WHO Prequalification of In Vitro Diagnostics
PUBLIC REPORT

Product: VISITECT CD4 Advanced Disease
WHO reference number: PQDx 0384-077-00

VISITECT CD4 Advanced Disease with product code **AB376**[1], manufactured by **AccuBio Ltd**[2]**., CE-mark regulatory version**, was accepted for the WHO list of prequalified in vitro diagnostics and was listed on 20 August 2020.

Summary of WHO prequalification assessment for VISITECT CD4 Advanced Disease

	Date	Outcome
Prequalification listing	20 August 2020	listed
Dossier assessment	17 July 2020	MR
Site inspection(s) of the quality management system	24-25 April 2023	MR
Product performance evaluation	2nd and 3rd quarters of 2022	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 WHO has been notified and has undertaken a review. Amendments to the report are summarised in the following table, and details of each amendment are provided below.

Version	Summary of amendment	Date of report amendment
2.0	Correction of regulatory version from RoW to CE-mark.	16 November 2020
3.0	Extension of timeline for commitment to conduct a prequalification performance evaluation for VISITECT CD4 Advanced Disease from 31 December 2020 to 31 December 2021.	18 July 2021

[1] Labelling has been changed per product rebranding. However, temporary labelling of the legacy brand with product code OD376 will be used in the market according to registration status in each country.
[2] The legal Manufacturer changed from Omega Diagnostics to AccuBio Ltd.

4.0	Extension of timeline for commitment to conduct prequalification performance evaluation for VISITECT CD4 Advanced Disease from 31 December 2021 to 31 July 2022	14 April 2022
5.0	Changed the Date of Manufacture and Expiry Date Format on the Buffer Bottle Label, Pouch Label and Kit Box Label; updated from displaying only Month and Year to YYYY-MMM-DD, which is intended to present customers with a more accurate representation of product shelf life. Changed the legal manufacturer from Omega Diagnostics Ltd to AccuBio Ltd and the product code from OD376 to AB376.	25 July 2023

Intended use:

According to the claim of intended use from AccuBio Ltd., "*the VISITECT CD4 Advanced Disease Rapid Test is a manually operated semi-quantitative assay for the estimation of CD4 protein on the surface of CD4+ T cells in human whole blood (capillary or EDTA venous) to indicate whether the level is above or below 200 cells/µL within pre-diagnosed HIV patients. The VISITECT CD4 Advanced Disease in vitro diagnostic test is for use as an aid in the management of patients with advanced HIV disease (patients with CD4 count below 200 cells/µL). This visually read test is designed to be used at the point-of-care and therefore has utility in decentralized diagnostic settings.*
VISITECT CD4 Advanced Disease is for professional use only.
VISITECT CD4 Advanced Disease is not intended for individuals <5 years of age.
VISITECT CD4 Advanced Disease is not intended for use in the determination of HIV status.
VISITECT CD4 Advanced Disease is not intended for self-testing."

Assay description:

According to the claim of assay description from AccuBio Ltd., "*the VISITECT CD4 Advanced Disease Rapid Test is an immunochromatographic assay that estimates full length CD4 protein associated with CD4+ T cells in human whole blood, and is directly correlated with CD4+ T cell levels.*
A capture monoclonal antibody (MAb) specific for the cytoplasmic domain of CD4 is applied as a line on the nitrocellulose membrane. Whole blood is added directly to the VISITECT CD4 Advanced Disease Rapid Test where red blood cells and monocytes are retained in the blood collection pad and following the addition of buffer, other white blood cells (including CD4+ T cells) migrate to a reaction area where cell lysis occurs, resulting in the release of full-length CD4 for capture in the test strip. Colloidal gold-labeled MAb conjugate against CD4 binds the captured CD4 and forms a test line. These complexes are visualized as a pink/purple line. A reference line (200 line) is included to allow estimation of CD4 levels by comparison to a set cut-off (equivalent to the signal level generated by samples containing 200 CD4+ T cells/µL). The 200 line and control line must be present for the assay result to be valid. The control line in the test device is not a sample addition control.

The VISITECT CD4 Advanced Disease test device has a results window where lines will appear. The Control line located in the results window marked "C".
The Reference line located in the results window marked "200" exhibits an intensity approximately equal to that seen with a sample containing 200 CD4+ T cells/µL.
The Test line located in the results window marked "T" exhibits an intensity that correlates to the number of CD4+ T cells in the sample.
The test result is interpreted by comparing the intensity of the Test (T) line with the Reference (200) line. If the Test (T) line has equal or weaker intensity than the Reference (200) line, the test result is "Below Reference" (≤200 CD4+ T cells/µL).
If the Test (T) line has stronger intensity than the Reference (200) line, the test result is "Above Reference" (>200 CD4+ T cells/µL)."

Test kit contents:

Component	**25 tests (product code AB376)**
Foil pouch containing test device and desiccant	25
Buffer	7 mL x 1 bottle
Sampling devices	25
Sterile retractable lancets	25
Alcohol swabs	25
Job aid for venous whole blood specimens	1
Job aid for capillary whole blood specimens	1
Instructions for use	1

Items required but not provided:

- New pair of disposable gloves
- Timer
- Pen
- Sharps/biohazard bin
- Dry gauze or tissue
- Precision pipette capable of delivering 30µL plus disposable tips (venous blood only)
- EDTA blood collection tube (venous blood only)
- Plaster

Storage:

The test kit must be stored at 2-30°C. DO NOT FREEZE

Shelf-life upon manufacture:

The shelf life of the product is currently 12 months based on accelerated studies; real-time stability studies are ongoing

Warnings/limitations:

Refer to the current version of the manufacturer's instructions for use attached to this public report.

Prioritization for prequalification:

Based on the established eligibility criteria, VISITECT CD4 Advanced Disease was given priority for the WHO prequalification assessment.

