

**510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
INSTRUMENT ONLY**

I Background Information:

A 510(k) Number

K191030

B Applicant

Life Technologies Corporation

C Proprietary and Established Names

Applied Biosystems™ 3500 Dx Genetic Analyzer and Applied Biosystems™ 3500xL Dx Genetic Analyzer

D Regulatory Information

Product Code(s)	Classification	Regulation Section	Panel
PCA	Class II Exempt, Meets the limitation of exemptions 862.9(a)	21 CFR 862.2570 - Instrumentation For Clinical Multiplex Test Systems	CH - Clinical Chemistry

II Submission/Device Overview:

A Purpose for Submission:

Change to the instrument software to provide fragment analysis of DNA

B Type of Test:

DNA Genetic Analyzer

III Intended Use/Indications for Use:

A Intended Use(s):

See Indications for Use below.

B Indication(s) for Use:

The Applied Biosystems™ 3500 Dx Genetic Analyzer and the Applied Biosystems™ 3500xL Dx Genetic Analyzer are in vitro diagnostic devices intended for detection of fluorescently-labeled human genomic deoxyribonucleic acid (DNA) nucleotides by capillary electrophoresis.

The Applied Biosystems™ 3500 Dx Genetic Analyzer and the Applied Biosystems™ 3500xL Dx Genetic Analyzer are indicated for sequencing and fragment analysis using FDA-cleared or approved assays.

C Special Conditions for Use Statement(s):

Rx - For Prescription Use Only

IV Device/System Characteristics:

A Device Description:

Device and consumables: The Applied Biosystems™ 3500 Dx Genetic Analyzer and Applied Biosystems™ 3500xL Dx Genetic Analyzer include the following components:

- 8-capillary (Applied Biosystems™ 3500 Dx Genetic Analyzer) or 24-capillary (Applied Biosystems™ 3500xL Dx Genetic Analyzer) array and separation matrix to separate DNA fragments by size (POP™ polymer)
- Reagents and consumables
- Computer workstation and monitor
- Integrated software for instrument control, data collection, quality control, base-calling, and size-calling of samples

The following consumables are required to operate the instrument:

- 50cm Capillary Array: enables the labeled DNA fragments to migrate from the cathode toward the anode for sequencing detection
- POP-6™ Polymer: used as a separation matrix to separate DNA fragments by size during electrophoresis for sequencing
- POP-7™ Polymer: used as a separation matrix for separating DNA fragments by size during electrophoresis for fragment analysis
- Hi-Di™ Formamide: sample re-suspension solution used for electro-kinetic injection and denaturing the DNA
- Sequencing Standard v1.1: used for spectral calibration of the instrument and instrument performance check
- Cathode Buffer Container: pre-filled with running buffer which maintains a source of ions and the correct pH for electrophoresis

- Anode Buffer Container: pre-filled with running buffer which maintains a source of ions and the correct pH for electrophoresis
- Conditioning Reagent: pre-filled pouch used for priming the polymer pump, washing the pump between polymer type changes, and during instrument shutdown
- DS-30 Matrix Standard – Dx: used for spectral calibration
- DS-33 Matrix Standard – Dx: used for spectral calibration
- DS-33 GeneScan™ Install Kit – Dx: used for instrument operational qualification
- GeneScan™ 600 LIZ® Size Standard v2.0 – Dx: used as a ladder for sizing DNA fragments
- Other accessories (e.g. sample plate holders, plate retainers, septa)

Software: The Applied Biosystems™ 3500 Dx Series Data Collection Software 3 IVD v3.2 provides control and monitoring of the instrument, collection of data during an injection, and primary analysis of injection data. The software provides three main functions:

1. Facilitates user entry of specific plate information, including plate and sample IDs, that are used by the instrument to perform the injection, to map the assay to wells on a plate, and to perform data reduction.
2. Communicates with the instrument to provide injection parameters and retrieve both raw instrument data and general instrument status.
3. Provides data reduction of instrument data for storage in sample files. These files can then be exported for analysis using a secondary, assay-specific software.

Principle of Operation: DNA, labeled with fluorescent dyes, is transferred to a capillary electrophoresis plate that is used for injection into the instrument. During capillary electrophoresis, fluorescently labeled PCR products are electrokinetically injected into capillaries. High voltage is applied to move DNA fragments toward the positive electrode. Shortly before reaching the positive electrode, the fluorescently labeled DNA fragments, separated by size, move through the path of a laser beam. The laser beam causes the dyes on the fragments to fluoresce. A charge coupled device (CCD) camera detects the fluorescence. The Applied Biosystems™ 3500 Dx Series Data Collection Software 3 IVD v3.2 converts the fluorescence signal to digital data and performs size calling operations on the data. The raw data files are then transferred to a computer with the assay-specific software for downstream analyses.

The Applied Biosystems™ 3500 Dx Genetic Analyzer and the Applied Biosystems™ 3500xL Dx Genetic Analyzer were cleared for in vitro diagnostic sequence analysis use in BK110039.

