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SUMMARY OF SAFETY AND EFFECTIVENESS DATA (SSED)

1. GENERAL INFORMATION

Device Generic Name:	HIV Self-Test
Device Trade Name:	INSTI® HIV Self Test
Device Product code:	QSS
Applicant's Name and Address:	bioLytical Laboratories Inc; Unit 406, 13251 Delf Place; Richmond; British Columbia; Canada.
Establishment Registration Number:	3003871407
Date(s) of Panel Recommendation:	None
Premarket Approval Application (PMA) Number:	BP251179
Date of FDA Notice of Approval:	**October 9, 2025**

X 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:

Anne Eder, M.D.
Director, OBRR/CBER

Breakthrough Device:

The INSTI HIV Self Test device met Criteria 1, 2b, and 2d described in the Breakthrough Devices Program guidance and was granted breakthrough device status on February 20, 2025 in BQ180308_S7.
The INSTI HIV Self Test is intended for use to aid in the diagnosis of HIV-1 and/or HIV-2 infections including acute or primary HIV-1 infection. HIV-1 and HIV-2 infections are life-threatening; without treatment, individuals infected with HIV will progress to Acquired Immunodeficiency Syndrome (AIDS), which is incurable and almost invariably fatal: depending on age and other factors, untreated individuals will typically survive about three years.
A reasonable potential for technical success in the intended population was demonstrated by the provided data and supporting literature demonstrating that antibodies to HIV-1 and HIV-2 can be detected in finger-prick capillary blood samples, and that users are likely to be able to use the self-test device; however, no blood-based self-tests are currently available in the U.S. These criteria fulfill the requirement for providing more effective treatment or diagnosis compared with the current standard of care. Thus, the INSTI HIV Self Test fulfills the criteria for breakthrough device designation.

2. INDICATIONS FOR USE

The INSTI HIV Self Test is a single use, rapid, in vitro diagnostic qualitative immunoassay for the detection of antibodies to Human Immunodeficiency Virus Type 1 (HIV-1) and/or Type 2 (HIV-2) in human fingerstick whole blood. This test is intended for over-the-counter (OTC) consumer use as an aid in the diagnosis of infection with HIV-1 and HIV-2. The test is intended for use as a self test by users 18 years or older. It is not intended to be used with specimens other than fingerstick whole blood.

3. DEVICE DESCRIPTION

A. Overview

The INSTI HIV Self Test is single use, manually performed, visually read, immunoassay for the qualitative detection of antibodies to Human Immunodeficiency Virus Type 1 (HIV-1) and Type 2 (HIV-2) in whole blood. The test is intended for use by untrained (lay) users as a self-test to aid in the diagnosis of HIV-1 and HIV-2 infection using a small drop (50µL) of blood obtained through fingerstick collection procedures. The test does not detect HIV directly but detects the antibodies specific to HIV infection response.

INSTI HIV Self Test is based on the current PMA approved and CLIA waived professional-use Point of Care (PoC) INSTI HIV-1/HIV-2 Antibody Test for use in venipuncture whole blood, fingerstick blood or plasma specimens (BP090032/7; approved on January 28, 2015). There were no changes made to either the design, reagents, or manufacturing process of the test device as was approved for PoC use, except for reformulation of sample dilution solution and elimination of a pipette in the specimen collection procedure. The following table describes the details of the

changes that were made to the INSTI HIV-1/HIV-2 Antibody Test to transition it to the INSTI HIV Self Test for untrained users.

Table 1: Summary of changes made to the professional use INSTI HIV-1/HIV-2 Antibody Test for development of the INSTI HIV Self Test

Device Component	Change
Sample Diluent	The (b) (4) composition of the Sample Diluent provided in Bottle 1 has changed.
Sample Collection procedure	Addition of drop of the blood directly in the Sample Diluent vial (Bottle 1) instead of using a pipette. The pipette was removed from the device.
Instruction for Use	A step-by-step Instruction for Use (IFU) is provided. Graphics were used to emphasize the critical steps and assist with understanding of the procedure of the test. The IFU also clearly depicts what to do as well as what not to do to avoid an invalid test result. In addition to the IFU, the INSTI HIV Self Test Training video is also provided. This training video is intended for users reference when performing the Self Test. The labeling references the toll-free number to the Consumer Support Center throughout, 8am to 8pm PST, 7 days/week.

B. Test Kit Components
The INSTI HIV Self Test consists of the following items, illustrated in Figure 1:

a. Blotted Membrane Unit (BMU): This is also called INSTI Test Device. Designed to filter, absorb and retain the test specimen and test reagents. This single use unit assembled with a membrane positioned atop an absorbent material in a plastic casing. The membrane has been spotted with HIV-1 and HIV-2 recombinant proteins, which reacts with HIV antibodies in the specimen. The membrane also includes a procedural control. The procedural control dot is printed on the membrane unit cassette as a 'C' mark. The membrane unit is individually packaged in a small aluminum pouch labeled with the name, lot number, manufacturer information, storage temperature and expiry date.

b. Sample diluent bottle (Bottle 1): is a buffered solution with cell lysis ingredients and an antimicrobial agent. This solution is colorless, free of particulate matter and ready to use when opened. The solution 1.5mL is contained in a red-capped, 4mL plastic vial that has adequate space for the addition of the blood sample. The vial can be recapped and shaken at least four times to mix the added blood sample. The vial is labelled number "1", with name, lot number and expiry date.

c. Color developer bottle (Bottle 2): is a buffered protein solution containing a blue dye color indicator and an antimicrobial agent. The solution (1.5mL), contained in a blue-capped, 4mL, plastic vial, is ready to use after shaking at least four times. Once opened, the solution is poured directly onto the nitrocellulose membrane in the well of the INSTI Membrane Unit. The bottle is labelled number "2", with name, lot number and expiry date.

d. Clarifying solution bottle (Bottle 3): is a buffered solution containing a detergent and an antimicrobial agent. This is ready-to-use solution (1.5mL), contained in a clear-capped, 4mL plastic vial. Vial is shaken four times, opened, and the solution is poured directly onto the membrane in the well of the INSTI Membrane Unit. The bottle is labelled "3", with the name, lot number, and expiry date.

e. Sterile single-use lancet

f. Adhesive bandage

g. Instructions for Use (IFU)

Figure 1: INSTI HIV Self Test pouch with components.

