WHO Prequalification of In Vitro Diagnostics
PUBLIC REPORT

Product: FalciVax - Rapid test for Malaria Pv/Pf
WHO reference number: PQDx 0290-025-00

FalciVax - Rapid test for Malaria Pv/Pf with product codes **503010025(1T), 503010010**, **503010025, 503010050, 503010100 and 503010025** manufactured by **Zephyr Biomedicals – A Division of Tulip Diagnostics (P) Ltd.**, **CE-mark**, was accepted for the WHO list of prequalified in vitro diagnostics and was listed on 3 June 2020.

Summary of WHO prequalification assessment for FalciVax - Rapid test for Malaria Pv/Pf

	Date	Outcome
Prequalification listing	3 June 2020	listed
Dossier assessment	20 January 2020	MR
Site inspection(s) of the quality management system	21-25 January 2019	MR
Product performance evaluation	2018	MR

MR: Meets Requirements

Report amendments and product changes

This public report has since been amended. Amendments may have arisen because of changes to the prequalified product for which the WHO has been notified and has undertaken a review. Amendments to the report are summarized in the following table, and details of each amendment are provided below.

Version	Summary of amendment	Date of report amendment
2.0	1. Change in use of specimen applicator from sample loops to Inverted cups. 2. Change in use of lancets from stainless steel sterile blood lancets to blood lancet plastic (twist off).	24 June 2022
3.0	Updates on commitments status.	7 July 2022
4.0	Addition of a pack size, with single tests in a pack of 25 tests (product code 503010025 (1T).	10 May 2023

Intended use

According to the claim of intended use from Zephyr Biomedicals – A Division of Tulip Diagnostics (P) Ltd., "*FalciVax* [- Rapid test for Malaria Pv/Pf] *is a rapid, qualitative, two site sandwich immunoassay utilizing capillary and venous whole blood specimens of symptomatic patients for the detection of P.falciparum specific histidine rich protein-2 (Pf. HRP-2) and P.vivax specific plasmodium Lactate Dehydrogenase (pLDH) antigens and it is used in aiding the diagnosis and differentiation of malaria infections caused by P.falciparum and P.vivax. It is intended to be used by trained healthcare or laboratory professionals or other health care workers who have received appropriate training. This product can be used by trained lay providers operating at point-of-care in resource-limited settings. This product is not intended for self-testing and it is not for blood donor screening. The test is not automated; it needs to be performed and interpreted manually by the user*".

Assay description

According to the claim of assay description from Zephyr Biomedicals – A Division of Tulip Diagnostics (P) Ltd., "*FalciVax* [- Rapid test for Malaria Pv/Pf*] utilizes the principle of agglutination of antibodies/ antisera with respective antigen in immuno-chromatography format along with use of nano gold particles as agglutination revealing agent. As the test specimen flows through the membrane assembly of the device after addition of the clearing buffer, the colored colloidal gold conjugates of the Agglutinating Sera for HRP-2 and the Agglutinating Sera for P. vivax specific pLDH complexes the HRP-2/ pLDH in the lysed specimen. This complex moves further on the membrane to the test region where it is immobilized by the Agglutinating Sera for Malaria specific pLDH and / or Agglutinating Sera for HRP-2 coated on the membrane leading to formation of pink-purple colored band/s which confirms a positive test result. A band will appear under Pf at the test region in falciparum positive specimens, while a band will appear under Pv in vivax malaria positive specimens. Appearance of band under Pf as well as Pv in the test region suggests a mixed infection.*
Absence of colored band/s in the test region indicates a negative test result. The unreacted conjugate and unbound complex if any, move further on the membrane and are subsequently immobilized by Agglutinating Sera for Rabbit globulin coated on the membrane at the control region, forming a pink-purple band. The control band formation is based on the 'Rabbit globulin / Agglutinating Sera for Rabbit globulin' system. Since it is completely independent of the analyte detection system, it facilitates formation of consistent control band signal independent of the analyte concentration. This control band serves to validate the test performance."

Test kit contents

Component	25 tests (product code 503010025(1T)	10 tests (product code 503010010)	25 tests (product code 503010025)	50 tests (product code 503010050)	100 tests (product code 503010100)
Pouch-sealed test with desiccant and specimen transfer device	25 x 1T (25 single kit test/kit)	10	25	50	100
Clearing buffer bottle	25 x 1.0 ml	1 bottle (total volume 3.0 ml)	1 bottle (total volume 4.0 ml)	2 bottles (total volume 8.0 ml)	4 bottles (total volume 16.0 ml)
Alcohol swabs	25	10	25	50	100
Sterile lancets	25	10	25	50	100
Instructions for Use	25	1	1	1	1
Pictorial instructions for use	25	1	1	1	1

Items required but not provided

Item	Description
Consumables: Disposable micropipette tips Venipuncture blood collection kit Additional alcohol swabs Additional sterile lancets	NA
Durables: Permanent marker Biohazard waste container	NA
Equipment: Calibrated micropipette Timer	Micropipette should be capable of delivering 5µl of specimen

Storage

The test kit should be stored between 1°C to 40°C.

Shelf-life upon manufacture

24 months

Warnings/limitations

Refer to the Instructions for Use (IFU) attached to this report.

Prioritization for prequalification

Based on the established criteria for acceptance in the WHO product testing of malaria RDTs Round 8[1], FalciVax - Rapid test for Malaria Pv/Pf was given priority for WHO prequalification assessment.

Dossier assessment

Zephyr Biomedicals – A Division of Tulip Diagnostics (P) Ltd. submitted a product dossier for FalciVax - Rapid test for Malaria Pv/Pf as per the "*Instructions for compilation of a product dossier*" (PQDx_018 version 3). The information (data and documentation) submitted in the product dossier was reviewed by WHO staff and external technical experts (assessors) appointed by WHO.

The manufacturer's responses to the nonconformities found during dossier screening and assessment findings were accepted on 20 January 2020.

Commitments for prequalification

1. The manufacturer will submit by 30 June 2020 an additional study investigating the potential interference of certain substances as per WHO document TSS-3. The commitment is under review.
2. The manufacturer will submit by 30 June 2020 an additional study investigating the potential cross-reactivity of certain substances as per WHO document TSS-3. The commitment is under review.

The manufacturer submitted additional studies. The additional information is currently under review.

Based on the product dossier screening and assessment findings, the product dossier for FalciVax - Rapid test for Malaria Pv/Pf meets WHO prequalification requirements.

[1] https://www.who.int/malaria/publications/atoz/9789241514965/en/

Manufacturing site inspection

An inspection of Zephyr Biomedicals – A Division of Tulip Diagnostics (P) Ltd. located at *M46-47, Phase III B, Verna, Goa, 403722, India,* was conducted between 21-25 January 2019. At the time of considering the product application for Prequalification, the Manufacturer of the product had a well-established quality management system and manufacturing practices in place that would support the manufacture of the product of consistent quality. Routine inspections of the Manufacturer will be conducted with copies of these WHO Public Inspection Reports (WHOPIRs) published on the WHO Prequalification web page as per Resolution WHA57.14 of the World Health Assembly. To note that a WHOPIR reflects the information on the most current inspection performed at a manufacturing site for in vitro diagnostic products and gives a summary of the inspection findings,

Information on the most current inspection can be found at:

https://extranet.who.int/pqweb/inspection-services/prequalification-reports/whopirs-vitro-diagnostics

All published WHOPIRs are with the agreement of the manufacturer.

Product performance evaluation

FalciVax - Rapid test for Malaria Pv/Pf was evaluated in the eighth[2] round of WHO product testing of RDTs for malaria antigen detection, completed in 2018.

