1. GENERAL INFORMATION

Device Generic Name:	HIV Supplemental Assay
Device Trade Name:	VioOne™ HIV Profile™ Supplemental Assay
Device Procode:	MZF
Applicant's Name and Address:	Avioq, Inc. 104 T.W. Alexander Drive Research Triangle Park North Carolina, 27709
Establishment Registration Number:	3008376326
Date of Panel Recommendation:	Not Applicable
Premarket Approval Application (PMA) Number:	BP180279

□ I concur with the summary review.

□ I concur with the summary review and include a separate review to add further analysis.

□ I do not concur with the summary review and include a separate review.

Office's Signatory Authority:

Nicole Verdun, M.D
Director, OBRR/CBER

Date of FDA Notice of Approval:

Material Reviewed/Consulted: The PMA, amendments to the PMA, and other specific documentation used in developing the Summary of Safety and Effectiveness (SSE).

Review memos from the following reviewers were used in developing the SSE:

Discipline Reviewed	Reviewer Names
Product Design	Julia Tait Lathrop
Preclinical and Clinical Studies	Julia Tait Lathrop Krishna Ketha Swati Verma Nevien Ismail
Chemistry/Manufacturing/Controls (CMC)	Mohan Haleyur Giri Setty Sreenivas Gannavaram Julia Tait Lathrop
Instrumentation and Software	NA
Statistician	Paul Hsheih
Bioresearch Monitoring Inspection	Colonius King
DMPQ/Pre-approval Inspection	Cecily Jones
Product and Promotion Labeling (OCBQ/DCM/APBL)	Dana Jones Julia Lathrop
Scientific and Programmatic Aspects	Pradip N. Akolkar David A. Leiby

2. INDICATIONS FOR USE

The VioOne™ HIV Profile™ Supplemental Assay is an enzyme-linked immunosorbent assay (ELISA) for confirmation and differentiation of individual antibodies directed to Human Immunodeficiency Virus Type 1 (HIV-1 Group M & Group O) and Type 2 (HIV-2) in human serum or plasma. The VioOne™ HIV Profile™ Supplemental Assay is intended as an aid in the diagnosis of infection with HIV-1 and/or HIV-2. It is intended as an additional, more specific test to confirm the presence of antibodies to HIV-1 and HIV-2 for specimens repeatedly reactive in diagnostic procedures, including pediatric patients (ages 2-20).

This device is not intended for use as a first line diagnostic test or for screening donors of blood, blood products, or human cells or tissues or cellular and tissue-based products (HCT/Ps).

3. DEVICE DESCRIPTION

The VioOne™ HIV Profile™ Supplemental Assay is a confirmatory test for specimens that are reactive on initial HIV antibody tests. The assay detects and distinguishes between antibodies to HIV-1 *env*, *pol*, and *gag* gene products as well as antibodies to HIV-2. This test uses HIV-1 *env*, *pol*, and *gag* gene products as recombinant antigens and an HIV-2 specific transmembrane peptide (gp36). These antigens are individually coated onto separate wells of microwell plate Strips (solid phase) in the following order:

Row A: No Viral Antigen

Row B: Clade B HIV-1 recombinant *pol* gene product (p65) (b) (4)

Row C: Clade C HIV-1 reduced concentration recombinant *env* gene product (gp160) (b) (4)

Row D: Clade C HIV-1 recombinant *env* gene product (gp160) (b) (4)

Row E: Clade B HIV-1 recombinant *env* gene product Group M (gp41) (b) (4) and HIV-1 Group O peptide (gp41)

Row F: Clade B HIV-1 recombinant *gag* gene product (p24) (b) (4)

Row G: Not applicable (NA)

Row H: HIV-2 peptide representing the immunodominant epitope of gp36 *env* protein

Upon addition of a diluted test specimen, antibodies to HIV-1 and/or HIV-2, if present, form immune complexes through the interaction between anti-HIV-1 or anti-HIV-2 antibodies in the specimen and HIV-1/HIV-2 antigens coated on microwells. The Sample Diluent contains biotinylated HIV-1 p24 antigen. If present, HIV-1 p24 antibody captured by solid phase HIV-1 p24 antigen also binds the biotinylated HIV-1 p24 antigen. Following incubation, the specimen/Sample Diluent mix containing biotinylated HIV-1 p24 antigen is aspirated and microwells

are washed with buffer. Subsequently, Conjugate containing horseradish peroxidase (HRP)-labeled NeutrAvidin™ and HRP-labeled HIV-1 and HIV-2 antigens is added to all microwells. Peroxidase-labeled NeutrAvidin binds to any biotinylated *gag* antigen / antibody complexes while HRP-labeled HIV-1 and HIV-2 antigens bind to any HIV-1 or HIV-2 antibodies captured on the solid phase. Following an aspiration and wash to remove excess Conjugate and incubation with Tetramethylbenzidine (TMB) substrate, a blue color is produced. The enzyme reaction is stopped by the addition of a sulfuric acid solution, which changes the color to yellow. The concentration of HIV specific antibodies in specimens is proportional to color intensity.

4. KIT COMPONENTS

24 Tests	Component Description
2 stripholders	Microelisa Strips – Twelve per holder, contained in a re-sealable foil pouch with silica gel desiccant. Each strip contains 8 wells coated with no viral antigen, HIV-1 antigens, and HIV-2 antigen.
1 bottle (25 mL)	Sample Diluent – Liquid specimen diluent with biotinylated HIV-1 p24 antigen; contains animal proteins, salt, surfactants, Patent Blue V as coloring reagent, and (0.03% (w/v) bromonitrodioxane as preservative.
1 vial (1.0 mL) CONTROL –	Negative Control Serum (Human) – Contains human serum with protein stabilizers and 0.05% (w/v) bromonitrodioxane as preservative; nonreactive to HBsAg and HIV-1 antigen, antibodies to HIV, HTLV-I/II, and HCV.
1 vial (1.0 mL) CONTROL +	HIV-1/2 Positive Control Serum – Inactivated serum containing protein stabilizers. Contains 0.05% (w/v) bromonitrodioxane as preservative and Amaranth as coloring agent; reactive for antibodies to HIV-1 / HIV-2.
4 vials	Conjugate – Lyophilized, horseradish peroxidase conjugated NeutrAvidin™, HIV-1 antigens, and HIV-2 antigens with protein stabilizers and Amaranth.
1 bottle (55 mL)	Conjugate Diluent – Phosphate buffered saline containing protein stabilizers and 0.03% (w/v) bromonitrodioxane as preservative.
1 bottle (22 mL)	TMB Solution – Citric acid containing 0.03% (w/v) tetramethylbenzidine 2HCl.
1 bottle (22 mL)	Peroxide Solution – Citric acid/sodium citrate buffer containing 0.04% urea peroxide.
10 sheets	Plate sealers – Adhesive.

- Wash Buffer Concentrate is provided as an accessory to the kit (500 mL/bottle). Do not use any other Wash Buffer for this assay. Wash Buffer Concentrate is stored at room temperature.
- The Stop Solution is 2N Sulfuric Acid and is not provided by Avioq, Inc. Do not use any other Stop Solution for this assay.
- NeutrAvidin™ is a trademark of Thermo Fisher

4.1 MATERIALS PROVIDED

- VioOne™ HIV Profile™ Strips
- Sample Diluent
- Negative Control Serum (Human)
- HIV-1/2 Positive Control Serum
- Conjugate
- Conjugate Diluent
- TMB Solution
- Peroxide Solution
- Wash Buffer Concentrate (provided separately as an accessory)
- Plate sealers – Adhesive

4.2 MATERIALS REQUIRED BUT NOT PROVIDED

- Automated diluter/dispenser system (minimum 10 µL with 10% accuracy), test tubes, or equivalent
- Aspiration/wash system: The aspiration/wash system must be capable of dispensing a minimum volume of 300 µL, and capable of performing a minimum 30 second soak cycle. Aspirated waste must be contained in a closed system.
- Incubator: A dry incubator or equivalent, capable of maintaining 37±2°C.
- Microplate reader: Any microplate reader capable of transmitting light at 450 nm ± 5 nm with a linear absorbance range of 0 to 2.000.
- 2 N Sulfuric acid
- Purified Water, USP7 or NCCLS Type I7 reagent water, or equivalent
- Stripholder with uncoated wells
- Absorbent paper
- V-shaped disposable troughs or equivalent
- Disposable gloves
- Sodium hypochlorite solution (5%) or liquid bleach
- Appropriate biohazard waste containers for materials potentially contaminated with infectious agents

4.3 KIT STORAGE AND STABILITY

VioOne™ HIV Profile™ Strips

The re-sealable foil pouches should be brought to room temperature (15-30°C) before opening to prevent condensation. After the airtight foil pouch has been opened, any remaining Strips should be resealed in the foil pouch using the ziplock closure and stored at 2-8°C. The silica gel bag must not be removed.

Stability of Strips resealed in the foil pouch after opening and stored at 2–8°C is 14 days.

Store kit reagents at 2–8°C. The expiration date of the kit is recorded on the kit label. Stability of kit reagents after reconstitution or dilution is listed in "REAGENT PREPARATION." Do not store frozen.

Chemical Or Physical Indications Of Instability

The colored or colorless solutions should be clear and visually free of particulate matter. Alterations in the physical appearance of test kit material may indicate instability or deterioration. The expiration date shown on component labels indicates the date beyond which product should not be used.

5. INSTRUMENTATION AND SOFTWARE

The VioOne HIV Profile Supplemental Assay uses a standard laboratory microplate reader and readily available laboratory equipment. There is no specialized instrumentation or software associated with the test.

6. TEST PROCEDURE

6.1 SPECIMEN COLLECTION, STORAGE AND SHIPMENT

Collection:

Serum or plasma derived from citrate, sodium heparin, or EDTA (ethylenediaminetetraacetate) as anticoagulants may be used.

Storage:

Specimens should be free of microbial contamination and can be stored at 2–8°C for up to 7 days. For long-term storage, specimens should be frozen at -20°C or colder. Specimens repeatedly frozen and thawed more than 5 times or those containing particulate matter may give erroneous results.

