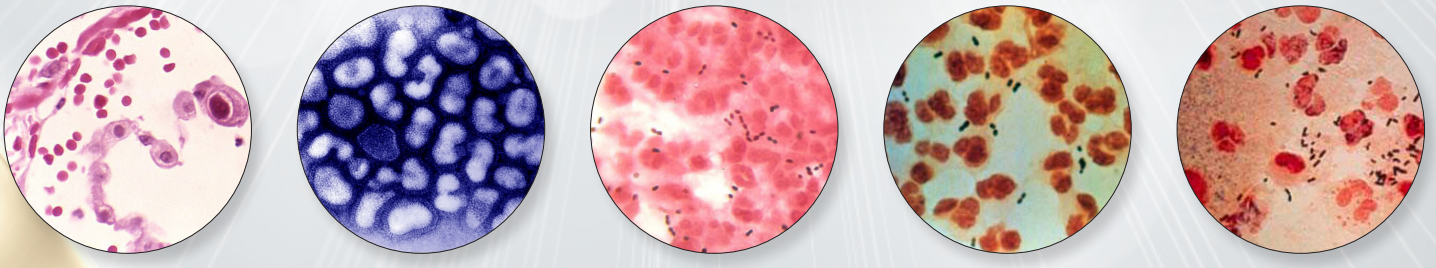
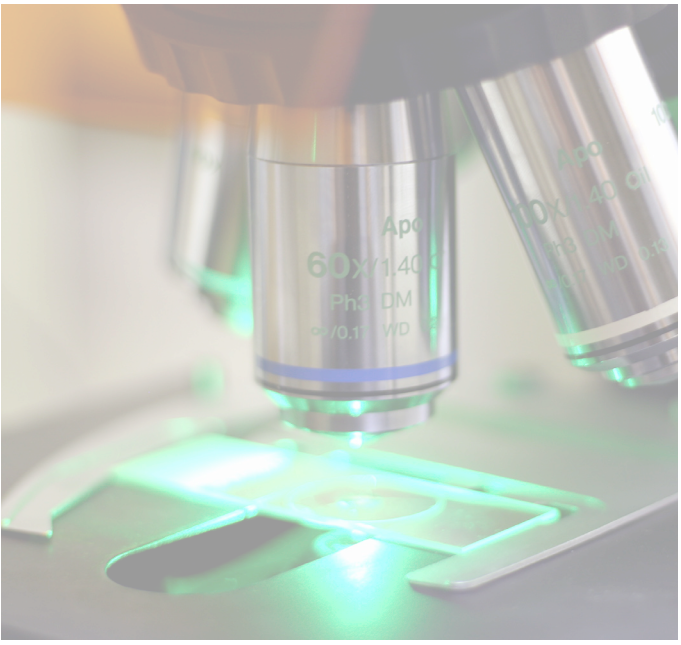
Medical Diagnostic Laboratories

A MEMBER OF GENESIS BIOTECHNOLOGY GROUP

Reference Guide for Available Tests





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A DIVISION OF GENESIS® CLINICAL DIAGNOSTICS

Medical Diagnostic Laboratories
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Specimen Guidelines

Proper collection, processing, and transport of specimens are vital to ensure specimen integrity for laboratory testing. Specific specimen requirements are listed under each test in the Test Listing sections. To avoid delays in testing/diagnosis and to prevent potential specimen rejection, be sure to follow these requirements when collecting a particular specimen. Upon receipt of a specimen, the condition of each sample will be assessed by laboratory personnel using specific guidelines to identify improper or inadequate specimens that offer the possibility of inaccurate results. Any sample that does not meet the acceptance criteria will be deemed suboptimal. All suboptimal specimens shall be evaluated by the Department of Quality Assurance & Quality Control.

Acceptance Criteria:

- Requested test is performed in this Laboratory.
- Sample is received in good condition and in the appropriate collection/transport vessel.
- Patient identifiers on sample match patient identifiers on the requisition.
- Sample is received at the proper temperature after transport.
- Sample is labeled with at least two patient identifiers.
- Sample is of sufficient volume.
- There is sufficient DNA following the extraction process for the test(s) to be performed.

Samples that meet the acceptance criteria, but are deemed to be suboptimal, may continue to be processed. As suboptimal sample conditions may impact test performance, a report will be sent to the referring health care provider detailing the suboptimal specimen condition(s). In the event that corrective action is possible, the referring health care provider may be contacted by our Specimen Resolution Center (SRC) for additional information or instruction.

Suboptimal Specimen Conditions:

- Tests requested are not appropriate for the specimen type received.
- Sample is received in an inappropriate collection/transport vessel.
- Blood is hemolyzed or lipemic depending on the particular test(s) ordered.
- Specimen is not received at the proper temperature.
- Sample is not labeled with at least two patient identifiers.
- Sample is of insufficient volume.

A repeat sample will only be requested in instances whereby the suboptimal specimen condition will negatively impact testing. Rejected specimens will not be processed further. A report will be generated to notify the referring health care provider of the reasons for the specimen rejection and a new sample may be requested, if appropriate. Please note, in the instance of irretrievable specimens, where recollection is NOT an option, the suboptimal criteria will be brought to the attention of the Director of Quality Control and will be reviewed on a case-by-case basis.

Specimen Labeling:

The College of American Pathologists (CAP) guidelines state that all primary clinical specimen containers should be labeled with two patient identifiers at the time of specimen collection. These identifiers must correspond to information provided on the test requisition form or accompanying documents. We will note on the result report when a specimen was received without the required two patient identifiers.

Preferred first identifier	Patient's first & last name
Preferred second identifier	Patient date of birth
Other acceptable identifiers	Social security number Requisition number Patient identification number Medical record number Accession number Unique random number
Additional desirable information	Date of collection Time of collection Specimen type Specimen source

Specimen Requirements

Biopsy (Formalin-fixed)

Collection vessel:	Sterile non-additive container with buffered formalin
Volume:	Minimum size requirement 1mm x 1mm section
Transport Conditions:	Stable at room temperature.
Collection Notes:	• Please list specimen source on the container and test requisition form. • Do not use the yellow top (ACD solution A) blood collection tubes.

Biopsy (fresh)

Collection vessel:	Sterile non-additive container with PBS buffer or sterile normal physiological saline solution.
Volume:	Minimum size requirement is 1mm X 1mm section.
Transport Conditions:	Stable at room temperature.
Collection Notes:	• Please list specimen source on the container and test requisition form. • Do not use the yellow top (ACD solution A) blood collection tubes.

Biopsy (paraffin block)

Collection vessel:	Sterile non-additive container
Volume:	Shave 5-7 sections of a paraffin block and place in a sterile container.
Transport Conditions:	Stable at room temperature.
Collection Notes:	• Please list specimen source on the container and test requisition form. • Do not use the yellow top (ACD solution A) blood collection tubes.

Cerebrospinal Fluid (CSF)

Collection vessel:	Sterile non-additive container.
Volume:	Minimum 1ml
Transport Conditions:	Stable at room temperature.
Collection Notes:	• Please list specimen source on the container and test requisition form. • Do not use the yellow top (ACD solution A) blood collection tubes.

NasoSwab®

Collection vessel:	Complete
Volume:	N/A
Transport Conditions:	Stable at room temperature.

OneSwab®

Collection vessel:	Complete
Volume:	N/A
Transport Conditions:	Stable at room temperature.

COVID-*OneSwab*®

Collection vessel:	Complete
Volume:	N/A
Transport Conditions:	Stable at room temperature.

Saliva

Collection vessel:	Saliva DNA self-collection vial with attached funnel
Volume:	N/A
Transport Conditions:	Stable at room temperature.
Collection Notes:	• Vigorously rinse your mouth with clean water 5 minutes prior to specimen collection (30 minutes prior is ideal). • After rinsing, do not brush your teeth, use mouthwash, eat, drink, chew gum or smoke prior to sample collection

Serum

Collection vessel:	• Serum separator tube (SST) • Red/gray or tiger top tube containing clot activator and gel for serum separation.
Volume:	Complete is preferred. Minimum volume is 1ml.
Transport Conditions:	Stable at room temperature.
Collection Notes:	• Immediately after blood collection, invert the tube(s) gently 5 times to ensure mixing of clot activator with blood. • Allow the tube to rest in an upright position for at least 30 minutes but not longer than 1 hour after collection to ensure proper clotting. • Centrifuge for at least 15 minutes at 2200-2500 RPM within one hour of collection. • Do not remove the stopper or pour off serum.

Synovial Fluid

Collection vessel:	Sterile non-additive container.
Volume:	Minimum 1ml
Transport Conditions:	Stable at room temperature.
Collection Notes:	• Please list specimen source on the container and test requisition form. • Do not use the yellow top (ACD solution A) blood collection tubes.

ThinPrep®

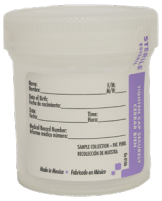
Collection vessel:	Complete
Volume:	N/A
Transport Conditions:	Stable at room temperature.

Tick

Collection vessel:	Clean non-additive container or zip-lock bag.
Volume:	N/A
Transport Conditions:	Stable at room temperature.
Collection Notes:	• Ticks can be submitted alive or dead. • Do not place in alcohol, burn, or place on tape. • Ticks are consumed during the extraction process and therefore cannot be returned after testing. • Turnaround time for tick testing is typically 3-5 days but may vary.

UroSwab®

Collection vessel:	Complete
Volume:	N/A
Transport Conditions:	Stable at room temperature.



Urine Collection Cup

Collection vessel:	Sterile Collection Cup
Volume:	Minimum volume of 33 mL required, 60 mL desired
Transport Conditions:	Stable at room temperature.
Collection Notes:	• Collect a second morning, clean-catch voided urine. • Store in refrigerator (4°C) until ready for transport • Pre-freeze cold packs flat to ensure fit in transport box • Do not collect/ship urine specimens on a Saturday

Whole Blood

Collection vessel:	Yellow top tube (ACD solution A)
Volume:	Complete
Transport Conditions:	Stable at room temperature.
Collection Notes:	• Completely fill the tube whenever possible to eliminate dilution from the anticoagulant and ensure the proper blood-to-anticoagulant ratio. • Immediately after blood collection, invert the tube(s) gently 8-10 times to ensure mixing of anticoagulant with blood to prevent clotting. • Do not shake tube(s). • Do not centrifuge specimen.

369 *Acinetobacter baumannii* by Real-Time PCR

Clinical significance: *Acinetobacter baumannii* is an aerobic, Gram-negative bacterium that is resistant to most antibiotic treatments and is responsible for many hospital patient deaths, the first case being linked directly to wounded soldiers returning from the Iraq war. An emerging, opportunistic, multi-drug resistant bacterium, *Acinetobacter baumannii* infection cases are expected to rise and have the potential to become the next superbug with a magnitude and scope similar to that of MRSA. *A. baumannii* is associated with long term wound, skin and soft tissue infections, catheter-associated UTIs, ventilator associated infections, bloodstream infections, surgical site infections, and co-infections with other bacteria, such as MRSA, is common. Those with compromised immunity are at greatest risk of infection. A few studies have looked for *A. baumannii* as well as MRSA colonization of anterior nares, skin, sputum, perianal, wounds, etc. This can be an environmental contaminant of hospitals and long-term care facilities. Colonization of healthy individuals occurs in an asymptomatic fashion but poses an increased risk of dissemination throughout hospital wards.

Method: Real-Time PCR

Specimen: ***UroSwab***®, ***NasoSwab***®, whole blood yellow top tube (ACD solution A)

Transport: Stable at room temperature

150 *Actinomyces europaeus* by Real-Time PCR

Clinical significance: Although *Actinomyces* species can be found as normal flora of the mouth, they are also considered opportunistic pathogens in infections associated with human bite wounds, abscesses, infections of the eye and mouth, as well as the gastrointestinal, genital, and urinary tracts. *A. europaeus* has been associated with cystitis and is often recovered from abscesses of various body sites. In this assay, DNA is extracted from the specimen and subjected to PCR amplification.

Method: Real-Time PCR

Specimen: ***OneSwab***®, ***UroSwab***®

Transport: Stable at room temperature

143 *Actinomyces israelii* by Real-Time PCR

Clinical significance: *Actinomyces israelii* is a filamentous, anaerobic, Gram-positive bacterium. The infection begins as an inflammatory soft tissue mass, which can enlarge into an abscess-like swelling. All species of Actinomyces are normal commensal inhabitants of the oral and buccal cavities in humans. The anaerobic actinomycetes are not transmitted sexually and are not generally considered as part of the normal vaginal flora. Colonization in the female genital tract is stimulated greatly by the presence of a foreign body, such as intrauterine contraceptive devices (IUCDs), hairpins, and even surgical sutures. Colonization may be asymptomatic or minimally symptomatic, presenting only as shedding of actinomycotic granules into the vaginal fluid. The clinical presentation includes foul-smelling vaginal discharge, intermittent pelvic pain, abnormal bleeding and one or more pelvic masses. In the acute phase, pelvic abscesses are often unilateral, involving a single fallopian tube and ovary. Single or multiple abscesses may form in the uterine wall, usually surrounding an embedded IUCD. The most extensive disease may present with a frozen or woody pelvis demonstrating extensive adhesions and scarring as part of the inflammatory response. A subset of genital actinomyces cases will present with some abnormalities of vaginal fluids on Pap smear. Anaerobic actinomycetes are successfully cultured in only about 10% of those cases investigated, which makes molecular amplification techniques a more feasible option for the clinical diagnosis of vaginal actinomyces. The anaerobic actinomycetes are considered universally susceptible to penicillin, which is the drug of choice if antibiotic therapy is needed.

Method: Real-Time PCR

Specimen: ***OneSwab***®, *ThinPrep*®

Transport: Stable at room temperature

149 *Actinomyces turicensis* by Real-Time PCR

Clinical significance: *Actinomyces turicensis* is a Gram-positive facultative anaerobe that is a commensal part of the oropharynx, gastrointestinal and female genital tracts. Although *Actinomyces* species are not considered to be pathogenic by nature, but rather part of the normal flora, they are capable of colonizing and establishing pathogenic infections within neighboring tissues upon a breach in the integrity of the mucosal membranes that typically sequester them. This may result in the chronic condition Actinomycosis. *A. turicensis* is one of the more commonly isolated species of the genus Actinomyces known to induce the Actinomycosis, a condition which is characterized by abscess formation, tissue fibrosis, and draining sinuses. While, clinically, infections of the oral and cervicofacial region are the most common, Actinomycosis also frequently occurs within the thoracic, abdominopelvic, and central nervous system compartments.

Method: Real-Time PCR

Specimen: ***OneSwab***®, ***UroSwab***®, whole blood yellow top tube (ACD solution A)

Transport: Stable at room temperature

222 Adenovirus by Real-Time PCR

Clinical significance: Adenoviruses cause a number of self-limiting, but often highly infectious, diseases that affect multiple organs, most commonly those associated with the respiratory and genitourinary tracts. Adenovirus is a relatively harmless pathogen in healthy individuals, but can cause a variety of symptoms in young children and the immunocompromised. Transmission can occur from direct, person-to-person contact or through contact with a contaminated surface or object. Adenovirus infections are usually asymptomatic and may cause a variety of symptoms, including: respiratory problems, gastroenteritis, pink eye, pharyngoconjunctival fever, skin rashes, and genitourinary tract infections including cervicitis, urethritis and hemorrhagic cystitis. The most severe cases of adenovirus infection may result in pneumonia, croup, and bronchitis. In this assay DNA is extracted from the specimen and subjected to PCR amplification.

Method: Real-Time PCR

Specimen: ***UroSwab***®, ***NasoSwab***®, whole blood yellow top tube (ACD solution A)

Transport: Stable at room temperature

182 Aerobic Vaginitis (AV) Panel by Real-Time PCR (GBS, *S. aureus*, *E. coli*, *E. faecalis*)

127 Group B Streptococcus (GBS) by Real-Time PCR
153 *Enterococcus faecalis* by Real-Time PCR
141 *Escherichia coli* by Real-Time PCR
184 *Staphylococcus aureus* by Real-Time PCR

Clinical Significance: Aerobic Vaginitis (AV) is caused by aerobic pathogens triggering a localized vaginal inflammatory and immune response as evidenced by the clinical signs and symptoms including the presence of leukocyte infiltration marked by a depletion of healthy *Lactobacillus* species. Group B Streptococcus (GBS), *Staphylococcus aureus*, *Escherichia coli*, and *Enterococcus faecalis* are often associated with AV. Its characteristics are different from those of Bacterial Vaginosis (BV). It is a common ailment often experienced by women diagnosed with BV who are then treated with traditional metronidazole therapy. Approximately 20% of women treated with metronidazole will fail to respond to therapy and will experience a recurrence of symptoms. It is believed that a subset of these may have been misdiagnosed and actually suffer from AV. AV may be implicated in complications of pregnancy such as ascending chorioamnionitis, premature rupture of the membranes, and preterm delivery. In this assay, DNA is extracted from the specimen and subjected to PCR amplification.

Method: Real-Time PCR

Specimen: ***OneSwab***®, *ThinPrep*®

Transport: Stable at room temperature

142 *Atopobium vaginae* by Real-Time PCR

Clinical significance: *Atopobium vaginae*, a facultative, anaerobic bacteria, is the first of a group of previously unremarked microorganisms that has recently become associated with Bacterial Vaginosis (BV) following the advent of PCR-based diagnostics. Mounting evidence has demonstrated a direct link between the presence of *A. vaginae* and BV, a condition which left untreated, may lead to adverse conditions such as pelvic inflammatory disease, preterm birth, and postpartum endometritis. Abnormal vaginal micro flora has also been associated with increased susceptibility to HIV, *Chlamydia trachomatis*, and *Neisseria gonorrhoeae* infections. The detection of *A. vaginae* by PCR has been shown to be as sensitive for BV as the detection of *Gardnerella vaginalis* (96% and 99% respectively). However, *A. vaginalis* was demonstrated to be more specific for BV than is *G. vaginalis* (77% and 35% respectively). In this assay DNA is extracted from the specimen and subjected to PCR amplification.

Method: Real-Time PCR

Specimen: ***OneSwab***®, *ThinPrep*®

Transport: Stable at room temperature

164 Bacterial Vaginosis Associated Bacterium 2 (BVAB2) by Real-Time PCR

Clinical significance: The most common alteration in vaginal microflora is a condition named Bacterial Vaginosis (BV). Bacterial Vaginosis Associated Bacterium 2 (BVAB2) is one of several bacteria described as indicative diagnostic markers of BV. It has been reported that in one study BVAB2 was detected in more than 80% of women with BV. Detection of BVAB2 provides high sensitivity and specificity for the diagnosis of BV. In addition, elimination of BVAB2 by antibiotic therapy is associated with disease resolution and its persistence is associated with chronic disease. In this assay, DNA is extracted from the specimen and subjected to PCR amplification.

Method: Real-Time PCR

Specimen: ***OneSwab***®, *ThinPrep*®

Transport: Stable at room temperature

759 Bacterial Vaginosis (BV) Panel with Lactobacillus Profiling by qPCR

(*Atopobium vaginae*, BVAB1, BVAB2, BVAB3, *Bacteroides fragilis*, *Bifidobacterium breve*, Megasphaera Type 1 & 2, *Gardnerella vaginalis*, *Mobiluncus curtisii*, *M. mulieris*, *Prevotella bivia*, *Sneathia sanguinegens*, *Streptococcus anginosus*)

Clinical Significance: The healthy human vagina is associated with relatively low microbial diversity dominated by a few *Lactobacillus* species, including *L. crispatus*, *L. gasseri*, *L. jensenii* and *L. acidophilus*, which is also a probiotic bacteria commonly used to restore vaginal microbial balance. Bacterial vaginosis (BV) is a common vaginal disorder among women of reproductive age characterized by the replacement of these healthy, lactic acid-producing *Lactobacilli* by a more diverse bacterial composition dominated by "pathogenic," volatile amine-producing anaerobic bacteria such as *Atopobium vaginae*, BVAB1/2/3, *Bacteroides fragilis*, *Gardnerella vaginalis*, Megasphaera type 1/2, Mobiluncus, Prevotella, Sneathia, and *Steptococcus anginosus*. At times during the progression or treatment of BV, the vaginal microflora may be transitioning between health and dysbiosis. An intermediate Nugent score may indicate this transitional state, but it has more recently been described by disruption of the relative abundance of healthy versus pathogenic bacteria, such as *G. vaginalis* and *L. iners*, or the presence of specific bacteria, such as *Bifidobacterium breve*. Although more than 50% of women may be asymptomatic, dysbiosis characteristic of BV may cause vaginal discharge, the presence of clue cells and a "fishy" odor, as well as an increase in vaginal pH and a reduction of hydrogen peroxide levels. In addition to causing symptoms for some women, BV has been shown to increase the risk of preterm delivery as well as gynecologic complications such as endometritis, cervicitis and postoperative pelvic infections. Furthermore, reducing Lactobacilli may also promote bacterial and viral sexually transmitted infections such as *Chlamydia trachomatis*, *Neisseria gonorrhoeae*, HSV, HIV and HPV. Therefore, the proper diagnosis and treatment of BV is essential for women's health. As BV closely represents a polymicrobial infectious process involving species that differ among patients and overlapping symptoms with other vaginal disorders, it is critical for an accurate diagnosis to include a comprehensive selection of "pathogenic" bacteria when testing for BV. It also is important to

include the detection of *Lactobacilli* that support vaginal health, whether naturally occurring or introduced by probiotic use, as well as any bacteria that more accurately may indicate the transition between a stable, healthy state and BV.

Method: Real-Time PCR

Specimen: ***OneSwab***®, *ThinPrep*®

Transport: Stable at room temperature

125 *Bacteroides fragilis* by Real-Time PCR

Clinical significance: *Bacteroides fragilis* is an anaerobic bacterium that is commonly associated with Bacterial Vaginosis (BV). BV is a leading cause of abnormal vaginal discharge and odor. BV constitutes a massive microecologic alteration of the vaginal flora that is characterized by: (1) decreased or absent *Lactobacillus* species, (2) a logarithmically increased concentration of *Gardnerella vaginalis* (> 10^8 to 10^11 CFU/g) and (3) logarithmically increased concentrations of a set of potentially pathogenic bacteria, including *Bacteroides* species. In this assay, DNA is extracted from the specimen and subjected to Real-Time PCR amplification.

Method: Real-Time PCR

Specimen: ***OneSwab***®, *ThinPrep*®

Transport: Stable at room temperature

147 *Bacteroides ureolyticus* by Real-Time PCR

When sampling a crusted over lesion, moisten the swab with sterile saline solution prior to swabbing.

Clinical significance: *Bacteroides ureolyticus* is an obligate, anaerobic, Gram-negative, rod-shaped bacterium that was first described in clinical specimens in 1948. It is the most commonly detected Bacteroides strain after *B. fragilis*. Identification of this organism from infections within the buccal cavity, intestinal tract, urogenital tract, and blood has been reported. It has also been isolated from mixed cultures of infections involving nearly every organ system in humans. *B. ureolyticus* is associated with ulcerative lesions of both the external and internal genitalia, including the perineal area, as well as abscesses and has been implicated in non-gonoccocal urethritis (NGU); one study reported its identification in 50% of the evaluated men with confirmed NGU. It is thought to cause damage to the urethral mucosa via its expression of an endotoxin. In this assay, DNA is extracted from the specimen and subjected to PCR amplification.

Method: Real-Time PCR

Specimen: ***OneSwab***®, ***UroSwab***®, whole blood yellow top tube (ACD solution A)

Transport: Stable at room temperature

551 *Candida albicans* by Real-Time PCR

Clinical significance: Between 70% to 90% of yeast strains isolated from the vagina belong to the species *Candida albicans*. *C. albicans* is one of the major causes of Candida Vaginitis (CV). In the United States, CV is currently the second most common cause of vaginal infection, with bacterial vaginosis the most common diagnostic entity. CV affects most females at least once during their lives at an estimated rate of 70% to 75%, of whom 40% to 50% will experience a recurrence. Studies indicate that CV is a frequent diagnosis among young women, affecting as many as 15% to 30% of symptomatic women visiting a clinician; by the age of 25, half of all college women will have experienced at least one episode of CV. *C. albicans* and *C. glabrata* represent the most common fungal causes of both complicated and uncomplicated urinary tract infections. *Candida* species produce a wide spectrum of diseases, ranging from superficial mucocutaneous disease to invasive illnesses, such as hepatosplenic candidiasis, Candida peritonitis, and systemic candidiasis. The expression of which depends primarily on the immune status of the host. In this assay, DNA is extracted from the specimen and subjected to Real-Time PCR amplification.

Method: Real-Time PCR

Specimen: ***OneSwab***®, ***UroSwab***®, *ThinPrep*®, whole blood yellow top tube (ACD solution A), CSF, synovial fluid

Transport: Stable at room temperature

581 *Candida albicans* fluconazole resistance by X-Plate Technology®

Only performed after test #551 is positive.
Charges will be the total of tests #551 + #581.

Clinical significance: In the United States, fungal infections have increased significantly over the past three decades. *Candida albicans* remains the primary species involved in Candida infections, 40% to 70%. Candida Vaginitis (CV) affects most females at least once during their lives, at an estimated rate of 70% to 75%. Identifying the species and the antimicrobial susceptibility of an isolate involved in infection is imperative for the proper course of treatment. If an isolate is resistant or susceptible-dose dependent, treatment with azole antifungals is ineffective and can increase resistance rapidly. *C. albicans* isolates are resistant in approximately 1% to 10% of cases.

Method: X-Plate Technology®

Specimen: ***OneSwab***®

Transport: Stable at room temperature

576 *Candida dubliniensis* by Real-Time PCR

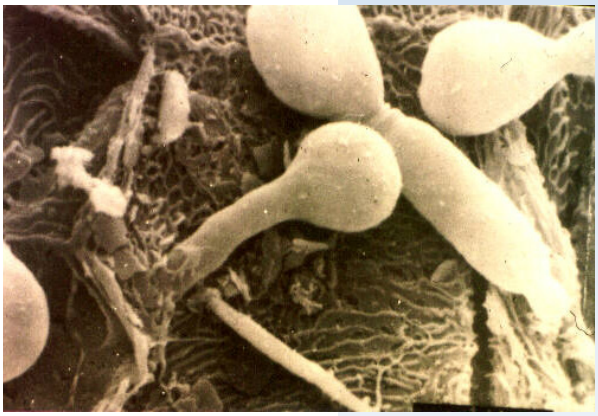
Clinical significance: First described in 1995, *Candida dubliniensis* is reported to have been previously misidentified as *Candida albicans*. It is associated with oral candidiasis and has been recovered from the vaginal tract of women. Although it is closely related to *C. albicans*, its differences in virulence and its ability to rapidly develop resistance to traditional antifungal agents makes it clinically relevant. *Candida* species produce a wide spectrum of diseases, ranging from superficial mucocutaneous disease to invasive illnesses, such as hepatosplenic candidiasis, Candida peritonitis, and systemic candidiasis. The expression of which depends primarily on the immune status of the host. *C. dubliniensis* is an opportunistic infection that is of particular concern in immunocompromised patients. The use of molecular techniques, such as PCR, enables the clinician to differentiate *C. dubliniensis* from other species of Candida to facilitate diagnosis and proper treatment. In this assay, DNA is extracted from the specimen and subjected to PCR amplification.

Method: Real-Time PCR

Specimen: ***OneSwab***®, ***UroSwab***®, whole blood yellow top tube (ACD solution A), synovial fluid

Transport: Stable at room temperature

559 *Candida glabrata* by Real-Time PCR



Clinical significance: *C. glabrata* has emerged as the second most common cause of invasive fungal infection and is the leading non-albicans species involved in Candida Vaginitis (CV), accounting for up to 20% of infections in immune-competent women. It is thought that the widespread use of topical antifungals, especially in short courses, may contribute to selection for non-albicans yeasts, which are less susceptible to these agents. *C. glabrata* has also been shown to intrinsically exhibit low level resistance but has the ability to rapidly acquire high level resistance to antifungals. *C. glabrata* is associated with CV and affects most females at least once during their lives at an estimated rate of 70% to 75%, of whom 40% to 50% will experience a recurrence. In the United States CV is currently the second most common cause of vaginal infections, with bacterial vaginosis the most common. Most studies indicate that CV is a frequent diagnosis among young women, affecting as many as 15% to 30% of symptomatic women visiting a clinician; by the age 25 years, half of all college women will have experienced at least one episode of CV. *C. albicans* and *C. glabrata* represent the most common fungal causes of both complicated and uncomplicated urinary tract infections. *Candida* species produce a wide spectrum of diseases, ranging from superficial mucocutaneous disease to invasive illnesses, such as hepatosplenic candidiasis, Candida peritonitis, and systemic candidiasis. The expression of which depends primarily on the immune status of the host. In this assay, DNA is extracted from the specimen and subjected to PCR amplification.

Method: Real-Time PCR

Specimen: ***OneSwab***®, ***UroSwab***®, *ThinPrep*®, whole blood yellow top tube (ACD solution A), CSF, synovial fluid

Transport: Stable at room temperature

582 *Candida glabrata* fluconazole resistance by X-Plate Technology®

Only performed after test #559 is positive.
Charges will be the total of tests #559 + #582.

Clinical significance: In the United States, fungal infections have increased significantly over the past three decades, especially amongst non-albicans species. Although *Candida albicans* remains the primary species involved in Candida infections (40% to 70%), *Candida glabrata* is now recognized as the second most common cause of infection, 10% to 30%. Candida Vaginitis (CV) affects most females at least once during their lives, at an estimated rate of 70% to 75%. The widespread use of azole antifungals may be a contributing factor in the emergence of non-albicans species. Identifying the species and the antimicrobial susceptibility of an isolate involved in infection is imperative for the proper course of treatment. Surveillance programs performed over the past few decades have demonstrated that azole resistance is becoming very common among *C. glabrata* and other non-albicans species. If an isolate is resistant or susceptible-dose dependent, treatment with azole antifungals is ineffective and can increase resistance rapidly.

Method: X-Plate Technology®

Specimen: ***OneSwab***®

Transport: Stable at room temperature

578 *Candida kefyr* by Real-Time PCR

Clinical significance: *Candida kefyr* is one of the six strains of Candida, of approximately 154 species, that is commonly associated with infections in humans. This species, previously reported in the literature by the obsolete name of *Candida pseudotropicalis*, has been reported as an emerging pathogen. Candidiasis has a wide clinical spectrum, capable of affecting almost any organ or system in the body. Infections range from localized, superficial infections to dissemination in the blood stream. Considered to be a relatively rare infection, found in approximately 1% of fungal isolates reported, *C. kefyr* infections have been documented from burn wounds, blood and vaginal infections. More recently, the frequency of *C. kefyr* infections has increased within oncohematologic patients, particularly those with neutropenic, myeloid and lymphoblastoid leukemias. In this assay, DNA is extracted from the specimen and subjected to PCR amplification.

Method: Real-Time PCR

Specimen: ***OneSwab***®, ***UroSwab***®, whole blood yellow top tube (ACD solution A)

Transport: Stable at room temperature

566 *Candida krusei* by Real-Time PCR

Clinical significance: *Candida krusei*, which has traditionally been implicated in urinary tract infections, has recently been associated with certain instances of fungal vaginitis, particularly recurrent fungal vaginitis. Candida Vaginitis (CV) resulting from *C. krusei* infection is often chronic due to the organism's inherent resistance to conventional anti-fungal therapies, necessitating the need for prolonged treatment courses. The incidence of *C. krusei* fungemia within leukemic populations has been on the rise within recent years, doubling within a five year span, and is highly lethal within the neutropenic subpopulation receiving fluconazole prophylaxis. As a result, treatment needs to be initiated quickly and aggressively. The use of molecular techniques, such as Real-Time PCR, enables the clinician to differentiate *C. krusei* from other *Candida* species to facilitate diagnosis and proper treatment. In this assay, DNA is extracted from the specimen and subjected to PCR amplification.

