

Value Framework Overview

In response to the growing need to demonstrate how diagnostic tests and technologies fit into the emerging value-based paradigm for providers, payers, and patients, AdvaMedDx launched a Strategic Value Initiative to develop an approach to value assessment for diagnostic tests and technologies that can be used by Medical technology companies as well as by health systems, payers, and other stakeholders.¹

The AdvaMedDx Value Assessment approach goes beyond traditional Health Economic Outcomes Research (HEOR) and clinical efficacy metrics to assess the value that diagnostic tests and technologies may contribute to improving patient care and experience, economic outcomes, and the overall health of populations. This approach uses four broad categories, or “value drivers,” to describe the value of diagnostic tests and technologies: clinical impact, non-clinical patient impact, care delivery revenue and cost impact, and public/population impact relevant to an array of stakeholders who may evaluate and measure value differently.

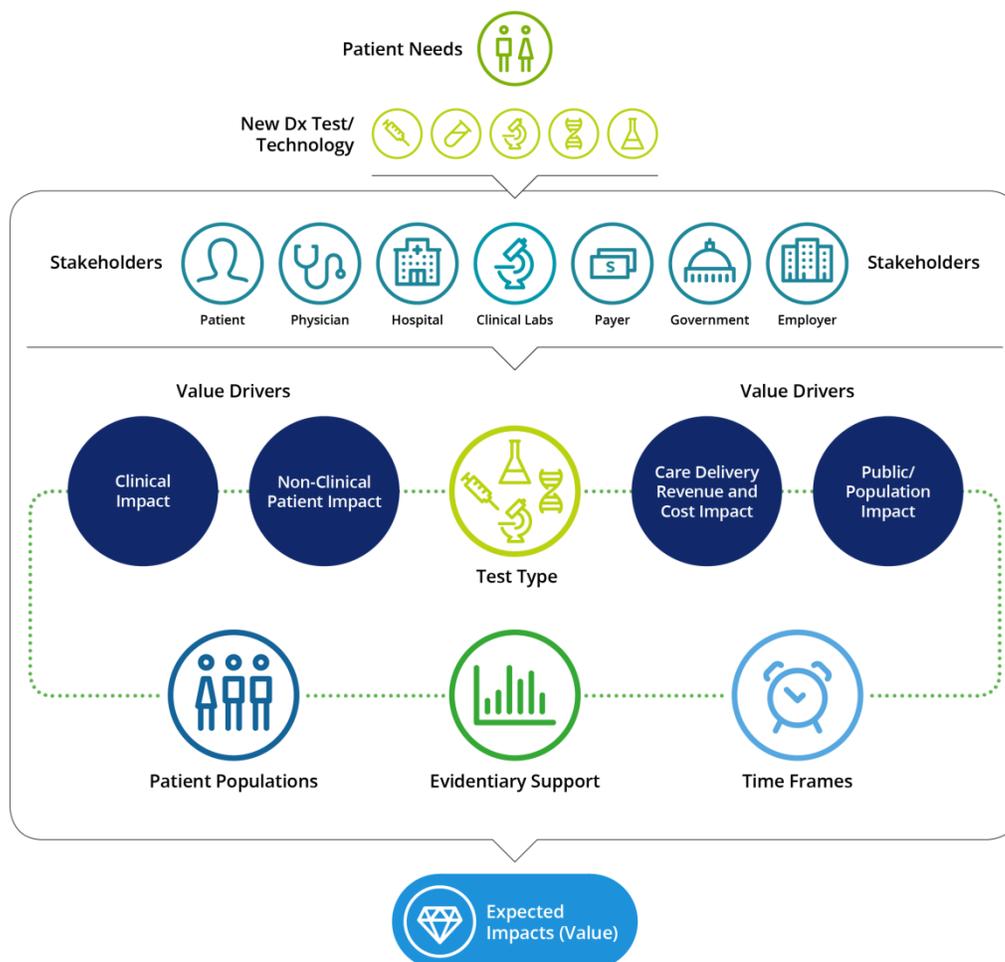
The AdvaMedDx Value Assessment approach can be used to guide the development of a value proposition that successfully communicates the full breadth of expected impacts offered by diagnostic tests and technologies while taking into account the demands of the changing health care ecosystem. The collection of information associated with the value drivers reflects quantitative and qualitative metrics of value, gives appropriate weight to patient experience and societal impacts, and also accounts for the consideration of evidence collected through a variety of methods. An illustration highlighting the value drivers and components of AdvaMed’s approach is on the following page.