Shipment:

Specimens to be shipped must be packaged in compliance with applicable regulations governing the transport of etiologic agents. Specimens may be shipped (b) (4), refrigerated (2–8°C), or frozen (-20°C or colder). Upon receipt, specimens should be stored at the recommended storage temperature described above.

6.2 PROCEDURAL NOTES

1. Check the Wash Buffer Concentrate for the presence of crystals or precipitate. If crystals or precipitate have formed in the solution, resolubilize by warming at 37ºC until crystals or precipitate dissolve. Wash Buffer Concentrate may appear slightly cloudy or show some phase separation after warming which is acceptable. Mix the Wash Buffer Concentrate before diluting.
2. Assay Strips, Conjugate, Negative Control, and Positive Control used in an assay must be from the same master lot number. Components and test specimens should

be at room temperature (15–30°C) before testing begins. Return the reagents to 2–8°C after use.

3. One microelisa strip containing 8 wells of HIV-1/2 Positive Control and one microelisa strip containing 8 wells of Negative Control must be included in each run.
4. Do not allow the microelisa wells to dry once the assay has begun. Fill the wells with the next required reagent immediately after washing; if not possible, fill the wells within 10 minutes. The assay should be repeated if the wells cannot be filled within 10 minutes after washing.
5. If a specimen is inadvertently not added in this assay, e.g., a well is missed, the results are invalid and the assay should be repeated, as the assay results for this specimen may be incorrectly interpreted as nonreactive for that antigen.
6. Manual plate washing should be validated before use. Use of an automated plate washer is recommended (refer to Additional materials required but not provided for automated washer requirements). Incomplete washing may adversely affect the test outcome.
7. Negative Control or HIV-1/2 Positive Control values that are not within the expected range (refer to Quality Control section) may indicate a problem with technique, product, or instrumentation.
8. Bubbles in the Strip wells may cause inaccurate microwell readings. Care should be taken to ensure that no bubbles are present.
9. Use only properly calibrated equipment.

Wash procedure

1. Incomplete washing will adversely affect the test outcome. Wash Solution must be at room temperature (15–30°C) before use.
2. Aspirate well contents into a waste bottle. Then fill the wells completely (approximately 0.3 ml) with Wash Solution, unless otherwise validated. Aspirate and fill the wells a total of four times. Allow a minimum of 30-second soak period after each addition of Wash Solution.
3. Note: Failure to incorporate these soak periods into the wash procedure may result in increased numbers of falsely reactive specimens.
4. Ensure the Strips are completely aspirated after the final aspiration. If necessary, invert stripholder and tap firmly on absorbent paper to absorb excess Wash Solution. Care should be taken not to dislodge any Strips (gentle pressure applied to the sides of the stripholder during inversion will prevent dislodging of Strips).

Preparation of Conjugate Concentrate

1. Pipet 1 mL Conjugate Diluent into one vial of Conjugate. Mix the contents thoroughly but avoid excessive foaming. Allow Conjugate Concentrate to rehydrate

a minimum of 30 minutes prior to use. Do not handle Conjugate Concentrate with gloves that have come into contact with serum or plasma.

2. The rehydrated Conjugate Concentrate cannot be stored and must be discarded after use.

Preparation of Conjugate Working Solution

3. Clean, preferably disposable/dedicated, polypropylene vessels should be used. Do not use polystyrene containers. Ensure reconstituted Conjugate Concentrate is well mixed and at room temperature before use. Transfer an appropriate amount of Conjugate Diluent to a vessel and add an appropriate amount of reconstituted Conjugate Concentrate to make a 1:12 Conjugate Working Solution. Return unused reconstituted Conjugate Concentrate to 2-8°C.
4. Once prepared, Conjugate Working Solution is stable for four hours at room temperature. Discard any unused Conjugate Working Solution after four hours.

Preparation of TMB Substrate

1. Prepare TMB Substrate in a clean, preferably disposable/dedicated, polypropylene container. Do not use polystyrene containers. Transfer a sufficient amount of Peroxide Solution to a container, add an equal amount of TMB Solution to the Peroxide Solution and mix thoroughly prior to use.
2. Each microwell plate requires at least 10 ml of TMB Substrate. More TMB Substrate may be needed depending upon the reagent dispenser used. See the instrument manufacturer's instructions for additional reagent requirements.
3. The TMB Substrate is stable for 6 hours when held at room temperature and should be colorless when used. Record the preparation and expiration times. If it is noticeably blue in color, discard and prepare more TMB Substrate as required.
4. Note: TMB Solution and TMB Substrate should be protected from exposure to light. Avoid contact with metal or metal ions as it may result in unwanted blue color formation.

6.3 TEST PROCEDURE FOR SERUM OR PLASMA SPECIMENS

1. Fit stripholder with the required number of Assay Strips. If less than twelve Strips re needed, use uncoated Strips to complete the plate when using a 96-well washer.
2. To each strip (Controls and test specimens) pipet 80 µL of Sample Diluent to each well if using the *direct manual method* shown below.
3. Pipet 20 µL of each serum or plasma test specimen, or Negative Control, or HIV-1/2 Positive Control into each of 8 wells of a designated Assay Strip and repeatedly aspirate and dispense to mix while trying to minimize the formation of bubbles. Include one Assay Strip containing 8 wells of Negative Control and one Assay Strip

containing 8 wells of HIV-1/2 Positive Control in each run. Include one Assay Strip containing 8 wells for each specimen tested.

4. NOTE: It is suggested to pipet HIV-1/2 Positive Control to column 1 of each plate and Negative Control to column 2 of each plate.
5. Caution: Use a clean tip for adding specimen or Controls to each well when using the *Direct manual method* described below. Do not pipet specimen into an empty well without Sample Diluent. Do not allow microelisa wells to dry once the assay has begun.
    a. *Direct manual method*: Pipet 80 µL of Sample Diluent to each well of a designated Assay Strip. Pipet 20 µL of specimen or Control into each well of the designated Assay Strip. Repeatedly aspirate and dispense to mix while trying to minimize the formation of bubbles.
    b. *Premixed manual method:* Pipet 200 µL specimen, Negative Control, or Positive Control into a clean test tube containing 800 µL Sample Diluent. Mix well but try to minimize bubble formation. Pipet 100 µL of the diluted specimen or Control into each well of the designated Assay Strip. Cover the Strips with an adhesive plate sealer or equivalent. Incubate Strips at 37± 2°C for 60 ± 5 minutes.
6. Wash each well four times with Wash Solution (refer to "Wash procedure") using a soak cycle of at least 30-seconds.
7. Pipet 100 µL of Conjugate Working Solution into each well.
8. Caution: Do not allow Conjugate to contaminate TMB Substrate. If the same equipment is used to add both reagents, new disposable tips must be used.
9. Cover the Strips with an adhesive plate sealer or equivalent. Incubate at 37±2°C for 30 ± 5 minutes.
10. Wash each well four times with Wash Solution (refer to "Wash procedure") using a soak cycle of at least 30 seconds.
11. Pipet 100 µL of TMB Substrate into each well. Do not mix or agitate. Do not cover the Strips.
12. Incubate at room temperature (15–30°C) for 30 ± 5 minutes.
13. Stop the reaction by adding 100 µL of 2N Sulfuric Acid to each well (maintain the same sequence and time intervals used for TMB Substrate addition). Plates should be read within 30 minutes.
14. Blank the microelisa reader on air (without stripholder and Strips) and read the absorbance of the solution in each well at 450 nm ± 5 nm.

6.4 QUALIFICATION OF CONTROLS AND CALCULATION OF RESULTS

6.4.1 Qualification of Negative Control (NC) values:

Individual NC absorbance is expected to be < 0.200. Eliminate any values ≥ 0.200 and calculate the NC mean. Absorbance of remaining individual NC values are expected to be less than or equal to 1.7 multiplied by NC mean and greater than or equal to 0.5 multiplied by NC mean (NCX). Eliminate any outliers and recalculate the mean NC (NCX). If more than two NC values total are eliminated, the run is invalid and must be repeated. If the NC mean is 0.100 absorbance or greater, the run is invalid and must be repeated.

6.4.2 Calculation of Cutoff Value (COV):

Calculate the cutoff value as follows: COV = NCX x 2.5

6.4.3 Qualification of HIV-1/2 Positive Control (PC) values:

The individual PC Signal to Cut-off ratio (S/CO) values must meet expected results shown below. If the expected results are not met, the run is invalid and must be repeated (Table 1).

Table 1. Qualification of Positive Control values

Well	Solid Phase Antigen	S/CO
A	No viral antigens	< 1.0
B	HIV-1 *pol* gene product (p65)	> 3.0
C	HIV-1 reduced *env* gene product (gp160) for assay control	< 2.5
D	HIV-1 *env* gene product (gp160)	> 4.0
E	HIV-1 *env* gene product (Group M & O gp41)	> 4.0
F	HIV-1 *gag* gene product (p24)	> 4.0
G	NA*	NA*
H	HIV-2 gp36	> 2.0

*Not Applicable except to calculate the Negative Control (NC) Mean

If the S/CO value of any PC well does not match the criteria shown in the above table the run is invalid and should be repeated.

6.4.4 Qualification of test specimens:

Any test specimens with an absorbance value greater than or equal to the cutoff value on Well A (no viral antigens), OR a reactive result in Well C and nonreactive

result in Well D, OR a reactive result in Well C greater than a reactive result in Well D is invalid and must be repeated.

7. RESULTS CALCULATION:

Calculations must be made separately for each stripholder. Representative results are presented in Table 2.