Dossier assessment

AccuBio Ltd. submitted a product dossier for VISITECT CD4 Advanced Disease as per the "*Instructions for compilation of a product dossier*" (PQDx_018). 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 17 July 2020.

Commitments for prequalification

1. Commitment to Prequalification 1: Please provide the Real Time Stability study reports ALV-018-STA08, ALV-018-STA10 and ALV-018-STA15 to WHO by 30 September 2020. The commitment was fulfilled. Issue closed.
2. Commitment to Prequalification 2: Please provide an updated timeline for submission of Real Time Stability study report ALV-018-STA20-PRO when it becomes available. The commitment was fulfilled. Issue closed.
3. Commitment to Prequalification 3: Please provide a commitment to submit the final study report for the multi-site evaluation, or a timeline for when this will be submitted. The commitment was fulfilled. Issue closed.
4. Commitment to Prequalification 1a1 and 1a2, which superseded commitments above: Please provide the interim study report for ALV-018-STA20-PRO in January 2023, with the final report to be provided in August 2023. The final report was submitted and is under review.

Based on the product dossier screening and assessment findings, the product dossier for VISITECT CD4 Advanced Disease meets WHO prequalification requirements.

Manufacturing site inspection

An inspection of AccuBio Ltd., located at Hillfoots Business Village, Alva, FK12 5DQ, United Kingdom, was conducted from 24-25 April 2023. 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 a product of consistent quality. Routine inspections of the Manufacturing site will be conducted with copies of the WHO Public Inspection Report (WHOPIR) published on the WHO Prequalification web page as per Resolution WHA57.14 of the World Health Assembly. Note that a WHOPIR reflects the information on the most current inspection or desk assessment performed at a manufacturing site for in vitro diagnostic products and gives a summary of the inspection or desk assessment findings.

Information on the most current inspection or desk assessment 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.
The manufacturer's responses to the nonconformities found at the time of the inspection were accepted on 11 July 2023.

Based on the site inspection or desk assessment and corrective action plan review, the quality management system for VISITECT CD4 Advanced Disease meets WHO prequalification requirements.

Product performance evaluation

Under the special circumstances linked to the Covid-19 pandemic, and considering that:

1. The product was assessed under full prequalification assessment, including the review of the product dossier;
2. The independent clinical evaluation data partly covering the requirements of the performance evaluation for prequalification assessment was provided;
3. The performance evaluation for this product requires prospective specimen collection, which is affected by the ongoing pandemic.

VISITECT CD4 Advanced Disease was evaluated in the 2nd and 3rd quarters of 2022 at Kenya Medical Research Institute, Centre for Global Health Research, HIV Research Laboratory, Kisumu, Kenya, on behalf of WHO according to protocol PQDx_340, version 1.

Clinical performance evaluation

In this limited evaluation of clinical performance characteristics, a panel of 300 venous whole blood and capillary blood specimens was used. The specimens were characterized using FACS Calibur on EDTA whole blood.

Clinical performance characteristics in comparison with an agreed reference standard		
	Venous whole blood	**Capillary whole blood**
Sensitivity for detection of specimens with ≤200 CD4+ T-cells/ µL % (N=100)	96.0% (95% CI: 90.1-98.9)	95.0 % (95% CI: 88.7-98.4)
Specificity (> 200 CD4+ T-cells/ µL) % (95% CI) (N= 200)	96.0 % (95% CI: 92.3-98.3)	97.0 % (95% CI: 93.6-98.9)
Inter-reader variability % (N= 300)	2.0%	0.3%
Invalid rate % (N= 600)	0%	

Analytical performance

Analytical performance characteristics	
Reproducibility	2 specimens with reference values <150 and 2 specimens with reference values >250 CD4+ T-cells/µL were correctly classified 20/20 times each over 2 days. 4 specimens with reference values between 150 and 250 CD4+ T-cells/ µL were consistently classified 20/20 times each over 2 days (3 were correctly classified, and 1 specimen with a reference value of 246 CD4+ T-cells/µL was consistently classified as below reference)
Lot-to-lot variation	Of 20 specimens tested on two different lots, none showed discrepant results between the two lots.

Ease of use and operational characteristics

VISITECT CD4 Advanced Disease was found to be easy to use. However, the operators noted that the images of the test on the IFU are not reflective of the actual images on the device. The VISITECT CD4 Advanced Disease test sometimes gives faint images; the reference and test lines are not as intense as shown on the IFU.

Adequate training is required. Due to the observed differences between results obtained during actual testing and IFU images, it was recommended to modify the IFU so that images better demonstrate the lines seen when performing the test. Training should focus on the actual results obtained during practical training at the laboratory.

This type of assay requires no sophisticated equipment and can therefore be performed in laboratories with limited facilities and non-laboratory settings.

Key operational characteristics	
Specimen type(s) and volume	30 µL of venous or capillary whole blood
Number of steps*	3 steps in total, including 2 steps with timing (add buffer to Well A after 3 minutes, add buffer to Well B after 17 minutes) 1 step with precision pipetting (only for venous whole blood)
Time to result	40 minutes
Endpoint stability (interval)	5 minutes
Internal QC	Yes, reagent addition control (not a specimen addition control)

Commitment to prequalification:

The manufacturer committed to revising the IFU to include test results images that resemble the true images when the users are performing the test when the next version of the IFU is issued**.**

Labelling

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

1. Labels

1.1 Carton artwork

AccuBio

VISITECT®
CD4 Advanced Disease

VISITECT®CD4 Advanced Disease
Rapid test for the estimation of CD4+ T cells in human whole blood

IVD : LOT

IFU Version :

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2°C 30°C

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CD4 Advanced Disease

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VISITECT®
CD4 Advanced Disease

