ABBOTT PRISM® HCV
Summary of Basis for Approval

Product Trade Name(s)	ABBOTT PRISM® HCV
Proper Name(s)	Hepatitis C Virus Encoded Antigens (Recombinant c100-3, HCr43, NS5)
Applicant	Abbott Laboratories Dept. 49C, Bldg. AP6C 100 Abbott Park Road Abbott Park, IL 60064
Submission Tracking Number(s)	BL 103762 (Prior Ref. No. PLA # 97-1220 and ELA # 97-1297)
Report Date	July 2007

I. Intended Use

The ABBOTT PRISM HCV assay is an *in vitro* chemiluminescent immunoassay (ChLIA) for the qualitative detection of antibodies to hepatitis C virus (anti-HCV) in human serum and plasma specimens. The ABBOTT PRISM HCV (ChLIA) is intended to screen individual human donors, including volunteer donors of whole blood and blood components, and other living donors for the presence of anti-HCV. It is also intended for use in testing blood and plasma specimens to screen organ donors when specimens are obtained while the donor's heart is still beating, and in testing blood specimens to screen cadaveric (non-heart-beating) donors. It is not intended for use on cord blood specimens.

II. Brief Description of Test

A. Description of the Test

The ABBOTT PRISM HCV assay utilizes microparticles coated with HCV recombinant antigens as the solid phase, to bind HCV antibodies present in human serum or plasma. A complex consisting of anti-biotin (mouse monoclonal):acridinium conjugate/biotinylated $F(ab')_2$ fragment (goat) anti-human IgG is then incubated with the microparticles.

A chemiluminescent signal is generated by addition of an alkaline hydrogen peroxide solution. The amount of light emitted is proportional to the amount of anti-HCV in the sample.

B. Reagents

1. The ABBOTT PRISM HCV Assay Kit (No. 6D18-68) contains the following components:

   a. 1 Bottle (325 mL) Hepatitis C Virus Encoded Antigens (Recombinant c100-3, HCr43, NS5) Coated Microparticles in phosphate buffered saline. Minimum concentration: 0.2% solids. Preservative: 0.1% sodium azide. (Symbol: ●)

   b. 1 Bottle (332 mL) Anti-biotin (Mouse Monoclonal):Acridinium Conjugate/Biotinylated $F(ab')_2$ Fragment (Goat) Anti-Human IgG (Gamma) in phosphate buffer, bovine serum albumin, and Triton®* X-100. Minimum concentration: 0.041 µg/mL. Preservative: 0.1% sodium azide. (Symbol:▲)

   *Triton is a registered trademark of Union Carbide Co., Inc.

   c. 3 Bottles (10.4 mL each) Negative Calibrator (Human). Recalcified plasma nonreactive for HBsAg, HIV-1 Ag or HIV-1 NAT, anti-HCV and anti-HIV-1/HIV-2. Preservative: 0.1% sodium azide. (Symbol: **NC**)

   d. 3 Bottles (10.4 mL each) Positive Calibrator (Human). Recalcified, inactivated plasma reactive for anti-HCV, nonreactive for HBsAg, HIV-1 Ag or HIV-1 NAT, and anti-HIV-1/HIV-2. Minimum S/CO: 1.25. Preservative: 0.1% sodium azide. (Symbol: **PC**)

   e. 1 Bottle (328 mL) Specimen Diluent. Borate buffered saline with Tween®** 20, bovine serum albumin, calf serum, and Triton® X-100. Preservative: 0.1% sodium azide. (Symbol: **X**)

   **Tween is a registered trademark of ICI Americas.

C. Other Reagents Required

1. The ABBOTT PRISM HCV Wash Kit (No. 6D18-58) contains the following components:

   a. 1 Bottle (3360 mL) Transfer Wash. Borate buffered saline with Tween® 20. Preservative: 0.1% sodium azide. (Symbol: ~)

b. 1 Bottle (1734 mL) Conjugate Wash. MES {2-(N-morpholino) ethanesulfonic acid} buffered saline. Preservative: 0.1% ProClin®*** 300. (Symbol:★)

***ProClin is a registered trademark of Rohm & Haas.

2. The ABBOTT PRISM Activator Concentrate (No. 1A75-02) contains the following component:

a. 4 Bottles (900 mL each) Activator Concentrate. 0.4% hydrogen peroxide/0.06% diethylenetriaminepentaacetic acid.