Method: Real-Time PCR

Specimen: ***OneSwab***®, ***UroSwab***®, whole blood yellow top tube (ACD solution A), CSF, synovial fluid

Transport: Stable at room temperature

577 *Candida lusitaniae* by Real-Time PCR

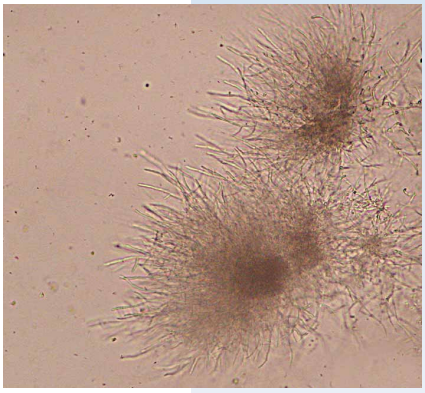
Clinical significance: *Candida lusitaniae* is considered a nosocomial bloodstream pathogen that is becoming increasingly associated with Candidemia. It is an opportunistic infection and therefore is associated with immunocompromised individuals. *C. lusitaniae* is known to enter the host through the urogenital and respiratory tracts or through intravascular catheters. It is also quite resistant to amphotericin B, a common antifungal treatment. In this assay, DNA is extracted from the specimen and subjected to PCR amplification.

Method: Real-Time PCR

Specimen: ***OneSwab***®, ***UroSwab***®, whole blood yellow top tube (ACD solution A)

Transport: Stable at room temperature

558 *Candida parapsilosis* by Real-Time PCR



Clinical significance: *C. parapsilosis* accounts for 1% of vaginal yeast isolates. It is thought that the widespread use of topical azole antifungals, especially in short courses, may contribute to selection for non-albicans yeasts, which are less susceptible to these agents than *C. albicans*. *C. parapsilosis* is associated with Candida Vaginitis (CV). CV affects most females at least once during their lives at an estimated rate of 70% to 75%, of whom 40% to 50% will experience a recurrence. In the United States CV is currently the second most common cause of vaginal infections, with bacterial vaginosis the most common diagnostic entity. Studies indicate that CV is a frequent diagnosis among young women, affecting as many as 15% to 30% of symptomatic women visiting a clinician; by the age of 25, half of all college women will have experienced at least one episode of CV. *Candida* species produce a wide spectrum of diseases, ranging from superficial mucocutaneous disease to invasive illnesses, such as hepatosplenic candidiasis, Candida peritonitis, and systemic candidiasis. The expression of which depends primarily on the immune status of the host. In this assay, DNA is extracted from the specimen and subjected to PCR amplification.

Method: Real-Time PCR

Specimen: ***OneSwab***®, ***UroSwab***®, *ThinPrep*®, whole blood yellow top tube (ACD solution A), CSF, synovial fluid

Transport: Stable at room temperature

583 *Candida parapsilosis* fluconazole resistance by X-Plate Technology®

Only performed after test #558 is positive.
Charges will be the total of tests #558 + #583.

Clinical significance: In the United States, fungal infections have increased significantly over the past three decades, especially amongst non-albicans species. Candida Vaginitis (CV) affects most females at least once during their lives, at an estimated rate of 70% to 75%. The widespread use of azole antifungals may be a contributing factor in the emergence of non-albicans species. Identifying the species and the antimicrobial susceptibility of an isolate involved in infection is imperative for the proper course of treatment. Surveillance programs performed over the past few decades have demonstrated that azole resistance is becoming very common among non-albicans species. If an isolate is resistant or susceptible-dose dependent, treatment with azole antifungals is ineffective and can increase resistance rapidly. *Candida parapsilosis* typically are not resistant to azoles, however approximately 1% of isolates are resistant.

Method: X-Plate Technology®

Specimen: ***OneSwab***®

Transport: Stable at room temperature

557 *Candida tropicalis* by Real-Time PCR

Clinical significance: *Candida tropicalis* accounts for 1% to 5% of vaginal yeast isolates and may be associated with a higher rate of recurrence after standard treatment. Although *C. tropicalis* is still very susceptible to azole antifungals, an increase in resistance has been observed in the US. It is thought that the widespread use of topical azole antifungals, especially in short courses, may contribute to selection for non-*albicans* yeasts, which are less susceptible to these agents than *C. albicans*. *C. tropicalis* is associated with Candida Vaginitis (CV). CV affects most females at least once during their lives, at an estimated rate of 70% to 75%, of whom 40% to 50% will experience a recurrence. In the United States CV is currently the second most common cause of vaginal infections, with bacterial vaginosis the most common diagnostic entity. Studies indicate that CV is a frequent diagnosis among young women, affecting as many as 15% to 30% of symptomatic women visiting a clinician; by the age of 25, half of all college women will have experienced at least one episode of CV. *Candida* species produce a wide spectrum of diseases, ranging from superficial mucocutaneous disease to invasive illnesses, such as hepatosplenic candidiasis, Candida peritonitis, and systemic candidiasis. The expression of which depends primarily on the immune status of the host. In this assay, DNA is extracted from the specimen and subjected to PCR amplification.

Method: Real-Time PCR

Specimen: ***OneSwab***®, ***UroSwab***®, *ThinPrep*®, whole blood yellow top tube (ACD solution A), CSF, synovial fluid

Transport: Stable at room temperature

584 *Candida tropicalis* fluconazole resistance by X-Plate Technology®

Only performed after test #557 is positive.
Charges will be the total of tests #557 + #584.

Clinical significance: In the United States, fungal infections have increased significantly over the past three decades, especially amongst non-albicans species. Candida Vaginitis (CV) affects most females at least once during their lives, at an estimated rate of 70% to 75%. The widespread use of azole antifungals may be a contributing factor in the emergence of non-albicans species. Identifying the species and the antimicrobial susceptibility of an isolate involved in infection is imperative for the proper course of treatment. Surveillance programs performed over the past few decades have demonstrated that azole resistance is becoming very common among non-albicans species. If an isolate is resistant or susceptible-dose dependent, treatment with azole antifungals is ineffective and can increase resistance rapidly.

Method: X-Plate Technology®

Specimen: ***OneSwab***®

Transport: Stable at room temperature

574 *Candida utilis* by Real-Time PCR

Clinical significance: *Candida utilis* has traditionally been described as an industrially significant yeast. However, it was recently implicated in a case of recurrent urinary tract infection and candidemia and has also been associated with fungal keratitis. The use of molecular techniques, such as Real-Time PCR, enables the clinician to differentiate *C. utilis* from other species of Candida to facilitate diagnosis and proper treatment. In this assay, DNA is extracted from the specimen and subjected to PCR amplification.

Method: Real-Time PCR

Specimen: ***UroSwab***®

Transport: Stable at room temperature

560 Candida Vaginitis Panel by Real-Time PCR

551 *Candida albicans* by Real-Time PCR
557 *Candida tropicalis* by Real-Time PCR
558 *Candida parapsilosis* by Real-Time PCR
559 *Candida glabrata* by Real-Time PCR
566 *Candida krusei* by Real-Time PCR

Clinical significance: The incidence of vulvovaginal candidiasis (VVC) is poorly documented, particularly since VVC is not a reportable entity. Regrettably, without laboratory confirmation, VVC is misdiagnosed in as many as 50% of cases. Seventy to ninety percent of yeast strains isolated from the vagina belong to the species of *Candida albicans*. Other vaginal yeast strains isolated include *C. glabrata*, *C. parapsilosis*, and *C. tropicalis*, accounting for the remaining VVC cases in the United States. Vulvovaginal candidiasis accounts for about one-third of all the vaginitis cases seen in private practices. Patients with VVC generally complain of perivaginal pruritus, often with little or no discharge. Currently, VVC diagnosis is based on the addition of 10% potassium hydroxide to vaginal discharge on a slide (the "whiff" test). However, the whiff test fails to elicit a confirmatory odor in most women with VVC. Direct microscopic examination of wet mount vaginal discharge fails to reveal the fungi in 30% to 50% of infected women. A commercially available latex agglutination test has a limited sensitivity of 60%. MDL has developed a highly sensitive and specific PCR based assay that can differentiate among the four VCC-causing pathogens. In this assay, DNA is extracted from the specimen and subjected to PCR amplification.

Method: Real-Time PCR

Specimen: ***OneSwab***®, ***UroSwab***®, *ThinPrep*®

Transport: Stable at room temperature

105 *Chlamydia trachomatis* by Real-Time PCR (*Reflex to antibiotic resistance by Molecular Analysis)

Applicable for *UroSwab*® specimens in adolescent females who are not candidates for pelvic exams.

Clinical significance: *Chlamydia trachomatis* is the causative agent of the disease Chlamydia and is the most common sexually transmitted bacterial agent. In women, this bacterium causes cervicitis, urethritis, endometritis and salpingitis. In more complicated cases, *C. trachomatis* infections may result in tubal scarring, infertility, and ectopic pregnancy. In men it causes urethritis and proctatitis. If left untreated, Chlamydia may develop into lymphogranuloma venereum. Other forms of infection also seen are trachoma, the most preventable form of blindness, and conjunctivitis in neonates. *Chlamydia trachomatis* has also been associated with reactive arthritis (RA), also called Reiter's syndrome, the most common type of inflammatory polyarthritis in young men. *C. trachomatis* infection is the most common antecedent of RA and accounts for most cases of venereal origin. It is important that proper treatment be initiated for both the patient and infected sexual partners to prevent spread of the disease and reinfection of the patient. *Chlamydia trachomatis* is typically thought to be easily treated with antibiotics. Previous studies have demonstrated that azithromycin and doxycycline were equally efficacious for the treatment of genital chlamydial infection. Azithromycin is a popular choice of treatment for those patients with unpredictable follow-up or poor treatment compliance since it can be administered as a single dose. However, recent studies suggest that treatment failure may occur in more than 5% of patients due to resistance to azithromycin. This emerging resistance of *Chlamydia trachomatis* to azithromycin is important when choosing proper antibiotic therapy. MDL can now detect azithromycin resistance in a subset of *C. trachomatis* positive specimens by Real-Time PCR. This new assay detects *C. trachomatis* to a single point mutation within the 23S rRNA gene of *C. trachomatis* that confers resistance to azithromycin. In this assay, DNA is extracted from the specimen and subjected to PCR amplification.

Method: Real-Time PCR

Specimen: ***OneSwab***®, ***UroSwab***®, *ThinPrep*®, whole blood yellow top tube (ACD solution A)

Transport: Stable at room temperature

554 *Cryptococcus neoformans* by Real-Time PCR

When sampling a crusted over lesion, moisten the swab with sterile saline solution prior to swabbing.

Clinical significance: *Cryptococcus neoformans* is found in aged pigeon droppings, such as those accumulated on window ledges and rooftops. Infection is commonly seen in AIDS and transplant patients on immunosuppressive therapies and primarily manifests as a respiratory infection causing severe pneumonia. It also causes central nervous system disturbances and skin lesions that may be non-specific but are often the first sign of infection. India ink smears can be useful as supportive evidence of infection but are not definitive. A combination of culture and smears with antibody or antigen detection assays are traditionally used. Molecular methods, such as PCR, offer a rapid route of diagnosis with increased sensitivity and specificity. In this assay, DNA is extracted from the specimen and subjected to PCR amplification.

Method: Real-Time PCR

Specimen: ***UroSwab***®, whole blood yellow top tube (ACD solution A), ***OneSwab***®

Transport: Stable at room temperature

207 Cytomegalovirus (CMV) by Real-Time PCR

Clinical significance: Cytomegalovirus (CMV) infects 50% to 80% of Americans by the age of 40 and is known to cause mild or asymptomatic infection in most healthy individuals. The virus is spread person-to-person through most bodily fluids. Congenital infection, which occurs when an infected mother passes the infection along to the fetus, may result in hearing, vision, neurologic and developmental problems shortly after birth. CMV viral shedding can be detected in the vaginal secretions of infected women. The use of molecular techniques, such as Real-Time PCR, enables the clinician to detect this viral shedding thus enabling diagnosis and treatment prior to delivery. In this assay, DNA is extracted from the specimen and subjected to PCR amplification. Ganciclovir resistance testing by Pyrosequencing is utilized for specimens that test positive for the presence of CMV to detect specific mutations associated with ganciclovir resistance.

Method: Real-Time PCR

Specimen: ***OneSwab***®, ***UroSwab***®, *ThinPrep*®, whole blood yellow top tube (ACD solution A), CSF

Transport: Stable at room temperature

175 *Eggerthella* species by Real-Time PCR

Clinical Significance: *Eggerthella* species is an anaerobic, non-sporulating, Gram-positive bacillus that is part of the normal human intestinal tract flora. The organism has been implicated in infections of the gastrointestinal and genital tracts including Bacterial Vaginosis (BV). *Eggerthella* species are generally sensitive to penicillin and metronidazole treatments. In this assay, DNA is extracted from the specimen and subjected to PCR amplification.

Method: Real-Time PCR

Specimen: ***OneSwab***®, *ThinPrep*®

Transport: Stable at room temperature

153 *Enterococcus faecalis* by Real-Time PCR (Reflex to vancomycin-resistant Van A & Van B by Real-Time PCR)

Reflex testing not available on UroSwab® specimens.

Clinical Significance: *Enterococcus faecalis* is a Gram-positive commensal bacterium inhabiting the gastrointestinal tract. *E. faecalis* can cause life-threatening infections, especially in a nosocomial or hospital environment, where the naturally high levels of antibiotic resistance found in *E. faecalis* contribute to its pathogenicity. Enterococci are important nosocomial pathogens. Their emergence in the past two decades is in many respects attributable to their resistance to many commonly used antimicrobial agents. Vancomycin-resistant Enterococcus (VRE) is the name given to a group of bacterial species of the genus *Enterococcus* that are resistant to the antibiotic vancomycin. Enterococci are enteric and can be found in the digestive and urinary tracts of some humans. VRE was first discovered in 1985 and is particularly dangerous to immunocompromised individuals. While infection of healthy individuals is uncommon, it is possible for them to become colonized with newly-resistant bacteria. VRE can then be carried by healthy people who have come in contact with the bacteria, this most likely occurs in hospital settings. There are six different types of vancomycin resistance shown by *Enterococcus*: Van-A, Van-B, Van-C, Van-D, Van-E, and Van-F. Of these, only Van-A, Van-B, and Van-C have been seen in general clinical practice thus far. Real-Time PCR is a rapid and accurate method for identifying *Enterococcus faecalis* in loose stool swab samples.

Method: Real-Time PCR

Specimen: ***OneSwab®***, ***UroSwab®***, *ThinPrep®*

Transport: Stable at room temperature

154 *Enterococcus faecium* by Real-Time PCR

Clinical Significance: *Enterococcus faecium* is a Gram-positive cocci bacterium and is one of the leading causes of gastrointestinal infection worldwide. The bacteria can be commensal in the human intestines, but may also act as a pathogen causing infections similar to neonatal meningitis. Enterococcus nosocomial infections are second to only to *E. coli*, and are known to cause intestinal and skin infections that can become life threatening in some instances. *E. faecium* has become a major concern in the medical community, because of the known resistant strains to many antibiotics, including penicillin and vancomycin. Enterococci frequently cause urinary tract infections, bloodstream infections, and wound infections in hospitalized patients. Real-Time PCR is a rapid and accurate method for identifying *Enterococcus faecium*.

Method: Real-Time PCR

Specimen: ***OneSwab®***, ***UroSwab®***

Transport: Stable at room temperature

205 Epstein-Barr virus (EBV) by Real-Time PCR

Clinical significance: EBV is the causative agent of infectious mononucleosis, which occurs primarily in late adolescence and early adulthood. It is characterized by malaise, fever, hepatosplenomegally, lymphadenopathy, and abdominal discomfort. EBV has also been associated with post-transplant lymphoma, Burkitt's lymphoma, and nasopharyngeal carcinoma. Reactivations of this disease are suspected in chronic fatigue syndrome. EBV is one of the most common human viruses and it is estimated that worldwide as many as 80% to 90% of all adults have at one time been infected. Although it is normally a self-limiting infection, complications can occur, such as splenomegaly, hepatitis, pericarditis, or central nervous system involvement. In certain rare instances, EBV infections may be fatal. In this assay, DNA is extracted from the specimen and subjected to PCR amplification.

Method: Real-Time PCR

Specimen: ***UroSwab®***, whole blood yellow top tube (ACD solution A)

Transport: Stable at room temperature

141 *Escherichia coli* by Real-Time PCR

Clinical significance: *Escherichia coli (E. coli)* are facultative anaerobic Gram-negative rods that normally live as commensal (i.e. non-pathogenic) organisms on the skin and within the gastrointestinal tract of humans and animals. Certain strains, referred to as uropathogenic *E. coli* (UPEC), exit the GI tract, colonize the perineum and, when they come in contact with the urethra, ascend into the bladder to cause a urinary tract infection (UTI). UPEC is also the cause of more than 90% of urinary tract infections (UTI), which primarily occur in young, sexually active women. However, UPEC is also the cause of 78% of male UTI, and is a significant cause of prostatitis. In this assay, DNA is extracted from the specimen and subjected to PCR amplification.

Method: Real-Time PCR

Specimen: ***OneSwab***®, ***UroSwab***®, *ThinPrep*®

Transport: Stable at room temperature

132 *Gardnerella vaginalis* by Real-Time PCR

Clinical significance: *Gardnerella vaginalis* is a Gram-variable anaerobic bacterium that can be present at low numbers as a normal constituent of the vaginal flora of some women. *G. vaginalis* is often present at high levels in women with Bacterial Vaginosis (BV) and the presence of this microorganism can be used to diagnose BV, usually in conjunction with a decrease in the numbers of Lactobacillus, and the presence of *Mobiluncus* species. In this assay, DNA is extracted from the specimen and subjected to PCR amplification.

Method: Real-Time PCR

Specimen: ***OneSwab***®, *ThinPrep*®

Transport: Stable at room temperature

115 Genital Ulcer Disease Panel (HSV-1 & HSV-2, *H. ducreyi, T. pallidum*) by Real-Time PCR

110 *Treponema pallidum* by Real-Time PCR
122 *Haemophilus ducreyi* by Real-Time PCR
126 Herpes subtype (HSV-1 & HSV-2) by Real-Time PCR

When sampling a crusted over lesion, moisten the swab with sterile saline solution prior to swabbing.

Clinical significance: The three major causes of Genital Ulcer Disease (GUD) in the United States are **Herpes simplex virus**, ***Treponema pallidum*** (syphilis), and ***Haemophilus ducreyi*** (chancroid). Currently, the diagnosis of GUD is based primarily on the clinical presentation of the ulcer itself. However, agent-specific diagnosis based solely on clinical evaluations are often obscured by multiple and mixed infections. As treatment options vary, it is medically necessary to identify the causative agent of GUD. In this assay, DNA is extracted from the specimen and subjected to PCR amplification for these three pathogens. The Herpes subtype assay, if positive, will determine whether the virus detected was HSV-1, HSV-2, or both HSV-1 and HSV-2.

Method: Real-Time PCR

Specimen: ***OneSwab***®, *ThinPrep*®

Transport: Stable at room temperature

1112 Group A Streptococcus by Real-Time PCR

Clinical significance: *Streptococcus pyogenes* (**Group A Streptococcus**) is a Gram-positive extracellular bacterium that colonizes the throat and skin. It is the cause of many human diseases which range from mild skin infections to invasive life threatening disease. Group A Streptococcus is the most common cause of bacterial pharyngitis (Strep throat) and is also associated with scarlet fever, impetigo, Streptococcal toxic shock syndrome and necrotizing fasciitis. Autoimmune mediated post infection sequelae such as rheumatic fever, rheumatic heart disease, glomerulonephritis and reactive arthritis can potentially result in disability or death. Group A Streptococcus has been shown to infect the vaginal mucosa and uterus leading to severe disease or septicemia. In this assay, DNA is extracted from the specimen and subjected to PCR amplification.

Method: Real-Time PCR

Specimen: ***OneSwab***®, ***NasoSwab***®

Transport: Stable at room temperature

127 Group-B Streptococcus (GBS) by Real-Time PCR

Obtaining specimens from both the anorectum and distal vagina increases the sensitivity of testing by a considerable percentage (5% to 25%) over vaginal swabbing alone.

Clinical significance: Group-B Streptococcus is the leading cause of neonatal infections, which can result in septicemia, pneumonia and meningitis. It is the most common cause of life-threatening infection in newborns. One out of every twenty babies with GBS dies from the infection. In pregnant women, GBS can cause bladder infections, womb infections, and stillbirths. Most adults are asymptomatic carriers of GBS in the bowel, vagina, bladder or throat. Diagnosis by traditional cultures may take several days to complete. Once diagnosed, GBS can be treated with antibiotics to prevent the spread from mother to baby. In this assay, DNA is extracted from the specimen and subjected to PCR amplification.

Method: Real-Time PCR

Specimen: ***OneSwab***®, ***UroSwab***®, *ThinPrep*®

Transport: Stable at room temperature

137 Group B Streptococcus (GBS) Antibiotic Resistance by Real-Time PCR

This test is appropriate for patients that are penicillin-allergic and clindamycin/erythromycin resistance determination is required for alternate treatment.
Only performed after test #127 is positive.
Charges will be the total of tests #127 + #137.

Clinical significance: The typical treatment for Group B Streptococcus-infected patients is penicillin G, of which there is no known resistance. However, up to 12% of the population reports allergies to penicillin. Therefore the macrolide (erythromycin) or lincosamide (clindamycin) classes of drugs need to be administered, particularly for those patients who are at high risk for anaphylactic shock. Previous reports cite an increase in resistance of GBS to erythromycin and clindamycin. For instance, in 2003, resistance to erythromycin and clindamycin was reported to be as high as 37% and 17%, respectively. The antibiotic resistance mechanisms are most commonly caused by three genes: *ermB*, *ermTR*, and *mefA*. MDL published a study where both the Clinical and Laboratory Standards Institute (formerly NCCLS) 2003 "Performance Standards for Antimicrobial Susceptibility Testing" protocols and a multiplex PCR assay were used to screen for the prevalence of these genes in 222 GBS clinical isolates (Gygax *et al.* 2006).These isolates were obtained from MDL's clinical swab samples which were procured with the ***OneSwab***® collection system. Of the 222 GBS clinical isolates, 84 strains (38%) were resistant to erythromycin and 46 strains (21%) were resistant to clindamycin. The multiplex PCR proved to be an efficient method to identify the three major antibiotic resistance genes in GBS. With the presence of these genes on mobile genetic elements, such as plasmids and/or transposons, the passing of these genes from bacteria to bacteria is likely and should be monitored to provide the physician with the vital information needed for proper patient treatment. MDL has developed a highly sensitive (94%) and (99%) specific multiplex polymerase chain reaction assay to identify GBS antibiotic resistance genes from GBS clinical isolates.

Method: Real-Time PCR

Specimen: ***OneSwab***®, ***UroSwab***®

Transport: Stable at room temperature

122 *Haemophilus ducreyi* by Real-Time PCR

When sampling a crusted over lesion, moisten the swab with sterile saline solution prior to swabbing.

Clinical significance: *H. ducreyi* is the causative agent of the sexually transmitted disease soft chancre or chancroid. It is most commonly diagnosed in males, probably due to the asymptomatic or inapparent infection that often occurs in females. It typically takes 5 to 7 days after exposure for symptoms to present, but may take as long as several weeks. A tender, small, solid, raised skin lesion will develop with a red base that may develop into a raised sore containing pus. It may then become an open ulcer within 2 days. These lesions are generally limited to the genitalia or perianal area. The lesion erodes to form a painful ulcer and swelling of lymph nodes in the groin area (bubo) in approximately 50% of patients. In this assay, DNA is extracted from the specimen and subjected to PCR amplification.

Method: Real-Time PCR

Specimen: ***OneSwab***®, *ThinPrep*®

Transport: Stable at room temperature

126 Herpes subtype (HSV-1 & HSV-2) by Real-Time PCR

When sampling a crusted over lesion, moisten the swab with sterile saline solution prior to swabbing.

Clinical significance: HSV infections are epidemic in the United States. Genital herpes is the most common cause of genital ulcer disease in the developed world. HSV-2 is the most common cause of genital ulcers in the United States and is the cause of more than 90% of recurrent disease. Most painful and annoying recurrent genital herpes is due to HSV-2 and almost all recurrent cold sores or fever blisters are due to HSV-1. HSV-1 classically presents as herpes gingivostomatitis, an infection of the oral mucosa. It can also cause conjunctivitis, keratitis, and herpetic whitlow. However, genital herpes also can be caused by HSV-1. It has been documented that as many as one third of herpes infections are due to HSV-1, particularly in adolescents and young adults. This type of genital herpes is much less frequently recurrent and each recurrence usually lasts only a few days. The main application for HSV subtyping is with regard to the clinical issue of recurrent infection. Although antigen detection systems for HSV can be specific and sensitive when applied to the evaluation of clinical genital lesions, the titer of HSV present during asymptomatic reactivations is 10- to 100-fold less than the titer present during symptomatic episodes. Therefore, methods based on the detection of viral proteins in such cases are less sensitive than DNA amplification assays. In this assay, DNA is extracted from the specimen and subjected to PCR amplification.

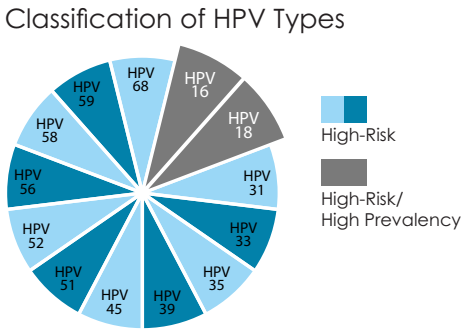
Method: Real-Time PCR

Specimen: ***OneSwab***®, *ThinPrep*®, whole blood yellow top tube (ACD solution A)

Transport: Stable at room temperature

739 HPV Type-Detect® 4.0 by Multiplex Real-Time PCR

Clinical significance: Papillomaviruses are a diverse group of viruses that have been found in more than 20 different mammalian species. To date, more than 115 distinct HPV types have been identified. HPV infection is very common, although most infected individuals eliminate evidence of the virus without developing clinical manifestations. Therefore, very few HPV-infected individuals progress to invasive cervical cancer. HPV type is a well established risk factor determinant for progression to cervical cancer. Over 40 HPV types infect the anogenital tract, 15 of them have been classified as high-risk for development of cervical cancer, 3 have been classified as probable high-risk, 12 have been classified as low-risk and 3 are considered undetermined-risk An HPV type is defined as a complete genome whose L1 gene sequence is at least 10% dissimilar to that of any other HPV type. Each Papillomavirus is highly tropic for a specific epithelium, and has its own degree of oncogenicity. HPV Type-Detect® 4.0 targets the L1 major capsid region. This region is a suitable target, because a diverse genetic region is contained within a more conserved region for all the detected HPV types. This assay detects and distinguishes between 13 different high-risk types.



Method: Multiplex Real-Time PCR

Specimen: ***OneSwab***®, *ThinPrep*®

Transport: Stable at room temperature

727 *Klebsiella oxytoca* by Real-Time PCR

Clinical significance: *Klebsiella oxytoca* is primarily a health care–associated pathogen acquired from environmental sources. *K. oxytoca* is emerging as an important bacterial isolate causing hospital-acquired infection in adults, most often involving immunocompromised patients or those requiring intensive care, and having multiple drug resistance to commonly used antibiotics. They may cause infection of the skin, blood, respiratory, urinary, and gastrointestinal tracts.

Method: Real-Time PCR

Specimen: ***OneSwab***®, ***UroSwab***®

Transport: Stable at room temperature

728 *Klebsiella pneumoniae* by Real-Time PCR

Clinical significance: *Klebsiella pneumoniae* is an important bacterial isolate causing hospital-acquired infection in adults, most often involving immunocompromised patients or those requiring intensive care, and having multiple drug resistance to commonly used antibiotics. It can cause different types of healthcare-associated infections, including pneumonia, bloodstream infections, wound or surgical site infections, and meningitis. *Klebsiella* bacteria can be spread through person-to-person contact, such as from patient to patient via the contaminated hands of healthcare personnel or, less commonly, by contamination of the environment.

Method: Real-Time PCR

Specimen: ***OneSwab***®, ***UroSwab***®

Transport: Stable at room temperature

121 Leukorrhea Panel (*N. gonorrhoeae**, *C. trachomatis**, *T. vaginalis****, *Mycoplasma genitalium*$^{\Psi}$) by Real-Time PCR

105 *Chlamydia trachomatis* by Real-Time PCR (*Reflex to antibiotic resistance by Molecular Analysis)
167 *Neisseria gonorrhoeae* by Real-Time PCR (*Reflex to antibiotic resistance by Molecular Analysis)
111 *Trichomonas vaginalis* by Real-Time PCR (***Reflex to metronidazole resistance)
129 *Mycoplasma genitalium* ($^{\Psi}$Reflex to azithromycin & fluoroquinolone resistance)
Applicable for *UroSwab*® specimens in adolescent females who are not candidates for pelvic exams.

Clinical significance: ***Chlamydia trachomatis***, ***Neisseria gonorrhoeae***, ***Trichomonas vaginalis and Mycoplasma genitalium*** are the major causes of leukorrhea. *C. trachomatis* is the most common sexually transmitted bacterial agent. In women, *C. trachomatis* causes cervicitis, urethritis, endometritis, and salpingitis. Prolonged *C. trachomatis* infection may result in tubal scarring, infertility, and ectopic pregnancy. *Neisseria gonorrhoeae* is the causative agent of the sexually transmitted disease gonorrhea. In women, the most common symptom of *N. gonorrhoeae* infection is endocervical infection which, if left untreated, may develop into vulvovaginitis and pelvic inflammatory disease. As a protozoan parasite, *Trichomonas vaginalis* is the causative agent of the sexually transmitted disease trichomoniasis. *T. vaginalis* infection is the primary cause of vaginitis, cervicitis and urethritis in women. Routine clinical diagnosis usually depends on microscopic identification of the parasite in wet mount preparations, which are only 60% sensitive as compared to culture-positive women. The sensitivity and specificity of PCR testing for *C. trachomatis* and *N. gonorrhoeae* are superior to the HCII (probe-based) assay which has a sensitivity/specificity of 75% / 97%, and 90.8% / 99.3%, respectively. Recent studies have shown that macrolide resistance to the *M. genitalium* primary antibiotic regimen (azithromycin), which highly correlates with treatment failure, ranges from 44% to 90% in the United States, Canada, Western Europe, and Australia. In the Sexually Transmitted Infections Treatment Guidelines, 2021, published by the Centers for Disease Control and Prevention (CDC), In this assay, DNA is extracted from the specimen and subjected to PCR amplification.

Method: Real-Time PCR

Specimen: ***OneSwab***®, ***UroSwab***®, *ThinPrep*®

Transport: Stable at room temperature

136 Lymphogranuloma venereum (LGV) by Real-Time PCR

When sampling a crusted over lesion, moisten the swab with sterile saline solution prior to swabbing.