VISITECT® CD4 Advanced Disease

Rapid test for the estimation of CD4+ T cells in human whole blood

2°C 30°C

Contents : 25 Test Devices
1 Bottle Containing Buffer
25 Sampling Devices
25 Retractable Lancets STERILE R
25 Alcohol Swabs
1 Job Aid for Venous Blood
1 Job Aid for Capillary Blood
1 IFU

REF :
LOT :

Required but not provided : Timer Sharps Bin
Gloves Dry Gauze/Tissue
Pen

VISITECT® CD4 Advanced Disease
Rapid test for the estimation of CD4+ T cells in human whole blood

2°C 30°C

Contents : 25 Test Devices
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1 Job Aid for Venous Blood
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1 IFU

REF :
LOT :

Required but not provided : Timer Sharps Bin
Gloves Dry Gauze/Tissue
Pen

WB065av3 6083 V1

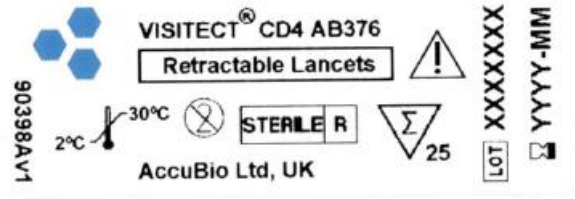
6083 V1 - WB065av3

1.2 VISITECT CD4 Advanced Disease Rapid Test

Component Labels

Buffer Bottle Label

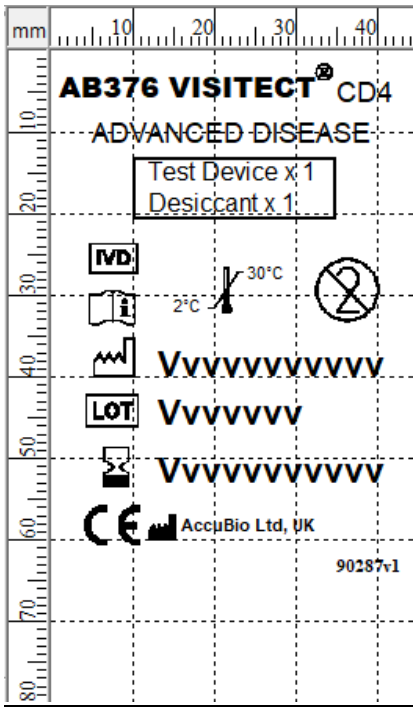
Retractable Lancet Label



Alcohol Swab Label

Sampling Device Label

Pouch Label Artwork



Pouch Image

2. Instructions for use and Job aid[2]

[2] 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.

REF AB376

VISITECT® CD4 Advanced Disease

Rapid test for the estimation of CD4+ T cells in human whole blood.
Store at 2-30°C. DO NOT FREEZE.
For professional use only.

IVD CE

INTENDED USE

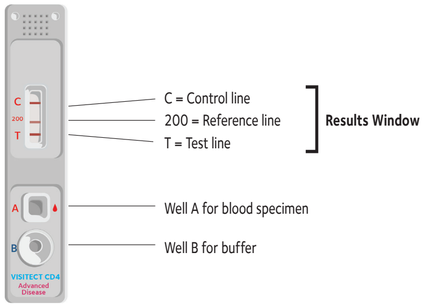
The VISITECT® CD4 Advanced Disease Rapid Test is a manually operated semi-quantitative assay for the estimation of CD4 protein on the surface of CD4+ T cells in human whole blood (capillary or EDTA venous) to indicate whether the level is above or below 200 cells/µL within pre-diagnosed HIV patients.
The VISITECT® CD4 Advanced Disease *in vitro* diagnostic test is for use as an aid in the management of patients with advanced HIV disease (patients with CD4 count below 200 cells/µL). This visually read test is designed to be used at the point-of-care and therefore has utility in decentralised diagnostic settings.
VISITECT® CD4 Advanced Disease is for professional use only.
VISITECT® CD4 Advanced Disease is not intended for individuals <5 years of age.
VISITECT® CD4 Advanced Disease is not intended for use in the determination of HIV status.
VISITECT® CD4 Advanced Disease is not intended for self-testing.

INTRODUCTION

The CD4+ T cell count has made a critical contribution to assessing the immune and clinical status of HIV patients over the last 35 years.[1]
Although the annual number of people dying of AIDS-related causes has reduced, this decline has stalled in recent years due to the challenges of advanced HIV disease, defined by WHO as <200 CD4+ T cells/µL or clinical stage III and IV disease.[2] Patients presenting with advanced HIV disease are at high risk of opportunistic infection and death, the risk increases with decreasing CD4 cell counts.
The role of CD4 cell counts has been re-assessed.[3] Current WHO guidelines for the management of advanced HIV disease recommend a package of care be offered to those presenting with advanced HIV disease depending on age and CD4 cell counts.[2] A HIV patient who has advanced disease requires additional testing and prophylaxis or treatment for opportunistic infections in order to safely initiate ART and decrease risk of death.[4]
The VISITECT® CD4 Advanced Disease *in vitro* diagnostic test is a rapid, instrument-free test, that provides actionable results at the point-of-care. The test provides an estimation of CD4 protein levels associated with T cells and indicates whether the patients' CD4+ T cell count is above or below 200 cells/µL and so HIV disease status.