3. The ABBOTT PRISM Activator Diluent (No. 1A75-01) contains the following component:

a. 4 Bottles (900 mL each) Activator Diluent. 0.3 *N* sodium hydroxide.

4. The ABBOTT PRISM Run Control Kit (No. 3E60-10) contains the following components:

a. 2 Bottles (10 mL each) Positive Control (Human). Purified anti-HBc IgG (Concentration: 0.9 - 2.6 PEI* Units/mL) and recalcified, inactivated plasma reactive for HBsAg (Concentration: 0.10 - 0.40 ng/mL), anti-HCV, anti-HIV-1 and anti-HTLV-I. Plasma is also tested for HIV-1 by either HIV-1 Ag and is nonreactive, or by HIV-1 NAT, and may be reactive. Positive Control may be cross-reactive with antibody to HTLV-II. Preservative: 0.1% sodium azide. (Symbol: **POS**)

b. 1 Bottle (10 mL) Supplemental Positive Control (Human). Recalcified, inactivated plasma reactive for anti-HIV-2 and anti-HTLV-II, nonreactive for HBsAg, anti-HCV and HIV-1 Ag or HIV-1 NAT. Supplemental Positive Control may be cross-reactive with antibody to HTLV-I. Preservative: 0.1% sodium azide. (Symbol: **SUP**)

c. 2 Bottles (10 mL each) Negative Control (Human). Recalcified plasma nonreactive for HBsAg, HIV-1 Ag or HIV-1 NAT, anti-HCV, anti-HIV-1/HIV-2, anti-HBc, anti-HBs and anti-HTLV-I/HTLV-II. Preservative: 0.1% sodium azide. (Symbol: **NEG**)

* Concentration standardized against the reference standard of the Paul Ehrlich Institute (PEI), Langen, Germany.

5. The ABBOTT PRISM Positive Run Control Kit (No. 3E60-11) contains the following component:

   a. 6 Bottles (10 mL each) Positive Control (Human). Purified anti-HBc IgG (Concentration: 0.9 - 2.6 PEI* Units/mL) and recalcified, inactivated plasma reactive for HBsAg (Concentration: 0.10 - 0.40 ng/mL), anti-HCV, anti-HIV-1 and anti-HTLV-I. Plasma is also tested for HIV-1 by either

   HIV-1 Ag and is nonreactive, or by HIV-1 NAT, and may be reactive. Positive Control may be cross-reactive with antibody to HTLV-II. Preservative: 0.1% sodium azide. (Symbol: **POS**).

   * Concentration standardized against the reference standard of the Paul Ehrlich Institute (PEI), Langen, Germany.

III. Manufacturing and Controls

A. Manufacturing and Controls

The ABBOTT PRISM HCV assay is manufactured by Abbott Laboratories and prepared under U.S. License Number 43.

Three recombinant antigens (HCV HCr43, c100-3 and NS5) that encompass four putative coding regions of HCV are used in the ABBOTT PRISM HCV assay. The HCr43 protein, expressed in *Escherichia coli* (*E. coli*), is composed of two non-contiguous coding regions of the HCV polyprotein sequence. The first of the two regions represents amino acids 1192 to 1457 of the HCV nonstructural region 3 (NS3) protein sequence. This is followed by a second region corresponding to amino acids 1 to 150 of the HCV core protein sequence. The c100-3 protein, expressed in *Saccharomyces cerevisiae* (*S. cerevisiae*) as a fusion protein with superoxide dimutase (SOD), includes amino acids 1569 to 1931 representing a portion of the NS3 and NS4 regions of the HCV polyprotein sequence. The NS5 protein, expressed in *S. cerevisiae* as a fusion protein with superoxide dimutase (SOD), includes amino acids 2054 to 2995 of the HCV polyprotein sequence. HCV antigens HCr43, c100-3, and NS5 are prepared under U.S. license, by Chiron Corporation, under a shared manufacturing agreement.

