September 25, 2025

Abbott Molecular Inc.
Jennifer Peterson
Associate Director Regulatory Affairs
1350 East Touhy Avenue
Des Plaines, Illinois 60018

Re: K252102
Trade/Device Name: Alinity m HCV
Regulation Number: 21 CFR 866.3170
Regulation Name: Nucleic Acid-Based Hepatitis C Virus Ribonucleic Acid Tests
Regulatory Class: Class II
Product Code: MZP
Dated: July 2, 2025
Received: July 3, 2025

Dear Jennifer Peterson:

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, Parts 800 to 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 Part 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 Part 807); labeling (21 CFR Part 801 and Part 809); medical device reporting (reporting of medical device-related adverse events) (21 CFR Part 803) for devices or postmarketing safety reporting (21 CFR Part 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 Part 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 Part 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 Part 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,

Bhawna Poonia -S

for

Uwe Scherf, M.Sc., Ph.D.
Director
Division of Microbiology Devices
OHT7: Office of In Vitro Diagnostics
Office of Product Evaluation and Quality
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)*
K252102

Device Name
Alinity m HCV

Indications for Use *(Describe)*
The Alinity m HCV assay is an in vitro reverse transcription-polymerase chain reaction (RT-PCR) assay for both the detection and quantitation of hepatitis C virus (HCV) RNA, in human plasma (EDTA, Acid Citrate Dextrose) or serum, from HCV antibody positive individuals. The assay is intended for use as an aid in the diagnosis of active HCV infection in individuals with antibody evidence of HCV infection, and to aid in the management of patients with known active HCV infection, including Sustained Virologic Response (SVR) determination.
The results from the Alinity m HCV assay must be interpreted within the context of all relevant clinical and laboratory findings.
The Alinity m HCV assay is not intended to be used in screening blood, plasma, serum, tissue or tissue donors for HCV.

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

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1.0 510(k) Summary

This 510(k) summary of safety and effectiveness information is being submitted in accordance with the requirement of 21 CFR Section 807.92(c).

1.1 Submitter

Applicant Name and Address:	Abbott Molecular Inc. 1300 E. Touhy Avenue Des Plaines, IL 60018
Contact Person:	Jennifer Peterson Associate Director Regulatory Affairs Abbott Molecular, Inc. 1300 E. Touhy Avenue Des Plaines, IL 60018 Phone: 224-361-7081 Mobile: 224-651-7305 Fax: 224-361-7269
Date Prepared:	July 2025

1.2 Device Information

Trade Name	Regulation Name	Product Code	Regulation No.	Class
Alinity m HCV	Nucleic Acid-Based Hepatitis C Virus Ribonucleic Acid Test	MZP	21 CFR 866.3170	II

1.3 Predicate Device

Device Name	Predicate Device	PMA	Approved
Alinity m HCV	Alinity m HCV	P190025	03/23/2020

1.4 Device Description

Alinity m HCV is an in vitro polymerase chain reaction (PCR) assay for both the detection and quantitation of HCV RNA in human plasma (EDTA, Acid Citrate Dextrose) or serum, from HCV antibody positive individuals.

This device is similar to the predicate device originally approved (PMA P190025) with the exception that the subject device may use a new DNA Polymerase as an alternative to the original DNA Polymerase and a new Reverse Transcriptase as an alternative to the original Reverse Transcriptase in the reagent formulation of the assay. This formulation difference does not introduce any changes to sample processing, assay procedure, or data reduction.

Additional studies were initiated to support the formulation of the assay with alternative DNA Polymerase and Reverse Transcriptase. Supplemental data from these studies were used with data previously obtained from the analytical and clinical testing studies submitted in P190025.

The steps of the Alinity m HCV assay consist of sample preparation, real-time PCR assembly, amplification/detection, result calculation, and reporting. All steps of the Alinity m HCV assay procedure are executed automatically by the Alinity m System. Manual dilutions may be performed for low-volume specimens to meet the minimum volume requirement and for high-titer specimens above the upper limit of quantitation (ULoQ). The Alinity m System is designed to be a random-access analyzer that can perform the Alinity m HCV assay in parallel with other Alinity m assays on the same instrument.

Alinity m HCV requires three separate assay specific kits as follows:

- **Alinity m HCV AMP Kit (List No. 08N50-095)**, consisting of 2 types of multi-well assay trays. The amplification trays (AMP Trays) contain lyophilized, unit-dose RT-PCR amplification/detection reagents and lyophilized, unit-dose IC in separate wells, and the activation trays (ACT Trays) contain liquid activation reagent. The intended storage condition for the Alinity m HCV AMP Kit is 2°C to 8°C.
- **Alinity m HCV CTRL Kit (List No. 08N50-085)**, consisting of negative controls, low positive controls, and high positive controls, each supplied as liquid in single-use tubes. The intended storage condition for the Alinity m HCV CTRL Kit is –25°C to –15°C.
- **Alinity m HCV CAL Kit (List No. 08N50-075)**, consisting of 2 calibrator levels, each supplied as liquid in single-use tubes. The intended storage condition for the Alinity m HCV CAL Kit is –25°C to –15°C.