PRINCIPLE OF THE TEST

The VISITECT® CD4 Advanced Disease Rapid Test is an immunochromatographic assay that estimates full length CD4 protein associated with CD4+ T cells in human whole blood, and is directly correlated with CD4+ T cell levels.
A capture monoclonal antibody (MAb) specific for the cytoplasmic domain of CD4 is applied as a line on the nitrocellulose membrane. Whole blood is added directly to the VISITECT® CD4 Advanced Disease Rapid Test where red blood cells and monocytes are retained in the blood collection pad and following the addition of buffer, other white blood cells (including CD4+ T cells) migrate to a reaction area where cell lysis occurs, resulting in the release of full-length CD4 for capture in the test strip. Colloidal gold-labeled MAb conjugate against CD4 binds the captured CD4 and forms a test line. These complexes are visualised as a pink/purple line. A reference line (200 line) is included to allow estimation of CD4 levels by comparison to a set cut-off (equivalent to the signal level generated by specimens containing 200 CD4+ T cells/µL). The 200 line and control line must be present for the assay result to be valid. The control line in the test device is not a specimen addition control.
The VISITECT® CD4 Advanced Disease test device has a results window where lines will appear.
The ***Control line***, located in the **results window marked "C"**.
The ***Reference line***, located in the **results window marked "200"** exhibits an intensity approximately equal to that seen with a specimen containing 200 CD4+ T cells/µL.
The ***Test line***, located in the **results window marked "T"** exhibits an intensity that correlates to the number of CD4+ T cells in the specimen.
The test result is interpreted by comparing the intensity of the Test (T) line with the Reference (200) line. If the **Test (T) line** has **equal or weaker intensity** than the Reference (200) line, the test result is **"Below Reference"** (**≤200 CD4+ T cells/µL**).
If the **Test (T) line** has **stronger intensity** than the Reference (200) line, the test result is **"Above Reference"** (**>200 CD4+ T cells/µL**).



CONTENTS OF THE VISITECT® CD4 ADVANCED DISEASE KIT

Materials provided:

- 25 foil pouches containing: one test device and one desiccant sachet
- 1 bottle with 7mL buffer containing 0.05% sodium azide
- 25 sampling devices
- 25 sterile retractable lancets
- 25 alcohol swabs
- 1 job aid for venous blood
- 1 job aid for capillary blood
- 1 instructions for use

Materials required, but not provided:

- New pair of disposable gloves
- Timer
- Pen
- Sharps/biohazard bin
- Dry gauze or tissue
- Precision pipette capable of delivering 30µL plus disposable tips (venous blood only)
- EDTA blood collection tube (venous blood only)
- Plaster

KIT STORAGE

The kit will perform within specification until the stated expiry date when stored at 2-30°C out of direct sunlight. Do not use the test device or buffer beyond the date of expiration. Do not freeze.

QUALITY CONTROL

The VISITECT® CD4 Advanced Disease test device contains an internal control which should exhibit a pink/purple coloured line independent of the Test (T) and Reference (200) lines. The Control (C) line must be present for the assay result to be valid. The Control (C) line in the test device is not a specimen addition control. There is no quality control standard available, however it is recommended that a specimen greater than 200 CD4+ T cells/µL (characterised by flow cytometry) is run and three pink/purple lines are visible. It is recommended that such a control is run on a regular basis according to local guidelines.

SPECIMEN COLLECTION AND TEST PROCEDURE

This assay is designed to be used only with peripheral whole blood collected by venepuncture into EDTA tubes or by finger-prick. **Capillary** or **venous blood** is transferred directly into Well A of the device. Read carefully the limitations, warnings and safety and handling precautions within these instructions for use. Long term kit storage is 2-30°C. Assay components must be run at 15-35°C. Place the test device on a horizontal surface.

Preparing for the test

1. Allow the test kit to come to operating temperature (15-35°C) before use. Check expiry on foil pouch and kit components are within date.
2. When you are ready to perform the test, tear open the foil pouch and remove materials. (VISITECT® CD4 Advanced Disease test devices should not be used more than 30 minutes after removal from the foil pouch.) Ensure a desiccant is present and discard. If no desiccant is present discard test device and use another test device. Dispose of all packaging in a general waste bin.
3. Write the patient's name or patient identifier on the test device.
4. Put on the disposable gloves. Use new gloves for each patient.

Specimen collection

5. Proceed to capillary or venous blood sampling, depending on blood collection type.

Capillary Blood Specimen

i. Take a supplied retractable lancet. ⚠ Check the cap seal is not broken before use. Ask the patient which is their non-dominant hand and clean the side of the finger with the alcohol swab where the prick will be performed. Allow the finger to air dry, twist off lancet cap and pierce the skin of the fingertip to the side of the ball of the finger. Dispose of the retractable lancet into the sharps/biohazard bin immediately.
ii. Wipe away the first drop of blood with a piece of dry gauze or tissue and dispose in the sharps/biohazard bin.
iii. Take a supplied sampling device. Gently squeeze the finger until a full drop of blood develops. DO NOT squeeze the finger too hard. Hold the sampling device provided horizontally and touch the tip of the sampling device to the blood specimen. Capillary action will draw blood to the black line (30µL). Do not squeeze the bulb to draw blood into the tube. Use immediately.

EDTA Venous Blood

i. Collect a venous specimen of blood using established techniques. Prepare the precision pipette volume to 30µL and attach a disposable tip.
ii. Mix the EDTA blood specimen by gentle inversion at least 8 times and ensure fully mixed. Open the EDTA blood tube.
iii. Press the plunger button of the pipette to the first stop. Immerse the disposable tip vertically into the EDTA tube. Smoothly release plunger button, drawing the blood into the disposable tip.

Test procedure

6. Touch the centre of **Well A** lightly and squeeze the bulb of the sampling device/depress the pipette plunger gently to ensure the full 30µL specimen is released into **Well A**.
7. Discard the sampling device/disposable tip into a sharps/biohazard bin.
8. Wait for **3 minutes**.
9. Hold the buffer bottle **vertically 1cm above Well A**. Add **1 drop** of buffer to **Well A** where the blood has been added.
10. Wait for **17 minutes**.
11. Hold the buffer bottle **vertically 1cm above Well B**. Carefully add **3 drops** of buffer to **Well B** allowing each drop to absorb into the well before adding the next drop.
12. Wait for **20 minutes**. After the test is complete, interpret the results within **5 minutes.**

INTERPRETATION OF RESULTS

13. Refer to examples of results on reverse.
The Control (C) line and Reference (200) line must be present when reading the test results for the test to be valid. Results are interpreted visually by comparing the colour intensity of the Test (T) line with the Reference (200) line.

