SPECIAL 510(k): Device Modification
OIR Decision Summary

To: THE FILE **RE:** k163359

This 510(k) submission contains information/data on modifications made to the SUBMITTER'S own Class II, Class III or Class I devices requiring 510(k). The following items are present and acceptable (delete/add items as necessary) for the ARK Methotrexate Assay.

1. The name and 510(k) number of the SUBMITTER'S previously cleared device.

   ARK Methotraxate Assay (k111904)

2. Submitter's statement that the **INDICATION/INTENDED USE** of the modified device as described in its labeling **HAS NOT CHANGED** along with the proposed labeling which includes instructions for use, package labeling, and, if available, advertisements or promotional materials (labeling changes are permitted as long as they do not affect the intended use).

3. A description of the device **MODIFICATION(S),** including clearly labeled diagrams, engineering drawings, photographs, user's and/or service manuals in sufficient detail to demonstrate that the **FUNDAMENTAL SCIENTIFIC TECHNOLOGY** of the modified device **has not changed**.

   This change was to add a cleared assay to a new cleared analyzer.

4. **Comparison Information** (similarities and differences) to applicant's legally marketed predicate device including labeling, intended use, physical characteristics, and performance studies of the ARK Methotrexate Assay.

5. A **Design Control Activities Summary** which includes:

   a) Identification of Risk Analysis method(s) used to assess the impact of the modification on the device and its components, and the results of the analysis

   b) Based on the Risk Analysis, an identification of the verification and/or validation activities required, including methods or tests used and acceptance criteria to be applied

The labeling for this modified subject device has been reviewed to verify that the indication/intended use for the device is unaffected by the modification. In addition, the submitter's description of the particular modification(s) and the comparative information between the modified and unmodified devices demonstrate that the fundamental scientific technology has not changed. The submitter has provided the design control information as specified in The New 510(k) Paradigm and on this basis, I recommend the device be determined substantially equivalent to the previously cleared (or their preamendment) device.

Special 510(k) Summary

This summary of safety and effectiveness information for the ARK™ Methotrexate Assay System on the Beckman Coulter AU680 automated clinical chemistry analyzer is being submitted in accordance with the requirements of SMDA 1990 and 21 CFR 807.92.

510(k) Number: k163359.

807.92 (a)(1): Name: **ARK Diagnostics, Inc.**

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Fremont, CA 94538

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Date Prepared: August 15, 2017

807.92 (a)(2): Device name – trade name and common name, and classification

Trade Name:	ARK™ Methotrexate Assay
Common Name:	Homogeneous Enzyme Immunoassay
Classification:	21 CFR 862 Clinical Chemistry Test System – Toxicology (91); Test Code LAO; Enzyme Immunoassay, Methotrexate Pre-Amendment Device, Unclassified

807.92 (a)(3): Identification of the legally marketed predicate device

Performance of the ARK Methotrexate Assay was established on the Roche/Hitachi 917 analyzer in the original 510(k) (k111904).

807.92 (a)(4): Device Description

The ARK Methotrexate Assay is a homogeneous immunoassay based on competition between drug in the specimen and Methotrexate labeled with the enzyme glucose-6-phosphate dehydrogenase (G6PDH) for binding to the antibody reagent. As the latter binds antibody, enzyme activity decreases. In the presence of drug from the specimen, enzyme activity increases and is directly proportional to the drug concentration. Active enzyme converts the coenzyme nicotinamide adenine dinucleotide (NAD) to NADH that is measured spectrophotometrically as a rate of change in absorbance. Endogenous serum G6PDH does not interfere with the results because the coenzyme NAD functions only with the bacterial enzyme used in the assay.

The ARK Methotrexate Assay consists of reagents R1 anti-Methotrexate polyclonal antibody with substrate and R2 Methotrexate labeled with bacterial G6PDH enzyme. The ARK Methotrexate Calibrator consists of a six-level set to calibrate the assay, and the ARK Methotrexate Control consists of a six-level set used for quality control of the assay (tri-level calibration range set and tri-level high range set). The ARK Methotrexate Dilution Buffer is equivalent to zero calibrator (Calibrator A).

807.92 (a)(5): Intended Use / Indications for Use

The ARK™ Methotrexate Assay is a homogeneous enzyme immunoassay intended for the quantitative determination of methotrexate in human serum or plasma on automated clinical chemistry analyzers. The measurements obtained are used in monitoring levels of methotrexate to help ensure appropriate therapy.

Specimens from patients who have received glucarpidase (carboxypeptidase G2) as a high dose methotrexate rescue therapy should ***not*** be tested with the ARK Methotrexate Assay.

Modification: The purpose of this submission is for a change in the platform analyzer used in the manufacture qualification of the ARK Methotrexate Assay from the Roche/Hitachi 917 analyzer to the Beckman Coulter AU680 analyzer.

807.92 (a)(6): Technological Similarities and Differences to the Predicate

SUBSTANTIAL EQUIVALENCE COMPARATIVE CHART

Characteristic	**Device** ARK™ Methotrexate Assay – Beckman Coulter AU680	**Predicate** ARK™ Methotrexate Assay – Roche/Hitachi 917
Intended Use	The ARK™ Methotrexate Assay is intended for the quantitative determination of methotrexate in human serum or plasma on automated clinical chemistry analyzers.	Same
Indications for Use	The measurements obtained are used in monitoring levels of methotrexate to help ensure appropriate therapy.	Same
Sample	Serum or plasma	Same
Methodology	Homogenous enzyme immunoassay (EIA)	Same
Reagent Components	Two (2) reagent system: Anti-Methotrexate Antibody/Substrate Reagent (R1) containing rabbit polyclonal antibodies to Methotrexate, glucose-6-phosphate, nicotinamide adenine dinucleotide, bovine serum albumin, preservatives, and stabilizers Enzyme Reagent (R2) containing Methotrexate labeled with bacterial G6PDH, buffer, bovine serum albumin, preservatives, and stabilizers	Same
Platform Required	Automated clinical chemistry analyzer	Same
Accessory Reagents	Calibrators (six levels) and controls (six levels) in a synthetic matrix; Dilution Buffer	Same
Testing Environment	Routine clinical laboratory	Same
Reagent Condition and Storage	Liquid, 2-8˚ C	Same

807.92 (b)(1) and 807.92 (b)(2): Brief Description of Nonclinical and Clinical Data

Validation and verification activities were performed which included analytical performance studies to ensure that the performance of the ARK Methotrexate Assay as used on the Beckman Coulter AU680 analyzer is substantially equivalent to the performance of the assay as used on the Roche/Hitachi 917 analyzer (k111904). The following performance characteristics were evaluated:

- Limit of Blank
- Limit of Detection
- Limit of Quantitation
- Recovery
- Linearity
- Accuracy (Method Comparison)
- Precision
- Specificity
- Cross-reactivity
- Carry-over
- Dilution Recovery
- On-board Stability

The pre-determined Pass/Fail acceptance criteria were met for all of the above performance studies.

807.92 (b)(3): Conclusions from Nonclinical Testing

The ARK Methotrexate Assay System (including the ARK Methotrexate Calibrator, ARK Methotrexate Control and ARK Methotrexate Dilution Buffer) as applied on the Beckman Coulter AU680 automated clinical chemistry analyzer is substantially equivalent to the ARK Methotrexate Assay System on the Roche/Hitachi 917 automated clinical chemistry analyzer. The ARK Methotrexate Assay System was shown to be safe and effective for its intended use based on performance studies.