TeaRx™ Test-- Diagnostic kit for the detection of Dry Eye Syndrome

Intended Use

The TeaRx™ Diagnostic Kit is a rapid, immunoassay for visual, semi-quantitative in vitro detection of lactoferrin, lysozyme and human serum albumin (HSA) levels in human tears. The integrated results of these three parameters, in conjunction with other methods of clinical evaluation, aid physicians with diagnosis and treatment of dry eye patients. This test is intended for prescription use at point-of-care sites only. The kit is intended for use by physicians, nurses, optometrists and other professional trained practitioners

Background

Dry eye syndrome (DES) is a multifactorial disease of the tears and ocular surface that results in symptoms of discomfort, visual disturbance, and tear film instability with potential damage to the ocular surface. It is accompanied by increased osmolarity of the tear film and inflammation of the ocular surface.

The clinical diagnosis of dry eye syndrome includes utilizing a combination of symptoms and signs [1]. A discomfort questionnaire is used to assess patient-reported presence of burning, stinging, pain, light sensitivity and fluctuating vision. Standard instrument used for screening patients with dry eye is the Ocular Surface Disease Index (OSDI). However, this provides a qualitative rather than a semi-quantitative analysis, as produced by the TeaRx™ kit. The clinical signs of dry eye syndrome include corneal staining and reduced tear break up time (TBUT) or analysis of MMP9 levels, which lack specificity for DES. In some cases, a Schirmer Tear Test might be used to confirm the presence of reduced tear production. Unlike these, TeaRx™ uses three protein markers in the tear film that originate from different locations in the eye, thus reflecting different pathologic processes resulting in dry eye. This will enable physicians to better understand the nature and root cause of DES for each of the patients.

The TeaRx™ Technology

The TeaRx™ is a point-of-care multi-assays diagnostic test that provides an objective, rapid, simple and semi-quantitative analysis of the tear film, based on lateral flow technology. The test measures the following tear constituents: lactoferrin, lysozyme and HSA. The selected combination of TeaRx™'s assays and the subject's demographics are used to build a predictive statistical model for assisting in the diagnosis of patients with dry eye syndrome.

Overall test time starting from tear collection through final result is approximately 12 minutes. Final test result is generated by dedicated software which integrates the subject's age, gender and the reading of each of the tested parameters.

Before running the test, please read the instructions carefully and view the training video.

Reagents and Materials

Provided Materials

The TeaRx™ Diagnostic Test contains the following materials:

Reusable materials:

TRX-SCD-001 1 pc. TeaRx™ Test line Intensity Scale card

Single use (disposable) materials:

TRX-CHP-001 20/40 pc. TeaRx™ Disposable cartridge.
TRX-TMC-001 20/40 pc. TeaRx™ Multichannel test cassette.
TRX-WRB-001 1 pc. Wash buffer dropper bottle.

Online Materials:

1 link to Online Calculator software.

Materials Not Provided:

- Timer.
- Gloves.
- Permanent marker.
- Slit lamp.

Warnings and Precautions

1. For invitro diagnostic use only.
2. Disposable Cartridge (TRX-CHP-001) and Multichannel Test Cassette (TRX-TMC-001) intended for **single use only!**
3. Open foil pouches containing Disposable Cartridge (TRX-CHP-001) and Multichannel Test Cassette (TRX-TMC-001) just before use.
4. Read test instructions carefully (TEST-TRX-001).
5. All used disposables should be treated as biohazard and disposed of in accordance with local regulations.
6. Wear disposable gloves while handling samples and wash hands after the test is complete.
7. Do not reuse the Disposable Cartridge (TRX-CHP-001) and Multichannel Test Cassette (TRX-TMC-001).
8. Do not substitute solutions or materials that are required for testing.

Storage and Handling Test Components

1. Store the TeaRx™ test components at Ambient temperature (between 59°F/15°C and 77°F/25°C). All tests components are stable at room temperature until expiration date marked on the external package.
2. If necessary, please ask DiagnosTear for Material Safety Data Sheet (MSDS).