Line Intensity	Interpretation of the test result
Test (T) line EQUAL to Reference (200) line	BELOW REFERENCE
Test (T) line MISSING	BELOW REFERENCE
Test (T) line LIGHTER than Reference (200) line	BELOW REFERENCE
Test (T) line DARKER than Reference (200) line	ABOVE REFERENCE
Reference (200) line MISSING	INVALID, REPEAT THE TEST
Control (C) line MISSING	INVALID, REPEAT THE TEST

14. Dispose of test device and gloves in a sharps/biohazard bin.

LIMITATIONS

- VISITECT® CD4 Advanced Disease is not intended for individuals less than 5 years of age.
- EDTA blood specimens must not be used more than 24 hours post collection when stored at 2-30°C.
- The presence of the Control (C) line only means that flow of the test has occurred. It does not guarantee that:
  i. the correct specimen has been used
  ii. the specimen has been applied correctly
  iii. the specimen and test have been correctly stored
  iv. the test procedure was followed correctly
- There is no re-use protocol for this product.
- VISITECT® CD4 Advanced Disease test devices should not be used more than 30 minutes after removal from the foil pouch.

WARNINGS

- Read the instructions carefully before performing the test. Failure to follow the instructions may lead to inaccurate test results.
- Use of any other buffer or fluid except the buffer supplied with the kit will invalidate the results.
- Do not use the kit beyond the expiry date.
- Do not use if any kit components are damaged.
- ⚠ Check the lancet cap seal is not broken before use.
- Do not use if the product has been exposed to excessive heat or humidity.
- Check for the presence of a desiccant immediately after opening the pouch. If no desiccant is present, do not use the test device and discard as appropriate.
- The test device, alcohol swab, lancet and sampling device are each intended for single use only.
- For finger-prick specimens, the use of any other sampling device except the sampling device supplied with the kit will invalidate the results.
- The use of specimens other than capillary or EDTA whole blood specimens have not been validated in this test.
- Clinical decisions should not be made solely on the findings of one test. When making an interpretation of the test all clinical data should be taken into consideration.
- Do not touch the test strip within the test device with your fingers.
- Do not use haemolysed, lipemic, coagulated or frozen bloods.
- No other anticoagulants other than EDTA can be used as they may give incorrect results.

SAFETY AND HANDLING PRECAUTIONS

- Safety Precautions
  i. Handle all specimens as potentially infectious.
  ii. Wear gloves and protective clothing while handling specimens and running the test.
  iii. Do not smoke, eat or drink while handling specimens or performing the test procedure.
  iv. Apply standard biosafety precautions for handling and disposal of potentially infective material. Dispose of all packaging in a general waste bin.
  v. Avoid splashing and aerosol formation.
  vi. Clean up spills thoroughly using an appropriate disinfectant.
- Handling Precautions
  i. Do not use if any kit components are damaged.
  ii. Do not use if the desiccant package is missing or damaged. Discard device and use a new test.
  iii. The test device, alcohol swab, lancet and sampling device are each intended for single use only.
  iv. Do not use kit components beyond the expiry date printed on the label. Always check expiry date prior to testing.
  v. Adequate lighting is required to read a test result.
  vi. All reagents and used test device should be treated as potential biohazards in use and disposal. Final disposal must be in accordance with local legislation. Do not ingest.
  vii. VISITECT® CD4 Advanced Disease buffer contains 0.05% sodium azide as a preservative which may be hazardous to health if ingested. Sodium azide may react with lead and copper plumbing to form highly explosive salts. On disposal, flush with large quantities of water.

PERFORMANCE CHARACTERISTICS

Performance Evaluation Data

All performance evaluations were carried out by hospital clinic sites.
Sensitivity: specimens ≤200 cells/µL correctly identified against Flow Cytometry (95% confidence intervals)
Specificity: specimens >200 cells/µL correctly identified against Flow Cytometry (95% confidence intervals)

VISITECT® Batch 1

VISITECT® CD4 Advanced Disease performance evaluation with venous blood performed in India (n=245).

Sensitivity (44/51)	**86.3%** (73.7% - 94.3%)
Specificity (180/194)	**92.8%** (88.2% - 96.0%)

Category (cells/µL)	≤100	101-200	201-350	351-500	>500
Correctly classified	100%	63%	75%	98%	100%

VISITECT® Batch 2

VISITECT® CD4 Advanced Disease performance evaluation with capillary blood performed in India (n=144).

Sensitivity (25/29)	**86.2%** (68.3% - 96.1%)
Specificity (109/115)	**94.8%** (89.0% - 98.1%)

Category (cells/µL)	≤100	101-200	201-350	351-500	>500
Correctly classified	100%	81%	74%	100%	100%

VISITECT® Batch 3

VISITECT® CD4 Advanced Disease performance evaluation with capillary blood performed in Zimbabwe (n=145).

Sensitivity (25/27)	**92.6%** (75.7% - 99.1%)
Specificity (107/118)	**89.8%** (82.9% - 94.6%)

Category (cells/µL)	≤100	101-200	201-350	351-500	>500
Correctly classified	100%	80%	67%	100%	94%

Other external test results

VISITECT® CD4 Advanced Disease test performance at several clinical sites in the UK, Zimbabwe and India with 1232 venous blood specimens demonstrated a sensitivity of 92% (88.0%-95.1%) and a specificity of 89.5% (87.4%-91.4%)

Category (cells/µL)	≤100	101-200	201-350	351-500	>500
Correctly classified	97%	87%	60%	92%	99%

Repeatability

Within run repeatability of the VISITECT® CD4 Advanced Disease test was determined by running ten replicates with an above and below reference specimens on one batch of devices by a single operator. All results were identified correctly 100% of the time.