Clinical significance: Lymphogranuloma venereum (LGV) is a sexually transmitted Chlamydial disease that should be part of the differential diagnosis for any patient presenting with a genital ulcer and/or inguinal lymphadenopathy. Treatment involves the use of antibiotics to clear the infection and to prevent tertiary sequelae. LGV is caused by *C. trachomatis* serotypes L1, L2, and L3. *C. trachomatis* serovars B and D-K are associated with causing non-gonococcal urethritis and cervicitis. While these other serotypes of *C. trachomatis* are limited to superficial infection of mucous membranes, serotypes L1, L2, and L3 are more invasive and virulent and tend to result in systemic disease.

LGV occurs in three distinct stages. The **first stage** is an incubation period of anywhere from three days to six weeks (10 to 14 days average) and is characterized by a painless genital papule which usually disappears after a few days. The onset of the **second stage** occurs 2 to 6 weeks later and often manifests as unilateral inguinal lymphadenopathy. Constitutional symptoms, such as fever, chills, malaise, myalgias, and arthralgias, are common in this stage of the disease. The **third stage** may occur years after the initial infection and is termed genitoanorectal syndrome. Women are more likely to present in this stage. Symptoms include fever, pain, tenesmus, pruritus, and purulent or bloody diarrhea. This Real-Time PCR assay is both highly sensitive and specific, capable of differentiating between LGV and *C. trachomatis* serotypes.

Method: Real-Time PCR

Specimen: ***OneSwab***®, ***UroSwab***®, *ThinPrep*®

Transport: Stable at room temperature

165 *Megasphaera* species (Type 1 and Type 2) by Real-Time PCR

Clinical Significance: Bacterial Vaginosis (BV) is the most common disorder that prompts women to seek gynecological care. The most common patient symptoms are discharge, odor and irritation. This condition is increasingly recognized as causing common and costly obstetric and gynecologic infectious complications worldwide. *Megasphaera* species are Gram-negative anaerobic organisms found in the digestive tracts of ruminants. A recent study has identified 16S rDNA present in BV patient samples as belonging to a *Megasphaera* species that has not yet been cultured. Detection of *Megasphaera* species 16S rDNA provides a sensitivity of 99% and 96%, and specificity of 89% and 84%, when compared to Amsel Criteria and Nugent Score, respectively. Successful antibiotic treatment of BV reduces the vaginal concentration of *Megasphaera* species and persistence of this organism is associated with chronic BV.

Method: Real-Time PCR

Specimen: ***OneSwab***®, *ThinPrep*®

Transport: Stable at room temperature

124 *Mobiluncus mulieris* and *Mobiluncus curtisii* by Real-Time PCR

Clinical significance: *Mobiluncus mulieris* and *Mobiluncus curtisii* are fastidious anaerobic curved Gram-variable bacteria. These bacterial species are not normal constituents of the bacterial flora and their presence in the vagina is a highly specific indicator of Bacterial Vaginosis (BV). Due to their fastidious nature and the low numbers present during BV, their absence from a vaginal specimen is not an indicator of healthy flora. In this assay, DNA is extracted from the specimen and subjected to PCR amplification.

Method: Real-Time PCR

Specimen: ***OneSwab***®, *ThinPrep*®

Transport: Stable at room temperature

128 Molluscum contagiosum virus (MCV) by Real-Time PCR

When sampling a crusted over lesion, moisten the swab with sterile saline solution prior to swabbing.

Clinical significance: Molluscum contagiosum virus (MCV) is a member of the human pox viruses which produces small raised papules or lesions with central umbilications and a white, firm, curd-like core. Infection occurs commonly in children under 5 years due to casual contact and in young adults due to skin-to-skin contact during sexual intercourse. MCV is a common infection in the United States and accounts for approximately 1% of all undiagnosed skin disorders. Many physician's find it necessary to differentiate MCV from Human Papillomavirus (HPV) or Herpes simplex virus (HSV) infections, which have greater mortality and morbidity. In this assay, DNA is extracted from a swab sample of lesions actively shedding the virus or biopsies of the actual lesion and subjected to PCR amplification.

Method: Real-Time PCR

Specimen: ***OneSwab***®, *ThinPrep*®

Transport: Stable at room temperature

1118 MRSA: Methicillin Resistant and Methicillin Susceptible (MSSA) *Staphylococcus aureus* by Conventional PCR

For nasal collection, please use a *NasoSwab*®

Clinical significance: *Staphylococcus aureus*, often referred to simply as "staph", are bacteria commonly carried on the skin or in the nose of healthy people. Methicillin-resistant *Staphylococcus aureus* (MRSA), often pronounced "mersa", is the resistant variant of this bacteria which is resistant to β-lactam antibiotics such as methicillin, oxacillin, penicillin, and amoxicillin. Risk of infection is greater for patients in hospitals, nursing homes, and other healthcare facilities who have open wounds and/or weakened immune systems. Colonization can occur in the anterior nares, skin, open wounds, and urinary tract. MRSA can be treated with alternate antibiotics which included glycopeptides (vancomycin and teichoplanin), linizolid, and daptomycin. Pre-screening patients upon admission for MRSA will also allow facilities to care for patients accordingly.

Method: Conventional PCR

Specimen: ***OneSwab***®, ***NasoSwab***®

Transport: Stable at room temperature

1119 CA-MRSA: Community-Associated MRSA. Panton-Valentine Leukocidin (PVL) DNA by Real-Time PCR

(Type IV + #1118 Req.)
[Community Acquired MRSA = Type IV MRSA+ and PVL+] Only performed after test #1118 is positive for Type IV.
Charges will be the total of tests #1118 + #1119.

Clinical significance: Staph infections, including MRSA, occur most frequently among persons in hospitals and healthcare facilities who have weakened immune systems. Staph and MRSA can also cause illness in persons outside of hospitals and healthcare facilities. MRSA infections that are acquired by persons who have not been hospitalized within the previous year or had a medical procedure are known as community acquired MRSA (CA-MRSA) infections. Staph or MRSA infections in the community usually manifest as skin infections, such as pimples and boils, and occur in otherwise healthy people. CA-MRSA strains were first reported in the late 1990s and were defined by a lack of exposure to the health care setting. In the next several years, it became clear that CA-MRSA infections were caused by strains of MRSA that have different genetic characteristics than other strains. Panton-Valentine leukocidin (PVL) is a cytotoxin which is associated with increased virulence of certain strains of *Staphylococcus aureus*. It is present in the majority [1] of community-associated methicillin-resistant *Staphylococcus aureus* (CA-MRSA) isolates studied and is the cause of necrotic ("flesh-eating") lesions involving the skin or mucosa, including necrotic hemorrhagic pneumonia. The new CA-MRSA strains have rapidly spread in the United States to become the most common cause of cultured skin infections among individuals seeking medical care for these infections at emergency rooms in cities. These strains also commonly cause skin infections in athletes, jail and prison detainees, and soldiers. In this assay, DNA is extracted from the specimen and subjected to PCR amplification.

Method: Real-Time PCR

Specimen: ***OneSwab***®, ***NasoSwab***®

Transport: Stable at room temperature

129 *Mycoplasma genitalium* by Real-Time PCR (Reflex to azithromycin & fluoroquinolone resistance by Pyrosequencing)

Clinical significance: *Mycoplasma genitalium* is a bacteria known to cause infection in men of the urethra, which causes pain and burning during urination and discharge. It has recently been associated with infections in women of the cervix, vagina, and endometrium. Recent studies have shown that *Mycoplasma genitalium* can be found in 10% - 30% of women with cervicitis making it more predominant than Gonorrhea. It is often seen as a coinfection with Chlamydia. There is a growing concern about antibiotic resistance. Recent studies have shown that macrolide resistance to the *M. genitalium* primary antibiotic regimen (azithromycin), which highly correlates with treatment failure, ranges from 44% to 90% in the United States, Canada, Western Europe, and Australia. In the Sexually Transmitted Infections Treatment Guidelines, 2021, published by the Centers for Disease Control and Prevention (CDC), they state that ideally, *Mycoplasma genitalium* antibiotic resistance testing should be performed and used to guide therapy. In this assay, DNA is extracted from the specimen and subjected to PCR amplification.

Method: Real-Time PCR

Specimen: ***OneSwab***®, ***UroSwab***®, *ThinPrep*®

Transport: Stable at room temperature

130 *Mycoplasma hominis* by Real-Time PCR

Clinical significance: Mycoplasmas are small (0.2 – 0.3 nm), membrane-bound organisms capable of independent self-replication. The most prevalent strains recoverable from the genital tract are *Ureaplasma urealyticum*, *Mycoplasma hominis* and *Mycoplasma genitalium*. Infants can become colonized with genital mycoplasmas during birth. *M. hominis* has been linked to pyelonephritis, pelvic inflammatory disease (PID), spontaneous abortion, and postpartum septicemia and fever. Genital mycoplasma infections are usually diagnosed by culture. However, it can take 2 to 5 days to culture *M. hominis*. In this assay, DNA is extracted from the specimen and subjected to PCR amplification.

Method: Real-Time PCR

Specimen: ***OneSwab***®, ***UroSwab***®, *ThinPrep*®, whole blood yellow top tube (ACD solution A), CSF, synovial fluid

Transport: Stable at room temperature

335 *Mycoplasma penetrans* by Real-Time PCR

Clinical significance: *Mycoplasma* species are the smallest and genetically simplest self-replicating bacteria. *Mycoplasma* species are ubiquitous in nature and are widely distributed throughout the animal kingdom. They have recently been associated with certain acute and chronic illnesses and can function as causative agents, cofactors, and opportunistic infectious agents. *M. penetrans* has been isolated from the urogenital tract and from HIV patients. It is a potential cofactor in AIDS progression. Mycoplasmas have been associated with respiratory illness, urogenital disease, immunosuppressive disease, such as HIV infection, cardiac diseases, arthritic syndromes, tick-borne illness, and chronic fatigue syndrome. In this assay, DNA is extracted from the specimen and subjected to PCR amplification.

Method: Real-Time PCR

Specimen: ***OneSwab***®, ***UroSwab***®, whole blood yellow top tube (ACD solution A)

Transport: Stable at room temperature

167 *Neisseria gonorrhoeae** by Real-Time PCR (*Reflex to antibiotic resistance by Molecular Analysis)

Applicable for *UroSwab*® specimens in adolescent females who are not candidates for pelvic exams.

Clinical Significance: *Neisseria gonorrhoeae* is the causative agent of the sexually transmitted disease Gonorrhea. In women the most common presentation is endocervical infection. If left untreated it may develop into vulvovaginitis, salpingitis, and pelvic inflammatory disease. Other forms of infection sometimes seen are infections of the oral and anal cavities, as well as the eye. Infections in men range from uncomplicated lower genital tract involvement such as urethritis, to the more serious epididymitis, prostatitis, and urethral stricture. Untreated asymptomatic infections may, in certain instances, develop into disseminated gonococcal infection.

Method: Real-Time PCR

Specimen: ***OneSwab***®, ***UroSwab***®, *ThinPrep*®, whole blood yellow top tube (ACD solution A), biopsy (fresh), biopsy (paraffin), synovial fluid

Transport: Stable at room temperature

109 *Neisseria gonorrhoeae**, *Chlamydia trachomatis** by Real-Time PCR

105 *Chlamydia trachomatis* by Real-Time PCR (*Reflex to antibiotic resistance by Molecular Analysis)
167 *Neisseria gonorrhoeae* by Real-Time PCR (*Reflex to antibiotic resistance by Molecular Analysis)

Applicable for *UroSwab*® specimens in adolescent females who are not candidates for pelvic exams.

Clinical significance: Genitourinary tract infections due to ***C. trachomatis*** and ***N. gonorrhoeae*** are a major cause of morbidity in sexually active individuals. In males infections with these pathogens may cause epididymitis and urethritis. In females, they can cause pelvic inflammatory disease (PID), ectopic pregnancy, and infertility. If left untreated, Chlamydia may develop into lymphogranuloma venereum and *N. gonorrhoeae* may develop into a disseminated gonococcal infection (DGI). In this assay, DNA is extracted from the specimen and subjected to PCR amplification.

Method: Real-Time PCR

Specimen: ***OneSwab***®, ***UroSwab***®, *ThinPrep*®

Transport: Stable at room temperature

138 Polyomavirus BK by Real-Time PCR

Clinical significance: Polyomavirus BK is a member of the Papovavirus family and infects up to 90% of the general population. After primary infection, which generally occurs in childhood without evident symptoms, the virus can remain latent in the urinary tract. Reactivation can be enhanced by immunosuppressive conditions, leading to overt clinical disease. Renal allograft recipients are particularly sensitive to reactivation as Polyomavirus BK has been implicated widely in dysfunction of the allograft. In this assay, DNA is extracted from the specimen and subjected to PCR amplification.

Method: Real-Time PCR

Specimen: ***UroSwab***®, whole blood yellow top tube (ACD solution A)

Transport: Stable at room temperature

139 Polyomavirus JC by Real-Time PCR

Clinical significance: Polyomavirus JC is a double-stranded DNA virus belonging to the Papovavirus family. It is estimated that 60% to 80% of adults in Europe and the United States have antibodies to JC virus, suggesting infectivity rates are quite high. It is proposed that JC virus establishes a latent infection in the kidney after a primary infection. JC virus has been linked to the development of hemorrhagic cystitis, ureteral stenosis and allograft dysfunction in renal transplant recipients. It is also believed to be the primary causative agent of both nephropathies after transplantation and progressive multifocal leukoencephalopathy. In this assay, DNA is extracted from the specimen and subjected to PCR amplification.

Method: Real-Time PCR

Specimen: ***UroSwab***®, whole blood yellow top tube (ACD solution A), biopsy (fresh), biopsy (paraffin)

Transport: Stable at room temperature

362 *Prevotella* Species Group 1 by Real-Time PCR (*P. bivia, P. disiens, P. intermedia, P. melaninogenica*)

Clinical significance: *Prevotella* species are Gram-negative non-motile rod-shaped singular cells that thrive in anaerobic growth conditions. *Prevotella* species can cause infections of the genital tract, urinary tract, wounds, bites, abscesses, bacteremia, and periodontal problems. *Prevotella* species involved in the Group 1 assay are *Prevotella bivia*, *Prevotella disiens*, *Prevotella intermedia*, and *Prevotella melaninogenica*. In this assay, DNA is extracted from the specimen and subjected to PCR amplification.

Method: Real-Time PCR

Specimen: ***OneSwab***®, ***UroSwab***®, whole blood yellow top tube (ACD solution A)

Transport: Stable at room temperature

363 *Prevotella* Species Group 2 by Real-Time PCR (*P. corporis*, *P. albensis*)

Clinical significance: *Prevotella* species are Gram-negative non-motile rod-shaped singular cells that thrive in anaerobic growth conditions. *Prevotella* species can cause infections of the genital tract, urinary tract, wounds, bites, abscesses, bacteremia, and periodontal problems. *Prevotella* species involved in the Group 2 assay are *P. corporis* and *P. albensis*. In this assay, DNA is extracted from the specimen and subjected to PCR amplification.

Method: Real-Time PCR

Specimen: ***OneSwab***®, ***UroSwab***®, whole blood yellow top tube (ACD solution A)

Transport: Stable at room temperature

146 *Proteus mirabilis* by Real-Time PCR

Clinical significance: *Proteus mirabilis*, a Gram-negative enteric bacterium, is one of the most common Gram-negative pathogens encountered in clinical specimens and can cause a variety of community or hospital-acquired illnesses, including urinary tract, wound, and bloodstream infections. *P. mirabilis* is one of the most common causes of urinary tract infections (UTI) in individuals with long-term indwelling urinary catheters, complicated UTI, and bacteremia among the elderly. Individuals suffering from UTIs caused by *P. mirabilis* often develop bacteriuria, kidney and bladder stones, catheter obstruction due to stone encrustation, acute pyelonephritis, and fever. In this assay, DNA is extracted from the patient specimen and subjected to PCR amplification.

Method: Real-Time PCR

Specimen: ***OneSwab***®, ***UroSwab***®

Transport: Stable at room temperature

174 *Pseudomonas aeruginosa* by Real-Time PCR

Clinical Significance: *Pseudomonas aeruginosa* is a Gram-negative, opportunistic bacterial pathogen and is mainly associated with nosocomial urinary tract infections (UTI) in hospital patients. However, it is known to be amongst the opportunistic strains colonizing the vaginal tract and is commonly tested against for specificity of diagnostics for Bacterial Vaginosis related pathogens. Routine clinical diagnosis usually takes up to 48 hours to report. In this assay, DNA is extracted from the specimen and subjected to PCR amplification.

Method: Real-Time PCR

Specimen: ***OneSwab***®, ***UroSwab***®, ***NasoSwab***®

Transport: Stable at room temperature

177 *Serratia marcescens* by Real-Time PCR

Clinical Significance: *Serratia marcescens* is a Gram-negative rod-shaped bacterium in the Enterobacteriaceae family which is known for its ability to produce a red/pink pigment. *S. marcesans* is an opportunistic pathogen and is commonly associated with hospital infections. *Serratia* species are associated with 1.4% of nosocomial bloodstream infections in the United States. Infection can be found in the urinary tract, blood stream, respiratory tract, surgical wounds as well as in skin and soft tissue infections. It is commonly found in the urinary tract of hospitalized adults. In this assay, DNA is extracted from the specimen and subjected to PCR amplification.

Method: Real-Time PCR

Specimen: ***OneSwab***®, ***UroSwab***®

Transport: Stable at room temperature

184 *Staphylococcus aureus* by Real-Time PCR

Clinical significance: Both community-associated and hospital-acquired infections with *Staphylococcus aureus* have increased in the past 20 years and are commonly referred to as “Staph Infections”. *S. aureus* can be associated with skin and soft tissue infections as well as Aerobic vaginitis (AV), among a host of other clinical conditions. AV is a state of abnormal vaginal flora that is distinct from the more common bacterial vaginosis (BV) in that *Staphylococcus aureus* may trigger a localized vaginal inflammatory immune response. In this assay, DNA is extracted from the specimen and subjected to PCR amplification.

Method: Real-Time PCR

Specimen: ***OneSwab***®, *ThinPrep*®

Transport: Stable at room temperature

151 *Staphylococcus saprophyticus* by Real-Time PCR

Clinical significance: *Staphylococcus saprophyticus* is a coagulase-negative *Staphylococcus* species which is implicated in 10% to 20% of urinary tract infections (UTI). In females between the ages of 17-27, it is the second most common cause of UTIs. It may also reside in the urinary tract and bladder of sexually active females. *S. saprophyticus* can cause UTIs in men often as a complication of bacterial infections of the prostate gland or kidney. Some of the symptoms may include a burning and frequency of urination, a ‘dripping effect’ after urination, weak bladder, bloated feeling with sharp razor pains in the lower abdomen around the bladder and ovary areas and razor-like pains during sexual intercourse. In this assay, DNA is extracted from the specimen and subjected to PCR amplification.

Method: Real-Time PCR

Specimen: ***OneSwab***®, ***UroSwab***®

Transport: Stable at room temperature

110 *Treponema pallidum* (syphilis) by Real-Time PCR

When sampling a crusted over lesion, moisten the swab with sterile saline solution prior to swabbing.

Clinical significance: *Treponema pallidum* is the causative agent of the sexually transmitted disease syphilis. The diagnosis of syphilis through traditional culture methods is complicated by the fact that *T. pallidum* is one of the few major bacterial pathogens of humans that cannot be cultivated on artificial medium. In this assay, we utilize a sensitive technique for *T. pallidum* identification that is based upon the amplification of the gene encoding the pathogen-specific and highly conserved 47-kDa membrane immunogen (tpp 47). In this assay, DNA is extracted from the specimen and subjected to PCR amplification.

Method: Real-Time PCR

Specimen: ***OneSwab***®, ***UroSwab***®, *ThinPrep*®, whole blood yellow top tube (ACD solution A), biopsy (fresh), biopsy (paraffin)

Transport: Stable at room temperature

111 *Trichomonas vaginalis* by Real-Time PCR (Reflex to metronidazole resistance)

When sampling a crusted over lesion, moisten the swab with sterile saline solution prior to swabbing

Clinical significance: *Trichomonas vaginalis*, a protozoan parasite, is the causative agent of trichomoniasis. The spread of *T. vaginalis* is usually, but not exclusively, through sexual contact. It is a major cause of vaginitis, cervicitis, and urethritis in women and may cause nongonococcal urethritis, prostatitis, and perhaps other genitourinary tract syndromes in men. Routine clinical diagnosis usually depends on microscopic identification of the parasite in wet mount preparations. Unfortunately, wet mount examination detects only 60% of culture-positive cases in women. Patients are normally treated with a single oral dose of metronidazole, an antibiotic used to treat infections caused by anaerobic bacteria and parasites. Although generally effective, some *T. vaginalis* strains are resistant to metronidazole. If metronidazole treatment fails, the only other approved treatment for *T. vaginalis* is the related drug tinidazole. Therefore, identifying *Trichomonas vaginalis* resistance to metronidazole can help guide clinicians in prescribing effective therapy for *Trichomonas* vaginitis patients. In this assay, DNA is extracted from the specimen and subjected to PCR amplification.

Method: Real-Time PCR

Specimen: ***OneSwab***®, ***UroSwab***®, *ThinPrep*®

Transport: Stable at room temperature

178 *Ureaplasma parvum* by Real-Time PCR (*Reflex to antibiotic resistance by Molecular Analysis)

Clinical Significance: *Ureaplasma*, of the family Mycoplasmataceae, are among the smallest free-living bacteria. *Ureaplasma parvum* can be found in the urinary tract of healthy female and male individuals and can also be associated with disease such as urethritis, pyelonephritis, wound infection, and pelvic inflammatory disease. In women it is also associated with adverse pregnancy outcomes and neonatal complications. In this assay, DNA is extracted from the specimen and subjected to PCR amplification.

Method: Real-Time PCR

Specimen: ***OneSwab***®, ***UroSwab***®

Transport: Stable at room temperature

320 *Ureaplasma urealyticum* by Real-Time PCR (*Reflex to antibiotic resistance by Molecular Analysis)

Clinical significance: *Ureaplasma*, of the family Mycoplasmataceae, are among the smallest free-living bacteria. Colonization, the presence and multiplication of microorganisms without tissue invasion or damage, usually begins at birth with passage through an infected mother's birth canal. Ureaplasmas have been isolated from the genital tract of 33% of infant girls and from the noses and throats of 15% of infant boys and girls. Carriage of these organisms does not usually persist beyond the age of 2. However, a small portion of pre-pubescent children will remain colonized and asymptomatic. As a result of sexual contact, the incidence of genital Ureaplasmas increases after puberty. In some pregnant women, Ureaplasma infections are considered to be the cause of chorioamnionitis and premature delivery. They are frequently transmitted from mothers to their infants, which may cause a variety of disorders including pneumonia, persistent pulmonary hypertension, and chronic infection of the central nervous system. In this assay, DNA is extracted from the specimen and subjected to PCR amplification.

Method: Real-Time PCR

Specimen: ***OneSwab***®, ***UroSwab***®, *ThinPrep*®, whole blood yellow top tube (ACD solution A), biopsy (fresh), biopsy (paraffin), CSF

Transport: Stable at room temperature

176 Urinary Pathogens Antibiotic Resistance [*E. coli, K. oxytoca, K. pneumonia*, *P. mirabilis*: amoxicillin-clavulanic acid, Cephalothin (cephalexin), trimethoprim-sulfamethoxazole, nitrofurantoin, ciprofloxacin, fosfomycin. *nterococcus faecalis*, *Enterococcus faecium:* ampicillin, nitrofurantoin, ciprofloxacin, fosfomycin, doxycycline, linizolid]

Positive results for test #'s 141, 153, 154, 727, 728, or 146 required.

Clinical significance: Urinary tract infections (UTIs) are definitively identified by the presence of bacteria in the urine (bacteriuria). Guidelines vary, but in general, a pure culture of > 105 colony-forming units (CFUs) per milliliter of urine is considered indicative of a community-acquired UTI. Additional guidelines for certain patient groups, such as catheter-associated UTIs (CAUTI), include > 103 and < 105 CFU/ml with no more than two bacterial species is considered indicative of a CAUTI. Most (> 80%) of these infections are caused by uropathogenic *E. coli* (UPEC), with *K. pneumoniae*, *P. mirabilis* and *S. saprophyticus* as the next most prevalent uropathogens. Community-acquired UTIs are normally treated with empirical antimicrobial therapy upon diagnosis. The recommended first-line antibiotic therapy for cystitis is a three day course of trimethoprim-sulfamethoxazole (SXT). Trimethoprim and sulfamethoxazole are both bacteriostatic inhibitors of the folate pathway required for bacterial synthesis of thymidine. With regards to β-lactam antibiotics, penicillins and first generation cephalosporins are not recommended for treatment unless staining confirms a Gram-positive pathogen, since resistance is prevalent among UPEC due to expression of β-lactamases. A combination of a β-lactam with a β-lactamase inhibitor (e.g. amoxicillin-clavulanic acid) can be used to overcome β-lactamase production. In geographic areas where UPEC resistance to SXT exceeds 15% to 20%, a three day course of a fluoroquinolone such as ciprofloxacin is recommended for non-pregnant women. As fluoroquinolones are assigned to FDA pregnancy risk "C" category (gestational risk in animal studies and no adequate human studies), pregnant patients are prescribed a 7-day course of nitrofurantoin, which in its reduced form damages bacterial DNA. Recent studies have found resistance rates of 21% for SXT and 6% for fluoroquinolones. In addition, 3% of isolates harbor extended-spectrum β-lactamases (ESBLs), capable of hydrolyzing third generation cephalosporins (e.g. ceftriaxone, ceftazidime). Therefore, antimicrobial susceptibility testing is critical to ensure appropriate treatment of UTI patients.

Method: Culture

Specimen: ***UroSwab***®

Transport: Stable at room temperature

575 Urogenital Candidiasis Panel by Real-Time PCR

551 *Candida albicans* by Real-Time PCR
559 *Candida glabrata* by Real-Time PCR
566 *Candida krusei* by Real-Time PCR
558 *Candida parapsilosis* by Real-Time PCR
557 *Candida tropicalis* by Real-Time PCR

Clinical significance: The incidence of Urogenital Candidiasis in men is poorly documented, particularly since it is not a reportable entity. Four major causes of Urogenital Candidiasis in men are *Candida albicans, C. glabrata, C. parapsilosis*, and *C. tropicalis*. Candida infection in men can cause urethritis and balanitis, an inflammation of the foreskin and glans of the penis in circumcised men. Prostatic infection with Candida has also been reported. Candidosis of the penis can be transmitted during sexual contact with partners with chronic vaginal or anal carriage. MDL has developed a highly sensitive and specific PCR based assay that can differentiate among these four pathogens

Method: Real-Time PCR

Specimen: ***OneSwab***®, ***UroSwab***®

Transport: Stable at room temperature

134 Urogenital Mycoplasma & Ureaplasma Panel by Real-Time PCR

129 *Mycoplasma genitalium* by Real-Time PCR (Reflex to azithromycin & fluoroquinolone resistance by Pyrosequencing)
130 *Mycoplasma hominis* by Real-Time PCR
320 *Ureaplasma urealyticum* by Real-Time PCR (*Reflex to antibiotic resistance by Molecular Analysis)

Clinical significance: Mycoplasmas are small (0.2 – 0.3 nm) membrane bound organisms capable of independent self-replication. The most prevalent strains recoverable from the genital tract are ***Ureaplasma urealyticum***, ***Mycoplasma hominis*** and ***Mycoplasma genitalium***. Infants can become colonized with genital mycoplasmas during birth. After puberty, colonization with mycoplasmas occurs primarily through sexual contact. Genital mycoplasmas are commonly isolated from gravid women at approximately the same recovery rate as in nonpregnant women with the same degree of sexual activity. Mycoplasmas and Ureaplasmas are strongly associated with infertility, intraamnionic infection, postpartum infection, pelvic inflammatory disease (PID), and histologic chorioamnionitis. Genital mycoplasma infections are usually diagnosed by culture. However, it can take from 2 to 5 days or up to 8 weeks to culture *M. hominis* and *M. genitalium*, respectively. Subspeciation of human urogenital mycoplasma infections is paramount for successful antimicrobial therapy due to differential antimicrobial susceptibilities. In this assay, DNA is extracted from the specimen and subjected to PCR amplification using a highly sensitive and specific PCR based assay developed by MDL that can differentiate among these bacterial species.

Method: Real-Time PCR

Specimen: ***OneSwab***®, ***UroSwab***®, *ThinPrep*®

Transport: Stable at room temperature

131 Urogenital Mycoplasma Panel by Real-Time PCR

129 *Mycoplasma genitalium* by Real-Time PCR (Reflex to azithromycin & fluoroquinolone resistance by Pyrosequencing)
130 *Mycoplasma hominis* by Real-Time PCR

Clinical significance: Mycoplasmas are small (0.2 – 0.3 nm), membrane-bound organisms capable of independent self-replication. The most prevalent strains recoverable from the genital tract are *Ureaplasma urealyticum*, ***Mycoplasma hominis*** and ***Mycoplasma genitalium***. Infants can become colonized with genital mycoplasmas during birth. After puberty, colonization with mycoplasmas occurs primarily through sexual contact. Genital mycoplasmas are commonly isolated from gravid women at approximately the same recovery rate as in nonpregnant women with the same degree of sexual activity. Mycoplasmas and Ureaplasmas are strongly associated with infertility, intraamnionic infection, postpartum infection, pelvic inflammatory disease (PID), and histologic chorioamnionitis. Genital mycoplasma infections are usually diagnosed by culture. However, it can take from 2 to 5 days or up to 8 weeks to culture *M. hominis* and *M. genitalium*, respectively. Subspeciation of human urogenital mycoplasma infections is paramount for successful antimicrobial therapy due to differential antimicrobial susceptibilities. In this assay, DNA is extracted from the specimen and subjected to PCR amplification using a highly sensitive and specific PCR based assay developed by MDL that can differentiate among these Mycoplasma species.

Method: Real-Time PCR

Specimen: ***OneSwab***®, ***UroSwab***®, *ThinPrep*®

Transport: Stable at room temperature

215 Varicella-zoster virus (VZV) by Real-Time PCR

When sampling a crusted over lesion, moisten the swab with sterile saline solution prior to swabbing.

Clinical significance: Varicella-Zoster Virus (VZV), also known as HHV3, is a member of the neurotrophic alpha herpes virus family, which is considered to be the most infectious of the human herpes viruses. The alpha herpes viruses' possess factors that increase their infectivity, including short reproductive cycles, the ability to replicate in multiple cell types and the ability to induce high levels of host cell tissue destruction quite rapidly. Humans serve as the alpha herpesviruses' only natural reservoir, which means transmission is person-to-person through either the aerosolization of virus in nasopharyngeal secretions or more directly by contact with vesicle fluids or respiratory secretions. Primary infections result in chickenpox and 95% occur during childhood. Presenting symptoms include rash, low-grade fever, headaches and malaise. Patients with chickenpox remain infective until the last skin lesion has dried and crusted over. Those who are infected during adulthood experience a greater number of complications and account for nearly half of all chickenpox-related deaths. Neonates and pregnant women are particularly susceptible to severe primary VZV infections. Complications associated with VZV infection include bacterial super-infections of the skin and lower respiratory tract. Diagnosis is typically based on clinical presentation, but in some instances, particularly immunocompromised individuals, clinical evaluation is necessary. Because VZV is capable of establishing a latent state within the sensory ganglia, infection is life-long and viral reactivation in the form of shingles or Ramsay Hunt Syndrome is possible at any age. Shingles occur in approximately 20% of the adult population at least once in their lives, with 1% experiencing multiple reactivations. Vaccination with the live attenuated Oka strain of VZV, Varivax, is available and recommended for adults over the age of sixty for the prevention of shingles. In this assay, DNA is extracted from the specimen and subjected to PCR amplification.