In order to demonstrate the application of this framework across different types of diagnostic tests and technologies, AdvaMedDx has partnered with member companies to develop use cases. These use cases address the clinical need for the diagnostic test or technology, alternative and existing technologies on the market, the expected impacts of the diagnostic test or technology, and the evidence to support such a value assessment. The use cases have been developed as a way to directly demonstrate the application of the AdvaMedDx Value Framework to the featured diagnostic test and should not be construed as an endorsement or promotion thereof.

Abbott

This use case demonstrates the value of Abbott’s 4th generation ARCHITECT HIV Antigen/Antibody combo (ARCHITECT HIV Ag/Ab Combo) test across all of the identified value drivers and for a range of stakeholders. The test works by simultaneously detecting HIV p24 antigen and antibodies to both HIV Type 1 and/or HIV Type 2 in human serum and plasma. It is intended for use as an aid in diagnosis of HIV-1/HIV-2, including acute/primary HIV-1 infection, in subjects age two and up and in pregnant women.

Illustration of AdvaMedDx Value Assessment Approach



Source: "A Framework for Comprehensive Assessment of the Value of Diagnostic Tests", co-developed with Deloitte Consulting LLP

Abbott ARCHITECT HIV Antigen/ Antibody Combo Test



Diagnostic test developers with a new product concept in development should start early, not only to address the FDA requirements, but also the value proposition that the diagnostic test conveys to patients, providers, and the health care system.

This use case demonstrates the value of Abbott's 4th generation ARCHITECT HIV Antigen/Antibody combo (ARCHITECT HIV Ag/Ab Combo) test across all of the identified value drivers and for a range of stakeholders.

There are three types of diagnostic tests for HIV: antibody tests, nucleic acid tests (NATs), and combination tests such as Abbott's ARCHITECT HIV Ag/Ab Combo assay.² Antibody tests detect the presence of antibodies, which typically reach detectable levels within 3-12 weeks after infection. Most rapid tests and home tests are antibody tests. NATs are the fastest type of HIV testing and are capable of detecting HIV 1-4 weeks after infection; however, the expense associated with the tests limits their use in diagnostic laboratories. Combination tests look for both HIV antibodies and antigens. Because antigens are present during the acute phase of HIV infection, combination tests can detect HIV 2-6 weeks after infection.³

Abbott's ARCHITECT HIV Ag/Ab Combo assay is a fourth generation test that simultaneously screens for both types of HIV antibodies (Type 1 and Type 2) and HIV-1 p24 antigen using a blood sample from the patient.

The ARCHITECT HIV Ag/Ab Combo assay is not intended for use in screening blood, plasma, or tissue donors, but may be used as a blood donor screening assay in urgent situations where other tests are unavailable or their use is impractical.



Unmet Need

AdvaMedDx's assessment process begins with understanding and addressing the unmet need and value imparted through the new diagnostic test.

Unmet patient need can be framed in terms of clinical validity, clinical utility, access, patient preferences, costs, quality of care, ease of use, etc.

At the end of 2013, there were an estimated 1.2 million people living with human immunodeficiency virus (HIV) in the United States.⁴ According to the CDC, approximately 1 in 8 (13%) of all people infected with HIV in the US do not know they are infected. In young people aged 13-24, the number is even higher, with 1 in 2 (51%) unaware of their HIV infection.⁵ Those who do not know their HIV status continue to spread the disease, accounting for approximately 30% of new infections.⁶ Testing and early diagnosis is critical to preventing new infections.

The US Preventative Services Task Force recommends that clinicians screen for HIV infection in adolescents and adults aged 15-65 years and all pregnant women.⁷



Patient Populations

Assessments should consider the extent to which a diagnostic test may be more or less effective for various patient populations and align with the population focus of the stakeholder evaluating the test.

This section demonstrates the value of the diagnostic test to patients by addressing the need for the test in the context of the affected patient sub-population and the available alternatives to treat their condition.

The ARCHITECT HIV Ag/Ab Combo assay can detect HIV infection earlier than tests that only detect antibodies, enabling detection of HIV up to 20 days earlier, when compared to an antibody test.⁸

This improved time to detection is critical to all groups of people with HIV. It allows people to prevent transmission of HIV to others and start treatment that improves quality of life and survival. It is also critical for pregnant women who, once diagnosed, receive treatment that may reduce the risk of transmitting HIV to their unborn child.