Table 2. Representative data

Well Designation	Solid Phase Antigen	NC Absorbance	PC Absorbance	PC S/CO
A	No viral antigens	0.086	0.094	0.62
B	HIV-1 *pol* gene product (p65)	0.063	1.388	9.07
C	HIV-1 reduced *env* gene product (gp160)for assay control	0.047	0.072	0.47
D	HIV-1 *env* gene product (gp160)	0.213	1.253	8.19
E	HIV-1 *env* gene product (Group M & O gp41)	0.061	0.987	6.45
F	HIV-1 *gag* gene product (p24)	0.048	1.166	7.62
G	NA	0.168	NA	NA
H	HIV-2 gp36	0.051	0.781	5.10

Acceptance Criteria: Eliminate any control absorbance values not meeting the following criteria:

Step 1: Eliminate NC values (≥ 0.200 absorbance; therefore, eliminate 0.213.
Calculate NCX (mean of NC values other than 0.213); NCX = 0.075
Calculate NC value acceptable range, which must fall between 0.5 NCX and 1.7NCX:
0.5NCX = 0.075 x 0.5 = 0.037
1.7NCX= 0.075 x 1.7 = 0.127;
The acceptable NC range is 0.037–1.127

Step 2: Eliminate NC values outside 0.037–1.127: eliminate 0.168 . The six remaining NC values are acceptable
Re-calculate NCX using remaining 6 NC values: NCX = 0.059

Step 3: 0.059 < 0.100 ; therefore, NC is acceptable

PC acceptance is defined in Qualification of PC S/CO values above.

NC mean acceptance is defined in Qualification of Negative Control (NC) values above

Calculate Cutoff Value (COV) (example):

NCX = 0.059
COV = NCX x 2.5
COV = 0.059 x 2.5 = 0.148

8. INTERPRETATION OF RESULTS

A summary of all results and their interpretation is presented in Table 3.

A. Specimen wells with absorbance values less than the cutoff value (S/CO < 1.0) are considered nonreactive for the antibody**.**

B. Specimen wells with absorbance values greater than or equal to the cutoff value (S/CO ≥ 1.0) are considered reactive for the antibody**.**

C. An HIV-1 infection is confirmed when the signal is equal to or above cutoff (S/CO ≥ 1.0) for any two or more of the wells coated with HIV-1 p65 (row B), HIV-1 gp160 (row D), HIV-1 gp41 (row E), and HIV-1 p24 (row F).

D. An HIV-2 infection is confirmed when the signal is equal to or above cutoff (S/CO ≥ 1.0) for the well coated with HIV-2 gp36 (row H).

Table 3. Results interpretation

	Test Results		Results Interpretation	
	HIV-1 Antigens	**HIV-2 Antigen**	**Interpretation**	**Symbol**
1	Nonreactive[1] for all HIV-1 Ags[2]	Nonreactive for HIV-2 Ag	HIV Negative	NEG
2	Reactive[1] for 1 HIV-1 Ag only	Nonreactive for HIV-2 Ag	HIV-1 Indeterminate	HIV-1 IND
3	Reactive for 2 or more HIV-1 Ags	Nonreactive for HIV-2 Ag	HIV-1 Positive	HIV-1 POS
4	Reactive for 1 or no HIV-1 Ag(s)	Reactive for HIV-2 Ag	HIV-2 Positive	HIV-2 POS
5	Reactive for 2 or more HIV-1 Ags	Reactive for HIV-2 Ag	a. HIV-1 Positive with Reactivity to HIV-2 Antigen (HIV-1 gp41 S/CO > HIV-2 gp36 S/CO) b. HIV-2 Positive with Reactivity to HIV-1 Antigens (HIV-1 gp41 S/CO ≤ HIV-2 gp36 S/CO)	a. HIV-1 POS*[3] b. HIV-2 POS*[3]

1. Negative: signal to cut-off ratio (S/CO) is less than 1.0; Positive: S/CO ≥ 1.0
2. Ags: antigens
3. HIV-1 POS* or HIV-2 POS* does not exclude the possibility of an HIV-1 and HIV-2 coinfection (rare)

Diagram 1 illustrates various possible reactivity patterns that can be expected from testing serum or plasma samples with the VioOne™ HIV Profile™ Supplemental assay. The highlighted wells are those with S/CO greater than or equal to 1.0.

Diagram 1. Representative results

		Strip / Sample Number											
Well #	Coated Antigen	1	2	3	4	5	6	7	8	9	10	11	12
A	No Viral Antigen			●									
B	HIV-1 p65	●	●		●	●	●	●					●
C	HIV-1 gp160 (low Ag control)	●			●		●						●
D	HIV-1 gp160	●	●	●		●	●						●
E	HIV-1 gp41 (Gp M / O)	●	●	●	●								●
F	HIV-1 p24	●	●				●		●			●	●
G	NA								●				
H	HIV-2 gp36									●	●	●	●

In this diagram, samples 3 and 4 are invalid. For sample 3, the signal for the no antigen well is greater than the cutoff. For sample 4, the signal for the well undercoated with gp160 (Well C) is above the cutoff and the well coated with normal level of gp160 (Well D) is below cutoff.

The test results for other samples are valid with the following interpretations: Sample 7 and 8 are HIV-1 indeterminate as there is only one HIV-1 antigen coated well with signal above the cutoff for each of these samples.

Samples 1, 2, 5 and 6 are confirmed for HIV-1 infection. Samples 9, 10, and 11 are confirmed for HIV-2 infection. Since all wells coated with HIV-1 or HIV-2 antigens result in signal above the cutoff, sample 12 result is interpreted according to Category 5a. or 5b. in Table 2.

9. WARNINGS AND PRECAUTIONS

1. Caution: Handle all HIV Profile™ biological materials as though capable of transmitting infectious agents. Positive control sera have been inactivated but should be handled as though they contain potentially infectious agents. Components prepared from human serum or plasma have been tested using FDA-licensed tests and found to be nonreactive for the presence of HIV antibody, HTLV-I/II antibody, Hepatitis B surface antigen (HBsAg) and HCV antibody. However, as no test method

can offer complete assurance that infectious agents are absent all materials of human origin should be handled as though they contain infectious agents.

2. Do not pipet any of the materials by mouth. Do not smoke, eat, or drink in areas where specimens or kit reagents are handled.

3. Do not perform the test in the presence of reactive vapors (e.g., from sodium hypochlorite, acids, alkalis, or aldehydes) or dust, because the enzymatic activity of the conjugate may be affected.

4. Use disposable gloves. Handle specimens and materials contacting specimens as potentially infectious biological materials in accordance with "Universal Precautions for Prevention of Transmission of Human Immunodeficiency Virus, Hepatitis B Virus, and Bloodborne Pathogens in Health-Care Setting" (CDC, MMWR, June 24, 1988). All test operators should adhere to the Occupational Safety and Health Administration (OSHA) regulations (29 CFR 1910). Consult a physician immediately in the event that contaminated materials are ingested or come in contact with open lacerations, lesions, or other breaks in the skin.

5. Immediately clean up any spillage of material potentially containing antigen or antibody with a 1:10 dilution of 5% sodium hypochlorite. Dispose of the cleaning material by an acceptable method.

6. Dispose of all specimens and materials used to perform the test according to local guidelines. For example:

    - Autoclave for 60 minutes at 121°C.
    - Incinerate disposable materials.
    - Mix liquid waste with 5% sodium hypochlorite solution so that the final concentration is approximately 0.5% sodium hypochlorite. Allow to stand at least 30 minutes before disposal.

      Note: Liquid waste containing acid must be neutralized prior to the addition of disinfectants and/or disposal.

7. Some components of this kit contain small concentrations of hazardous chemicals (TMB Solution and Peroxide Solution).

8. 2N Sulfuric Acid used as stop solution is corrosive and should be handled with care to prevent exposure to skin and eyes. If this reagent comes into contact with skin or eyes, wash thoroughly with water.

10. LIMITATIONS

1. For *in vitro* diagnostic use.
2. For prescription use only.
3. This device is not intended for use as a first line diagnostic test or for screening donors of blood, blood products, or human cells or tissues or cellular and tissue-based products (HCT/Ps).
4. Serum, or plasma derived from sodium citrate, CPD (citrate phosphate dextrose), heparin, or EDTA (ethylenediaminetetraacetate) as anticoagulants may be used with the VioOne™ HIV Profile™ Supplemental assay. Using other types of samples may not yield accurate results.
5. The VioOne™ HIV Profile™ Supplemental assay must be used in accordance with the instructions for use in the package insert to obtain accurate results.
6. The VioOne™ HIV Profile™ Supplemental assay is not intended as an initial diagnostic test or for monitoring individuals who are undergoing treatment for HIV infection.
7. All test results should be interpreted in conjunction with the individual's clinical presentation, history, and other laboratory results.
8. A VioOne™ HIV Profile™ Supplemental assay result that is INVALID should not be reported and the sample(s) should be retested.
9. A positive VioOne™ HIV Profile™ Supplemental assay result interpretation confirms the presence of specific antibodies to HIV-1 and/or HIV-2 in the sample. HIV and AIDS-related conditions are clinical syndromes caused by HIV-1 and HIV-2 and their diagnosis can only be established clinically.
10. A person who has antibodies to HIV-1 or HIV-2 is presumed to be infected with the virus, however, false positive results may be obtained if a person who has participated in an HIV vaccine study may develop antibodies to the vaccine and may or may not be infected with HIV. A comprehensive risk history and clinical judgement should be considered before concluding that an individual is not infected with HIV.
11. False negative results may be obtained under the following conditions:
    a. In individuals infected with HIV-1 and/or HIV-2 who are receiving medication for treatment for HIV infection (ART) or prevention of infection (PrEP or PEP).
    b. A negative result does not preclude the possibility of exposure to HIV or infection with HIV. An antibody response to a recent exposure may take several weeks to months to reach detectable levels. It is recommended that testing be repeated on a specimen freshly drawn after 2–4 weeks.
    c. Immunosuppressed or immunocompromised individuals infected with HIV-1 and/or HIV-2 may not produce antibodies to the virus.

d. Antibodies to a variant strain of HIV-1 and/or HIV-2 in the patient that do not react with specific antigens utilized in the assay configuration.