C. Principles of Operation

The membrane of the Blotted Membrane Unit (BMU) has been spotted with HIV-1 and HIV-2 antibody-binding recombinant proteins, which react with the HIV antibodies in the specimen to produce a distinct visual signal (a blue dot) on the membrane. To ensure the test has been performed correctly, a procedural control spot is also present on the BMU. The procedural control consists of a protein-A-treated spot capable of capturing human immunoglobulin antibodies present in blood. The human immunoglobulin antibodies then react with a proprietary chromatic agent to

produce a visual signal on the BMU. Since human immunoglobulin antibodies are present in blood (irrespective of HIV status), the control spot provides a visual signal when the test procedure has been followed, and the correct type of sample applied. The absence of a Control spot indicates invalid test.
In the test spot, recombinant HIV proteins are embedded in the membrane to capture HIV-specific antibodies if present in the specimen. Antibodies captured in the test spot react with a chromatic agent to produce a second visible dot on the membrane. The presence of both the control and test dot indicates a reactive HIV result. The presence of the control dot and no test dot is a non-reactive result.
The test is performed by adding the fingerstick whole blood into the vial of Sample Diluent (Bottle 1), which lyses the blood cells. Then, the diluent solution plus specimen poured into the well of the BMU. HIV-1 and HIV-2 antibodies, if present in the specimen, are captured by proteins on the filtration membrane. Color Developer (Bottle 2) is then added to the Membrane Unit. The Color Developer reacts with the captured antibodies to generate a distinct blue dot at the location of the control spot and, in the case, where HIV-1/HIV-2 antibodies are present in the specimen, a blue dot also appears at the location of the test spot on the membrane.
In the final step, the Clarifying Solution (Bottle 3) is added to the BMU to decrease background color and make the control and test spots visible and more distinct. The results are interpreted immediately and up to an hour after the Clarifying Solution is fully absorbed into the BMU.
An illustration of the immunoassay reaction principles of the assay design is provided under Figure 2.

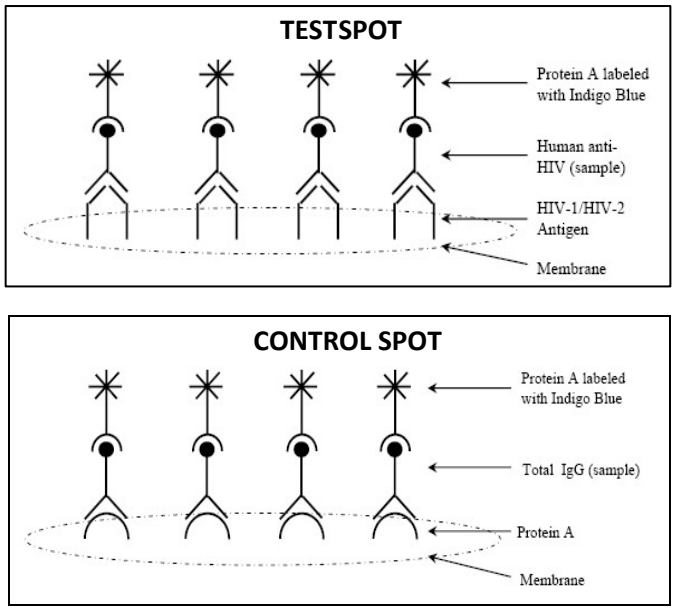


Figure 2: Assay principle of the INSTI HIV Self Test

D. Test Results and Interpretation
An illustration of the INSTI HIV Self Test results interpretation is provided below in Figure 3.

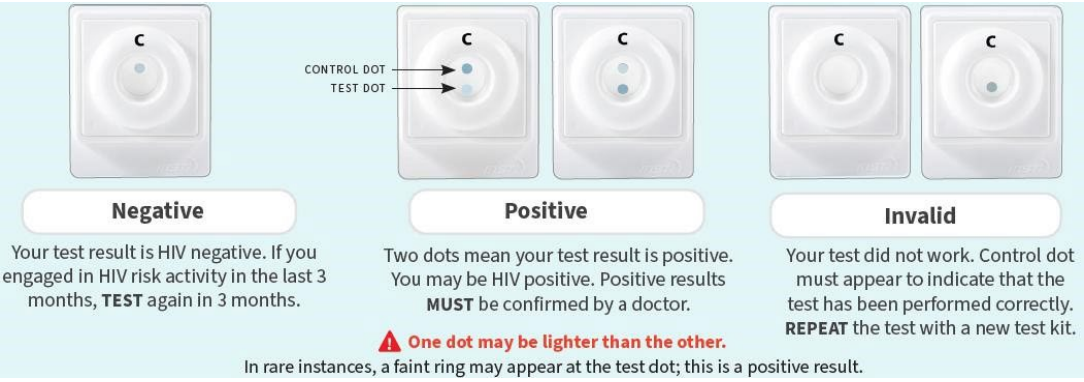


Figure 3: Result Interpretation of the INSTI HIV Self Test

E. INSTI-HIV Self Test Consumer Support Center
If the individual running the test has any questions regarding the test or encounters any problems while performing the test, they can call the bioLytical Laboratories Technical Support/Customer Service Center as indicated in the IFU. The customer service is available 8:00 AM to 8:00 PM PST, 7 days a week/ 365 days a year with bilingual capability (English and Spanish).

4. CONTRAINDICATIONS

There are no known contraindications for use for this test.

5. WARNINGS, PRECAUTIONS, AND LIMITATIONS

a. For in vitro diagnostic use only.

b. Read instructions carefully before use.

c. The test is not for individuals younger than 18 years.

d. To assist with the understanding of the test procedural steps, a training video is available upon scanning the QR code. Individual should watch this video before they perform the test.

e. Do not use this test if you are afraid of needles.

f. Do not use if past expiration date is on outer packaging.

g. Do not use if the test pouch has been damaged or if any of the components are missing.

h. Do not open the pouch until you begin the test.

i. Adequate lighting is required to perform the test and to read the test result.

j. Allow test to reach room temperature if stored refrigerated.

k. Do not use this test if you are taking Anti-retroviral Treatment (ART).

l. Do not use this test if you are using pre-exposure prophylaxis (PrEP) or post-exposure prophylaxis (PEP) treatment.

m. Do not use this test if you have participated in a HIV vaccine study.

n. Do not use this test if you have bleeding disorders, multiple myeloma or have higher than normal hemoglobin.

o. This test is approved by FDA for use with the fingerstick whole blood specimens only. Use of other types of specimens may not yield accurate results.

p. All positive test results must be confirmed by a laboratory test.

q. As with many tests, there is a chance for false results. If you have a negative result but you were involved in an HIV-risk activity in the past 3 months, you could be in what is called the "window period" and it is recommended to repeat testing in 3 months.