The human plasma, which is reactive for anti-HCV and used in the manufacture of the ABBOTT PRISM HCV Positive Calibrator,-----.

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Raw materials intended for use in the product are subjected to quality control evaluations before they are accepted for use in manufacturing. All components have established acceptance criteria and performance specifications. Final components are subjected to performance testing and assembled into kits. The final ABBOTT PRISM HCV Assay Kit is then further subjected to final performance testing.

Each lot of ABBOTT PRISM HCV assay kit is tested with in-house panels of samples with varying levels of anti-HCV reactivity, as well as the CBER HCV Reference Panel, and must meet the performance requirements of both panels.

B. Stability Studies

Components of the ABBOTT PRISM HCV Assay Kit, ABBOTT PRISM HCV Wash Kit, ABBOTT PRISM Run Control Kit, ABBOTT PRISM Positive Run Control Kit, as well as the ABBOTT PRISM Activator Concentrate and ABBOTT PRISM Activator Diluent were entered into a stability program to establish the recommended storage conditions and the expiration dating. Three different lots of each component were manufactured, tested, assembled into kits and evaluated during storage. The studies support a 12 month dating period for the components of the Assay Kit, Wash Kit, both Run Control Kits, the Activator Concentrate and the Activator Diluent. The expiration date of the kit lot is the same as that of the shortest dated kit component.

C. Methods of Validation

Production of components is monitored by in-process testing. Product potency is assured through evaluation of product appearance, sterility or bioburden testing and performance testing. Product consistency is assured through lot uniformity testing of components.

Product performance is assessed through laboratory evaluations of each test kit lot against in-house panels and the CBER HCV Reference Panel. Each lot of product and protocols summarizing pertinent product testing are submitted for evaluation and approval by FDA prior to release for distribution.

D. Labeling

The product labeling, including immediate container, package labels, and package insert (directions for use), are in compliance with 21 CFR 610 Subpart G, 21 CFR 801 Subpart A and 21 CFR 809.10. The product trade name, ABBOTT PRISM HCV, is not known to conflict with any other biologic or device trade name.

E. Establishment Inspection

A pre-licensing inspection of the areas where product is manufactured, tested, stored and shipped was most recently conducted in October 2006. Facilities and procedures for this product were found to be in substantial conformity with the Quality System Regulation.

F. Environmental Impact Analysis Report (EIAR)

Abbott Laboratories has filed a detailed EIAR. This product has no significant environmental impact.

IV. Biological Principles of the Procedure

The ABBOTT PRISM HCV assay is a two-step sandwich ChLIA. The reactions occur within the ABBOTT PRISM System in the following sequence:

- Microparticles coated with HCV recombinant antigens are incubated with Specimen Diluent and sample (either plasma, serum, calibrator, or control) in the incubation well of the reaction tray. During incubation, HCV antibodies present in the sample binds to the antigens on the Microparticles.

- After this first incubation is complete, the reaction mixture is transferred to the glass fiber matrix (matrix) of the reaction tray using the Transfer Wash. The Microparticles are captured by the matrix while the remaining mixture flows through to the absorbent blotter.

- The Anti-Biotin (Mouse Monoclonal):Acridinium Conjugate/Biotinylated $F(ab')_2$ Fragment (Goat) Anti-Human IgG is added to the Microparticles on the matrix and incubated. After this second incubation, the unbound Conjugate is washed into the blotter with the Conjugate Wash.

- The chemiluminescent signal is generated by addition of an alkaline hydrogen peroxide solution. The resultant photons are counted.