Results interpretation limitations:

1. HIV-2 positive samples exhibited a high degree of cross-reactivity to HIV-1 antigens in the VioOne HIV Profile Supplemental Assay (see Table 20, footnote a).
2. VioOne™ HIV Profile™ Supplemental results that meet the HIV-2 Positive criteria can show reactivity on one or more HIV-1 antigens. This profile that confirms an HIV-2 infection does not exclude the rare possibility of a co-infection.
3. VioOne™ HIV Profile™ Supplemental results that meet both the HIV-1 and HIV-2 Positive criteria are interpreted as either HIV-1 Positive with reactivity to HIV-2 antigen or HIV-2 Positive with reactivity to HIV-1 antigens. However, neither test result excludes the possibility of an HIV-1 and HIV-2 coinfection (rare).
4. An Indeterminate interpretation does not exclude the possibility of early seroconversion of the test subject or a cross-reactivity with other retroviruses. The homology between HIV-1 and HIV-2 viruses can lead to cross-reactivities between anti-HIV-1 and anti-HIV-2 antibodies. It is recommended that testing be repeated on a specimen freshly drawn after 2–4 weeks.

11. MARKETING HISTORY

The VioOne™ HIV Profile™ Supplemental Assay has not been marketed in the United States or in any foreign country.

12. CONTRAINDICATIONS

There are no known contraindications.

13. ALTERNATIVE PRACTICES AND PROCEDURES

There are other FDA-approved HIV supplemental serology tests available to confirm and differentiate antibodies to HIV-1 and HIV-2. There are FDA-approved nucleic acid tests with a supplemental claim.

14. POTENTIAL ADVERSE EFFECTS OF THE DEVICE

Potential adverse effects of the VioOne™ HIV Profile™ Supplemental Assay relate to the risk of false positive and false negative results. While performance studies indicate this risk is likely to be very low, the potential for incorrect results exists. The risk of incorrect results is minimized by following the procedures and instructions provided in the package insert. False negative results can lead to a delay in diagnosis or treatment, and to possible transmission of the infection. False positive results can lead to unnecessary treatment and adverse psychosocial consequences.

15. SUMMARY OF PRECLINICAL STUDIES

15.1 ANALYTICAL SENSITIVITY

The analytical sensitivity of the VioOne™ HIV Profile™ Supplemental Assay evaluated by testing a panel of HIV-1 and HIV-2 confirmed-positive samples with

the assay. Members of a study panel consisting of four HIV-1 and four HIV-2 samples were terminally diluted to undetectable levels of HIV1 and HIV-2 antibodies in HIV-antibody negative human serum and tested. These samples were tested with the HIV Profile™ Assay. The same samples were blinded and sent to a qualified third party laboratory for testing with an FDA approved HIV-1/2 supplemental assay (Table 4).

Table 4. Analytical sensitivity

			VioOne™ HIV Profile™ Assay					
			HIV-1 (n=24)			HIV-2 (n=29)		
			POS	IND	NEG	POS	IND	NEG
HIV-1/2 Supplemental Assay (Comparator)	HIV-1	POS	0	0	0			
		IND	2	0	0			
		NEG	11	3	8			
	HIV-2	POS				12	0	0
		IND				5	0	1
		NEG				2	0	9

Of the 24 diluted HIV-1 samples, VioOne™ HIV Profile™ Supplemental Assay detected 13 as HIV-1 positive and three as HIV-1 indeterminate compared to none detected as HIV-1 positive and only two detected as HIV-1 indeterminate by an FDA approved HIV-1/2 supplemental assay (the comparator assay). Of the 29 diluted HIV-2 samples, the HIV Profile™ Assay detected 19 as HIV-2 positive and 10 as negative including one sample detected as HIV-2 indeterminate by the comparator. The comparator assay detected 12 as HIV-2 positive, 11 as negative including 2 detected as HIV-2 positive by the HIV Profile™ Assay, and 6 as HIV-2 or HIV indeterminate.

These results indicate that the VioOne™ HIV Profile™ Supplemental assay has equivalent analytical sensitivity to an FDA-approved HIV Supplemental assay.

15.2 PRECISION/REPRODUCIBILITY

Testing was performed at three sites, one internal and two external, using three lots of kit reagents. Each sample was tested in duplicate on one plate with each of the three lots, in two runs per day for five days at each site by one technician, yielding 180 replicates per sample with one positive and one negative control per plate. The test panel consisted of five samples: one negative sample (R1) and four separate antibody positive samples specific for HIV-1 p65/p24 (R2), HIV-1 gp160 (R3), HIV-1 gp41 (R4), and HIV-2 gp36 (R5) all with antibody target levels contrived in normal human serum to be within approximately 25% of the assay cutoff (Table 5).

Table 5. Precision and reproducibility

				Within Run		Between Run		Between Days		Lot-to-Lot		Site-to-Site		Total Reproducibility	
Sample	**Ag Well**	**Mean**	**n**	**SD**	**%CV**	**SD**	**%CV**	**SD**	**%CV**	**SD**	**%CV**	**SD**	**%CV**	**SD**	**%CV**
PC	No Viral Ag	0.47	91	0.06	12.07	0.11	23.26	0.05	9.80	0*	0*	0.08	16.17	0.15	32.32
	p65	15.41	91	1.59	10.33	0*	0*	0.58	3.76	2.30	14.89	0.84	5.47	2.97	19.30
	gp160-D	1.19	91	0.12	10.06	0.06	4.69	0.11	9.36	0.07	5.95	0.07	5.70	0.20	16.69
	gp160	21.78	91	1.74	7.98	0*	0*	0.98	4.51	0.86	3.95	1.19	5.48	2.48	11.39
	gp41	16.18	91	2.20	13.60	0*	0*	0.67	4.13	1.75	10.84	0.65	4.04	2.96	18.33
	p24	14.65	91	1.80	12.31	0*	0*	0.74	5.06	2.04	13.92	1.38	9.40	3.14	21.43
	G5	8.92	91	0.89	10.01	0*	0*	0.42	4.71	0.77	8.68	0.80	8.95	1.49	16.67
NC	No Viral Ag	0.38	88	0.04	9.94	0.05	12.69	0.01	3.52	0*	0*	0.01	3.30	0.06	16.83
	p65	0.48	91	0.02	3.23	0.03	7.29	0*	0*	0.05	10.22	0.01	3.14	0.06	13.34
	gp160-D	0.33	91	0.05	14.67	0*	0*	0*	0*	0.01	4.06	0.00	1.13	0.05	15.26
	gp160	0.45	91	0.04	9.72	0*	0*	0*	0*	0.02	4.20	0.01	3.33	0.05	11.10
	gp41	0.47	91	0.04	9.43	0*	0*	0*	0*	0.01	3.08	0.00	0.84	0.05	9.95
	p24	0.37	91	0.03	6.87	0.05	12.26	0*	0*	0*	0*	0*	0*	0.05	14.06
	G5	0.37	91	0.04	11.76	0*	0*	0.02	5.52	0.01	2.38	0.01	3.49	0.05	13.66
R-1 (-)	No Viral Ag	0.37	180	0.05	12.26	0.04	10.20	0.01	3.31	0.02	4.33	0.01	3.72	0.06	17.26
	p65	0.42	180	0.06	14.85	0.04	8.70	0.03	6.22	0.02	5.44	0.02	4.17	0.08	19.54
	gp160-D	0.34	180	0.11	31.29	0.04	11.26	0.02	5.72	0*	0*	0.02	4.68	0.12	34.06
	gp160	0.41	180	0.08	18.65	0.04	8.67	0.04	9.64	0*	0*	0.03	7.71	0.10	23.99
	gp41	0.45	180	0.11	23.99	0.01	2.01	0.05	11.35	0.02	5.15	0.03	6.54	0.13	27.89
	p24	0.37	180	0.06	15.26	0.02	4.88	0.03	8.48	0*	0*	0.02	4.70	0.07	18.73
	G5	0.37	180	0.05	12.57	0.04	11.00	0.03	7.88	0*	0*	0.01	2.35	0.07	18.62
R-2 (+)	No Viral Ag	0.38	180	0.06	15.10	0.02	6.13	0.01	2.86	0*	0*	0.03	6.70	0.07	17.85
	p65	1.35	180	0.08	5.71	0.08	5.73	0.07	5.22	0.13	9.28	0.07	5.34	0.19	14.40
	gp160-D	0.37	180	0.04	10.21	0*	0*	0.02	6.16	0.02	4.63	0.01	2.15	0.05	12.97
	gp160	2.24	180	0.12	5.52	0.14	6.32	0.07	3.06	0.12	5.37	0.15	6.49	0.28	12.28
	gp41	0.90	180	0.06	6.83	0.04	5.00	0.03	3.30	0.05	5.14	0.04	4.61	0.10	11.41
	p24	1.45	180	0.10	7.00	0.07	4.90	0.08	5.63	0.14	9.62	0.05	3.19	0.21	14.41