6. ALTERNATIVE PRACTICES AND PROCEDURES

The detection of HIV antibodies in individuals is primarily conducted with laboratory based or PoC rapid tests performed in clinics or physicians' offices that use blood, serum, plasma, and oral fluids as the specimen. All initially reactive results must be confirmed using a second test. There is one FDA-approved OTC HIV test, that uses oral fluid as the sample type, available in the U.S. that allows an untrained user to test for HIV antibodies in home/self-test environment.

7. MARKETING HISTORY

The INSTI HIV Self Test is currently marketed in Europe, Canada, and other countries including Vietnam, Thailand, Kenya, and South Africa. This device has not been withdrawn from marketing for any reason related to its safety or effectiveness.

8. POTENTIAL ADVERSE EFFECTS OF THE DEVICE ON HEALTH

INSTI HIV Self Test is a home-use HIV test kit. This means that an untrained user is responsible for blood specimen collection, execution of the test, and interpretation of test result without any counseling support present while they perform the test.
Key Adverse Health Effects may be:

- Psychological effect of positive results.
- Delayed medical care from false negative results.
- Transmission risk from undetected infection.

9. SUMMARY OF NON-CLINICAL STUDIES

A. Laboratory Studies Conducted for INSTI HIV-1/HIV-2 Antibody Test professional use, Point of Care Test (BP090032/0 and BP090032/07)

The INSTI HIV Self Test uses the same reagents, design, and manufacturing process as the approved INSTI HIV-1/HIV-2 Antibody Test (BP090032/0, approved on November, 2010, and BP0090032/7, approved on January, 2015). The following non-clinical laboratory-based studies that were conducted to assess the performance of the INSTI HIV-1™ Antibody Test were used as a basis for approval of the INSTI HIV Self Test:

a. **Reproducibility:** The reproducibility of the INSTI HIV-1 Antibody Test was tested at three laboratory sites using three lots of the INSTI HIV-1 Antibody Test on three separate days with nine operators (three per site). A panel of five blind-coded contrived plasma specimens, consisting of four HIV-1 antibody-positive (one strong positive and three low positive) and one HIV antibody-negative specimen was tested at each site. A total of 405 tests were conducted, 135 at each site, with a total of 81 tests per panel specimen. The overall reproducibility of the INSTI HIV-1 Antibody Test was 405/405 = 100%.

b. **Reactivity with HIV-1 Seroconversion Panels:** Twenty-three seroconversion panels were tested, and the INSTI HIV-1 Antibody Test results were compared with licensed or approved anti-HIV enzyme immunoassays (EIAs). In this study, the INSTI HIV-1 Antibody Test demonstrated the ability to detect HIV-1 antibodies during seroconversion equivalent to the FDA licensed or approved HIV EIAs.

c. **Reactivity with HIV-1 Low-Titer Panel:** One HIV-1 low titer panel was tested with three lots of INSTI HIV-1 Antibody Test and results were compared with FDA licensed or approved HIV EIA assays. In this study, the INSTI HIV-1 Antibody Test demonstrated the capability of detecting low levels of antibodies to HIV-1 equivalent to FDA licensed or approved EIAs.

d. **Potentially Interfering Medical Conditions:** To assess the impact of potentially unrelated medical conditions on the sensitivity (samples spiked with HIV-1) and specificity (samples without HIV-1) of the INSTI HIV-1 Antibody Test, 195

serum/plasma specimens from a cross section of medical conditions unrelated to HIV-1 infection were tested. Reactivity of the samples of following medical conditions were tested: toxoplasmosis, rheumatoid factor, multiple myeloma, syphilis, rubella, cytomegalovirus, Epstein Barr virus, HTLV-I/II, HBV and HAV. INSTI HIV-1 Antibody Test generated positive results with all HIV-1-positive samples and nonreactive results with all HIV-1-negative samples.

e. **Potentially Interfering Substances:** To assess the impact of potentially interfering substances on the sensitivity (samples spiked with HIV-1) and specificity (samples without HIV-1) of the INSTI HIV-1 Antibody Test, 217 specimens with potentially interfering substances were tested. Reactivity of the samples of following interfering substances were tested: bilirubin (>8.0mg/dL), lipemic, visual hemolysis, triglyceride (≥292mg/dL), hemoglobin (>12g/100mL), albumin (11.5-13g/dL), EDTA, sodium heparin, sodium citrate, and bacterially contaminated samples. All HIV-1-positive samples were INSTI HIV-1 Antibody Test reactive, and all HIV-1-negative samples were non-reactive.

f. **Detection of Anti-HIV-1 non-B Subtypes:** To assess the sensitivity of the INSTI HIV-1 Antibody Test for detection of antibodies to non-B subtypes of HIV-1, 207 serum/plasma specimens collected from individuals from various geographic regions who were infected with non-B subtypes of HIV-1 were tested. Of these 207 specimens, 206 were reactive with the INSTI HIV-1 Antibody Test, for an overall sensitivity of 99.5% (95% CI = 97.3-99.9%). One subtype A specimen tested false non-reactive.

B. Laboratory Studies Conducted in Support of the new sample diluent used in INSTI HIV Self Test

A change to the sample diluent was implemented for the INSTI HIV-1/HIV-2 Antibody Test post-reclassification of HIV Diagnostic devices from class III to class II (2022). The change was internally documented by the Sponsor as required by 510(k) regulations; however, as the change affects the class III INSTI HIV Self Test, validation of the change was included in BP251179. Results relevant to the INSTI HIV Self-Test are included below.

Due to the lack of availability of the approved (b) (4) in the Sample Diluent (Solution 1), a new (b) (4) was evaluated as an alternative raw material. Validation of the reformulated Solution 1, identified here as Sample Diluent 3 (SD3) was performed by producing (b) (4) lots of SD3 using (b) (4) different vendor lots of the new (b) (4) . Testing was performed on INSTI HIV-1 Antibody Tests to evaluate equivalence between the current Solution 1 formulation identified here as Sample Diluent 1 (SD1) and SD3. Results of testing demonstrate the change in (b) (4) had no effect on test performance and performance with the reformulated Solution 1 with SD3 was equivalent to performance of the test with SD1. The updated Solution 1 (SD3) was used in the validation as well as in clinical study of the INSTI HIV Self Test.