The amount of light emitted is proportional to the amount of anti-HCV in the sample. The presence or absence of anti-HCV in the sample is determined by comparing the number of photons collected from the sample to a cutoff value determined from a calibration performed in the same batch. If the number of photons collected from a test sample is less than the cutoff value, the sample is considered nonreactive for anti-HCV by the criteria of the ABBOTT PRISM HCV assay. These specimens need not be further tested. If the number of photons collected from a test sample is greater than or equal to the cutoff value, the sample is considered reactive for anti-HCV by the criteria of the ABBOTT PRISM HCV assay.

Specimens that are initially reactive must be handled according to the package insert instructions and retested in duplicate. Follow appropriate FDA recommendations and regulations for specimens found to be repeatedly reactive.

V. Performance Characteristics

A. Summary of Non-Clinical Studies

The following studies were performed: 1) specimen collection----------; 2) specimen handling ---------- specimen freeze-thaw effects; 3) effects of potentially interfering substances (including triglycerides, bilirubin, hemoglobin, protein and red blood cells); 4) assay detectability studies (including fresh serum vs. plasma specimens); 5) reagent studies (including microbial challenge of kit reagents, ABBOTT PRISM Positive Control ----------and evaluation of within-run variability and validation of batch size); and 6) cadaveric serum specimens.

1. Specimen Collection

Results of in-house studies showed that the following specimen collection containers and anticoagulants are suitable for use in the ABBOTT PRISM HCV assay: serum, serum separator tubes, EDTA, potassium oxalate, sodium citrate, ACD-A, ACD-B, CP2D, CPD, CPDA-1 or segmented tubing. ---------- methods employing heparin ---------- were shown to cause a reduction in Sample Net Counts and in Sample Net Counts/Cutoff Value (S/CO). Since the ABBOTT PRISM System pipettes samples simultaneously for all assays and due to the anticoagulant testing limitations, the package insert states: “CAUTION: Do not use specimens collected in heparin. Use of heparin as an anticoagulant may cause a reduction in Sample Net Counts and in Sample Net Counts/Cutoff Value (S/CO).”

No qualitative differences in results were observed between matched donor serum and EDTA plasma specimens.

2. Specimen Handling

The results of in-house studies showed no significant differences when using anti-HCV nonreactive or reactive specimens that have been ----------.
However, as a precautionary measure, the package insert states: "Specimens may be stored for up to 14 days at 2 - 8 °C."

---------- However, as a precautionary measure, the package insert states: "Do not use heat-inactivated specimens."

Studies were conducted to evaluate the effect of microbial contamination of specimens on assay performance in ABBOTT PRISM HCV. These studies showed that no significant assay performance differences were observed when anti-HCV nonreactive and reactive specimens were inoculated with ----------. However, as a precautionary
measure, the package insert states: "Do not use specimens with obvious microbial contamination."

Results from the freeze-thaw studies showed that ----------. However, as a precautionary measure, the package insert
states: "Some specimens that have undergone multiple freeze-thaw cycles or have been stored frozen for prolonged periods may give erroneous or inconsistent test results."

3. Potentially Interfering Substances

No qualitative performance differences were observed for the ABBOTT PRISM HCV assay in controlled studies using anti-HCV nonreactive and reactive specimens when testing the following potentially interfering substances at the specified levels: bilirubin (≤ 20 mg/dL), hemoglobin (≤ 500 mg/dL), red blood cells (≤ 0.4% v/v), triglycerides (≤ 3,000 mg/dL) or protein (≤ 12 g/dL).

4. Detectability Studies

In order to evaluate whether the ABBOTT PRISM HCV assay is susceptible to the fresh serum effects observed in some assays, freshly collected serum and EDTA plasma specimens were ----------. There were no significant differences observed between
the fresh vs. stored serum, or between fresh serum vs. plasma specimens.

5. Reagent Studies

The data for the microbial challenge of kit components indicate that the preservative used in the ABBOTT PRISM HCV assay (sodium azide) is effective in preventing microbial growth of----------.

--(environmental isolate).

