February 28, 2025

Cepheid
Samir Ghevariya
Regulatory Affairs Principal
904 Caribbean Drive
Sunnyvale, California 94089

Re: K243730

Trade/Device Name:	Xpert *C. difficile/Epi*
Regulation Number:	21 CFR 866.3130
Regulation Name:	Clostridium Difficile Toxin Gene Amplification Assay
Regulatory Class:	Class II
Product Code:	OZN, OOI
Dated:	December 3, 2024
Received:	December 3, 2024

Dear Samir Ghevariya:

We have reviewed your section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (the Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. Although this letter refers to your product as a device, please be aware that some cleared products may instead be combination products. The 510(k) Premarket Notification Database available at https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpmn/pmn.cfm identifies combination product submissions. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration. Please note: CDRH does not evaluate information related to contract liability warranties. We remind you, however, that device labeling must be truthful and not misleading.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, §800–898. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Additional information about changes that may require a new premarket notification are provided in the FDA guidance documents entitled "Deciding When to Submit a 510(k) for a Change to an Existing Device" (https://www.fda.gov/media/99812/download) and "Deciding When to Submit a 510(k) for a Software Change to an Existing Device" (https://www.fda.gov/media/99785/download).

Your device is also subject to, among other requirements, the Quality System (QS) regulation (21 CFR §820), which includes, but is not limited to, 21 CFR §820.30, Design controls; 21 CFR §820.90, Nonconforming product; and 21 CFR §820.100, Corrective and preventive action. Please note that regardless of whether a change requires premarket review, the QS regulation requires device manufacturers to review

and approve changes to device design and production (21 CFR §820.30 and 21 CFR §820.70) and document changes and approvals in the device master record (21 CFR §820.181).

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR §807); labeling (21 CFR §801 and §809); medical device reporting (reporting of medical device-related adverse events) (21 CFR §803) for devices or postmarketing safety reporting (21 CFR §4, Subpart B) for combination products (see https://www.fda.gov/combination-products/guidance-regulatory-information/postmarketing-safety-reporting-combination-products); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR §820) for devices or current good manufacturing practices (21 CFR Part 4, Subpart A) for combination products; and, if applicable, the electronic product radiation control provisions (Sections 531–542 of the Act); 21 CFR Parts 1000–1050.

All medical devices, including Class I and unclassified devices and combination product device constituent parts are required to be in compliance with the final Unique Device Identification System rule ("UDI Rule"). The UDI Rule requires, among other things, that a device bear a unique device identifier (UDI) on its label and package (21 CFR §801.20(a)) unless an exception or alternative applies (21 CFR 801.20(b)) and that the dates on the device label be formatted in accordance with 21 CFR §801.18. The UDI Rule (21 CFR §830.300(a) and §830.320(b)) also requires that certain information be submitted to the Global Unique Device Identification Database (GUDID) (21 CFR §830 Subpart E). For additional information on these requirements, please see the UDI System webpage at https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance/unique-device-identification-system-udi-system.

Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR §807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR §803), please go to https://www.fda.gov/medical-devices/medical-device-safety/medical-device-reporting-mdr-how-report-medical-device-problems.

For comprehensive regulatory information about medical devices and radiation-emitting products, including information about labeling regulations, please see Device Advice (https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance) and CDRH Learn (https://www.fda.gov/training-and-continuing-education/cdrh-learn). Additionally, you may contact the Division of Industry and Consumer Education (DICE) to ask a question about a specific regulatory topic. See the DICE website (https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance/contact-us-division-industry-and-consumer-education-dice) for more information or contact DICE by email (DICE@fda.hhs.gov) or phone (1-800-638-2041 or 301-796-7100).

Sincerely,

Ribhi Shawar -S

Ribhi Shawar, PhD (ABMM)
Branch Chief
General Bacteriology and Antimicrobial Susceptibility Branch
DMD: Division of Microbiology Devices
OHT7: Office of In Vitro Diagnostics
OPEQ: Office of Product Evaluation and Quality
CDRH: Center for Devices and Radiological Health

Enclosure

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

Indications for Use

Form Approved: OMB No. 0910-0120
Expiration Date: 07/31/2026
See PRA Statement below.