Reproducibility

Within run reproducibility of the VISITECT® CD4 Advanced Disease test was determined by running three replicates with an above and below reference specimens on one batch by three operators in three separate locations.
Between batch reproducibility of the VISITECT® CD4 Advanced Disease test was determined by running ten replicates with an above and a below reference specimens on three batches of test devices. All results were identified 100% of the time.

Interfering Substances

No interference in the performance of the VISITECT® CD4 Advanced Disease was evident when above and below reference blood specimens were spiked with the following endogenous interferents: Bilirubin (conjugated) up to 30µmol/L, Bilirubin (Unconjugated) up to 48µmol/L, Total Protein up to 120mg/mL, Lipids up to 37mmol/L, Rheumatoid Factor up to 100IU/mL and Haemoglobin at 2g/L. Additionally, no interference was observed with Biotin at 50ng/mL, Soluble CD4 at 12ng/mL, Human Anti-Mouse Antibody at 300ng/mL and Monocytes up to 1000cells/µL.

SYMBOL LEGEND

The following symbols may have been used within the labelling of this product.

CE	This product fulfils the requirements of Directive 98/79/EC on *in vitro* diagnostic medical devices.	!	Harmful
LOT	Batch code	IVD	*In vitro* diagnostic medical device
	Biological risks		Keep dry
REF	Catalogue number		Keep away from sunlight
⚠	Caution		Manufacturer
	Consult instructions for use	SN	Serial number
Σ	Contains sufficient for "n" tests	STERILE R	Sterilised using irradiation
	Date of manufacture		Temperature limit
	Do not re-use		Use-by date

REFERENCES

1. D Barnett et al. CD4 immunophenotyping in HIV infection. Nat Rev Microbiol. 2008; 6: S7-S15.
2. World Health Organization. Guidelines for managing advanced HIV disease and rapid initiation of antiretroviral therapy. Geneva, Switzerland: WHO, 2017.
3. N Ford et al. The evolving role of CD4 cell counts in HIV care. Curr Opin HIV AIDS. 2017;12: 123-128.
4. N Ford et al. Managing Advanced HIV Disease in a Public Health Approach. Clin Infect Dis. 2018; 66: (S2): S106-S110.

8476 V1 JUNE 2023

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AN ISO 13485 CERTIFIED COMPANY

MATERIALS PROVIDED

TEST DEVICE AND DESICCANT

SAMPLING DEVICE **(FOR CAPILLARY BLOOD COLLECTION ONLY)**

BOTTLE CONTAINING BUFFER

ALCOHOL SWAB

STERILE RETRACTABLE LANCET

MATERIALS REQUIRED, BUT NOT PROVIDED

DISPOSABLE GLOVES

TIMER

PEN

SHARPS/ BIOHAZARD BIN

DRY GAUZE OR TISSUE

PRECISION PIPETTE CAPABLE OF DELIVERING 30µL PLUS DISPOSABLE TIPS **(VENOUS BLOOD ONLY)**

EDTA BLOOD COLLECTION TUBE **(VENOUS BLOOD ONLY)**

PLASTER

COLLECT ALL THE REQUIRED MATERIALS BEFORE STARTING THE TEST. READ INSTRUCTIONS CAREFULLY

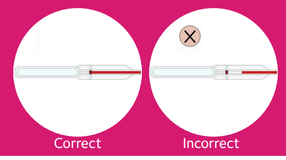
Do's and Don'ts

DO NOT RE-USE THE TEST

BUFFER BOTTLE

Correct Incorrect

SAMPLING DEVICE

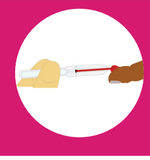


Correct Incorrect

FINGER WIPE

Do not wipe first drop of blood with alcohol swab but with a piece of clean dry gauze or tissue

BLOOD DRAW



Do not squeeze bulb of sampling device to draw the blood

PREPARING FOR THE TEST

1 Check expiry on foil pouch, and that kit components are within date and are at operating temperature (15–35°C) before use.

2

Tear open foil pouch and remove materials.

Discard desiccant sachet.

Dispose of all packaging in a general waste bin.

3 Write patient's identifier on device.

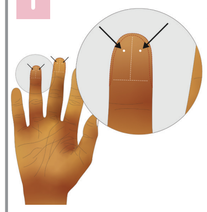
4 Put on a new pair of disposable gloves.

SPECIMEN COLLECTION

5 Proceed to capillary or venous blood sampling, depending on blood collection type.

CAPILLARY

i

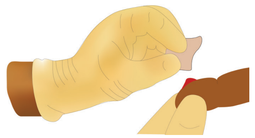


Ask patient which is their non-dominant hand, clean side of finger with alcohol swab where prick will be performed.

Allow finger to air dry, twist off lancet cap and pierce skin of fingertip to the side of the ball of the finger.

Dispose of the retractable lancet into a sharps/biohazard bin immediately.

ii Wipe away first drop of blood with piece of dry gauze or tissue, dispose of in sharps/biohazard bin.



iii Gently squeeze the finger until a full drop of blood develops.

Hold sampling device horizontally and touch the tip to the blood specimen. Capillary action will draw blood to the black line (30µL). Do not squeeze the bulb to draw blood into the tube. Use immediately.

EDTA VENOUS BLOOD

i

Collect venous specimen of blood using established techniques.

Prepare precision pipette volume to 30µL and attach disposable tip.

ii

Mix the EDTA blood specimen by gentle inversion at least 8 times and ensure fully mixed.

Open the EDTA blood tube.

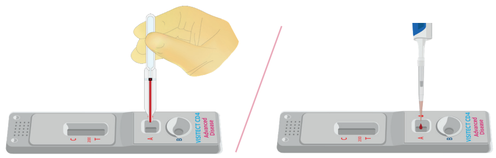
iii

Press the plunger button of the pipette to the first stop.

Immerse the disposable tip vertically into the EDTA tube. Smoothly release plunger button, drawing the blood into the disposable tip.

TEST PROCEDURE

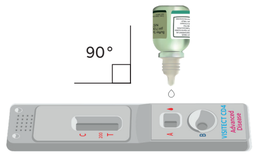
6 Touch the centre of **Well A** lightly and squeeze the bulb/depress the plunger gently to ensure the full 30µL specimen is released into **Well A**.



7 Discard the sampling device/ disposable tip into a sharps/ biohazard bin.

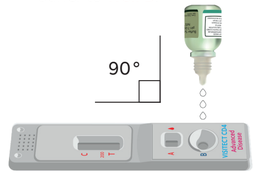
8 Wait for **3 MINUTES**.

9 Hold the buffer bottle vertically 1cm above **Well A**. Add 1 drop of buffer to **Well A**.



10 Wait for **17 MINUTES**.

11 Hold the buffer bottle vertically 1cm above **Well B**. Add 3 drops of buffer to **Well B**.

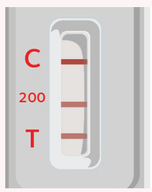


12 Wait for **20 MINUTES**.

Interpret the results within **5 MINUTES**.

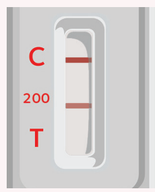
INTERPRETATION OF RESULTS

13 The Control (C) line and the Reference (200) line must be present when reading the test results for the test to be valid. Results are interpreted visually by comparing the colour intensity of the Test (T) line with the Reference (200) line.



Test (T) line EQUAL INTENSITY to Reference (200) line
CD4 count equal to or below 200 cells/µL

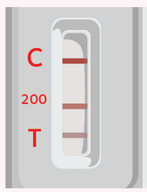
Test result is **BELOW REFERENCE**



Test (T) line MISSING

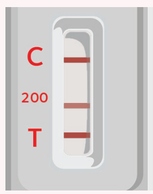
CD4 count below 200 cells/µL

Test result is **BELOW REFERENCE**



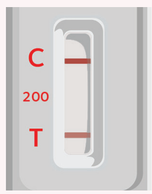
Test (T) line LIGHTER than Reference (200) line
CD4 count below 200 cells/µL

Test result is **BELOW REFERENCE**



Test (T) DARKER than Reference (200) line
CD4 count above 200 cells/µL

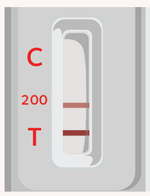
Test result is **ABOVE REFERENCE**



Reference (200) line MISSING

Test result is **INVALID**

Repeat the test



Control (C) line MISSING

Test result is **INVALID**

Repeat the test

14 Dispose of the test device and gloves in a sharps/biohazard bin.

en **JOB AID** CAPILLARY

VISITECT® AB376
CD4 Advanced Disease

MATERIALS PROVIDED


TEST DEVICE AND DESICCANT

SAMPLING DEVICE


BOTTLE CONTAINING BUFFER


ALCOHOL SWAB


STERILE RETRACTABLE LANCET

MATERIALS REQUIRED, BUT NOT PROVIDED


DISPOSABLE GLOVES

TIMER


PEN


SHARPS/ BIOHAZARD BIN

DRY GAUZE OR TISSUE


PLASTER

COLLECT ALL THE REQUIRED MATERIALS BEFORE STARTING THE TEST. READ INSTRUCTIONS CAREFULLY.

PREPARING FOR THE TEST

1 Check expiry on foil pouch and kit components are within date and are at operating temperature (15-35°C) before use.

2

Tear open foil pouch and remove materials.

Discard desiccant sachet.

Dispose of all packaging in a general waste bin.

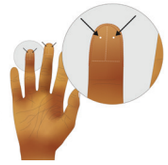
3 Write patient's identifier on device.

4 Put on a new pair of disposable gloves.

SPECIMEN COLLECTION

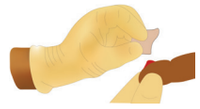
5 i Ask patient which is their non-dominant hand, clean side of finger with alcohol swab where prick will be performed.

Allow finger to air dry, twist off lancet cap and pierce skin of fingertip to the side of the ball of the finger.



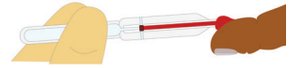
Dispose of the retractable lancet into a sharps/biohazard bin immediately.

ii Wipe away first drop of blood with piece of dry gauze or tissue, dispose of in sharps/ biohazard bin.



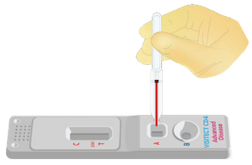
iii Gently squeeze the finger until a full drop of blood develops.

Hold sampling device horizontally and touch the tip to the blood specimen. Capillary action will draw blood to the black line (30µL). Do not squeeze the bulb to draw blood into the tube. Use immediately.



TEST PROCEDURE

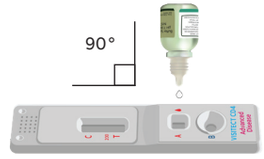
6 Touch the centre of **Well A** lightly and squeeze the bulb gently to ensure the full 30µL specimen is released into **Well A**.



7 Discard the sampling device into a sharps/ biohazard bin.

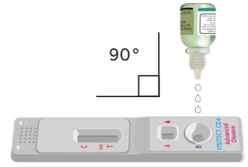
8 Wait for **3 MINUTES**.