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No significant within-run variability in the S/CO of the ABBOTT PRISM Positive Run Control was observed during in-house investigations. There is minimal variation in the ABBOTT PRISM Positive Run Control S/CO with time over the duration of an --------
ABBOTT PRISM batch.

6. Performance Characteristics of Cadaveric Serum Testing

a. Reproducibility

Inter-assay reproducibility of the PRISM HCV assay was assessed using 11 postmortem donor sera. These sera specimens were spiked with human plasma reactive for anti-HCV to create low-level reactive specimens. Each of the specimens was tested in triplicate on three different days on each of three reagent lots of PRISM HCV at one site for a total of 297 replicates. Fifteen replicates had insufficient sample volume and were excluded from the analysis. For intra-assay reproducibility, the %CV ranged from 3.4 to 11.3 for the low level reactive specimens.

For inter-assay reproducibility over all lots, the percent coefficient of variation (%CV) ranged from 5.5 to 13.2 for the low-level reactive specimens. The total reproducibility ranged from 9.7 to 17.0 for the low level reactive specimens. Note: Inter-assay reproducibility includes intra-assay and inter-assay variation. Total reproducibility includes intra-assay, inter-assay and inter-lot variations.

b. Specificity

Specificity was evaluated using 53 postmortem donor specimens and 55 normal donor specimens. Each of the specimens was tested once on each of three reagent lots of PRISM HCV. The mean sample to cutoff (S/CO) ratio for the 155 nonreactive postmortem replicates (53 specimens with three reagent lots; see Table I, footnote a) was 0.15, and the mean S/CO for 165 normal donor replicates (55 specimens with three reagent lots) was 0.10. Results are presented in Table I.

The PRISM HCV assay has an estimated specificity of 100.00% (155/155) (binomial confidence interval = [97.65%, 100.00%]) in postmortem serum specimens collected up to a maximum of 18.8 hours after death.

c. Sensitivity

Sensitivity was evaluated using 51 postmortem specimens and 54 normal donor specimens that were pre-screened for anti-HCV and found to be negative. The 105 specimens were spiked with human plasma reactive for anti-HCV to create low-level reactive specimens. Each of the specimens was tested once on each of three reagent lots of PRISM HCV. The mean sample to cutoff (S/CO) for the 150 postmortem replicates (51 specimens, with three reagent lots; see Table II, footnote a) was 1.67, and the mean S/CO ratio for the 156 normal donor replicates (54 specimens, with three reagent lots; see Table II footnote a) was 1.64. Results are presented in Table II.

The PRISM HCV assay has an estimated sensitivity of 97.33% (146/150) (95% binomial confidence interval = [93.31%, 99.27%]) in postmortem serum specimens collected up to 18.8 hours after death.

B. Summary of Clinical Studies

1. Assay Reproducibility

Assay reproducibility was determined by testing a three-member panel consisting of two diluted specimens reactive for anti-HCV (panel members 1 and 2) and one specimen nonreactive for anti-HCV (panel member 3). Panel members were prepared in recalcified human plasma. Each panel member was tested in replicates of four in five runs over five days with each of three reagent lots at six sites. In addition, each panel member was tested in replicates of four in five runs over five days with one of the three reagent lots at four of the six sites.

The Negative and Positive Controls were tested once at the beginning and end of each run on each subchannel. The Negative and Positive Calibrators were automatically tested in triplicate at the beginning of each run on each subchannel. The intra-assay and inter-assay standard deviation (SD) and percent coefficient of variation (%CV) were determined with a variance component analysis for a mixed model (Table III).

2. Assay Specificity

A total of 25,595 fresh serum and plasma specimens from volunteer whole blood donors and plasmapheresis donors were collected and tested at six geographically distinct blood centers (Table IV). Two sites tested a total of 8,252 serum specimens with initial and repeat reactive rates of 0.27% (22/8,252) and 0.25% (21/8,252), respectively.