510(k) Number *(if known)*
K243730

Device Name
Xpert® *C. difficile/Epi*

Indications for Use *(Describe)*
The Xpert® *C. difficile/Epi* test is a qualitative *in vitro* diagnostic test for detection of toxin B gene sequences and for presumptive identification of 027/NAP1/BI strains of toxigenic *Clostridioides difficile* from unformed (liquid or soft) stool specimens collected from patients suspected of having *C. difficile* infection (CDI). Presumptive identification of 027/NAP1/BI strains of *C. difficile* is by detection of binary toxin (CDT) gene sequences and the single base pair deletion at nucleotide 117 in the *tcdC* gene. The *tcdC* gene encodes for a negative regulator in *C. difficile* toxin production. The test is performed on the GeneXpert® Instrument Systems and utilizes automated real-time polymerase chain reaction (PCR) to detect toxin gene sequences associated with toxin producing *C. difficile*. The Xpert *C. difficile/Epi* test is intended as an aid in the diagnosis of CDI. Detection of 027/NAP1/BI strains of *C. difficile* by the Xpert *C. difficile/Epi* test is presumptive and is solely for epidemiological purposes and is not intended to guide or monitor treatment for *C. difficile* infections. Concomitant culture is necessary only if further typing or organism recovery is required.

Type of Use *(Select one or both, as applicable)*

☒ Prescription Use (Part 21 CFR 801 Subpart D) ☐ Over-The-Counter Use (21 CFR 801 Subpart C)

CONTINUE ON A SEPARATE PAGE IF NEEDED.

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510(k) Summary
for
Xpert® *C. difficile/Epi*

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1 510(k) Summary

As required by 21 CFR Section §807.92

Submitted by:	Cepheid 904 Caribbean Drive Sunnyvale, CA 90489 Phone number: (408) 541-4191
Contact:	Samir Ghevariya, Regulatory Affairs Principal
Date of Preparation:	February 5, 2025
Device:	
Trade name:	Xpert® *C. difficile/Epi*
Common name:	Xpert *C. difficile/Epi* test
Type of Test:	Qualitative Nucleic Acid Amplification Test for *C. difficile* toxin B and binary toxin gene sequences and the single base pair deletion at nucleotide 117 in *tcdC* from unformed stool specimens.
Classification:	Class II
Classification name:	Clostridium difficile toxin gene amplification assay
Product code:	OZN, OOI
Regulation number:	21 CFR §866.3130
Classification Advisory Panel:	Microbiology
Prescription Use:	Yes
Predicate Device:	cobas® Cdiff Nucleic acid test for use on the cobas® Liat® System (K212427)

1.1 Device Description

The Xpert *C. difficile/Epi* test is an automated *in vitro* diagnostic test for qualitative detection of toxin producing *Clostridioides difficile* (formerly known as *Clostridium difficile*) directly from unformed (liquid or soft) stool specimens of patients suspected of having *Clostridioides difficile* infection (CDI). The test detects the toxin B gene (*tcdB*), the binary toxin (CDT) gene, and the single base pair deletion at nucleotide 117 (*tcdC*Δ117) within the gene encoding TcdC, a negative regulator of toxin production. The combined presence of the genes encoding toxin B and binary toxin and the *tcdC*Δ117 deletion has been associated with a hypervirulent *C. difficile*

strain known as 027/NAP1/BI, which has been associated with severe disease outbreaks in healthcare facilities worldwide.

The test is performed on the GeneXpert® Instrument Systems (comprised of the GeneXpert® Dx System, GeneXpert® System with Touchscreen, and GeneXpert® Infinity System). In the GeneXpert® Instrument Systems, sample preparation, amplification, and real-time detection are all fully automated and completely integrated. The single-use disposable Xpert *C. difficile/Epi* cartridge, required by the platform for use, holds the PCR reagents and hosts the PCR process. Because the cartridge is self-contained, cross-contamination between samples is minimized.

The Xpert *C. difficile/Epi* test includes reagents for the detection of toxigenic *C. difficile* and the detection of sequences for presumptive identification of 027/NAP1/BI strains. In addition, the test reagents include an internal sample processing control (SPC) to ensure adequate processing of the target bacteria and to monitor the presence of inhibitor(s) in the PCR Assay. The SPC also ensures that the PCR conditions (temperature and time) are appropriate for the amplification reaction and that the PCR reagents are functional. The Probe Check Control (PCC) verifies reagent rehydration, PCR tube filling in the cartridge, probe integrity, and dye stability.

