iScan™Dx Instrument

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Package Insert

FOR IN VITRO DIAGNOSTIC USE.

Intended Use

The iScanDx Instrument is an *in vitro* diagnostic (IVD) device intended to be used by trained personnel in a professional laboratory environment for automated and quantitative detection of fluorescent signal intensities from Illumina Infinium BeadChips (bead-based microarrays) containing nucleic acid probes for human genomic variants. The resulting fluorescent intensity signals are intended for use with user-defined IVD applications.

Principles of Procedure

The iScanDx is an imager of Illumina BeadArray products. The iScanDx generates fluorescent intensities from Illumina BeadArrays and outputs intensity results that can be used for application specific analysis.

In the Illumina microarray workflow, the iScanDx functions as follows.

- Reads the fluorescent intensities associated with individual beads in the BeadChip.

- Performs data aggregation.

- Outputs the aggregated intensities for each BeadType.

Limitations of the Procedure

- For *in vitro* diagnostic use.

- The iScanDx is validated for use with BeadChips with 1-micron and 1.2-micron beads.

- The iScanDx Instrument is intended for *in vitro* diagnostic use with registered and listed, cleared, or approved reagents or assays.

- The iScanDx is validated for use with Illumina BeadArrays. The beadarray consumable itself is not included as part of the iScanDx system. However, incorrect results may occur as a result of beadarray limitations including (but not limited to) beadarray decoding, number of replicates per beadtype, variation in hybridization capture, amplification issues, evaporation issues, or non-uniformity of beadarray.

- Product limitations:

  - The iScanDx does not have a specific(s) clinical application, and hence can be used across various clinical applications and specimen types (subject to the approved intended use). The clinical limitations vary based on the clinical application use case.

  - Use errors, malfunctions, reduced optical performance, laser power variation, or other failures can lead to poor data quality or increased data variability.

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    – Software and algorithm limitations including (but not limited to) poor registration performance can lead to poor data quality.

Product Components

The Illumina iScanDx Instrument consists of the iScanDx Instrument (Catalog # 20081314).

The following software is required for instrument operation:

Software Application	Function	Description
iScanDx Operating Software	Controls instrument operation	The iDOS software application manages the operation of the instrument during loading and scanning of BeadChips. The iDOS also generates, registers, and extracts images acquired during the scanning process. For more information, refer to *iScanDx Instrument Product Documentation (document # 200014809)*.

Storage and Handling

Element	Specification
Temperature	Transportation and Storage: 5°C to 50°C (41°F to 122°F) Operating Conditions: 15°C to 30°C (59°F to 86°F) During a run, do not allow the ambient temperature to vary by more than ±2°C.
Humidity	Transportation and Storage: 15–90% relative humidity (non-condensing) Operating Conditions: 20–80% relative humidity (non-condensing)

Equipment and Materials Required, Not Provided

BeadChips

Before you begin scanning, complete the appropriate assay for your BeadChip and application.

User-Supplied Consumables

Make sure that the following user-supplied consumables are available before beginning a scan. These consumables are needed when handling and cleaning the back side of the BeadChip.

Consumable	Supplier
Gloves, powder-free, disposable, latex or nitrile	General lab supplier

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Consumable	Supplier
Alcohol wipes, 70% Isopropyl, Medium	VWR, catalog # 15648-981
Lab tissue, low-lint	VWR, catalog # 21905-026
[Optional] Ethanol, 99.5%, ACS, absolute	Fisher Scientific, catalog # AC61509-5000

Warnings and Precautions

Immediately report any serious incidents related to this product to Illumina and the Competent Authorities of the member states in which the user and the patient are established.

⚠ Follow all operating instructions when working in areas marked with this label to minimize risk to personnel or the instrument.

The operator of the iScanDx Instrument is assumed to be trained in the correct position of the instrument and the safety issues involved.

⚠ The iScanDx Reader is a Class 1 laser instrument that houses two Class 3B lasers and, under the normal operating procedures specified in this document, does not permit operator exposure to laser light. The lasers, with power up to 110 mW, are accessible in the interior of the instrument. All laser radiation accessible to the operator is in accordance with IEC 60825-1 accessible limits for Class 1 laser products.

Do not attempt to gain access to the interior of the instrument through any opening. Exposure to laser light can cause injury. For example, viewing the laser light directly can cause blindness.

The iScanDx Instrument is a Class 1 laser product.

⚠ WARNING

Avoid leaning on the iScanDx Instrument or applying excessive force to components, especially to parts that detach.

⚠ WARNING

Keep hands away from moving parts while they are in operation.

⚠ CAUTION

Avoid contamination as follows:

- Always wear gloves when handling BeadChips.
- Only touch the barcode end of the BeadChip. Do not touch the sample area.

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⚠ CAUTION

Federal law restricts this device to sale by or on the order of a physician or other practitioner licensed by the law of the State in which they practice, to use or order the use of the device.