FalciVax - Rapid test for Malaria Pv/Pf was evaluated against a *Plasmodium falciparum* cultured line panel, *P. falciparum wild-type* parasite panel, *P. vivax* wild type parasite panel and a *P. falciparum* and *P. vivax* negative panel.

[2] https://www.who.int/malaria/publications/atoz/9789241514965/en/

Performance characteristics		
	P. falciparum	***P. vivax***
Panel detection score at 200 parasites/µL (Pf N=100) (Pv N=35)	95	*100*
False positive results % (N= 208)	0.5	
Invalid rate % (N= 1210)	0	
Inter-reader variability %*	Not applicable	
Lowest concentration of HRP2/pLDH detected using the 1st WHO International standard for Pf antigens (NIBSC code: 16/376)*	*Not applicable.*	

** Not applicable for assays evaluated in WHO product testing of RDTs for malaria antigen detection*

Operational characteristics and ease of use

This assay does not require laboratory equipment and can be performed in laboratories with limited facilities or non-laboratory settings.

Key operational characteristics	
Number of steps*	2 steps in total
Time to result	20 minutes
Endpoint stability (interval)	10 minutes (the test can be read between 20 and 30 minutes after the addition of diluent)
Internal QC	Yes. The test has a control line. The test has an internal control line. The presence of the control line indicates that migration of liquid has occurred; however, it does not guarantee that the correct specimen type or volume was added or that the test procedure was followed correctly.

** Definition: each action required to obtain a result (excluding specimen collection, device preparation – opening the pouch), e.g. for RDTs: add specimen, add buffer (2 steps).*

Based on these results, the performance evaluation for FalciVax - Rapid test for Malaria Pv/Pf meets the WHO prequalification requirements.

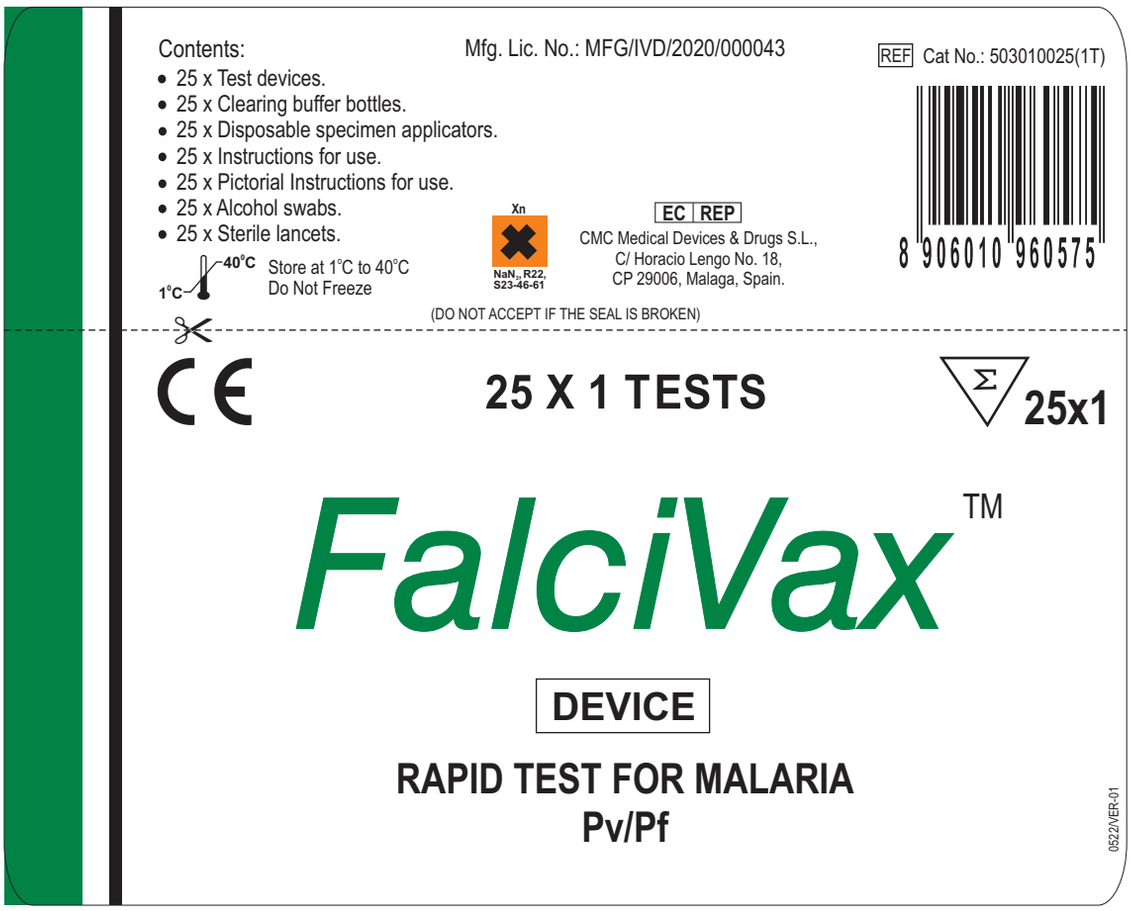
Labelling

1. **Labels**
2. **Instructions for use**

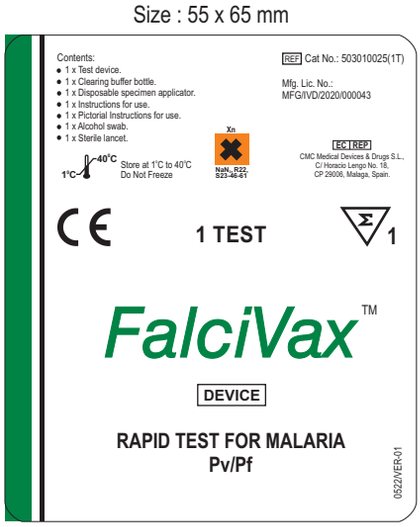
1. Labels

1.1 Kit box labels

Size : 150 x 120 mm



Size : 55 x 65 mm



Size : 55 x 18 mm

Contents:

- 10 x Test devices.
- 1 x Clearing buffer bottle.
- 10 x Disposable specimen applicators.
- 1 x Instructions for use.
- 1 x Pictorial Instructions for use.
- 10 x Alcohol swabs.
- 10 x Sterile lancets.

1°C 40°C Store at 1°C to 40°C
Do Not Freeze

Mfg. Lic. No.: MFG/IVD/2020/000043

Xn
NaN., R22.
S23-46-61

EC REP
CMC Medical Devices & Drugs S.L.,
C/ Horacio Lengo No. 18,
CP 29006, Malaga, Spain.

REF Cat No.: 503010010

8 906010 960070

(DO NOT ACCEPT IF THE SEAL IS BROKEN)

CE

10 TESTS

Σ 10

FalciVax™

DEVICE

RAPID TEST FOR MALARIA
Pv / Pf

0322/VER-05

Contents:

- 25 x Test devices.
- 1 x Clearing buffer bottle.
- 25 x Disposable specimen applicators.
- 1 x Instructions for use.
- 1 x Pictorial Instructions for use.
- 25 x Alcohol swabs.
- 25 x Sterile lancets.

1°C 40°C Store at 1°C to 40°C
Do Not Freeze

Xn
NaN, R22, S23-46-61

EC REP
CMC Medical Devices & Drugs S.L.,
C/ Horacio Lengo No. 18,
CP 29006, Malaga, Spain.