Method: Real-Time PCR

Specimen: ***OneSwab***®, ***UroSwab***®, whole blood yellow top tube (ACD solution A), CSF

Transport: Stable at room temperature

2605 Hereditary Melanoma Cancer Panel (10 genes) by Next Generation Sequencing (BAP1, BRCA1, BRCA2, CDK4, CDKN2A, MITF, POT1, PTEN, RB1, TP53)

Clinical Significance: genetic testing may confirm a diagnosis and help guide treatment and management decisions. Identification of a disease-causing variant would also guide testing and diagnosis of at-risk relatives. Pathogenic variants in multiple genes have been implicated in hereditary melanoma.

Method: Gene Sequencing and Deletion/ Duplication Analysis

Specimen: Whole blood (ACD solution A) or saliva

Transport: Stable at room temperature

2603 Hereditary Prostate Cancer Panel (18 genes) by Gene Sequencing and Deletion/ Duplication Analysis (ATM, BRCA1, BRCA2, BRIP1, CHEK2, EPCAM, FANCA, HOXB13, MITF, MLH1, MSH2, MSH6, NBN, PALB2, PMS2, RAD51C, RAD51D, TP53)

Clinical Significance: Hereditary Prostate Cancer genetic testing analyzes genes associated with a hereditary predisposition to prostate cancer. Men with pathogenic variants in these genes have an increased risk of developing prostate cancer and, in some cases, other cancers as well.

Method: Gene Sequencing and Deletion/ Duplication Analysis

Specimen: Whole blood (ACD solution A) or saliva

Transport: Stable at room temperature

2604 Hereditary Renal Cancer Panel (19 genes) by Gene Sequencing and Deletion/ Duplication Analysis (BAP1, EPCAM, FH, FLCN, MET, MITF, MLH1, MSH2, MSH6, PALB2, PMS2, PTEN, SDHB, SDHC, SDHD, TP53, TSC1, TSC2, VHL)

Clinical Significance: Hereditary Renal Cancer genetic testing may confirm a diagnosis and help guide treatment and management decisions. Identification of a disease-causing variant would also guide testing and diagnosis of at-risk relatives. Pathogenic variants in multiple genes have been implicated in hereditary renal cancer.

Method: Gene Sequencing and Deletion/ Duplication Analysis

Specimen: Whole blood (ACD solution A) or saliva

Transport: Stable at room temperature

149 *Actinomyces turicensis* by Real-Time PCR

Clinical significance: *Actinomyces turicensis* is a Gram-positive facultative anaerobe that is a commensal part of the oropharynx, gastrointestinal tract, and female genital tract. Although *Actinomyces* species are not considered to be pathogenic by nature, but rather part of the normal flora, they are capable of colonizing and establishing pathogenic infections within neighboring tissues upon a breach in the integrity of the mucosal membranes that typically sequester them resulting in the chronic condition Actinomycosis. *A. turicensis* is one of the more commonly isolated species of the genus Actinomyces known to induce the Actinomycosis, a condition which is characterized by abscess formation, tissue fibrosis, and draining sinuses. While, clinically, infections of the oral and cervicofacial region are the most common, Actinomycosis also frequently occurs within the thoracic, abdominopelvic, and central nervous system compartments.

Method: Real-Time PCR

Specimen: ***OneSwab***®, ***UroSwab***®, whole blood yellow top tube (ACD solution A)

Transport: Stable at room temperature

147 *Bacteroides ureolyticus* by Real-Time PCR

When sampling a crusted over lesion, moisten the swab with sterile saline solution prior to swabbing.

Clinical significance: *Bacteroides ureolyticus* is an obligate anaerobic Gram-negative rod-shaped bacterium that was first described in clinical specimens in 1948. It is the most commonly detected Bacteroides strain after *B. fragilis*. Identification of this organism from infections within the buccal cavity, intestinal tract, urogenital tract, and blood has been reported. It has also been isolated from mixed cultures of infections involving nearly every organ system in humans. *B. ureolyticus* is associated with ulcerative lesions of both the external and internal genitalia, including the perineal area, as well as abscesses and has been implicated in non-gonoccocal urethritis (NGU); one study reported its identification in 50% of the evaluated men with confirmed NGU. It is thought to cause damage to the urethral mucosa via its expression of an endotoxin. In this assay, DNA is extracted from the specimen and subjected to PCR amplification.

Method: Real-Time PCR

Specimen: ***OneSwab***®, ***UroSwab***®, whole blood yellow top tube (ACD solution A)

Transport: Stable at room temperature

326 *Bartonella bacilliformis* by Real-Time PCR

Clinical significance: The genus Bartonella contains aerobic, fastidious, Gram-negative bacteria that belong to the alpha-2 subgroup of the class Proteobacteria. Due to the limited distribution of its vector, the sand fly, *Bartonella bacilliformis* is found predominantly at high elevations in the Andes Mountains. It is the causative agent of Carriõn's disease. This biphasic syndrome is comprised of two disorders: Oroya Fever and verruga peruana. Oroya fever is characterized by an acute septicemic phase of severe hemolytic anemia. The chronic form, verruga peruana, is the second phase and is characterized by reddish papular skin lesions that are highly vascular in nature. Verruga peruana is very similar to bacillary angiomatosis which is caused by *B. henselae*. Without appropriate antimicrobial therapy, they may be fatal. In this assay, DNA is extracted from the specimen and subjected to PCR amplification.

Method: Real-Time PCR

Specimen: Whole blood yellow top tube (ACD solution A), ticks

Transport: Stable at room temperature

325 *Bartonella clarridgeiae* by Real-Time PCR

Clinical significance: The genus Bartonella contains aerobic, fastidious, Gram-negative bacteria that belong to the alpha-2 subgroup of the class Proteobacteria. *Bartonella clarridgeiae* is predominantly associated with infection in cats. However, it has been documented as an additional cause of Cat Scratch Disease (CSD) along with *Bartonella henselae*. Transmission from cats to humans has also been documented. In this assay, DNA is extracted from the specimen and subjected to PCR amplification.

Method: Real-Time PCR

Specimen: Whole blood yellow top tube (ACD solution A), ticks

Transport: Stable at room temperature

339 *Bartonella elizabethae* by Real-Time PCR

Clinical significance: The genus Bartonella contains aerobic, fastidious, Gram-negative bacteria that belong to the alpha-2 subgroup of the class Proteobacteria. *Bartonella elizabethae* has been associated with endocarditis. The means of transmission of *B. elizabethae* is unknown, but is believed to be via an arthropod vector. It has been isolated in a human patient and in rats. In this assay, DNA is extracted from the specimen and subjected to PCR amplification.

Method: Real-Time PCR

Specimen: Whole blood yellow top tube (ACD solution A), CSF, ticks

Transport: Stable at room temperature

376 *Bartonella henselae* IgG by ELISA

Serum required

Clinical significance: *Bartonella henselae* is the causative agent of cat scratch disease (CSD) as well as other conditions. It is commonly seen in immunocompromised patients, particularly those suffering from HIV infection. The classic clinical presentation of CSD is a self-limiting regional lymphadenopathy, usually caused by a cat scratch or bite. The disease starts with a lesion at the site of infection, which may become a papule. Transmission of the disease has been linked to cats and is also suspected to occur via fleas and ticks. Recently, Bartonella has been detected in immunocompromised patients as well as in *Ixodes scapularis* ticks, the same ticks that transmit Lyme disease. Evidence is mounting that *Bartonella* species are also transmitted from ticks to humans and can contribute to the disease manifestations of Lyme disease. Traditionally, clinical diagnostics have relied on direct culturing and immunofluorescent antibody (IFA) technologies. The culturing of Bartonella from blood samples is technically challenging and is a low-yield procedure with recommended growth conditions including lengthy incubation periods of at least 21 days. *B. henselae* IFAs have high sensitivity and specificity. However, cross-reactivity with other human pathogens has been reported. In addition, IFAs rely heavily on technicians for the determination of test results, are time-consuming to score, and require expensive fluorescent microscopes. Detection of antibodies using an ELISA assay allows diagnosis of an infection when other methods, such as culture or IFA, are impractical or yield negative results. In this assay, patient serum is analyzed by ELISA for the presence of *Bartonella henselae*-specific IgG antibodies.

Method: ELISA

Specimen: Serum

Transport: Stable at room temperature

317 *Bartonella henselae* by Real-Time PCR

Clinical significance: *Bartonella henselae* is the causative agent of Cat Scratch Disease (CSD) as well as other conditions. It is commonly seen in immunocompromised patients, particularly those suffering from HIV infection. The classic clinical presentation of CSD is a self-limiting, regional lymphadenopathy, usually caused by a cat scratch or bite. The disease starts with a lesion at the site of infection, which may become a papule. Transmission of the disease has been linked to cats and is also suspected to occur via fleas and ticks. Recently, *B. henselae* has been detected in immunocompromised patients as well as in *Ixodes scapularis* ticks, the same ticks that transmit Lyme disease. Evidence is mounting that *Bartonella* species are also transmitted from ticks to humans and can contribute to the disease manifestations of Lyme disease. Proper identification is essential such that the necessary treatments are administered. In this assay, DNA is extracted from the specimen and subjected to PCR amplification.

Method: Real-Time PCR

Specimen: Whole blood yellow top tube (ACD solution A), CSF, ticks

Transport: Stable at room temperature

342 *Bartonella quintana* by Real-Time PCR

Clinical significance: The genus Bartonella contains aerobic, fastidious, Gram-negative bacteria that belong to the alpha-2 subgroup of the class Proteobacteria. *B. quintana* was first identified as an important human pathogen during World War I when it caused epidemics of louse-borne trench fever. *B. quintana* infections were rarely recognized from the end of World War II until the 1980s, when the organism re-emerged as an opportunistic pathogen among HIV-infected persons. It has since been identified in cases of bacillary angiomatosis, endocarditis and bacteremia, isolated from AIDS patients, and, more recently, in homeless populations. In this assay, DNA is extracted from the specimen and subjected to PCR amplification.

Method: Real-Time PCR

Specimen: Whole blood yellow top tube (ACD solution A), CSF, ticks

Transport: Stable at room temperature

356 *Bartonella* Species by Real-Time PCR

Clinical significance: The genus Bartonella contains aerobic, fastidious, Gram-negative bacteria which belong to the alpha-2 subgroup of the class Proteobacteria. MDL has developed a rapid and sensitive PCR-based method for the simultaneous detection and differentiation of *Bartonella* sub-species, *B. henselae* and *B. quintana*, from specimens. In this assay, DNA is extracted from the specimen and subjected to PCR amplification.

Method: Real-Time PCR

Specimen: Whole blood yellow top tube (ACD solution A), CSF, ticks

Transport: Stable at room temperature

352 *Bordetella pertussis* (IgG/IgA) by Western blot

Serum required

Clinical significance: Pertussis, commonly known as whooping cough, results from an upper respiratory tract infection with *Bordetella pertussis*. This infection was a significant cause of childhood morbidity and mortality in the early part of the twentieth century and reemerged as a significant health concern in the late 1990's. The upward trend in childhood pertussis cases has been primarily attributed to decreased vaccine usage, while the increase in adult pertussis cases is attributed to waning vaccine-induced immunity and the lack of a vaccine approved for use in adults. In this assay, IgG and IgA antibodies to *B. pertussis* in human serum are detected.

Method: Western blot

Specimen: Serum

Transport: Stable at room temperature

359 *Brucella* species (*B. abortus, B. canis, B. melitensis, B. ovis* and *B. suis*) by Real-Time PCR

Clinical Significance: Brucellosis is an important zoonosis of public health in many countries. Due to the fact that clinical presentation of this disease varies so greatly, diagnosis can really only be made based on laboratory methods. *Brucella melitensis* is the species that primarily causes infection in humans. Human brucellosis, also known as 'undulant fever' or 'Bang's disease' can change from an occupational disease for farmers, veterinarians and other animal health professionals to a food-borne disease when people consume non-pasteurized milk and cheeses made with raw milk from infected cattle. Human symptoms of brucellosis infection include fever, night sweats, undue fatigue, anorexia, weight loss, headache, and arthralgia. Severe infections of the central nervous system or lining of the heart may occur. Brucellosis can also cause long-lasting or chronic symptoms that include recurrent fevers, joint pain, and fatigue. Our PCR-based testing permits the identification of four species of Brucella—*Brucella abortus*, *B. melitensis*, *B. ovis*, and *B. suis*. In this assay, DNA is extracted from the specimen and subjected to PCR amplification.

Method: Real-Time PCR

Specimen: Whole blood yellow top tube (ACD solution A)

Transport: Stable at room temperature

105 *Chlamydia trachomatis* by Real-Time PCR (*Reflex to antibiotic resistance by Molecular Analysis)

Applicable for *UroSwab*® specimens in adolescent females who are not candidates for pelvic exams.

Clinical significance: *Chlamydia trachomatis* is the causative agent of the disease Chlamydia and is the most common sexually transmitted bacterial agent. In women this bacterium causes cervicitis, urethritis, endometritis and salpingitis. In more complicated cases, *C. trachomatis* infections may result in tubal scarring, infertility, and ectopic pregnancy. In men it causes urethritis and proctatitis. If left untreated, Chlamydia may develop into lymphogranuloma venereum. Other forms of infection also seen are trachoma, the most preventable form of blindness, and conjunctivitis in neonates. *Chlamydia trachomatis* has also been associated with reactive arthritis (RA), also called Reiter's syndrome, the most common type of inflammatory polyarthritis in young men. *C. trachomatis* infection is the most common antecedent of RA and accounts for most cases of venereal origin. It is important that proper treatment be initiated for both the patient and infected sexual partners to prevent spread of the disease and reinfection of the patient. *Chlamydia trachomatis* is typically thought to be easily treated with antibiotics. Previous studies have demonstrated that azithromycin and doxycycline were equally efficacious for the treatment of genital chlamydial infection. Azithromycin is a popular choice of treatment for those patients with unpredictable follow-up or poor treatment compliance since it can be administered as a single dose. However, recent studies suggest that treatment failure may occur in more than 5% of patients due to resistance to azithromycin. This emerging resistance of *Chlamydia trachomatis* to azithromycin is important when choosing proper antibiotic therapy. MDL can now detect azithromycin resistance in a subset of *C. trachomatis* positive specimens by Real-Time PCR. This new assay detects *C. trachomatis* to a single point mutation within the 23S rRNA gene of *C. trachomatis* that confers resistance to azithromycin. In this assay, DNA is extracted from the specimen and subjected to PCR amplification.

Method: Real-Time PCR

Specimen: ***OneSwab***®, ***UroSwab***®, *ThinPrep*®, whole blood yellow top tube (ACD solution A)

Transport: Stable at room temperature

364 Chlamydiales species (*Chlamydophila pneumoniae*, *Chlamydophila psittaci*, and *Chlamydia trachomatis*) by Real-Time PCR

Clinical significance: There are three subtypes associated with causing disease in humans. ***Chlamydophila pneumoniae*** causes pneumonia, sinusitis, bronchitis, pharyngitis and has been associated with adult onset asthma, atherosclerotic cardiovascular disease, arthritis, and chronic fatigue syndrome. ***Chlamydophila psittaci*** is the causative agent of psittacosis or parrot fever. ***Chlamydia trachomatis*** is a sexually transmitted disease that also causes conjunctivitis, pneumonia, proctitis, and lymphogranuloma venereum. It is also the cause of ocular trachoma, the leading cause of preventable blindness. Sensitive screening methods are necessary for early detection of Chlamydial infections. Rapid treatment could control and decrease the spread of the disease. MDL has developed a rapid and sensitive Real-Time PCR-based method for the detection and differentiation of Chlamydia sub-species from specimens. In this assay, DNA is extracted from the specimen and subjected to PCR amplification.

Method: Real-Time PCR

Specimen: Whole blood yellow top tube (ACD solution A), CSF

Transport: Stable at room temperature

319 *Chlamydophila pneumoniae* by Real-Time PCR

Clinical significance: Chlamydophila are obligate intracellular parasites. *Chlamydophila pneumoniae*, also known as TWAR, is the most recently identified of the *Chlamydophila* species. It is a common cause of infection throughout the world. Although first isolated in 1965, it was not established as a human pathogen until it was obtained from a respiratory specimen in 1983. Infection is spread via exposure to respiratory secretions. It has been associated with community acquired acute respiratory infection, adult onset asthma, atherosclerotic cardiovascular disease, arthritis, and chronic fatigue syndrome. In this assay, DNA is extracted from the specimen and subjected to PCR amplification.

Method: Real-Time PCR

Specimen: ***NasoSwab***®, whole blood yellow top tube (ACD solution A), CSF

Transport: Stable at room temperature

327 *Chlamydophila pneumoniae* IgG/IgM by ELISA

Serum required

Clinical significance: *Chlamydophila pneumoniae* is the most recently identified of the *Chlamydophila* species and is a common cause of infection throughout the world. Seropositivity rates are very low in children under 5 years of age. By the time most people reach early adulthood, 50% are seropositive with rates reaching approximately 75% in the elderly. *C. pneumoniae* specific IgM antibodies appear approximately 3 weeks after onset of illness; whereas, *C. pneumoniae*-specific IgG antibodies begin to appear about 6-8 weeks after onset. Detection of antibodies allows diagnosis of an infection when other methods, such as culture or antigen detection, are impractical or yield negative results.

Method: ELISA

Specimen: Serum

Transport: Stable at room temperature

361 *Chlamydophila psittaci* by Real-Time PCR

Clinical significance: *Chlamydophila psittaci*, an obligate intracellular bacterium, is the causative agent of psittacosis in birds and humans. It is a well-established pathogen responsible for regular outbreaks of disease in psittacine birds and domestic poultry, as well as cases of atypical pneumonia in exposed persons. Infection is acquired by inhaling dried secretions from infected birds. Psittacosis often starts with flu-like symptoms including fever, chills, headache, dyspnoea, and cough which may develop into a life-threatening pneumonia. In this assay, DNA is extracted from the specimen and subjected to PCR amplification

Method: Real-Time PCR

Specimen: Whole blood yellow top tube (ACD solution A)

Transport: Stable at room temperature

360 *Francisella* Species (*F. tularensis, F. holarctica*) by Real-Time PCR

Clinical significance: Five subspecies of Francisella are found in the Northern hemisphere, but only *F. tularensis* subsp. *tularensis* and subsp. *holarctica* cause disease in humans. *F. tularensis* is the causative agent of tularemia, a zoonotic disease of humans, rabbits, rodents, and hares. It is typically transmitted by inhalation, the bite of an infected tick, contact with infected animal products or by the ingestion of contaminated water. Clinical manifestations of tularemia vary depending on the virulence of the strain and the route of inoculation. Inhalation results in the pneumonic form. Acquisition through a tick bite or from contact with an infected animal, results in the ulceroglandular form of the disease. Francisella can also be contracted through the conjunctiva, causing the oculoglandular form of tularemia. Less commonly, ingestion of contaminated foods or water may result in clinical symptoms. Once the bacterium enters the body, it travels to the draining lymph nodes and then spreads to the liver, lungs, and spleen of infected humans or animals, where it replicates to high numbers. In this assay DNA is extracted from the specimen and subjected to PCR amplification.

Method: Real-Time PCR

Specimen: Whole blood yellow top tube (ACD solution A)

Transport: Stable at room temperature

353 *Helicobacter pylori* (IgG/IgA) by Western blot

Serum required

Clinical significance: Infection with *Helicobacter pylori* is the leading cause of gastric cancers. It can also present clinically as a variety of gastrointestinal diseases, including duodenal and gastric ulcers, malt lymphoma, gastric cancer and non-gastric dyspepsia. With approximately 50% of the world's population colonized with this organism, concern for the diagnosis and subsequent treatment of *H. pylori* infection is growing. Some diseases not associated with the gastrointestinal tract (i.e. liver disease, acne rosacea, chronic urticaria, atherosclerosis, and iron deficiency anemia) may be associated with *H. pylori* infection. Infection by *H. pylori* can also lead to loss of normal gastric function, including the ability to absorb micronutrients such as Vitamin B12, folic acid, beta-carotene and iron. In the assay, we detect IgG and IgA antibodies to *H. pylori* in human serum.

Method: Western Blot

Specimen: Serum

Transport: Stable at room temperature

310 *Helicobacter pylori* by Real-Time PCR

Clinical significance: *Helicobacter pylori* resides within the mucous membrane of the gastric epithelium and occasionally the duodenal or esophageal mucosal epithelium as well. It can lead to inflammation of the mucosa and, if untreated, chronic superficial gastritis. This inflammation process has been linked to peptic ulceration and gastric cancer. *Helicobacter pylori* is now established as the most common cause of gastritis. In this procedure, we perform a PCR assay for the sensitive and specific detection of *H. pylori*. The assay is based on the DNA sequence of a species-specific protein antigen, which is present in all strains of *H. pylori* tested. The specificity of this assay and the fidelity of the chosen region was verified by the lack of cross-reactivity with other enteric bacteria (whose coding sequence did not hybridize to the DNA of numerous enteric bacteria). In this assay, DNA is extracted from the specimen and subjected to PCR amplification.

Method: Real-Time PCR

Specimen: Whole blood yellow top tube (ACD solution A), gastric biopsy (fresh), gastric biopsy (paraffin)

Transport: Stable at room temperature

318 *Legionella pneumophila* by Real-Time PCR

Clinical significance: *Legionella pneumophila*, a rod-shaped, Gram-negative bacterium, is the causative agent of Legionella, also referred to as Legionnaire's disease, and Pontiac fever. *L. pneumophila* is involved in more than 95% of cases of severe, atypical pneumonia. This disease is most often contracted by inhaling mist from *L. pneumophila* contaminated water sources. Thus far, no cases of person-to-person transmission have been documented. It is commonly seen in immunocompromised patients, transplant patients, and people with impaired pulmonary function, such as heavy smokers. Traditional isolation of the organism from bronchoalveolar lavage (BAL) specimens is very invasive and time consuming. In addition, it has been demonstrated that certain strains cannot be cultured. Traditional serological means of diagnosis is often difficult due to the delay in seroconversion with respect to the timing of the onset of illness. In this assay, DNA is extracted from the specimen and subjected to PCR amplification.

Method: Real-Time PCR

Specimen: Whole blood yellow top tube (ACD solution A)

Transport: Stable at room temperature

158 *Listeria monocytogenes* by Real-Time PCR

Clinical Significance: *Listeria monocytogenes* is a Gram-positive, facultative intracellular parasite and is the causative agent of listeriosis. *L. monocytogenes* infections can cause septicemia, encephalitis, meningitis, and gastroenteritis. The bacteria is capable of entering most cells. Transmission occurs through contaminated foods including raw meat and fish, unpasteurized dairy products, and uncooked vegetables. *L. monocytogenes* has also been found in processed foods that have become contaminated after processing such as soft cheeses, deli cold cuts, sliced or grated cheese, and ice cream. The infective dose for oral transmission is unknown but is thought to depend on the strain and the susceptibility of the person. Healthy people seem to be able to eat most Listeria-contaminated foods without clinical signs; however, in susceptible persons, the infective dose is probably fewer than 1,000 organisms. The incubation period in susceptible adults is 3 to 70 days, with the median incubation period estimated to be 3 weeks. *L. monocytogenes* is relatively resistant to freezing, drying and heat and can proliferate at refrigeration temperatures on contaminated foods. Real-Time PCR is a rapid and accurate method for identifying *Listeria monocytogenes* in loose stool swab samples.

Method: Real-Time PCR

Specimen: Whole blood yellow top tube (ACD solution A), CSF

Transport: Stable at room temperature

332 *Mycoplasma fermentans* by Real-Time PCR

Clinical significance: *Mycoplasma* species are the smallest and genetically simplest self-replicating bacteria. *Mycoplasma* species are ubiquitous in nature and are widely distributed throughout the animal kingdom. *Mycoplasma fermentans*' potential role as a causative agent in chronic fatigue syndrome has generated much controversy. The potential invasive nature of this species has been demonstrated following the organism's detection in lung tissue from previously immunocompetent adult respiratory distress syndrome patients. *M. fermentans* has also been implicated as a cofactor in rheumatoid arthritis patients, where its presence in the synovial fluid of RA patients has been repeatedly demonstrated by both culture and molecular techniques. Its role as an opportunistic infection has also been demonstrated in patients with HIV infection. In this assay, DNA is extracted from the specimen and subjected to PCR amplification.

Method: Real-Time PCR

Specimen: Whole blood yellow top tube (ACD solution A), synovial fluid

Transport: Stable at room temperature

301 Mycoplasma general by Qualitative PCR

Clinical significance: *Mycoplasma* species are the smallest and genetically simplest self-replicating bacteria. *Mycoplasma* species are ubiquitous in nature and are widely distributed throughout the animal kingdom. They have recently been associated with certain acute and chronic illnesses and can function as causative agents, cofactors, and opportunistic infectious agents. Mycoplasmas have been associated with respiratory illness, urogenital disease, immunosuppressive disease, such as HIV infection, cardiac diseases, arthritic syndromes, tick-borne illness, and chronic fatigue syndrome. In this assay, DNA is extracted from the specimen and subjected to PCR amplification.

Method: PCR

Specimen: Whole blood yellow top tube (ACD solution A),Ticks

Transport: Stable at room temperature

130 *Mycoplasma hominis* by Real-Time PCR

Clinical significance: Mycoplasmas are small (0.2 – 0.3 nm), membrane-bound organisms capable of independent self-replication. The most prevalent strains recoverable from the genital tract are *Ureaplasma urealyticum*, *Mycoplasma hominis* and *Mycoplasma genitalium*. Infants can become colonized with genital mycoplasmas during birth. *M. hominis* has been linked to pyelonephritis, pelvic inflammatory disease (PID), spontaneous abortion, and postpartum septicemia and fever. Genital mycoplasma infections are usually diagnosed by culture. However, it can take 2 to 5 days to culture *M. hominis*. In this assay, DNA is extracted from the specimen and subjected to PCR amplification.

Method: Real-Time PCR

Specimen: ***UroSwab***®, whole blood yellow top tube (ACD solution A), CSF, synovial fluid

Transport: Stable at room temperature

335 *Mycoplasma penetrans* by Real-Time PCR

Clinical significance: *Mycoplasma* species are the smallest and genetically simplest self-replicating bacteria. *Mycoplasma* species are ubiquitous in nature and are widely distributed throughout the animal kingdom. They have recently been associated with certain acute and chronic illnesses and can function as causative agents, cofactors, and opportunistic infectious agents. *M. penetrans* has been isolated from the urogenital tract and from HIV patients. It is a potential cofactor in AIDS progression. Mycoplasmas have been associated with respiratory illness, urogenital disease, immunosuppressive disease, such as HIV infection, cardiac diseases, arthritic syndromes, tick-borne illness, and chronic fatigue syndrome. In this assay, DNA is extracted from the specimen and subjected to PCR amplification.

Method: Real-Time PCR

Specimen: ***UroSwab***®, whole blood yellow top tube (ACD solution A)

Transport: Stable at room temperature

336 *Mycoplasma pneumoniae* by Real-Time PCR

Clinical significance: *Mycoplasma* species are the smallest and genetically simplest self-replicating bacteria. *Mycoplasma* species are ubiquitous in nature and are widely distributed throughout the animal kingdom. *Mycoplasma pneumoniae* is the most common cause of pneumonia and febrile upper-respiratory tract infections. Transmission occurs person-to-person via respiratory droplets produced by coughing. Other complications may develop with infections ranging from mild to life threatening. In this assay, DNA is extracted from the specimen and subjected to PCR amplification.

Method: Real-Time PCR

Specimen: Whole blood yellow top tube (ACD solution A), ***NasoSwab***®, CSF

Transport: Stable at room temperature

340 *Mycoplasma pneumoniae* IgG/IgM by ELISA

Serum required

Clinical significance: *Mycoplasma* species are the smallest and genetically simplest self-replicating bacteria. *Mycoplasma* species are ubiquitous in nature and are widely distributed throughout the animal kingdom. *Mycoplasma pneumoniae* is the most common cause of pneumonia and febrile upper-respiratory tract infections. Other complications may develop with this disease ranging from mild to life threatening. Species-specific antibodies to surface antigens are known to exist and are readily detected by ELISA, even in the early stages of the disease. In the assay, IgG and IgM antibodies to *M. pneumoniae* in human serum are detected.

Method: ELISA

Specimen: Serum

Transport: Stable at room temperature

362 *Prevotella* Species Group 1 by Real-Time PCR (*P. bivia, P. disiens, P. intermedia, P. melaninogenica*)

Clinical significance: *Prevotella* species are Gram-negative non-motile rod-shaped singular cells that thrive in anaerobic growth conditions. *Prevotella* species can cause infections of the genital tract, urinary tract, wounds, bites, abscesses, bacteremia, and periodontal problems. *Prevotella* species involved in the Group 1 assay are *Prevotella bivia*, *Prevotella disiens*, *Prevotella intermedia*, and *Prevotella melaninogenica*. In this assay, DNA is extracted from the specimen and subjected to PCR amplification.

Method: Real-Time PCR

Specimen: ***OneSwab***®, ***UroSwab***®, whole blood yellow top tube (ACD solution A)

Transport: Stable at room temperature

363 *Prevotella* Species Group 2 by Real-Time PCR (*P. corporis, P. albensis*)

Clinical significance: *Prevotella* species are Gram-negative non-motile rod-shaped singular cells that thrive in anaerobic growth conditions. *Prevotella* species can cause infections of the genital tract, urinary tract, wounds, bites, abscesses, bacteremia, and periodontal problems. *Prevotella* species involved in the Group 2 assay are *P. corporis* and *P. albensis*. In this assay, DNA is extracted from the specimen and subjected to PCR amplification.

Method: Real-Time PCR

Specimen: ***OneSwab***®, ***UroSwab***®, whole blood yellow top tube (ACD solution A)

Transport: Stable at room temperature

151 *Staphylococcus saprophyticus* by Real-Time PCR

Clinical significance: *Staphylococcus saprophyticus* is a coagulase-negative *Staphylococcus* species which is implicated in 10% to 20% of urinary tract infections (UTI). In females between the ages of 17-27, it is the second most common cause of UTIs. It may also reside in the urinary tract and bladder of sexually active females. *S. saprophyticus* can cause UTIs in men often as a complication of bacterial infections of the prostate gland or kidney. Some of the symptoms may include a burning and frequency of urination, a 'dripping effect' after urination, weak bladder, bloated feeling with sharp razor pains in the lower abdomen around the bladder and ovary areas and razor-like pains during sexual intercourse. In this assay, DNA is extracted from the specimen and subjected to PCR amplification.

Method: Real-Time PCR

Specimen: ***UroSwab***®

Transport: Stable at room temperature

308 *Toxoplasma gondii* by Real-Time PCR

Clinical significance: *Toxoplasma gondii* is a single-celled parasite and the causative agent of the disease known as toxoplasmosis. According to the CDC, more than 60 million people in the US may be infected with the Toxoplasma parasite. Although symptoms are not always apparent in healthy individuals, pregnant women and those with compromised immune systems can present with more serious health issues. Such symptoms can include fever, sore throat, muscle pain and tiredness. In severe toxoplasmosis, damage to the brain and vision complications are possible. Infection of an unborn child early in pregnancy can result in miscarriage, poor growth, early delivery, or stillbirth. In this assay, DNA is extracted from the specimen and subjected to PCR amplification.