In addition to shortening the length of time to diagnosis, the ARCHITECT HIV Ag/Ab Combo assay may also shorten the time between testing and reporting of the first test result. Results from the ARCHITECT HIV Ag/Ab Combo test are available less than 30 minutes after test initiation on the instrument, which can allow patients to receive results before leaving the site of testing—potentially improving patient compliance and follow-up.



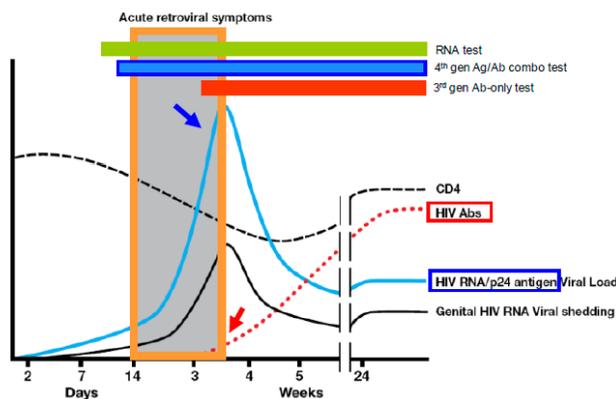
Time Frames

The assessment should identify time frames that are important in understanding the value of the diagnostic test.

HIV infection can be divided into three stages: acute infection, clinical latency, and acquired immunodeficiency syndrome (AIDS).⁹

- Acute HIV infection occurs within the first few weeks following infection. Within two to four weeks after infection, people with acute HIV infection have extremely high viral loads and may or may not experience symptoms resembling a flu-like virus. During this time, they are highly contagious. Because they may or may not have symptoms, people with acute HIV are often unaware they are infected and may spread HIV. This is a time period in which it is important that patients are tested so they can take steps to reduce the spread of HIV to others and begin treatment.
- Clinical latency (also called asymptomatic or chronic HIV infection) is the phase during which HIV is still active but reproduces at low levels. People in this stage who are being

The Phases of HIV and Diagnostic HIV Assays



Adapted from: Marquez, MLO February 2008, "HIV Testing: An Update."

treated with antiretroviral medications (ART) and have low levels of virus in their blood are less likely to transmit HIV to others, though it is still possible. This stage can last for a decade or longer.

- People with HIV progress to acquired immunodeficiency syndrome (AIDS) once their viral loads increase and their CD4 cell counts drop below a certain level. People with AIDS often acquire

opportunistic infections as a result of their damaged immune systems. They can have a high viral load and can be very infectious.

Early diagnosis is critical to avoiding the spread of HIV by someone who does not know his or her infection status. The early diagnosis of HIV is also critical to reducing healthcare costs. In 2015, there were almost 40,000 new cases of HIV diagnosed in the US.¹⁰ The lifetime cost of HIV infection treatment and care is estimated to be \$379,668 per person.¹¹ Early diagnosis can reduce the spread of HIV and the number of new cases, avoiding those lifetime costs for people who otherwise may become infected. People who get an early HIV-positive diagnosis may receive treatment that suppresses their viral loads and allows them to continue in the workforce. Treatment may also help these patients avoid opportunistic infections, which can reduce both immediate and long-term health system costs. These factors reduce the economic burden of HIV.



Stakeholders

The intended audience for a value assessment affects the framing of the assessment and the drivers and metrics that could be highlighted.

Both the intended audience/stakeholders and the purpose of the assessment should dictate which types of value are considered and emphasized via the assessment process, as well as the types and quality of evidence needed to support evidence development needs and appropriate strategies for collecting annual performance information.

It is important for stakeholders to consider the full range of value drivers and impacts.

The chart on the following page highlights potential value for various stakeholders based on use of the Abbott ARCHITECT HIV Ag/Ab Combo test in regular testing for HIV:

