Numero di catalogo	Katalognummer	Número do catálogo	Kataloški broj	Katalognummer	Catalogus nr.
	Caution	Attention	Precaución	Attenzione	Gebrauchsanweisung beachten	Atenção	Oprez	Försiktighet	Waarschuwing
	Manufacturer	Fabricant	Fabricante	Produttore	Hersteller	Fabricante	Proizvođač	Tillverkare	Fabrikant
	Importer	Importateur	Importador	Importatori	Importeur	Importador	Uvoznik	Importörernas	Importeur
	Authorized representative of the European Community	Représentant autorisé de la Communauté européenne	Representante autorizado en la Comunidad Europea	Rappresentante autorizzato nella Comunità Europea	Bevollmächtigter in der Europäischen Union	Representante autorizado da Comunidade Europeia	Ovlašteni predstavnik Europske zajednice	Behörig företrädare för Europeiskage menskapen	Bevoegde verte genwoordiger van de Europese Gemeenschap
	In vitro diagnostic medical device	Dispositif médical de diagnostic in vitro	Dispositivo médico de diagnóstico In vitro	Dispositivo medico-diagnostico in vitro	Bevollmächtigter in der Europäischen Union	Dispositivo médico para diagnóstico in vitro	In vitro dijagnostički medicinski uređaj	Medicinsk utrustning för in vitro-diagnostik	In vitro diagnostisch medisch hulpmiddel
	Temperature limit	Limite de température	Límite de temperatura	Limite di temperatura	Temperaturbegrenzung	Limite de temperatura	Temperaturni režim	Temperatur gräns	Temperatuur grens
	Do not reuse	Ne pas réutiliser	No reutilizar	Non riutilizzare	Nicht zur Wiederverwendung	Não reutilizar	Ne ponovno upotrijebiti	Återanvänd inte	Niet opnieuw gebruiken
	This product fulfills the requirements of the Directive 98/79/EC on in vitro diagnostic medical devices	Ce produit est conforme aux exigences de la Directive 98/79/EC sur les dispositifs médicaux de diagnostic in vitro	Este producto cumple con los requisitos de la Directiva 98/79/EC sobre dispositivos de diagnóstico In vitro	Questo prodotto soddisfa i requisiti della Direttiva 98/79/CE sui dispositivi medici diagnostici in vitro	Dieses Produkt entspricht den Anforderungen der europäischen Richtlinie 98/79/EG über In-vitro-Diagnostika	Este produto cumpre os requisitos da Diretiva 98/79/CE sobre dispositivos médicos de diagnóstico in vitro	Ovaj proizvod ispunjava zahtjeve Direktive 98/79/EC o in vitro dijagnostičkim medicinskim uređajima	Denna produkt uppfyller kraven i direktiv 98/79/EG om medicintekniska produkter för in vitro-diagnostik	Dit product voldoet aan de vereisten van de Richtlijn 98/79/EG op in vitro diagnostisch medisch hulpmiddelen

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ez-Tracker

Anti-Infliximab

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ez-Tracker Anti-Infliximab

INTENDED USE

ez-Tracker Anti-Infliximab is a fluorescence immunoassay (FIA) for the semi-quantitative determination of free antibodies against infliximab in human whole blood/serum.

For *in vitro* diagnostic use only.

INTRODUCTION

Infliximab is a chimeric monoclonal antibody against Tumor Necrosis Factor-α (TNF-α) used for treatment of a wide variety of inflammatory conditions such as Rheumatoid Arthritis (RA), Crohn's Disease (CD), ulcerative colitis (UC), and Ankylosing Spondylitis, etc. [1,2]

Most biological drugs can induce an immunogenic response, where the appearance of antibodies against a drug has a negative effect such as secondary treatment failure. [3,4]

In large, randomized clinical trials with infliximab, treatment failure is significantly associated with antibodies to infliximab formation at steady state. [5,6] Therefore, the detection of ATI has potential value in biologic therapy. Thus, the detection of ATI in patient receiving infliximab is potential value to guide therapeutic decisions in clinical practice.

ez-Tracker Anti-Infliximab used for a semi-quantitative detection of free antibodies to infliximab. This assay is helpful for physician to optimize the appropriate therapeutic treatment.