				Within Run		Between Run		Between Days		Lot-to-Lot		Site-to-Site		Total Reproducibility	
	G5	0.36	180	0.06	15.33	0.03	7.61	0.03	7.21	0.01	2.50	0.02	5.42	0.07	19.51
R-3 (+)	No Viral Ag	0.38	180	0.05	13.51	0.04	10.78	0.01	2.72	0.01	2.53	0.02	6.42	0.07	18.81
	p65	0.98	180	0.07	6.84	0.07	6.64	0.05	5.34	0.05	5.49	0.04	4.48	0.13	13.03
	gp160-D	0.35	180	0.05	14.42	0.02	5.07	0.02	4.81	0*	0*	0*	0*	0.06	16.03
	gp160	1.43	180	0.08	5.86	0.10	6.75	0.02	1.72	0.08	5.46	0.06	4.06	0.16	11.36
	gp41	0.70	180	0.05	6.60	0.05	6.90	0.01	0.73	0.02	3.24	0.03	3.88	0.08	10.83
	p24	0.96	180	0.07	7.34	0.06	6.07	0.05	5.25	0.09	9.16	0.02	2.33	0.14	14.41
	G5	0.35	180	0.04	11.56	0.03	8.46	0.02	5.38	0.02	5.68	0.02	4.55	0.06	16.94
R-4 (+)	No Viral Ag	0.38	180	0.04	11.08	0.03	8.37	0.02	4.17	0.01	3.75	0.02	5.09	0.06	15.82
	p65	2.31	180	0.13	5.68	0.15	6.39	0.12	5.00	0.41	17.87	0.11	4.86	0.49	21.01
	gp160-D	0.38	180	0.03	9.14	0.02	5.03	0.02	4.97	0.01	3.12	0*	0*	0.05	11.97
	gp160	2.98	180	0.17	5.85	0.20	6.68	0.11	3.64	0.24	8.04	0.12	3.93	0.39	13.12
	gp41	1.50	180	0.09	5.68	0.11	7.40	0.06	4.05	0.09	5.91	0.06	4.26	0.19	12.51
	p24	0.83	180	0.06	7.27	0.05	5.90	0.04	5.14	0.10	11.75	0.04	4.28	0.14	16.45
	G5	0.36	180	0.06	15.73	0.02	4.25	0.04	11.38	0.02	5.12	0.02	6.16	0.08	21.42
R-5 (+)	No Viral Ag	0.38	180	0.04	9.41	0.04	9.59	0.03	7.28	0*	0*	0.02	4.21	0.06	15.85
	p65	0.47	180	0.04	8.80	0.03	6.79	0.03	6.77	0.04	7.84	0*	0*	0.07	15.19
	gp160-D	0.34	180	0.03	10.06	0.02	5.55	0.02	6.41	0*	0*	0.02	6.20	0.05	14.54
	gp160	0.43	180	0.05	12.18	0.00	0.92	0.02	5.34	0.01	1.88	0.03	6.22	0.06	14.83
	gp41	0.47	180	0.06	12.94	0.02	3.41	0.03	6.20	0.02	3.54	0*	0*	0.07	15.16
	p24	0.35	180	0.04	11.47	0.01	3.74	0.02	5.83	0*	0*	0.02	5.50	0.05	14.48
	G5	1.24	180	0.08	6.49	0.07	5.42	0.06	5.20	0.12	9.99	0.12	10.05	0.22	17.30

0* Results with variance values < 0 are reported as 0

All samples produced the expected qualitative classification of reactive or non-reactive for each antigen. The data presented indicate that the VioOne™ HIV Profile™ Supplemental Assay has acceptance variability under the conditions tested.

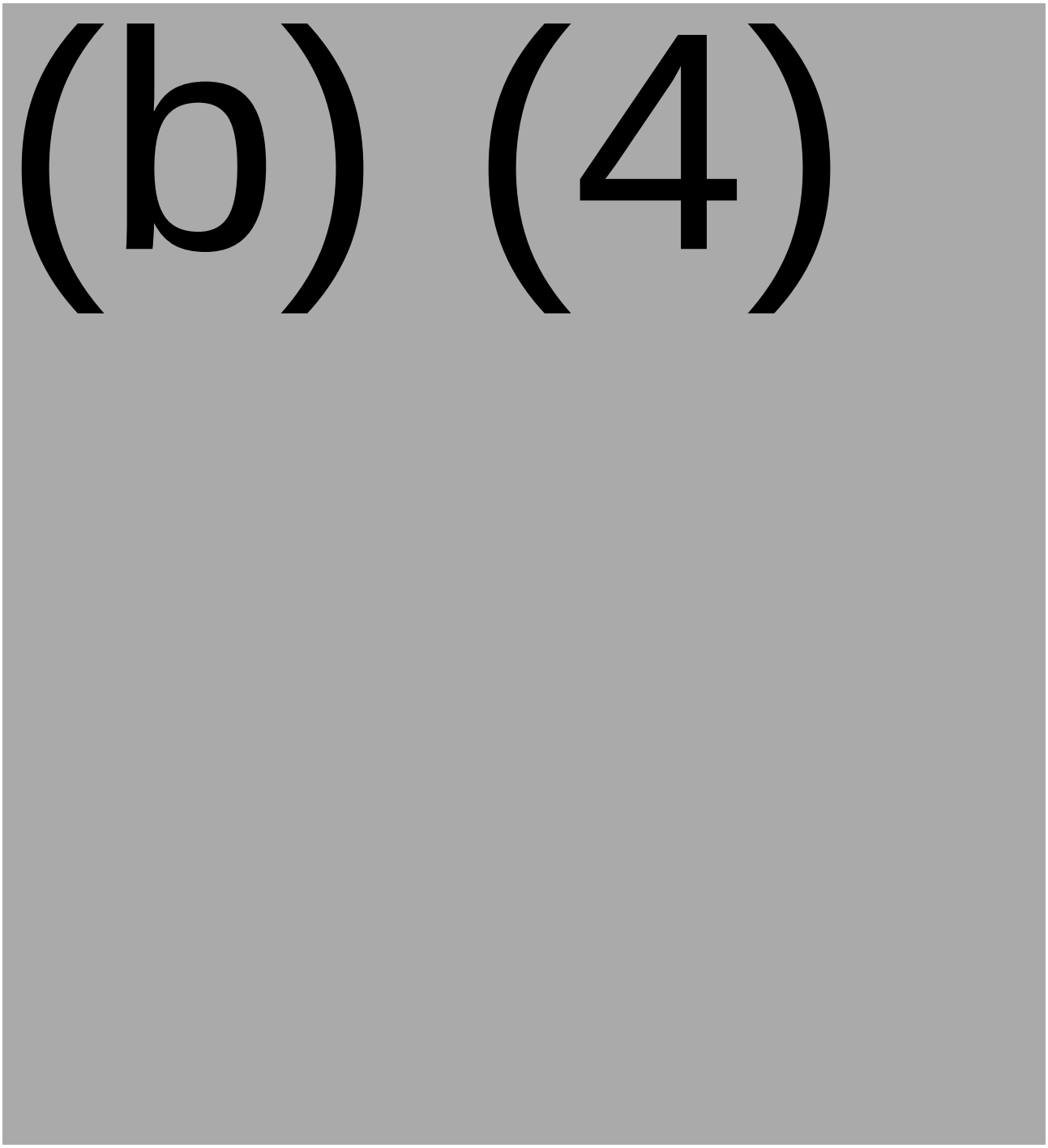
15.3 LOT-TO-LOT REPRODUCIBILITY

A separate lot-to-lot study was performed to further evaluate the reproducibility between different lots of the device. (b) (4)

The samples were tested in (b) (4) on one plate with each of three lots of Profile

kits in (b) (4) test runs during (b) (4) at Avioq by one technician, yielding (b) (4) replicates for each sample (b) (4) replicates per lot) with one positive (PC) and one negative control (NC) per plate. In one of the (b) (4) plates from one lot the NC mean exceeded an upper OD limit; per the instructions for use, this plate was considered invalid and the results from this plate were removed. The results of the remaining plates are presented in Table 6.

Table 6. Lot-to-lot reproducibility



(b) (4)

The results from this study indicate that the lot-to-lot variability of the VioOne™ HIV Profile™ Supplemental Assay is acceptable.

15.4 PERFORMANCE PANELS

Seroconversion Panels

Eighty-eight samples from twenty commercially available seroconversion panels were tested with the VioOne HIV Profile™ Supplemental Assay and an FDA supplemental assay by a qualified third party laboratory (Table 7).

Table 7. Seroconversion panels

Panel			First Confirmed Positive Bleed (Collection Day)	
Panel ID	**Number of Panel Members**	**Collection Days**	**VioOne HIV Profile Supplemental Assay**	**Supplemental test**
1	4	17, 38, 49, 51	49	49 (Ind*)
2	3	59, 62, 67	67 (Ind)	67
3	3	3,10, 49	49	49
4	3	7, 10 14	14 (Ind)	14 (Ind)
5	5	10, 14, 18, 21, 25	21	18
6	3	18, 25, 30	30	30
7	4	33, 35, 40, 42	40	40
8	3	13, 15, 20	20 (Ind)	20 (Ind)
9	3	17, 19, 24	24	24
10	4	0, 27, 30, 34	34 (Ind)	34 (Ind)
11	10	52, 57, 59, 64, 67, 71, 74, 78, 81 88,	57	52
12	10	56, 58, 65, 70, 72, 77, 79, 84, 86, 91	65	58
13	4	63, 70, 72, 77	72	77
14	3	0, 3, 8	8	8
15	3	10, 18, 21	21	18
16	4	0, 24, 26, 33	26	26

17	5	117, 119, 124, 126, 129	124	126
18	5	28, 30, 36, 45, 53	45	36
19	4	26, 28, 33, 35	33	33
20	5	2, 12, 24, 29, 31	12	24

*Ind: Indeterminate

These data indicate that the VioOne™ HIV Profile™ Supplemental Assay has equivalent sensitivity to an FDA-approved supplemental assay.

HIV-1 Incidence/Prevalence Panel

All 15 members of the SeraCare PRB601 Incidence/Prevalence Panel, consisting of seven known HIV-1 positive incidence (new infections) members and eight known HIV-1 positive prevalence (long standing infections) members, were found to be HIV-1 antibody positive and HIV-2 antibody negative with the VioOne™ HIV Profile™ Supplemental Assay (Table 8).

Table 8. Incidence (I)/prevalence (P) panel

Sample	No Viral Ag	p65	gp160-D	gp160	gp41	HIV-1 p24	HIV-2 gp36	VioOne Profile
PRB601-1 (I)	0.55	13.58	0.74	23.58	4.81	25.41	0.52	HIV-1 Pos
PRB601-2 (I)	0.49	6.97	0.74	22.77	3.69	25.19	0.45	HIV-1 Pos
PRB601-3 (P)	0.41	22.58	2.19	28.13	23.83	25.90	0.49	HIV-1 Pos
PRB601-4 (P)	0.54	27.76	2.48	28.49	24.35	22.60	0.52	HIV-1 Pos
PRB601-5 (I)	0.57	5.13	0.46	16.95	2.51	22.96	0.38	HIV-1 Pos
PRB601-6 (P)	0.60	16.35	1.52	28.18	24.40	21.43	0.56	HIV-1 Pos
PRB601-7 (I)	0.45	2.49	0.83	25.50	6.30	19.95	0.37	HIV-1 Pos
PRB601-8 (P)	0.44	26.17	5.68	28.66	27.19	9.39	0.41	HIV-1 Pos
PRB601-9 (I)	0.41	16.41	1.01	27.19	10.89	21.96	0.35	HIV-1 Pos
PRB601-10 (P)	0.53	27.68	3.28	28.72	27.08	13.24	0.39	HIV-1 Pos
PRB601-11 (P)	0.51	25.50	2.52	26.29	25.58	16.51	0.43	HIV-1 Pos
PRB601-12 (I)	0.49	23.09	0.89	24.63	12.12	18.76	0.39	HIV-1 Pos
PRB601-13 (P)	0.63	22.13	3.85	26.25	25.33	12.00	0.69	HIV-1 Pos
PRB601-14 (I)	0.65	24.25	0.56	17.20	3.13	14.27	0.60	HIV-1 Pos
PRB601-15 (P)	0.65	25.80	1.64	24.66	18.34	14.02	0.53	HIV-1 Pos

*Row G: NA

HIV-1/HIV-2 Performance Panel

All 15 members of the SeraCare HIV-1/HIV-2 Performance Panel 0800-0331, containing seven HIV-1 positive, seven HIV-2 positive, and one negative panel members were correctly identified and differentiated by the VioOne™ HIV Profile™ Supplemental Assay (Table 9).