B Instrument Description Information:

Modes of Operation	Yes	No
Does the applicant’s device contain the ability to transmit data to a computer, webserver, or mobile device?	<input checked="" type="checkbox"/>	<input type="checkbox"/>
Does the applicant’s device transmit data to a computer, webserver, or mobile device using wireless transmission?	<input checked="" type="checkbox"/>	<input type="checkbox"/>
Software		
FDA has reviewed applicant’s Hazard Analysis and software development processes for this line of product types.	<input checked="" type="checkbox"/>	<input type="checkbox"/>

1. Instrument Name:

Applied Biosystems™ 3500 Dx Genetic Analyzer and Applied Biosystems™ 3500xL Dx Genetic Analyzer

2. Specimen Identification:

The user can use either use a handheld barcode reader or can manually enter the barcodes identified on the test plates. The user manually enters individual sample IDs per well on a plate.

3. Specimen Sampling and Handling:

Human genomic DNA, from EDTA-anticoagulated whole human blood (fresh or stored under validated storage conditions) may be isolated using laboratory-validated sample preparation methodologies (precipitation, silica column, or magnetic beads). PCR products from FDA- cleared or approved devices intended to be used with the Applied Biosystems™ 3500 Dx Genetic Analyzer and Applied Biosystems™ 3500xL Dx Genetic Analyzer may be used immediately or stored under validated storage conditions (protected from light) prior to capillary electrophoresis analysis. The PCR product is plated onto a 96-well plate for use with the analyzer.

4. Calibration:

Two calibrations are required to prepare the instrument for sample runs:

1. Spatial calibration: The software uses images collected during the spatial calibration to establish a relationship between the signal emitted by each capillary and the position where that signal is detected by the CCD camera. Spatial calibrations should be performed after removal or replacement of the capillary array. The instrument requires spatial calibration when it detects a newly installed capillary array. During the calibration, the software performs quality checks to ensure that sequence and fragment analysis attributes do not exceed the set thresholds.
2. Spectral calibration: The spectral calibration creates a de-convolution matrix for each capillary that compensates for dye overlap (reduces raw data from the instrument) in the dye data stored in each sample file and this information is used to convert the 20-color data into 4-, 5-, or 6-dye data. Spectral calibration should be performed when a new dye is used, when the capillary is removed or replaced, or when the user observes a decrease in spectral separation in the data peaks of raw or analyzed data. The instrument must be calibrated for the detection of each fluorescent dye used with the assay.

5. Quality Control:

Size standards are present in each sample (internal control) and are labeled with the fluorescent dye, LIZ, for quality control. The assay may also include external positive and negative controls in each run for the assay software to interpret sample results correctly.

V Substantial Equivalence Information:

A Predicate Device Name(s):

3500 Dx/3500xL Dx Genetic Analyzer CS2 and 3500 Dx Series Software

B Predicate 510(k) Number(s):

BK110039

C Comparison with Predicate(s):

Similarities and Differences		
Device & Predicate Device(s):	<u>K191030</u>	<u>BK110039</u>
Intended Use	For detection of fluorescently labeled DNA by capillary electrophoresis	Same
Analysis Type	Sequencing and fragment analysis	Sequencing analysis
Software	3500 Series Dx Data Collection Software 3 IVD v3.2	3500 Dx Data Collection Software 2011 v1.01
Environment of Use	Prescription use	Same
Specimen Type	Whole blood	Same
Input Sample	Human genomic DNA	Same
Technology	Capillary electrophoresis, 8- and 24-capillary configurations	Same

VI Standards/Guidance Documents Referenced:

- IEC 60601-1-2: Medical electrical equipment - Part 1-2: General requirements for basic safety and essential performance - Collateral Standard: Electromagnetic disturbances - Requirements and tests
- UL 61010-1: Safety Requirements for Electrical Equipment for Measurement, Control, and Laboratory Use - Part 1: General Requirements
- Class II Special Controls Guidance Document: Instrumentation for Clinical Multiplex Test Systems, 2005

VII Performance Characteristics (if/when applicable):

A Analytical Performance:

The Applied Biosystems™ 3500 Dx Genetic Analyzer and Applied Biosystems™ 3500xL Dx Genetic Analyzer were previously legally marketed for sequencing analysis (see BK110039). The performance information referenced below (AmplideX® Fragile X Dx & Carrier Screen Kit, approved under DEN190023) supports the performance of the Applied Biosystems™ 3500 Dx

Genetic Analyzer and Applied Biosystems™ 3500xL Dx Genetic Analyzer for DNA fragment analysis.

1. Precision/Reproducibility:

See DEN190023.

2. Linearity:

Not applicable.

3. Analytical Specificity/Interference:

See DEN190023.

4. Accuracy (Instrument):

See DEN190023.

5. Carry-Over:

See DEN190023.

B Other Supportive Instrument Performance Characteristics Data:

DNA input, DNA extraction equivalence, and specimen handling stability studies were also conducted using the assay. See DEN190023.

VIII Proposed Labeling:

The labeling supports the finding of substantial equivalence for this device.

IX Conclusion:

The submitted information in this premarket notification is complete and supports a substantial equivalence decision.