PRINCIPLE

ez-Tracker Anti-Infliximab test uses a bridging immunoassay for detection of antibodies to infliximab. Anti-infliximab antibodies from sample are bridged with fluorescent and biotin labeled infliximab which results in formation of an immune complex. This immune complex is migrated through nitrocellulose matrix and are captured by the immobilized streptavidin on the test strip.

The more antibodies to infliximab in the sample forms the more immune complex and leads to stronger intensity of fluorescence signal which is processed by the instrument ez-Tracker tests to show anti-infliximab antibodies concentration.

COMPONENT

ez-Tracker Anti-Infliximab consists of 'cartridges'.

- Each sealed aluminum pouch contains two cartridges.
- Each cartridge packaged in an aluminum pouch has three components including a cartridge part, a detector part, and a diluent part.
- The cartridge part contains the membrane called a test strip which has streptavidin at the test line, and chicken IgY at the control line.
- The detector part contains infliximab-fluorescence conjugate, anti-chicken IgY-fluorescence conjugate, infliximab-biotin conjugate, mouse IgG, sucrose, bromophenol blue, and bovine serum albumin (BSA) as a stabilizer in tris-hydrochloride buffer.
- The diluent part contains tween 20, sodium chloride, and sodium azide as a preservative in phosphate buffered saline.

WARNING AND PRECAUTIONS

- For *in vitro* diagnostic use only.
- Follow the instructions and procedures described in this 'Instructions for use'.
- Use only fresh samples and avoid direct sunlight.
- Lot numbers of all the test components (cartridge and ID chip) must match each other.
- Do not interchange the test components between different lots or use the test components after the expiration date, either of which might yield incorrect test result(s).
- Do not reuse cartridges. A cartridge should be used for testing one sample only.
- The cartridge should remain sealed in its original pouch until just before use. Do not use a cartridge, if the pouch is damaged or has already been opened.
- Frozen sample should be thawed only once. For shipping, samples must be packed in accordance with local regulations. Sample with severe hemolysis and/or hyperlipidemia must not be used.
- If test components and/or sample are stored in refrigerator, then allow cartridge and sample to be at room temperature for approximately 30 minutes before use.
- The instrument for ez-Tracker tests may generate slight vibration during use.
- Used cartridges, C-tips and pipette tips should be handled carefully and discarded by an appropriate method in accordance with relevant local regulations.
- The cartridge contains sodium azide (NaN_3), and they may cause certain health issues like convulsions, low blood pressure and heart rate, loss of consciousness, lung injury and respiratory failure. Avoid contact with skin, eyes, and clothing. In case of contact, rinse immediately with running water.
- No Biotin interference was observed in **ez-Tracker Anti-Infliximab** when biotin concentration in the sample 500 ng/mL was below. If a patient has been taking biotin at dosage of more than 0.03 mg a day, it is recommended to test again 24 hours after discontinuation of biotin intake.
- **ez-Tracker Anti-Infliximab** will provide accurate and reliable results subject to the below conditions.
  - **ez-Tracker Anti-Infliximab** should be used only in conjunction with the instrument for ez-Tracker tests.
  - Have to use recommended anticoagulant.

Recommended anticoagulant
K_2 EDTA, Na_2 EDTA, Na Citrate, Lithium heparin, Na heparin

- **C-tip should be used when the following conditions are met.**
  - C-tip provided with the kit is recommended to obtain correct test result.
  - Capillary blood should be immediately tested after collection.
  - Do not perform a test with C-tip on General Mode. It might cause an erroneous result.
  - Excess capillary blood around the C-tip should be wiped off.
  - In order to avoid cross-contamination, please do not re-use C-tip for multiple samples.
  - ez-Tracker cartridge should be inserted and positioned in the cartridge holder prior to the blood sample collection.
  - While collecting blood, be careful not to create air bubbles in the C-tip.