First Use Test Preparation

Prior to first use of the kit, do the following:

1. Enter the DiagnosTear online calculator using QR barcode provided inside the kit packaging or in the appendix below or use the link – http://calculator.diagnostear.com/#/do-test.
2. Please watch the training movie using the QR barcode provided inside the kit packaging or in the appendix below.
3. Test the Calculator software integrity by using Table 1. Make sure that the TeaRx™ scoring you receive by using the calculator is identical to the score specified in Table 1.

In case the received score is not equal to results in Table 1, please contact DiagnosTear Ltd before proceeding to test use.

Sample#	Test Score			Age	Gender	TeaRx score
	LF	HSA	Lys			
1	1	1.5	0.25	61	1 (F)	100
2	0.5	0.5	1	72	-1 (M)	17

Table 1: Parameters to be used for Calculator Algorithm integrity test.

Test Preparation

1. Take one new Disposable Cartridge. Open the aluminum pouch. Ensure that the Disposable Cartridge is not damaged and appears as shown in Fig. 1.

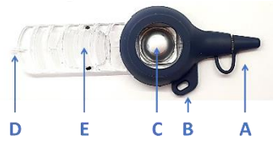

Figure 1: Disposable Cartridge

A– cap, B– cap holder, C– dispensing blister, D– dispensing capillary, E– mixing chamber.

Figure 2: Multichannel cassette

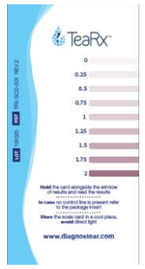

Figure 3: Intensity Scale Card

2. Open the aluminum pouch with the Multichannel Cassette and place it on the table with sample wells facing upwards (Fig.2).
3. Unscrew the cap of the wash reagent dropper bottle and place it on the table.
4. Place the TeaRx™ Test Line Intensity Scale Card (Fig. 3) on the table, as well as the printed TeaRx™ results table (Optional) – if used.

Tear Sample Collection and Dilution

Note: The TeaRx™ Test is designed for use on tear specimens collected with TeaRx™ Cartridge. Tear samples should be collected from the patient before adding any eye drops, including fluorescein or drops for dilating the pupil. *It is recommended to use a Slit lamp for tear collection.*

1. Remove cap from capillary (Fig. 4-A) and secure it in cap holder (Fig. 4-B), as shown.
2. Hold the TeaRx™ Cartridge and place it gently on the patient's cheek while the collection capillary (Fig. 4-A) is lightly touching the tear film on the eye's lateral canthus as demonstrated in Fig. 5 (it is recommended to hold it at 30-90 degrees with the canthus).
3. Avoid collecting tears when there is active tearing.
4. Keep the TeaRx™ Cartridge at that position until visually confirming collection of one microliter (1 µL) of tears. Note -orange-yellow color in collection capillary turns bright yellow - See Fig. 6A-C using Slit lamp).
5. Gently remove the TeaRx™ Cartridge from the patient's eye and re-cap the collection capillary.
6. To dilute the tear, press the blister (Fig. 1-C), while holding the cartridge pointing down with collecting capillary closed until diluted solution fills the reservoir up to the marked dots.
7. Shake the cartridge for 5 seconds by moving your hand from left to right.
8. The diluted tear is now ready for dispensing into the Multichannel Test Cassette.

Figure 4

A- Collection capillary
B- Secured cap

Figure 5

Capillary lightly touching the tear film on the lateral canthus

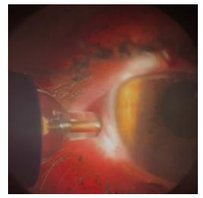

Figure 6-A

Capillary prior to tear collection – Orange-yellow.

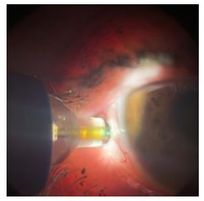

Figure 6-B

Capillary half filled.