Method: Real-Time PCR

Specimen: Whole blood yellow top tube (ACD solution A)

Transport: Stable at room temperature

110 *Treponema pallidum* (syphilis) by Real-Time PCR

When sampling a crusted over lesion, moisten the swab with sterile saline solution prior to swabbing.

Clinical significance: *Treponema pallidum* is the causative agent of the sexually transmitted disease syphilis. The diagnosis of syphilis through traditional culture methods is complicated by the fact that *T. pallidum* is one of the few major bacterial pathogens of humans that cannot be cultivated on artificial medium. In this assay, we utilize a sensitive technique for *T. pallidum* identification that is based upon the amplification of the gene encoding the pathogen-specific and highly conserved 47-kDa membrane immunogen (tpp 47). In this assay, DNA is extracted from the specimen and subjected to PCR amplification.

Method: Real-Time PCR

Specimen: ***OneSwab***®, ***UroSwab***®, *ThinPrep*®, whole blood yellow top tube (ACD solution A), biopsy (fresh), biopsy (paraffin)

Transport: Stable at room temperature

358 *Tropheryma whippelii* by Real-Time PCR

Clinical significance: *Tropheryma whippelii* is the causative agent of Whipple's disease. Although most frequently associated with malabsorption syndrome accompanied by diarrhea, arthritis is the most common extraintestinal manifestation and affects up to 90% of patients. It can also affect the central nervous, pulmonary and cardiovascular systems. Worldwide Whipple's disease is extremely rare with only several hundred clinical cases being reported. It occurs primarily in Caucasian males over forty years of age. Although readily treated with antibiotics, it almost universally fatal in patients who fail to receive accurate diagnosis and treatment within one year. In this assay DNA is extracted from the specimen and subjected to PCR amplification.

Method: Real-Time PCR

Specimen: Whole blood yellow top tube (ACD solution A)

Transport: Stable at room temperature

320 *Ureaplasma urealyticum* by Real-Time PCR (*Reflex to antibiotic resistance by Molecular Analysis)

Clinical significance: *Ureaplasma*, of the family Mycoplasmataceae, are among the smallest free-living bacteria. Colonization, the presence and multiplication of microorganisms without tissue invasion or damage, usually begins at birth with passage through an infected mother's birth canal. Ureaplasmas have been isolated from the genital tract of 33% of infant girls and from the noses and throats of 15% of infant boys and girls. Carriage of these organisms does not usually persist beyond the age of 2. However, a small portion of pre-pubescent children will remain colonized and asymptomatic. As a result of sexual contact, the incidence of genital Ureaplasmas increases after puberty. In some pregnant women, Ureaplasma infections are considered to be the cause of chorioamnionitis and premature delivery. They are frequently transmitted from mothers to their infants, which may cause a variety of disorders including pneumonia, persistent pulmonary hypertension, and chronic infection of the central nervous system. In this assay, DNA is extracted from the specimen and subjected to PCR amplification.

Method: Real-Time PCR

Specimen: ***OneSwab***®, ***UroSwab***®, *ThinPrep*®, whole blood yellow top tube (ACD solution A), biopsy (fresh), biopsy (paraffin), CSF

Transport: Stable at room temperature

354 Yersinia species (IgG/IgA) by Western blot

Serum required

Clinical significance: The genus Yersinia encompasses a group of Gram-negative, non-motile, rod-shaped bacteria. Three (*Y. pestis*, *Y. enterocolitica*, and *Y. pseudotuberculosis*) of the eleven species in this genus are human pathogens. *Y. enterocolitica* and *Y. pseudotuberculosis* are responsible for an estimated 17, 000 cases of yersiniosis (hallmarked by enteritis) per year in the United States. In addition, approximately 20% of patients with ankylosing spondylitis, Reiter's disease, or reactive arthritis are culture positive for Yersinia species. Cases of *Y. pestis*, the causative agent of the plague, occur with far less frequency with an estimated 13 cases per year in the United States. Infection with *Y. enterocolitica* typically occurs in young children. Patients may present with fever, abdominal pain, and acute enteritis. In the assay, we detect IgG and IgA antibodies to Yersinia species in human serum.

Method: Western Blot

Specimen: Serum

Transport: Stable at room temperature

365 *Campylobacter jejuni* by Real-Time PCR

Clinical Significance: *Campylobacter jejuni* is a species of curved, rod-shaped, non-spore forming, Gram-negative microaerophilic, bacteria commonly found in animal feces. *C. jejuni* is the most commonly reported bacterial cause of food borne infection in the United States with an estimated 2.1 to 2.4 million cases of human campylobacteriosis occurring each year with illnesses ranging room loose stools to dysentery. *Campylobacter jejuni* results in enteritis, which is characterized by abdominal pain, cramping, diarrhea, fever, and malaise within two to five days after exposure to the organism. The diarrhea may be bloody and can be accompanied by nausea and vomiting. The illness typically lasts one week. Food poisoning caused by *Campylobacter* species in persons with compromised immune systems may spread to the bloodstream and cause a serious life-threatening infection. Real-Time PCR is a rapid and accurate method for identifying *Campylobacter jejuni* in loose stool swab samples.

Method: Real-Time PCR

Specimen: ***OneSwab***® (loose stool)

Transport: Stable at room temperature

162 *Clostridium difficile* (Toxins A and B) by Real-Time PCR

Clinical Significance: *Clostridium difficile* is an anaerobic Gram-positive spore forming bacteria. *C. difficile* is the most serious cause of antibiotic-associated diarrhea (AAD) and can lead to pseudomembranous colitis, a severe infection of the colon, often resulting from eradication of the normal gut flora by antibiotics. *C. difficile* is frequently found in hospitals, nursing homes, extended care facilities, and nurseries for newborn infants. Found in feces, *C. difficile* is spread by ingestion of the spores from the environment which lie dormant in the body until antibiotics disrupt the normal bacteria. Then the spore becomes active and produces the active *C. difficile* bacteria. Infection can occur when someone touches items or surfaces that are contaminated with feces and then touch their mouth or mucous membranes. Healthcare workers can spread the bacteria to other patients or contaminate surfaces through hand contact. Symptoms of infection may include watery diarrhea (at least three bowel movements per day for two or more days), fever, loss of appetite, nausea, and abdominal pain/tenderness. Real-Time PCR is a rapid and accurate method for identifying *Clostridium difficile* in loose stool swab samples

Method: Real-Time PCR

Specimen: ***OneSwab***® (loose stool)

Transport: Stable at room temperature

371 *Cryptosporidium parvum* by Real-Time PCR

Clinical significance: *Cryptosporidium parvum* is a microscopic parasite that is one of the most prevalent species that causes the diarrheal disease cryptosporidiosis. The parasite is protected by an outer shell that allows it to survive outside of the body for long periods of time and makes it very tolerant to chlorine disinfectant. The parasite is spread by ingesting contaminated water and occasionally through food sources. Outbreaks have been associated with recreational water parks, community swimming pools, and child care centers. Patients typically present with acute, watery, non-bloody diarrhea, abdominal cramps, and low-grade fever. In this assay, DNA is extracted from the specimen and subjected to PCR amplification.

Method: Real-Time PCR

Specimen: ***OneSwab***® (loose stool)

Transport: Stable at room temperature

372 *Entamoeba histolytica* by Real-Time PCR

Clinical Significance: *Entamoeba histolytica* is an anaerobic protozoan and the causative agent of amebiasis. Transmission occurs through ingestion of the infective cystic form via the fecal-oral route and is commonly associated with fecal contamination of food and water supplies. Although many infections are asymptomatic, when symptoms do occur they can vary from mild gastrointestinal distress to dysentery. Invasive extraintestinal infection can occur and result in abscess of hepatic, pleuropulmonary, cardiac, cerebral, renal, genitourinary, and cutaneous sites. Diagnosis can be complicated because of the similar appearance of *E. histolytica* to other parasites when visualized under a microscope. In this assay, DNA is extracted from the specimen and subjected to PCR amplification.

Method: Real-Time PCR

Specimen: ***OneSwab***® (loose stool)

Transport: Stable at room temperature

168 *Enteropathogenic Escherichia coli* (O157 and Shiga toxin) by Real-Time PCR

Clinical Significance: *Escherichia coli* (*E. coli*) is the head of the large bacterial family, *Enterobacteriaceae*, the enteric bacteria, which are facultatively anaerobic Gram-negative rods that live in the intestinal. *E. coli* serogroup O157 is largely found in cattle, but also has been isolated from sheep, goats, pigs, and turkeys. It also exists as an enterohemorrhagic pathogen in the human intestinal tract. O157 is typically contracted orally through consumption of under-cooked contaminated meat, as well as unpasteurized milk or cider, fresh vegetables, contaminated water sources, and infected persons. Symptoms of infection present as watery diarrhea, but may progress to bloody diarrhea (hemorrhagic colitis), kidney failure, anemia due to blood loss, and low platelet count (hemolytic uremic syndrome). Children and the elderly are more susceptible to the severe symptoms of infection. Real-Time PCR is a rapid and accurate method for identifying *Escherichia coli* (O157 and Shiga toxin) in loose stool swab samples.

Method: Real-Time PCR

Specimen: ***OneSwab***® (loose stool)

Transport: Stable at room temperature

370 *Giardia intestinalis* by Real-Time PCR

Clinical significance: *Giardia intestinalis* is a microscopic, anaerobic, flagellated protozoan parasite that is the causative agent of the diarrheal illness known as giardiasis. Transmission occurs through contact with contaminated water, soil or food. The majority of infections are thought to originate from person-to-person through poor hygiene, travel in underdeveloped nations or contact with surfaces that have been contaminated with feces from infected humans or animals. Day care centers and contaminated lakes and swimming holes also serve as ready sources of infection. Because Giardia cysts can be excreted intermittently, it is important to use a highly sensitive and specific assay for detection. In this assay, DNA is extracted from the specimen and subjected to Real-Time PCR amplification. Real-Time PCR is a rapid and accurate method for identifying *Giardia intestinalis* in loose stool swab samples.

Method: Real-Time PCR

Specimen: ***OneSwab***® (loose stool)

Transport: Stable at room temperature

310 *Helicobacter pylori* by Real-Time PCR

Clinical significance: *Helicobacter pylori* resides within the mucous membrane of the gastric epithelium and occasionally the duodenal or esophageal mucosal epithelium as well. It can lead to inflammation of the mucosa and, if untreated, chronic superficial gastritis. This inflammation process has been linked to peptic ulceration and gastric cancer. *Helicobacter pylori* is now established as the most common cause of gastritis. In this procedure, we perform a PCR assay for the sensitive and specific detection of *H. pylori*. The assay is based on the DNA sequence of a species-specific protein antigen, which is present in all strains of *H. pylori* tested. The specificity of this assay and the fidelity of the chosen region was verified by the lack of cross-reactivity with other enteric bacteria (whose coding sequence did not hybridize to the DNA of numerous enteric bacteria). In this assay, DNA is extracted from the specimen and subjected to PCR amplification.

Method: Real-Time PCR

Specimen: ***OneSwab***® (loose stool)

Transport: Stable at room temperature

274 Human Rotavirus A by Real-Time PCR

Clinical Significance: Human Rotavirus is a double stranded RNA virus. Rotavirus is the single most important cause of severe gastroenteritis in infants and young children. Every year in the United States, there are an estimated 55,000 to 70,000 hospitalizations and 205,000 to 272,000 emergency department visits due to rotavirus gastroenteritis among children under the age of 5Of the seven species of Human Rotavirus (denoted A through G), species HRV A is the most common. Infection is usually through fecal-oral transmission. The incubation period is around two days followed by three to eight days of sickness. The severity of rotavirus infection ranges from asymptomatic infection to severe gastroenteritis. Real-Time PCR is a rapid and accurate method for identifying Human Rotavirus A in loose stool swab samples.

Method: Real-Time PCR

Specimen: ***OneSwab***® (loose stool)

Transport: Stable at room temperature

158 *Listeria monocytogenes* by Real-Time PCR

Clinical Significance: *Listeria monocytogenes* is a Gram-positive, facultative intracellular parasite and is the causative agent of listeriosis. *L. monocytogenes* infections can cause septicemia, encephalitis, meningitis, and gastroenteritis. The bacteria is capable of entering most cells. Transmission occurs through contaminated foods including raw meat and fish, unpasteurized dairy products, and uncooked vegetables. *L. monocytogenes* has also been found in processed foods that have become contaminated after processing such as soft cheeses, deli cold cuts, sliced or grated cheese, and ice cream. The infective dose for oral transmission is unknown but is thought to depend on the strain and the susceptibility of the person. Healthy people seem to be able to eat most Listeria-contaminated foods without clinical signs; however, in susceptible persons, the infective dose is probably fewer than 1,000 organisms. The incubation period in susceptible adults is 3 to 70 days, with the median incubation period estimated to be 3 weeks. *L. monocytogenes* is relatively resistant to freezing, drying and heat and can proliferate at refrigeration temperatures on contaminated foods. Real-Time PCR is a rapid and accurate method for identifying *Listeria monocytogenes* in loose stool swab samples.

Method: Real-Time PCR

Specimen: ***OneSwab***® (loose stool)

Transport: Stable at room temperature

272 Norwalk Virus (Norovirus) by Real-Time PCR

Clinical Significance: Norwalk Virus is a small, round, structured RNA virus of the Caliciviridae taxonomic family. This virus causes approximately 90% of epidemic non-bacterial outbreaks of gastroenteritis around the world, and may be responsible for 50% of all food-borne outbreaks of gastroenteritis in the United States. The virus is transmitted by food or water contaminated with feces and by person-to-person contact. Outbreaks of infection often occur in closed or semi-closed communities, such as long-term care facilities, hospitals, prisons, dormitories, and cruise ships where once the virus has been introduced, the infection spreads very rapidly. Usual symptoms include nausea, vomiting, diarrhea, and abdominal pain. Headache and low-grade fever may also accompany this disease. The disease is usually mild and brief. Symptoms will develop 24-48 hours after contaminated food or water is ingested and lasts for 24-60 hours. Symptoms may become life-threatening (approximately 300 cases per year) in the young, the elderly, or the immune-compromised if dehydration is ignored or not treated. Real-Time PCR is a rapid and accurate method for identifying Norwalk Virus in loose stool swab samples.

Method: Real-Time PCR

Specimen: ***OneSwab***® (loose stool)

Transport: Stable at room temperature

160 Salmonella by Real-Time PCR

Clinical Significance: Salmonella is a genus of Gram-negative, rod-shaped motile bacilli. Salmonella infections cause diarrheal illness in humans. Transmission occurs through contaminated foods including raw meat and fish, unpasteurized dairy products, and uncooked vegetables. Salmonella has also been found in processed foods that have become contaminated after processing such as soft cheeses, deli cold cuts, sliced or grated cheese, and ice cream. The infective dose for oral transmission is unknown. Most people experience diarrhea, abdominal cramps, and fever within 8 to 72 hours after the consumption of contaminated food. Most of the symptoms disappear within 4 to 7 days without treatment of antibiotics. Salmonella carries the *invA* gene which is not carried by any other bacterial species and enables the bacteria to invade cells. Real-Time PCR is a rapid and accurate method for identifying Salmonella in loose stool swab samples.

Method: Real-Time PCR

Specimen: ***OneSwab***® (loose stool)

Transport: Stable at room temperature

161 Shigella by Real-Time PCR

Clinical Significance: Shigella is a genus of Gram-negative, rod-shaped bacteria including four serotypes: A (*S. dysenteriae*), B (*S. flexneri*), C (*S. boydii*), D (*S. sonnei*). *Shigella* species are the cause of shigellosis and are typically transmitted via a fecaloral route. *Shigella* species normally cause dysentery. Most cases in adults are mild and self-limiting. In some cases, a range of antibiotics can be used to treat the infection. In more severe cases, the bacteria can produce toxins that cause hemolytic uremic syndrome. Real-Time PCR is a rapid and accurate method for identifying *Shigella* species in loose stool swab samples.

Method: Real-Time PCR

Specimen: ***OneSwab***® (loose stool)

Transport: Stable at room temperature

553 *Aspergillus fumigatus* by Real-Time PCR

Clinical significance: Aspergillosis is the second most common fungal infection requiring hospitalization in the United States. It is associated with infections of the eye, ear, sinuses, skin and respiratory system. It can also cause allergic reactions with worsening of pulmonary function in asthmatics and cystic fibrosis patients. There are certain predisposing factors associated with Aspergillus such as prosthetic devices, immunocompromised patients such as those undergoing chemotherapy, organ transplantation and suffering from AIDS. Traditional diagnostic methods consist of microscopic analysis, culture and special stains that cannot speciate. Molecular methods, such as PCR, offer the physician a rapid and extremely sensitive means of diagnosis. In this assay, DNA is extracted from the specimen and subjected to PCR amplification.

Method: Real-Time PCR

Specimen: Whole blood yellow top tube (ACD solution A), CSF, synovial fluid

Transport: Stable at room temperature

551 *Candida albicans* by Real-Time PCR

Clinical significance: Between 70% to 90% of yeast strains isolated from the vagina belong to the species *Candida albicans*. *C. albicans* is one of the major causes of Candida Vaginitis (CV). In the United States, CV is currently the second most common cause of vaginal infection, with bacterial vaginosis the most common diagnostic entity. CV affects most females at least once during their lives at an estimated rate of 70% to 75%, of whom 40% to 50% will experience a recurrence. Studies indicate that CV is a frequent diagnosis among young women, affecting as many as 15% to 30% of symptomatic women visiting a clinician; by the age of 25, half of all college women will have experienced at least one episode of CV. *C. albicans* and *C. glabrata* represent the most common fungal causes of both complicated and uncomplicated urinary tract infections. *Candida* species produce a wide spectrum of diseases, ranging from superficial mucocutaneous disease to invasive illnesses, such as hepatosplenic candidiasis, Candida peritonitis, and systemic candidiasis. The expression of which depends primarily on the immune status of the host. In this assay, DNA is extracted from the specimen and subjected to Real-Time PCR amplification.

Method: Real-Time PCR

Specimen: ***OneSwab***®, ***UroSwab***®, *ThinPrep*®, whole blood yellow top tube (ACD solution A), CSF, synovial fluid

Transport: Stable at room temperature

576 *Candida dubliniensis* by Real-Time PCR

Clinical significance: First described in 1995, *Candida dubliniensis* is reported to have been previously misidentified as *Candida albicans*. It is associated with oral candidiasis and has been recovered from the vaginal tract of women. Although it is closely related to *C. albicans*, its differences in virulence and its ability to rapidly develop resistance to traditional antifungal agents makes it clinically relevant. *Candida* species produce a wide spectrum of diseases, ranging from superficial mucocutaneous disease to invasive illnesses, such as hepatosplenic candidiasis, Candida peritonitis, and systemic candidiasis. The expression of which depends primarily on the immune status of the host. *C. dubliniensis* is an opportunistic infection that is of particular concern in immunocompromised patients. The use of molecular techniques, such as PCR, enables the clinician to differentiate *C. dubliniensis* from other species of Candida to facilitate diagnosis and proper treatment. In this assay, DNA is extracted from the specimen and subjected to PCR amplification.

Method: Real-Time PCR

Specimen: ***OneSwab***®, ***UroSwab***®, whole blood yellow top tube (ACD solution A), synovial fluid

Transport: Stable at room temperature

559 *Candida glabrata* by Real-Time PCR

Clinical significance: *C. glabrata* has emerged as the second most common cause of invasive fungal infection and is the leading non-albicans species involved in Candida Vaginitis (CV), accounting for up to 20% of infections in immune-competent women. It is thought that the widespread use of topical antifungals, especially in short courses, may contribute to selection for non-albicans yeasts, which are less susceptible to these agents. *C. glabrata* has also been shown to intrinsically exhibit low level resistance but has the ability to rapidly acquire high level resistance to antifungals. *C. glabrata* is associated with CV and affects most females at least once during their lives at an estimated rate of 70% to 75%, of whom 40% to 50% will experience a recurrence. In the United States CV is currently the second most common cause of vaginal infections, with bacterial vaginosis the most common. Most studies indicate that CV is a frequent diagnosis among young women, affecting as many as 15% to 30% of symptomatic women visiting a clinician; by the age 25 years, half of all college women will have experienced at least one episode of CV. *C. albicans* and *C. glabrata* represent the most common fungal causes of both complicated and uncomplicated urinary tract infections. *Candida* species produce a wide spectrum of diseases, ranging from superficial mucocutaneous disease to invasive illnesses, such as hepatosplenic candidiasis, Candida peritonitis, and systemic candidiasis. The expression of which depends primarily on the immune status of the host. In this assay, DNA is extracted from the specimen and subjected to PCR amplification.

Method: Real-Time PCR

Specimen: ***OneSwab***®, ***UroSwab***®, *ThinPrep*®, whole blood yellow top tube (ACD solution A), CSF, synovial fluid

Transport: Stable at room temperature

578 *Candida kefyr* by Real-Time PCR

Clinical significance: *Candida kefyr* is one of the six strains of Candida, of approximately 154 species, that is commonly associated with infections in humans. This species, previously reported in the literature by the obsolete name of *Candida pseudotropicalis*, has been reported as an emerging pathogen. Candidiasis has a wide clinical spectrum, capable of affecting almost any organ or system in the body. Infections range from localized, superficial infections to dissemination in the blood stream. Considered to be a relatively rare infection, found in approximately 1% of fungal isolates reported, *C. kefyr* infections have been documented from burn wounds, blood and vaginal infections. More recently, the frequency of *C. kefyr* infections has increased within oncohematologic patients, particularly those with neutropenic, myeloid and lymphoblastoid leukemias. In this assay, DNA is extracted from the specimen and subjected to PCR amplification.

Method: Real-Time PCR

Specimen: ***OneSwab***®, ***UroSwab***®, whole blood yellow top tube (ACD solution A)

Transport: Stable at room temperature

566 *Candida krusei* by Real-Time PCR

Clinical significance: *Candida krusei*, which has traditionally been implicated in urinary tract infections, has recently been associated with certain instances of fungal vaginitis, particularly recurrent fungal vaginitis. Candida Vaginitis (CV) resulting from *C. krusei* infection is often chronic due to the organism's inherent resistance to conventional anti-fungal therapies, necessitating the need for prolonged treatment courses. The incidence of *C. krusei* fungemia within leukemic populations has been on the rise within recent years, doubling within a five year span, and is highly lethal within the neutropenic subpopulation receiving fluconazole prophylaxis. As a result, treatment needs to be initiated quickly and aggressively. The use of molecular techniques, such as Real-Time PCR, enables the clinician to differentiate *C. krusei* from other *Candida* species to facilitate diagnosis and proper treatment. In this assay, DNA is extracted from the specimen and subjected to PCR amplification.

Method: Real-Time PCR

Specimen: ***OneSwab***®, ***UroSwab***®, whole blood yellow top tube (ACD solution A), CSF, synovial fluid

Transport: Stable at room temperature

577 *Candida lusitaniae* by Real-Time PCR

Clinical significance: *Candida lusitaniae* is considered a nosocomial bloodstream pathogen that is becoming increasingly associated with Candidemia. It is an opportunistic infection and therefore is associated with immunocompromised individuals. *C. lusitaniae* is known to enter the host through the urogenital and respiratory tracts or through intravascular catheters. It is also quite resistant to amphotericin B, a common antifungal treatment. In this assay, DNA is extracted from the specimen and subjected to PCR amplification.

Method: Real-Time PCR

Specimen: ***OneSwab***®, ***UroSwab***®, whole blood yellow top tube (ACD solution A)

Transport: Stable at room temperature

558 *Candida parapsilosis* by Real-Time PCR

Clinical significance: *C. parapsilosis* accounts for 1% of vaginal yeast isolates. It is thought that the widespread use of topical azole antifungals, especially in short courses, may contribute to selection for non-albicans yeasts, which are less susceptible to these agents than *C. albicans*. *C. parapsilosis* is associated with Candida Vaginitis (CV). CV affects most females at least once during their lives at an estimated rate of 70% to 75%, of whom 40% to 50% will experience a recurrence. In the United States CV is currently the second most common cause of vaginal infections, with bacterial vaginosis the most common diagnostic entity. Studies indicate that CV is a frequent diagnosis among young women, affecting as many as 15% to 30% of symptomatic women visiting a clinician; by the age of 25, half of all college women will have experienced at least one episode of CV. *Candida* species produce a wide spectrum of diseases, ranging from superficial mucocutaneous disease to invasive illnesses, such as hepatosplenic candidiasis, Candida peritonitis, and systemic candidiasis. The expression of which depends primarily on the immune status of the host. In this assay, DNA is extracted from the specimen and subjected to PCR amplification.

Method: Real-Time PCR

Specimen: ***OneSwab***®, ***UroSwab***®, *ThinPrep*®, whole blood yellow top tube (ACD solution A), CSF, synovial fluid

Transport: Stable at room temperature

557 *Candida tropicalis* by Real-Time PCR

Clinical significance: *Candida tropicalis* accounts for 1% to 5% of vaginal yeast isolates and may be associated with a higher rate of recurrence after standard treatment. Although *C. tropicalis* is still very susceptible to azole antifungals, an increase in resistance has been observed in the US. It is thought that the widespread use of topical azole antifungals, especially in short courses, may contribute to selection for non-*albicans* yeasts, which are less susceptible to these agents than *C. albicans*. *C. tropicalis* is associated with Candida Vaginitis (CV). CV affects most females at least once during their lives, at an estimated rate of 70% to 75%, of whom 40% to 50% will experience a recurrence. In the United States CV is currently the second most common cause of vaginal infections, with bacterial vaginosis the most common diagnostic entity. Studies indicate that CV is a frequent diagnosis among young women, affecting as many as 15% to 30% of symptomatic women visiting a clinician; by the age of 25, half of all college women will have experienced at least one episode of CV. *Candida* species produce a wide spectrum of diseases, ranging from superficial mucocutaneous disease to invasive illnesses, such as hepatosplenic candidiasis, Candida peritonitis, and systemic candidiasis. The expression of which depends primarily on the immune status of the host. In this assay, DNA is extracted from the specimen and subjected to PCR amplification.

Method: Real-Time PCR

Specimen: ***OneSwab***®, ***UroSwab***®, *ThinPrep*®, whole blood yellow top tube (ACD solution A), CSF, synovial fluid

Transport: Stable at room temperature

580 *Coccidioides* Species (*C. immitis, C. posadasii*) by Real-Time PCR

Clinical Significance: *Coccidioides* species are fungi that cause coccidioidomycosis, also known as Valley fever, California Valley fever, San Joaquin Valley Fever and desert fever. This disease is endemic in American deserts and is found most frequently in Southern California, Southern Arizona, and in certain areas of Mexico, Central and South America. Infection occurs via respiratory inhalation of spores disseminated in their natural habitat. In 40% of cases, patients will experience flu-like symptoms such as fever, cough, headaches, rash, and myalgia (muscle pain). Some patients fail to recover and develop chronic pulmonary infection or widespread disseminated infection, affecting the meninges, soft tissues, joints and bone. Severe pulmonary disease may develop in HIV-infected persons. In this assay DNA is extracted from the specimen and subjected to PCR amplification.

Method: Real-Time PCR

Specimen: Whole blood yellow top tube (ACD solution A)

Transport: Stable at room temperature

554 *Cryptococcus neoformans* by Real-Time PCR

When sampling a crusted over lesion, moisten the swab with sterile saline solution prior to swabbing.

Clinical significance: *Cryptococcus neoformans* is found in aged pigeon droppings, such as those accumulated on window ledges and rooftops. Infection is commonly seen in AIDS and transplant patients on immunosuppressive therapies and primarily manifests as a respiratory infection causing severe pneumonia. It also causes central nervous system disturbances and skin lesions that may be non-specific but are often the first sign of infection. India ink smears can be useful as supportive evidence of infection but are not definitive. A combination of culture and smears with antibody or antigen detection assays are traditionally used. Molecular methods, such as PCR, offer a rapid route of diagnosis with increased sensitivity and specificity. In this assay, DNA is extracted from the specimen and subjected to PCR amplification.

Method: Real-Time PCR

Specimen: ***UroSwab***®, whole blood yellow top tube (ACD solution A), ***OneSwab***®

Transport: Stable at room temperature

550 *Pneumocystis carinii* by Real-Time PCR

Clinical significance: *Pneumocystis carinii* is an opportunistic pathogen which can cause a fatal pneumonia in patients under immunosuppressed or immune deficient conditions due to AIDS, cancer, chemotherapy, or immunosuppressive therapy for organ transplantation. Traditionally, the clinical samples for diagnosis of *P. carinii* infection by microscopic analysis are mostly from samples obtained during invasive procedures such as open lung biopsy and bronchoscopic alveolar lavage. In this assay, DNA is extracted from the specimen and subjected to PCR amplification.

Method: Real-Time PCR

Specimen: Whole blood yellow top tube (ACD solution A)

Transport: Stable at room temperature

555 Trichosporon by Qualitative PCR

Clinical significance: Trichosporonosis is caused by six species, some of which can be considered normal flora. The usual clinical manifestation is a superficial infection of the scalp, facial and pubic hair. *S. cerevisiae* has been implicated in thrush, fungemia, and vulvovaginitis. It has been reported that exposure to bakers yeast may be a predisposing factor for infection. In an immunocompromised patient, Trichosporonosis can disseminate to multiple organs rapidly developing into respiratory failure, renal failure, disseminated intravascular coagulation, and death. Treatment of this invasive form is only effective if initiated early in the infectious process. In this assay, DNA is extracted from the specimen and subjected to PCR amplification.

Method: Qualitative PCR

Specimen: Whole blood yellow top tube (ACD solution A), biopsy (fresh), biopsy (paraffin), CSF

Transport: Stable at room temperature

369 *Acinetobacter baumannii* by Real-Time PCR

Clinical significance: *Acinetobacter baumannii* is an aerobic, Gram-negative bacterium that is resistant to most antibiotic treatments and is responsible for many hospital patient deaths, the first case being linked directly to wounded soldiers returning from the Iraq war. An emerging, opportunistic, multi-drug resistant bacterium, *Acinetobacter baumannii* infection cases are expected to rise and have the potential to become the next superbug with a magnitude and scope similar to that of MRSA. *A. baumannii* is associated with long term wound skin and soft tissue infections, catheter-associated UTIs, ventilator associated infections, bloodstream infections, surgical site infections, and co-infections with other bacteria is common such as MRSA. Those with compromised immunity are at greatest risk of infection. A few studies have looked for *A. baumannii* as well as MRSA colonization of anterior nares, skin, sputum, perianal, wounds, etc. This can be an environmental contaminant of hospitals and long-term care facilities. Colonization of healthy individuals occurs in an asymptomatic fashion but poses an increased risk of dissemination throughout hospital wards.

Method: Real-Time PCR

Specimen: ***NasoSwab***®

Transport: Stable at room temperature

222 Adenovirus by Real-Time PCR

Clinical significance: Adenoviruses cause a number of self-limiting, but often highly infectious, diseases that affect multiple organs, most commonly those associated with the respiratory and genitourinary tracts. Adenovirus is a relatively harmless pathogen in healthy individuals, but can cause a variety of symptoms in young children and the immunocompromised. Transmission can occur from direct, person-to-person contact or through contact with a contaminated surface or object. Adenovirus infections are usually asymptomatic and may cause a variety of symptoms, including: respiratory problems, gastroenteritis, pink eye, pharyngoconjunctival fever, skin rashes, and genitourinary tract infections including cervicitis, urethritis and hemorrhagic cystitis. The most severe cases of adenovirus infection may result in pneumonia, croup, and bronchitis. In this assay DNA is extracted from the specimen and subjected to PCR amplification.

