WHO Prequalification of Diagnostics Programme
PUBLIC REPORT
Product: Pima CD4 Test
Number: PQDx 0099-032-00

Abstract

The Pima\textsuperscript{TM} CD4 Test with product codes 260100100, 260100025 and 260300001, manufactured by Alere Technologies GmbH, Loebstedter Str. 103-105, Jena 07749, Germany, CE-marked regulatory version, was accepted for the WHO list of prequalified diagnostics and was listed on 25 November 2011.

Pima CD4 is an automated, image-based immune haematology test intended for the rapid in vitro quantitative measurement of CD3+/CD4+ T cells (T-helper cells) in capillary or venous whole blood. Pima CD4 determines the absolute count of CD3+/CD4+ cells and is intended to be used for the on-going monitoring of absolute CD4 lymphocyte counts in patients with documented diagnosis of an immunodeficiency disease. The Pima CD4 test is intended for in vitro diagnostic use.

The Pima CD4 test comprises a disposable Pima CD4 test cartridge and the Pima Analyser, and enables the determination of absolute counts of T-helper cells in whole blood. The disposable Pima CD4 test cartridge is equipped with means to take up approximately 25 μL of sample and contains dried reagents needed to perform the test. The Pima CD4 test is performed within the Pima CD4 test cartridge and no part of the Pima Analyser has contact with the sample at any time in the testing process. This minimises the risk of Analyser contamination and sample carryover between measurements.

After insertion of the Pima CD4 test cartridge into the Analyser, peristaltic movement first transports the sample into the incubation compartment where the sample interacts with specific antibodies labelled with two different fluorescent dyes emitting light at two different wavelengths (dye 1 and dye 2). One antibody is an anti-human CD3 monoclonal antibody conjugated to dye 1. The second antibody is an anti-human CD4 monoclonal antibody conjugated to dye 2. After a defined incubation time, the stained sample is transferred into the detection channel of the cartridge.

The Pima Analyser is equipped with miniaturized multi-colour fluorescence imaging optics. Fluorescence signals are detected by an on-board camera and analysed using proprietary software algorithms on board an embedded computer. T-helper cells carry both CD3 and CD4 surface antigens and therefore emit light at wavelengths specific for both antibody-dye conjugates. This allows the specific differentiation of T-helper cells from other blood cell types carrying only one of the two surface antigens. Results are displayed by the Pima

\footnote{1 See page 2 for a list of components required to perform the assay}
Analyser as cells/μL. Results are also stored in an on-board archive and are assigned to a sample ID that has been entered into the Pima Analyser by the operator and the date/time the test was carried out. Data can be retrieved and downloaded by the operator at any time after the test. An external Pima Printer can be attached via USB to the Pima Analyser to print test results.

In order to perform the assay, the following components are required:

**Instrumentation:**
- Pima™ Analyser (260300001)

**Reagents:**
- Disposable Pima CD4 cartridge, test kits containing 100 cartridges (260100100) or 25 cartridges (260100025)
- Pima Bead Standard (260400011)

**Software:**
- The Pima Analyser has embedded software

**Accessories:**
- Finger stick sample collection kit (100x) (260400199) containing:
  - 4x units of safety lancets (x28) (260400101)
  - 4x units of gauze swabs (x25) (260400104)
  - 1x unit of alcoholic swabs (x100) (260400103)
  - 4x units of plasters (x26) (260400102)

**Optional:**
- Alere Pima™ Printer (260300001)
- External barcode reader (260400008)
- Pima Analyser bag (260300001)
- Pima Printer paper I (260400009)
- Pima Printer Paper II (260400010)
- Volumetric or transfer pipette (for venous blood)²

**Storage:**
The Alere Pima CD4 cartridge should be stored at 2-30°C temperature range.

**Shelf-life:**
The shelf life of the Pima CD4 cartridge is 12 months at 2-30°C temperature range.

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² Not provided by the manufacturer.
Summary of prequalification status for Pima™ CD4 Test: PQDx 0099-032-00

<table>
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<tr>
<th>Status on PQ list</th>
<th>Date</th>
<th>Outcome</th>
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<td></td>
<td>25 November 2011</td>
<td>listed</td>
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<tr>
<td>Dossier assessment</td>
<td>30 September 2011</td>
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<tr>
<td>Inspection status</td>
<td>01 October 2011</td>
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</tr>
<tr>
<td>Laboratory evaluation</td>
<td>ongoing</td>
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MR: Meets Requirements, NA: Not Applicable, FT: Fast-tracked

The Pima™ CD4 Test was conditionally accepted for the WHO list of prequalified diagnostics on the basis of the dossier assessment, inspection findings, publicly available information and in view of the potential high public health impact of the PIMA CD4 counter, which is a unique and innovative point of care CD4 technology.

Background information

Alere Technologies GmbH submitted an application for prequalification of Pima CD4 Test. Based on the established WHO prioritization criteria, Pima CD4 Test was given priority for prequalification.

Product dossier assessment

Alere Technologies GmbH submitted a product dossier for Pima CD4 Test as per the Instructions for compilation of a product dossier (PQDx_018 v1). The information submitted in the product dossier was reviewed by WHO staff and external experts (assessors) appointed by WHO in accordance with the internal procedure on the screening and assessment of a product dossier (PQDx_009 v2). The product dossier screening and assessment findings met the requirements, a recommendation was made to accept the product dossier for Pima CD4 Test.

Commitments for prequalification:
The manufacturer committed to amend and submit additional documentation on the following issue:
1. Shipping stability at high humidity and variable temperature.