⚠ WARNING

This set of reagents contains potentially hazardous chemicals. Personal injury can occur through inhalation, ingestion, skin contact, and eye contact. Wear protective equipment, including eye protection, gloves, and laboratory coat appropriate for risk of exposure. Handle used reagents as chemical waste and discard in accordance with applicable regional, national, and local laws and regulations. For additional environmental, health, and safety information, see the SDS at support.illumina.com/sds.html.

Instructions for Use

The following sections provide general instructions for using the iScanDx Instrument. Before you begin scanning, complete the appropriate assay for your BeadChip and application. For detailed steps and illustrations, refer to the *iScanDx Instrument Product Documentation (document # 200014809)*.

Start the iScanDx Instrument

To start the iScanDx Instrument, perform the following steps:

1. Power on the iScanDx Instrument computer.
2. Power on the iScanDx Reader.
3. Start the iScanDx Operating Software.

Load and Scan BeadChips

NOTE   Before starting a scan, the lasers must stabilize. Make sure that the iScanDx Reader has been on for at least 5 minutes before beginning a scan.

⚠ CAUTION

Avoid contamination as follows:

- Always wear gloves when handling BeadChips.
- Only touch the barcode end of the BeadChip. Do not touch the sample area.

Load BeadChips

NOTE   If using the AutoLoader to automate BeadChip loading, refer to the *AutoLoader 2.x User Guide (document # 15015394)* for the available menu options.

⚠ CAUTION

Only handle BeadChips by the edges. Always inspect BeadChips for damage or imperfections before loading them onto the carrier. Always load BeadChips onto the carrier before placing the carrier into the iScanDx Reader tray to avoid putting pressure on the tray.

Clean BeadChips

1. Using an alcohol wipe (70% isopropyl) or a lint-free tissue moistened with ethanol (90%) or isopropanol (70%), carefully wipe the *back side* of the BeadChip.
2. Let the surface air dry before loading the BeadChip onto a carrier.

Load BeadChips onto Carrier

1. Hold the BeadChip by the barcode end.
2. Place the BeadChip in a slot so that the end of the BeadChip without the barcode presses up against the raised stop on the carrier.
3. Place up to four BeadChips onto the carrier, each in its own slot, as follows.
4. To prevent scanning errors, make sure that the BeadChips are settled down firmly into the slots and are perfectly flat.

Load Carrier into iScanDx Reader

1. If the iScanDx Reader tray is not already open, open it using one of the following methods:

NOTE   Make sure that nothing is blocking the tray of the iScanDx before you open it.

- From the iScanDx Operating Software welcome screen, select Start. The iScanDx reader tray automatically opens.
- From the yellow arrow icon in the upper left corner of iScanDx Operating Software, select **Scanner**, and then select **Open Tray**.
- Press the **Open/Close Tray** button on the front of the iScanDx Reader, below the status LEDs.

2. Line up the notches on the carrier with the silver beads on the adapter plate in the iScanDx Reader tray.

NOTE   When loading the BeadChip carrier, make sure to orient it properly in the iScanDx tray.

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⚠ CAUTION

When transferring the carrier to the tray, handle the carrier by the edges to prevent dislocating the BeadChips.

3. Lower the carrier gently onto the tray with the BeadChip barcode ends near the front of tray, making sure that the carrier fits securely. Avoid pressing down on the iScanDx Reader tray.

4. Select **Next** to close the iScanDx Reader tray.

⚠ WARNING

Keep hands away from the tray when it is closing.

When the barcodes have been recorded, the iDOS Setup screen displays. The BeadChips are shown on screen in the locations that correspond to their positions in the carrier.
If the barcode scanner finds an empty slot barcode, the iDOS identifies that slot with the word EMPTY. Other BeadChips loaded in the carrier are processed normally.

Specify Input and Output Paths

The iScanDx Instrument obtains processing file information from the input path. The output path is the location where all files are saved upon scan completion. When the iScanDx Instrument is running under Illumina LIMS, you cannot change the input or output paths. These paths are designated by the LIMS project management software.

For information on specifying input and output paths, refer to the *iScanDx Instrument Product Documentation (document # 200014809)*.

Scan BeadChips

NOTE   Before starting a scan, the lasers must stabilize. Make sure that the iScanDx Reader has been on for at least 5 minutes before beginning a scan.

To start a scan:

1. On the iScanDx Operating Software Setup screen, select **Scan**.

The iDOS performs prescan steps. The scan process begins automatically after these steps are complete.

As each section is scanned, image and intensity data are saved on the instrument control computer or in a network location in the output path specified on the iDOS Setup screen.

Monitor the Scan Progress

As the iScanDx Reader scans, the colored strip at the top of each iDOS screen shows the scan status.

• **Dark orange with small text**—Step is complete.

• **Dark orange with large text**—Step is in progress.

- **Light orange**—Step is not complete.

You can also use the progress indicator, image preview, status bar, and information bar to monitor scan progress. For details on these components, refer to *iScanDx Instrument Product Documentation (document # 200014809)*.

Pause or Stop a Scan

You can pause or stop a scan at any time.