The Xpert *C. difficile/Epi* test system performs sample preparation and real-time, multiplex polymerase chain reaction (PCR) for detection of target-specific DNA. A swab is inserted into the stool specimen and then placed in a tube containing Sample Reagent. Following brief vortexing, the content of the Sample Reagent is transferred to the Sample Chamber of the disposable fluidic cartridge (the Xpert *C. difficile/Epi* cartridge). The user initiates a test from the system user interface of the GeneXpert® Instrument Systems and places the cartridge with sample into a GeneXpert® instrument system which performs hands-off real-time PCR for detection of *C. difficile* DNA.

Depending on the specific instrument, a GeneXpert® instrument system may contain 1–80 modules, each of which are randomly accessible and capable of performing separate sample preparation and real-time PCR tests for the detection of gene sequences for *C. difficile* toxin B and binary toxin and the *tcdC*Δ117 deletion in less than 45 minutes. Each module contains a syringe drive for dispensing fluids (i.e., the syringe drive activates the plunger that works in concert with the rotary valve in the cartridge to move fluids between chambers), an ultrasonic horn for lysing cells or spores, and a proprietary I-CORE® thermocycler for performing real-time PCR and detection.

Each instrument in the GeneXpert® instrument family is equipped with a Windows OS-based personal computer that is preloaded with software applications for running the tests and viewing the results, as described in **Table 1**.

Table 1: Instrument Systems and Software in the GeneXpert® Instrument Family Members

Instrument Family	Instrument Family Members	System Software	GeneXpert Instruments
GeneXpert® Instrument Systems	GeneXpert® Dx System	*GeneXpert Dx*	• GX-I† • GX-II • GX-IV • GX-XVI
	GeneXpert® System with Touchscreen	*Cepheid OS*	• GX-II • GX-IV • GX-XVI
	GeneXpert® Infinity System	*GeneXpert Xpertise*	• GeneXpert Infinity-48s • GeneXpert Infinity-80

† No longer manufactured but is in circulation in the market.

1.2 Intended Use

The Xpert® *C. difficile/Epi* test is a qualitative *in vitro* diagnostic test for detection of toxin B gene sequences and for presumptive identification of 027/NAP1/BI strains of toxigenic *Clostridioides difficile* from unformed (liquid or soft) stool specimens collected from patients suspected of having *C. difficile* infection (CDI). Presumptive identification of 027/NAP1/BI strains of *C. difficile* is by detection of binary toxin (CDT) gene sequences and the single base pair deletion at nucleotide 117 in the *tcdC* gene. The *tcdC* gene encodes for a negative regulator in *C. difficile* toxin production. The test is performed on the GeneXpert® Instrument Systems and utilizes automated real-time polymerase chain reaction (PCR) to detect toxin gene sequences associated with toxin producing *C. difficile*. The Xpert® *C. difficile/Epi* test is intended as an aid in the diagnosis of CDI. Detection of 027/NAP1/BI strains of *C. difficile* by the Xpert® *C. difficile/Epi* test is presumptive and is solely for epidemiological purposes and is not intended to guide or monitor treatment for *C. difficile* infections. Concomitant culture is necessary only if further typing or organism recovery is required.

1.3 Technical Characteristics

The Xpert *C. difficile/Epi* test has similar technological characteristics to those of the predicate device. Briefly, Xpert *C. difficile/Epi* test is an *in vitro* qualitative nucleic acid (DNA) amplification test using real time polymerase chain reaction (PCR) that utilizes primers and TaqMan probes specific for toxigenic *C. difficile* toxin genes with fluorogenic target-specific hybridization.

1.4 Substantial Equivalence

The purpose of this 510(k) submission is to obtain a substantial equivalence determination for Cepheid's Xpert *C. difficile/Epi* test for use with Cepheid-manufactured GeneXpert® Instrument Systems family of instruments (see **Table 1** above) and to update device labeling to reflect the inclusion of a member of the GeneXpert® Instrument Systems family—namely, the GeneXpert® Infinity System, along with systems software (GeneXpert Xpertise)—in addition to other instrument members of the same family, which were previously cleared for use with or added to

the Xpert *C. difficile/Epi* test, namely, the GeneXpert® Dx System (K110203) and the GeneXpert® System with Touchscreen (CR240176).

For the determination of substantial equivalence with the legally marketed predicate device, cobas® Cdiff nucleic acid test for use on the cobas® Liat® System (K212427), the similarities and differences between the Xpert *C. difficile/Epi* test and predicate are noted, respectively, in **Table 2** and **Table 3**. The Intended Use and the technological characteristics of the Xpert *C. difficile/Epi* test and the predicate device are equivalent, and the noted differences between the candidate and predicate devices do not raise new or different questions of safety and effectiveness.

Table 2. Similarities between Xpert *C. difficile/Epi* and Predicate

Similarities		
Attribute	**Candidate Device (K243730)**	**Predicate (K212427)**
	Xpert® *C. difficile/Epi*	**cobas® Cdiff Nucleic Acid Test for use on the cobas® Liat® System**
Device class	Same	Class II
Product code	Same	OZN (*C. difficile* toxin gene amplification assay) OOI (Real Time Nucleic Acid Amplification System)
Regulation	Same	**21 CFR §866.3130** (Clostridium difficile toxin gene amplification assay)
Intended Use	The Xpert® *C. difficile/Epi* test is a qualitative *in vitro* diagnostic test for detection of toxin B gene sequences and for presumptive identification of 027/NAP1/BI strains of toxigenic *Clostridioides difficile* from unformed (liquid or soft) stool specimens collected from patients suspected of having *C. difficile* infection (CDI). Presumptive identification of 027/NAP1/BI strains of *C. difficile* is by detection of binary toxin (CDT) gene sequences and the single base pair deletion at nucleotide 117 in the *tcdC* gene. The *tcdC* gene encodes for a negative regulator in *C. difficile* toxin production. The test is performed on the GeneXpert® Instrument Systems and utilizes automated real-time polymerase chain reaction (PCR) to detect toxin gene sequences associated with toxin producing *C. difficile*. The Xpert® *C. difficile/Epi* test is intended as an aid in the diagnosis of CDI. Detection of 027/NAP1/BI strains of *C. difficile* by the Xpert® *C. difficile/Epi* test is presumptive and is solely for epidemiological purposes and is not intended to guide or monitor treatment for *C. difficile* infections. Concomitant culture is necessary only if further typing or organism recovery is required.	The cobas® Cdiff Nucleic acid test for use on the cobas® Liat® System is an automated, qualitative *in vitro* diagnostic test that uses real-time polymerase chain reaction (PCR) for the detection of the toxin B (*tcdB*) gene of toxigenic *Clostridioides difficile* (C. *difficile*) in unformed (liquid or soft) stool specimens obtained from patients suspected of having *C. difficile* infection (CDI). The cobas® Cdiff Nucleic acid test for use on the cobas® Liat® System is intended for use as an aid in the diagnosis of CDI in humans in conjunction with clinical and epidemiological risk factors.
Specimen	Same	Unformed (liquid or soft) stool

Similarities		
Attribute	**Candidate Device (K243730)**	**Predicate (K212427)**
	Xpert® *C. difficile/Epi*	**cobas® Cdiff Nucleic Acid Test for use on the cobas® Liat® System**
Test Technology	Same	Real time PCR
Detection Technique	Same	Multiplex assay using different reporter dyes for each target
Test Automation	Same	Fully automated DNA extraction, detection, and results interpretation
Test Format	Same	Disposable single-use, multi-chambered, fluidic cartridge
Intended Use Environment	Same	Trained users
Test Access	Same	Prescription use only

Table 3. Differences between Xpert *C. difficile/Epi* and Predicate

Attribute	Differences	
	Candidate Device	**Predicate (K212427)**
	Xpert® *C. difficile/Epi*	**cobas® Cdiff Nucleic Acid Test for use on the cobas® Liat® System**
Purpose of Use	Detection of toxin B gene sequences and presumptive identification of 027/NAP1/BI strains of toxigenic *Clostridioides difficile*	Detection of toxin B gene sequences of toxigenic *Clostridioides difficile*
DNA Target Sequence	• toxin B gene • binary toxin gene • *tcdC* gene by deletion of nucleotide 117 (*tcdC*Δ117)	• toxin B gene
Internal Controls	• Sample Processing Control (SPC) • Probe Check Control (PCC)	• A gram-positive *Bacillus thuringiensis israelensis* bacterial organism to monitor the full process of cobas® Liat® Analyzer. Native sequence in the bacteria is used as the Internal Control Target.
Instrument Systems	• GeneXpert® Dx System • GeneXpert® System with Touchscreen • GeneXpert® Infinity System	• cobas® Liat® System
Collection Device	Cepheid Sample Collection Device	cobas® PCR Media Swab Sample Kit
Time to Results	Less than 45 minutes	~20 minutes