a. **Limit of Blank (LOB) and Limit of Detection (LOD):** The purpose of this study was to determine whether LOB and LOD remain unchanged with the INSTI HIV-1/HIV-2 Antibody Test kit containing SD3. The LOB and LOD with the new (b) (4) were verified with (b) (4) lot of INSTI HIV-1/HIV-2 Antibody Test kit containing SD3.
The LOB was verified using (b) (4) confirmed HIV-negative whole blood samples. The panel members were tested in (b) (4) replicates on (b) (4) INSTI HIV-1/HIV-2 Antibody test kit lot over (b) (4) days for (b) (4) total replicates. All panel members were non-reactive.
The LOD was verified using (b) (4) HIV-negative whole blood samples, each spiked with (b) (4) HIV-1 antibody-positive specimen (b) (4) and (b) (4) HIV-2 antibody-positive specimen (b) (4) All panel members were tested in (b) (4) replicates with (b) (4) INSTI HIV-1/HIV-2 Antibody Test kit lot over (b) (4) days for (b) (4) total replicates. All samples were reactive.

b. **Low-Titer Panel Study:** The purpose of this study was to determine if analytical sensitivity remained unchanged with the INSTI HIV-1/HIV-2 Antibody Test kit containing SD3. (b) (4) commercially available low titer HIV performance panels were tested with (b) (4) INSTI HIV-1/HIV-2 Antibody Test kit lot containing SD1 and (b) (4) kit lot containing SD3. The results from (b) (4) kit lots were equivalent (Table 2). No invalid results were observed.

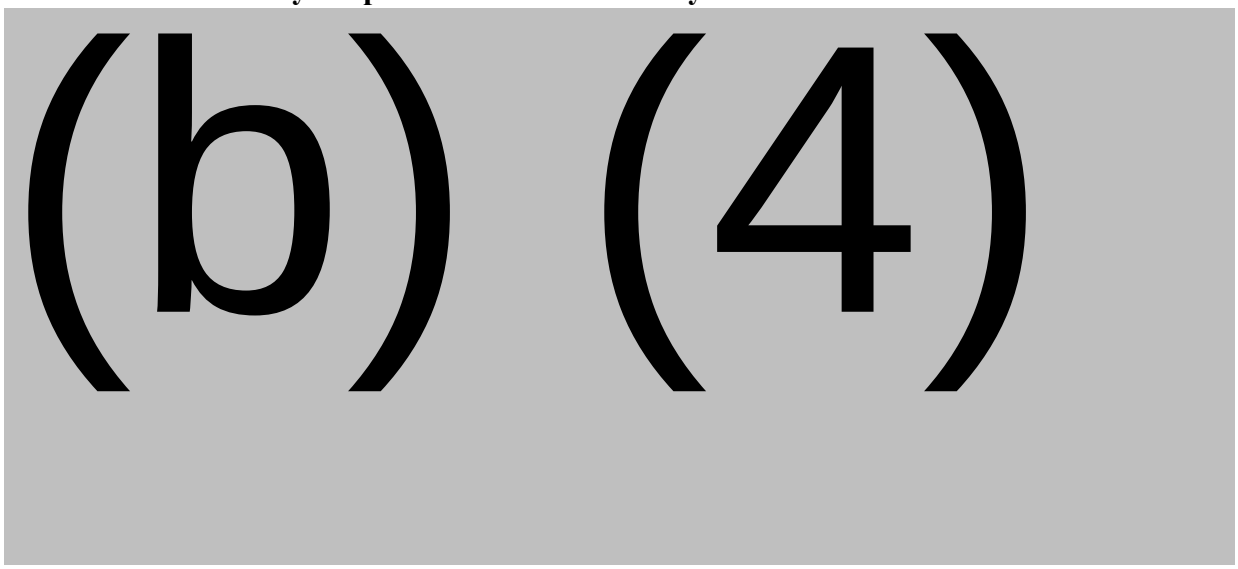
Table 2: Summary of Low titer panel study results

(b) (4)

c. **Seroconversion Panel Study:** The purpose of this study was to determine if the sensitivity remains unchanged with the INSTI HIV Self Test kits containing SD3. (b) (4) panel members were tested from (b) (4) commercially available panels with (b) (4) INSTI HIV-1/HIV-2 Antibody Test kit (b) (4) containing SD1 (b) (4) kit (b) (4) containing SD3. All panel members that were reactive with SD1 were also reactive with SD3, and all panel members that were non-reactive with SD1 were also non-Reactive with SD3. No invalid results were observed in this study.

d. **Validation of Specimen Type:** The purpose of this study was to verify whether the performance of the INSTI HIV-1/HIV-2 Antibody Test kit containing SD1 and SD3 is similar when tested with (b) (4) matched sample matrices. Testing was performed on (b) (4) matched panels consisting of whole blood and plasma. All samples were tested with (b) (4) INSTI HIV-1/HIV-2 Antibody Test kit (b) (4) containing SD1 (b) (4) kit (b) (4) containing SD3 and provided identical results (Table 3). No invalid results were observed in this study.

Table 3: Summary of specimen validation study results



e. **In-use Stability Study:** An in-use stability study was conducted to determine the effect of storing the INSTI HIV-1/HIV-2 Antibody Test containing the reformulated SD3 at elevated temperatures after being removed from the primary package. The sensitivity and specificity of the test kits stored for a short time (b) (4) minutes and (b) (4) minutes) under a variety of conditions (15°C and (b) (4) relative humidity, 30°C at (b) (4) relative humidity, and (b) (4) and (b) (4) relative humidity) were evaluated using a panel of (b) (4) specimens consisting of plasma and whole blood matrices un-spiked or spiked with HIV-1/HIV-2 positive plasma to a low ((b) (4) LoD) to moderate (b) (4) LoD) level of reactivity. The panel members were tested on (b) (4) lots of INSTI HIV-1/HIV-2 Antibody Test Kit, (b) (4) containing SD1 (b) (4) containing SD3, (b) (4) . All positive samples were reactive, and all negative samples were non-reactive. No invalid results were observed.

f. **Validation of Reading Times:** The purpose of this study was to evaluate the equivalence of SD1 and SD3 with test result reading time at the intended operational temperature and humidity range. This study was performed using a panel of (b) (4) specimens (plasma and whole blood) consisting of negative and (b) (4) positive ((b) (4) LoD) HIV-1 and HIV-2 antibody titers. Each panel member was tested (b) (4) times after storing the vials of SD1 and SD3 at different temperatures and relative humidity conditions. Test results were observed and recorded at following time points: t= (b) (4) (b) (4) . The results were identical across (b) (4) kit lots.