Mfg. Lic. No.: MFG/IVD/2020/000043

REF Cat No.: 503010025

8 906010 960087

(DO NOT ACCEPT IF THE SEAL IS BROKEN)

CE

25 TESTS

Σ 25

FalciVax™

DEVICE

RAPID TEST FOR MALARIA
Pv / Pf

0322/VER-05

Contents:

- 50 x Test devices.
- 2 x Clearing buffer bottles.
- 50 x Disposable specimen applicators.
- 1 x Instructions for use.
- 1 x Pictorial Instructions for use.
- 50 x Alcohol swabs.
- 50 x Sterile lancets.

Store at 1°C to 40°C
Do Not Freeze

Mfg. Lic. No.: MFG/IVD/2020/000043

EC REP
CMC Medical Devices & Drugs S.L.,
C/ Horacio Lengo No. 18,
CP 29006, Malaga, Spain.

REF Cat No.: 503010050

(DO NOT ACCEPT IF THE SEAL IS BROKEN)

CE

50 TESTS

Σ 50

FalciVax™

DEVICE

RAPID TEST FOR MALARIA
Pv / Pf

0322/VER-05

Contents:

- 100 x Test devices.
- 4 x Clearing buffer bottles.
- 100 x Disposable specimen applicators.
- 1 x Instructions for use.
- 1 x Pictorial Instructions for use.
- 100 x Alcohol swabs.
- 100 x Sterile lancets.

1°C – 40°C Store at 1°C to 40°C
Do Not Freeze

Mfg. Lic. No.: MFG/IVD/2020/000043

Xn
NaN_3 R22,
S23-46-61

EC REP
CMC Medical Devices & Drugs S.L.,
C/ Horacio Lengo No. 18,
CP 29006, Malaga, Spain.

REF Cat No.: 503010100

8 906010 960582

(DO NOT ACCEPT IF THE SEAL IS BROKEN)

CE

100 TESTS

Σ 100

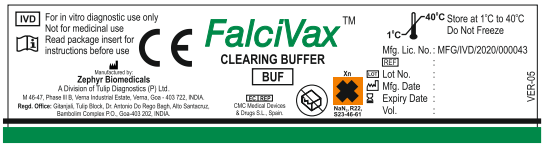
FalciVax™

DEVICE

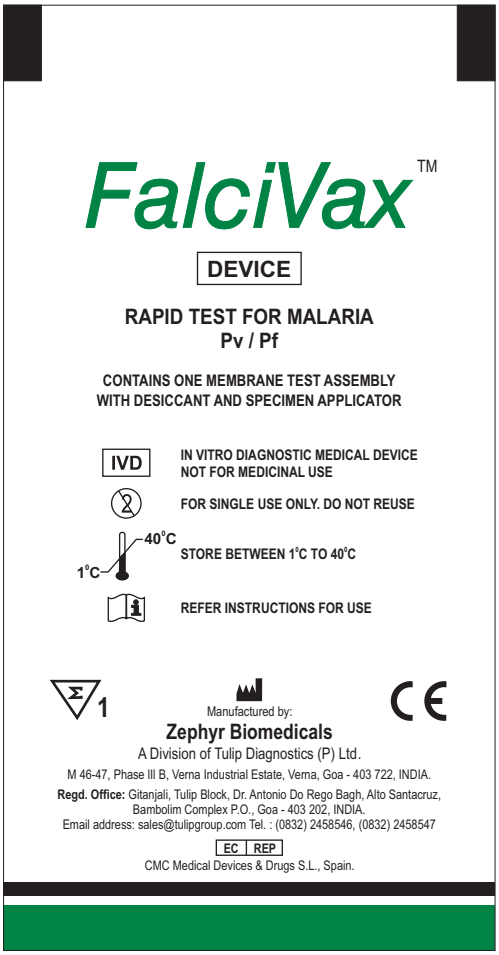
RAPID TEST FOR MALARIA
Pv / Pf

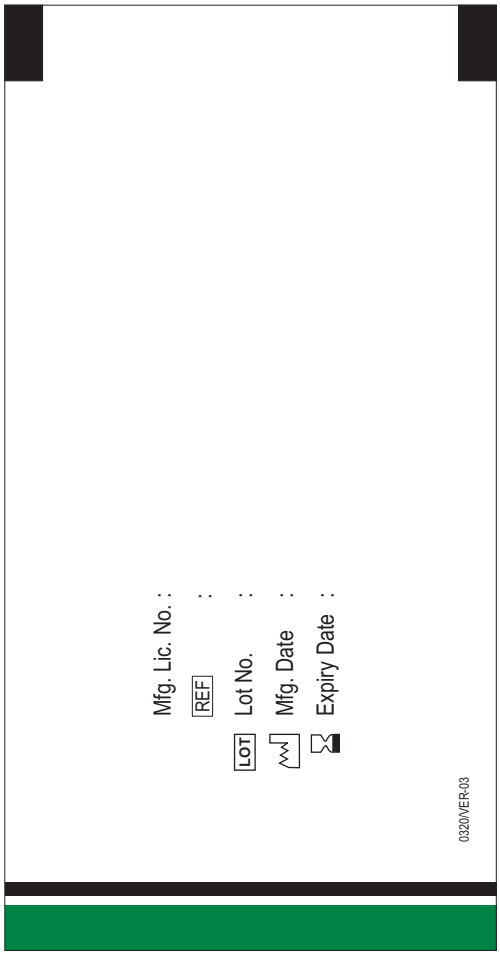
0322/VER-05

1.2 Clearing buffer label



1.3 Device pouch label





1.4 Kit box cartons for all configurations

1 Tests Carton
Size: 70 mm x 22 mm X 130 mm

LOT Lot No. :
Mfg. Date :
Expiry Date :
M.R.P. (₹) :
(Inclusive of all taxes)

An ISO 13485
Certified Company

This side up

Manufactured by:

Zephyr Biomedicals

A Division of Tulip Diagnostics (P) Ltd.

M 46-47, Phase III B, Verna Industrial Estate,
Verna, Goa - 403 722, INDIA.

Regd. Office: Gitanjali, Tulip Block,
Dr. Antonio Do Rego Bagh, Alto Santacruz,
Bambolim Complex P.O.,
Goa - 403 202, INDIA.

IN VITRO DIAGNOSTIC MEDICAL DEVICE
NOT FOR MEDICINAL USE
REFER PACKAGE INSERT
FOR INSTRUCTIONS
BEFORE USE

IVD

0522/VER-01

25 x 1 Test Carton
Size: 300 mm x 135 mm X 145 mm

Manufactured by:

Zephyr Biomedicals

A Division of Tulip Diagnostics (P) Ltd.

M 46-47, Phase III B, Verna Industrial Estate, Verna, Goa - 403 722, INDIA.

Regd. Office: Gitanjali, Tulip Block, Dr. Antonio Do Rego Bagh, Alto Santacruz, Bambolim Complex P.O., Goa - 403 202, INDIA.
Email address: sales@tulipgroup.com
Tel. : (0832) 2458546, (0832) 2458547

9522/VER-01

LOT **Lot No.** :

Mfg. Date :

Expiry Date :

M.R.P. (₹) :
(Inclusive of all taxes)

This side up

An ISO 13485 Certified Company

IVD **IN VITRO DIAGNOSTIC MEDICAL DEVICE NOT FOR MEDICINAL USE**

REFER PACKAGE INSERT FOR INSTRUCTIONS BEFORE USE

10 Tests Carton (Device)
Size: 132 mm x 90 mm X 70 mm

Manufactured by:

Zephyr Biomedicals

A Division of Tulip Diagnostics (P) Ltd.

M 46-47, Phase III B, Verna Industrial Estate, Verna, Goa - 403 722, INDIA.

Regd. Office: Gitanjali, Tulip Block, Dr. Antonio Do Rego Bagh, Alto Santacruz, Bambolim Complex P.O., Goa - 403 202, INDIA.

Email address: sales@tulipgroup.com

Tel. : (0832) 2458546, (0832) 2458547

LOT Lot No. :

Mfg. Date :

Expiry Date :

M.R.P. (₹) :

(Inclusive of all taxes)

This side up

An ISO 13485 Certified Company

IVD IN VITRO DIAGNOSTIC MEDICAL DEVICE NOT FOR MEDICINAL USE

REFER PACKAGE INSERT FOR INSTRUCTIONS BEFORE USE

0320/VER-03

50 Tests Carton
Size: 200 mm x 132 mm

Manufactured by:

Zephyr Biomedicals

A Division of Tulip Diagnostics (P) Ltd.

M 46-47, Phase III B, Verna Industrial Estate, Verna, Goa - 403 722, INDIA.

Regd. Office: Gitanjali, Tulip Block, Dr. Antonio Do Rego Bagh, Alto Santacruz, Bambolim Complex P.O., Goa - 403 202, INDIA.

Email address: sales@tulipgroup.com

Tel. : (0832) 2458546, (0832) 2458547

0320/VER-03

This side up

Lot No. :

Mfg. Date :

Expiry Date :

M.R.P. (₹) :
(Inclusive of all taxes)

An ISO 13485
Certified Company

IVD **IN VITRO DIAGNOSTIC MEDICAL DEVICE**
NOT FOR MEDICINAL USE

REFER PACKAGE INSERT FOR
INSTRUCTIONS BEFORE USE

25 Tests Carton
Size: 200 mm x 132 mm X 70 mm

Manufactured by:

Zephyr Biomedicals

A Division of Tulip Diagnostics (P) Ltd.

M 46-47, Phase III B, Verna Industrial Estate, Verna, Goa - 403 722, INDIA.

Regd. Office: Gitanjali, Tulip Block, Dr. Antonio Do Rego Bagh, Alto Santacruz, Bambolim Complex P.O., Goa - 403 202. INDIA.

Email address: sales@tulipgroup.com

Tel. : (0832) 2458546, (0832) 2458547

0320/VER-03

LOT **Lot No.** :

Mfg. Date :

Expiry Date :

M.R.P. (₹) :

(Inclusive of all taxes)

This side up

An ISO 13485 Certified Company

IVD **IN VITRO DIAGNOSTIC MEDICAL DEVICE NOT FOR MEDICINAL USE**

REFER PACKAGE INSERT FOR INSTRUCTIONS BEFORE USE

100 Tests Carton
Size: 240 mm x 128 mm X 190 mm

Manufactured by:

Zephyr Biomedicals

A Division of Tulip Diagnostics (P) Ltd.

M 46-47, Phase III B, Verna Industrial Estate, Verna, Goa - 403 722, INDIA.

Regd. Office: Gitanjali, Tulip Block, Dr. Antonio Do Rego Bagh, Alto Santacruz, Bambolim Complex P.O., Goa - 403 202, INDIA.

Email address: sales@tulipgroup.com

Tel. : (0832) 2458546, (0832) 2458547

LOT Lot No. :

Mfg. Date :

Expiry Date :

M.R.P. (₹) :
(Inclusive of all taxes)

This side up

An ISO 13485 Certified Company

IVD **IN VITRO DIAGNOSTIC MEDICAL DEVICE NOT FOR MEDICINAL USE**

REFER PACKAGE INSERT FOR INSTRUCTIONS BEFORE USE

0320/VER-03

2. Instructions for use[3]

[3] English version of the IFU was the one that was assessed by WHO. It is the responsibility of the manufacturer to ensure correct translation into other languages.

CE

FalciVax™

REF	503010025(1T)	503010010	503010025	503010050	503010100

RAPID TEST FOR MALARIA
Pv/Pf
DEVICE

INTENDED USE
FalciVax™ is a rapid, qualitative, two site sandwich immunoassay utilizing capillary and venous whole blood specimens of symptomatic patients for the detection of *P.falciparum* specific histidine rich protein-2 (Pf. HRP-2) and *P.vivax* specific plasmodium Lactate Dehydrogenase (pLDH) antigens and it is used in aiding the diagnosis and differentiation of malaria infections caused by *P.falciparum* and *P.vivax*.
It is intended to be used by trained healthcare or laboratory professionals or other health care workers who have received appropriate training. This product can be used by trained lay providers operating at point-of-care in resource-limited settings. This product is not intended for self-testing and it is not for blood donor screening. The test is not automated; it needs to be performed and interpreted manually by the user.

SUMMARY
Four species of the Plasmodium parasites are responsible for malarial infections in human viz. *P. falciparum* , *P.vivax*, *P.ovale* and *P.malariae*. Of these *P. falciparum* and *P. vivax* are considered the "Big Two" due to incidence of cerebral malaria and drug resistance associated with *P. falciparum* malaria, and high rate of infectivity and relapse associated with *P.vivax*. As the course of treatment is dependent on the species, differentiation between *P.falciparum* and *P.vivax* is of utmost importance for better patient management and speedy recovery.
In ***FalciVax***™**,** the detection system for *P.falciparum* malaria is based on the detection of *P.falciparum* specific histidine rich protein-2 (Pf. HRP-2), which is a water soluble protein that is released from parasitised red blood cells of infected individuals. The detection system for *P.vivax* malaria is based on presence of *P.vivax* specific pLDH.

PRINCIPLE
FalciVax™ utilizes the principle of agglutination of antibodies/ antisera with respective antigen in immuno-chromatography format along with use of nano gold particles as agglutination revealing agent. As the test specimen flows through the membrane assembly of the device after addition of the clearing buffer, the colored colloidal gold conjugates of the Agglutinating Sera for HRP-2 and the Agglutinating Sera for *P. vivax* specific pLDH complexes the HRP-2/ pLDH in the lysed specimen. This complex moves further on the membrane to the test region where it is immobilized by the Agglutinating Sera for Malaria specific pLDH and / or Agglutinating Sera for HRP-2 coated on the membrane leading to formation of pink-purple colored band/s which confirms a positive test result. A band will appear under Pf at the test region in falciparum positive specimens, while a band will appear under Pv in vivax malaria positive specimens. Appearance of band under Pf as well as Pv in the test region suggests a mixed infection.
Absence of colored band/s in the test region indicates a negative test result. The unreacted conjugate and unbound complex if any, move further on the membrane and are subsequently immobilized by Agglutinating Sera for Rabbit globulin coated on the membrane at the control region, forming a pink-purple band. The control band formation is based on the 'Rabbit globulin / Agglutinating Sera for Rabbit globulin' system. Since it is completely independent of the analyte detection system, it facilitates formation of consistent control band signal independent of the analyte concentration. This control band serves to validate the test performance.

REAGENTS AND MATERIALS SUPPLIED
FalciVax™ kit contains:
A. Individual pouches, each containing:
   1. DEVICE Membrane assembly pre-dispensed with Agglutinating Sera for HRP-2 - colloidal gold conjugate, Agglutinating Sera for *P. vivax* specific pLDH - colloidal gold conjugate, rabbit globulin colloidal gold conjugate, Agglutinating Sera for HRP-2, Agglutinating Sera for Malaria specific pLDH and Agglutinating Sera for Rabbit globulin at the respective regions.
   2. Desiccant pouch.
   3. PIPETTE Disposable Plastic Specimen Applicator.
B. BUF Clearing buffer in a dropper bottle.
C. Instructions for use.
D. Pictorial instructions for use.
E. Alcohol swabs – 70% Isopropyl alcohol.
F. Sterile lancets.

Product codes REF	503010025(1T)	503010010	503010025	503010050	503010100
Pouch Sealed tests Σ	25 x 1T (25 single kit test/kit)	10	25	50	100
Clearing buffer bottles	25 x 1.0ml	01 x 3.0ml	01 x 4.0ml	02 x 4.0ml	04 x 4.0ml
Alcohol swabs	25	10	25	50	100
Sterile lancets	25	10	25	50	100
Instructions for use	25	01	01	01	01
Pictorial instructions for use	25	01	01	01	01

MATERIALS REQUIRED BUT NOT PROVIDED
Calibrated micropipette capable of delivering 5µl specimen accurately, disposable micropipette tips.
Permanent marker Pen/pencil, disposable gloves, timer.
Biosafety sharps container and Biohazard waste container (for potentially infectious waste).
Venipuncture blood collection kit (if whole blood is collected by venepuncture).
Additional alcohol swabs (if any included in the kit are found dry) and additional sterile lancets (if any included in the kit have the sterility seal broken).

STORAGE AND STABILITY
The sealed pouches in the test kit & the kit components may be stored between 1°C to 40°C till the duration of the shelf life as indicated on the pouch/ carton. DO NOT FREEZE. After first opening of the clearing buffer bottle, it can be stored between 1°C to 40°C for the remaining duration of its shelf life.

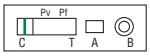
WARNINGS
Read the instructions carefully before performing the test.
For in vitro diagnostic use only. NOT FOR MEDICINAL USE. For professional use.
The test is for aiding in diagnosis of malaria infection and not for screening which requires confirmation.
Do not use beyond expiry date.
Do not use components from different lots of the product.
The device, specimen applicator, alcohol swab and blood lancet are for single use only.
Contact with the contents of desiccant pouch containing, among other substances, cobalt chloride (CAS# 7646-79-9) should be kept to a minimum. Inhalation / swallowing may cause harm.
Handle all specimens as potentially infectious.
Follow standard biosafety guidelines for handling and disposal of potentially infectious material.
Clearing buffer contains Sodium Azide(0.1%), avoid skin contact with this reagent. Azide may react with lead and copper in the plumbing system and form highly explosive metal oxides. Flush with large volumes of water to prevent azide build up in the plumbing.

SPECIMEN COLLECTION AND PREPARATION
For specimen collection, refer to pictorial instructions for use.
Fresh capillary/venous whole blood from finger prick / puncture should be used as a test specimen. However, fresh anti-coagulated venous whole blood may also be used as a test specimen. Using standard blood collection practices, collect venous whole blood into the commercially available anti-coagulant tube such as EDTA or CPDA or Heparin or Oxalate or Tri-sodium Citrate. If immediate testing is not possible then the specimen may be stored at 2°C to 8°C for upto 72 hours before testing and should be brought to room temperature (20°C to 30°C) before use on the test. Clotted, hemolysed or lipaemic whole blood specimens should not be used for performing the test.

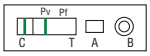
TESTING PROCEDURE AND INTERPRETATION OF RESULTS

1. Bring the ***FalciVax***™ kit components to room temperature (20°C to 30°C) before testing.
2. Open the pouch and retrieve the device, specimen applicator and desiccant pouch. Check the color of the desiccant. It should be blue, if it has turned colorless or pink, discard the device and use another device. ***Once opened, the device must be used immediately.***
3. Label the test device with patient identifier.
4. Place the testing device on a flat horizontal surface.
5. Tighten the cap of the clearing buffer bottle provided with the kit in the clockwise direction to pierce the buffer bottle nozzle.
6. **Specimen application**
   - **6.1 Venous whole blood:** Evenly mix the anti-coagulated whole blood by gentle swirling. Dip the specimen applicator into the whole blood. Ensuring that an applicator full of blood is retrieved, immediately blot the blood so collected in the specimen port 'A'(This delivers approximately 5µl of the whole blood specimen). Alternatively, 5µl of the anti-coagulated venous whole blood specimen may be delivered in the specimen port 'A' using a micropipette.
   - **6.2 Capillary whole blood:** Touch the specimen applicator to the whole blood on the finger prick. Ensuring that an applicator full of blood is retrieved, immediately blot the blood so collected in the specimen port 'A'(Care should be taken that whole blood specimen is not clotted and transfer to the specimen port is immediate). Alternatively, 5µl of the capillary finger-prick whole blood specimen may be delivered in the specimen port 'A' using a micropipette.

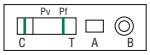
   Note: Ensure that the whole blood from the specimen applicator has been completely taken up at the specimen port 'A'.
7. Immediately dispense **two drops** of clearing buffer into buffer port 'B' holding the buffer bottle vertically and switch on the timer. To avoid contamination of clearing buffer bottle, do not touch the buffer port 'B' with the tip of clearing buffer bottle.
8. Read the results at the end of **20 minutes** as follows:



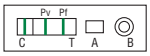
NEGATIVE for malaria : Only one pink-purple band appears in the control window 'C'.



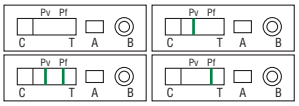
POSITIVE for *P.vivax* malaria : In addition to the control band, a pink-purple band also appears under the region marked 'Pv' in the test window 'T'. Appearance of a coloured band of any intensity (faint to dark) at 'Pv' should be considered as positive result for *P.vivax* malaria.



POSITIVE for *P.falciparum* malaria : In addition to the control band, a pink-purple band also appears under the region marked 'Pf' in the test window 'T'. Appearance of a coloured band of any intensity(faint to dark) at 'Pf' should be considered as positive result for *P.falciparum* malaria.



POSITIVE for *P.falciparum* and *P.vivax* malaria : In addition to the control band, two pink-purple bands appear under the regions marked 'Pf' and 'Pv' in the test window 'T'. Appearance of coloured bands of any intensity (faint to dark) at 'Pf' and 'Pv' should be considered as positive results for *P.falciparum* and *P.vivax* malaria.



INVALID RESULT: The test should be considered invalid if no bands appear on the device. The test should also be considered invalid if only test bands (Pv and/or Pf) appear and no control band appears. Repeat the test with a new device ensuring that the test procedure has been followed accurately.

CAUTION : Do not read results after 30 minutes as it may show erroneous results.

PERFORMANCE CHARACTERISTICS

A. Analytical Performance Study

A1. Potentially interfering exogenous and endogenous substances :

The following Potentially interfering substances have no impact on test results of ***FalciVax***™ :

Type of Specimen		Sr. No.	Potential Interfering substances
Endogenous substance		1	Total Protein
		2	Bilirubin, conjugated
		3	Cholesterol
		4	Triglycerides
		5	Haemoglobin
Common Drugs	Antibiotic	1	Amoxicillin
		2	Ciprofloxacin
	Anti-inflammatory	1	Aspirin
		2	Ibuprofen
Exogenous Substance	Anti-Malaria Drugs	1	Chloroquine
		2	Doxycycline
		3	ACT
		4	Primaquine
		5	Mefloquine
		6	Sulfadoxine
		7	Pyrimethamine
	Anti-TB Drugs	1	Ethambutol
		2	Isoniazide
		3	Rifampin
	Anti-Retroviral Drugs	1	Lamivudine
		2	Efavirenz
		3	Emtricitabine
		4	Tenofovir
		5	Atazanavir

A2. Cross Reacting infections, disease and medical conditions:

The following 17 potential cross reacting infections/diseases/conditions did not affect the performance of ***FalciVax***™.

Potential Cross reacting infections/diseases/conditions			
1	*T. cruzi*	10	*Toxoplasma gondii*
2	Dengue virus	11	Influenza A/B
3	*Leishmania spp*	12	Yellow fever virus
4	*Brucella spp*	13	*Leptospira spp*
5	Measles virus (Rubeola virus)	14	*Treponema pallidum*
6	HAV	15	HAMA
7	HBV	16	ANA
8	HCV	17	Rheumatoid factor
9	HIV-1/HIV-2		

A3. Precision (Repeatability)

Within run, precision was determined using 10 replicates of 5 different venous whole blood specimens in 03 different lots of ***FalciVax***™ which is summarized below:

*Quality control Panel	Accuracy (%)
Malaria Negative	100%
P.falciparum Positive (Moderate Positive)	100%
P.falciparum Positive (Weak Positive)	100%
P.vivax Positive (Moderate Positive)	100%
P.vivax Positive (Weak Positive)	100%

A4. Precision (Reproducibility)

Between run, precision was determined using 5 different blinded venous whole blood specimens in 3 different lots of ***FalciVax***™ X 3 different operators X 3 different sites X 5 different days which is summarized below:

*Quality control Panel	Accuracy (%)			
	Between Day	Between Operator	Between lot	Between site
Malaria Negative	100%	100%	100%	100%
P.falciparum Positive (Moderate Positive)	100%	100%	100%	100%
P.falciparum Positive (Weak Positive)	100%	97.7%	100%	100%
P.vivax Positive (Moderate Positive)	100%	100%	100%	100%
P.vivax Positive (Weak Positive)	100%	100%	100%	100%

*Quality control panel specimens have been confirmed by microscopy as malaria negative and malaria positive. Malaria positive specimens were classified as moderate or weak positive based on respective parasite counts as determined by microscopy.

A5. Analytical Sensitivity

The sensitivity of ***FalciVax***™ for *P.falciparum* is 100 parasites/µl and for *P.vivax* is 200 parasite/µl based on microscopy results.

B. Clinical Performance study: Diagnostic Specificity and Diagnostic Sensitivity

B1. In an in-house study, a panel of 200 venous whole blood specimens whose results were earlier confirmed with microscopy were tested with ***FalciVax***™. The results obtained are as follows:

Specimens	Total no. of specimens tested	***FalciVax***™		Sensitivity (95% CI)	Specificity (95% CI)
		Positive	Negative		
P.falciparum	20	20	0	100% (83.16% to 100.00%)	-
P.vivax	25	25	0	100% (86.28% to 100.00%)	-
Pf and *Pv* Malaria Negative	155	0	155	-	100% (97.65% to 100.00%)

B2. External evaluation studies:

Table 1

Study Site	Total Number of Malaria Negative specimens Tested	Specimen Type		Number of specimens Negative by Microscopy	Number of specimens Negative in ***FalciVax***™	Number of specimens falsely Positive in ***FalciVax***™
		Population type	Mode of Collection			
Jharkhand, India	985	Hospitalized Patients	Finger prick/ venous phlebotomy	985	985	0
Maharashtra, India.	1000	Blood Donors	Venous whole blood	1000	1000	0
Goa, India.	39	Symptomatic/ Asymptomatic Individuals	Capillary Whole Blood	39	39	0
			Venous Whole Blood	39	39	0
Odisha, India	545	Pregnant Women	Venous Whole Blood	545	545	0
Odisha, India	497	Neonates	Heel Prick	497	497	0

Based on above data:

Total Nos. tested	Overall Specificity	95% Confidence Interval
3105	100%	99.88% to 100.00%

Table 2

Study Site	Total Number of Malaria Positive specimens Tested	Population type	Specimen Type		Number of specimens Positive by Microscopy	Number of specimens Positive in ***FalciVax***™	Number of specimens falsely Negative in ***FalciVax***™
			Mode of Collection	Species Type			
India	403	Hospitalized Patients	Finger prick/ venous phlebotomy	*P.falciparum*	403	403	0
	312			*P.vivax*	312	312	0
	26	Symptomatic/ Asymptomatic Individuals	Capillary and Venous Whole Blood	*P.falciparum*	26	26	0
	29			*P.vivax*	29	29	0
	06			*P.falciparum* + *P.vivax*	06	06	0
	01	Pregnant Women	Venous Whole Blood	*P.falciparum*	01	01	0
	04			*P.vivax*	04	04	0
	01	Neonates	Heel Prick	*P.falciparum*	01	01	0
	02			*P.vivax*	02	02	0

Based on above data:

Plasmodium species	Total Nos. tested	Overall Sensitivity	95% Confidence Interval
P.falciparum	431	100%	99.15% to 100.00%
P.vivax	347	100%	98.94% to 100.00%
P.falciparum + *P.vivax*	06	100%	54.07% to 100.00%

LIMITATIONS OF THE TEST

1. As with all diagnostic tests, the results must always be correlated with clinical findings.
2. The results of test are to be interpreted within the epidemiological, clinical and therapeutic context.
3. Any modification to the above procedure and / or use of other reagents will invalidate the test procedure.
4. Hook effect may be observed at parasite density ≥3,00,000 parasite/µl. In such cases, repeat the test by using different dilutions of same specimen. Other clinical data (e.g symptoms, travel history, risky factors) should be used in conjunction with the test results.
5. Potential cross-reacting diseases such as HAT, Tick-borne Encephalitis and those caused by *Schistosoma spp* have not been tested in this product, and their associated interference in ***FalciVax***™ is not known.
6. Interference due to presence of heterophile antibodies in patient's specimen can lead to erroneous analyte detection in immunoassay, has been reported in various studies. ***FalciVax***™ uses HETEROPHILIC BLOCKING REAGENT (HBR) to inhibit majority of these interferences.
7. In case of (Pv+Pf) mixed infections, ***FalciVax***™ detects *P.vivax* as low as 200 parasite/µl even in presence of high *P.falciparum* densities of ~2,00,000 parasite/µl. In suspected cases of *P. falciparum* densities > 2,00,000 parasite/µl, confirm the results with microscopy.
8. ***FalciVax***™ is 100% sensitive to *P. falciparum* and *P. vivax* malaria. However, a negative test result does not rule out the possibility of infection with *P.ovale* and *P. malariae*.
9. In *P. falciparum* malaria infection, Pf. HRP-2 is not secreted in gametogony stage. Hence in "Carriers", the 'Pf' band may be absent.
10. Since Pf. HRP-2 persists for upto a fortnight even after successful therapy, a positive test result does not indicate a failed therapeutic response. If the reaction of the test remains positive with the same intensity after 5-10 days, post treatment, the possibility of a resistant strain of malaria has to be considered.

WARRANTY

This product is designed to perform as described on the label and Instructions for use. The manufacturer disclaims any implied warranty of use and sale for any other purpose. In the event of performance changes or product malfunction, please contact manufacturer.

BIBLIOGRAPHY

1. Howard, R.J., et al., 1986: Secretion of a Malarial Histidine-rich Protein (Pf. HRP II) from *Plasmodium falciparum*-infected Erythrocytes.J. Cell Biol., 103, 1269-1277.
2. Parra, M.E., et al., 1991: Identification of *Plasmodium falciparum* Histidine-Rich Protein 2 in the Plasma of Humans with Malaria.J. Clin. Microbiol., 29, 1629-1634.
3. Rodriguez-Del Valle, M., et al., 1991: Detection of Antigens and Antibodies in the Urine of Humans with *Plasmodium falciparum* Malaria. J. Clin. Microbiol., 29, 1236-1242.
4. Piper, R. C., et al., (1999) Immuno-capture diagnostic assays for malaria utilizing *Plasmodium* Lactate Dehydrogenase (pLDH) Am. J. Trop. Med. Hyg. 60(1) 109-118.
5. Hunte-Cooke A., et al., (1999) Comparison of a Parasite Lactate Dehydrogenase-based Immunochromatographic Antigen Detection assay (OptiMAL®) with Microscopy for the Detection of Malaria Parasites in Human Blood Samples. Am J.Trop Med 60(2). 173-176.
6. Quintana M., et al., (1998) Malaria diagnosis by dipstick assay in a Honduran Population with coendemic *Plasmodium falciparum* and *Plasmodium vivax*. Am. J. Trop. Med. Hyg. 59(6) 868-871.
7. Palmer, C. J., (1998) Evaluation of OptiMal test for rapid diagnosis of *Plasmodium vivax* and *Plasmodium falciparum*. J. Clin Microbiol. 36(1) 203-206.
8. Moody A., et al., (2000) Performance of the OptiMAL® malaria antigen capture dipstick for malaria diagnosis and treatment monitoring. British Journal of Hematology, 109, 1-5.
9. Data on file: Zephyr Biomedicals.

SYMBOL KEYS

Temperature Limitation	Manufacturer	DEVICE Device	EC REP Authorised Representative in the European Community
Use by	Consult Instructions for use	PIPETTE Disposable Plastic Specimen Applicator	
Date of Manufacture	REF Catalogue Number	BUF Clearing Buffer	Xn NaN., R22, S23-46-61 Harmful if swallowed. Do not breathe vapour. If swallowed, seek medical advice immediately and show this container or label. Avoid release to the environment. Refer to special instructions.
LOT Batch Number / Lot Number	IVD *In vitro* Diagnostic Medical Device	This side up	
Σ Contains sufficient for <n> tests	Do not reuse	Do not use if package is damaged	

Manufactured by:

Zephyr Biomedicals

A Division of Tulip Diagnostics (P) Ltd.

M 46-47, Phase III B, Verna Industrial Estate, Verna, Goa - 403 722, INDIA.

Regd. Office: Gitanjali, Tulip Block, Dr. Antonio Do Rego Bagh, Alto Santacruz, Bambolim Complex P.O., Goa - 403 202, INDIA.

Email address: sales@tulipgroup.com

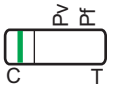
Tel. : (0832) 2458546, (0832) 2458547

EC REP

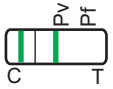
CMC Medical Devices & Drugs S.L., Spain.

0522/VER-05
Date of issue: 2023-01

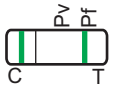
Interpretation of Results



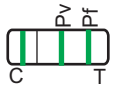
Band on 'C' Area
NEGATIVE
for Malaria



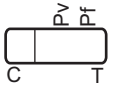
Band on 'C'&'T'-Pv Area
POSITIVE
for *P.vivax*



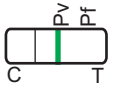
Band on 'C'&'T'-Pf Area
POSITIVE
for *P.falciparum*



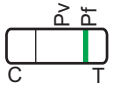
Band on 'C'&'T'-Pv,Pf Area
POSITIVE
for *P. v.* & *P. f.*



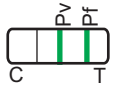
No band on 'C'&'T' Area
INVALID
Repeat the test



No band on 'C'.
Band on 'T'-Pv Area
INVALID
Repeat the test



No band on 'C'.
Band on 'T'-Pf Area
INVALID
Repeat the test



No band on 'C'.
Band on 'T'-Pv & Pf Area
INVALID
Repeat the test

Note : Coloured bands of any intensity (faint to dark) at 'Pv' and/or 'Pf' should be considered as positive result.

For further information, contact :

Zephyr Biomedicals

A Division of Tulip Diagnostics (P) Ltd.

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EC REP

CMC Medical Devices & Drugs S.L., Spain.

0522/VER-05
Date of issue: 2023-01

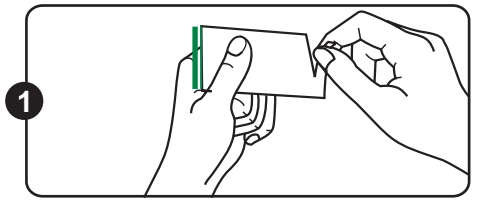
CE

FalciVax™

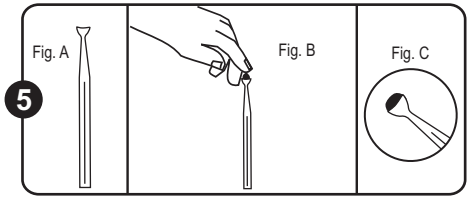
REF | 503010025(1T) | 503010010 | 503010025 | 503010050 | 503010100

RAPID TEST FOR MALARIA
Pv / Pf

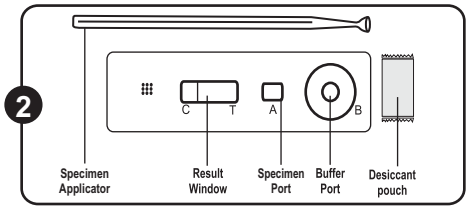
Test Procedure using Capillary whole blood specimen



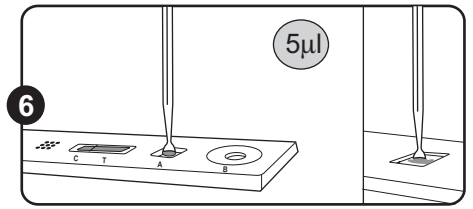
Open pouch at cut mark and remove all content; the device, disposable specimen applicator & desiccant pouch. Once opened, the device must be used immediately.
Note: Before opening the pouch, check the date of expiration on the back side of the pouch. Do not use beyond expiry date.



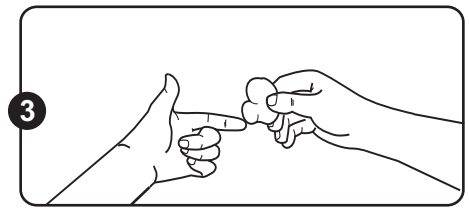
For blood collection, hold the specimen applicator vertically as shown above Fig A. With the pricked finger facing downwards towards the specimen applicator, allow the blood drop to touch the cup side of specimen applicator, Fig.B. Ensure that the cup full of blood is retrieved Fig C.



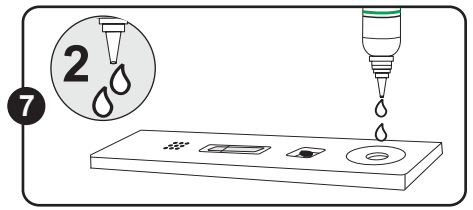
Component details are shown above. Check the colour of the desiccant. It should be blue, if it has turned colourless or pink, discard the device & use a new device.



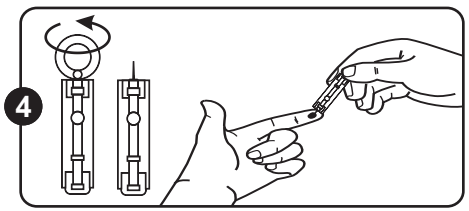
Blot the collected blood (5µl) in the specimen port 'A' by touching applicator vertically straight onto the specimen pad. Ensure that the blood from the applicator has been completely taken up at the specimen pad.



Clean finger to be pricked with an alcohol swab. Allow to dry. "Avoid finger with callus".



Hold the clearing buffer bottle vertically straight over the buffer port 'B' without having contact with the pad to avoid contamination & add exactly 2 drops of buffer onto the buffer port. Start the stop watch.



Take a sterile lancet. Open the lancet by twisting the cap. Squeeze the finger tip then prick the lateral side of the tip with sterile lancet. Safely dispose off the used lancet as biohazardous sharps waste.

Read the test Results at the end of 20 minutes. Do not read test results after 30 minutes.

FalciVax™

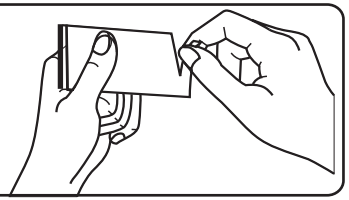
RAPID TEST FOR MALARIA

Pv / Pf

REF	503010025(1T)	503010010	503010025	503010050	503010100

Test Procedure for Venous Whole Blood Specimen

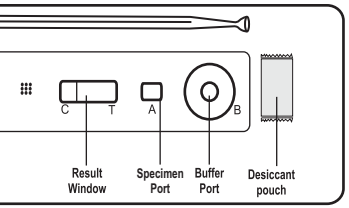
1



Open pouch at cut mark and remove all content; the device, disposable specimen applicator & desiccant pouch. Once opened, the device must be used immediately.

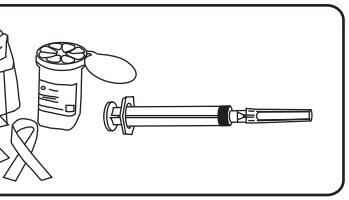
Note: Before opening the pouch, check the date of expiration on the back side of the pouch. Do not use beyond expiry date.

2



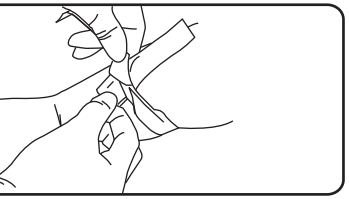
Component details are shown above. Check the colour of the desiccant. It should be blue, if it has turned colourless or pink, discard the device & use a new device.

3



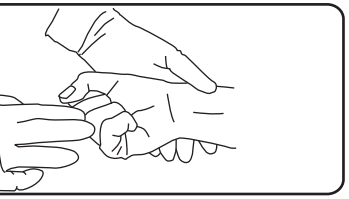
Assemble equipment & include needle & syringe.

4



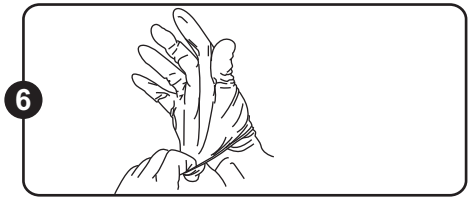
Apply a tourniquet, about 4 to 5 finger widths above the selected venepuncture site.

5



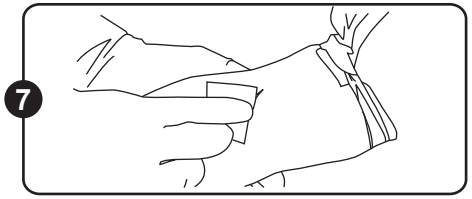
Ask the patient to form a fist.

6



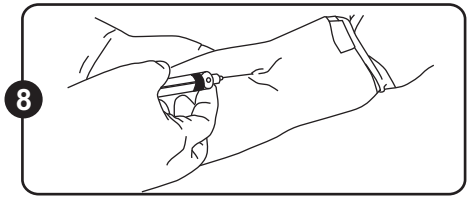
Put on well fitting non-sterile gloves.

7



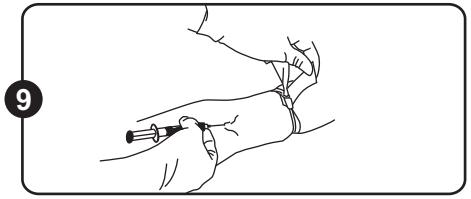
Disinfect the site using 70% Isopropyl Alcohol and let it dry completely.

8



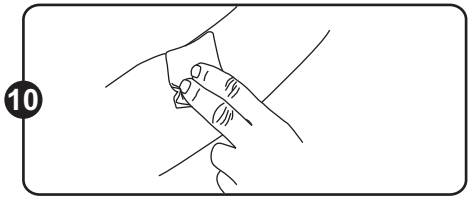
Enter the syringe in vein swiftly at a 30^0 angle.

9



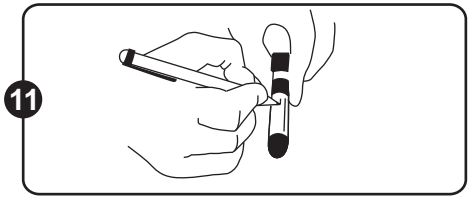
Release the tourniquet once sufficient blood has been collected.

10



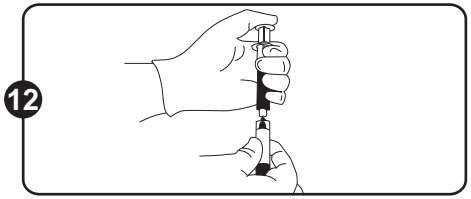
Withdraw the needle gently and then give the patient a clean cotton.

11



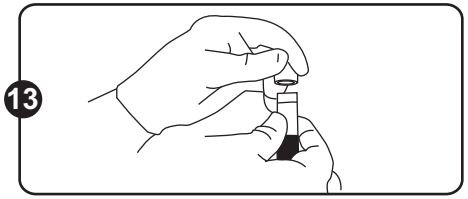
Label the tube with respective patient's name.

12



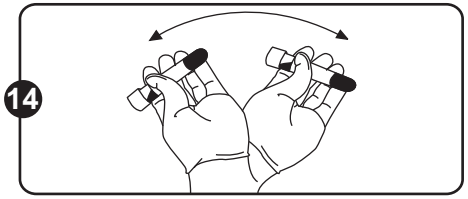
Transfer blood to the labeled tube.

13



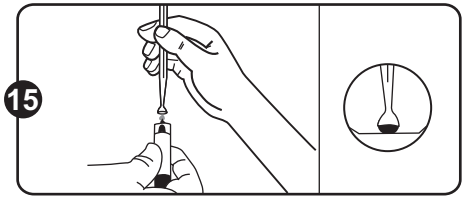
Place the cap in the tube.

14



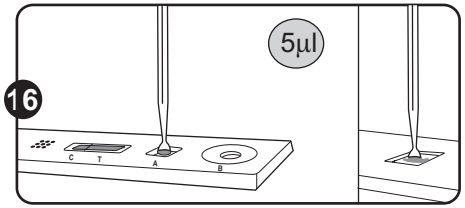
Invert specimen tube back and forth 5-10 times to mix the additives with the whole blood.

15



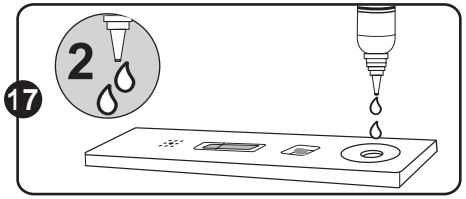
Dip the cup side of the specimen applicator in the tube. Ensure that an applicator full of blood is retrieved as shown in the above figure.

16



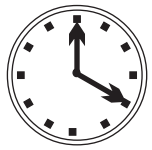
Blot the collected blood (5µl) in the specimen port 'A' by touching applicator vertically straight onto specimen pad. Ensure that the blood from the applicator has been completely taken up at the specimen pad.

17



Hold the clearing buffer bottle vertically straight over the buffer port 'B' without having contact with the pad to avoid contamination & add exactly 2 drops of buffer onto the buffer port. Start the stop watch.

18 **20 Minutes**



Read the test result at the end of 20 minutes. Do not read test result after 30 minutes.