Table 9. HIV-1/HIV-2 Performance panel

Sample	No Viral Ag	p65	gp160-D	gp160	gp41	HIV-1 p24	HIV-2 gp36	VioOne Profile
0800-0331-1	0.55	0.75	0.36	6.24	0.82	5.89	0.44	HIV-1 Pos
0800-0331-2	0.68	1.28	0.46	3.02	0.67	3.12	0.38	HIV-1 Pos
0800-0331-3	0.44	4.28	0.44	13.78	3.16	21.15	0.37	HIV-1 Pos
0800-0331-4	0.44	1.87	0.43	5.79	0.84	16.20	0.38	HIV-1 Pos
0800-0331-5	0.51	3.97	0.40	4.85	0.99	13.91	0.39	HIV-1 Pos
0800-0331-6	0.43	3.77	0.53	15.33	2.14	24.60	0.44	HIV-1 Pos
0800-0331-7	0.39	7.28	0.85	25.04	8.06	22.02	0.36	HIV-1 Pos
0800-0331-8	0.45	0.73	0.40	1.25	0.68	1.37	15.75	HIV-2 Pos*
0800-0331-9	0.71	1.03	0.56	0.79	0.52	23.17	16.84	HIV-2 Pos*
0800-0331-10	0.36	0.57	0.36	0.49	0.47	13.19	16.12	HIV-2 Pos
0800-0331-11	0.37	0.92	0.43	0.45	0.45	0.77	17.96	HIV-2 Pos
0800-0331-12	0.46	0.50	0.35	0.60	0.52	0.52	15.24	HIV-2 Pos
0800-0331-13	0.41	0.58	0.33	1.00	0.60	2.54	15.43	HIV-2 Pos
0800-0331-14	0.43	0.55	0.37	1.04	0.64	0.89	17.10	HIV-2 Pos
0800-0331-15	0.44	0.49	0.37	0.60	0.53	0.40	0.51	Neg

HIV-2 Pos = HIV-2 Positive with reactivity to HIV-1 antigens
Column G: NA

These data indicate that the VioOne™ HIV Profile™ Supplemental Assay appropriately detects HIV-1 in performance panels and incidence/prevalence panels.

HIV-1 Group M Clades Studies

Nine major HIV-1 Group M clades and 13 CRFs consisting of 96 samples from commercial sources were tested in singlicate with the VioOne™ HIV Profile™ Supplemental Assay. All 96 Group M clade samples and CRFs were tested positive for HIV-1 with the VioOne™ HIV Profile™ Supplemental Assay with 100% reactivity rate and a 95% confidence interval of 95.8% to 100%. Of the 96 samples tested, all were tested as HIV-1 positive; one of the Clade C samples was

also reactive to HIV-2 antigen because of a weak reactive result for HIV-2 gp36 (Table 10).

Table 10. HIV-1 Clade M

HIV-1 Group M Clade	N	VioOne™ HIV Profile™		
		NEG	IND	POS
A	10	0	0	10
B	10	0	0	10
C	10	0	0	10*
D	10	0	0	10
F	11	0	0	11
G	10	0	0	10
H	10	0	0	10
J	3	0	0	3
K	9	0	0	9
CRF_01_AE	4	0	0	4
CRF02_AG	2	0	0	2
CRF18_cpx	1	0	0	1
CRF11_cpx	1	0	0	1
CRF25_cpx	1	0	0	1
CRF06_cpx	2	0	0	2
CRF14_BG	2	0	0	2
TOTAL	**96**	**0**	**0**	**96**
*One of the Clade C samples tested HIV-1 positive with reactivity to HIV-2 antigen				

These data indicate that the VioOne™ HIV Profile™ Supplemental Assay acceptably detects HIV-1 from a variety of clades and circulating forms.

15.5 SAMPLES REPEATEDLY REACTIVE/CONFIRMED NEGATIVE

Ninety-four repeatedly reactive samples with a screening or diagnostic HIV assay but confirmed negative (RRN) were used for this study. There was 100% concordance with approved supplemental and rapid tests*. Of the 56 samples confirmed negative with an IFA assay, 54 were negative and two were indeterminate with the VioOne Profile assay, for an overall concordance of 97.9% (Table 11).

Table 11. Repeat reactive/confirmed negative

	Assay	N	VioOne™ HIV Profile™ Supplemental Assay		
			Negative	Indeterminate	Positive
Samples Repeatedly Reactive	HIV-1/2 Supplemental Assay NEG**	21	21	0	0

	Assay	N	VioOne™ HIV Profile™ Supplemental Assay		
			Negative	Indeterminate	Positive
with a Diagnostic or Screening HIV Test	HIV-1/HIV-2 Rapid* Test NEG	17	17	0	0
	IFA NEG	56	54	2	0
	Total	**94**	**92 (97.9%)**	**2 (2.1%)**	**0**

* Rapid test approved for differentiation of antibodies to HIV-1 and HIV-2 as part of CDC HIV testing algorithm.

**NEG: negative

These data indicate that the VioOne HIV Profile Supplemental Assay performance is acceptable for confirming previously negative results in a diagnostic screening assay.

15.6 SAMPLES REPEATEDLY REACTIVE/CONFIRMED INDETERMINATE

Ninety-nine samples repeatedly reactive with a screening or diagnostic HIV assay and indeterminate (RRI) by different FDA-approved assays were used for this study. One sample confirmed negative on the IFA was indeterminate on the VioOne HIV Profile Supplemental Assay (1%) and 98 (99%) were confirmed negative on the VioOne™ HIV Profile™ Supplemental Assay. In addition, fifteen repeatedly reactive samples that were positive by IFA but were indeterminate by Western Blot were positive on the VioOne HIV Profile™ Supplemental Assay (100%). (Table 12).

Table 12. Repeat reactive/confirmed indeterminate

	Assay	N	VioOne™ HIV Profile™ Supplemental Assay		
			Negative	Indeterminate	Positive
Samples Repeatedly Reactive with a Diagnostic or Screening HIV Test	HIV-1/2 Supplemental Assay IND*	1	1	0	0
	IFA IND	98	97	1	0
	Total	**99**	**98 (99.0%)**	**1 (1.0%)**	**0**
	IFA POS, Western Blot IND	15	0	0	**15 (100%)**

*IND: indeterminate

These data indicate that the VioOne HIV Profile Supplemental Assay performance is acceptable for resolving the status of Repeatedly Reactive/confirmed indeterminate samples in a diagnostic screening assay.

15.7 INTERFERING SUBSTANCES

Ten samples from patients with the 13 different medical conditions unrelated to HIV infection were tested unspiked and spiked with HIV-1, HIV-2, or HIV-1/HIV-2 antibodies. The samples were tested in (b) (4) using (b) (4) VioOne HIV Profile assay lot.

125 samples were negative. Five samples produced reactive or indeterminate results and were re-tested in duplicate. One Candida sample and one post-

influenza sample were non-reactive upon repeat. One Candida sample lacked sufficient volume for re-testing and remained as indeterminate. One sample from a multiparous pregnant patient demonstrated cross-reactivity and one yeast (Candida) retained an indeterminate result upon retesting (Table 13).

Table 13. Unspiked samples

Potentially Interfering Factor	N	VioOne™ HIV Profile™		
		NEG	IND	POS
Autoimmune disease	10	10	0	0
Dialysis patients	10	10	0	0
EBV infection	10	10	0	0
HBsAg infection	10	10	0	0
HCV infection	10	10	0	0
High rheumatoid factor	10	10	0	0
Multiparous (pregnant) females	10	9	0	1[a]
Post influenza vaccine	10	9	1[b]	0
Yeast (Candida) reactive	10	7	3[c]	0
Vaccinia vaccine samples	10	10	0	0
HTLV-I/II antibody positive	10	10	0	0
Multiple transfusions	10	10	0	0
Hemophilia	10	10	0	0
TOTAL	**130**	**125 (98.5%)**	**4 (3.1%)**	**1 (0.77%)**

[a]HIV-2 positive, which was negative upon repeat testing in duplicate.
[b]HIV-1 indeterminate, which was negative upon repeat testing only in singlicate due to volume limitation.
[c]Of these three HIV-1 indeterminate samples, one was indeterminate upon repeat testing in duplicate, one was negative upon repeat testing in duplicate, and one was invalid for repeat testing.

When the samples were spiked with an HIV-1 or HIV-2 positive sample or HIV-1 and HIV-2 to mimic coinfection all samples were positive for HIV-1, HIV-2, or both HIV-1 and HIV-2 (Tables 14–16). One HIV-1-spiked specimen from a subject with an autoimmune disease demonstrated borderline reactivity with the HIV-2 gp36 (G5) well (Table 14). Five HIV-2 samples produced HIV-1 positive results (Table 15). Four were confirmed to be HIV-1 positive with Western Blot and one with an FDA-approved HIV-1/2 Supplemental assay.