Abbott ARCHITECT HIV Ag/Ab Combo Test Value Drivers Impact by Stakeholder

	Clinical Impact	Non-Clinical Impact	Care Delivery Revenue and Cost Impact	Public/Population Impact
Patient	<ul style="list-style-type: none"> • 100% sensitivity (post-seroconversion) to correctly identify those with HIV¹² • 99.77% specificity to correctly identify those without HIV (post-seroconversion)¹³ • 89.1% sensitivity during acute phase (compared to 42.4% for 3rd gen. antibody test), allowing for earlier diagnosis¹⁴ • Allows for earlier start of ART if HIV positive, which may reduce risk of transmission to uninfected partner by up to 96%¹⁵ • Low risk of adverse reaction (risk typical of any dx blood test) • Fewer retests needed due to high clinical validity • Confirmatory testing performed on positive test results 	<ul style="list-style-type: none"> • Ability to be tested in a variety of healthcare settings (inpatient, outpatient, etc.) • Results obtained in under 30 minutes, so patients may receive results prior to leaving the site of testing • Improved patient compliance and follow-up due to availability of same-day result 	<ul style="list-style-type: none"> • Earlier diagnosis can lead to earlier initiation of treatment, which may reduce need for further doctor's office and hospital visits • Lower out of pocket costs for testing than with NATs • Potentially reduced costs associated with adverse events or retesting 	<ul style="list-style-type: none"> • Earlier detection and treatment may lead to longer life expectancy and higher quality of life • Earlier detection allows for earlier treatment to control HIV, which may allow patient to continue working and reduce absenteeism and presenteeism • Fewer missed cases compared to testing with antibody tests or NATs that may miss individuals during or at the end of the acute phase • Potentially lower overall individual healthcare cost due to increased awareness of disease status and earlier treatment • Earlier detection may lead to less transmission and reduced incidence of HIV
Doctor	<ul style="list-style-type: none"> • Provides ability to detect HIV earlier and intervene earlier than 3rd generation antibody tests • Low risk of adverse reaction (risk typical of any dx blood test) • Allows for earlier start of ART if HIV positive, which may reduce risk of transmission to uninfected partner by up to 96%¹⁶ • Informs need for treatment 	<ul style="list-style-type: none"> • No special training needed to administer test • Results obtained in 30 minutes of test initiation, so patient can be counseled before leaving office or test setting • Potentially improved patient compliance and follow-up due to availability of same-day result 	<ul style="list-style-type: none"> • Can be performed in outpatient settings • Earlier diagnosis can lead to earlier initiation of treatment, which may reduce need for further doctor's office and hospital visits • Potentially reduced costs associated with adverse events or retesting 	<ul style="list-style-type: none"> • Earlier detection may lead to less transmission and reduced incidence of HIV
Hospital/Outpatient Clinic	<ul style="list-style-type: none"> • Provides ability to detect HIV earlier and intervene earlier than 3rd generation antibody tests • Low risk of adverse reaction (risk typical of any dx blood test) 	<ul style="list-style-type: none"> • Potentially improved patient compliance and follow-up due to availability of same-day result • No special training needed to administer test 		<ul style="list-style-type: none"> • Earlier detection may lead to less transmission and reduced incidence of HIV

	Clinical Impact	Non-Clinical Impact	Care Delivery Revenue and Cost Impact	Public/Population Impact
Insurer	<ul style="list-style-type: none"> Provides ability to detect HIV earlier and intervene earlier than 3rd generation antibody tests Low risk of adverse reaction (risk typical of any dx blood test) 	<ul style="list-style-type: none"> Potentially improved patient compliance and follow-up due to availability of same-day result 	<ul style="list-style-type: none"> Less expensive testing method than NATs Earlier diagnosis can lead to earlier initiation of treatment, which may reduce further doctor's office and hospital visits Lower overall healthcare costs due to increased awareness of disease status, potentially fewer transmissions, and fewer missed cases 	<ul style="list-style-type: none"> Earlier detection may lead to less transmission and reduced incidence of HIV



Evidence Across the Value Drivers

Diagnostic test innovators must determine the best way to show value with evidence. This can vary based upon the type of test.

It is critical to identify and evaluate the quantity and quality of available types of evidence for the diagnostic test early in product development and on an ongoing basis to determine how it can be used across the relevant drivers to offer robust evidentiary support.

Abbott's evidence focuses on the ARCHITECT HIV Ag/Ab Combo assay's clinical validity and ability to detect HIV infection earlier than antibody-only test methods. Abbott has conducted its own non-clinical and clinical studies, and has contributed and co-authored a number of published studies that use the ARCHITECT HIV Ag/Ab Combo test. Abbott also supported an economic modeling study that examined both the clinical implications and cost-effectiveness of their testing method.

