

Summary of Safety and Effectiveness Data

I. GENERAL INFORMATION:

Device Generic Name: Antibody to Hepatitis C Virus (HCV)

Device Trade Name: ARCHITECT® Anti-HCV Reagent Kit
ARCHITECT® Anti-HCV Calibrator
ARCHITECT® Anti-HCV Controls

Name and Address of Applicant: Abbott Laboratories
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Date of Panel Recommendation: None

Premarket Approval Application (PMA) Number: P050042

Date of Notice of Approval to the Applicant: June 7, 2006

II. INDICATIONS FOR USE:

ARCHITECT® Anti-HCV Reagent Kit

The ARCHITECT Anti-HCV assay is a chemiluminescent microparticle immunoassay (CMIA) for the qualitative detection of immunoglobulin G (IgG) and immunoglobulin M (IgM) antibodies to hepatitis C virus (anti-HCV) in human adult serum and plasma (potassium EDTA, lithium heparin, and sodium heparin). Assay results, in conjunction with other laboratory results and clinical information, may be used to provide presumptive evidence of infection with HCV (state of infection or associated disease not determined) in persons with signs and symptoms of hepatitis and in persons at risk for hepatitis C infection.

ARCHITECT® Anti-HCV Calibrator

The ARCHITECT Anti-HCV Calibrator is used for the calibration of the ARCHITECT *i* System when the system is used for the qualitative detection of immunoglobulin G (IgG) and immunoglobulin M (IgM) antibodies to hepatitis C virus (anti-HCV) using the ARCHITECT Anti-HCV Reagent Kit.

ARCHITECT® Anti-HCV Controls

The ARCHITECT Anti-HCV Controls are used for monitoring the performance of the ARCHITECT *i* System when used for the qualitative detection of immunoglobulin G (IgG) and immunoglobulin M (IgM) antibodies to hepatitis C virus (anti-HCV) when using the ARCHITECT Anti-HCV Reagent Kit.

III. CONTRAINDICATIONS: None known.

IV. WARNINGS AND PRECAUTIONS: For *in vitro* diagnostic use only.

Warnings and precautions for ARCHITECT Anti-HCV Reagent Kit, ARCHITECT Anti-HCV Calibrator, and ARCHITECT Anti-HCV Controls are stated in the respective product labeling.

V. DEVICE DESCRIPTION:

Kit Configurations and Components

For detection of antibodies to hepatitis C virus, the ARCHITECT Anti-HCV Reagent Kit is composed of the following three components:

- ARCHITECT Anti-HCV Microparticles: 1 or 4 Bottle(s) (6.6 mL/27.0 mL) HCV antigen (recombinant *E. coli*, recombinant yeast) coated microparticles in MES buffer. Minimum concentration: 0.14% solids. Preservatives: antimicrobial agents.
- ARCHITECT Anti-HCV Conjugate: 1 or 4 Bottle(s) (5.9 mL/26.3 mL) murine anti-human IgG/IgM acridinium-labeled conjugate in MES buffer with protein (bovine) additive (152 µM) and surfactant. Minimum concentration: (IgG) 8 ng/mL / (IgM) 0.8 ng/mL. Preservatives: antimicrobial agents.
- ARCHITECT Anti-HCV Assay Diluent: 1 or 4 Bottle(s) (10.0 mL/ 50.9 mL) anti-HCV assay diluent containing TRIS buffer with protein (goat) additive (102.6 g/L) and surfactant. Preservative: ProClin® 300.

In addition, the following components are required for the ARCHITECT Anti-HCV Reagent Kit:

- ARCHITECT *i* System is an analyzer designed to perform automated immunoassay tests based on the use of CMIA detection technology.
- ARCHITECT Anti-HCV Calibrator, which consists of one calibrator level for the calibration of the instrument.
- ARCHITECT Anti-HCV Controls (or other control material), which consist of a negative control and a positive control.
- ARCHITECT *i* Pre-Trigger Solution contains 1.32% (w/v) hydrogen peroxide.
- ARCHITECT *i* Trigger Solution contains 0.35N sodium hydroxide.
- ARCHITECT *i* Wash Buffer contains phosphate buffered saline solution with preservative.

The ARCHITECT Anti-HCV Calibrator Kit contains:

- 1 Bottle (4 mL) ARCHITECT Anti-HCV Calibrator 1 is recalcified, heat-inactivated anti-HCV positive human plasma in recalcified anti-HCV negative human plasma. Calibrator 1 is green and contains Acid Yellow No. 23 and Acid Blue No. 9 dyes. Preservative: sodium azide.

The ARCHITECT Anti-HCV Control Kit contains:

- 2 Bottles (8 mL each) of ARCHITECT Anti-HCV Controls (1 bottle of negative control and 1 bottle of positive control).
- The negative control is recalcified human plasma. Preservative: sodium azide.
- The positive control is recalcified, heat-inactivated anti-HCV positive human plasma in recalcified anti-HCV negative human plasma. The positive control is blue and contains Acid Blue No. 9 dye. Preservative: sodium azide.

Assay Principle and Format

The ARCHITECT Anti-HCV assay is a two-step immunoassay for the qualitative detection of anti-HCV in human serum and plasma using CMIA technology with flexible assay protocols, referred to as Chemiflex®.

In the first step, sample, recombinant HCV antigen coated paramagnetic microparticles, and assay diluent are combined. Anti-HCV present in the sample binds to the HCV coated microparticles. After washing, anti-human IgG/IgM acridinium-labeled conjugate is added in the second step. Following another wash cycle, pre-trigger and trigger solutions are added to the reaction mixture. The resulting chemiluminescent reaction is measured as relative light units (RLUs). A relationship exists between the amount of anti-HCV in the sample and the RLUs detected by the ARCHITECT *i* optical system.

The ARCHITECT Anti-HCV Calibrator Kit is used to calibrate the ARCHITECT *i* System. The presence or absence of anti-HCV in the sample is determined by comparing the chemiluminescent signal in the reaction to the cutoff signal determined from an active ARCHITECT Anti-HCV calibration curve. If the chemiluminescent signal of the sample is greater than or equal to the cutoff signal, the sample is considered reactive for anti-HCV.

Results

The ARCHITECT *i* System calculates the cutoff RLU from the mean chemiluminescent signal of three Anti-HCV Calibrator 1 replicates and stores the result. The cutoff RLU is determined by multiplying the Anti-HCV Calibrator 1 mean RLU by 0.074.

$$\text{Cutoff RLU} = \text{Calibrator 1 Mean RLU} \times 0.074$$

The ARCHITECT *i* System calculates a result based on the ratio of the sample RLU to the cutoff RLU (S/CO) for each specimen and control.

$$\text{S/CO} = \text{Sample RLU/Cutoff RLU ratio.}$$

Interpretation of Results

Initial ARCHITECT Anti-HCV Results			
Initial Result (S/CO)	Instrument Flag	Interpretation	Retest Procedure
" \geq 1.00	REACTIVE	Reactive	No retest required.
0.80 to 0.99	GRAYZONE	Grayzone	Retest in duplicate.
0.00 to 0.79	NONREACTIVE	Nonreactive	No retest required.

ARCHITECT Anti-HCV Results			
Initial Result	Retest Result	Result	Interpretation
Reactive	No retest required.	Reactive	Presumptive evidence of antibodies to HCV; follow CDC recommendations for supplemental testing.
Grayzone	Both of the duplicate retests are reactive.	Reactive	Presumptive evidence of antibodies to HCV; follow CDC recommendations for supplemental testing.
	One or both of the duplicate retests are repeatedly in the grayzone or one retest is reactive and the other nonreactive.	Equivocal	Antibodies to HCV may or may not be present; another specimen should be obtained from the individual for further testing or follow CDC recommendations for supplemental testing.
	Both of the duplicate retests are nonreactive.	Nonreactive	Antibodies to HCV not detected; does not exclude the possibility of exposure to HCV.
Nonreactive	No retest required.	Nonreactive	Antibodies to HCV not detected; does not exclude the possibility of exposure to HCV.

VI. ALTERNATIVE PRACTICES AND PROCEDURES

Determining the presence of HCV in patients may be achieved by using a variety of commercially available, FDA-approved, serological tests. When these test results are used in combination with a physician's assessment and other laboratory test results, infection with HCV can be identified.

VII. MARKETING HISTORY

ARCHITECT Anti-HCV, List No. 1L79, has not been marketed in any other country.

VIII. POTENTIAL ADVERSE EFFECTS OF THE DEVICE ON HEALTH

The ARCHITECT Anti-HCV materials are for in vitro diagnostic use, thus there is no direct adverse effect on the patient. Failure of the product to perform as intended, or errors in the use of the product, may lead to a false result. A false reactive (false positive) result using an anti-HCV assay is not considered a patient or public health concern because a reactive enzyme immunoassay (EIA) result in a clinical lab should be followed up with supplemental tests (e.g., strip immunoblot assay (SIA) and/or polymerase

chain reaction (PCR) for detection of HCV RNA) to determine inactive or resolved infection versus active HCV replication.' Treatment of the patient with chronic HCV infection is initiated only after extensive clinical, laboratory and behavioral assessment of the patient (e.g., elevated ALT levels for six months, detectable serum HCV RNA, liver biopsy with portal fibrosis, patient compliance, and abstinence from drugs and alcohol). A false nonreactive (false negative) anti-HCV result in a diagnostic setting may lead to a patient with HCV going unidentified. Under these circumstances, there is a safety concern for both the patient and the public, since such individuals may be capable of transmitting HCV infection. However, if a patient is known to be at high risk of HCV infection, or is symptomatic, and the physician's suspicion of HCV infection is high, HCV RNA testing is often employed and is of diagnostic value, even after an initial negative anti-HCV test result.

IX. SUMMARY OF NONCLINICAL STUDIES

Nonclinical studies were performed at Abbott Laboratories to evaluate the performance characteristics of the ARCHITECT Anti-HCV assay. The studies are described below.

Tube Type Interference

A study was conducted to evaluate which anticoagulants (blood collection tube types) are acceptable for use with the ARCHITECT Anti-HCV assay. Sample sets of human specimens were collected in the control tube type (glass serum) and the blood collection tube types selected for evaluation. The blood collection tubes for the sample sets were supplemented with anti-HCV positive serum or plasma to prepare high negative samples (targeted to 0.80 S/CO) and low positive samples (targeted to 1.20 S/CO) and were tested.

On average, the tube types listed in Table 1 below showed less than a 10% difference when compared to the control tube type (glass serum) for high negative samples (S/CO range: 0.60 to 0.99) and low positive samples (S/CO range: 1.00 to 1.40).

**Table 1
ARCHITECT Anti-HCV
Tube Type Interference
Distribution of Differences**

Tube Type	Distribution of the differences		
	< 10%	≥ 10% to ≤ 20%	> 20%
Glass Serum Separator	85.0% (34/40)	15.0% (6/40)	-
Plastic Serum	95.0% (38/40)	5.0% (2/40)	-
Plastic Serum Separator	90.0%	7.5%	2.5%

	(36/40)	(3/40)	(1/40)
Plastic Lithium Heparin Plasma Separator	72.5% (29/40)	22.5% (9/40)	5.0% (2/40)
Plastic Sodium Heparin	75.0% (30/40)	22.5% (9/40)	2.5% (1/40)
Plastic Dipotassium EDTA	72.5% (29/40)	20.0% (8/40)	7.5% (3/40)

The data support the use of the following blood collection tube types in the ARCHITECT Anti-HCV assay:

Glass tubes

- Serum
- Serum separator

Plastic tubes

- Serum
- Serum separator
- Dipotassium EDTA
- Lithium heparin plasma separator
- Sodium heparin

Interferences – Bilirubin, Hemoglobin, Total Protein, and Triglycerides

A study was conducted to evaluate the susceptibility of the ARCHITECT Anti-HCV assay to potentially interfering substances based on guidance from the Clinical Laboratory Standards Institute (CLSI) document EP7-A.

A bilirubin test sample was prepared by supplementing high negative and low positive samples with bilirubin (conjugated and unconjugated) at > 20 mg/dL (targeted to 22 mg/dL). A hemoglobin test sample was prepared by supplementing the high negative and low positive samples with hemolysate at > 500 mg/dL (targeted to 550 mg/dL). A high protein test sample (> 12 g/dL [targeted to 13.2 g/dL]) was prepared by concentrating a nonreactive, normal protein specimen and supplementing with anti-HCV positive stock to yield two test samples with different analyte levels (0.80 and 1.20 S/CO). A triglyceride test sample was prepared by supplementing the high negative and low positive samples with Liposyn[®] III at > 3000 mg/dL (targeted to 3300 mg/dL). Control samples were prepared for each test sample at each analyte level. The control and test samples were tested.

At the concentrations listed below, bilirubin, hemoglobin, total protein, and triglycerides showed less than 10% interference in the ARCHITECT Anti-HCV assay for high negative samples targeted to 0.80 S/CO (S/CO range: 0.60 to 0.99) and low positive samples targeted to 1.20 S/CO (S/CO range: 1.00 to 1.40):

- Bilirubin (≤ 20 mg/dL)
- Hemoglobin (≤ 500 mg/dL)
- Total Protein (≤ 12 g/dL)
- Triglycerides (≤ 3000 mg/dL)

Sample Stability of Serum and Plasma

A study was conducted to evaluate the sample storage temperatures and number of freeze/thaw cycles for each blood collection tube type acceptable for use with the ARCHITECT Anti-HCV assay. Sample sets of human specimens were collected in each of the blood collection tube types and supplemented with anti-HCV positive stock (targeted at 1.1 S/CO). The samples were tested at time point 0 and after being stored at 2 to 8°C for > 7 days, at room temperature (study performed at 20 to 23°C) for > 3 days, and after being subjected to three freeze/thaw cycles. Specimens that were stored at the room temperature condition and 2 to 8°C condition were tested from the blood collection tubes, as on the clot represents worst-case condition (*i.e.* specimen contact with the red blood cells). The specimens that were subjected to the freeze/thaw conditions were tested off the clot.

The data demonstrate that human serum (including serum collected in serum separator tubes) or plasma collected in dipotassium EDTA, lithium heparin plasma separator, or sodium heparin tubes may be used with the ARCHITECT Anti-HCV assay when:

- stored at 2 to 8°C for up to 7 days
- stored at room temperature (study performed at 20 to 23°C) for up to 3 days
- subjected to up to 3 freeze/thaw cycles.

Sample On Board Stability

A study was conducted to evaluate samples when stored on the ARCHITECT *i* System (on board storage) and tested with the ARCHITECT Anti-HCV assay. High negative samples (targeted to 0.80 S/CO) and low positive samples (targeted to 1.20 S/CO) were tested using one lot of reagents, one lot of calibrator, and one

lot of controls on two instruments (one *i2000* and one *i2000_{SR}*). Time point 0 consisted of testing the two analyte levels immediately after pipetting the samples. Time point 1 consisted of testing the two analyte levels after being stored on board the instrument for longer than 3 hours.

The data support sample storage of up to 3 hours on board the ARCHITECT *i* System when tested with the ARCHITECT Anti-HCV assay.

Within-Laboratory Precision

A 20-day precision study was conducted to evaluate the precision performance of the ARCHITECT Anti-HCV assay based on guidance from the Clinical and Laboratory Standards Institute (CLSI) document EP5-A2. Testing was performed using three ARCHITECT Anti-HCV reagent lots, three calibrator lots, and one control lot on two instruments (one *i 2000* and one *i 2000_{SR}*). The ARCHITECT Anti-HCV Negative Control and Positive Control, high negative panel (targeted to 0.80 S/CO) and low positive panel (targeted to 1.20 S/CO) were assayed in replicates of two at two separate times of day for 20 testing days.

The ARCHITECT Anti-HCV assay demonstrates the following precision in Tables 2a and 2b beginning on page 8.

Table 2a
ARCHITECT Anti-HCV
Within-Laboratory Precision Study - Overall Precision
Individual Components

Instrument	Sample	n	Grand Mean S/CO	Within-run		Between-run		Between-day		Between-lot		Total ^a	
				SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV
i 2000	Positive Control	240	3.54	0.088	2.5	0.039	1.1	0.053	1.5	0.071	2.0	0.110	3.1
	High Negative	240	0.77	0.026	3.4	0.011	1.4	0.000	0.0	0.025	3.3	0.028	3.7
	Low Positive	240	1.13	0.039	3.5	0.012	1.1	0.000	0.0	0.027	2.4	0.041	3.6
	Negative Control	240	0.20	0.013	NA	0.035	NA	0.061	NA	0.021	NA	0.071	NA
i 2000 _{SR}	Positive Control	240	3.52	0.100	2.8	0.000	0.0	0.061	1.7	0.063	1.8	0.117	3.3
	High Negative	240	0.76	0.029	3.8	0.000	0.0	0.016	2.1	0.034	4.4	0.033	4.3
	Low Positive	240	1.13	0.041	3.6	0.000	0.0	0.013	1.1	0.037	3.3	0.043	3.8
	Negative Control	240	0.17	0.009	NA	0.022	NA	0.019	NA	0.021	NA	0.031	NA

^a Total variability contains within-run, between-run, and between-day variance components.

NA = not applicable

Table 2b
ARCHITECT Anti-HCV
Within-Laboratory Precision Study - Overall Precision
Cumulative Components

Instrument	Sample	n	Grand Mean S/CO	Within-Run		Within-Day		Within-Laboratory Precision	
				SD	%CV	SD	%CV	SD	%CV
i 2000	Positive Control	240	3.54	0.088	2.5	0.096	2.7	0.131	3.7
	High Negative	240	0.77	0.026	3.4	0.028	3.7	0.038	4.9
	Low Positive	240	1.13	0.039	3.5	0.041	3.6	0.049	4.3
	Negative Control	240	0.20	0.013	NA	0.037	NA	0.075	NA
i 2000 _{SR}	Positive Control	240	3.52	0.100	2.8	0.100	2.8	0.133	3.8
	High Negative	240	0.76	0.029	3.8	0.029	3.8	0.047	6.2
	Low Positive	240	1.13	0.041	3.6	0.041	3.6	0.057	5.0
	Negative Control	240	0.17	0.009	NA	0.024	NA	0.037	NA

Within-Laboratory Precision contains within-run, between-run, between-day and between-lot variance components.
 NA = not applicable

Analytical Specificity

A study was conducted to evaluate the ARCHITECT Anti-HCV assay for potential cross-reactivity for specimens from individuals with medical conditions unrelated to HCV infection. Specimens with various medical conditions were obtained and tested with the ARCHITECT Anti-HCV assay and the comparator anti-HCV assay. The final results for each of the specimens were compared between the two assays. Specimen results that were discordant between the two assays were sent to an external reference laboratory for supplemental testing.

For the medical conditions evaluated, the ARCHITECT Anti-HCV assay demonstrates no potential cross-reactivity for specimens from individuals with medical conditions unrelated to HCV. The data are summarized in Table 3 on page 13.

Table 3
Reactivity of the ARCHITECT Anti-HCV Assay in Individuals with Medical Conditions Unrelated to HCV Infection

Category	n	Comparator Anti-HCV assay								
		Nonreactive			Equivocal			Reactive ^a		
		ARCHITECT Anti-HCV			ARCHITECT Anti-HCV			ARCHITECT Anti-HCV		
	NR ^b	EQ ^b	R ^b	NR ^b	EQ ^b	R ^b	NR ^b	EQ ^b	R ^b	
Cytomegalovirus (anti-CMV positive)	10	10	0	0	0	0	0	0	0	0
Epstein-Barr Virus (anti-EBV positive)	10	10	0	0	0	0	0	0	0	0
Hepatitis A Virus (anti-HAV positive)	10	8	0	0	1 ^c	0	0	0	0	1
Hepatitis B Virus (anti-HBV positive)	10	10	0	0	0	0	0	0	0	0
Human Immunodeficiency Virus (anti-HIV-1 positive)	10	6	0	0	0	0	0	1 ^d	0	3
Anti-Nuclear Antibody (ANA)	10	10	0	0	0	0	0	0	0	0
<i>Escherichia coli</i> (<i>E.Coli</i>)	3	3	0	0	0	0	0	0	0	0
Elevated IgG	10	9	0	0	0	0	0	0	0	1
Elevated IgM	10	8	0	0	0	0	0	0	0	2
Elevated total bilirubin	10	4	0	0	0	0	0	0	0	6
Elevated total protein	8	5	0	0	0	0	0	0	0	3
Herpes Simplex Virus (HSV) IgG	5	5	0	0	0	0	0	0	0	0
Human T-cell Lymphotropic Virus (HTLV)	10	10	0	0	0	0	0	0	0	0
Human anti-mouse antibodies (HAMA) positive	10	10	0	0	0	0	0	0	0	0
Influenza vaccine recipients	10	9	0	0	0	0	0	0	0	1
Multiparous female	10	10	0	0	0	0	0	0	0	0
Non-viral liver disease	10	10	0	0	0	0	0	0	0	0
Rheumatoid factor positive	10	10	0	0	0	0	0	0	0	0
Rubella	10	10	0	0	0	0	0	0	0	0
Syphilis	10	6	0	0	0	0	0	1 ^c	0	3
Systemic Lupus Erythematosus (SLE)	4	4	0	0	0	0	0	0	0	0
Toxoplasmosis IgG positive	9	9	0	0	0	0	0	0	0	0
Varicella Zoster (VZV) positive	10	9	0	0	0	0	0	0	0	1
Yeast infection	9	9	0	0	0	0	0	0	0	0
Total	218	194	0	0	1	0	0	2	0	21

^a Each reactive anti-HCV result was verified using the comparator anti-HCV assay.

^b NR = Nonreactive, EQ = Equivocal, R = Reactive

^c The final result of the anti-HAV positive specimen was anti-HCV negative when tested using the Chiron RIBA[®] HCV 3.0 Strip Immunoblot Assay (SIA) and HCV RNA negative when tested using the Roche COBAS AMPLICOR[™] Hepatitis C Virus (HCV) Test v2.0.

^d The final result of the anti-HIV-1 positive specimen was anti-HCV indeterminate when tested using the Chiron RIBA HCV 3.0 SIA and HCV RNA negative when tested using the Roche COBAS AMPLICOR HCV Test v2.0.

		Comparator Anti-HCV assay								
		Nonreactive			Equivocal			Reactive ^a		
		ARCHITECT Anti-HCV			ARCHITECT Anti-HCV			ARCHITECT Anti-HCV		
Category	n	NR ^b	EQ ^b	R ^b	NR ^b	EQ ^b	R ^b	NR ^b	EQ ^b	R ^b

^a The final result of the syphilis specimen was anti-HCV negative when tested using the Chiron RIBA HCV 3.0 SIA and HCV RNA negative when tested using the Roche COBAS AMPLICOR HCV Test v2.0.

Seroconversion Panels

A study was conducted to evaluate the seroconversion detection of the ARCHITECT Anti-HCV assay when compared to the comparator anti-HCV assay. Nineteen anti-HCV patient seroconversion panel sets were obtained from two commercial vendors and tested using the ARCHITECT Anti-HCV assay and the comparator anti-HCV assay. For members of panels that had a reactive status in the ARCHITECT Anti-HCV assay earlier than in the comparator anti-HCV assay, supplemental testing with the Chiron RIBA HCV 3.0 SIA and the Roche COBAS AMPLICOR HCV Test v2.0 was performed on the reactive panel members.

The ARCHITECT Anti-HCV assay demonstrates acceptable seroconversion detection when compared to the comparator anti-HCV assay. The data are summarized in Table 4 on page 15.

Table 4
ARCHITECT Anti-HCV Assay
Days to Evidence of HCV Infection
Seroconversion Panels

Panel ID	Comparator Anti-HCV assay			ARCHITECT Anti-HCV assay			Chiron RIBA HCV 3.0 SIA			Roche COBAS AMPLICOR HCV Test v2.0		Difference in Days to Anti-HCV Reactive Results Comparator - ARCHITECT ^b
	NR ^a	EQ ^a	R ^a	NR ^a	EQ ^a	R ^a	-	IND ^a	+	-	+	
PHV904	7	9	14	7		9	9				9	5
PHV905	11	14	18	7		11	11	14			11	7
PHV906			0			0	--	--	--	--	--	0
PHV907	13		18	13		18	--	--	--	--	--	0
PHV908	11	13	19	5		11	11	13			11	8
PHV909	30		*** ^c	0		28		30			28	*** ^c
PHV910	4		8	4		8	--	--	--	--	--	0
PHV911	3		14	3		14	--	--	--	--	--	0
PHV912	4		7	4		7	--	--	--	--	--	0
PHV914	19		24	12		16		19			16	8
PHV916	9	16	19	9		16	16				16	3
PHV917	22		85	22		85	--	--	--	--	--	0
PHV918	16		24	16		24	--	--	--	--	--	0
PHV920	7	13	16	7		13	13				13	3
HCV 6212	0		12	0		12	--	--	--	--	--	0
HCV 6213	35		37	35		37	--	--	--	--	--	0
HCV 6214	23		25	25		30	--	--	--	--	--	-5
HCV 6216	17	23	*** ^c	17		23		23		23		*** ^c
HCV 6229	10	17	20	10		17	17				17	3

^a NR = Nonreactive, EQ = Equivocal, R = Reactive, IND = Indeterminate

^b The dates of the first reactive test results were compared in the comparator assay and ARCHITECT Anti-HCV assay. If the first reactive test result occurred on the same day, then the difference is 0; if ARCHITECT Anti-HCV assay had an earlier date, then the difference is positive; if ARCHITECT Anti-HCV assay had a later date, then the difference is negative.

^c The panel never seroconverted from a nonreactive status to a reactive status with the comparator anti-HCV assay.

-- Supplemental testing was not performed.

Genotype Detection

A study was conducted to evaluate the genotype detection of the ARCHITECT Anti-HCV assay for the most commonly recognized genotypes when compared to the comparator anti-HCV assay. Two lots of HCV genotype panels were obtained from Teragenix Corporation which consisted of the following genotypes, as determined by the vendor: 1a, 1b, 1c, 2, 2a, 2b, 2c, 3a, 3b, 4, 4a, 4c, 4d, 5, 5a, and 6a. The lots were tested with the ARCHITECT Anti-HCV assay and the comparator anti-HCV assay, and the final results were compared.

The ARCHITECT and comparator anti-HCV assay final results were in 100% agreement for the genotypes of HCV. Therefore, the ARCHITECT Anti-HCV assay demonstrates acceptable genotype detection for the most commonly recognized genotypes.

Calibration Curve Storage

A study was conducted to evaluate the acceptability of an ARCHITECT Anti-HCV calibration curve stored on the ARCHITECT *i* System for a minimum of 30 days. Testing was performed using three ARCHITECT Anti-HCV reagent lots, three calibrator lots, and one control lot on two instruments (one *i* 2000 and one *i* 2000_{SR}). Each reagent lot was matched with a different calibrator lot. Three calibrations were performed on each instrument for each reagent lot and the calibration curve generated was stored on each instrument for the duration of the study. The ARCHITECT Anti-HCV Negative Control and Positive Control were assayed in replicates of two, at two times per day, for a total of 20 time points across a minimum of 31 days. The last time point was performed at least 31 days after calibration.

The data support the storage of an ARCHITECT Anti-HCV calibration curve on the ARCHITECT *i* System for a minimum of 30 days.

Instrument Percent Agreement

A study was conducted to confirm that the ARCHITECT Anti-HCV assay can be used on the ARCHITECT *i* 2000 and *i* 2000_{SR} systems. Surplus serum specimens were obtained from a commercial vendor and tested on both ARCHITECT instrument systems using a minimum of two lots of reagents and one lot of calibrator and controls. One replicate of each specimen was tested with the same reagent lot on both instruments.

The negative percent agreement between the two ARCHITECT instrument systems was 99.8% (919/921) with 95% confidence interval of 99.2% to 100% and the positive percent agreement between the two ARCHITECT instrument systems was 100% (329/329) with 95% confidence interval of 98.9% to 100%. The ARCHITECT Anti-HCV assay demonstrates acceptable agreement between the ARCHITECT *i* 2000 and *i* 2000_{SR}.

High Dose Hook Effect

A study was conducted to characterize the performance of the ARCHITECT Anti-HCV assay when used to test specimens containing high levels of anti-HCV that have the potential to cause a high dose hook effect. Two unique stocks of recalcified anti-HCV positive human plasma with S/CO values of > 15 after a minimum of a 1:4 dilution were each serially diluted with recalcified anti-HCV negative human plasma and tested on the ARCHITECT *i* System.

The data demonstrate that the ARCHITECT Anti-HCV assay is not susceptible to interference from specimens with high levels of anti-HCV.

Within-Assay Sample Carryover

A study was conducted to evaluate the susceptibility of within-assay sample carryover within the ARCHITECT Anti-HCV assay by comparing the results of a low anti-HCV (0.80 S/CO) sample when tested before (protected low sample) and after testing a high anti-HCV sample with target S/CO of >15 S/CO (unprotected low sample).

The difference between the protected low sample and the unprotected low sample mean S/CO values was 0.00 S/CO with 95% confidence interval of -0.02 to 0.02. This indicated that within-assay sample carryover was not detected. Therefore, the ARCHITECT Anti-HCV assay is not susceptible to within-assay sample carryover.

ARCHITECT Anti-HCV Microbial Challenge Characterization

A Microbial Challenge Characterization (MCC) evaluation was performed for the ARCHITECT Anti-HCV Reagents, Calibrator, and Controls, which consisted of an Antimicrobial Effectiveness Testing (AET) evaluation and a Microbial Interference Characterization (MIC) evaluation. The MCC evaluation integrated the results from both AET and MIC, which determined that the product is adequately protected.

Reagent, Calibrator, and Control Developmental Stability

The developmental stability is an on-going study to establish the stability (shelf-life integrity) of the ARCHITECT Anti-HCV Reagents, Calibrator, and Controls at the intended storage condition of 2 to 8°C and during on board storage (for reagents only).

In addition, the developmental stability includes the in-use and freeze/thaw conditions. The in-use condition for the reagents, calibrator, and controls simulates customer use over time. The freeze/thaw condition for the reagents, calibrator, and controls supports the transport simulation study described below.

Stability testing is performed on three lots of 100-test kit reagents, two lots of 500-test kit reagents, three lots of calibrators, and three lots of controls.

The developmental stability is scheduled to continue for a maximum of 15 months (with a minimum of 6 months). The data support 6 months of expiration dating for the ARCHITECT Anti-HCV Reagents and 7 months of expiration dating for the ARCHITECT Anti-HCV Calibrator and Controls.

Reagent Transport Stability

A study was conducted to support the stability of the ARCHITECT Anti-HCV Reagents following simulated transport stress conditions. One 100-test kit lot and one 500-test kit lot of the ARCHITECT Anti-HCV Reagents were tested after being subjected to simulated transport stress.

The data support the stability of the ARCHITECT Anti-HCV Reagents following transport at ambient temperatures.

Calibrator and Control Transport Stability

A study was conducted to support the stability of the ARCHITECT Anti-HCV Calibrator and Controls following simulated transport stress conditions. One lot each of the ARCHITECT Anti-HCV Calibrator and Controls was tested after being subjected to simulated transport stress.

The data support the stability of the ARCHITECT Anti-HCV Calibrator and Controls following transport at ambient temperatures.

X. SUMMARY OF CLINICAL STUDIES

A multi-center study was conducted to evaluate the efficacy of the ARCHITECT Anti-HCV assay for the qualitative detection of anti-HCV in human serum and plasma as measured by precision and method comparison.

System Reproducibility

The precision (reproducibility) of the ARCHITECT Anti-HCV assay was evaluated by testing three master lots each of ARCHITECT Anti-HCV Reagents, Calibrator, and Controls at each of three clinical sites for five days. Precision testing was performed on one ARCHITECT *i* 2000 System and two ARCHITECT *i* 2000_{SR} Systems across the three clinical sites.

The ARCHITECT Anti-HCV Negative Control and Positive Control, and a high negative panel member (Panel 1) (targeted to 0.80 S/CO) and low positive panel member (Panel 2) (targeted to 1.20 S/CO) were assayed in replicates of four at two separate times

per day for five days. The analysis method of data was based on guidance from CLSI documents EP5-A2 and EP15-A2. The overall precision data are summarized in Tables 5a and 5b beginning on page 18.

Table 5a
ARCHITECT Anti-HCV
System Reproducibility (5-Day Precision Study)
Individual Components

Sample	n	Grand Mean S/CO	Within-run		Between-run		Between-day		Total ^a		Between-lot		Between-site		Overall ^b	
			SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV
Positive Control	360	3.68	0.118	3.2	0.028	0.8	0.037	1.0	0.127	3.5	0.049	1.3	0.048	1.3	0.136	3.7
High Negative	360	0.77	0.045	5.9	0.016	2.0	0.000	0.0	0.048	6.2	0.055	7.1	0.010	1.3	0.074	9.5
Low Positive	360	1.15	0.064	5.6	0.014	1.2	0.009	0.8	0.066	5.8	0.083	7.2	0.020	1.7	0.107	9.3
Negative Control	360	0.12	0.006	NA	0.000	NA	0.003	2.8	0.007	NA	0.054	NA	0.007	NA	0.055	NA

^a Total variability contains within-run, between-run and between-day variance components.

^b Overall variability contains within-run, between-run, between-day, between-lot, between-site and lot-site interaction variance components.

NA = not applicable

Table 5b
ARCHITECT Anti-HCV
System Reproducibility (5-Day Precision Study)
Cumulative Components

Sample	n	Grand Mean S/CO	Within-Run		Within-Day		Within-Laboratory Precision (Total)		Precision with Additional Component of Between-Site		Precision with Additional Component of Between-Lot		Precision with Additional Components of Site and Lot (Overall)	
			SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV
Positive Control	360	3.68	0.118	3.2	0.122	3.3	0.127	3.5	0.136	3.7	0.136	3.7	0.136	3.7
High Negative Panel	360	0.77	0.045	5.9	0.048	6.2	0.048	6.2	0.049	6.4	0.073	9.5	0.074	9.5
Low Positive Panel	360	1.15	0.064	5.6	0.066	5.7	0.066	5.8	0.069	6.0	0.106	9.2	0.107	9.3
Negative Control	360	0.12	0.006	NA	0.006	NA	0.007	NA	0.010	NA	0.055	NA	0.055	NA

NA = not applicable

Method Comparison

Clinical Performance

A prospective multi-center study was conducted to evaluate the ability of the ARCHITECT Anti-HCV assay to detect anti-HCV antibodies in specimens from an intended use diagnostic population.

Of the 2,027 specimens tested in the ARCHITECT Anti-HCV clinical study, 1,310 specimens were obtained from individuals at increased risk of HCV infection (increased risk population) due to lifestyle, behavior, occupation, disease state, or known exposure event; and 717 specimens were obtained from individuals with signs and symptoms of a hepatitis infection.

The 2,027 specimens were collected from specimen collection sites or were purchased from specimen vendors. The number and percent of specimens obtained from each specimen collection site/specimen vendor are listed in Table 6 below.

**Table 6
Number and Percent of Specimens by Specimen Collection Sites/Specimen Vendors
for Overall Specimen Population**

Collection Site/Vendor	Site/Location	Group (n)	Total (n) ^a	Percent (%)
Collection Site				
Galveston, TX	1	757	2027	37.35
Dallas, TX	2	126	2027	6.22
Miami, FL	3	94	2027	4.64
St. Petersburg, FL	4	81	2027	4.00
Chicago, IL	5	181	2027	8.93
Denver, CO	6	140	2027	6.91
Collection Vendor				
Vendor 1: High Point, NC	1	185	2027	9.13
Vendor 1: Colton, CA	2	118	2027	5.82
Vendor 1: Plymouth, MA	3	345	2027	17.02

A demographic summary of the overall specimen population by race/ethnic group is provided in Table 7 below.

Table 7
Demographic Summary of Overall Specimen Population by Race/Ethnic Group

Race/Ethnic Group	Group (n)	Total (n) ^a	Percent (%)
African American	631	2027	31.13
American Indian/Alaska Native	12	2027	0.59
Asian	30	2027	1.48
Caucasian	1035	2027	51.06
Hispanic	294	2027	14.50
Other	25	2027	1.23

Of the 2,027 subjects, 1,126 (55.55%) were female and 901 (44.45%) were male. The age was not reported for three subjects. Of the remaining 2,024 subjects, the mean age was 41 years (age range: 18 to 83 years).

The HCV status was determined for each specimen using the comparator anti-HCV assay and, as necessary, supplemental assays (Chiron RIBA HCV 3.0 SIA and Roche COBAS AMPLICOR HCV Test v2.0). During the clinical study, all comparator and supplemental testing was performed following manufacturers' instructions. Each specimen was also tested using the ARCHITECT Anti-HCV assay at the three clinical testing sites located in Galveston, TX; Hershey, PA; and Milwaukee, WI.

Results by Specimen Classification

Following testing using the comparator anti-HCV assay and the supplemental assays, as necessary, the 2,027 specimens were assigned an HCV status of *HCV Infected*, *HCV Not Determined*, or *HCV Not Infected* based on the HCV status algorithm provided in Table 8 below.

**Table 8
HCV Status Algorithm**

Comparator Anti-HCV Final Test Results	Supplemental Test Results		HCV Status²³
Nonreactive	--		Not infected ^a
	Chiron RIBA HCV 3.0 SIA	Roche COBAS AMPLICOR HCV Test v2.0	
Reactive	Positive	--	Infected ^b
Reactive	Indeterminate or Negative	Positive	Infected ^c
Reactive	Indeterminate or Negative	Equivocal	Not Determined ^d
Reactive	Indeterminate or Negative	Negative	Not infected ^a
Equivocal	Positive	--	Infected ^b
Equivocal	Indeterminate or Negative	Positive	Infected ^c
Equivocal	Indeterminate or Negative	Equivocal	Not Determined ^d
Equivocal	Indeterminate or Negative	Negative	Not infected ^a

^a A negative test result does not exclude the possibility of exposure to hepatitis C virus.

^b State or associated disease Not Determined.

^c Indicates active HCV infection.

^d HCV status cannot be determined.

-- = not performed

Comparison of Results

The ARCHITECT Anti-HCV assay results were compared to HCV status for the increased risk and signs and symptoms populations. The increased risk population was ranked according to the risk of HCV infection in study subjects. The risk of HCV infection was ranked based on a clinical evaluation of the likelihood of acquiring HCV through each mode of transmission. The mode of transmission was ranked higher if the likelihood of acquiring HCV was greater. Each specimen was assigned only one risk (highest ranked risk). Of the 2,027 specimens analyzed, the status of 616 specimens was *HCV Infected*. The status of 1,411 specimens was *HCV Not Infected*. No specimens had the status *HCV Not Determined*. The comparison of ARCHITECT Anti-HCV results by HCV status is presented in Table 9 on page 26.

Table 9
Comparison of ARCHITECT Anti-HCV Results to HCV Status - Overall
Increased Risk (by Risk) and Signs and Symptoms Populations

Specimen Population	HCV Status ^b												Total	
	HCV Infected						HCV Not Infected							
	Reactive		Equivocal		Nonreactive		Reactive		Equivocal		Nonreactive			
n	%	n	%	n	%	n	%	n	%	n	%	n	%	
Individuals with increased risk of HCV infection														
Recipients of clotting factor concentrate prior to 1987	1	0.05	0	0.00	0	0.00	0	0.00	0	0.00	2	0.10	3	0.15
Users of injecting drugs	97	4.79	0	0.00	0	0.00	8	0.39	0	0.00	85	4.19	190	9.37
Multiple sex partners	53	2.61	0	0.00	1	0.05	6	0.30	1	0.05	587	28.96	648	31.97
Transfusion recipient prior to July 1992 or received blood from donor later to be found HCV positive	18	0.89	0	0.00	0	0.00	2	0.10	0	0.00	22	1.09	42	2.07
Perinatal exposure; mother was infected with hepatitis C	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00	3	0.15	3	0.15
Men who have sex with men	1	0.05	0	0.00	0	0.00	2	0.10	0	0.00	11	0.54	14	0.69
Needle stick or mucosal exposure on the job	13	0.64	0	0.00	0	0.00	3	0.15	2	0.10	252	12.43	270	13.32
Other ^a : Household contact with hepatitis C infected individual and/or intranasal cocaine user	31	1.53	0	0.00	0	0.00	2	0.10	0	0.00	107	5.28	140	6.91
Individuals with signs and symptoms of hepatitis infection	400	19.73	0	0.00	1	0.05	7	0.35	0	0.00	309	15.24	717	35.37
Total	614	30.29	0	0.00	2	0.10	30	1.48	3	0.15	1378	67.98	2027	100.00

^a Not ranked based on CDC recommendations.

^b No specimens had the status *HCV Not Determined*.

Percent Agreement

The positive percent agreement and negative percent agreement between the ARCHITECT Anti-HCV assay result and HCV status, and their corresponding 95% confidence intervals were calculated for the overall population (increased risk and signs and symptoms) and for the increased risk population. The results are summarized in Table 10 below.

Table 10
ARCHITECT Anti-HCV Results versus HCV Status
Overall Population
(n=2027)

ARCHITECT Anti-HCV Result	HCV Status	
	HCV Infected	HCV Not Infected
Reactive	614	30
Equivocal	0	3
Nonreactive	2	1378
Total	616	1411

The positive percent agreement between the ARCHITECT Anti-HCV assay results and the *HCV Infected* status for the overall population (n=2,027) was 99.68% (614/616) with a 95% confidence interval of 98.83% to 99.96%. Among the specimens with *HCV Infected* status, there were 0.00% (0/616) equivocal results by ARCHITECT Anti-HCV assay (95% confidence interval is 0.00% to 0.60%). The negative percent agreement between the ARCHITECT Anti-HCV assay results and the *HCV Not Infected* status for the overall population (n=2,027) was 97.66% (1,378/1,411) with a 95% confidence interval of 96.73% to 98.38%. Among the specimens with *HCV Not Infected* status, there were 0.21% (3/1,411) equivocal results by ARCHITECT Anti-HCV assay (95% confidence interval is 0.04% to 0.62%).

The positive percent agreement and negative percent agreement results for the increased risk population by hepatitis risk group are presented in Table 11 on page 28.

Table 11
ARCHITECT Anti-HCV Results versus HCV Status
Percent Agreement for Increased Risk Population

Hepatitis C Ranked Risk Group	Positive Percent Agreement % (x/n)^a	95% Confidence Interval	Negative Percent Agreement % (x/n)^b	95% Confidence Interval
Recipients of clotting factor concentrate prior to 1987	100.00 (1/1)	2.50 - 100.00	100.00 (2/2)	15.81 - 100.00
Users of injecting drugs	100.00 (97/97)	96.27 - 100.00	91.40 (85/93)	83.75 - 96.21
Multiple sex partners	98.15 (53/54)	90.11 - 99.95	98.82 (587/594)	97.59 - 99.52
Transfusion recipient prior to July 1992 or received blood from donor later to be found HCV positive	100.00 (18/18)	81.47 - 100.00	91.67 (22/24)	73.00 - 98.97
Perinatal exposure; mother was infected with hepatitis C	NA (0/0)	NA	100.00 (3/3)	29.24 - 100.00
Men who have sex with men	100.00 (1/1)	2.50 - 100.00	84.62 (11/13)	54.55 - 98.08
Needle stick or mucosal exposure on the job	100.00 (13/13)	75.29 - 100.00	98.05 (252/257)	95.52 - 99.37
Other ^a : Household contact with hepatitis C infected individual and/or intranasal cocaine user	100.00 (31/31)	88.78 - 100.00	98.17 (107/109)	93.53 - 99.78
Total	99.53 (214/215)	97.44 - 99.99	97.63 (1069/1095)	96.54 - 98.44

^a Not ranked based on CDC recommendations.

^b x = the number of reactive (or nonreactive) ARCHITECT Anti-HCV results that were generated with the HCV status as determined by comparator or supplemental testing;
n = the total number of *HCV Infected* status (or *HCV Not Infected* status) results as determined by comparator or supplemental testing.

Expected Results (Increased Risk Population)

Of the 2,027 specimens analyzed in the ARCHITECT Anti-HCV clinical investigation, a total of 1,310 (64.63%) specimens were from the individuals at increased risk of HCV infection. All subjects were at risk of HCV infection due to lifestyle, behavior, occupation, or known exposure event but were asymptomatic and reported no current signs or symptoms of hepatitis.

The 1,310 increased risk specimens were collected from specimen collection sites or were purchased from specimen vendors. The number and percent of specimens obtained from each collection site/vendor are listed in Table 12 below.

**Table 12
Number and Percent of Specimens by Specimen Collection Sites/Specimen Vendors
for Increased Risk Population**

Collection Site/Vendor	Site/Location	Group (n)	Total (n)	Percent (%)
Collection Site				
Galveston, TX	1	707	1310	53.97
Dallas, TX	2	64	1310	4.89
Miami, FL	3	56	1310	4.27
St. Petersburg, FL	4	56	1310	4.27
Chicago, IL	5	19	1310	1.45
Denver, CO	6	44	1310	3.36
Collection Vendor				
High Point, NC	1	185	1310	14.12
Colton, CA	2	76	1310	5.80
Plymouth, MA	3	103	1310	7.86

A demographic summary of the increased risk population by race/ethnic group is provided in Table 13 on page 30.

Table 13
Demographic Summary of Increased Risk Population by Race/Ethnic Group

Race/Ethnic Group	Group (n)	Total (n)	Percent (%)
African American	522	1310	39.85
American Indian/Alaska Native	9	1310	0.69
Asian	10	1310	0.76
Caucasian	589	1310	44.96
Hispanic	165	1310	12.60
Other	15	1310	1.15

Of the 1,310 increased risk subjects, 864 (65.95%) were female and 446 (34.05%) were male. The age was not reported for three subjects. Of the remaining 1,307 subjects, the mean age was 40 years (age range: 18 to 73 years).

The ARCHITECT Anti-HCV assay was reactive in 237 (18.09%) of the individuals in the increased risk population. The number and percent of ARCHITECT Anti-HCV reactive results obtained at each collection location are presented in Table 14 below. Testing of the specimens was performed at the three clinical testing sites located in Galveston, TX; Hershey, PA; and Milwaukee, WI.

Table 14
ARCHITECT Anti-HCV Percent Reactive Results by Collection Location for Increased Risk Population

Collection Site/Vendor	Site/Location	Reactive (n)	Total (n)	Percent Reactive (%)
Collection Site				
Galveston, TX	1	132	707	18.67
Dallas, TX	2	15	64	23.44
Miami, FL	3	10	56	17.86
St. Petersburg, FL	4	10	56	17.86
Chicago, IL	5	14	19	73.68
Denver, CO	6	13	44	29.55
Collection Vendor				
High Point, NC	1	10	185	5.41
Colton, CA	2	1	76	1.32
Plymouth, MA	3	32	103	31.07
Total		237	1310	18.09

The distribution of ARCHITECT Anti-HCV reactive, equivocal and nonreactive results by age range and gender is presented in Table 15 below.

Table 15
ARCHITECT Anti-HCV Results by Age Range and Gender
for Individuals at Increased Risk of HCV Infection

Age Group (Years)	Gender	ARCHITECT Anti-HCV Result			Total
		Reactive n (%)	Equivocal n (%)	Nonreactive n (%)	
0 to 17	Female	0 (0.00)	0 (0.00)	0 (0.00)	0
	Male	0 (0.00)	0 (0.00)	0 (0.00)	0
18 to 29	Female	12 (5.58%)	1 (0.47%)	202 (93.95%)	215
	Male	8 (8.99%)	0 (0.00%)	81 (91.01%)	89
30 to 39	Female	15 (7.21)	1 (0.48)	192 (92.31)	208
	Male	18 (18.56)	1 (1.03)	78 (80.41)	97
40 to 49	Female	48 (18.25)	0 (0.00)	215 (81.75)	263
	Male	55 (37.16)	0 (0.00)	93 (62.84)	148
50 to 59	Female	26 (18.98)	0 (0.00)	111 (81.02)	137
	Male	47 (51.09)	0 (0.00)	45 (48.91)	92
60 to 69	Female	1 (3.03)	0 (0.00)	32 (96.97)	33
	Male	4 (25.00)	0 (0.00)	12 (75.00)	16
70 to 79	Female	1 (16.67)	0 (0.00)	5 (83.33)	6
	Male	1 (33.33)	0 (0.00)	2 (66.67)	3
Total		236 (18.06)	3 (0.23)	1068 (81.71)	1307^a

^a Age was not reported for three subjects.

XI. CONCLUSIONS DRAWN FROM THE STUDIES

The data from the nonclinical studies demonstrated acceptable precision, analytical specificity, seroconversion panel detection, and genotype detection of the ARCHITECT Anti-HCV assay when used according to the instructions for use as stated in the labeling, the warnings and precautions, and the Specimen Collection and Preparation for Analysis and Limitations sections of the labeling.

The clinical studies in this application indicate that the ARCHITECT Anti-HCV assay is safe and effective when used according to the directions for use in the labeling.

RISK BENEFIT ANALYSIS

As a diagnostic test, the ARCHITECT Anti-HCV assay involves removal of blood from an individual for testing purposes. This test presents no more of a safety hazard to an individual than is presented to an individual who is having their blood drawn for any other diagnostic evaluation. The benefits to HCV-infected individuals tested by the assay outweigh any potential adverse event or risk to the patient or user due to assay malfunction or operator error.

The potential risks encountered with this *in vitro* diagnostic test are not unusual in the clinical laboratory setting. Appropriate warnings for these risks are contained in the labeling and package inserts for the device. Standard good laboratory practices are considered sufficient to mitigate the risks to the end user.

SAFETY

Based on the results of the preclinical and clinical laboratory studies, the ARCHITECT Anti-HCV assay, when used according to the provided directions and in conjunction with other serological and clinical information, should be safe and effective and pose minimal risk to the patient due to false test results.

EFFECTIVENESS

The effectiveness of the ARCHITECT Anti-HCV assay has been demonstrated for use in determining if antibodies to Hepatitis C virus are present in an individual's serum or plasma. A reasonable determination of effectiveness of the ARCHITECT Anti-HCV assay for aiding in the status of HCV infection in suspected individuals has been demonstrated.

XII. PANEL RECOMMENDATIONS

In accordance with the provisions of section 515(c)(2) of the act as amended by the Safe Medical Devices Act of 1990, this PMA was not referred to the Microbiology Advisory Panel, an FDA advisory committee, for review and recommendation because the information in the PMA substantially duplicates information previously reviewed by this panel.

XIII. CDRH DECISION

FDA issued an approval order on June 7, 2006.

The applicant's manufacturing facility was inspected on 5/8/06 (N. Chicago), 5/16/06 (Abbott Park), and 5/19/06 (Puerto Rico) and found to be in compliance with the Quality Systems Regulation (21 CFR 820).

XIV. APPROVAL SPECIFICATIONS

Directions for use: See the labeling.

Hazards to Health from Use of the Device: See Indications, Contraindications, Warnings, Precautions and Adverse Events in the labeling.

Postapproval Requirements and Restrictions: See approval order.