Manufacturing site inspection

An inspection was conducted at the site of manufacture of the Pima CD4 test at Alere Technologies GmbH (Loebstedter Str.103-105 D-07749 Jena, Germany) on 12-15 April 2011 in accordance with the procedure described in ‘Information for manufacturers on WHO
prequalification inspection procedures for the sites of manufacture of diagnostics (PQDx_014 v1)’.

The inspection found that the manufacturer had a well-established quality management system and manufacturing practices in place that would ensure the manufacture of a product of consistent quality. The manufacturer’s final responses to the minor nonconformities noted at the time of the inspection were accepted on 1 October 2011.

Commitments for prequalification:
1. Labeling will be improved for easier understanding by end users in resource limited and environmentally challenging regions to which the product is distributed.
2. Alere Technologies GmbH will inform WHO of changes made subsequent to the site inspection, such as change in location of site of manufacture of major components of the test, or other changes to the manufacturing process that may affect the quality of the product.

Laboratory evaluation

In view of the potential high public health impact of the Pima CD4 counter, which is a unique and innovative point of care CD4 technology, the product is prequalified on a conditional basis. The continuing prequalification status is subject to a satisfactory outcome of WHO laboratory comparative evaluation studies.
1. Labels
2. Instructions for use
1. Labels

Pouch Label Pima CD4

Box Label Pima CD4 100x
Box Label Pima CD4 25x

Finger Stick Sample Collection Kit for 100 Blood Collections

Collection of Devices as indicated on separate label

Safety Lancet Super
4 bags, each bag with 28 pcs.

Soft Zellin Alcohol prep pads
1 box with 100 pcs.

Cosmoplast Plaster
4 boxes, each box with 26 pcs.

Medicomp Extra
4 boxes, each box with 25x2 pcs.
Box Label Pima Bead Standard “Normal” and “Low”

**Pima Beads [Normal]**

Detection Range
719 - 1335 c/μl

LOT 01894
dpos 00006

Stable up to 6 months upon opening.

Pouch Label Pima Bead Standard

**Pima Bead Standard**

REF 260400011

LOT 00061 2013-02

Alere Technologies GmbH
Loebstettler Str. 103-105
D-07749 Jena, Germany
www.pimatest.com

Stable up to 6 months upon opening.
Device Label Pima Analyser

Pima Analyser

SN: PIMA-D-xxxxxx

Alere Technologies GmbH
Loebstedter Str. 103-105
D-07749 Jena, Germany
www.pimatest.com

DC OUTPUT:
18 V === 3.5 A

Box Label Pima Analyser

Pima Analyser incl.
Power Transformer (18 V)
& Power Cable
SN: PIMA-D-002252

Pima Bead Standard
LOT 00066

Alere Technologies GmbH
Loebstedter Str. 103-105
D-07749 Jena, Germany
www.pimatest.com
Box Label Pima Analyser Bag

Pima Analyser Bag

REF 260400001

Alere Technologies GmbH
Loebstedter Str. 103-105
D-07749 Jena, Germany
www.pimatest.com

Device Label Pima Printer

Pima Printer

SN: PPr-xxxxxx

Alere Technologies GmbH
Loebstedter Str. 103-105
D-07749 Jena, Germany
www.pimatest.com

NiMH

DC OUTPUT: 5V===0.5A

Box Label Pima Printer

Pima Printer

REF 260400007

SN  PPr-002502

Alere Technologies GmbH
Loebstedter Str. 103-105
D-07749 Jena, Germany
www.pimatest.com
2. Instructions for use

2.1. Pima CD4 Cartridge Guide
2.2. Pima Bead Standard User Guide
Pima Bead Standard
The Pima Bead Standard is an internal standard for daily quality control (QC) on the Pima Analyser. It comprises two ready-to-use test cartridges, Pima Beads “Normal” and Pima Beads “Low”, with set amounts of immobilised fluorescent beads. Daily QC should be performed before testing of patient samples or after any relocation of the Pima Analyser. Each test takes approx. 9 minutes.

Stability and Storage
The Pima Bead Standard is a re-usable dry standard material that is stable until the expiry date indicated on the package label, as long as the sealed foil pouch is not opened. Once the sealed foil pouch is opened, the Pima Bead Standard can be used for 6 months. Store the Pima Bead Standard cartridges in their storage box at ambient temperature and protected from bright light.
Bead Count
For expected result ranges please refer to the LOT specific information sheet provided with each Pima Bead Standard.

⚠ Daily QC of a particular Pima Analyser should always be performed with the same set of Pima Bead Standard.

Testing the Pima Bead Standard
Control material is sealed within each Pima Bead Standard cartridge. No addition of liquid reagent or sample is needed.

To perform a Pima Beads measurement press the button on the Pima Analyser and insert a Pima Bead Standard cartridge when prompted by the Analyser. The Analyser automatically recognises the cartridge and initiates the Pima Beads test.
• Once an Operator and Sample ID has been entered into the Pima Analyser the «Analysis in Progress» window appears. «Pima Beads» is displayed in the status line.

• After successful completion of the analysis, remove the Pima Bead Standard cartridge. Once the cartridge is removed, the Pima Analyser automatically displays the first «Pima Beads» result window, showing the Sample ID and test result in c/μL.
There are four result windows for every Pima Beads test. Because Pima Bead Standard is a dry material, the QC features for «Volume» and «Reagent» are inactivated. All other QC parameters are tested as usual. The test results are stored in the Analyser archive.

For further information on viewing and printing test results please refer to the Pima Analyser User Guide.

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Pima Bead Standard User Guide

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