1.5 Performance Studies

There have been no changes to the analytical and clinical performance data for the Xpert *C. difficile/Epi* test since the device's original clearance in K110203. In accordance with Cepheid's design control process, additional analytical verification studies were performed with the Xpert *C. difficile/Epi* test for use on GeneXpert® Infinity System and to establish compliance with

Class II Special Controls Guidelines appropriate for 21 CFR §866.3130. These verification studies are summarized below.

1.5.1 Verification Studies to Demonstrate Performance on GeneXpert Infinity System

The performance of the Xpert *C. difficile/Epi* test when used with the GeneXpert® Infinity System instruments was assessed through two (2) verification studies, namely, a prepared cartridge hold time study and a functional testing study. The study results support the use of the Xpert *C. difficile/Epi* test on the additional GeneXpert® Instrument Systems family member (i.e., GeneXpert® Infinity System).

Prepared Cartridge Hold Time Study

Hold time refers to the duration between the preparation of the cartridge (i.e., addition of processed specimen to the cartridge) and the initiation of the Xpert *C. difficile/Epi* test. A prepared cartridge hold time study was conducted using contrived positive (*C. difficile* cells added to negative matrix) and negative (negative matrix only) samples held for various times under three (3) hold environments, i.e., at ambient (22°C), elevated (25°C) with high humidity, or high (35°C) temperatures. The maximum acceptable hold time for a prepared cartridge was verified as 4 hours under all environments.

Functional Testing

Functional testing was conducted using both contrived positive (*C. difficile* cells added to negative matrix) and negative (negative matrix only) samples to evaluate differences (if any) in the performance of the Xpert *C. difficile/Epi* test on the previously cleared GeneXpert® Dx System and the GeneXpert® Infinity System, running respectively under systems software GeneXpert® Dx (v6.5) and GeneXpert® Xpertise (v6.8 or v7.1). The study results showed 100% agreement with the expected results, with no statistically significant differences in Ct values observed among test runs in all instrument/software combinations. This study demonstrated equivalent performance of the Xpert *C. difficile/Epi* test when performed on any member of the GeneXpert® Instrument Systems family of instruments.

1.5.2 Verification Studies to Establish Compliance with Special Controls Guidelines

Inclusivity Study

A study to determine the Analytical Reactivity (Inclusivity) of the Xpert *C. difficile/Epi* test was previously conducted in support of K110203 with *C. difficile* strains selected to broadly represent the majority of *C. difficile* toxinotypes encountered in practice. This study utilized eighteen (18) toxigenic *C. difficile* strains representing toxinotype 0 and other variant toxinotypes, including 027/NAP1/BI toxinotype III isolates. With the current submission (K243730), to comply with the requirements of FDA's Class II Special Controls Guideline document "Toxin Gene Amplification Assays for the Detection of *Clostridium difficile*" (issued on August 27, 2015) as appropriate for this Class II device under regulation 21 CFR §866.3130, a supplemental inclusivity study was conducted with Xpert *C. difficile/Epi* test using another eight (8) *C. difficile* strains. Overall, the inclusivity study results showed that Xpert *C. difficile/Epi* test met the requirements of the Class II Special Controls and accurately identified all strains of toxigenic *C.*

difficile tested, thereby demonstrating an inclusivity rate of 100% for the Xpert *C. difficile/Epi* test.

1.6 Conclusion

Overall, analytical and clinical studies conducted with Xpert *C. difficile/Epi*

- Demonstrate the safe and effective use of the Xpert *C. difficile/Epi* test, when performed on the members of the GeneXpert® Instrument Systems family (including the GeneXpert® Infinity System),
- Demonstrate compliance with the Class II Special Controls under regulation 21 CFR §866.3130, and
- Support the finding of Substantial Equivalence with the predicate.