g. **Effect of Variable Sample Volumes:** The purpose of this study was to evaluate the equivalence of SD1 and SD3 when specimen volumes vary. This study was performed using a panel of (b) (4) specimens (plasma and whole blood) consisting of negative and (b) (4) positive (b) (4) LoD) HIV-1 and HIV-2 antibodies. (b) (4) of INSTI HIV-1/HIV-2 Antibody Test kit containing SD1 and (b) (4) INSTI HIV-1/HIV-2 Antibody Test kit (b) (4) containing SD3 was used in this study. Each panel member was tested (b) (4) times

by each of the INSTI HIV-1/HIV-2 Antibody Test kit with following specimen volumes: (b) (4). The results were identical across (b) (4) kit (b) (4)

h. **Effect of Elapsed Time between Addition of INSTI Solutions:** The purpose of this study was to evaluate the equivalence of SD1 and SD3 when a time delay is introduced before the addition of the sample in Solution 1 to the BMU. Time intervals of 0, 5, 10, (b) (4) minutes between the addition of sample in Solution 1 to the BMU were tested with (b) (4) different reagent kit lots of the INSTI HIV-1/HIV-2 Antibody Test. Expected results were obtained for 0, 5, and 10 minutes delay when tested across (b) (4) kits. However, (b) (4) delay produced expected results for SD3, but produced (b) (4) false positive results with SD1 for negative whole blood. A (b) (4) delay produced (b) (4) false positive results with SD1 and (b) (4) false positive result with SD3 for negative whole blood. A warning statement was added to the IFU to avoid delay in adding INSTI solutions to reduce the risk of false positive results.

i. **Effect on Sensitivity/Specificity of INSTI at Reduced Reagent Volumes:** The purpose of this study was to evaluate the equivalence of SD1 and SD3 with reduced reagent volumes. This study was performed using a panel of (b) (4) specimens (plasma and whole blood) consisting of negative and (b) (4) positive ((b) (4) LoD) HIV-1 and HIV-2 samples. The addition of panel members to SD1 or SD3 volumes of (b) (4) were tested with (b) (4) of INSTI HIV-1/HIV-2 Antibody Test kit containing SD1 and (b) (4) of INSTI HIV Test kit containing SD3. The results were identical across (b) (4) kit lots.

j. **Insufficient Mixing of Solutions:** The purpose of this study was to evaluate the equivalence of SD1 and SD3 with insufficient mixing of whole blood with Solution 1 prior to adding into the BMU (b) (4). All panel members tested provided identical results on (b) (4) lots of INSTI HIV-1/HIV-2 Antibody Test kits with SD1 or SD3.

k. **Real-time Shelf-life Stability Study:** Reagent real-time stability was validated using (b) (4) lots of test kits containing SD3 stored at 2°C and 30°C up to (b) (4) months. Venous whole blood and plasma/serum samples were tested in (b) (4) at each time point. Acceptable performance was observed supporting stability of the test kit containing SD3 for up to (b) (4) months.

10. SUMMARY OF PRIMARY CLINICAL STUDIES

A summary of the clinical studies supporting the self-testing with the INSTI HIV Self Test is presented below. The original clinical studies in support of the INSTI HIV-1/HIV-2 Antibody Test are included to demonstrate the baseline clinical sensitivity and specificity of the test in the hands of trained users.

Table 4: Objective of clinical studies

Number	Title	Objective
Study 1	Evaluation of the performance of the test by trained users and untrained users in CLIA-waived sites	a) Characterized sensitivity and specificity of the professional use, Point of Care (PoC) INSTI HIV-1/HIV-2 Antibody Test (BP0950032 and BP090032/7) b) CLIA-waiver study evaluating positive percent agreement (PPA) and negative percent agreement (NPA) of waived users with trained users in fingerstick whole blood (CR180016)
Study 2	Evaluation of the performance of the test in the hands of untrained intended users under observation	a) Determine INSTI HIV Self Test PPA and NPA percent agreement, compared with the INSTI HIV-1/HIV-2 Antibody PoC Test b) Evaluate the usability of the test c) Ability of individuals to interpret possible results in contrived tests
Study 3	Evaluation of the performance of the test in the hands of untrained intended users when unobserved	Determine INSTI HIV Self Test PPA and NPA compared with the INSTI HIV-1/HIV-2 Antibody PoC Test

A. Study 1: Performance of the professional use, PoC HIV-1/HIV-2 Antibody Test:

Clinical sensitivity and specificity by trained users: The sensitivity and specificity of the test in the hands of trained users was determined in a study with fingerstick whole blood conducted at 14 geographically diverse sites in the U.S. in support of the INSTI HIV-1/HIV-2 Antibody Test approvals in 2010 (HIV-1) and 2015 (addition of HIV-2).

HIV-1: The sensitivity of the INSTI HIV-1 Antibody test in fingerstick whole blood was evaluated in individuals known to be HIV positive or at high-risk for HIV infection, while the specificity of the device was evaluated in individuals at low-risk of HIV infection. Individuals at high-risk who were confirmed to be HIV negative in the sensitivity study were included in the calculations of specificity. The clinical study results are summarized in Tables 5-7.

A sensitivity study was performed using fingerstick blood from 1075 individuals known to be HIV positive and 22 individuals were confirmed HIV positive from 782 individuals from HIV high-risk group.

Table 5: Sensitivity of INSTI HIV-1 Antibody Test from known positive and high-risk population

INSTI Test Result	Approved Test Reactive	Approved Test Non-reactive	Total
Reactive	1095	1[1]	1096
Non-Reactive	2[2]	755	757
Invalid	0	4	4
Total	1097	760	1857

[1] One individual that produced a false reactive result by INSTI HIV-1 Test was from the high-risk group.
[2] One individual was from HIV-known positive and one individual from HIV high-risk group.

The overall sensitivity of the INSTI HIV-1 Antibody Test in fingerstick whole blood specimens for the confirmed HIV-1 positive participants in the combined high-risk and known HIV-1 positive populations that produced valid results was 1095/1097= 99.8% (95% CI = 99.3% – 99.9%). Two INSTI false negative results (one from the HIV-1 known positive and one from the high-risk for HIV infection populations) were generated. There were four invalid results from the INSTI HIV-1 Antibody test.

The specificity study was performed using fingerstick blood from 626 individuals from HIV low-risk and 760 individuals from known to be HIV negative from high-risk group.

Table 6: Specificity analysis from low-risk population

INSTI Test Result	Approved Test Reactive	Approved Test Non-reactive	Total
Reactive	0	6	6
Non-Reactive	0	620	620
Invalid	0	0	0
Total	0	626	626

Table 7: Specificity analysis from high-risk population

INSTI Test Result	Approved Test Reactive	Approved Test Non-reactive	Total
Reactive	21	1	22
Non-Reactive	1	755	756
Invalid	0	4	4
Total	22	760	782

The overall specificity of the INSTI HIV-1 Antibody Test in fingerstick whole blood specimens for the confirmed HIV negative participants in the combined high-risk

and low or unknown risk populations that produced valid results was 1375/1382 = 99.5% (95% CI = 99.0% – 99.8%). Seven false reactive results (one from the high-risk group, six from the low or unknown risk group) were generated from the 1382 specimens from HIV-negative individuals that produced valid INSTI results. There were four invalid results from the INSTI HIV-1 Antibody test.