Method: Real-Time PCR

Specimen: ***NasoSwab***®

Transport: Stable at room temperature

1101 *Bordetella parapertussis* by Real-Time PCR

Clinical significance: *Bordetella pertussis* and *Bordetella parapertussis* are Gram-negative aerobic coccobacilli that cause pharyngitis and Whooping Cough. *Bordetella parapertussis*, lacking many of *B. pertussis*' virulence factors, induces milder forms of disease. Despite their association with Whooping Cough, they are not the only pathogenic causes; *Bordetella bronchiseptica*, *Mycoplasma pneumoniae* and *Chlamydophila trachomatis* have also been associated. Once a highly lethal infection in children and infants, vaccination has decreased the major risks associated with infection. However, studies have demonstrated a drop in immunity 3-5 years post-vaccination that reaches undetectable levels within 12 years. Since the 1980's the incidence rate has increased cyclically, peaking every 3-4 years. Seasonality is from June through September. Infection is in three stages: catarrhal, paroxysmal, and convalescent. The initial stage, catarrhal, is largely indistinguishable from other common respiratory tract infections, which might be problematic considering it is the most infectious stage. In this assay, DNA is extracted from the specimen and subjected to PCR amplification.

Method: Real-Time PCR

Specimen: ***NasoSwab***®

Transport: Stable at room temperature

1102 *Bordetella pertussis* by Real-Time PCR (Reflex to *Bordetella holmesii* by Real-Time PCR)

Clinical significance: *Bordetella pertussis* and *Bordetella parapertussis* are Gram-negative aerobic coccobacilli that cause pharyngitis and Whooping Cough. *Bordetella parapertussis*, lacking many of *B. pertussis*' virulence factors, induces milder forms of disease. Despite their association with Whooping Cough, they are not the only pathogenic causes; *Bordetella bronchiseptica*, *Mycoplasma pneumoniae* and *Chlamydophila trachomatis* have also been associated. Once a highly lethal infection in children and infants, vaccination has decreased the major risks associated with infection. However, studies have demonstrated a drop in immunity 3-5 years post-vaccination that reaches undetectable levels within 12 years. Since the 1980's the incidence rate has increased cyclically, peaking every 3-4 years. Seasonality is from June through September. Infection is in three stages: catarrhal, paroxysmal, and convalescent. The initial stage, catarrhal, is largely indistinguishable from other common respiratory tract infections, which might be problematic considering it is the most infectious stage. In this assay, DNA is extracted from the specimen and subjected to PCR amplification.

Method: Real-Time PCR

Specimen: ***Naso*Swab®**

Transport: Stable at room temperature

319 *Chlamydophila pneumoniae* by Real-Time PCR

Clinical significance: Chlamydophila are obligate intracellular parasites. *Chlamydophila pneumoniae*, also known as TWAR, is the most recently identified of the *Chlamydophila* species. It is a common cause of infection throughout the world. Although first isolated in 1965, it was not established as a human pathogen until it was obtained from a respiratory specimen in 1983. Infection is spread via exposure to respiratory secretions. It has been associated with community acquired acute respiratory infection, adult onset asthma, atherosclerotic cardiovascular disease, arthritis, and chronic fatigue syndrome. In this assay, DNA is extracted from the specimen and subjected to PCR amplification.

Method: Real-Time PCR

Specimen: ***Naso*Swab®**

Transport: Stable at room temperature

1134 CombiVid Panel by Real-Time PCR

1131 SARS-CoV-2 virus (COVID-19) by Real-Time Reverse Transcription PCR (CDC N1, N2, RP targets)
1124 Influenza A virus
1107 Influenza B virus

Coronavirus Disease 2019 (COVID-19) is an acute respiratory disease caused by a viral infection with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). The virus, which has infected and caused deaths of millions of people worldwide, has rapidly escalated to pandemic status since it first appeared in Wuhan, China in December 2019. Influenza virus is a segmented, negative-sense, single-stranded RNA virus capable of infecting epithelial cells of the upper respiratory tract. Infection results in the desquamation of the epithelial cells and viral entry of the lungs, which could result in influenza pneumonia. Due to overlapping symptoms, laboratory testing is important for an accurate diagnosis and to assist in guiding triage, patient care, and treatment decisions to prevent further transmission.

Method: Real-Time PCR

Specimen: **COVID-*One*Swab®, *Naso*Swab®**

Transport: Stable at room temperature

273 Coxsackie virus A & B by Pyrosequencing

Clinical significance: Coxsackieviruses are a part of the Picornaviridae family belonging to the Enterovirus genus. There are two groups of Coxsackieviruses, A and B, differentiated by their effects on mice. Generally, Coxsackie A infects the skin and mucous membranes, causing hand, foot and mouth disease, a common childhood illness. Symptoms associated with hand, foot and mouth disease include: fever, herpangina (blisters in the mouth), and blisters on the palms and fingers of the hand or on the soles of the feet. Acute hemorrhagic conjunctivitis can also be onset from Coxsackie A viral infection. Group B Coxsackie virus causes pleurodynia or Bornholm disease. Symptoms found associated with Coxsackie B virus include fever, headache, sore throat, chest and muscle pain, and gastrointestinal distress. In some instances, Coxsackievirus B may lead to infectious pericarditis or viral myocarditis. Both group A and group B Coxsackieviruses can cause nonspecific febrile illnesses, rashes, upper respiratory tract disease, and aseptic meningitis.

Method: Pyrosequencing

Specimen: ***NasoSwab***®

Transport: Stable at room temperature

1128 Enterovirus D68 by Real-Time PCR

Clinical significance: Although Enteroviruses are associated with various clinical symptoms including mild respiratory illness, febrile rash illness, and neurologic illness, such as aseptic meningitis and encephalitis, Enterovirus D68 (EV-D68) primarily causes respiratory illness. EV-D68 causes a spectrum of symptoms ranging from mild which may include fever, runny nose, sneezing, cough, body and muscle aches, up to severe such as wheezing and difficulty breathing. EV-D68 is known to cause infections primarily in children but has been known to infect adults. An outbreak of EV-D68 in 2014 was notable for its high number of hospitalizations involving infected children. In this assay, DNA is extracted from the specimen and subjected to PCR amplification to rapidly detect Enterovirus D68.

Method: Real-Time PCR

Specimen: ***NasoSwab***®

Transport: Stable at room temperature

1112 Group A Streptococcus by Real-Time PCR

Clinical significance: *Streptococcus pyogenes* (**Group A Streptococcus**) is a Gram-positive extracellular bacteria that colonizes the throat and skin. It is the cause of many human diseases which range from mild skin infections to invasive life threatening disease. Group A Streptococcus is the most common cause of bacterial pharyngitis (Strep throat) and is also associated with scarlet fever, impetigo, Streptococcal toxic shock syndrome and necrotizing fasciitis. Autoimmune mediated post infection sequelae such as rheumatic fever, rheumatic heart disease, glomerulonephritis and reactive arthritis can potentially result in disability or death. Group A Streptococcus has been shown to infect the vaginal mucosa and uterus leading to severe disease or septicemia. In this assay, DNA is extracted from the specimen and subjected to PCR amplification.

Method: Real-Time PCR

Specimen: ***NasoSwab***®

Transport: Stable at room temperature

1117 *Haemophilus influenzae* by Real-Time PCR

Clinical significance: *Haemophilus influenzae* is a small, nonmotile Gram-negative bacterium. *H. influenzae* most commonly causes ear, eye and sinus infections as well as pneumonia. A more serious strain of the bacteria called *H. influenzae* type b has been nearly abolished in the United States due to effective vaccine development, which has been available since 1988. The more serious strain can be found in cerebrospinal fluid and is responsible for causing meningitis (infection of the membranes that surround the brain) and a life-threatening infection called epiglottitis (infection of the area of the throat that covers and protects the voice box and trachea during swallowing). In rare cases, children may still develop *H. influenzae* type b infections. This can occur if the child has not completed their series of immunizations or in older children who did not receive the vaccine as an infant. In this assay, DNA is extracted from the specimen and subjected to PCR amplification.

Method: Real-Time PCR

Specimen: ***NasoSwab***®

Transport: Stable at room temperature

1114 Human Bocavirus by Real-Time PCR

Clinical significance: Human Bocavirus (HBoV) is a relatively new and poorly characterized respiratory pathogen. Identified in 2005 as a novel parvovirus closely related to both bovine and canine strains, it is capable of infecting humans. Due to its recent isolation, the full clinical relevance of HBoV has yet to be fully realized. The initial study in which it was identified has associated HBoV infection with 3.1% of children hospitalized with respiratory distress. A retrospective study that followed reported an infectivity rate of 5.6% during the winter months, half of which were co-infected with another respiratory pathogen. In this assay, DNA is extracted from the specimen and subjected to PCR amplification.

Method: Real-Time PCR

Specimen: ***NasoSwab***®

Transport: Stable at room temperature

1115 Human Coronavirus (Human Coronaviruses 229E, OC43, NL-63) by Real-Time PCR

Clinical significance: Human Coronaviruses are single-stranded, enveloped RNA viruses. Although there are many viral strains capable of infecting various mammals, only four human strains exist: 229E, OC43, NL-63 and SARS. Coronaviruses are responsible for 10% to 30% of all common colds and, to date, only the 229E and OC43 strains have been associated with high rates of infection within the United States. Infection occurs across large age groups, although the more severe infections occur among the young and the elderly. Reinfection with the same serotype is quite common, suggesting a short-lived humoral response. Confirmatory tests should exclude standard culturing methods due to the fastidious nature of these viruses. In this assay, RNA is extracted from the specimen and subjected to PCR amplification.

Method: Real-Time PCR

Specimen: ***NasoSwab***®

Transport: Stable at room temperature

1105 Human Metapneumovirus by Real-Time PCR

Clinical significance: Human Metapneumovirus (hMPV) is a negative sense, non-segmented RNA virus that was identified in 2001 as a new respiratory pathogen. The spectrum of symptoms that result are often indistinguishable from other respiratory infections, especially RSV, including fever, severe cough, breathing difficulties and wheezing. It is one of four pathogens known to induce bronchiolitis and is estimated to account for 5% to 15% of all bronchiolitis cases. Instances of severe respiratory distress requiring mechanical ventilation have been associated with hMPV. Infections are very common in the United States and 78% of infections occur between the months of December and April. Standard culture identification is difficult due to the virus' slow growth making PCR and ELISA more suitable methods. In this assay, RNA is extracted from the specimen and subjected to PCR amplification.

Method: Real-Time PCR

Specimen: ***NasoSwab***®

Transport: Stable at room temperature

1136 Influenza A and Influenza B by Multiplex CFX rRT-PCR

Clinical significance: Influenza virus is a segmented, negative-sense, single-stranded RNA virus capable of infecting epithelial cells of the upper respiratory tract. Infection results in the desquamation of the epithelial cells and viral entry of the lungs, which could result in influenza pneumonia. Three infectious strains exist, A, B and C; only A and B strains pose a threat to humans. Infections follow a winter seasonal pattern within the United States. The high degree of mutation and reassortment associated with influenza viruses makes them a public health issue. Vaccination is highly effective at mitigating the infectious process and is recommended annually for adults 55 and over and two doses are recommended for children who have never been immunized or infected previously. In this assay, RNA is extracted from the specimen and subjected to multiplex PCR amplification.

Method: Real-Time PCR

Specimen: ***NasoSwab***®**, COVID-*****OneSwab***®

Transport: Stable at room temperature

1109 *Moraxella catarrhalis* by Real-Time PCR

Clinical significance: *Moraxella catarrhalis* is a Gram-negative, aerobic, diplococcus clinically associated with bronchitis, sinusitis, laryngitis and otitis media. It is the third leading cause of otitis media within the United States. Infectious outcome is somewhat age dependent, affecting the upper respiratory tract in children and lower tract in adults. Colonization of children does occur, peaking at age 2, but wanes in adulthood. *M. catarrhalis* is also associated with chronic pulmonary disease in the elderly and long-time smokers and is known to exacerbate chronic obstructive pulmonary disease (COPD). Treatment should not include penicillin as the majority of the isolated organisms demonstrate penicillin resistance. In this assay, DNA is extracted from the specimen and subjected to PCR amplification.

Method: Real-Time PCR

Specimen: ***NasoSwab***®

Transport: Stable at room temperature

1118 MRSA: Methicillin-Resistant *Staphylococcus aureus* by Conventional PCR

Clinical significance: *Staphylococcus aureus*, often referred to simply as "staph" are bacteria commonly carried on the skin or in the nose of healthy people. Methicillin-resistant *Staphylococcus aureus* (MRSA), often pronounced "mersa", is the resistant variant of this bacteria which is resistant to β-lactam antibiotics such as methicillin, oxacillin, penicillin, and amoxicillin. Risk of infection is greater for patients in hospitals, nursing homes, and other healthcare facilities who have open wounds and/or weakened immune systems. Colonization can occur in the anterior nares, skin, open wounds, and urinary tract. MRSA can be treated with alternate antibiotics which included glycopeptides (vancomycin and teichoplanin), linizolid, and daptomycin. Pre-screening patients upon admission for MRSA will also allow facilities to care for patients accordingly.

Method: Conventional PCR

Specimen: ***NasoSwab***®

Transport: Stable at room temperature

1119 CA-MRSA: Community-Associated MRSA. Panton-Valentine Leukocidin (PVL) DNA by Real-Time PCR

(Type IV + #1118 Req.) [Community Acquired MRSA = Type IV MRSA+ and PVL+]
Only performed after a test #1118 is positive for Type IV. Charges will be the total of tests #1118 + #1119.

Clinical significance: Staph infections, including MRSA, occur most frequently among persons in hospitals and healthcare facilities who have weakened immune systems. Staph and MRSA can also cause illness in persons outside of hospitals and healthcare facilities. MRSA infections that are acquired by persons who have not been hospitalized within the previous year or had a medical procedure are known as community acquired MRSA (CA-MRSA) infections. They usually manifest as skin infections, such as pimples and boils, and occur in otherwise healthy people. It became clear that CA-MRSA infections were caused by strains of MRSA that have different genetic characteristics than other strains. Panton-Valentine leukocidin (PVL) is a cytotoxin which is associated with increased virulence of certain strains of *Staphylococcus aureus*. Present in the majority of community-associated CA-MRSA isolates studied, it is the cause of necrotic ("flesh-eating") lesions involving the skin or mucosa, including necrotic hemorrhagic pneumonia. The new CA-MRSA strains have rapidly spread in the US to become the most common cause of cultured skin infections among individuals seeking medical care for these infections at emergency rooms in cities. These strains also commonly cause skin infections in athletes, jail and prison detainees, and soldiers. In this assay, DNA is extracted from the specimen and subjected to PCR amplification.

Method: Real-Time PCR

Specimen: ***NasoSwab***®

Transport: Stable at room temperature

336 *Mycoplasma pneumoniae* by Real-Time PCR

Clinical significance: *Mycoplasma* species are the smallest and genetically simplest self-replicating bacteria. *Mycoplasma* species are ubiquitous in nature and are widely distributed throughout the animal kingdom. *Mycoplasma pneumoniae* is the most common cause of pneumonia and febrile upper-respiratory tract infections. Transmission occurs person-to-person via respiratory droplets produced by coughing. Other complications may develop with infections ranging from mild to life threatening. In this assay, DNA is extracted from the specimen and subjected to PCR amplification.

Method: Real-Time PCR

Specimen: ***NasoSwab***®

Transport: Stable at room temperature

1121 *Neisseria meningitidis* by Real-Time PCR

Clinical significance: *Neisseria meningitidis*, also simply known as meningococcus, is a Gram-negative diplococcal bacterium. It is only known to infect humans and can be found as normal flora in the nasopharynx of 40% of adults. Meningococcal disease includes serious infections of the fluid and lining surrounding the brain (meningitis), bloodstream (bacteremia and sepsis), lungs (pneumonia), and joints (arthritis). It causes the only form of bacterial meningitis known to cause epidemics. *N. meningitidis* is responsible for considerable morbidity and mortality throughout the world. Meningococcus is spread through the exchange of saliva and other respiratory secretions during activities like coughing and kissing. Though it initially produces with general symptoms like fatigue, it can rapidly progress from fever, headache and neck stiffness to coma and death. Death occurs in approximately 10% of cases. Those with impaired immunity may be at particular risk of meningococcus. In this assay, DNA is extracted from the specimen and subjected to PCR amplification.

Method: Real-Time PCR

Specimen: ***NasoSwab***®

Transport: Stable at room temperature

1110 Parainfluenza viruses 1-4 by Real-Time PCR

Clinical significance: Human Parainfluenza viruses are RNA viruses that serve as a common cause of upper and lower respiratory tract infections, second only to Respiratory Syncytial virus. There are four viral serotypes, designated 1 thru 4, each having varying infectious frequencies and clinical outcomes; therefore, speciation offers a diagnostic advantage. HPIVs 1 and 2 are both associated with croup in children; however, HPIV-1 is more common. Bronchiolitis and pneumonia are more often associated with HPIV-3, while HPIV-4 has thus far only been associated with mild disease. The incubation period ranges from one to seven days. Symptoms include fever, irritability, barky cough and harsh breathing. In this assay, RNA is extracted from the specimen and subjected to PCR amplification.

Method: Real-Time PCR

Specimen: ***NasoSwab***®

Transport: Stable at room temperature

174 *Pseudomonas aeruginosa* by Real-Time PCR

Clinical Significance: *Pseudomonas aeruginosa* is a Gram-negative, opportunistic bacterial pathogen and is mainly associated with nosocomial urinary tract infections (UTI) in hospital patients. It is the most common pathogen isolated from patients who have been hospitalized longer than 1 week. Pseudomonal infections are complicated and can be life-threatening. However, it is known to be amongst the opportunistic strains colonizing the vaginal tract. Routine clinical diagnosis usually takes up to 48 hours to report. In this assay, DNA is extracted from the specimen and subjected to PCR amplification.

Method: Real-Time PCR

Specimen: ***NasoSwab***®

Transport: Stable at room temperature

1103 Respiratory Syncytial virus A (RSV A) by Real-Time PCR

Clinical significance: Respiratory Syncytial virus (RSV) is a negative-sense, enveloped RNA virus and is the most common cause of bronchiolitis. Although infections can occur throughout ones lifetime, bronchiolitis is typically limited to the first infection whereby approximately 25% to 40% of children demonstrate signs and symptoms of bronchiolitis and 0.5% to 2% require hospitalization. Subsequent infections are limited to moderate-to-severe cold-like symptoms in healthy adults and children but pose a significant health issue to the elderly and those with compromised pulmonary, cardiac, or immune systems. Treatment varies from acetaminophen in mild infections to ribavirin aerosolization in more severe cases. In this assay, RNA is extracted from the specimen and subjected to PCR amplification.

Method: Real-Time PCR

Specimen: ***NasoSwab***®

Transport: Stable at room temperature

1116 Respiratory Syncytial virus A and B by Real-Time PCR

Clinical significance: Respiratory syncytial virus (RSV) is a common viral pathogen which causes yearly winter epidemics that are widely associated with lower respiratory tract infections (LRTI), as well as bronchiolitis and viral pneumonia. Yearly outbreaks adversely affect infants and the elderly most severely. Within the United States, RSV-induced LRTIs occur in 4-5 million children of which an estimated 18,000-75,000 children require hospitalization and 90-1,900 succumb to their infection annually. Two viral subtypes are known, A and B, each having multiple genotypes. Studies have demonstrated greater annual circulation rates, as well as greater virulence to be associated with RSV A. However, there have been years when RSV B strains predominated and some studies have indicated a higher preponderance of RSV B infections during the early portion of the infectious season. In this assay, RNA is extracted from the specimen and subjected to reverse transcriptase PCR amplification utilizing an assay capable of speciating the infectious strain.

Method: Real-Time PCR

Specimen: ***NasoSwab***®

Transport: Stable at room temperature

1104 Respiratory Syncytial virus B (RSV B) by Real-Time PCR

Clinical significance: Respiratory Syncytial Virus (RSV) is a negative-sense, enveloped RNA virus and is the most common cause of bronchiolitis. Although infections can occur throughout ones lifetime, bronchiolitis is typically limited to the first infection whereby approximately 25% to 40% of children demonstrate signs and symptoms of bronchiolitis and 0.5% to 2% require hospitalization. Subsequent infections are limited to moderate-to-severe cold-like symptoms in healthy adults and children but pose a significant health issue to the elderly and those with compromised pulmonary, cardiac, or immune systems. Treatment varies from acetaminophen in mild infections to ribavirin aerosolization in more severe cases. In this assay, RNA is extracted from the specimen and subjected to PCR amplification.

Method: Real-Time PCR

Specimen: ***NasoSwab***®

Transport: Stable at room temperature

1127 Rhinovirus and Enterovirus by Real-Time PCR

Clinical Significance: Rhinoviruses and non-polio Enteroviruses are very common infections and are the predominant cause of the common cold. These viruses are ubiquitous and are transmitted person-to-person via direct contact with viral particles shed in the feces and upper respiratory tract secretions. Viral shedding may persist for days prior to the onset of symptoms. The average incubation period is 3-10 days. Although infections occur year-round, there is a seasonal distribution with the highest incidences in the fall and spring. Only 70%-80% of person exposed to these viruses will experience symptoms which are usually mild and self-limiting. Infections are typically limited to the upper respiratory tract. However, they may cause otitis media and sinusitis, as well as exacerbate asthma, cystic fibrosis, chronic bronchitis, and cause serious lower respiratory tract illness in infants, the elderly and immunocompromised. Real-time PCR has been shown to be a rapid and effective way of detecting these viruses and has been proposed as the clinical detection method of choice. In this assay, DNA is extracted from the specimen and subjected to PCR amplification.

Method: Real-Time PCR

Specimen: ***Naso*Swab®**

Transport: Stable at room temperature

1131 SARS-CoV-2 [COVID-19] by Reverse Transcription Real-Time PCR (CDC N1, N2, RP Targets)

Coronavirus Disease 2019 (COVID-19) is an acute respiratory disease caused by a viral infection with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). The virus, which has infected and caused deaths of millions of people worldwide, has rapidly escalated to pandemic status since it first appeared in Wuhan, China in December 2019. Additional cases have now been reported in the United States. An infection with coronavirus 229E, NL63, OC43, or HKU1 is not the same as a COVID-19. Patients with COVID-19 are evaluated and cared for differently than patients with common coronavirus diagnosis. In this assay, RNA is extracted from the specimen and subjected to Reverse Transcription Real-Time PCR amplification.

Method: Reverse Transcription Real-Time PCR

Specimen: **COVID-*One*Swab®**, ***Naso*Swab®**

Transport: Stable at room temperature

1132 SARS-CoV-2 [COVID-19] IgG/IgM by ELISA (serum required)

Testing for IgM and IgG antibodies, produced by a patient's immune system in response to the presence of SARS-CoV-2 virus, is available on serum specimens by ELISA. The presence of certain antibodies can indicate an immune response to SARS-CoV-2, whether symptoms developed from infection or the infection was asymptomatic. The type of antibody and its relative levels could also be used to indicate the stage of infection and estimate time since exposure for contact tracing.

Method: ELISA

Specimen: Serum

Transport: Stable at room temperature

1138 SARS-CoV-2 IgG by quantitative ELISA

Prepayment required. Testing will not performed if payment is not submitted with the specimen.

Clinical Significance: Testing for IgM and IgG antibodies, produced by a patient's immune system in response to the presence of SARS-CoV-2 virus, is available on serum specimens by ELISA. The presence of certain antibodies can indicate an immune response to SARS-CoV-2, whether symptoms developed from infection or the infection was asymptomatic. The type of antibody and its relative levels could also be used to indicate the stage of infection and estimate time since exposure for contact tracing. This assay is used for the quantitative detection of the IgG antibodies to SARS-CoV-2 in the tested specimen.

Method: Quantitative ELISA

Specimen: Serum

Transport: Stable at room temperature

1120 Severe Acute Respiratory Syndrome (SARS) by Real-Time PCR

Clinical significance: Severe acute respiratory syndrome, SARS, is a highly contagious RNA viral disease (BSL-3 containment) of the *Coronaviridae* family, which caused the first pandemic infectious disease of the new millennium. SARS results in infection of both the upper and lower respiratory tracts and sometimes leads to gastroenteritis. A common symptom among patients is high fever above 38°C (100.4°F); other symptoms may include myalgia, lethargy, gastrointestinal symptoms, cough, sore throat, and other non-specific symptoms. Early diagnosis is crucial for appropriate treatment and survival of the patient; therefore, a Real-Time reverse transcriptase PCR assay was developed for the rapid detection of SARS.

Method: Real-Time PCR

Specimen: ***NasoSwab®***

Transport: Stable at room temperature

1111 *Streptococcus pneumoniae* by Real-Time PCR

Clinical significance: *Streptococcus pneumoniae* is a Gram-positive, alpha hemolytic diplococcus that is a major cause of pneumonia as well as one of the most common causes of death in the United States. Approximately 5% to 10% of healthy adults and 20% to 40% of children are colonized with *S. pneumoniae* and, as a result, can spread it to others through the aerosolization of their respiratory secretions and coughing. Its polysaccharide coat protects it from phagocytosis; therefore, antibiotic treatment is required. Resistance to multiple antibiotic classes (penicillin, cephalopsporins, macrolides, tetracycline) has been reported. An effective vaccine is available and is recommended for children under the age of 2 and adults over the age of 65. In this assay, DNA is extracted from the specimen and subjected to PCR amplification.

Method: Real-Time PCR

Specimen: ***NasoSwab®***

Transport: Stable at room temperature

369 *Acinetobacter baumannii* by Real-Time PCR

Clinical significance: *Acinetobacter baumannii* is an aerobic, Gram-negative bacterium that is resistant to most antibiotic treatments and is responsible for many hospital patient deaths, the first case being linked directly to wounded soldiers returning from the Iraq war. An emerging, opportunistic, multi-drug resistant bacterium, *Acinetobacter baumannii* infection cases are expected to rise and have the potential to become the next superbug with a magnitude and scope similar to that of MRSA. *A. baumannii* is associated with long term wound skin and soft tissue infections, catheter-associated UTIs, ventilator associated infections, bloodstream infections, surgical site infections, and co-infections with other bacteria, such as MRSA, is common. Those with compromised immunity are at greatest risk of infection. A few studies have looked for *A. baumannii* as well as MRSA colonization of anterior nares, skin, sputum, perianal, wounds, etc. This can be an environmental contaminant of hospitals and long-term care facilities. Colonization of healthy individuals occurs in an asymptomatic fashion but poses an increased risk of dissemination throughout hospital wards.

Method: Real-Time PCR

Specimen: ***OneSwab***®

Transport: Stable at room temperature

553 *Aspergillus fumigatus* by Real-Time PCR

Clinical significance: *Aspergillus fumigatus* is a species of fungus. Cutaneous aspergillosis usually involves sites of skin injury such intravenous access catheter sites and at sites associated with trauma, occlusive dressings, burns, or surgery and occasionally, outbreaks of are due to contaminated biomedical equipment. Skin changes are most commonly a consequence of widespread infection with aspergillus in patients with impaired immunity. Lesions include single or multiple red or violet hardened plaques or papules that evolve into pus- or blood-filled blisters which eventually become necrotic blackened ulcers or scabs. Primary cutaneous aspergillosis most commonly develops at the site of an intravenous cannula insertion or venipuncture (wound from a blood test). Lesions initially appear similar to cellulitis, then develop into a necrotic ulcer or scab.

Method: Real-Time PCR

Specimen: ***OneSwab***®

Transport: Stable at room temperature

286 Dermatologic Viruses Panel [HSV-1, HSV-2, HPV, HHV-6, HHV-7, Molluscum contagiosum virus, Varicella-zoster virus]

126	Herpes subtype (HSV-1, HSV-2) by Real-Time PCR
439	HPV Type-Detect® 4.0 by Multiplex Real-Time PCR
219	Human herpesvirus-6 (HHV-6) Variants A & B by Real-Time PCR
263	Human herpesvirus-7 (HHV-7) by Real-Time PCR
128	Molluscum contagiosum virus (MCV) by Real-Time PCR
215	Varicella-zoster virus (VZV) by Real-Time PCR

Clinical significance: Viral skin infections are common, can affect individuals of any age and can be difficult to diagnose. They range from mild to severe and may be self-limiting or highly contagious depending on the type of infection. It is important to distinguish between the various causes of a viral rash. Although a thorough history and examination of the patient are vital, laboratory tests can help the clinician to make an accurate diagnosis. Diagnostic tests are indicated when the cause of a skin lesion or disease is not obvious from history and physical examination alone. In this assay, DNA is extracted from the specimen and subjected to PCR amplification.

Method: Real-Time PCR

Specimen: ***OneSwab***®

Transport: Stable at room temperature

368 *Fusobacterium* species by Real-Time PCR

Clinical significance: *Fusobacterium* species are obligate anaerobic, Gram-negative, rod-shaped bacteria found in the microflora of mucosal membranes. They are found as normal flora of the oropharyngeal, gastrointestinal, and genitourinary tracts of healthy humans. After trauma of the mucosal layer or a weakness in the host mucosal barrier due to preceding illness, these bacteria can enter the underlying tissue and cause an infection and potentially infect the bloodstream causing systemic infection. *Fusobacterium* species are commonly associated with topical skin ulcers, oropharyngeal infections including tonsillitis and which can progress to Lemierre's syndrome. Transmission can occur from human-to-human or animal-to-humans and infection is frequently associated with dog bites. In this assay, DNA is extracted from the specimen and subjected to PCR amplification.

Method: Real-Time PCR

Specimen: ***OneSwab***®

Transport: Stable at room temperature

285 Monkeypox virus (Non-variola Orthopoxvirus) by Real-Time PCR

Clinical Significance: Monkeypox virus belongs to the Orthopoxvirus genus, which includes the variola (smallpox) virus. Monkeypox is a rare viral infection that does not usually cause serious illness. However, it can result in hospitalization. Since May 2022, monkeypox has been spreading from person to person in countries where the virus is not usually found, including the United States. In this assay, DNA is extracted from the specimen and subjected to Real-Time PCR amplification

Method: Real-Time PCR

Specimen: ***OneSwab***®

Transport: Stable at room temperature

366 Skin & Soft Tissue Infections (SSTI) Panel [A. *fumigatus*, *B. fragilis, E. faecalis. E. coli*, *Fusobacterium* species, GAS, GBS, *Klebsiella* species, Prevotella Groups 1 & 2, *P. mirabilis, P. aeruginosa, S. aureus*, MRSA, Community Associated MRSA (CA-MRSA)]

553	*Aspergillus fumigatus* by Real-Time PCR
125	*Bacteroides fragilis* by Real-Time PCR
153	*Enterococcus faecalis* by Real-Time PCR
141	*Escherichia coli* by Real-Time PCR
368	*Fusobacterium* species by Real-Time PCR
1112	Group A Streptococcus by Real-Time PCR
127	Group B Streptococcus (GBS) by Real-Time PCR
172	*Klebsiella* species by Real-Time PCR (Reflex to Speciation by Pyrosequencing)
362	Prevotella species Group 1 (*P. bivia, P. disiens, P. intermedia, P. melaninogenica*) by Real-Time PCR
363	Prevotella species Group 2 (*P. corporis, P. albensis*) by Real-Time PCR
146	*Proteus mirabilis* by Real-Time PCR
174	*Pseudomonas aeruginosa* by Real-Time PCR
1118	MRSA: Methicillin-Resistant *Staphylococcus aureus* by Conventional PCR
1119	CA-MRSA: Community-Associated MRSA. Panton-Valentine Leukocidin (PVL) DNA by Real-Time PCR (Type IV + #1118 Req.)