- To pause the scan, select **Pause**.

- To stop the scan, select **Cancel**.

Complete a Scan

When all the BeadChips are scanned, a completion message appears.

⚠️ CAUTION

If you want to review the scan results in the iDOS after BeadChip data has been saved, avoid clicking OK to complete the scan. For information on viewing scan results, refer to the *iScanDx Instrument Product Documentation (document # 200014809)*.

To complete a scan:

- Select **OK** to continue to the Review screen to verify data has been sent successfully.

When using Illumina Lab Information Management System (LIMS) or Illumina Connected Analytics (ICA), if all sections of a BeadChip are successfully scanned, the BeadChip data are automatically saved to these systems.

If any sections are not successfully scanned, the entire scan can be canceled, the scan data can be submitted as-is, or the section can be rescanned.

To rescan a BeadChip:

- On the iDOS Review screen, select **Rescan**. The iDOS only rescans the sections that are not successfully scanned.

Results

Scan Metrics

The Instrument software evaluates each run against quality control metrics. The scan metrics for each BeadChip display in the Scan Metrics table at the top of the Review screen. Use the table to review intensity values in the red and green channels, and to check focus and registration metrics for each BeadChip stripe. You can also use the table to determine whether intensity data was normalized for each scanned BeadChip section.

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Focus Metrics

The focus metric ranges between 0 and 1. The higher the focus score, the sharper and more well-defined the bead images are. A low focus score means that the bead images are not well-defined and bead colors bleed into each other.

Registration Metrics

The registration value varies depending on the type of BeadChip. The value ranges between 0 and 1 (multiple swaths per BeadChip) or between 0 and 2 (single swath per BeadChip). When the stripe registration is < 0.75, the stripe is flagged as potentially misregistered and is colored red in the Scan Progress Indicator window. Misregistered sections can be rescanned.

Scan Metrics Text Files

Scan metrics are also stored in two text files, `Metrics.txt` and `[Barcode]_qc.txt`, where `[Barcode]` represents the barcode number for a single BeadChip. If there is a rescan, the scan metrics will transfer the existing data to a new file with a number at the end (eg, `Metrics00.txt`) and overwrite the data in the `Metrics.txt` file.

Performance Characteristics

All studies were performed on the iScanDx Instrument.

Definitions of Calculations Used in Performance Characteristics

The following BeadChip types were used to evaluate the intra-instrument scan intensity repeatability:

- 1-micron beads and 48 samples
- 1.2-micron beads and 8 samples
- 1.2-micron beads and 24 samples

Four test BeadChips were each scanned four times on the same iScanDx Instrument (with four iScanDxs used for this study) to render raw `IDAT` files. These files contain the intensity values for each bead type (probe type). The final raw data sets contain 64 `IDAT` files from 16 test BeadChips for each BeadChip type.

The per-BeadType intensity values for each sample were then bleaching-corrected across four scans. The per-BeadType CV values were calculated based on the bleaching-corrected intensity values. Next, the sample-wise scan intensity CV is represented by the median of the per-BeadType CV values in that sample. The overall intra-instrument scan intensity repeatability for each type of BeadChip was calculated by averaging the sample-wise scan intensity CV values from all the samples in 16 test BeadChips. The scan repeatability for the red and green channels were analyzed separately.

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Inter-instrument scan intensity reproducibility was evaluated on four iScanDx Instruments with the three types of BeadChips. Four test BeadChips from each type were consecutively scanned on four iScanDxs to render raw `IDAT` files containing the per-BeadType (probe type) intensity values. The per-BeadType CV value for each sample was then calculated across four scans. The sample-wise scan intensity CV is represented by the median of the per-BeadType CV values. The overall inter-instrument scan intensity reproducibility for each type of BeadChip was calculated by averaging the sample-wise scan intensity CV values from all the samples in four test BeadChips. The scan repeatability from the red and green channels was analyzed separately.

Repeatability

The following table shows the repeatability data for the iScanDx Instrument.

BeadChip Type	Channel	Min	Max	Mean	Median	Number of Samples
1-micron beads (48 samples)	Green	1.9%	2.7%	2.1%	2.1%	768
	Red	2.2%	3.1%	2.5%	2.5%	
1.2-micron beads (8 samples)	Green	1.6%	2.3%	2.0%	2.0%	128
	Red	1.6%	2.4%	2.1%	2.1%	
1.2-micron beads (24 samples)	Green	1.7%	7.3%	2.2%	2.1%	357
	Red	2.0%	7.2%	2.4%	2.3%	

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Revision History

Document #	Date	Description of Change
200024657 v02	July 2024	Added trademark symbol to iScan in title. In *Contact Information* section, made the following changes: • Added importer symbol to the EC REP address. • Added Australian Sponsor address. • Updated Illumina to Illumina, Inc. Updated Intended Use statement. Updated warnings and precautions.
200024657 v01	August 2023	Removed *Reproducibility* section.
200024657 v00	March 2023	Initial release.

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