Table 14. Spiked with HIV-1

Potential Interfering Factor	N	VioOne™ HIV Profile™			
		NEG	IND	HIV-1 POS	HIV-2 POS
AutoImmune disease	10	0	0	10	1*
Dialysis patients	10	0	0	10	0
EBV infection	10	0	0	10	0
HBsAg infection	10	0	0	10	0
HCV infection	10	0	0	10	0
High rheumatoid factor	10	0	0	10	0
Multiparous (pregnant) females	10	0	0	10	0
Post influenza vaccine	10	0	0	10	0
Yeast (Candida) reactive	10	0	0	10	0
Vaccinia vaccine samples	10	0	0	10	0
HTLV-I/II antibody positive	10	0	0	10	0
Multiple transfusions	10	0	0	10	0
Hemophilia	10	0	0	10	0
TOTAL	**130**	**0**	**0**	**130 (100.0%)**	**1 (0.77%)**

*1 of 10 samples was HIV-1 positive and HIV-2 gp36 reactive.

Table 15. Spiked with HIV-2

Potential Interfering Factor	N	VioOne™ HIV Profile™			
		NEG	IND	HIV-1 POS	HIV-2 POS
AutoImmune disease	10	0	0	0	10
Dialysis patients	9	0	0	0	9
Dialysis patient with HIV-1 infection	1	0	0	1[a]	1
EBV infection	10	0	0	0	10
HBsAg infection	10	0	0	0	10
HCV infection	7	0	0	0	7
HCV/HIV-1 Co-infection	3	0	0	3[b]	3
High rheumatoid factor	10	0	0	0	10
Multiparous (pregnant) females	10	0	0	0	10
Post influenza vaccine	10	0	0	0	10
Yeast (Candida) infection	9	0	0	0	9
Yeast (Candida) / HIV-1 coinfection	1	0	0	1[b]	1
Vaccinia vaccine samples	10	0	0	0	10
HTLV-I/II antibody positive	10	0	0	0	10
Multiple transfusions	10	0	0	0	10
Hemophilia	10	0	0	0	10
TOTAL	**130**	**0**	**0**	**5 (3.85%)**	**130 (100%)**

[a]Confirmed positive by an HIV 1/2 Supplemental Assay
[b]Confirmed positive by a Western Blot Test

Table 16. Spiked with both HIV-1 and HIV-2

Potential Interfering Factor	N	VioOne™ HIV Profile™		
		NEG	HIV-1 POS	HIV-2 POS
AutoImmune disease	10	0	10	10
Dialysis patients	9	0	9	9
Dialysis patient with HIV-1	1	0	1	1
EBV infection	10	0	10	10
HBsAg infection	10	0	10	10
HCV infection	7	0	7	7
HCV/HIV-1 Co-infection	3	0	3	3
High rheumatoid factor	10	0	10	10
Multiparous (pregnant) females	10	0	10	10
Post influenza vaccine	10	0	10	10
Yeast (Candida) infection	9	0	9	9
Yeast (Candida) / HIV-1 coinfection	1	0	1	1
Vaccinia vaccine samples	10	0	10	10
HTLV-I/II antibody positive	10	0	10	10
Multiple transfusions	10	0	10	10
Hemophilia	10	0	10	10
TOTAL	**130**	**0**	**130 (100%)**	**130 (100%)**

A panel of 47 samples with five to seven each from patients with additional, potentially cross-reactive conditions were tested for cross-reactivity in un-spiked samples. All produced negative results, indicating that there was no cross-reactivity observed from these conditions (Table 17).

Table 17. Additional conditions

Disease State Samples	N	VioOne™ HIV Profile™		
		NEG	IND	POS
Cirrhosis	5	5	0	0
Hepatitis A	7	7	0	0
Cancer	5	5	0	0
HSV IgG	5	5	0	0
Malaria: *P. falciparum*	5	5	0	0
Rubella IgG	5	5	0	0
Syphilis	5	5	0	0
Toxoplasmosis IgG	5	5	0	0
CMV IgG	5	5	0	0
TOTAL	**47**	**47**	**0**	**0**

These data indicate that no significant interference with detection of HIV-1, HIV-2, or HIV-1 and HIV-2 coinfection was observed with any of the potentially interfering conditions.

15.8 BIOTIN INTERFERENCE

This sample group was constructed by spiking a normal human serum sample with biotin at 3600 ng/mL. This sample containing elevated biotin and the same sample without biotin was tested with the VioOne Profile Assay unspiked, spiked with HIV-1, HIV-2, or both HIV-1 and HIV-2 antibodies.

No interference from biotin was demonstrated in any of the samples at 3600 ng/mL.

15.9 ENDOGENOUS INTERFERENCE

Negative samples were spiked to various levels of bilirubin, lipid (triglycerides), hemoglobin, or HAMA (human anti-mouse antibody) and tested with the VioOne HIV Profile Assay. The test results demonstrated that these substances did not cross react with the assay. One HAMA sample containing 27.1 ng/mL HAMA antibody was initially a low reactive on the HIV-1 gp41 well but failed to repeat in duplicate; no reactivity was found in other level of HAMA antibody (Table 18).

Table 18. Endogenous interference

Panel Member Samples		N	VioOne™ HIV Profile™		
			NEG	IND	POS
Total Bilirubin	0.20 mg/dL	1	1	0	0
	2.00 mg/dL	1	1	0	0
	4.00 mg/dL	1	1	0	0
	6.70 mg/dL	1	1	0	0
	11.43 mg/dL	1	1	0	0
Lipemia - Triglycerides	150 mg/dL	1	1	0	0
	272 mg/dL	1	1	0	0
	379 mg/dL	1	1	0	0
	1013 mg/dL	1	1	0	0
	2375 mg/dL	1	1	0	0
Hemoglobin	Normal	1	1	0	0
	140 mg/dL	1	1	0	0
	275 mg/dL	1	1	0	0
	550 mg/dL	1	1	0	0
	1100 mg/dL	1	1	0	0
HAMA	Negative	1	1	0	0

Panel Member Samples		N	VioOne™ HIV Profile™		
			NEG	IND	POS
(Human anti mouse antibody)	Negative	1	1	0	0
	4.0 ng/mL	1	1	0	0
	4.7 ng/mL	1	1	0	0
	7.2 ng/mL	1	1	0	0
	9.6 ng/mL	1	1	0	0
	13.0 ng/mL	1	1	0	0
	27.1 ng/mL	1	0	1	0
	30.0 ng/mL	1	1	0	0
	38.8 ng/mL	1	1	0	0
	52.7 ng/mL	1	1	0	0
	74.0 ng/mL	1	1	0	0
TOTAL		**27**	**26 (96.30%)**	**1 (3.70%)**	**0**

Thus, the data presented indicate no endogenous interference with the assay from the interferents tested.

15.10 MATRIX COMPARISON

(b) (4) matched samples were collected from individual donors into tubes containing the following anticoagulants: (b) (4) EDTA, Sodium Citrate, and (b) (4) Heparin, (b) (4) EDTA, CPD or (b) (4) heparin. These samples were tested unspiked or spiked with three levels (low, medium and high) of HIV-1 and HIV-2 antibody (a blend of HIV-1 and HIV-2 positive samples). The serum samples were used for comparison. Testing was performed with (b) (4) or (b) (4) (other anticoagulants) of the VioOne™ HIV Profile™ Supplemental Assay. The S/CO was compared with that from serum as reference and the % difference calculated. The results of this study indicated that the claimed matrices performed with only minor differences between them.

15.11 HOOK EFFECT

This study was designed to evaluate if high titer samples would alter the interpretation of the test results, i.e., change the result from positive to negative or indeterminate.

For the hook effect study, (b) (4) panel members with high antibody titers for HIV-1 and HIV-2 within the top 20% of the titers found in the clinical study were evaluated. No hook effect was observed in this study.

15.12 STABILITY

15.12.1 Kit shelf-life stability

A panel of (b) (4) samples consisting of (b) (4) negative sample and (b) (4) positive samples along with the kit Negative Control and kit Positive Control was utilized for stability

testing at each time point. Each positive sample had S/CO (signal-to-cutoff) values close to borderline (target S/CO range (b) (4)-2.5) for at least (b) (4) antigen. Baseline testing was performed to generate acceptance criteria at the start of this protocol. (b) (4) replicates for each test sample panel member were assayed on each of the (b) (4) VioOne HIV Profile Supplemental Assays to establish the baseline. Samples were tested at each timepoint to evaluate if the performance degraded over time.

The data submitted supports a shelf-life stability claim of 13 months when stored at 2–8°C.

15.12.2 Open kit stability

Open vial and on-board stability were evaluated as part of the shelf-life stability study with the kits tested at each time point and at 14 days after opening. The data submitted support a claim for 14 days stability after opening when stored at 2–8°C.

The reconstituted reagents are single-use only. The kit provides four vials of reagents which are intended to be discarded after use.

15.12.3 Sample stability/ Freeze-thaw

Both fresh serum and CPD plasma samples were prepared and used in this study. (b) (4) replicates of serum samples and plasma samples were spiked with low levels (S/CO between (b) (4)) of HIV-1 or HIV- 2 antibodies. (b) (4) replicates were tested at Time 0 with (b) (4) of the VioOne assay to establish the baseline. Samples were stored at 2–8°C for 2, 5, 7, (b) (4) days. Samples also were subjected to 1,3,5, (b) (4) freeze/thaw (FT) cycles during storage at -20°C as well as long term storage at -20°C.

The data submitted supports a claim of up to five freeze-thaw cycles, storage for seven days at 2–8°C, and (b) (4) months at -20°C.

15.12.4 Transport stability

Kits were exposed to 37°C or -20°C for (b) (4) days to simulate extremes of temperature to which the kits may reasonably be exposed during shipping. Baseline testing was performed to establish the expected performance. After stressing, the kits were stored at 2-8°C until testing. Testing was performed six months after stressing, then monthly for (b) (4) months using a panel of (b) (4) samples with concentrations near the cutoff for each analyte.

The data submitted support a claim of stability following shipping of seven months when shipped in styrofoam containers.