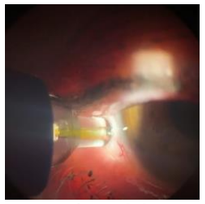

Figure 6-C

Full capillary following tear collection – Bright yellow.

Running the Test

1. Take the TeaRx™ Cartridge with the collected tears and hold it vertically, above the first sample well (on left side) of the Multichannel Test Cassette, while the dispensing capillary (Fig. 1-D) is pointing down.
2. Dispense the first drop of diluted tear in left well, by applying gentle pressure on the transparent membrane (Fig. 6), until one drop is dispensed (drop should fall by gravitational force. Do not apply direct contact with well).

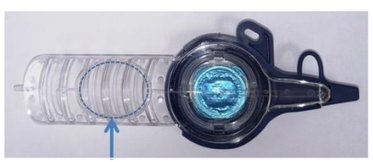

Figure 6: Back of the Disposable Cartridge. The arrow points to the transparent membrane of the mixing chamber.

3. Repeat dispensing a drop over the middle and right sample wells.
4. Following sample application, take the uncapped dropper bottle and dispense one drop of Wash Buffer to each of the sample wells, starting from left side of the cassette.
5. Incubate at room temperature for 9 minutes.
6. Close the Wash Buffer bottle.

Reading Test Results

1. Read results after 9 minutes from Wash Buffer addition.
2. Read the results from the left slot (slot 1, i.e. - LF) to right slot (slot 3, i.e. - Lys).
3. Determine intensity of TeaRx™ Test Lines (Fig. 8) using the included TeaRx™ Intensity Scale Card (Fig. 3).
4. Write the identified score for each Test Line on the cassette using a permanent marker or use Table 2 (see appendix).
5. Type in the recorded intensity values, age and gender from Cassette/Table 2 in designated slots of the DiagnosTear Calculator:

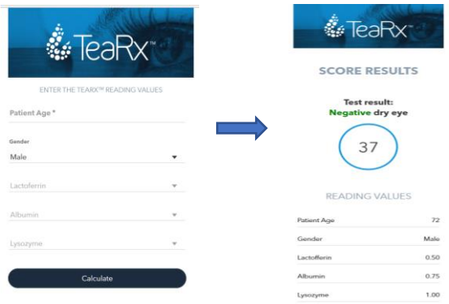

Figure 7: DiagnosTear Calculator Algorithm

6. Score reflects integration of all input parameters, such that 0-54 indicates healthy condition and 55-99 confirms DES.
7. Record TeaRx™ score and interpretation.
8. Dispose the cartridge and cassette according to the local regulatory guidelines.

Validity of the Results

1. **Valid Results:** TeaRx™ includes an internal validity control – a pink to red line appearing in the control line (labelled with "C") in each of the channels. The test line (marked with "T") may or may not appear, depending on the concentration of the analyte in the sample (Fig. 8-A).
2. **Invalid Results:** The absence of a pink to red line in any one of the control lines ("C", Fig 8-B) invalidates the test and requires to repeat the test.

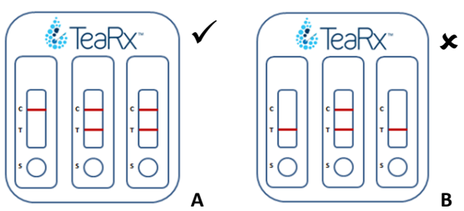

Figure 8: TeaRx™ Multichannel Test Cassette
(A –valid results, B – invalid results)