The clinical sensitivity and specificity met the acceptance criteria for PoC HIV diagnostic devices.

HIV-2: The sensitivity of the INSTI HIV-1/HIV-2 Antibody Test for detecting HIV-2 in plasma specimens was determined using commercially available plasma (190 HIV-2 positive) as well as plasma specimens (12 HIV-2 positive) from HIV-2 endemic region (Ivory Coast) was 201/202 = 99.5% (95% CI = 97.2% – 99.9%).

CLIA-waiver study: A CLIA- waiver study was conducted to evaluate the performance of the INSTI HIV-1/HIV-2 Antibody Test in the hands of untrained users in a professional use setting; it did not evaluate self-testing performance. A CLIA waiver prospective study was conducted over four months at three geographically diverse sites in the U.S. At each site, testing was conducted by (b) (4) untrained operators who had no laboratory experience and were representative of users at CLIA waived testing sites. A total of 905 individuals with unknown HIV status and 483 known HIV-positive individuals participated in the study. The individuals with unknown HIV status were tested with both the INSTI HIV-1/HIV-2 Antibody Test and the comparator test. The individuals known to be HIV-positive were tested with INSTI HIV-1/HIV-2 Antibody Test and their HIV status was not known to the operators.

The PPA in known-positive individuals was 483/483 = 100% (95% CI 99.2 – 100%) and the PPA for new diagnoses in individuals with unknown status was 34/34= 100%. The NPA in individuals with unknown status was 869/871 = 99.8% (95% CI 99.2 – 99.9%). The results demonstrated that the INSTI HIV-1/2 Antibody Test performance in CLIA-waived sites by untrained users was equivalent to that of trained users.

B. Study 2: Performance of the test in the hands of untrained intended users under observation:

This study was conducted in three parts:

a. The first part was designed to evaluate the performance of the INSTI HIV Self Test when used by individuals with unknown HIV status to self-test while under observation by a trained operator at the clinical sites. Participants who were enrolled and signed the consent form were provided with one INSTI HIV Self Test kit. The participant performed the test and documented the test result in the provided form. The observer did not interact with the participant but documented any errors made by the participants during test procedure. Once the

participant completed interpretation of the test result, the observer also interpreted the participants self-test result and recorded their interpretation. The participant was then tested by the trained operator with the approved PoC INSTI HIV-1/HIV-2 Antibody Test (comparator device).

b. Participants who agreed to participate provided their feedback on the Usability Questionnaire. The questionnaire asked participants 24 questions about their experience using INSTI HIV Self Test, including whether they found the test easy to use, whether the illustrations, training video and instructions in the package insert were clear, if they would use this again or recommend the test to others. It also assessed participants' understanding of information provided in the package insert and instructions for use video.

c. The operator presented the participant with five contrived INSTI HIV Self Test device (one with a positive test result, one with a weak positive test result, one with a negative test result, two with invalid; either invalid with results or invalid due to lack of a control spot in the presence of a reactive test spot) for participant's interpretation of each test result.

In case of discordant results between the INSTI HIV Self Test and the comparator test, the investigators collected venous blood from the participants for a subsequent laboratory test conducted by a central laboratory to confirm the individual's status.

The following three objectives were assessed from this study:

a. Performance analysis by percent agreement: PPA and NPA between valid INSTI HIV Self Test results obtained and interpreted by the participant and comparator INSTI HIV-1/HIV-2 Antibody Test result obtained by the trained operator were calculated. The failure rate of the test was also assessed and calculated based on all individuals who were provided with the test but failed to achieve a result, regardless of whether use errors were made.

b. Usability Evaluation by Questionnaire: Only the questions about ease of use and comprehensibility were used to evaluate usability.

c. Interpretation Evaluation: Participants were presented with five INSTI HIV Self Test devices that had been prepared with contrived potential results and asked to provide their interpretation. The operator recorded their answers on a form.

Study 2, was conducted at six clinical sites geographically distributed in the U.S. A total of 1596 participants were screened through inclusion and exclusion criteria (Table 8) and 1593 participants were enrolled. Test performance was evaluated by calculating the PPA and NPA between INSTI-HIV Self Test results obtained and interpreted by the participants and Comparator INSTI HIV-1/HIV-2 Antibody Test result obtained by the trained operator.

Table 8: Inclusion and exclusion criteria for participation in the Observed clinical study

Number	Inclusion Criteria
1	18 years of age or older
2	Unknown HIV Status
3	Participant to sign and date the Informed Consent form
4	Able to speak, read and write English or Spanish
5	Willingness to provide the fingerstick blood sample and if necessary, the volume of blood collected through venous blood draw
6	Willingness to participate in the study sites standard of care HIV counseling and testing program and receive the study site's standard of care test results
	Exclusion Criteria
1	Has participated in any prior trial of HIV self-tests
2	Is a practicing medical healthcare professional
3	Is currently on a PrEP regimen
4	Has received any experimental HIV vaccine
5	Is known HIV positive
6	Uses Anti-Retroviral medication
7	Has bleeding disorders

Demographics of participants are summarized in the Table 9 below. The age category with the most participants was >55 years, and the age category with the fewest enrolled participants was 18-25 years. The rate of male and female enrollment was comparable.

Table 9: Demographics of Observed clinical study

Parameter	INSTI HIV Self Test N = 1593; n (%)
Age Group (Years)	
18-25	198 (12.4)
26-35	263 (16.5)
36-45	281 (17.6)
46-55	297 (18.6)
>55	554 (34.8)
Sex	
Male	834 (52.4)
Female	759 (47.6)
Race	
American Indian	4 (0.3)
Asian	68 (34.3)
Black or African American	956 (60.0)
Native Hawaiian or Pacific Islander	3 (0.2)
White	547 (34.3)
Other	15 (0.9)
Ethnicity	
Hispanic or Latino	231 (14.5)
Not Hispanic or Latino	1362 (85.5)

A summary of the clinical study results is described below.

a. Performance analysis: A total of 1593 participants initiated the testing procedures. Six were invalid only in comparator (1587); 39 tests were invalid in the HIV Self Test (1548); and three were invalid in both tests (1545); One individual was unable to complete the testing procedure. Overall, 1544 participants obtained valid test results in both INSTI HIV Self Test and comparator test. A total of 1521 test results were negative and 23 test results were positive, and there were no discordant results between the INSTI HIV Self Test and comparator tests. The point estimate for NPA and PPA are summarized the Table 10 A and B.