Three sites tested a total of 14,262 plasma specimens with initial and repeat reactive rates of 0.20% (29/14,262) and 0.20% (28/14,262), respectively. One site tested a total of 3,081 plasmapheresis donors with initial and repeat reactive rates of 0.88% (27/3,081). Based on supplemental test results from a licensed and/or research immunoblot assay and/or research HCV RNA PCR, 47 of the 76 repeatedly reactive specimens were anti-HCV positive, 12 specimens were indeterminate, and 17 specimens were anti-HCV negative.

Specificity based on assumed zero prevalence of anti-HCV in blood and plasmapheresis donors was estimated in these studies to be 99.89% (25,519/25,548) with a 95% confidence interval (CI) of 99.84% to 99.92%. Forty-seven repeatedly reactive specimens determined to be positive by supplemental testing were excluded from these calculations.

One site evaluated 340 serum or plasma repository specimens collected from individuals with medical conditions unrelated to HCV infection or containing potentially interfering substances (Table IV). Twenty-two of the 340 specimens (6.47%) were initially reactive and 21 of the 340 specimens (6.18%) were repeatedly reactive. All 21 specimens (100.00%) were positive by a licensed immunoblot assay.

3. Assay Sensitivity

A total of 834 serum and plasma repository specimens from 400 individuals known to be positive for HCV antibodies, 20 individuals with acute HCV infection, 154 individuals with chronic HCV infection, 260 individuals at increased risk for HCV infection were tested with the ABBOTT PRISM HCV assay. A total of 834 specimens, 725 specimens (86.93%) were repeatedly reactive, and 723 specimens (99.72%) were positive by a licensed or research immunoblot assay (Table V). Overall sensitivity was estimated in these studies to be 100.00% (723/723) with a 95% CI of 99.49% to 100.00%.

The ability of the ABBOTT PRISM HCV assay to detect HCV antibodies was evaluated by testing 10 commercially available seroconversion panels collected from blood and plasmapheresis donors who seroconverted over the course of their donation history. The panels were also tested by an FDA licensed anti-HCV assay. The ABBOTT PRISM HCV assay detected anti-HCV 3 to 14 days earlier than the licensed assay in five of the 10 panels and equivalently in the other five panels.

VI. Package Insert

See the package insert (directions for use) for the ABBOTT PRISM HCV assay.

TABLE I

Specificity of Cadaveric Specimens with PRISM HCV

Population	Number of Specimens	Number of Replicates	Mean S/CO	Nonreactive	Initial Reactive
Postmortem	53	155[a]	0.15	155 (100.00%)	0 (0.00%)
Normal Donor	55	165	0.10	165 (100.00%)	0 (0.00%)

[a] No results were obtained for 1 specimen on one lot due to a reagent dispense error and 1 specimen on three lots due to drain time errors.

TABLE II

Sensitivity of Cadaveric Specimens with PRISM HCV

Population	Number of Specimens	Number of Replicates	Mean S/CO	Nonreactive	Initial Reactive
Postmortem	51	150[a]	1.67	4 (2.67%)	146 (97.33%)
Normal Donor	54	156[a]	1.64	0 (0.00%)	156 (100.00%)

[a] No results were obtained for 1 postmortem specimen and 2 normal donor specimens using 3 reagent lots due to drain time errors.

TABLE III

ABBOTT PRISM HCV Assay Reproducibility

Panel Member or Control	Number of Replicates	Mean S/CO*	Intra-assay SD	Intra-assay %CV	Inter-assay[a] SD	Inter-assay[a] %CV
1	439[b]	3.53	0.249	7.1	0.287	8.1
2	437[c]	1.54	0.120	7.8	0.140	9.1
3	440	0.12	0.011	9.2	0.013	10.8
Negative Control	440	0.17	0.017	10.3	0.019	11.4
Positive Control	440	2.34	0.186	7.9	0.195	8.3

* Cutoff Value = Mean Negative Calibrator Net Counts + (0.55 x Mean Positive Calibrator Net Counts)

Calibrator	Number of Replicates	Mean Net Counts	Intra-assay SD	Intra-assay %CV	Inter-assay[a] SD	Inter-assay[a] %CV
Negative	660	3,299	342.3	10.4	636.6	19.3
Positive	659[d]	40,025	3,839.8	9.6	3,839.8	9.6

[a] Inter-assay variability contains intra-assay variability.