Troubleshooting

Troubleshooting Guide for TeaRx™		
Problem	**Cause**	**Solutions**
No control line, while the Test Line is present.	**Wash Buffer was not added after sample dispensing into the multichannel cassette.**	**In case the sample pad looks wet replace the Multi-channel Test Cassette with a new one and repeat sample dispensing followed by 1 drop of wash reagent to each sample well.**
	Test strip is invalid.	**In case the sample pad looks wet replace the Multi-channel Test Cassette with a new one and repeat sample dispensing followed by 1 drop of wash reagent to each sample well.**
No results (no lines appear in the Control and Test Line) in the window following 9 minutes from sample application onto the cassette.	**Tear samples were not added to device.**	**In case the sample pad looks wet replace the Multi-channel Test Cassette with a new one and repeat sample dispensing followed by 1 drop of wash reagent to each sample well.**
	Wash Buffer was not added after sample dispensing on multichannel cassette or test strip is invalid.	**If sample pad is dry, discard the Multichannel Test Cassette and use a new cassette. Start the run by applying the diluted sample followed by1 drop of Wash Buffer.**
Unable to collect tears with collector. Orange-yellow color in collection capillary does not turn bright yellow.	**Cartridge cap was not removed.**	**Remove cartridge cap.**
	Wrong positioning of cartridge or damaged cartridge.	**Try using a Slit lamp or wait a few more seconds or try collecting the tears in different angles (usually 30-90 degrees to the canthus) or make sure cartridge capillary is only lightly touching the tear film or make sure correct cartridge grip to avoid any pressure on membrane. If the cartridge keeps failing more than 3 times – replace with a new cartridge.**
Following tear collection – no flow is seen towards lower capillary	**Cartridge was damaged – transparent membrane is not working properly.**	**Check for possible tares in transparent membrane, preventing liquid flow.**

Limitations

1. The TeaRx™ Test is one of the indicators which aid the diagnosis of dry eye syndrome. A valid test result should not be used as the sole basis for treatment or other management decisions.
2. Results obtained with this test should be used in conjunction with other clinical information available to the physician.

References

1. The International Dry-Eye Workshop (DEWS Report). The Definition and Classification of Dry Eye Syndrome: Report of the Definition and Classification Subcommittee of the International Dry Eye Workshop. Ocul Surf. 2007; 5:75-92.
2. Chong E, Harissi-Dagher M, and Dana R. Wetting of the Ocular Surface and Dry-Eye Disorders. In: *Albert & Jakobiec's* Principles and Practices of Ophthalmology 3rd ed. Canada; Elsevier. 2008:773-788.
3. Gayton JL. Etiology, prevalence, and treatment of dry eye syndrome. Clin Ophthal. 2009; 3:405-412.

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Borkstrasse 10, 48163 Münster,
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Contact: contact@mednet-cerep.com

Read instructions before use

Do not re-use

Manufacturer Information

Do not use if package is damaged

Expiration Date

Storage Temperature

LOT Lot Number

REF Catalog Number

IVD In Vitro Diagnostics Medical Device

EC REP Authorized Representative information

Appendix

Table 2

TeaRx results table

Date:___/___/___ **Patient Name:** _____

1. Did the patient get any eye drops during the visit, including fluorescein or drops for dilating the pupil?
   Yes / No

   If "Yes"- the patient is not eligible for testing by TeaRx™. Collection from the patient must be prior to adding any eye drops.
2. If "No"- the patient is eligible for testing by TeaRx™. Run the test and write the intensity values for the
   parameters, following 9 minutes from Wash buffer dispensing.
3. Observe the control lines and mark "V" if all control lines are valid. If one or more parameters have a Non-Valid Control line, mark "NV" and re-run the test by using a new cassette.
4. Fill-in the age and gender information in the table. In the gender column, mark (-1) for Male and (1) for Female.
5. Enter the data collected into the calculator software to calculate the TearRx™ score and final result. You may record the TearRx™ score and final result in the table below.

Eye	TeaRx Cassette Results			Control line	Demographics			TeaRx score	Interpretation
	Lactoferrin	HSA	Lysozyme	Valid (V)/ Not valid (NV)	Age	Gender			
						M/F	(-1)/(1)		
Right									
Left									

Person performed the test:

_____ _____ _____
Name Title Signature

Person reviewed the results:

_____ _____ _____
Name Title Signature

Training video

To view the training video – please scan the following barcode:

DiagnosTear online calculator

To enter TeaRx™ calculator – please scan the following barcode: