



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

I Background Information:

A 510(k) Number

K262368

B Applicant

Centers for Disease Control and Prevention

C Proprietary and Established Names

B. anthracis Real-time PCR Assay

D Regulatory Information

Product Code(s)	Classification	Regulation Section	Panel
NHT	Class II	21 CFR 866.3045 - In Vitro Diagnostic Device For <i>Bacillus</i> Spp. Detection	MI - Microbiology

II Submission/Device Overview:

A Purpose for Submission:

To establish a Pre-determined Change Control Plan (PCCP) to validate certain future device modifications for the CDC *B. anthracis* Real-time PCR Assay.

B Measurand:

Target DNA sequences from *Bacillus anthracis* (*B. anthracis*)

C Type of Test:

Real-time PCR assay

III Intended Use/Indications for Use:

A Intended Use(s):

See Indications for Use below.

B Indication(s) for Use:

The *B. anthracis* Real-time PCR Assay is an *in vitro* diagnostic test for the qualitative detection of plasmid and chromosomal DNA sequences from *Bacillus anthracis*. The assay can be used to test human respiratory samples, whole blood, serum, plasma, swabs from lesions, CSF, pleural fluid, and bacterial culture isolates from individuals suspected of having anthrax.

Results generated from direct specimen testing are presumptive for the identification of *B. anthracis*. Results generated from culture isolate testing should be used in conjunction with other conventional methods for identification of *Bacillus anthracis* isolates as part of the LRN *Bacillus anthracis* Testing Algorithm. The diagnosis of anthrax infection must be made based on history, signs, symptoms, exposure likelihood, and other laboratory evidences, in addition to the identification of *B. anthracis* from cultures or detection directly in clinical specimens.

Negative results do not preclude infection with the biothreat microbial agents targeted by the device and should not be used as the sole basis for diagnosis, treatment, or other patient management decisions.

Use is limited to Centers for Disease Control and Prevention (CDC) designated laboratories.

The *B. anthracis* Real-time PCR Assay is also intended for environmental specimen testing for bio threat detection and response. FDA has not evaluated claims related to use of this assay on environmental specimens.

C Special Conditions for Use Statement(s):

Rx - For Prescription Use Only

D Special Instrument Requirements:

Not Applicable.

IV Device/System Characteristics:

A Device Description:

No changes were made to the device description under the PCCP. Refer to the public summary for K192871 for the device description.

B Principle of Operation:

No changes were made to the principle of operation under the PCCP. Refer to the public summary for K192871 for a description of test operation.

V Substantial Equivalence Information:

A Predicate Device Name(s):

B. anthracis Real-time PCR Assay

B Predicate 510(k) Number(s):
K192871

C Comparison with Predicate(s):

Device & Predicate Device(s):	<u>K262368</u>	<u>K192871</u>
Device Trade Name	<i>B. anthracis</i> Real-time PCR Assay	<i>B. anthracis</i> Real-time PCR Assay
General Device Characteristic Similarities		
Intended Use/Indications For Use	The <i>B. anthracis</i> Real-time PCR Assay is an <i>in vitro</i> diagnostic test for the qualitative detection of plasmid and chromosomal DNA sequences from <i>Bacillus anthracis</i>. The assay can be used to test human respiratory samples, whole blood, serum, plasma, swabs from lesions, CSF, pleural fluid, and bacterial culture isolates from individuals suspected of having anthrax. Results generated from direct specimen testing are presumptive for the identification of <i>B. anthracis</i>. Results generated from culture isolate testing should be used in conjunction with other conventional methods for identification of <i>Bacillus anthracis</i> isolates as part of the LRN <i>Bacillus anthracis</i> Testing Algorithm. The diagnosis of anthrax infection must be made based on history, signs, symptoms, exposure likelihood, and other laboratory evidences, in addition to the identification of <i>B. anthracis</i> from cultures or detection directly in clinical specimens. Negative results do not preclude infection with the biothreat microbial agents targeted by the device and should not be used as the sole basis for diagnosis, treatment, or other patient management decisions.	The <i>B. anthracis</i> Real-time PCR Assay is an <i>in vitro</i> diagnostic test for the qualitative detection of plasmid and chromosomal DNA sequences from <i>Bacillus anthracis</i>. The assay can be used to test human respiratory samples, whole blood, serum, plasma, swabs from lesions, CSF, pleural fluid, and bacterial culture isolates from individuals suspected of having anthrax. Results generated from direct specimen testing are presumptive for the identification of <i>B. anthracis</i>. Results generated from culture isolate testing should be used in conjunction with other conventional methods for identification of <i>Bacillus anthracis</i> isolates as part of the LRN <i>Bacillus anthracis</i> Testing Algorithm. The diagnosis of anthrax infection must be made based on history, signs, symptoms, exposure likelihood, and other laboratory evidences, in addition to the identification of <i>B. anthracis</i> from cultures or detection directly in clinical specimens. Use is limited to Centers for Disease Control and Prevention (CDC) designated laboratories. The <i>B. anthracis</i> Real-time PCR Assay is also intended for environmental specimen testing for bio threat detection and response. FDA has not evaluated claims related to use of this assay on

	Use is limited to Centers for Disease Control and Prevention (CDC) designated laboratories. The <i>B. anthracis</i> Real-time PCR Assay is also intended for environmental specimen testing for bio threat detection and response. FDA has not evaluated claims related to use of this assay on environmental specimens.	environmental specimens.
Analytes Detected	Same	<i>Bacillus anthracis</i> virulence plasmids and chromosomal DNA
Sample Types	Same	• Swabs from lesions and vesicular material • Whole Blood (EDTA or sodium citrate) • Serum/Plasma • Respiratory specimens (transtracheal aspirates, bronchial lavage, and sputum) • Cerebrospinal fluid • Pleural Fluid Bacterial culture isolates
Principle of Operation	Same	Nucleic acid amplification and fluorescent probe detection
Instrumentation	Same	• Applied Biosystems 7500 Fast Dx Real-Time PCR Instrument • QuantStudio Dx Real-Time PCR Instrument

The subject device is similar to the predicate (K192871), having the same intended use, and the same technological characteristics, with the exception of implementation of a PCCP for modifications to the FDA-cleared CDC *B. anthracis* Real-time PCR Assay that specifies the validation protocols and acceptance criteria for evaluating the following modifications:

1. Addition of a real-time PCR instrument that is *in vitro* diagnostic (IVD)-labeled and used in accordance with its instructions for use.
2. Addition of PCR master mix that is IVD-labeled and used in accordance with its instructions for use or is research use only (RUO)-labeled and qualified lot-by-lot by the CDC Ancillary Reagent Qualification Program.
3. Addition of:
 - a) A manual extraction method that is IVD-labeled and used in accordance with its instructions for use or is RUO-labeled and qualified lot-by-lot by the CDC Ancillary Reagent Qualification Program.

- b) Nucleic acid extraction reagents that are IVD-labeled and used in accordance with their instructions for use or are RUO-labeled and qualified lot-by-lot by the CDC Ancillary Reagent Qualification Program as part of a cleared manual extraction procedure.
 - c) An automated extraction instrument that is IVD-labeled and used in accordance with its instructions for use.
- 4. Addition of oligonucleotide chemistries that are manufactured under good manufacturing practices (GMP).

VI Standards/Guidance Documents Referenced:

Not applicable.

VII Validation Studies and Acceptance Criteria to Support PCCP Modifications:

Specific test methods for clinical and analytical validation are specified in the PCCP for modifications to the *B. anthracis* Real-time PCR assay. The following validation studies will be performed in accordance with the PCCP depending on the device modification:

1. Clinical evaluation designed using established and FDA-accepted approaches, with pre-defined acceptance criteria cleared by FDA during this review, to demonstrate substantial equivalence to the predicate device. Clinical performance studies will be conducted to evaluate the following changes according to the established PCCP: addition of a real-time PCR instrument, addition of an automated extraction instrument, addition of nucleic acid extraction reagents or manual extraction method, addition of PCR master mix, or modification of the quencher on the oligonucleotide probes.
2. Limit of Detection (LoD) determination with representative, well-characterized strains of *B. anthracis* according to established and FDA-accepted approaches. Pre-defined acceptance criteria were found to be appropriate by FDA during this review to demonstrate substantial equivalence to the predicate device. An LoD study will be conducted, according to the established PCCP, to evaluate the addition of a real-time PCR instrument, addition of an automated extraction instrument, addition of nucleic acid extraction reagents or manual extraction method, addition of PCR master mix, or modification of oligonucleotide chemistries.
3. Reproducibility study that is designed according to established and FDA-accepted approaches. Pre-defined acceptance criteria were found to be appropriate by FDA during this review to demonstrate substantial equivalence to the predicate device. A reproducibility study will be conducted, according to the established PCCP, to evaluate addition of a real-time PCR instrument or addition of an automated extraction instrument.
4. Carry-over contamination study demonstrating agreement with expected results compared to the predicate device. A carry-over study will be conducted, according to the established PCCP, to evaluate addition of a real-time PCR instrument or addition of an automated extraction instrument.

VIII Performance Characteristics (if/when applicable):

A Analytical Performance:

1. Precision/Reproducibility:

Precision/reproducibility data for the CDC *B. anthracis* Real-time PCR Assay were reviewed and accepted previously in K140426 and K192871. A reproducibility study will be conducted to evaluate addition of a real-time PCR instrument and addition of an automated extraction instrument, according to the established PCCP. Data demonstrating pre-specified agreement with the expected results will be considered acceptable to support these modifications to the device.

2. Linearity:

Not Applicable. This is a qualitative test.

3. Analytical Specificity/Interference:

Analytical specificity/interference data for the CDC *B. anthracis* Real-time PCR Assay were reviewed and accepted previously in K140426 and K192871.

4. Assay Reportable Range:

Not Applicable. This is a qualitative test.

5. Traceability, Stability, Expected Values (Controls, Calibrators, or Methods):

Quality control data for the CDC *B. anthracis* Real-time PCR Assay were reviewed and accepted previously in K140426 and K192871.

6. Detection Limit:

Limit of Detection (LoD) data for the CDC *B. anthracis* Real-time PCR Assay were reviewed and accepted previously in K140426 and K192871. An LoD study will be conducted to evaluate the addition of a real-time PCR instrument, addition of an automated extraction instrument, addition of nucleic acid extraction reagents or manual extraction method, addition of PCR master mix, or modification of the quencher on the oligonucleotide probes, according to the established PCCP. Data demonstrating LoD equivalency will be considered acceptable to support these modifications to the device.

7. Assay Cut-Off:

Assay cut-offs for the CDC *B. anthracis* Real-time PCR Assay were reviewed and accepted previously in K140426.

B Comparison Studies:

1. Method Comparison with Predicate Device:

Refer to the “Clinical Studies” section.

2. Matrix Comparison:

Not applicable.

C Clinical Studies:

Clinical data for the CDC *B. anthracis* Real-time PCR Assay were reviewed and accepted previously in K140426. Testing of clinical samples will be conducted to evaluate addition of a real-time PCR instrument, addition of an automated extraction instrument, addition of nucleic acid extraction reagents or manual extraction method, addition of PCR master mix, or modification of the quencher on the probes, according to the established PCCP. Data demonstrating that the performance meets or exceeds pre-specified point estimates for both positive and negative percent agreement (PPA and NPA) and the associated lower bounds of the 95% confidence intervals when compared to comparator will be considered acceptable to support these modifications to the device.

D Clinical Cut-Off:

Not applicable.

E Expected Values/Reference Range:

Not applicable.

IX Proposed Change in Labeling:

If the validation studies are performed according to the specified protocols in the PCCP and the validation data meet the specified acceptance criteria established in the PCCP, the modification and supporting validation study results will be included in updated device labeling. The labeling will clearly describe the added modification(s).

X Conclusion:

The submitted information in this premarket notification, which includes a PCCP for modifications to the *B. anthracis* Real-time PCR assay, is complete and supports a substantial equivalence decision.