LIMITATIONS OF THE TEST SYSTEM

- The test may yield false positive result(s) due to the cross-reactions and/or non-specific adhesion of certain sample components to the capture/detector antibodies.
- The test may yield false negative result(s) due to the non-responsiveness of the anti-drug antibody which is the most common if the epitope is masked by some unknown components, so therefore not being able to be detected or captured by the antibodies. The instability or degradation of the anti-drug antibody with time and/or temperature may also cause false negative result as it makes the drug unrecognizable by the antibodies.
- Other factors may interfere with the test and cause erroneous results, such as technical/procedural errors, degradation of the test components/reagents or presence of interfering substances in the test samples.
- Any clinical diagnosis based on the test result must be supported by a comprehensive judgment of the concerned physician in conjunction with clinical symptoms and other relevant test results.

STORAGE AND STABILITY

	Storage condition		
Component	Storage Temperature	Shelf life	Note
Cartridge	2 – 30 °C	20 months	Unopened
		1 months	Resealed

- Return an unused cartridge to the spare cartridge zipper bag containing the desiccant pack. Reseal along entire edge of zip-seal.

MATERIALS SUPPLIED

REF ETI 003-24

Components of **ez-Tracker Anti-Infliximab**

Cartridge	CART	24
Pipette tip (Zipper bag)	P-T	24
C-tip (Zipper bag)	C-T	24
ID chip	ID-C	1
Spare cartridge zipper bag	SCZB	1
Instructions for use	IFU	1

MATERIALS REQUIRED BUT SUPPLIED ON DEMAND

Following items can be purchased separately from **ez-Tracker Anti-Infliximab.**

Please contact our sales division for more information.

- **ez-Track**[1] REF ET 001
- **ez-Traker Anti-Infliximab Control** REF ETI 003-C
- **ez-Traker Anti-Infliximab Calibrator** REF ETI 003-CAL

SAMPLE COLLECTION AND PROCESSING

The sample type for **ez-Tracker Anti-Infliximab** is human whole blood/serum.

- It is recommended to test the sample within 24 hours after collection.
- The serum should be separated from the clot by centrifugation within 3 hours after the collection of whole blood.
- The serum may be stored for a week at 2-8 °C prior to being tested. If testing will be delayed more than a week, serum should be frozen at -20 °C.
- The serum stored frozen at -20 °C for 1 month showed no performance difference.
- However, the whole blood sample should not be kept in a freezer in any case.
- As a repeated freeze-thaw cycle may affect the test result, do not refreeze previously frozen samples.
- Collection of capillary blood sample using C-tip

① Hold the C-tip horizontally and touch the surface of blood drop with the tip of the C-tip.

② Capillary action will automatically draw the blood sample to C-tip and stop.

③ Wipe off any excess blood around the tip.

④ Double-check if capillary blood is filled accurately in the C-tip and instrument for ez-Tracker tests is ready for a test on the 'C-tip mode'.

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TEST SETUP

- Check the components of the **ez-Tracker Anti-Infliximab** as described below: Cartridges, pipette tips, C-tips, an ID chip, a spare cartridge zipper bag and an instructions for use.
- If the sealed cartridge has been stored in a refrigerator, place them on a clean and flat surface at room temperature for at least 30 minutes before testing.
- Ensure that the lot number of the cartridge matches that of the ID chip.
- Turn on the instrument for ez-Tracker tests.
- Empty the tip box.
- Insert the ID chip into the 'ID chip port'.

※ **Please refer to the instrument for ez-Tracker tests operation manual for complete information and operating instructions.**

TEST PROCEDURE

General mode

1) Insert a cartridge into the cartridge holder.
2) Insert a tip into the tip hole of the cartridge.
3) Select the 'General mode' in the instrument for ez-Tracker tests.
4) Take 100 µL of the sample (whole blood/serum /control) using a pipette and dispense it into the sample well of the cartridge.
5) Tap the 'Start' button on the screen.
6) The test result will be displayed on the screen after 12 minutes.

C-tip Mode

1) Insert a cartridge into the cartridge holder.
2) Take 30 µL of capillary blood using a C-tip.
3) Insert the capillary blood-filled C-tip into the tip hole of the cartridge.
4) Select the 'C-tip mode' in the instrument for ez-Tracker tests.
5) Tap the 'Start' button on the screen.
6) The test result will be displayed on the screen after 12 minutes.

