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 AB376¹, manufactured by AccuBio Ltd², 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

<table>
<thead>
<tr>
<th>Date</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prequalification listing</td>
<td>20 August 2020</td>
</tr>
<tr>
<td>Dossier assessment</td>
<td>17 July 2020</td>
</tr>
<tr>
<td>Site inspection(s) of the quality management system</td>
<td>24-25 April 2023</td>
</tr>
<tr>
<td>Product performance evaluation</td>
<td>2nd and 3rd quarters of 2022</td>
</tr>
</tbody>
</table>

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.

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

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

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-MM-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.

**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:

<table>
<thead>
<tr>
<th>Component</th>
<th>25 tests (product code AB376)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Foil pouch containing test device and desiccant</td>
<td>25</td>
</tr>
<tr>
<td>Buffer</td>
<td>7 mL x 1 bottle</td>
</tr>
<tr>
<td>Sampling devices</td>
<td>25</td>
</tr>
<tr>
<td>Sterile retractable lancets</td>
<td>25</td>
</tr>
<tr>
<td>Alcohol swabs</td>
<td>25</td>
</tr>
<tr>
<td>Job aid for venous whole blood specimens</td>
<td>1</td>
</tr>
<tr>
<td>Job aid for capillary whole blood specimens</td>
<td>1</td>
</tr>
<tr>
<td>Instructions for use</td>
<td>1</td>
</tr>
</tbody>
</table>

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.

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

Analytical performance

<table>
<thead>
<tr>
<th>Analytical performance characteristics</th>
<th>2 specimens with reference values &lt;150 and 2 specimens with reference values &gt;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)</th>
<th>Of 20 specimens tested on two different lots, none showed discrepant results between the two lots.</th>
</tr>
</thead>
</table>
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

<table>
<thead>
<tr>
<th>Specimen type(s) and volume</th>
<th>30 µL of venous or capillary whole blood</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of steps*</td>
<td>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)</td>
</tr>
<tr>
<td>Time to result</td>
<td>40 minutes</td>
</tr>
<tr>
<td>Endpoint stability (interval)</td>
<td>5 minutes</td>
</tr>
<tr>
<td>Internal QC</td>
<td>Yes, reagent addition control (not a specimen addition control)</td>
</tr>
</tbody>
</table>

**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
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

AB376 VISITECT® CD4
ADVANCED DISEASE

Test Device x 1
Desiccant x 1

Lot:

Accutree Ltd. UK

90237v1

Pouch Image

VISITECT®
CD4 Advanced Disease
2. Instructions for use and Job aid\textsuperscript{2}

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\textsuperscript{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.
The VISITECT® CD4 Advanced Disease Rapid Test is a manually operated semi-quantitative assay for the estimation of CD4+ T cells in human whole blood.

**INTENDED USE**
The VISITECT® CD4 Advanced Disease test is not intended for individuals less than 15 years of age.

**ACCUBIO**

**INTERPRETATION OF RESULTS**

1. **Diagnosis of test device and gloves is a sharp hazard.**

LIMITATIONS

- The VISITECT® CD4 Advanced Disease is not intended for individuals less than 5 years of age.
- EDTA blood specimens should not be used more than 24-hours post collection when stored at 2-8°C.
- The presence of the Control (C) line only means the test has occurred. It does not guarantee that:
  - the correct specimen has been used.
  - the specimen has been applied correctly.
  - the test has been correctly performed.
- There is no re-use protocol for this product.
- The VISITECT® CD4 Advanced Disease test devices should not be used more than 30 minutes after removal from the foil pack.

**WARNING**

- Read the instructions carefully before performing the test. Failure to follow the instructions may lead to inaccurate test results.
- Do not use a test device or buffer except the supplied with the kit will void the results.
- Do not use the test beyond the expiry date. The test result is uncertain if the test has expired.
- Check the last cap seal is not broken before use.
- Do not use in lot if the product has been exposed to excessive heat or humidity.
- Do not use the test device and assay kit beyond the expiration date.
- This test is unclassified at single condition test on one batch only.
- The results of virucidal tests except the sampling device supplied with the kit will void 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 readings of one test. When making an interpretation of the test all clinical data should be taken into consideration.
- Do not touch the test window with your fingers. When this product is used for qualitative testing using a test strip the operator must identify the test window.
- Do not haemolyse, spermatic, coagulated or frozen blood.
- No other anticoagulants other than EDTA used can give inaccurate results.

**GENERAL INSTRUCTIONS**

- **Do not re-use.** Discard the sampling device/disposable tip into a sharps/biohazard bin.
- **Do not self-test.**
- **Do not use in lot if the product has been exposed to excessive heat or humidity.