Clinical Significance: Skin and soft tissue infections (SSTI), wounds, and surgical site infections (SSI) are a major issue of morbidity and mortality in the community and healthcare system. Skin or our epidermal layer provides us with a protective barrier between the microbial environment and our sub-dermal tissue, organs, and blood stream. Whenever that barrier is breached by trauma, surgery, or infectious abscess, a strong immune response is triggered to the infecting organism. SSTI, wound infections, and SSI can be caused by a single bacteria or can be polymicrobial depending on the site and length of time of the infection. The initial stages of a SSTI, wound infection, and SSI usually involve the Gram-positive *Staphylococcus, Streptococcus, or Enterococcus* species. Other bacteria can cause the infections, such as the facultative anaerobic Gram-negative rods *Escherichia coli*, *Klebsiella* species, *Proteus mirabilis*, and *Pseudomonas aeruginosa*. These bacteria are usually present at wounds lasting for weeks or surgical site infections, especially those associated with gut or OB/GYN surgeries. Chronic wounds lasting weeks can be due to other facultative anaerobic bacteria such as *Bacteriodes fragilis*, Peptostretococcus, and facultative anaerobic Gram-negative rods such as *Pseudomonas aeruginosa* and *Enterobacter* species. In this assay, DNA is extracted from the specimen and subjected to PCR amplification.

Method: Real-Time PCR

Specimen: ***OneSwab***®

Transport: Stable at room temperature

709 *Staphylococcus epidermidis* by Real-Time PCR

Clinical significance: *Staphylococcus epidermidis* in recent years has emerged as an important opportunistic pathogen. It is now a frequent cause of nosocomial infections. In particular, *S. epidermidis* represents the most common source of infections on prosthetic devices and indwelling medical devices such as catheters. This likely stems from the fact that *S. epidermidis* is a permanent and ubiquitous colonizer of human skin. For this reason, it is also commonly found as a pathogen in surgical wounds. In this assay, DNA is extracted from the specimen and subjected to PCR amplification.

Method: Real-Time PCR

Specimen: *OneSwab*®

Transport: Stable at room temperature

367 SSTI Panel Antibiotic Resistance [*Enterococcus faecalis*, *E. coli*, GAS, GBS, *Klebsiella* species, *P. mirabilis, P. aeruginosa,* CA-MRSA: amoxicillin-clavulanic acid, ampicillin (for *E. faecalis*), cephalothin (cephalexin), clindamycin, doxycycline, trimethoprim-sulfamethoxazole, ciprofloxacin, cefepime, piperacillin-tazobactam, imipenem, gentamicin]

Only performed after 153, 141, 1112, 127, 172, 146, 174, or 118 is positive.

Clinical Significance: Skin and soft tissue infections (SSTI), wounds, and surgical site infections (SSI) are a major issue of morbidity and mortality in the community and healthcare system. Skin or our epidermal layer provides us with a protective barrier between the microbial environment and our sub-dermal tissue, organs, and blood stream. Whenever that barrier is breached by trauma, surgery, or infectious abscess, a strong immune response is triggered to the infecting organism. SSTI, wound infections, and SSI can be caused by a single bacteria or can be polymicrobial depending on the site and length of time of the infection. The initial stages of a SSTI, wound infection, and SSI usually involve the Gram-positive *Staphylococcus, Streptococcus, or Enterococcus* species. Other bacteria can cause the infections, such as the facultative anaerobic Gram-negative rods *Escherichia coli*, *Klebsiella* species, *Proteus mirabilis*, and *Pseudomonas aeruginosa.* These bacteria are usually present at wounds lasting for weeks or surgical site infections, especially those associated with gut or OB/GYN surgeries. Chronic wounds lasting weeks can be due to other facultative anaerobic bacteria such as *Bacteriodes fragilis*, Peptostretococcus, and facultative anaerobic Gram-negative rods such as *Pseudomonas aeruginosa* and *Enterobacter* species. Both topical and systemic antibiotics are used to treat these infections depending on the clinical presentation. Antibiotics suggested by the Infectious Disease Society of America (IDSA), provider survey, and the Clinical and Laboratory Standards Institute (CLSI) were selected for this antibiotic susceptibility assay.

Method: Culture

Specimen: *OneSwab*®

Transport: Stable at room temperature

TICK-BORNE DISEASE

Anaplasmosis & Ehrlichiosis

439 *Anaplasma phagocytophilum* (IgG/IgM) by IFA

Serum required

Clinical Significance: Ehrlichia is the causative agent of Ehrlichiosis. This obligate intracellular bacterium is transmitted by the Ixodes tick, the same vector implicated in Lyme disease and Babesiosis. Human Ehrlichiosis was described in the United States for the first time in 1986. Unusual inclusions are noted in patient's mononuclear cells and were later recognized as being characteristic of the genus *Ehrlichia*. Human Ehrlichiosis has a fatality rate approaching 5% if treatment with the appropriate antibiotic is not administered in a timely fashion. Two types of human Ehrlichiosis have been recognized, depending on the type of infected blood cells. Human Monocytotropic Ehrlichiosis (HME) is caused by infection of mononuclear cells and Human Granulocytic Ehrlichiosis (HGE) is caused by infection of granulocytes.

Method: IFA

Specimen: Serum

Transport: Stable at room temperature

411 *Ehrlichia chaffeensis* (HME) & *Anaplasma phagocytophilum* by Real-Time PCR

Clinical significance: *Ehrlichia* is the causative agent of Ehrlichiosis. This obligate intracellular bacteria is transmitted by the Ixodes tick, the same vector implicated in Lyme disease and Babesiosis. Human Ehrlichiosis was described in the United States for the first time in 1986. Unusual inclusions are noted in patient's mononuclear cells and were later recognized as being characteristic of the genus *Ehrlichia*. Human Ehrlichiosis has a fatality rate approaching 5% if treatment with the appropriate antibiotic is not administered in a timely fashion. Two types of human Ehrlichiosis have been recognized, depending on the type of infected blood cells. Human Monocytotropic Ehrlichiosis (HME) is caused by infection of mononuclear cells and Human Granulocytic Ehrlichiosis (HGE) is caused by infection of granulocytes. In this assay, DNA is extracted from the specimen and subjected to PCR amplification.

Method: Real-Time PCR

Specimen: Whole blood yellow top tube (ACD solution A), CSF, synovial fluid, ticks

Transport: Stable at room temperature

456 *Ehrlichia ewingii* by Real-Time PCR

Clinical significance: *Ehrlichia ewingii* is one of three *Ehrlichia* species associated with Human Monocytic Ehrlichiosis (HME). HME occurs mostly in the southeastern and south-central United States, from the East Coast to Texas, overlapping with the geographic distribution of Rocky Mountain Spotted Fever Rickettsiosis. However, significant cases have also been reported in Maryland, Delaware, New Jersey, New York, Connecticut, and Rhode Island. The Lone Star tick (*Amblyomma americanum*) is primarily responsible for the transmission of *E. ewingii*. *Ehrlichia* species have similar clinical presentation having an incubation period of one to two weeks. Signs and symptoms include fever, chills, headache, malaise, muscle pain, gastrointestinal symptoms (nausea, vomiting, diarrhea, and anorexia), altered mental status and rash (more common among children). Of the *Ehrlichia* species, *E. ewingii* infections are typically less severe than the more common *E. chaffeensis*.

Method: Real-Time PCR

Specimen: Whole blood yellow top tube (ACD solution A)

Transport: Stable at room temperature

Babesiosis

431 *Babesia duncani* (Wa1) by Real-Time PCR

Clinical significance: Babesiosis is a zoonotic disease which requires transmission from an animal reservoir to humans via a tick vector. In the northeastern United States, the black-legged deer tick *Ixodes scapularis*, the same vector that transmits Lyme disease, is the principal vector for the transmission of the etiologic agent of Babesiosis, *Babesia microti*. *Babesia* species from rodents, primarily the white-footed deer mouse but also the field mouse, vole, rat, and chipmunk, are transmitted to humans during tick bites in endemic areas. Human infections occurring on the West Coast of the United States have been caused by Babesia-like organisms designated WA-1 type Babesia (where the prefix "WA" stands for Washington State in which the first human case was described). Based upon sequencing data, WA-1 type Babesia shows more affinity to small babesial isolates from dogs and wildlife in California than to *B. microti*. Although WA1 is morphologically similar to *B. microti*, several differences were noted, including antigenic cross-reactivity, virulence in hamsters (100% fatality within 10 days), and Southern restriction fragment length polymorphisms of DNA digests. All of these data indicated that ***Babesia duncani* (WA-1)** is a new human pathogen that is distinct from *B. microti*.

Method: Real-Time PCR

Specimen: Whole blood yellow top tube (ACD solution A), ticks

Transport: Stable at room temperature

410 *Babesia microti* by Real-Time PCR

Clinical significance: *Babesia* species are the causative agent of babesiosis. Babesia are probably the most frequent mammalian intraerythrocytic parasites, with the exception of trypanosomes. In the host, intraerythrocytic *Babesia* species vary in size from 1 to 5µm in length and are oval, round or pear-shaped. Babesia and *Borrelia burgdorferi* are transmitted by the same vector, black-legged ticks of the genus Ixodes. The disease is transmitted to humans mostly by the nymph and occasionally by the adult ticks. In general, patients infected with Babesia do not recall receiving a tick bite. After an incubation period of 1 to 4 weeks (or 6 to 9 weeks following transmission by blood transfusion), symptoms and signs gradually appear. The symptoms are not specific and can include fatigue, anorexia, myalgia, nausea, depression and dark urine. In this assay, DNA is extracted from the specimen and subjected to PCR amplification.

Method: Real-Time PCR

Specimen: Whole blood yellow top tube (ACD solution A), CSF, synovial fluid, ticks

Transport: Stable at room temperature

440 *Babesia microti* (IgG/IgM) by IFA

Serum required

Human babesiosis is an emerging tick-borne disease that may be life-threatening. Babesia IFA detects the long-lasting human immune system response, or IgG antibodies, to Babesia antigen, as well as primary and early infections through the detection of IgM antibodies.

Method: IFA

Specimen: Serum

Transport: Stable at room temperature

Borreliosis - Lyme disease

424 *Borrelia afzelii* by Real-Time PCR

Clinical significance: *Borrelia afzelii* and *Borrelia garinii* are part of the "*B. burgdorferi* sensu lato" group and are distinguished from the species "*B. burgdorferi* sensu stricto" (strict sense of *B. burgdorferi*). Human infection due to *B. burgdorferi* sensu lato may involve multiple organs or tissues, resulting in skin, cardiac, neurological and musculoskeletal disorders. *B. burgdorferi* sensu stricto is widely distributed in the Northeast, Midwest and Western regions of the United States. *B. burgdorferi* sensu stricto, *B. garinii*, and *B. afzelii* have been documented in Europe. The principal vectors of *B. burgdorferi* sensu lato are ticks of the *I. ricinus* complex, including *I. scapularis* and *I. pacificus* in the United States, *I. ricinus* in Europe, and *I. persulcatus* in Asian Russia, China and Japan. The European sheep tick, *I. ricinus*, has been recognized as a vector of all three human pathogenic Borrelia species, *B. burgdorferi* sensu stricto, *B. garinii*, and *B. afzelii*. Acrodermatitis chronica atrophicans (ACA) is associated with *B. afzelii* infection. ACA is a late cutaneous manifestation of LB characterized by chronic and long-lasting progressive red and bluish-red lesions, usually on the extensor of the extremities. Molecular studies of ACA isolates from patients in several European countries have provided evidence that *B. afzelii* is the predominant etiologic agent of ACA. Lyme carditis is a well known clinical manifestation in both North American and European patients with LB. Neuroborreliosis is the most frequent manifestation of disseminated infection in Europe and is a common symptom in North American LB patients as well. All three species, *B. burgdorferi* sensu stricto, *B. garinii*, and *B. afzelii*, are known to cause Lyme neuroborreliosis. In European patients, *B. garinii* constituted 72% of the Borrelia isolates or DNAs detected in human CSF samples, whereas 8% and 20% of the specimens were identified as *B. burgdorferi* sensu stricto and *B. afzelii*, respectively.

Method: Real-Time PCR

Specimen: Whole blood yellow top tube (ACD solution A), CSF, synovial fluid, ticks

Transport: Stable at room temperature

441 *Borrelia afzelii* (Europe) by Western blot (IgG/IgM) (serum required)

Clinical significance: This assay is for the qualitative in vitro detection of human IgG or IgM antibodies to individual proteins of *Borrelia afzelii* in human serum. The Western blot is useful for characterizing the specificity of the antibody response to *B. afzelii* It is utilized as a second-step method to differentiate between IgM and IgG antibodies to specific *B. afzelii* proteins. Other serological tests, such as IFA or EIA, only measure total antibody response.

Method: Western blot

Specimen: Serum

Transport: Stable at room temperature

305 Lyme disease (*B. burgdorferi*) by Real-Time PCR

Clinical significance: *Borrelia burgdorferi* is the causative agent of Lyme disease. Transmission of Lyme disease occurs primarily by way of infected black-legged ticks of the genus Ixodes. If left untreated the bacterium usually travels through the bloodstream, establishes itself in various body tissues, and can cause a number of symptoms ranging from a relatively benign skin rash to severe arthritic, neurologic and cardiac manifestations. The clinical symptoms of Lyme disease vary among individuals and during the course of an infection. The characteristics of *Borrelia burgdorferi* infections makes diagnosis of the disease difficult. Most of the displayed associated clinical symptoms are not unique to Lyme disease. In this assay, DNA is extracted from the specimen and subjected to PCR amplification.

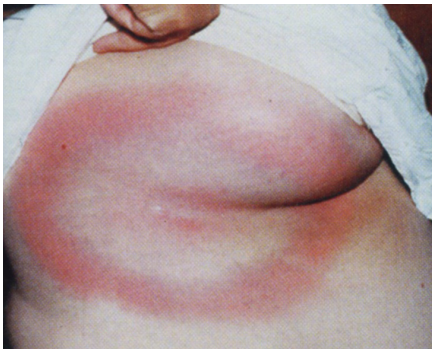
Method: Real-Time PCR

Specimen: Whole blood yellow top tube (ACD solution A), ***UroSwab***®, CSF, synovial fluid, ticks

Transport: Stable at room temperature

425 *Borrelia garinii* by Real-Time PCR

Clinical significance: *Borrelia afzelii* and *Borrelia garinii* are part of the "*B. burgdorferi* sensu lato" group and are distinguished from the species "*B. burgdorferi* sensu stricto" (strict sense of *B. burgdorferi*). Human infection due to *B. burgdorferi* sensu lato may involve multiple organs or tissues, resulting in skin, cardiac, neurological and musculoskeletal disorders. *B. burgdorferi* sensu stricto is widely distributed in the Northeast, Midwest and Western regions of the United States. *B. burgdorferi* sensu stricto, *B. garinii*, and *B. afzelii* have been documented in Europe. The principal vectors of *B. burgdorferi* sensu lato are ticks of the *I. ricinus* complex, including *I. scapularis* and *I. pacificus* in the United States, *I. ricinus* in Europe, and *I. persulcatus* in Asian Russia, China and Japan. The European sheep tick, *I. ricinus*, has been recognized as a vector of all three human pathogenic Borrelia species, *B. burgdorferi* sensu stricto, *B. garinii*, and *B. afzelii*. Acrodermatitis chronica atrophicans (ACA) is associated with *B. afzelii* infection. ACA is a late cutaneous manifestation of LB characterized by chronic and long-lasting progressive red and bluish-red lesions, usually on the extensor of the extremities. Molecular studies of ACA isolates from patients in several European countries have provided evidence that *B. afzelii* is the predominant etiologic agent of ACA. Lyme carditis is a well known clinical manifestation in both North American and European patients with LB. Neuroborreliosis is the most frequent manifestation of disseminated infection in Europe and is a common symptom in North American LB patients as well. All three species, *B. burgdorferi* sensu stricto, *B. garinii*, and *B. afzelii*, are known to cause Lyme neuroborreliosis. In European patients, *B. garinii* constituted 72% of the Borrelia isolates or DNAs detected in human CSF samples, whereas 8% and 20% of the specimens were identified as *B. burgdorferi* sensu stricto and *B. afzelii*, respectively.



Method: Real-Time PCR

Specimen: Whole blood yellow top tube (ACD solution A), CSF, synovial fluid, ticks

Transport: Stable at room temperature

442 *Borrelia garinii* (Europe) by Western blot (IgG/IgM) (serum required)

Clinical significance: This assay is for the qualitative in vitro detection of human IgG or IgM antibodies to individual proteins of *Borrelia garinii* in human serum. The Western blot is useful for characterizing the specificity of the antibody response to *B. garinii*. It is utilized to differentiate between IgM and IgG antibodies to specific *B. garinii* proteins. Other serological tests, such as IFA or EIA, only measure total antibody response.

Method: Western blot

Specimen: Serum

Transport: Stable at room temperature

449 *Borrelia mayonii* (United States) by Real-Time PCR

Clinical significance: *Borrelia mayonii* is a new *Borrelia* species recently found to cause Lyme disease in the upper Midwestern United States. While genetically distinct from the three other species of *Borrelia*, it is the only species besides *B. burgdorferi* shown to cause Lyme disease in North America. The associated illness is still called Lyme disease or Lyme borreliosis. In addition to the traditional Lyme disease symptoms, unlike *Borrelia burgdorferi*, *B. mayonii* appears to be associated with nausea and vomiting, diffuse rashes, and a higher concentration of bacteria in the blood. *B. mayonii* has also been identified in blacklegged (or "deer") ticks collected in several counties in northwestern Wisconsin and Minnesota.

Method: Real-Time PCR

Specimen: Whole blood yellow top tube (ACD solution A)

Transport: Stable at room temperature

427 Lyme disease IgG/IgM by ELISA

Serum required

Clinical significance: This assay tests for the qualitative detection of total (IgG and IgM) antibodies to *Borrelia burgdorferi* in human serum. Detection of antibodies allows diagnosis of an infection when other methods, such as culture or antigen detection, are impractical or yield negative results. This test is the first of a two-step system to provide supportive evidence of exposure to *B. burgdorferi*, which could support a clinical diagnosis of Lyme disease. This assay should not be used as a sole criterion for diagnosis.

Method: ELISA

Specimen: Serum

Transport: Stable at room temperature

417 Lyme disease C6 Peptide by ELISA

Serum required

Clinical significance: This assay utilizes a synthetic peptide (C6 peptide) which is derived from the VisE protein of *B. burgdorferi*. This peptide has been shown to be both specific and highly immunogenic. The peptide sequence is conserved and equally antigenic in humans infected with *Borrelia burgdorferi* or with European genospecies including *B. afzelii* and *B. garinii*. As the antigen represents a defined sequence within the protein, potential cross-reactivity in individuals with unrelated and partially related antigens found in other organisms is greatly reduced. Likewise, cross-reactivity in individuals vaccinated with licensed recombinant OspA Lyme disease vaccine (Lymerix) is not observed.

Method: ELISA

Specimen: Serum

Transport: Stable at room temperature

313 Lyme disease IgG/IgM by Western blot

Serum required

Clinical significance: This assay is for the qualitative in vitro detection of human IgG or IgM antibodies to individual proteins of *Borrelia burgdorferi* in human serum. The Western blot is useful for characterizing the specificity of the antibody response to *B. burgdorferi*. It is utilized as a second-step method to differentiate between IgM and IgG antibodies to specific *B. burgdorferi* proteins. Other serological tests, such as IFA or EIA, only measure total antibody response.

Method: Western blot

Specimen: Serum

Transport: Stable at room temperature

Borreliosis - Southern Tick-associated Rash Illness (STARI

430 *Borrelia lonestari* by Real-Time PCR

Clinical significance: In the southeastern and south central United States, the prevalence of Lyme disease caused by *B. burgdorferi* sensu stricto is much lower than that found in the northeastern United States. However, another Lyme disease-like illness that develops following the bite of the Lone Star tick, *Amblyomma americanum*, has been described. Individuals affected with this illness, termed "southern tick-associated rash illness", or STARI, commonly develop a localized expanding circular skin rash (erythema migrans [EM]) at the site of the tick bite similar to that seen with classic Lyme disease. A mild illness characterized by generalized fatigue, headache, stiff neck, and occasionally fever and other constitutional signs also develop. STARI appears to respond to antibiotic treatment and has been attributed to infection with an as-of-yet-uncultivated spirochete tentatively referred to as *Borrelia lonestari*. Cases consistent with this clinical presentation have been reported from several southeastern and south central states, including Missouri, Maryland, Georgia, South Carolina, and North Carolina. The majority of patients with STARI do not have laboratory evidence of infection with *B. burgdorferi* sensu stricto. Moreover, a new spirochete, *B. lonestari*, was described from *A. americanum* on the basis of polymerase chain reaction (PCR) amplification of the flagellin and 16s rRNA genes. Virtually identical sequences have been found in ticks from geographic regions as disparate as New Jersey and Texas, suggesting this organism is widely distributed. Likewise, Borrelia spirochetes have been detected in *A. americanum* and *I. scapularis* ticks in Alabama. Despite relatively widespread documentation of this organism in ticks, a vertebrate reservoir host that could be responsible for maintaining infection in the tick population has not yet been identified.

Method: Real-Time PCR

Specimen: Whole blood yellow top tube (ACD solution A), CSF, ticks

Transport: Stable at room temperature

Borreliosis - Tick-borne Relapsing Fever

450 *Borrelia hermsii* by Real-Time PCR

Clinical significance: *Borrelia hermsii* is one of three *Borrelia* species associated with Tick-borne Relapsing Fever (TBRF). TBRF occurs mostly in 14 western states: Arizona, California, Colorado, Idaho, Kansas, Montana, Nevada, New Mexico, Oklahoma, Oregon, Texas, Utah, Washington, and Wyoming. Most cases of TBRF occur in rodent infested cabins and may be associated with cave exposure in Texas. *B. hermsii* is carried by the Soft Bodied tick (*Ornithodoros spp.*). The incubation period of the infection is approximately 7 days, followed by recurring febrile episodes that last 3 days and separated by afebrile periods of 7 days. Signs and symptoms include relapsing fever, headache, myalgia, chills, nausea, vomiting, arthralgia, and facial palsy (rare).

Method: Real-Time PCR

Specimen: Whole blood yellow top tube (ACD solution A)

Transport: Stable at room temperature

443 *Borrelia miyamotoi* by Real-Time PCR

Clinical significance: *Borrelia miyamotoi,* associated with Tick-borne Relapsing Fever**,** is found in the Upper Midwest, Northeast, and mid-Atlantic United States, in places where Lyme Disease is endemic. It may be spread by larval blacklegged tick (*Ixodes scapularis)* which are already known to transmit several diseases, including Lyme disease, anaplasmosis, and babesiosis. Common symptoms include Fever, chills, fatigue, severe headaches, arthralgia, and myalgia. Laboratory diagnosis includes the use of polymerase chain reaction (PCR) testing to detect DNA from the organism to indicate active infection. Antibody-based testing including C6 peptide for Lyme disease by ELISA may also be positive.

Method: Real-Time PCR

Specimen: Whole blood yellow top tube (ACD solution A), ticks

Transport: Stable at room temperature

451 *Borrelia parkeri* by Real-Time PCR

Clinical significance: Tick-borne relapsing fever (TBRF) is a potentially serious vector-borne disease endemic to the western United States. TBRF is caused by 8 or more *Borrelia* species including *Borrelia parkeri* which are transmitted to humans by the bite of an infected *Ornithodoros* tick. Relapsing fever is characterized by recurring episodes of fever and nonspecific symptoms such as headache, myalgia, arthralgia, shaking chills, and abdominal complaints.

Method: Real-Time PCR

Specimen: Whole blood yellow top tube (ACD solution A), ticks

Transport: Stable at room temperature

445 *Borrelia turicatae* by Real-Time PCR

Clinical significance: *Borrelia turicatae* is one of several spirochetes associated with Tick-borne Relapsing Fever. Relapsing fever is an acute disease characterized by recurrent episodes of fever and spirochetemia separated by afebrile periods, uncontrollable chills, nausea, vomiting, miscarriage, and potential death if untreated. Endemic TBRF is a zoonotic disease transmitted worldwide by softbody ticks of the genus Ornithodoros.

Method: Real-Time PCR

Specimen: Whole blood yellow top tube (ACD solution A)

Transport: Stable at room temperature

Spotted Fever Group Rickettsiosis

448 *Rickettsia parkeri* by Real-Time PCR

Clinical significance: *Rickettsia parkeri* is found in the Southeast and mid-Atlantic United States, and parts of southern Arizona. It is transmitted by the Gulf Coast tick (*Amblyomma maculatum). R. parkeri* rickettsiosis has overlapping symptoms with RMSF, but less severe. It's almost always associated with an inoculation eschar (ulcerated, necrotic lesion) at the site of tick attachment. Several days after an eschar appears, so do fevers, headaches, rashes (sparse maculopapular or papulovescicular eruptions on the trunk and extremities), and muscle aches. In this assay, DNA is extracted from the specimen and subjected to PCR amplification.

Method: Real-Time PCR

Specimen: Whole blood yellow top tube (ACD solution A), ticks

Transport: Stable at room temperature

452 *Rickettsia philipii* (364D) by Real-Time PCR

Clinical significance: *Rickettsia philipii* (364D) is the causative agent of Pacific Coast tick fever (PCTF). Transmitted to people by the Pacific Coast tick, *Dermacentor occidentalis*. Although most human cases of PCTF have been reported from northern California, surveillance suggests that *R. philipii* may occur throughout the distribution range of *D. occidentalis* including most of California, southern Oregon, and northern Baja California, Mexico. The hallmark feature of PCTF is the presence of at least one necrotic lesion, known as an eschar, where dead tissue falls off (sheds) from healthy skin. Symptoms also include fever and headache.

Method: Real-Time PCR

Specimen: Whole blood yellow top tube (ACD solution A), ticks

Transport: Stable at room temperature

447 *Rickettsia rickettsii* by Real-Time PCR

Clinical significance: *Rickettsia rickettsii* is an obligate intracellular parasite that seems to target endothelial cells. It is the causative agent of Rocky Mountain Spotted Fever (RMSF). It is a tick-borne disease that can be transmitted by ticks of the genus Ixodes, the same ticks which transmit Lyme disease, Babesiosis, and Ehrlichiosis. This disease is characterized by fever, myalgia, and headache at onset. The major diagnostic sign is a rash that may characteristically affect the palms of the hands and soles of the feet. Early diagnosis of this disease is important so that appropriate antibiotic therapy may be initiated. Failure to initiate proper therapy within 5 days after onset of symptoms has been associated with increased mortality. Traditional laboratory tests lack sensitivity and can be very time consuming. Recent advances in molecular diagnostic techniques, such as PCR, provide a highly sensitive and specific means of early diagnosis. In this assay, DNA is extracted from the specimen and subjected to PCR amplification.

Method: Real-Time PCR

Specimen: Whole blood yellow top tube (ACD solution A), ticks

Transport: Stable at room temperature

446 *Rickettsia* species (Rickettsiosis) by Real-Time PCR

Clinical significance: *Rickettsia rickettsii* is an obligate intracellular parasite that seems to target endothelial cells. It is the causative agent of Rocky Mountain Spotted Fever (RMSF). It is a tick-borne disease that can be transmitted by ticks of the genus Ixodes, the same ticks which transmit Lyme disease, Babesiosis, and Ehrlichiosis. This disease is characterized by fever, myalgia, and headache at onset. The major diagnostic sign is a rash that may characteristically affect the palms of the hands and soles of the feet. Early diagnosis of this disease is important so that appropriate antibiotic therapy may be initiated. Failure to initiate proper therapy within 5 days after onset of symptoms has been associated with increased mortality. Traditional laboratory tests lack sensitivity and can be very time consuming. Recent advances in molecular diagnostic techniques, such as PCR, provide a highly sensitive and specific means of early diagnosis. In this assay, DNA is extracted from the specimen and subjected to PCR amplification.

Method: Real-Time PCR

Specimen: Whole blood yellow top tube (ACD solution A), ticks

Transport: Stable at room temperature

Tick-borne Viruses

434 Colorado Tick Fever virus by Real-Time PCR

Clinical significance: Colorado tick fever is an acute viral infection transmitted from the bite of an infected *Dermacentor andersoni* (wood) tick, and in rare instances by blood transfusion. It is found most commonly in the western United States and Canada, with particular concentration in the mountainous regions of Colorado and Idaho. This disease most commonly develops from March to September, with the highest numbers of infections occurring in May and June. Symptoms start about 3 to 6 days after the tick bite. Symptoms of a two-staged illness present with initial fever for 3 days, resolve, and then return 1 to 3 days later for another few days. Infection can be severe in young children resulting in hospitalization. Possible complications include ascetic meningitis, encephalitis and hemorrhagic fever. In this assay DNA is extracted from the specimen and subjected to PCR amplification.

Method: Real-Time PCR

Specimen: Whole blood yellow top tube (ACD solution A)

Transport: Stable at room temperature

436 Heartland virus (Phlebovirus) by Real-Time PCR

Clinical significance: On August 30, 2012, a new tick-borne viral pathogen was reported in the New England Journal of Medicine called the Heartland virus. The Heartland virus is a phlebovirus of the Bunyaviridiae family. It is a single-stranded, negative-sense RNA virus. Infection with Phleboviridiae result in diverse pathologies, many associated with fever such as Rift Valley Fever. Although there is no available epidemiologic data, a potential vector may be Amblyoma americanum (the Lone Star tick). The clinical presentation closely resembles infection with Human Granulocytic Anaplasmosis and STFSV including fever, fatigue, thrombocytopenia, and diarrhea. Recognition may be important to differentiate it from infection with Human Granulocytic Anaplasmosis due to the similar clinical presentation. In this assay, DNA is extracted from the specimen and subjected to Real-Time PCR amplification.

Method: Real-Time PCR

Specimen: Whole blood yellow top tube (ACD solution A), tick

Transport: Stable at room temperature

282 Powassan virus IgG/IgM by ELISA (serum required)

Clinical significance: Powassan virus belongs to the Flavivirus genus that includes the Zika, Dengue, and West Nile viruses. Powassan virus is associated with a tick-borne disease located mainly in the Great Lakes region and Northeastern states. The Blacklegged tick (*Ixodes scapularis*) and Groundhog tick (*Ixodes cookei*) are primarily responsible for the transmission of the virus. Many people who become infected do not have symptoms. Signs and symptoms include fever, headache, vomiting, and generalized weakness. Symptoms usually progress to meningoencephalitis that may include meningeal signs, altered mental status, seizures, aphasia, paresis, movement disorders, or cranial nerve palsies. Approximately 50% of survivors have permanent neurological symptoms such as recurrent headaches, muscle wasting, and memory problems. Approximately 10% of Powassan virus encephalitis cases are fatal. Due to the common Blacklegged tick (*Ixodes scapularis*) vector, co-infection with *Anaplasma phagocytophilum*, *Borrelia burgdorferi*, or *Babesia microti* is possible.