Table 10: Summary of INSTI HIV Self Test and comparator test results and agreement analysis

A) Cross-tabulation Results:

INSTI HIV Self Test Result	Comparator Test: Positive	Comparator Test: Negative	Comparator Test: Invalid/ Test did not work	Comparator Test: Do not know/not sure	Total
Positive	23	0	1	0	24
Negative	0	1521	5	0	1526
Invalid/test did not work	1	38	3	0	42
Do not know/not sure	0	1	0	0	1
Total	24	1560	9	0	1593

B) Performance Metrics

Metric	Value	95% Confidence Interval
PPA	100% (23/23)	(85.69%, 100%)
NPA	100% (1521/1521)	(99.75%, 100%)

The PPA of the INSTI HIV Self Test in the Observed study was 100% with a 95% CI of 85.69 – 100%. The NPA of the INSTI HIV Self Test was 100% with a 95% CI of 99.75 – 100%, which met the recommended performance criteria.

Failure Rate: The failure rate of INSTI HIV Self Test was determined by participants who were provided a self-test but failed to obtain a valid test result, whether it was caused by user error or device malfunction. An observer present while the participant was performing the test documented any procedural errors made by the participant. There were 42 invalid results due to participant actions, for an overall failure rate of INSTI HIV Self Test of 2.7%. Out of 42 invalid test

results, 36 were from a single site. Upon investigation, it was determined that the most common reasons for invalid results were that the participants smeared or scraped their finger on the bottle (16/42) and not producing sufficient blood to run the test (21/42). The IFU and the training video were updated to reduce the likelihood of these user errors. As these updates were not independently validated, CBER is requiring a post-market study with annual reporting of questions and comments that are made to the customer call center/technical support line to evaluate potential user signals (see section 17).

b. Usability Questionnaire Analysis result: The usability questionnaire containing 24-questions to assess participants' experience using INSTI HIV Self Test was completed by 452 of the participants in the self-testing arm who consented to this arm of the study. In this study the answers to two critical questions were considered: 1, "Was the test easy", 98.6% (446/452) participants found the INSTI HIV Self Test easy to use. 2, "How easy were the test instructions in the Package Insert", 99.5% (450/452) found the test instructions easy to use. The remaining questions were related to test procedural steps, audio-video instructions, and personal recommendations of this test.

c. Test Result Interpretation Analysis: All participants who participated in the self-testing arm were offered the opportunity to participate in the Results Interpretation Analysis arm of the study, and 495 participants agreed to participate. Participants were presented with five INSTI HIV Self Test devices that had been prepared with contrived potential results and asked to provide their interpretation. The following results were obtained: 94.9% of participants correctly interpreted a positive result, 90.0% of participants correctly interpreted a weak positive result, 98.1% of participants correctly interpreted a negative result, 94.2% of participants correctly interpreted an invalid blank result, and 89.3% of participants correctly interpreted an invalid test with a test dot. These results met the acceptance criteria.

C. Study 3: Performance of the INSTI HIV Self Test in the hands of untrained intended users when Unobserved:

In this study participants performed the INSTI HIV Self Test at a clinical site in an unobserved setting. The participant performed the self-test per the instructions, interpreted the test result, and documented their result in the provided form. Once the participant completed interpretation of the test result, an operator entered the room and also interpreted the self-tester's test result. The participant was then tested by the operator utilizing the comparator INSTI HIV-1/HIV-2 Antibody Test with fingerstick whole blood. In case of discordant results between the INSTI HIV Self Test and the comparator test, the investigators would collect venous blood from the participants for a subsequent laboratory test conducted by a central laboratory to confirm the individual's status.

A total of 122 participants were enrolled based on inclusion and exclusion criteria (Table 11) across two clinical sites. The demographics of participants are summarized below (Table 12)

Table 11: Inclusion and exclusion criteria for participation in the Unobserved clinical study

Number	Inclusion Criteria
1	18 years of age or older
2	Unknown HIV Status or known HIV positive status with less than 12 months of Anti-Retroviral Treatment (ART)
3	For known HIV positive status individuals, willingness to share ART start date
4	Participant to sign and date the Informed Consent form
5	Able to speak, read and write English or Spanish
6	Willingness to provide the fingerstick blood sample and if necessary, the volume of blood collected through venous blood draw
7	Willingness to participate in the study sites standard of care HIV counseling and testing program and receive the study site's standard of care test results
	Exclusion Criteria
1	Has participated in any prior trial of HIV self-tests
2	Is a practicing medical healthcare professional
3	Known HIV positive individual and currently on an ART for 12 months or longer.
4	Has received any experimental HIV vaccine
5	Has bleeding disorders
6	Has received any experimental HIV vaccine

Table 12: Demographics of Unobserved clinical study

Parameter	INSTI HIV Self Test N = 122; n (%)
Age Group (Years)	
18-25	29 (23.8)
26-35	19 (15.6)
36-45	6 (4.9)
46-55	18 (14.8)
>55	50 (41.0)
Sex	
Male	45 (36.9)
Female	77 (63.1)
Race	
American Indian	0 (0)
Asian	11 (9.0)
Black or African American	74 (60.7)
Native Hawaiian or Pacific Islander	0 (0.0)
White	35 (28.7)
Other	2 (1.6)
Ethnicity	
Hispanic or Latino	10 (8.2)
Not Hispanic or Latino	112 (91.8)

Table 13: Summary of INSTI HIV Self Test and comparator test results and agreement analysis

A) Cross-tabulation Results:

INSTI HIV Self Test Result	Comparator Test: Positive	Comparator Test: Negative	Comparator Test: Invalid/ Test did not work	Comparator Test: Do not know/not sure	Total
Positive	10	0	0	0	10
Negative	0	107	0	0	107
Invalid/test did not work	0	4	0	0	4
Do not know/not sure	0	1	0	0	1
Total	10	112	0	0	122

B) Performance Metrics

Metric	Value	95% Confidence Interval
PPA	100% (10/10)	(69.15%, 100%)
NPA	100% (107/107)	(96.61%, 100%)

There were 10 positive results, 107 negative results, four invalid results, and one participant recorded their result as "do not know/ not sure' (Table 13 A). There were five positive results from previously undiagnosed participants, and five positive results from known HIV-positive participants. All 10 participants had positive results in both the INSTI HIV Self Test and the comparator device, resulting point estimate of PPA as 100%. All 107 participants had negative results in both the INSTI HIV Self Test and the comparator device, resulting NPA 100% (95% Two-Sided CI; 96.61 – 100%) (Table 13 B). The overall failure rate of the device in this study was 5/122, or 4.1%. One of the five participants with invalid results was due to the participant recording their INSTI HIV Self Test result as invalid, although the trained observer interpreted their result as Negative, and which was confirmed with the comparator test; with this result excluded from test failures, the overall invalid rate was 4/122, or 3.3%.