9 Hold the buffer bottle vertically 1cm above **Well A**. Add 1 drop of buffer to **Well A**.



10 Wait for **17 MINUTES**.

11 Hold the buffer bottle vertically 1cm above **Well B**. Add 3 drops of buffer to **Well B**.



12 Wait for **20 MINUTES**.

Interpret the results within **5 MINUTES**.

INTEPRETATION OF RESULTS

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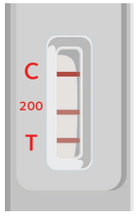
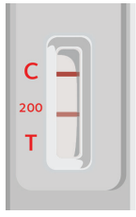


Test (T) line EQUAL INTENSITY to Reference (200) line
CD4 count equal to or below 200 cells/µL

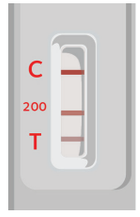
Test result is **BELOW REFERENCE**



Test (T) line MISSING

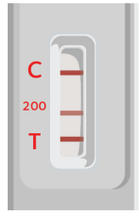
CD4 count below 200 cells/µL

Test result is **BELOW REFERENCE**



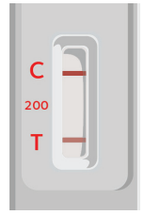
Test (T) line LIGHTER than Reference (200) line
CD4 count below 200 cells/µL

Test result is **BELOW REFERENCE**



Test (T) DARKER than 200 line
CD4 count above 200 cells/µL

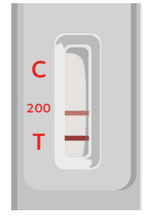
Test result is **ABOVE REFERENCE**



Reference (200) MISSING

Test result is **INVALID**

Repeat the test



Control (C) line MISSING

Test result is **INVALID**

Repeat the test

14 Dispose of the test device and gloves in a sharps/biohazard bin.

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Always refer to the instructions for use for the most up to date version of the test procedure

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AN ISO 13485 CERTIFIED COMPANY

en **JOB AID** VENOUS WITH EDTA

VISITECT® AB376
CD4 Advanced Disease

MATERIALS PROVIDED


TEST DEVICE AND DESICCANT

SAMPLING DEVICE


BOTTLE CONTAINING BUFFER


ALCOHOL SWAB


STERILE RETRACTABLE LANCET

MATERIALS REQUIRED, BUT NOT PROVIDED


DISPOSABLE GLOVES

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PRECISION PIPETTE CAPABLE OF DELIVERING 30µL PLUS DISPOSABLE TIPS


EDTA BLOOD COLLECTION TUBE


PLASTER

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PREPARING FOR THE TEST

1 Check expiry on foil pouch and kit components are within date and are at operating temperature (15-35°C) before use.

2

Tear open foil pouch and remove materials.

Discard desiccant sachet.

Dispose of all packaging in a general waste bin.

3 Write patient's identifier on device.

4 Put on a new pair of disposable gloves.

SPECIMEN COLLECTION

5 i Collect venous specimen of blood using established techniques.

Prepare precision pipette volume to 30µL and attach disposable tip.

ii Mix the EDTA blood specimen by gentle inversion at least 8 times and ensure fully mixed.

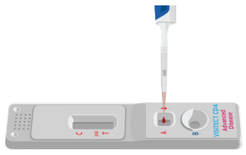
Open the EDTA blood tube.

iii Press the plunger button of the pipette to the first stop.

Immerse the disposable tip vertically into the EDTA tube. Smoothly release plunger button, drawing the blood into the disposable tip.

TEST PROCEDURE

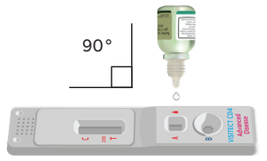
6 Touch the centre of **Well A** lightly and depress the plunger gently to ensure the full 30µL specimen is released into **Well A**.



7 Discard the disposable tip into a sharps/ biohazard bin.

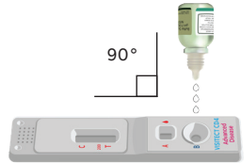
8 Wait for **3 MINUTES**.

9 Hold the buffer bottle vertically 1cm above **Well A**. Add 1 drop of buffer to **Well A**.



10 Wait for **17 MINUTES**.

11 Hold the buffer bottle vertically 1cm above **Well B**. Add 3 drops of buffer to **Well B**.



12 Wait for **20 MINUTES**.

Interpret the results within **5 MINUTES**.

INTEPRETATION OF RESULTS

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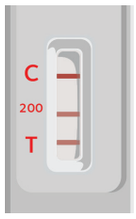
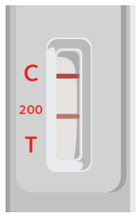


Test (T) line EQUAL INTENSITY to Reference (200) line
CD4 count equal to or below 200 cells/µL

Test result is **BELOW REFERENCE**



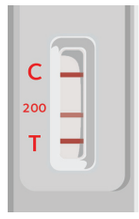
Test (T) line MISSING

CD4 count below 200 cells/µL

Test result is **BELOW REFERENCE**

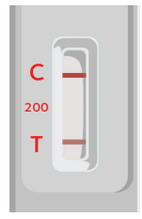
Test (T) line LIGHTER than Reference (200) line
CD4 count below 200 cells/µL

Test result is **BELOW REFERENCE**



Test (T) DARKER than 200 line
CD4 count above 200 cells/µL

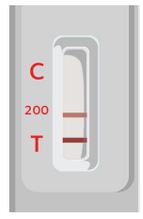
Test result is **ABOVE REFERENCE**



Reference (200) MISSING

Test result is **INVALID**

Repeat the test



Control (C) line MISSING

Test result is **INVALID**

Repeat the test

14 Dispose of the test device and gloves in a sharps/biohazard bin.

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Always refer to the instructions for use for the most up to date version of the test procedure

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