16. SUMMARY OF PRIMARY CLINICAL STUDIES

16.1 CLINICAL SPECIFICITY

Clinical specificity was evaluated by testing 280 serum samples and 300 plasma samples from a low-risk population. All serum and plasma specimens were previously screened and found to be non-reactive with FDA licensed or approved HIV-1/2 assays. In addition, 20 serum samples from a pediatric population were also tested in the specificity study. Of these 20 pediatric samples, 10 were from

children aged 2–11 and 10 from children aged 12–18. Thus, a total of 600 samples were tested in the specificity study. One sample was excluded for a total of 599 samples from which performance was obtained.

These samples were tested at three external sites with at least one lot in common at all three clinical sites. The overall clinical specificity for the VioOne™ HIV Profile™ Supplemental Assay was 98.16% (95% CI: 96.74%–99.08%) (Table 19).

Table 19. Clinical specificity

Sample Type	Number	Negative	Indeterminate	Positive
Serum	279[a]	272	5[b]	2[d]
Pediatric Serum 2–11	10	10	0	0
Pediatric Serum 12–18	10	10	0	0
Plasma	300	296	3[c]	1[e]
TOTAL	**599**	**588 (98.16%)**	**8 (1.36%)**	**3 (0.50%)**

[a] One sample was repeatedly invalid and excluded from analysis.
[b] All five samples were HIV-1 indeterminate and negative upon repeat testing in duplicate.
[c] All three samples were HIV-1 indeterminate and negative on repeat testing in duplicate.
[d] Of the two samples, one was HIV-1 positive and one was HIV-2 positive and both were negative upon repeat testing in duplicate.
[e]Sample was HIV-2 positive and negative upon repeat testing in duplicate

16.2 CLINICAL SENSITIVITY

The HIV-positive samples used in this study consisted of both serum and plasma repository samples from individuals known to have been infected with HIV (n= 502). The sensitivity samples consisted of 266 HIV-1 positives, 21from HIV-1 clades, 125 HIV-2 positives, 30 samples from AIDS patients, 27 pediatric HIV positive samples, 10 HIV-1 Group O positives, 8 HIV-1/HIV-2 co-infected positives and 15 HIV-positive samples from pregnant females distributed through each trimester.

An earlier version of the device was used to conduct for testing of 744 clinical samples (400 HIV-1 Positive, 202 HIV-2 positive, 10 HIV-1/HIV-2 coinfection, 15 HIV-1 Group O, 50 AIDs, 40 HIV-1 pediatric, and 27 HIV-1 Pregnant women) at five clinical sites, four external and one internal. Following updates to the device, a bridging study demonstrated that further testing for clinical sensitivity could be performed at a single internal site. The results of the internal testing are presented below for establishing clinical sensitivity.

One sample from an HIV-1 positive patient was negative by initial and repeat testing in the VioOne™ HIV Profile™ Supplemental Assay.

The overall clinical sensitivity for the VioOne™ HIV Profile™ Supplemental Assay was 99.88% (95% CI: 98.88%–99.96%) (Table 20).

Table 20. Clinical sensitivity

Sample Type	Number	Positive	Indeterminate	Negative
HIV-1 Positive	266	265	0	1
HIV-1 Clades	21	21	0	0
HIV-2 Positive; HIV-2 with cross-reactivity to HIV-1	125	125 (63[a])	0	0
HIV-1/HIV-2 Coinfection	8	8[b]	0	0
HIV-1 Group O	10	10	0	0
AIDS	30	30	0	0
HIV-1 Positive Pediatrics	27	27	0	0
HIV-1+ Pregnant Females	15	15	0	0
TOTAL	**502**	**501 (99.8%)**	**0 (0%)**	**1 (0.2%)**

[a]Sixty-three of 125 samples were interpreted as HIV-2 positive with reactivity to HIV-1 antigens

[b]AII samples were interpreted as HIV-2 positive with reactivity to HIV-1 antigens

HIV-2/HIV-1 crossreactivity

HIV-2 positive samples exhibited a high degree of cross-reactivity to HIV-1 antigens in the VioOne HIV Profile Supplemental Assay. Sixty-three of 125 HIV-2 samples (50.4%) had Profile results of HIV-2 positive with reactivity to HIV-1 antigens and 8 of 8 (100%) HIV-1/HIV-2 co-infection samples had Profile results of HIV-2 positive with reactivity to HIV-1 antigens.

16.3 SAFETY AND EFFECTIVENESS RESULTS

Safety Results

The risk of the device is based on data collected in the non-clinical and clinical studies conducted to support PMA approval as described above. Based on the results from both studies, VioOne™ HIV Profile™ assay, when used according to the provided directions and in conjunction with all relevant clinical and laboratory findings, should be safe to use and poses minimal risk to the patient due to false test results.

Effectiveness Conclusions

The effectiveness of the VioOne™ HIV Profile™ assay has been demonstrated by the sensitivity and specificity which has been comparable with the current commercially available FDA-approved HIV supplemental assay among all

populations tested. The results from both the non-clinical and clinical studies indicate that the VioOne™ HIV Profile™ Supplemental assay is safe and effective for the confirmation of results from an initially reactive diagnostic screening test.

16.4 PEDIATRIC SAMPLE POPULATION

The reactivity of the Avioq VioOne HIV Profile Supplemental Assay for HIV-1 positive pediatric patients was evaluated by testing HIV-1 antibody positive pediatric samples from individuals aged 2–20. The number of specimens of each pediatric age groups tested was as follows:

Ten samples were obtained from children aged 2–11 and 10 from children aged 12–18 in the clinical specificity study. Twenty-seven samples were from children aged 2–18 in the clinical sensitivity study.

16.5 FINANCIAL DISCLOSURE

The Financial Disclosure by Clinical Investigators regulation (21 CFR 54) requires applicants who submit a marketing application to include certain information concerning the compensation to, and financial interests and arrangement of, any clinical investigator conducting clinical studies covered by the regulation. The pivotal clinical study included four investigators. None of the clinical investigators had disclosable financial interests/arrangements as defined in sections 54.2(a), (b), (c), and (f). The information provided does not raise any questions about the reliability of the data.

17. INSPECTIONS

17.1 MANUFACTURING FACILITY

The technology, product design, component formulations, and production processes for the VioOne™ HIV Profile™ Supplemental Assay are similar or identical to those for the other two FDA approved or licensed products (Avioq HIV-1Microelisa System and Avioq HTLV-I/II Microelisa System). For this device, the only new manufacturing equipment is for (b) (4) , and this equipment is considered similar in design to the currently approved (b) (4) machines. All other equipment is in routine use for existing products. There is no new space qualified for this kit as the lines being used are in existing, qualified manufacturing space.

The facility was last inspected February 21–27, 2019. The inspection was classified Voluntary Action Indicated (VAI) and all inspectional issues have been resolved. Therefore, the pre-market inspection was waived.

17.2 BIORESEARCH MONITORING (BIMO) INSPECTION

CBER Bioresearch Monitoring (BIMO) issued three inspection assignments at three testing sites in the United States. These inspections did not reveal significant problems that impact the data submitted in this PMA. The inspections were classified as No Action Indicated (NAI).

18. CONCLUSIONS DRAWN FROM PRECLINICAL AND CLINICAL STUDIES

18.1 SAFETY AND EFFECTIVENESS CONCLUSIONS

Performance studies demonstrated that the overall rate of indeterminate results for the Avioq VioOne™ HIV Profile™ Supplemental Assay is low for all specimen types studied. The Avioq VioOne™ HIV Profile™ Supplemental Assay has high sensitivity and specificity for all specimen types studied, resulting in few indeterminate test results for specimens that are repeatedly reactive on a diagnostic screening assay.

18.2 BENEFIT-RISK DETERMINATION

The probable benefits of the device are based on data collected in a clinical study conducted to support PMA approval as described above. The benefits include confirming HIV infection in subjects who have had a repeatedly reactive initial HIV diagnostic test. Confirmation of the initial results will ensure that only those subjects with actual HIV infection will be treated, sparing those with initial false reactive results from unnecessary treatment.

The probable risks of the device are also based on data collected in a clinical study conducted to support PMA approval as described above. The risks to patients from this device are the risk of a false negative result, denying needed treatment, or a false positive result, subjecting the individual to unneeded treatment. The performance of the Avioq VioOne HIV Profile Supplemental Assay as demonstrated in the information provided indicates high sensitivity and specificity. The rate of indeterminate results is low.

This submission did not include specific information on patient perspectives for this device.

In conclusion, given the available information above, the data support that the probable benefits outweigh the probable risks from use of the Avioq VioOne™ HIV Profile™ Supplemental Assay for use as a supplemental assay to confirm initial reactive results.

18.3 OVERALL CONCLUSIONS

The data in this application support the reasonable assurance of safety and effectiveness of this device when used in accordance with the indications for use.

19. APPROVAL SPECIFICATIONS

Directions for use: See device labeling.

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

Post-approval Requirements and Restrictions: See approval order.

1. Endogenous interference using spiked samples
   Provide the results of testing the interference of bilirubin, hemoglobin, triglycerides, and HAMA with using HIV-1, HIV-2, and HIV-1/2-positive samples so that we may evaluate the effect of endogenous interferents on the

performance of the VioOne™ HIV Profile™ Supplemental Assay. It is acceptable to use spiked samples to perform the study, with analyte levels near the cutoff. The concentrations of interferents tested and sample numbers should be equivalent to those tested in the unspiked study. Please note that if you do not see any interference at the highest concentration of the interferent tested you do not need to also evaluate lower, non-negative concentrations.

This study should be completed by the anniversary of approval of the PMA. The results of this study may be provided in the PMA annual report submitted per 21 CFR 814.84. Upon completion and approval of the study the package insert should be updated to include the results of this study.

2. Complaint reporting
   For five years following approval, Avioq should yearly provide the complaint log that they are required to maintain per 21 CFR 820.198. This report should be submitted annually on the anniversary of the device approval. This can be part of the regular Annual Report submitted per 21 CFR 814.84.

20. PANEL RECOMMENDATIONS

Not Applicable- this product was not submitted for review by the Blood Products Advisory Committee.

21. FDA/CBER DECISION

The PMA BP180279 is recommended for approval.

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