**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 compared with CD4+ T cell counts.

**SPECIMENS**

- Whole blood from a finger stick
- Whole blood from a venous source
- EDTA blood
- Serum
- Plasmas
- Whole blood (unanted)
- Cerebrospinal fluid
- Sputum
- Urine
- Saliva
- Other body fluids

- **CONTENTS OF THE VISITECT® CD4 ADVANCED DISEASE KIT**

- 50 foil pouches containing: one test device and one desiccant sachet
- 1 bottle with 700 μL containing 0.5% sodium azide
- 25 sampling devices
- 25 sterile reagent lancets
- 25 alcohol swabs
- 1 job aid for venous blood

- 1 job aid for capillary blood
- 1 instruction for use
- Materials required, but not provided:
  - New pair of disposable gloves
  - Pen
  - Sharp/hand-held lancets

**References**

**Materials Provided**

- **Test Device and Desiccant**
- **Sampling Device** (for capillary blood collection only)
- **Buffer Bottle**
- **Disposables**
- **Ethylenediaminetetraacetic Acid (EDTA) Blood Collection Tube** (Venous Blood Only)
- **Plaster**

**Materials Required, But Not Provided**

- **Disposable Gloves**
- **Timer**
- **Pen**
- **Sample Bin**
- **Dry Gauze or Tissue**
- **Precision Pipette Capable of Delivering 30µl Plus Disposable Tip** (Venous Blood Only)
- **EDTA Blood Collection Tube** (Venous Blood Only)

**Collect All the Required Materials Before Starting the Test. Read Instructions Carefully**

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**Specimen Collection**

**Capillary**

1. Ask patient which is their non-dominant hand, clean side of finger with alcohol swab where prick will be performed.
2. Allow finger to air dry, twist off lancet cap and place skin of finger up to the side of the ball of the finger.
3. Dispose of the retractor lancet into a sharps/biohazard bin immediately.

**Test Procedure**

6. Touch the centre of Well A lightly and squeeze the bulb of 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.

**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 LIGHTER than Reference (200) line**
  - CD4 count below 200 cells/µL.
  - Test result is BELOW REFERENCE.
- **Test (T) line DARKER than Reference (200) line**
  - CD4 count above 200 cells/µL.
  - Test result is ABOVE REFERENCE.
- **Test result is INVALID**
  - Repeat the test.

14. Dispose of the test device and gloves in a sharps/biohazard bin.
COLLECT ALL THE REQUIRED MATERIALS BEFORE STARTING THE TEST. READ INSTRUCTIONS CAREFULLY.

MATERIALS PROVIDED
- Test device
- Sampling device
- Bottle containing buffer
- Alcohol swab
- Sterile retractable lancet
- Disposable gloves
- Timer
- Pen
- Sharps/biohazard bin
- Dry gauze or tissue
- Plaster

MATERIALS REQUIRED, BUT NOT PROVIDED
- Job aid
- Capillary
- Centrifuge
- Microscope
- Pipette
- Vial

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.
3. Discard desiccant sachet.
4. Dispose of all packaging in a general waste bin.

SPECIMEN COLLECTION
5. Ask patient which is their non-dominant hand, clean side of finger with alcohol swab where prick will be performed.
6. Allow finger to air dry, twist off lancet cap and pierce skin of fingertip to the side of the ball of the finger.
7. Dispose of the retractable lancet into a sharps/biohazard bin immediately.
8. Wipe away first drop of blood with piece of dry gauze or tissue, dispose of in sharps/biohazard bin.
9. Gently squeeze the finger until a full drop of blood develops.
10. 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.
11. Hold the buffer bottle vertically 1cm above Well A. Add 1 drop of buffer to Well A.
12. Hold the buffer bottle vertically 1cm above Well B. Add 3 drops of buffer to Well B.

TEST PROCEDURE
13. Wait for 3 MINUTES.
14. Hold the buffer bottle vertically 1cm above Well A. Add 1 drop of buffer to Well A.
15. Wait for 17 MINUTES.
16. Hold the buffer bottle vertically 1cm above Well B. Add 3 drops of buffer to Well B.
17. Wait for 20 MINUTES.

INTERPRETATION OF RESULTS
18. Interpret the results within 5 MINUTES.

- 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 LIGHTER than Reference (200) line CD4 count above 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) line MISSING
  - Test result is INVALID
  - Repeat the test
- Control (C) line MISSING
  - Test result is INVALID
  - Repeat the test

Dispose of the test device and gloves in a sharps/biohazard bin.
# VISITECT® AB376 CD4 Advanced Disease

## 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.
3. Write patient’s identifier on device.
5. Collect venous specimen of blood using established techniques.
6. Prepare precision pipette volume to 30µL and attach disposable tip.

## Specimen Collection
- Mix the EDTA blood specimen by gentle inversion at least 8 times and ensure fully mixed.
- Open the EDTA blood tube.
- 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
1. Touch the centre of Well A lightly and depress the plunger gently to ensure the full 30µL specimen is released into Well A.
2. Discard the disposable tip into a sharps/biohazard bin.
3. Wait for 3 MINUTES.
4. Hold the buffer bottle vertically 1 cm above Well A. Add 1 drop of buffer to Well A.
5. Wait for 17 MINUTES.
6. Hold the buffer bottle vertically 1 cm above Well B. Add 3 drops of buffer to Well B.
7. Wait for 20 MINUTES.

## Interpretation of Results
1. 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.

<table>
<thead>
<tr>
<th>Test (T) line</th>
<th>Reference (200) line</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Equal</strong></td>
<td><strong>200</strong></td>
</tr>
<tr>
<td><strong>Lighter</strong></td>
<td><strong>200</strong></td>
</tr>
<tr>
<td><strong>Darker</strong></td>
<td><strong>200</strong></td>
</tr>
</tbody>
</table>

- **Test result is BELOW REFERENCE**
- **Test result is ABOVE REFERENCE**
- **Test result is INVALID**
- **Repeat the test**

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