[b] One replicate was invalid due to instrument detection of a dispense error.

[c] Three replicates were invalid due to instrument detection of a sample to negative calibrator error, low net counts for a sample, and high dark counts for a sample.

[d] One replicate was invalid due to instrument detection of high net counts for a sample.

TABLE IV

Reactivity of the ABBOTT PRISM HCV Assay in Whole Blood and Plasmapheresis Donors, in Specimens from Individuals with Medical Conditions Unrelated to HCV Infection and in Specimens Containing Potentially Interfering Substances

Category	Number Tested	IR (% of Total) (95% CI)	RR (% of Total) (95% CI)
Volunteer Blood Donors			
Serum	8,252	22 (0.27) (0.17 – 0.40)	21 (0.25) (0.16 – 0.39)
Plasma	14,262	29 (0.20) (0.14 – 0.29)	28 (0.20) (0.13 – 0.28)
Plasmapheresis Donors	3,081	27 (0.88) (0.58 – 1.27)	27 (0.88) (0.58 – 1.27)
Total Donors	25,595	78 (0.30) (0.24 – 0.38)	76 (0.30) (0.23 – 0.37)
Medical Conditions Unrelated to HCV Infection and Specimens Containing Potentially Interfering Substances[a]	340	22 (6.47)	21[b] (6.18)

IR = Initial Reactive; RR = Repeat Reactive; CI = Confidence Interval

[a] Specimens from individuals with medical conditions unrelated to HCV infection and specimens containing potentially interfering substances included the following categories: anti-CMV positive (12), anti-EBV positive (12), anti-HSV positive (12), anti-HAV positive (22), HBsAg positive (12), anti-HIV-1 positive (12), anti-HIV-2 positive (5), anti-HTLV-I antibody positive (12), anti-HTLV-II positive (12), rubella antibody positive (12), toxoplasma antibody positive (12), yeast infections (12), *E. coli* infections (5), syphilis serology positive (12), dengue antibody positive (7), anti-nuclear antibody positive (12), rheumatoid factor positive (12), influenza vaccine recipients (52), elevated IgG and elevated IgM (24), elevated triglycerides (12), elevated bilirubin (12), elevated hemoglobin (12), and non-viral liver diseases (33).

[b] The 21 repeatedly reactive specimens included the following categories: HBsAg positive (1), anti-HIV-1 positive (3), anti-HTLV-I positive (3), anti-HTLV-II positive (5), autoimmune hepatitis (3), yeast infections (5) and rheumatoid factor positive (1).

TABLE V

ABBOTT PRISM HCV Reactivity in Specimens from Individuals Known to be anti-HCV Positive or at Increased Risk for HCV Infection

Category	Number Tested	Number Repeatedly Reactive (% of Total)	Number Positive By Supplemental Testing (% of RR)
Preselected anti-HCV Positive	400	400[a] (100.00)	400[a] (100.00)
Acute Infection	20	20 (100.00)	20 (100.00)
Chronic Infection	154	154 (100.00)	154 (100.00)
Increased Risk for HCV Infection[b]	260	151[c] (58.08)	149[d] (98.68)
Total	834	725 (86.93)	723 (99.72)

[a] Specimens from the preselected anti-HCV positive category were only tested once.

[b] Individuals at increased risk for HCV infection included intravenous drug users (210) and hemophilia patients (50).

[c] The 151 repeatedly reactive specimens included intravenous drug users (101) and hemophilia patients (50).

[d] Of the 151 specimens, 149 were confirmed anti-HCV positive based on supplemental test results using a licensed and/or research immunoblot assay. Two of the 151 repeatedly reactive specimens were indeterminate based on the supplemental test results. All specimens in this category (260 specimens) that were repeatedly reactive by the licensed anti-HCV assay were repeatedly reactive by the PRISM assay.