The chart on the following page applies to patients tested for HIV using the ARCHITECT HIV Ag/Ab Combo Assay:

ARCHITECT HIV Ag/Ab Combo Assay Test Value Drivers by Evidence Source

Evidence	Type of Evidence	Clinical Impact	Non-Clinical Impact	Care Delivery Revenue and Cost Impact	Public/Population Impact
Abbott Safety and Effectiveness Data¹⁷	Clinical Study	<ul style="list-style-type: none"> High sensitivity and specificity for both low and high risk populations and all patient groups (pregnant women, children, etc.) Reduced time to detection of HIV by up to 20 days (compared to 3rd generation antibody test) 			
Health Economics Modeling Study (published)¹⁸	Health Economic Modeling/Analysis	<ul style="list-style-type: none"> Earlier detection of HIV with 4th generation test (ARCHITECT) More HIV cases detected with ARCHITECT than 3rd generation antibody test 		<ul style="list-style-type: none"> 4th generation assay is cost-effective method for detecting HIV in appropriate settings 	<ul style="list-style-type: none"> Earlier detection and treatment may lead to fewer transmissions, longer life expectancy, and higher quality of life
Analysis of HIV diagnosis algorithm¹⁹	Clinical Study	<ul style="list-style-type: none"> ARCHITECT assay able to detect HIV up to 20 days before positive antibody tests High sensitivity for HIV ARCHITECT increased detection of HIV results compared to 3rd generation tests 			
Detection of HIV-1 study²⁰	Clinical Study	<ul style="list-style-type: none"> 61.9% sensitivity for acute infections (compared to 14.3% by 3rd generation test) Detects acute and chronic infections in a single step 	<ul style="list-style-type: none"> Results delivered to patients faster than NATs 	<ul style="list-style-type: none"> ARCHITECT has lower cost than NATs Less laboratory labor required than for NATs 	
Assessment of ARCHITECT HIV Ag/Ab²¹ Combo assay in high-risk setting	Clinical Study	<ul style="list-style-type: none"> ARCHITECT capable of providing positive result in absence of HIV antibodies Detected 85.7% of acute infections incorrectly diagnosed by 3rd generation test 			



Expected Impacts (Value)

The value assessment should clearly demonstrate the impact of the diagnostic test across select value drivers including clinical impact, non-clinical patient impact, care delivery revenue and cost impact, and patient/population impact.

These impacts would be offset by the cost of acquiring the technology to derive the total expected value impacts.

Clinical Impact Value – Abbott’s ARCHITECT HIV Ag/Ab Combo assay provides benefits to both the patient using the test and the clinician and healthcare systems involved in that patient’s care. The ARCHITECT HIV Ag/Ab Combo test has high sensitivity and specificity for HIV and can test for both acute and chronic infections simultaneously. The test’s improved ability for detecting acute infections compared to 3rd generation antibody tests allows patients to be diagnosed sooner and to receive treatment faster than with other testing methods. The risk of adverse reactions to the test is low, and results are available quickly.

Non-Clinical Impact Value – The ARCHITECT HIV Ag/Ab Combo test has a wide range of beneficial non-clinical impacts for a range of stakeholders. Additionally, the test can be administered in a range of settings and the quick time-to-result allows patients to receive results while still in the healthcare setting where they were tested—potentially improving patient compliance and follow-up.

Care Delivery Revenue and Cost Impact Value – The ARCHITECT HIV Ag/Ab Combo may generate both short and long term healthcare system cost savings. The ARCHITECT HIV Ag/Ab Combo test may be less expensive to the patient, healthcare setting, and insurer than other test methods that cannot detect HIV in the acute phase. An earlier diagnosis can lead to earlier initiation of treatment, which may reduce the need for additional healthcare visits and treatments. In addition, the ARCHITECT HIV Ag/Ab Combo test requires no additional training for healthcare providers, less laboratory labor than NATs, and its high clinical validity reduces the need for and costs associated with retesting—creating lower costs for both the patient and hospital.

Public/Population Impact Value – The ARCHITECT HIV Ag/Ab Combo test has likely beneficial societal impact through earlier identification and treatment, potentially leading to reduced new incidences of HIV and lowered burden of disease on society. An accurate diagnosis during the acute phase is also critical in preventing the transmission of HIV to uninfected individuals.

¹ "A Framework for Comprehensive Assessment of the Value of Diagnostic Tests", co-developed with Deloitte Consulting LLP, available at www.advamed.org and co-developed with Deloitte Consulting LLP

² "HIV Testing." CDC.

³ Ibid

⁴ "HIV/AIDS Basic Statistics." Centers for Disease Control and Prevention.

⁵ Ibid

⁶ "HIV Testing." Centers for Disease Control and Prevention.

⁷ "Human Immunodeficiency Virus (HIV) Infection: Screening." U.S. Preventive Services TASK FORCE.

⁸ "Summary of Safety and Effectiveness Data - Abbott ARCHITECT HIV Ag/Ab Combo PMA." US Food and Drug Administration.