HCV RNA from human plasma or serum is extracted automatically on-board in the Alinity m System using the Alinity m Sample Prep Kit 2, Alinity m Lysis Solution, and Alinity m Diluent Solution. The Alinity m System employs magnetic microparticle technology to facilitate nucleic acid capture, wash, and elution. The resulting purified nucleic acids are then combined with liquid unit-dose Alinity m HCV activation reagent and lyophilized unit-dose Alinity m HCV amplification/detection reagents and transferred into a reaction vessel. Alinity m Vapor Barrier Solution is then added to the reaction vessel which is then transferred to an amplification/detection unit for PCR amplification, and real-time fluorescence detection of HCV targets.

At the beginning of the Alinity m HCV sample preparation process, a lyophilized unit-dose IC on the AMP Tray is rehydrated by the Alinity m System and delivered into each sample preparation reaction. The IC is then processed through the entire sample preparation and real-time PCR procedure along with the specimens, calibrators, and controls to demonstrate proper sample processing and validity.

The Alinity m HCV amplification/detection reagents consist of enzymes, primers, probes, and activation reagents that enable reverse transcription, polymerization, and detection.

An HCV calibration curve is required for determination of HCV RNA concentration. Two levels of calibrators are processed through sample preparation and RT-PCR to generate the calibration curve. The concentration of HCV RNA in specimens and controls is then calculated from the stored calibration curve.

Assay controls are tested at or above an established minimum frequency to help ensure that instrument and reagent performance remains satisfactory. During each control event, a negative control, a low-positive control, and a high-positive control are processed through sample preparation and RT-PCR procedures that are identical to those used for specimens.

The Alinity m HCV assay also utilizes the following:

- Alinity m HCV Application Specification File, (List No. 08N50-03B)
- Alinity m System and System Software (List No. 08N53)
- Alinity m Sample Prep Kit 2 (List No. 09N12-001)
- Alinity m Specimen Dilution Kit I (List No. 09N50-001)
- Alinity m System Solutions, (List No. 09N20):
    - Alinity m Lysis Solution (List No. 09N20-001)
    - Alinity m Diluent Solution (List No. 09N20-003)
    - Alinity m Vapor Barrier Solution, (List No. 09N20-004)
- Alinity m Tubes and Caps (List No. 09N49):
    - Alinity m LRV Tube (List No. 09N49-001)
    - Alinity m Transport Tubes Pierceable Capped (List No. 09N49-010)
    - Alinity m Transport Tube (List No. 09N49-011)
    - Alinity m Pierceable Cap (List No. 09N49-012)
    - Alinity m Aliquot Tube (List No. 09N49-013)

1.5 Intended Use

The Alinity m HCV assay is an in vitro reverse transcription-polymerase chain reaction (RT-PCR) assay for both the detection and quantitation of hepatitis C virus (HCV) RNA, in human plasma (EDTA, Acid Citrate Dextrose) or serum, from HCV antibody positive individuals. The assay is intended for use as an aid in the diagnosis of active HCV infection in individuals with antibody evidence of HCV infection, and to aid in the management of patients with known active HCV infection, including Sustained Virologic Response (SVR) determination.

The results from the Alinity m HCV assay must be interpreted within the context of all relevant clinical and laboratory findings.

The Alinity m HCV assay is not intended to be used in screening blood, plasma, serum, tissue or tissue donors for HCV.

1.6 Similarities and Differences to Predicate Device

The primary functional components of the Alinity m HCV assay are substantially equivalent to the current on-market Alinity m HCV assay (PMA 190025), which is a legally marketed Nucleic Acid-Based Hepatitis C Virus Ribonucleic Acid Test.

The Alinity m HCV assay has the same intended use as the predicate device. The subject device and predicate device differ only in the DNA polymerase and Reverse Transcriptase enzymes that may be used in manufacture of the assay; this formulation difference does not raise new types of safety or effectiveness questions.

These devices are similar in that they are designed to prepare nucleic acids for amplification, amplify specific HCV RNA sequences, detect the amplified products, and report quantitative results.

The primary similarities and differences between the Alinity m HCV assay and the predicate device are shown in **Table 1** and **Table 2**.

Table 1. Similarities Between Alinity m HCV and Predicate Device

Description	Subject Device	Predicate Device
	Alinity m HCV	**Alinity m HCV (PMA 190025)**
Intended Use	Same	The Alinity m HCV assay is an in vitro reverse transcription-polymerase chain reaction (RT-PCR) assay for both the detection and quantitation of hepatitis C virus (HCV) RNA, in human plasma (EDTA, Acid Citrate Dextrose) or serum, from HCV antibody positive individuals. The assay is intended for use as an aid in the diagnosis of active HCV infection in individuals with antibody evidence of HCV infection, and to aid in the management of patients with known active HCV infection, including Sustained Virologic Response (SVR) determination. The results from the Alinity m HCV assay must be interpreted within the context of all relevant clinical and laboratory findings. The Alinity m HCV assay is not intended to be used in screening blood, plasma, serum, tissue or tissue donors for HCV.
Assay Type	Same	Quantitative
Assay Targets	Same	highly conserved sequence within the 5’ untranslated region (5’utr) of the HCV genome
Specimen Types	Same	ACD Plasma, EDTA Plasma, Serum
Sample Preparation Procedure	Same	Automated liquid handling and robotic manipulation platform
Amplification Technology	Same	Real-time polymerase chain reaction

Table 1. Similarities Between Alinity m HCV and Predicate Device

Description	Subject Device	Predicate Device
	Alinity m HCV	**Alinity m HCV (PMA 190025)**
Assay Controls	Same	• Negative Control • Low Positive Control • High Positive Control • Internal Control (IC)

Table 2. *Differences* Between Alinity m HCV and Predicate Device

Feature	Current Application	Predicate Device
	Alinity m HCV	**Alinity m HCV (P190025)**
Amplification Enzymes	Original DNA Polymerase *or alternative DNA Polymerase* enzyme used for DNA amplification. Original *or alternative* enzyme to convert target RNA to complimentary DNA (cDNA).	Original DNA Polymerase enzyme used for DNA amplification. Original enzyme to convert target RNA to complimentary DNA (cDNA).

1.7 Performance Data

The following performance data were provided in support of substantial equivalence determination of the device.

1.7.1 Specific Performance Characteristics

The subject device is similar to the predicate device originally approved (P190025) with the exception that the subject device may use a new DNA Polymerase as an alternative to the original DNA Polymerase and a new Reverse Transcriptase as an alternative to the original Reverse Transcriptase in the reagent formulation of the assay. Apart from the DNA polymerase and Reverse Transcriptase enzymes used, the reagent formulation, including all oligonucleotide primers and probes (components and concentrations) is identical between the subject device and predicate device. There are no differences in the intended use, end-user workflow, instrument workflow, assay software, reagent manufacturing, or final product release specifications.

Additional analytical performance studies listed in **Table 3** were conducted to confirm the ability of the Alinity m HCV assay formulated with alternative DNA Polymerase and alternative Reverse Transcriptase (subject device) to meet the performance claims established in the corresponding studies submitted in P190025 for the Alinity m HCV assay formulated with the original DNA Polymerase and the original Reverse Transcriptase (predicate device).

Table 3. Additional Supporting Studies (Alternate Enzymes Formulation)

Study Description / Performance Characteristic	**510(k) Summary Section**
Limit of Detection	**1.7.1.1**
Linear Range	**1.7.1.2**
Precision	**1.7.1.3**
Lower Limit of Quantitation	**1.7.1.4**

All other specific performance characteristics of the subject device are supported by the studies submitted in P190025. Refer to **Table 4**.

Table 4. Supporting Studies Submitted in P190025

Study Description / Performance Characteristic	Reference
Traceability to the WHO Standard	Original submission
Genotype Limit of Detection	Original submission
Genotype Linearity	Original submission
Analytical Specificity – Potential Cross-Reactants	Original submission
Analytical Specificity – Potentially Interfering Substances	Original submission
Carryover	Original submission
Alinity m HCV Testing Using Dilution Procedure	Original submission
Precision of Alinity m HCV Using Dilution Procedure	Original submission
Confirmation of LLoQ Using Dilution Procedure	Original submission

1.7.1.1 Limit of Detection

A limit of detection (LoD) study was conducted previously to support the approval of P190025. Please refer to the decision summary for P190025.

An additional study was conducted to confirm the LoD claim of Alinity m HCV (12 IU/mL) for the formulation of the assay using the alternative enzymes.

The LoD for HCV was evaluated by testing dilutions of a World Health Organization (WHO) HCV Standard (NIBSC code 18/184) prepared in HCV negative human plasma. Testing for each HCV DNA concentration was performed with 3 lots of amplification reagents across multiple days.

The data from the study demonstrated that the Alinity m HCV assay formulated with the alternative DNA Polymerase and the alternative Reverse Transcriptase had an overall detection rate of 98.6% at 12 IU/mL. Refer to **Table 5**.

Table 5. Alinity m HCV (Alternat Enzymes Formulation) Limit of Detection (LoD) Results

Target Concentration (IU/mL)	AMP Kit Reagent Lot	Number of Total Replicates	Number of Replicates Detected	Detection Rate (%)	95% Score Confidence Interval (%)
9	1	48	46	95.8	(86.0, 98.8)
	2	48	45	93.8	(83.2, 97.9)
	3	48	47	97.9	(89.1, 99.6)
	All Combined	144	138	95.8	(91.2, 98.1)
12[a]	1	48	48	100.0	(92.6, 100.0)
	2	48	46	95.8	(86.0, 98.8)
	3	47	47	100.0	(92.4, 100.0)
	All Combined	143	141	98.6	(95.0, 99.6)
16	1	47	47	100.0	(92.4, 100.0)
	2	48	48	100.0	(92.6, 100.0)
	3	45	45	100.0	(92.1, 100.0)
	All Combined	140	140	100.0	(97.3, 100.0)

[a] Alinity m HCV assay limit of detection (LoD) claim

1.7.1.2 Linear Range

A linearity study was conducted previously to support the approval of P190025. Please refer to the decision summary for P190025.

An additional study was conducted to confirm that the Alinity m HCV assay formulated with the alternative DNA Polymerase and the alternative Reverse Transcriptase was linear across the claimed quantitation range (12 IU/mL [1.08 Log IU/mL] to 100,000,000 IU/mL [8.00 Log IU/mL]).

Linearity was evaluated by testing 12 panel members that spanned the intended quantitation range of the assay(12 IU/mL to 100,000,000 IU/mL), including a panel member below the expected Lower Limit of Quantification (LLoQ) at 10 IU/mL and a panel member exceeding the expected Upper Limit of Quantification (ULoQ) at 200,000,000 IU/mL. Refer to **Table 6**.

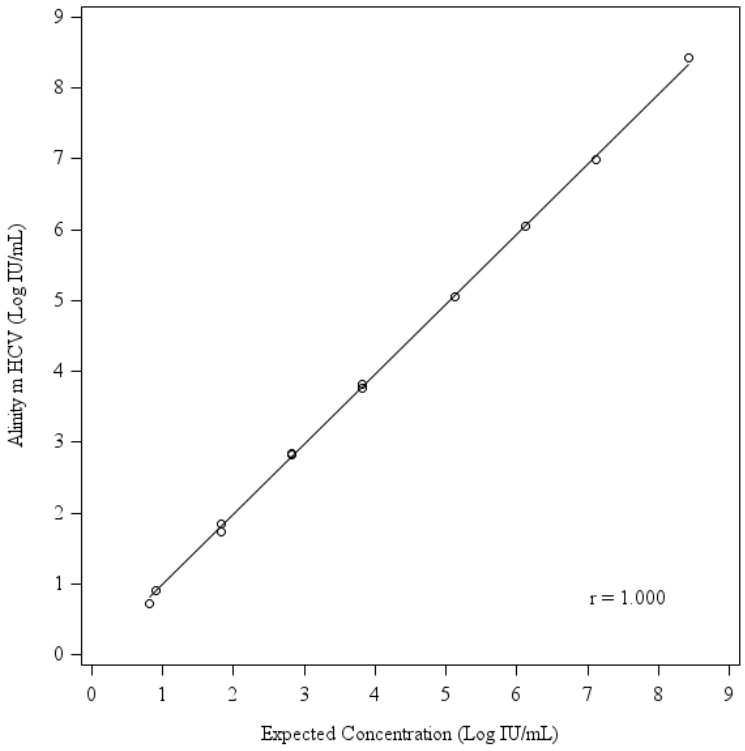
Table 6. Panel Members for Linearity

Panel Member	Targeted HCV Concentration		Source
	IU/mL	Log IU/mL	
01	200,000,000	8.30	aRNA
02	10,000,000	7.00	aRNA
03	1,000,000	6.00	aRNA
04	100,000	5.00	aRNA
05	10,000	4.00	Clinical Sample
06	5,000	3.70	aRNA
07	1,000	3.00	Clinical Sample
08	500	2.70	aRNA
09	100	2.00	Clinical Sample
10	50	1.70	aRNA
11[a]	12	1.08	Clinical Sample
12	10	1.00	Clinical Sample

[a] The assay's claimed LLoQ is 12 IU/mL per package insert.

The data from the study demonstrated that the Alinity m HCV assay formulated with the alternative DNA Polymerase and the alternative Reverse Transcriptase was linear across the quantitative range from 12 IU/mL to 100,000,000 IU/mL (1.08 Log IU/mL to 8.00 Log IU/mL). Results for Alinity m HCV linearity performance are shown in **Figure 1**.

Figure 1. Alinity m HCV (Alternate Enzymes Formulation) Linearity



1.7.1.3 Precision

A precision study was conducted previously to support the approval of P190025. Please refer to the decision summary for P190025.

An additional study was conducted to confirm the precision claim of Alinity m HCV (as follows) for the alternative DNA Polymerase and the alternative Reverse Transcriptase formulation of the assay:

- Within-laboratory standard deviation (SD) of ≤ 0.25 Log IU/mL for samples between 100 IU/mL to 200,000,000 IU/mL (2.00 Log IU/mL to 8.30 Log IU/mL) HCV RNA
- Within-laboratory SD of ≤ 0.35 Log IU/mL for samples with target concentrations from the claimed LLoQ to 3x LLoQ (12 IU/mL to 36 IU/mL or 1.08 Log IU/mL to 1.56 Log IU/mL) HCV RNA

Precision was evaluated by testing 8 panel members with HCV concentrations ranging from 12 IU/mL to 200,000,000 IU/mL (1.08 Log IU/mL to 8.30 Log IU/mL). Panel members were prepared by diluting HCV positive specimen or armored RNA (aRNA) in human EDTA plasma. aRNA was only used for panel members with high concentrations (> 5.00 Log IU/mL).

Three lots of Alinity m HCV amplification reagents manufactured with the alternative DNA Polymerase and the alternative Reverse Transcriptase were run on 1 Alinity m System. Three replicates of each panel member were run twice each day for 15 days for each lot with a minimum separation of 2 hours between successive runs of a panel member.

The overall precision analysis summary for the Alinity m HCV assay formulated with the alternative enzymes is presented in **Table 7**.

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The results demonstrated that the Alinity m HCV assay has a within-laboratory SD of 0.25 Log IU/mL or less for samples targeted between 100 IU/mL to 200,000,000 IU/mL (2.00 Log IU/mL to 8.30 Log IU/mL) HCV RNA, and a within-laboratory SD of 0.35 Log IU/mL or less for samples with target concentrations from the claimed LLoQ to 3x LLoQ (12 IU/mL to 36 IU/mL or 1.08 Log IU/mL to 1.56 Log IU/mL) HCV RNA

Table 7. Alinity m HCV (Alternate Enzymes Formulation) Precision Analysis – All Reagent Lots

		Mean	Within-Run Component		Between-Run Component		Between-Day Component		Within-Laboratory [a]		Between-Lot Component		Total [b]	
Panel	N	Concentration (Log IU/mL)	SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV
01	269	0.96	0.24	24.6	0.00	0.0	0.10	10.2	0.26	26.6	0.09	9.1	0.27	28.2
02	270	1.61	0.14	8.8	0.06	3.5	0.00	0.0	0.15	9.5	0.08	4.8	0.17	10.6
03	270	1.80	0.11	6.2	0.06	3.1	0.00	0.0	0.13	7.0	0.07	4.1	0.15	8.1
04	270	2.88	0.09	3.0	0.05	1.6	0.00	0.0	0.10	3.4	0.07	2.3	0.12	4.1
05	270	3.78	0.07	1.9	0.04	1.1	0.00	0.0	0.08	2.2	0.06	1.6	0.10	2.7
06	270	5.85	0.06	1.1	0.02	0.3	0.03	0.5	0.07	1.2	0.05	0.9	0.09	1.5
07	270	6.89	0.04	0.5	0.02	0.2	0.00	0.0	0.04	0.6	0.06	0.9	0.07	1.1
08	270	8.26	0.04	0.5	0.01	0.1	0.02	0.2	0.05	0.6	0.10	1.2	0.11	1.3

[a] Within-Laboratory includes Within-Run, Between-Run, and Between-Day Components.
[b] Total includes Within-Run, Between-Run, Between-Day, and Between-Lot Components.

The Total SD and Total %CV for each panel member in this study were compared with the Total SD and Total %CV from the original precision study submitted in P190025. Refer to **Table 8**.

Table 8. Equivalence Evaluation of Total SD and Total %CV (New [a] vs. Original [b])

	Mean Concentration		Total SD		Total %CV		Ratios and 95% CI	
Panel Member	**New [a] Mean (Log IU/mL)**	**Original [b] Mean (Log IU/mL)**	**New [a] SD**	**Original [b] SD**	**New [a] % CV**	**Original [b] % CV**	**SD**	**%CV**
01	0.96	1.07	0.27	0.21	28.2	19.7	1.28 (1.01, 1.63)	1.43 (1.12, 1.81)
02	1.61	1.42	0.17	0.18	10.6	12.6	0.96 (0.68, 1.34)	0.85 (0.60, 1.19)
03	1.80	1.91	0.15	0.17	8.1	8.7	0.88 (0.53, 1.46)	0.94 (0.57, 1.55)
04	2.88	2.88	0.12	0.17	4.1	5.8	0.71 (0.40, 1.26)	0.71 (0.40, 1.26)
05	3.78	3.94	0.10	0.14	2.7	3.6	0.73 (0.47, 1.12)	0.76 (0.49, 1.16)
06[c]	5.85	6.14	0.09	0.11	1.5	1.8	0.77 (0.33, 1.80)	0.81 (0.35, 1.89)
07[d]	6.89	7.11	0.07	0.16	1.1	2.3	0.45 (0.22, 0.92)	0.47 (0.23, 0.95)
08 [e]	8.26	8.55	0.11	0.16	1.3	1.9	0.69 (0.17, 2.87)	0.72 (0.17, 2.97)

[a] "New" Mean, SD, and %CV data for Alinity m HCV assay formulated with alternative DNA Polymerase and alternative Reverse Transcriptase.

[b] "Original" Mean, SD, and %CV data for Alinity m HCV assay formulated with original DNA Polymerase and original Reverse Transcriptase (per P190025)

[c] Panel 06 in the New Precision protocol targeting 6.0 Log IU/mL is compared to panel 07 in the Original Precision protocol targeting 6.0 Log IU/mL

[d] Panel 07 in the New Precision protocol targeting 7.0 Log IU/mL is compared to panel 08 in the Original Precision protocol targeting 7.0 Log IU/mL.

[e] Panel 08 in the New Precision protocol targeting 8.3 Log IU/mL is compared to panel 09 in the Original Precision protocol targeting 8.3 Log IU/mL.

NOTE: Panel 06 in the Original Precision protocol targeting 5.0 Log IU/mL is not analyzed for comparison.

1.7.1.4 Lower Limit of Quantitation (LLoQ)

A lower limit of quantitation (LLoQ) study was conducted previously to support the approval of P190025. Please refer to the decision summary for P190025.

An additional study was conducted to confirm the LLoQ claim of Alinity m HCV (12 IU/mL) for the alternative DNA Polymerase and alternative Reverse Transcriptase formulation of the assay.

The LLoQ is defined as the lowest concentration at which HCV RNA is reliably quantitated within an acceptable total error. Total error was estimated for detected samples from the LoD study (**Section 1.7.1.1**), the Linearity study (**Section 1.7.1.2**), and the Precision study (**Section 1.7.1.3**) by 2 methods:

- Total Analytical Error (TAE) = |bias| + 2 × SD, (where bias = mean concentration – assigned target concentration)

and

- Total Error (TE) = SQRT(2) × 2 × SD

Panel members were dilutions of a World Health Organization (WHO) HCV Standard (NIBSC code 18/184) prepared in HCV negative human plasma.

The results of the calculations are shown in **Table 9**.

The results of these analyses support a claimed LLoQ of 12 IU/mL (1.08 Log IU/mL), with an acceptable level of accuracy and precision (ie, TAE and TE less than or equal to 1.00 Log IU/mL).

Table 9. Alinity m HCV (Alternate Enzyme Formulation) TAE and TE

Study	Panel	Target (IU/mL)	N	Target (Log IU/mL)	Mean (Log IU/mL)	Bias (Log IU/mL)	SD	TAE	TE
Linearity	11	12	24	1.08	0.90	-0.18	0.27	0.72	0.76
	12	10	24	1.00	0.72	-0.28	0.32	0.93	0.92
Precision	01	12	269	1.08	0.96	-0.12	0.26	0.63	0.73
Sensitivity	1	9	138	0.95	0.77	-0.18	0.26	0.70	0.74
	2	12	141	1.08	0.85	-0.23	0.27	0.77	0.76
	3	16	140	1.20	1.06	-0.15	0.21	0.57	0.59

1.7.1 Performance Characteristics

1.7.1.1 Reproducibility

A reproducibility study was conducted previously to support the approval of P190025. Please refer to the decision summary for P190025.

An additional study was conducted to evaluate the reproducibility of the Alinity m HCV assay formulated with alternative DNA Polymerase and alternative Reverse Transcriptase.

Reproducibility performance of Alinity m HCV was evaluated by testing an 11-member reproducibility panel, which included 10 positive panel members and 1 negative panel member. Panel members were prepared in base-matrix (EDTA plasma) and spanned the linear range of Alinity m HCV assay. One panel member was negative for HCV. Ten positive panel members represented the two different genotypes 1a & 2. Panel members were prepared by diluting HCV positive clinical specimen or HCV armored RNA (aRNA) in HCV negative plasma. HCV aRNA was only used for panel members with high concentrations (>5.0 Log IU/mL).

One lot each of Alinity m HCV AMP Kit, Alinity m HCV CAL Kit, Alinity m HCV CTRL Kit, and Alinity m Sample Prep Kit 2 lots were used. Testing was performed at 3 clinical sites on 5 non-consecutive days with 2 runs per day. Four replicates of each panel member were tested on each of 5 days to ensure a minimum of 3 valid replicates for analysis.

The reproducibility results are summarized in **Table 10** (for the positive panel members) and in **Table 11** (for the negative panel member).

Table 10. Alinity m HCV (Alternate Enzymes Formulation) Overall Variance Component Analysis

Genotype	Panel	N	Mean Concentration (Log IU/mL)	Within-Run Component		Between-Run Component		Between-Day Component		Within-Laboratory [a]		Between-Site Component		Total [b]	
				SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV
1a	1	118	7.71	0.20	2.6	0.08	1.1	0.10	1.4	0.24	3.1	0.06	0.8	0.25	3.2
1a	2	115	5.72	0.06	1.1	0.05	0.8	0.00	0.0	0.08	1.4	0.06	1.1	0.10	1.8
1a	3	115	3.53	0.06	1.6	0.04	1.1	0.03	0.9	0.08	2.2	0.03	0.9	0.08	2.4
1a	4	119	1.84	0.11	5.9	0.07	4.1	0.00	0.0	0.13	7.2	0.06	3.0	0.14	7.8
1a	5	116	0.89	0.21	23.8	0.07	7.4	0.01	1.4	0.22	24.9	0.10	11.5	0.24	27.5
1a	6	116	0.80	0.25	31.5	0.04	5.5	0.00	0.0	0.26	31.9	0.06	8.1	0.26	32.9
2	7	120	6.97	0.06	0.9	0.03	0.5	0.05	0.6	0.08	1.2	0.02	0.3	0.09	1.3
2	8	116	2.99	0.08	2.6	0.02	0.8	0.03	1.1	0.09	2.9	0.03	0.8	0.09	3.0
2	9	118	1.65	0.14	8.5	0.00	0.0	0.05	2.8	0.15	9.0	0.06	3.7	0.16	9.7
2	10	119	1.05	0.22	21.3	0.00	0.0	0.06	5.9	0.23	22.1	0.07	6.5	0.24	23.1

[a] Within-Laboratory includes Within-Run, Between-Run, and Between-Day Variance Components.
[b] Total (Overall) includes Within-Run, Between-Run, Between-Day, and Between-Site Variance Components.

Table 11. Alinity m HCV (Alternate Enzymes Formulation) Overall Negative Agreement Analysis

Panel	Site	N			Negative Agreement Rate	95% CI
		Total	Positive	Negative		
11	All	120	0	120	100.0%	(96.9%, 100.0%)

The Total SD and Total %CV for each panel member in this study were compared with the Total SD and Total %CV from the original reproducibility study submitted in P190025. Refer to **Table 12**.

Table 12. Equivalence Evaluation of Total SD and Total %CV (New [a] vs. Original [b])

		Mean Concentration		Total SD		Total %CV		Ratios and 95% CI	
Genotype	Panel	New Mean (Log IU/mL)	Original Mean (Log IU/mL)	New SD	Original SD	New %CV	Original %CV	SD	%CV
1a	1	7.71	8.50	0.25	0.15	3.2	1.7	1.68 (0.97, 2.92)	1.85 (1.06, 3.21)
1a	2	5.72	6.15	0.10	0.16	1.8	2.6	0.64 (0.44, 0.93)	0.69 (0.48, 1.00)
1a	3	3.53	3.89	0.08	0.18	2.4	4.5	0.47 (0.36, 0.61)	0.52 (0.40, 0.68)
1a	4	1.84	1.95	0.14	0.22	7.8	11.0	0.66 (0.52, 0.84)	0.70 (0.55, 0.90)
1a	5	0.89	1.06	0.24	0.35	27.5	33.0	0.70 (0.53, 0.94)	0.83 (0.63, 1.11)
1a	6	0.80	0.65	0.26	0.37	32.9	56.8	0.71 (0.58, 0.87)	0.58 (0.47, 0.71)
2	7	6.97	7.30	0.09	0.11	1.3	1.5	0.83 (0.59, 1.16)	0.87 (0.62, 1.21)
2	8	2.99	3.06	0.09	0.21	3.0	6.7	0.44 (0.36, 0.54)	0.45 (0.36, 0.56)
2	9	1.65	1.44	0.16	0.24	9.7	17.0	0.66 (0.51, 0.85)	0.57 (0.44, 0.74)
2	10	1.05	0.88	0.24	0.30	23.1	34.2	0.80 (0.66, 0.98)	0.67 (0.55, 0.83)

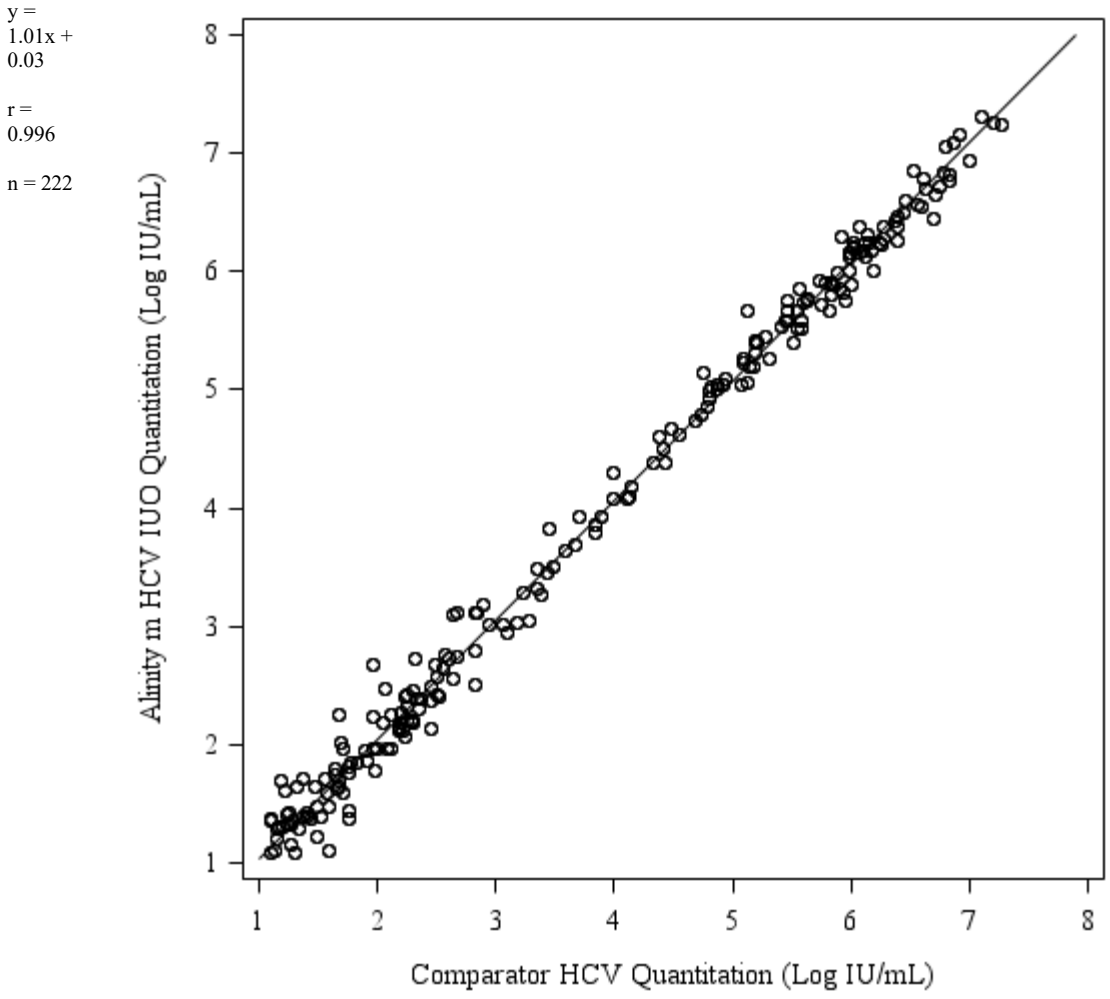
[a] "New" Mean Concentration, Total SD, and Total %CV data for Alinity m HCV assay formulated with alternative enzymes.
[b] "Original" Mean Concentration, Total SD, and Total %CV data for on-market Alinity m HCV assay (submitted in P190025).

1.7.1.2 Method Comparison

A method comparison study was conducted with the Alinity m HCV assay formulated with the alternative DNA Polymerase and the alternative Reverse Transcriptase to demonstrate equivalence to the FDA-approved (on-market) Alinity m HCV assay formulated with the original DNA Polymerase and the original Reverse Transcriptase (P190025).

Regression and bias analysis included a total of 222 samples with results that were within the common quantitation range of both the Alinity m HCV assay formulated with alternative enzymes formulation (Alinity m HCV IUO) and the comparator assay (on-market Alinity m HCV). **Figure 2** shows the results of the Deming regression analysis with a slope of 1.01, an intercept of 0.03, and a correlation coefficient of 0.996. The mean bias between Alinity m HCV IUO and the comparator (Alinity m HCV IUO minus comparator) was 0.06 Log IU/mL with a 95% Confidence Interval of (0.04, 0.09).

Figure 2. Deming Regression Analysis



The Systematic difference between Alinity m HCV assay formulated with alternate enzymes and the on-market Alinity m HCV assay (comparator) at 4 selected viral load levels is shown in **Table 13**.

Table 13. Systematic Difference at Selected Viral Load Levels		
Target Viral Load Level (per comparator)	**Systematic Difference**	**95% CI (Log IU/mL)**
1.08 Log IU/mL	0.04 Log IU/mL	(-0.00, 0.09)
1.40 Log IU/mL	0.05 Log IU/mL	(0.00, 0.09)
3.60 Log IU/mL	0.06 Log IU/mL	(0.04, 0.09)
5.80 Log IU/mL	0.08 Log IU/mL	(0.05, 0.11)

1.8 Conclusions Drawn from the Studies

The additional analytical and clinical study results demonstrate that the Alinity m HCV assay formulated with the alternative DNA Polymerase and the alternative Reverse Transcriptase performs comparably to the FDA approved Alinity m HCV assay formulated with the original DNA Polymerase and the original Reverse Transcriptase.

The results support a substantial equivalence decision for Alinity m HCV formulated with the alternative DNA Polymerase and the alternative Reverse Transcriptase.