INTERPRETATION OF TEST RESULT

- The instrument for ez-Tracker tests calculate the test result automatically and displays anti-infliximab concentration of the test sample in terms AU/mL.
- Working range: 4 - 250 AU/mL
- The cut-off: 10 AU/mL

Range	Interpretation
> 10 AU/mL	Positive
≤ 10 AU/ml	Negative

QUALITY CONTROL

- Quality control tests are a part of the good testing practice to confirm the expected results and validity of the assay and should be performed at regular intervals.
- Quality control tests should also be performed whenever there is any question concerning the validity of the test results.
- Control materials are provided on demand with **ez-Tracker Anti-Infliximab**. For more information regarding obtaining the control materials, contact Theradiag's Sales Division for assistance.
(Please refer to the instructions for use of control material.)

PERFORMANCE CHARACTERISTICS

- **Analytical sensitivity**
  - Limit of Blank (LoB) 2.50 AU/mL
  - Limit of Detection (LoD) 4.00 AU/mL
- **High-dose Hook Effect**
  There is no high-dose hook effect at anti-infliximab concentration up to 20,000 AU/mL.
- **Analytical specificity**
  - Cross-reactivity
    ez-Tracker Anti-Infliximab test results did not show any significant cross-reactivity with these biomolecules.

Cross-reactivity materials	Concentration
Adalimumab	100 µg/mL
Etanercept	100 µg/mL
Golimumab	100 µg/mL
Anti- adalimumab antibody	1,000 ng/mL
Anti-etanercept antibody	1,000 ng/mL
Anti-golimumab antibody	1,000 ng/mL

  - Interference
    Interferents listed in the following table were added to the test sample at the concentration mentioned below. **ez-Tracker Anti-Infliximab** test results did not show any significant interference with these materials.

Interference materials	Concentration
Hemoglobin	1,000 mg/dL
Bilirubin	40 mg/dL
Triglyceride	2,000 mg/dL
Rheumatoid factor	200 IU/mL
Human serum albumin	12 g/dL

- **Precision**
  - Single-site study
    Repeatability (within-run precision)
    within-laboratory precision (Total precision)
    Lot to lot precision
    3 Lots of **ez-Tracker Anti-Infliximab** were tested for 20 days. Each standard material was tested 2 times per day. For each test, each material was duplicated.
  - Multi-site study
    Reproducibility
    1 Lot of **ez-Tracker Anti-Infliximab** was tested for 5 days in 3 different sites (1 person per 1 site, 1 instrument per 1 site). Each standard material was tested 1 time per and 5 replicates per day.

Anti-Infliximab antibody [AU/mL]	Repeatability		Total precision	
	AVG	CV (%)	AVG	CV (%)
15	14.82	6.8	14.94	6.0
100	99.62	5.8	100.80	5.8
200	199.08	5.4	199.77	5.8
Anti-Infliximab antibody [AU/mL]	Lot to lot precision		Reproducibility	
	AVG	CV (%)	AVG	CV (%)
15	14.92	6.0	14.99	6.2
100	99.93	5.8	99.48	5.7
200	200.71	5.9	200.36	5.1

- **Accuracy**
  The accuracy was confirmed by testing with 3 different lots of **ez-Tracker Anti-Infliximab**. The tests were repeated 10 times at each concentration of the control standard.

Anti-Infliximab antibody [AU/mL]	Lot 1	Lot 2	Lot 3	AVG	Recovery (%)
24.25	23.72	24.31	24.82	24.28	100.1
33.50	34.62	33.41	34.09	34.04	101.6
52.00	54.14	53.98	52.41	53.51	102.9
89.00	88.89	85.96	87.64	87.50	98.3
126.00	124.57	129.05	130.77	128.13	101.7
181.50	188.67	192.46	183.64	188.26	103.7

- **Clinical performance evaluation**
  ez-Tracker Anti-Infliximab has demonstrated the following clinical performance results.

Total (n=69)		n	ez-Tracker Anti-Infliximab	
			Positive	Negative
Comparator A	Positive	15	14	1
	Negative	54	2	52
Positive Agreement (> 10 AU/mL)			93.3%	
Negative Agreement (≤10 AU/mL)			96.2%	
Total Agreement			95.6%	

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