⁹ "About HIV/AIDS." Centers for Disease Control and Prevention.

¹⁰ "HIV/AIDS Basic Statistics." CDC.

¹¹ "HIV Cost-effectiveness." Centers for Disease Control and Prevention.

¹² Cragin et al. "Cost-effectiveness of a Fourth-Generation Combination Immunoassay for Human Immunodeficiency Virus (HIV) Antibody and p24 Antigen for the Detection of HIV Infections in the United States." *HIV Clinical Trials* 13. 1 (2012): 11-22.

¹³ Ibid

¹⁴ Ibid

¹⁵ Cohen et al. "Prevention of HIV-1 Infection with Early Antiretroviral Therapy." *The New England Journal of Medicine* 365.6 (2011): 493-505.

¹⁶ Ibid

¹⁷ "Summary of Safety and Effectiveness Data - Abbott ARCHITECT HIV Ag/Ab Combo PMA." FDA.

¹⁸ Cragin et al. "Cost-effectiveness of a Fourth-Generation Combination Immunoassay for Human Immunodeficiency Virus (HIV) Antibody and p24 Antigen for the Detection of HIV Infections in the United States." *HIV Clinical Trials* 13. 1 (2012): 11-22.

¹⁹ Masciotra et al. "Evaluation of an alternative HIV diagnostic algorithm using specimens from seroconversion panels and persons with established HIV infections." *Journal of Clinical Virology* 52.1 (2011): 17-22.

²⁰ Eshleman et al. "Detection of Individuals With Acute HIV-1 Infection Using the ARCHITECT HIV Ag/Ab Combo Assay." *Journal of Acquired Immune Deficiency Syndromes* 52. 1 (2009): 121-124.

²¹ Pandori et al. "Assessment of the Ability of a Fourth-Generation Immunoassay for Human Immunodeficiency Virus (HIV) Antibody and p24 Antigen To Detect both Acute and Recent HIV Infections in a High-Risk Setting." *Journal of Clinical Microbiology* 47.8 (2009): 2639-2642.

AdvaMedDx Value Assessment Framework *in Practice*

Abbott- 4th Generation ARCHITECT HIV Antigen/Antibody Combo Test

At the end of 2013, there were an estimated 1.2 million people living with human immunodeficiency virus (HIV) in the United States. According to the CDC, approximately 1 in 8 (13%) of all people infected with HIV in the US do not know they are infected. In young people aged 13-24, the number is even higher, with 1 in 2 (51%) unaware of their HIV infection. Those who do not know their HIV status continue to spread the disease, accounting for approximately 30% of new infections. Testing and early diagnosis is critical to preventing new infections.



Patient Needs



New Dx Test/ Technology



Stakeholders



Patient



Physician



Hospital



Clinical Labs



Payer



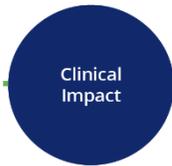
Government



Employer

Stakeholders

Value Drivers



Clinical Impact

- High sensitivity
- Allows earlier start of treatment
- Low risk of adverse reaction
- Fewer retests needed



Non-Clinical Patient Impact

- Testing in a variety of healthcare settings
- Results in under 30 minutes
- Improved patient compliance



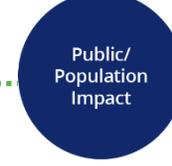
Test Type



Care Delivery Revenue and Cost Impact

- Lower out of pocket costs than NATs
- Reduced need for additional doctors visits
- Reduced retesting costs

Value Drivers



Public/Population Impact

- May reduce transmission and incidence of HIV
- May decrease individual overall costs due to earlier treatment and status awareness
- Reduced absenteeism and presenteeism



Patient Populations

- People with all phases of HIV infection



Evidentiary Support

- Safety and Effectiveness Data
- Health Economic Modeling Study
- Analysis of HIV diagnosis algorithm
- Detection of HIV-1 Study
- Assessment of ARCHITECT HIV Ag/Ab Combo assay in high-risk setting



Time Frames

- Detecting all stages of HIV:
 - Acute infection
 - Clinical latency
 - AIDS



Expected Impacts (Value)

- Earlier diagnosis
- Faster treatment
- Reduced risk of adverse reaction
- Quick results
- Earlier initiation of treatment
- Improved patient compliance and follow-up
- Healthcare savings: short and long term
- Lower costs than some other acute phase tests
- Reduced patient visits
- Lower costs to patients and hospitals
- Less missed work