11. FINANCIAL DISCLOSURE

The applicant has adequately disclosed the financial interest/arrangements with clinical investigators. The information provided does not raise any questions about the reliability of the data.

12. PEDIATRIC EXTRAPOLATION

Individuals aged 18-21 years old participated in this clinical study to support the intended use in this population. Existing clinical data was not leveraged to support approval of

other pediatric patient populations as the intended use population includes only individuals aged 18 and older.

13. SUMMARY OF SUPPLEMENTAL CLINICAL INFORMATION

Data generated to support the approval of the INSTI HIV Self Test in Canada, Congo, and South Africa in clinical studies performed in these countries was used to demonstrate the efficacy of the INSTI HIV Self Test to identify new HIV diagnoses. The study designs, testing in untrained users, exclusion criteria, and inclusion criteria were similar to the studies conducted in the U.S. Self-test results were compared with the true clinical status of the participants as determined by venous whole blood testing. Table 14 A and B presents the combined PPA and NPA results from all clinical studies conducted outside of the U.S. One hundred twelve new diagnoses were identified in these studies.

Table 14: Summary result of performance of INSTI HIV Self Test Outside of the U.S.

A) Cross tabulation Results

INSTI HIV ST Results	Confirmatory Results - Positive	Confirmatory Results - Negative	Total
Positive	112	3	115
Negative	5*	1,854	1,859
Total	117	1,857	1,974

*Includes two participants who recorded their results as negative although the observer recorded the Self Test result as positive, which was concordant with the clinical status of the individuals.

B) Performance Metrics

Metric	Value	95% Confidence Interval
PPA	95.73% (112/117)	(90.31%, 98.60%)
NPA	99.84% (1,854/1,857)	(99.53%, 99.97%)

14. PANEL MEETING RECOMMENDATION AND FDA'S POST-PANEL ACTION

Not applicable- This product was not submitted for review by the Blood Products Advisory Committee.

15. INSPECTIONS

A. Manufacturing Facilities:

bioLytical Laboratories, Inc.
Manufacturing Facility
13251 Delf Place Unit 406,
Richmond, BC,
Canada, V6V2A2

Establishment inspection dates: 0616/2025 – 06/20/2025
FEI # 3003871407
Functions: Manufacturing and Quality

At the conclusion of the inspection, a Form FDA 483, Inspectional Observations, was not issued. No Action Indicated.

B. Bioresearch Monitoring (BIMO):

Seven clinical sites participated in this study. Four clinical site inspections were performed. The factors used to select the sites for inspection included the following: prior inspection reports, the study protocol, study participant enrollment, clinical investigators not previously inspected, and invalid test result rates. The inspections focused on specific questions concerning the study protocol and the comparison of information from the PMA to source documents.
The inspections at three of the four sites revealed no deviations from applicable regulations for clinical research involving investigational devices. Validation data from one of the clinical studies is pending. Therefore, FDA excluded the data from that site for clinical performance evaluation. The clinical trial data from the remaining sites are sufficient to make a determination of safety and effectiveness of this device.

16. CONCLUSIONS DRAWN FROM PRECLINICAL AND CLINICAL STUDIES

a. Effectiveness Conclusions

The Clinical performance and non-clinical study results support the effectiveness of INSTI HIV Self Test for the diagnosis of HIV infection in the previously undiagnosed intended users. Both PPA (sensitivity) as well as NPA (specificity) results demonstrated 100% concordance between the HIV Self Test performed by lay intended users and the approved, professional use PoC INSTI HIV-1/HIV-2 Antibody Test performed by a trained operator. Further support of the effectiveness of the INSTI HIV Self Test is provided by the outside the U.S. INSTI HIV Self Test results, the CLIA-waiver study results, and the baseline INSTI HIV-1/HIV-2 Antibody Test clinical sensitivity and specificity results, which met the Special Control requirements of 21 CFR 866.3956 of a lower bound of the 95% CI of ≥ 98%.

However, as HIV prevalence is low in the U.S. it is difficult to get new HIV infection from the previously undiagnosed HIV infection. CBER considered 23 new diagnoses, combined with the new diagnoses obtained outside the U.S. for this device, sufficient to demonstrate acceptable clinical sensitivity of the device in the hands of untrained users.

In addition, five new diagnoses in the unobserved study support the value of the INSTI HIV Self Test for detecting new diagnoses in previously untested individuals.

b. Safety Conclusions

The risks of the device are based on the analytical studies conducted for the INSTI HIV-1/HIV-2 Antibody Test as well as data collected in clinical studies conducted to support PMA approval as described above.

Based on the results of the clinical studies, the INSTI HIV Self Test, when used according to the labeling, is safe to use and poses minimal risk to the patient due to false test results. However, 2–4% of the participants were unable to obtain interpretable results, as found in observed and unobserved clinical studies. Based on the observations during the observed clinical study, bioLytical updated the IFU with proper schematic diagrams to mitigate the risk and reduce the use errors. To guide the users regarding proper usage of this test, relevant limitations were included in the IFU and a training video which demonstrates the entire test procedure was provided. No significant adverse events were observed in any of the clinical studies conducted.

c. Benefit-Risk Determination

The probable benefits of the device are also based on data collected in clinical studies conducted to support PMA approval as described above. An easily accessible over the counter rapid test for self-testing with fingerstick whole blood provides significant advantages for testing individuals who are engaged in high-risk activities. If the individual turned out to be HIV positive by INSTI HIV Self Test, they could seek further confirmatory testing and immediate medical care. Additionally, if the individuals are aware of their status, they may take appropriate precautions to reduce the transmission of infection. This is helpful to patients and public health surveillance initiatives.
The risk of false reactive or false non-reactive results with the INST HIV Self Test is small, as demonstrated by clinical studies. If the test procedure is not followed as indicated in the IFU, the individual may get an invalid test result and need retesting. Overall, findings of the clinical studies indicates that the benefits of INSTI HIV Self Test outweigh the risks associated with its use.

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.

17. POST-APPROVAL REQUIREMENTS:

CBER issued an approval order on October 9, 2025. The final conditions of approval cited in the approval order are described below:
From the customer support/technical support, bioLytical will collect information on the number of individuals reporting positive results, negative results, unknown results, and demographic information as well as problems or issues with the test. bioLytical will provide this information annually in PMA Post-Approval Study Reports.

18. 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.

19. FDA/CBER DECISION

The PMA BP251179 is recommended for approval.