Method: ELISA

Specimen: Serum

Transport: Stable at room temperature

281 Tick-borne Encephalitis virus IgG/IgM by ELISA (serum required)

Clinical significance: This assay is for the qualitative in vitro detection of human IgG or IgM antibodies to individual proteins of Tick-borne Encephalitis virus in human serum. Tick-borne encephalitis virus (TBEV) is a member of the family *Flaviviridae* and was initially isolated in 1937. It is transmitted to humans predominantly by ticks of the Ixodideae family, but can also occur via the consumption of unpasteurized contaminated dairy products. Most TBEV infections are asymptomatic, but the symptomatic cases typically have neurological manifestations, such as meningitis, encephalitis, and meningoencephalitis which, together, are referred to as tick-borne encephalitis (TBE). TBE is a severe disease that often results in life-long neurological complications and can lead to death.

Method: ELISA

Specimen: Serum

Transport: Stable at room temperature

Tularemia

360 *Francisella* Species (*F. tularensis, F. holarctica*) by Real-Time PCR

Clinical significance: Five subspecies of Francisella are found in the Northern hemisphere, but only *F. tularensis* subsp. *tularensis* and subsp. *holarctica* cause disease in humans. *F. tularensis* is the causative agent of tularemia, a zoonotic disease of humans, rabbits, rodents, and hares. It is typically transmitted by inhalation, the bite of an infected tick, contact with infected animal products or by the ingestion of contaminated water. Clinical manifestations of tularemia vary depending on the virulence of the strain and the route of inoculation. Inhalation results in the pneumonic form. Acquisition through a tick bite or from contact with an infected animal, results in the ulceroglandular form of the disease. Francisella can also be contracted through the conjunctiva, causing the oculoglandular form of tularemia. Less commonly, ingestion of contaminated foods or water may result in clinical symptoms. Once the bacterium enters the body, it travels to the draining lymph nodes and then spreads to the liver, lungs, and spleen of infected humans or animals, where it replicates to high numbers. In this assay DNA is extracted from the specimen and subjected to PCR amplification.

Method: Real-Time PCR

Specimen: Whole blood yellow top tube (ACD solution A)

Transport: Stable at room temperature

MOSQUITO-BORNE VIRUSES

280 Chikungunya virus IgG/IgM by ELISA (serum required)

Clinical significance: This assay is for the qualitative in vitro detection of human IgG or IgM antibodies to individual proteins of Chikungunya virus in human serum. Chikungunya virus is spread to people by the bite of an infected mosquito. Symptoms usually begin 3–7 days after being bitten by an infected mosquito and primarily include fever and joint pain. Other symptoms may include headache, muscle pain, joint swelling, or rash. In late 2013, chikungunya virus was found for the first time in the Americas on islands in the Caribbean.

Method: ELISA

Specimen: Serum

Transport: Stable at room temperature

270 Dengue viruses 1-4 by Real-Time PCR

Clinical significance: Dengue virus (DV) is an arthropod-borne virus (arbovirus) transmitted by Aedes mosquitoes. There are four closely related, but antigenically distinct, Dengue virus serotypes (DEN 1, DEN 2, DEN 3 and DEN 4). Infection with one of these serotypes provides immunity to only that serotype for life. DV may cause Dengue fever (DF) which usually starts with a high fever, rash, severe headache, pain behind the eyes and muscle and joint pain. A DV infection may also progress to Dengue hemorrhagic fever (DHF) which is fatal in about 5 percent of cases. Important risk factors for DHF include the strain of the infecting virus, as well as the age, and especially the prior dengue infection history of the patient. In the United States, approximately 100 cases of dengue are reported each year in travelers returning from tropical areas. Aedes mosquitoes are found in Texas, Florida and other southern states, and locally acquired dengue has been reported three times since 1980 in southern Texas. There is no treatment or vaccine for dengue. Prevention centers on public health action to control mosquitoes, and on individual action to avoid mosquito bites. A Real-Time polymerase chain reaction (PCR) assay provides a rapid, specific and sensitive approach for detection of this virus.

Method: Real-Time PCR

Specimen: Whole blood yellow top tube (ACD solution A)

Transport: Stable at room temperature

279 Dengue virus IgG/IgM by ELISA (serum required)

Clinical significance: This assay is for the qualitative in vitro detection of human IgG or IgM antibodies to individual proteins of Dengue virus in human serum. The Western blot is useful for characterizing the specificity of the antibody response to Dengue virus. It is utilized to differentiate between IgM and IgG antibodies to specific Dengue virus proteins. Other serological tests, such as IFA or EIA, only measure total antibody response.

Method: ELISA

Specimen: Serum

Transport: Stable at room temperature

269 Eastern Equine Encephalitis virus by Real-Time PCR

Clinical significance: Eastern Equine Encephalitis virus (EEE) is an arthropod-borne virus (arbovirus) transmitted by mosquitoes. It is found mainly along the eastern seaboard of the United States and on the eastern Gulf coast. EEE can affect the central nervous system and cause severe complications, including death. The symptoms may also include fever, headache, drowsiness, irritability, nausea, and vomiting, followed by confusion, weakness, and coma. Young infants often suffer seizures. Since 1964, there have been 163 confirmed cases in the United States. There is no treatment or vaccine for EEE. Prevention centers on public health action to control mosquitoes, and on individual action to avoid mosquito bites. A Real-Time polymerase chain reaction (PCR) test provides a rapid, specific, and sensitive approach to detection of this virus.

Method: Real-Time PCR

Specimen: Whole blood yellow top tube (ACD solution A)

Transport: Stable at room temperature

283 Japanese Encephalitis virus IgG/IgM by ELISA (serum required)

Clinical significance: Japanese Encephalitis (JE) virus belongs to the Flavivirus genus that includes Powassan, Zika, Dengue, and West Nile viruses. JE virus is a leading cause of encephalitis in Asia and the western Pacific transmitted by the bite of the Culex species of mosquito. The lifecycle of JE virus is dependent upon its propagation between the mosquito and vertebrate hosts such as pigs and wading birds. Human infections are considered a dead-end since viral concentrations in humans is not high enough to infect mosquitoes and continue the cycle. Although risk of JE viral infection is relatively low and most people infected with JE have only mild or no symptoms. Less than 1% of infected people will develop initial signs and symptoms that include fever, headache, and vomiting typically after a 5 to 15 day incubation period. Additionally, changes in mental status, neurologic symptoms, weakness, and movement disorders might develop and seizures are common, especially among children. Of the patients who develop encephalitis, the mortality rate is 20 - 30% and 30 - 50% of those who recover continue to have neurologic, cognitive, or psychiatric symptoms. The JE virus infection is preventable due to the availability of the JE vaccine. Risk of infection is associated with unvaccinated travelers to the region.

Method: ELISA

Specimen: Serum

Transport: Stable at room temperature

266 La Crosse Encephalitis virus by Real-Time PCR

Clinical significance: La Crosse virus (LAC) is the causative agent of La Crosse encephalitis. This vector-borne disease is transmitted through the bite of an infected *Aedes triseriatus* tree hole mosquito. Laboratory confirmed cases of La Crosse virus occur with decreasing frequencies from North to South and the vast majority of infections occur within the eastern half of the United States. LAC is traditionally active in the upper Midwest and Great Lakes areas; however, in recent years there has been an increase in frequency in the Mid-Atlantic States. Most LAC infections are subclinical; however, when symptoms are evident, the onset is abrupt. LAC virus produces an acute encephalitis that begins with a mild fever and illness lasting on average 1 to 3 days and sometimes persisting for up to one week. Patients typically present with fever, chills, abdominal pain, and headache with or without photophobia. One can also experience upper respiratory symptoms with or without sore throat as well as cough. More serious illness can occur, characterized by vomiting, nuchal rigidity, lethargy and coma. In this assay, RNA is extracted from the specimen and subjected to reverse transcriptase PCR amplification.

Method: Real-Time PCR

Specimen: Whole blood yellow top tube (ACD solution A)

Transport: Stable at room temperature

264 St. Louis Encephalitis virus by Real-Time PCR

Clinical significance: St. Louis Encephalitis virus (SLE) is a flavivirus capable of inducing aseptic meningitis or encephalitis in infected individuals. Transmission is via a bite from an infected mosquito and can occur anywhere within the continental United States, although the CDC reports the highest prevalence in Indiana, Illinois, Mississippi, Ohio and Texas. The incubation period is typically from five to fifteen days. Symptoms range from mild, limited to fever and headache, to severe, marked by headache, high fever, disorientation, stupor, neck stiffness and occasional convulsion and paralysis. Hospitalization for CNS infection occurs for 95% of recognized cases with a reported 3% to 30% mortality rate. There is no specific treatment for SLE and no available vaccine. In this assay, RNA is extracted from the patient specimen and subjected to PCR amplification.

Method: Real-Time PCR

Specimen: Whole blood yellow top tube (ACD solution A)

Transport: Stable at room temperature

243 West Nile virus by Real-Time PCR

Clinical significance: West Nile virus (WNV) is spread most often by infected mosquitoes. In 1999, the CDC reported that there were 62 human cases of WNV infection in New York State. Since then, this flavivirus has rapidly spread throughout the continental United States. Although about 80% of infected people show no symptoms upon infection, the remaining 20% exhibit mild symptoms such as fever, headache, body aches, nausea and vomiting. Symptoms typically present 3 to 14 days post infection. In about 1 out of 150 infected people, symptoms are much more severe and range from high fever, neck stiffness, stupor and disorientation to coma, tremors, convulsions, muscle weakness, vision loss, numbness, and even paralysis. Real-Time PCR is most successful for detection when utilized immediately after infection. Subsequently, serological assays are available to determine exposure to WNV.

Method: Real-Time PCR

Specimen: Whole blood yellow top tube (ACD solution A), biopsy (fresh), biopsy (paraffin), CSF

Transport: Stable at room temperature

244 West Nile virus IgG/IgM by ELISA

Serum required

Clinical significance: Diagnosis of WNV infection relies on high clinical suspicion. Virus isolation is rarely a viable option because this technique is laborious, time-consuming, and requires expensive facilities. The IgM antibody-capture enzyme-linked immunosorbent assay (ELISA) is currently the most efficient diagnostic method. MDL has developed a convenient and specific serology test for the detection of antibodies against WNV; this ELISA-based assay represents an advancement over currently available diagnostic tests because it is designed to eliminate antigenic cross-reactivity with other flaviviruses.

Method: ELISA

Specimen: Serum

Transport: Stable at room temperature

265 Western Equine Encephalitis virus by Real-Time PCR

Clinical significance: Western Equine Encephalitis virus is a mosquito-transmitted disease that affects both humans and horses. A member of the Togoviridae family, it is one of several mosquito-borne viruses that induce serious, sometimes fatal, infections that affect the central nervous system. Symptoms range from mild, with few or no overt symptoms, to severe and possibly fatal and may take five to ten days to manifest following a mosquito bite. The more severe cases can be distinguished from the less severe by the presence of a high fever with sudden onset, drowsiness, nausea, vomiting and irritability that is followed by weakness, confusion and coma. Infections in young infants often present with seizures. While there is no specific treatment, medical intervention is necessary to limit complications, which include brain damage in 13% of cases and are fatal in 3% of persons exhibiting severe symptoms. Seasonality within the United States is primarily during June and July. Prevention consists of limiting exposure to mosquitoes, covering exposed flesh and the use of insect repellents. In this assay, DNA is extracted from the patient specimen and subjected to PCR amplification.

Method: Real-Time PCR

Specimen: Whole blood yellow top tube (ACD solution A)

Transport: Stable at room temperature

FLEA, FLY, LOUSE, MITE & TICK-BORNE DISEASE

326 *Bartonella bacilliformis* by Real-Time PCR

Clinical significance: The genus Bartonella contains aerobic, fastidious, Gram-negative bacteria that belong to the alpha-2 subgroup of the class Proteobacteria. Due to the limited distribution of its vector, the sand fly, *Bartonella bacilliformis* is found predominantly at high elevations in the Andes Mountains. It is the causative agent of Carriõn's disease. This biphasic syndrome is comprised of two disorders: Oroya Fever and verruga peruana. Oroya fever is characterized by an acute septicemic phase of severe hemolytic anemia. The chronic form, verruga peruana, is the second phase and is characterized by reddish papular skin lesions that are highly vascular in nature. Verruga peruana is very similar to bacillary angiomatosis which is caused by *B. henselae*. Without appropriate antimicrobial therapy, they may be fatal. In this assay, DNA is extracted from the specimen and subjected to PCR amplification.

Method: Real-Time PCR

Specimen: Whole blood yellow top tube (ACD solution A), ticks

Transport: Stable at room temperature

325 *Bartonella clarridgeiae* by Real-Time PCR

Clinical significance: The genus Bartonella contains aerobic, fastidious, Gram-negative bacteria that belong to the alpha-2 subgroup of the class Proteobacteria. *Bartonella clarridgeiae* is predominantly associated with infection in cats. However, it has been documented as an additional cause of Cat Scratch Disease (CSD) along with *Bartonella henselae*. Transmission from cats to humans has also been documented. In this assay, DNA is extracted from the specimen and subjected to PCR amplification.

Method: Real-Time PCR

Specimen: Whole blood yellow top tube (ACD solution A), ticks

Transport: Stable at room temperature

339 *Bartonella elizabethae* by Real-Time PCR

Clinical significance: The genus Bartonella contains aerobic, fastidious, Gram-negative bacteria that belong to the alpha-2 subgroup of the class Proteobacteria. *Bartonella elizabethae* has been associated with endocarditis. The means of transmission of *B. elizabethae* is unknown, but is believed to be via an arthropod vector. It has been isolated in a human patient and in rats. In this assay, DNA is extracted from the specimen and subjected to PCR amplification.

Method: Real-Time PCR

Specimen: Whole blood yellow top tube (ACD solution A), CSF, ticks

Transport: Stable at room temperature

317 *Bartonella henselae* by Real-Time PCR

Clinical significance: *Bartonella henselae* is the causative agent of Cat Scratch Disease (CSD) as well as other conditions. It is commonly seen in immunocompromised patients, particularly those suffering from HIV infection. The classic clinical presentation of CSD is a self-limiting, regional lymphadenopathy, usually caused by a cat scratch or bite. The disease starts with a lesion at the site of infection, which may become a papule. Transmission of the disease has been linked to cats and is also suspected to occur via fleas and ticks. Recently, *B. henselae* has been detected in immunocompromised patients as well as in *Ixodes scapularis* ticks, the same ticks that transmit Lyme disease. Evidence is mounting that *Bartonella* species are also transmitted from ticks to humans and can contribute to the disease manifestations of Lyme disease. Proper identification is essential such that the necessary treatments are administered. In this assay, DNA is extracted from the specimen and subjected to PCR amplification.

Method: Real-Time PCR

Specimen: Whole blood yellow top tube (ACD solution A), CSF, ticks

Transport: Stable at room temperature

376 *Bartonella henselae* IgG by ELISA

Serum required

Clinical significance: *Bartonella henselae* is the causative agent of cat scratch disease (CSD) as well as other conditions. It is commonly seen in immunocompromised patients, particularly those suffering from HIV infection. The classic clinical presentation of CSD is a self-limiting regional lymphadenopathy, usually caused by a cat scratch or bite. The disease starts with a lesion at the site of infection, which may become a papule. Transmission of the disease has been linked to cats and is also suspected to occur via fleas and ticks. Recently, Bartonella has been detected in immunocompromised patients as well as in *Ixodes scapularis* ticks, the same ticks that transmit Lyme disease. Evidence is mounting that *Bartonella* species are also transmitted from ticks to humans and can contribute to the disease manifestations of Lyme disease. Traditionally, clinical diagnostics have relied on direct culturing and immunofluorescent antibody (IFA) technologies. The culturing of Bartonella from blood samples is technically challenging and is a low-yield procedure with recommended growth conditions including lengthy incubation periods of at least 21 days. *B. henselae* IFAs have high sensitivity and specificity. However, cross-reactivity with other human pathogens has been reported. In addition, IFAs rely heavily on technicians for the determination of test results, are time-consuming to score, and require expensive fluorescent microscopes. Detection of antibodies using an ELISA assay allows diagnosis of an infection when other methods, such as culture or IFA, are impractical or yield negative results. In this assay, patient serum is analyzed by ELISA for the presence of *Bartonella henselae*-specific IgG antibodies.

Method: ELISA

Specimen: Serum

Transport: Stable at room temperature

342 *Bartonella quintana* by Real-Time PCR

Clinical significance: The genus Bartonella contains aerobic, fastidious, Gram-negative bacteria that belong to the alpha-2 subgroup of the class Proteobacteria. *B. quintana* was first identified as an important human pathogen during World War I when it caused epidemics of louse-borne trench fever. *B. quintana* infections were rarely recognized from the end of World War II until the 1980s, when the organism re-emerged as an opportunistic pathogen among HIV-infected persons. It has since been identified in cases of bacillary angiomatosis, endocarditis and bacteremia, isolated from AIDS patients, and, more recently, in homeless populations. In this assay, DNA is extracted from the specimen and subjected to PCR amplification.

Method: Real-Time PCR

Specimen: Whole blood yellow top tube (ACD solution A), CSF, ticks

Transport: Stable at room temperature

356 *Bartonella species (B. henselae, B. quintana)* by Real-Time PCR

Clinical significance: The genus Bartonella contains aerobic, fastidious, Gram-negative bacteria which belong to the alpha-2 subgroup of the class Proteobacteria. MDL has developed a rapid and sensitive PCR-based method for the simultaneous detection and differentiation of *Bartonella* sub-species, *B. henselae* and *B. quintana*, from specimens. In this assay, DNA is extracted from the specimen and subjected to PCR amplification.

Method: Real-Time PCR

Specimen: Whole blood yellow top tube (ACD solution A), CSF, ticks

Transport: Stable at room temperature

453 *Rickettsia akari* (house mouse mite) by Real-Time PCR

Clinical significance: *Rickettsia akari* is the etiologic agent of rickettsialpox. *R. akari* is transmitted by the house mouse mite, *Liponyssoides sanguineus*. When a mite infected with rickettsiae is unable to locate its natural host and is forced to obtain a blood meal from a human host. Because of its minute size, this mite is almost never seen by patients. Symptoms initially present as fever, sweating, headache, and myalgia. One week after a mite bite, a vesicle appears which dries up leaving an eschar. The rash is often papular but can also be vesicular resembling chickenpox, hence the name rickettsialpox. Rickettsialpox was initially described in New York City and has been reported in other US towns and states.

Method: Real-Time PCR

Specimen: Whole blood yellow top tube (ACD solution A)

Transport: Stable at room temperature

455 *Trypanosoma cruzi* (Chagas Disease) by Real-Time PCR

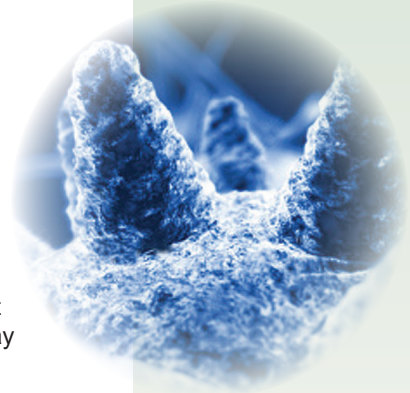
Clinical significance: Chagas Disease is caused by the parasite *Trypanosoma cruzi*, which is transmitted through the bite of an insect vector called the 'kissing bug,' i.e. Triatomine species. The Triatomine bug transmits the *T. cruzi* parasite into the body via the bite wound or the mucous membranes. At these sites, the parasite will start to multiply within host cells until they burst out and enter the bloodstream, subsequently causing intracellular infections at new tissues sites. *T. cruzi* can also be transmitted through blood transfusions, organ transplantation, and transplacentally from the mother to the fetus. Chagas disease manifests in an acute phase and a chronic phase. In the acute phase, which occurs immediately after infection, the parasites can be found circulating in the blood usually causing mild signs and symptoms or can be asymptomatic. Acute phase signs and symptoms, which can last a few weeks or months, include fever or swelling around the primary site of infection of skin or mucous membranes and in rare cases may cause severe inflammation of the heart or brain and meninges. Following the acute phase of infection, people usually fall into a period of asymptomatic chronic infection where the parasite is often undetectable in the blood. Many people are chronically infected without symptoms for life. However, 20 - 30% of these people with chronic infections will develop severe and sometimes life-threatening medical problems such as heart arrhythmia that can lead to sudden death, heart malfunctions, or a dilated esophagus or colon. Immunosuppression can reactivate the *T. cruzi* parasite in the host potentially leading to severe disease. Most infections occur in Central and South America within poor housing conditions. The CDC estimates that there are about 300,000 infected people in the United States, 30,000 to 40,000 with undiagnosed Chagas cardiomyopathy, and 63 to 315 congential *T. cruzi* infections per year. Although Triatomine bugs are usually found in the southern U.S., they have been reported to be migrating north. However, primary *T. cruzi* infections and Chagas Disease is still rare in the U.S. at this point.

Method: Real-Time PCR

Specimen: Whole blood yellow top tube (ACD solution A)

Transport: Stable at room temperature

222 Adenovirus by Real-Time PCR



Clinical significance: Adenoviruses cause a number of self-limiting, but often highly infectious, diseases that affect multiple organs, most commonly those associated with the respiratory and genitourinary tracts. Adenovirus is a relatively harmless pathogen in healthy individuals, but can cause a variety of symptoms in young children and the immunocompromised. Transmission can occur from direct, person-to-person contact or through contact with a contaminated surface or object. Adenovirus infections are usually asymptomatic and may cause a variety of symptoms, including: respiratory problems, gastroenteritis, pink eye, pharyngoconjunctival fever, skin rashes, and genitourinary tract infections including cervicitis, urethritis and hemorrhagic cystitis. The most severe cases of adenovirus infection may result in pneumonia, croup, and bronchitis. In this assay DNA is extracted from the specimen and subjected to PCR amplification.

Method: Real-Time PCR

Specimen: ***UroSwab***®, ***NasoSwab***®, whole blood yellow top tube (ACD solution A)

Transport: Stable at room temperature

434 Colorado Tick Fever virus by Real-Time PCR

Clinical significance: Colorado tick fever is an acute viral infection transmitted from the bite of an infected *Dermacentor andersoni* (wood) tick, and in rare instances by blood transfusion. It is found most commonly in the western United States and Canada, with particular concentration in the mountainous regions of Colorado and Idaho. This disease most commonly develops from March to September, with the highest numbers of infections occurring in May and June. Symptoms start about 3 to 6 days after the tick bite. Symptoms of a two-staged illness present with initial fever for 3 days, resolve, and then return 1 to 3 days later for another few days. Infection can be severe in young children resulting in hospitalization. Possible complications include ascetic meningitis, encephalitis and hemorrhagic fever. In this assay DNA is extracted from the specimen and subjected to PCR amplification.

Method: Real-Time PCR

Specimen: Whole blood yellow top tube (ACD solution A)

Transport: Stable at room temperature

273 Coxsackie virus A & B by Pyrosequencing

Clinical significance: Coxsackieviruses are a part of the Picornaviridae family belonging to the Enterovirus genus. There are two groups of Coxsackieviruses, A and B, differentiated by their effects on mice. Generally, Coxsackie A infects the skin and mucous membranes, causing hand, foot and mouth disease, a common childhood illness. Symptoms associated with hand, foot and mouth disease include: fever, herpangina (blisters in the mouth), and blisters on the palms and fingers of the hand or on the soles of the feet. Acute hemorrhagic conjunctivitis can also be onset from Coxsackie A viral infection. Group B Coxsackie virus causes pleurodynia or Bornholm disease. Symptoms found associated with Coxsackie B virus include fever, headache, sore throat, chest and muscle pain, and gastrointestinal distress. In some instances, Coxsackievirus B may lead to infectious pericarditis or viral myocarditis. Both group A and group B Coxsackieviruses can cause nonspecific febrile illnesses, rashes, upper respiratory tract disease, and aseptic meningitis.

Method: Pyrosequencing

Specimen: ***NasoSwab***®, whole blood yellow top tube (ACD solution A), CSF

Transport: Stable at room temperature

207 Cytomegalovirus (CMV) by Real-Time PCR

Clinical significance: Cytomegalovirus (CMV) infects 50% to 80% of Americans by the age of 40 and is known to cause mild or asymptomatic infection in most healthy individuals. The virus is spread person-to-person through most bodily fluids. Congenital infection, which occurs when an infected mother passes the infection along to the fetus, may result in hearing, vision, neurologic and developmental problems shortly after birth. CMV viral shedding can be detected in the vaginal secretions of infected women. The use of molecular techniques, such as Real-Time PCR, enables the clinician to detect this viral shedding thus enabling diagnosis and treatment prior to delivery. In this assay, DNA is extracted from the specimen and subjected to PCR amplification. Ganciclovir resistance testing by Pyrosequencing is utilized for specimens that test positive for the presence of CMV to detect specific mutations associated with ganciclovir resistance.

Method: Real-Time PCR

Specimen: ***OneSwab***®, ***UroSwab***®, *ThinPrep*®, whole blood yellow top tube (ACD solution A), CSF

Transport: Stable at room temperature

233 Cytomegalovirus (CMV) IgG/IgM by ELISA

Serum required

Clinical significance: CMV is implicated in congenital disease in newborns, transfusion and transplant related infections as well as infections in immunocompromised individuals. CMV is known to cause mild or asymptomatic infection in most healthy individuals but can cause symptomatic infection in immunosuppressed hosts. It is transmitted from person-to-person through contact with a person excreting the virus in their saliva, urine, blood, tears, semen, and breast milk but can also be transmitted through blood transfusions and transplanted organs. Until recently, the detection of CMV in these clinical specimens depended on the detection of early antigen expression, or isolation in conventional cell culture, which may take 2 and 14 days, respectively. This test can be used to determine if acute infection, previous infection, or passively acquired maternal antibody in an infant is present. In this assay, patient serum is analyzed by ELISA for the presence of CMV-specific IgG and IgM antibodies.

Method: ELISA

Specimen: Serum

Transport: Stable at room temperature

270 Dengue viruses 1-4 by Real-Time PCR

Clinical significance: Dengue virus (DV) is an arthropod-borne virus (arbovirus) transmitted by Aedes mosquitoes. There are four closely related, but antigenically distinct, Dengue virus serotypes (DEN 1, DEN 2, DEN 3 and DEN 4). Infection with one of these serotypes provides immunity to only that serotype for life. DV may cause Dengue fever (DF) which usually starts with a high fever, rash, severe headache, pain behind the eyes and muscle and joint pain. A DV infection may also progress to Dengue hemorrhagic fever (DHF) which is fatal in about 5 percent of cases. Important risk factors for DHF include the strain of the infecting virus, as well as the age, and especially the prior dengue infection history of the patient. In the United States, approximately 100 cases of dengue are reported each year in travelers returning from tropical areas. Aedes mosquitoes are found in Texas, Florida and other southern states, and locally acquired dengue has been reported three times since 1980 in southern Texas. There is no treatment or vaccine for dengue. Prevention centers on public health action to control mosquitoes, and on individual action to avoid mosquito bites. A Real-Time polymerase chain reaction (PCR) assay provides a rapid, specific and sensitive approach for detection of this virus.

Method: Real-Time PCR

Specimen: Whole blood yellow top tube (ACD solution A)

Transport: Stable at room temperature

269 Eastern Equine Encephalitis virus by Real-Time PCR

Clinical significance: Eastern Equine Encephalitis virus (EEE) is an arthropod-borne virus (arbovirus) transmitted by mosquitoes. It is found mainly along the eastern seaboard of the United States and on the eastern Gulf coast. EEE can affect the central nervous system and cause severe complications, including death. The symptoms may also include fever, headache, drowsiness, irritability, nausea, and vomiting, followed by confusion, weakness, and coma. Young infants often suffer seizures. Since 1964, there have been 163 confirmed cases in the United States. There is no treatment or vaccine for EEE. Prevention centers on public health action to control mosquitoes, and on individual action to avoid mosquito bites. A Real-Time polymerase chain reaction (PCR) test provides a rapid, specific, and sensitive approach to detection of this virus.

Method: Real-Time PCR

Specimen: Whole blood yellow top tube (ACD solution A)

Transport: Stable at room temperature

231 EBV-EA-D IgG/IgM by ELISA

Serum required

Clinical significance: Antibody to early antigen (EA) appears at approximately the same time as anti-VCA antibody (acute phase) and typically falls to undetectable levels after 3 to 6 months. Detection of anti-EA antibodies is often an indication of active infection. Reactivated infection is suggested by the elevation of EA antibodies in the presence of antibodies to EBNA. However, 20% of healthy people may have detectable anti-EA antibody for several years after initial infection. For this reason, detection of this antibody does not necessarily indicate that a patient's medical condition is caused by EBV. In this assay, patient serum is analyzed by ELISA for the presence of EBV-EA-D-specific IgG and IgM antibodies.

Method: ELISA

Specimen: Serum

Transport: Stable at room temperature

230 EBV-EBNA-1 IgG/IgM by ELISA

Serum required

Clinical significance: Antibody to Epstein-Barr Nuclear Antigen (EBNA) is not present during the acute phase of infection but typically appears 2 to 4 months after onset and may remain detectable throughout a patient's lifetime. The presence of VCA-IgM antibody with the absence of antibody to EBNA after at least 4 weeks of infection is suggestive of primary infection. Past infection (4 to 6 months earlier) is usually determined by the presence of both VCA antibodies and EBNA antibodies. An increase of EA antibodies in the presence of EBNA antibodies is suggestive of reactivation. In this assay, patient serum is analyzed by ELISA for the presence of EBV-EBNA-1-specific IgG and IgM antibodies.

Method: ELISA

Specimen: Serum

Transport: Stable at room temperature

229 EBV-VCA IgG/IgM by ELISA

Serum required

Clinical significance: Antibody to viral capsid antigen (VCA) is the most valuable of the EBV specific antibody tests. IgM-VCA appears early in infection and typically disappears within 4 to 6 weeks. IgG-VCA is produced during the late acute phase, peaks at 2 to 4 weeks after onset of infection, and may persist throughout a patient's lifetime. The presence of VCA-IgM antibody with the absence of antibody to EBNA after at least 4 weeks of infection is suggestive of primary infection. Past infection (4 to 6 months earlier) is usually determined by the presence of both VCA antibodies and EBNA antibodies. Differentiation of the VCA IgG and IgM antibodies is also useful for confirmation when the Monospot test is negative. Susceptibility to EBV infection is also determined by the absence of antibodies to viral capsid antigens. In this assay, patient serum is analyzed by ELISA for the presence of EBV-VCA-specific IgG and IgM antibodies.

Method: ELISA

Specimen: Serum

Transport: Stable at room temperature

205 Epstein-Barr virus (EBV) by Real-Time PCR

Clinical significance: EBV is the causative agent of infectious mononucleosis, which occurs primarily in late adolescence and early adulthood. It is characterized by malaise, fever, hepatosplenomegally, lymphadenopathy, and abdominal discomfort. EBV has also been associated with post-transplant lymphoma, Burkitt's lymphoma, and nasopharyngeal carcinoma. Reactivations of this disease are suspected in chronic fatigue syndrome. EBV is one of the most common human viruses and it is estimated that worldwide as many as 80% to 90% of all adults have at one time been infected. Although it is normally a self-limiting infection, complications can occur, such as splenomegaly, hepatitis, pericarditis, or central nervous system involvement. In certain rare instances, EBV infections may be fatal. In this assay, DNA is extracted from the specimen and subjected to PCR amplification.

Method: Real-Time PCR

Specimen: ***UroSwab***®, whole blood yellow top tube (ACD solution A)

Transport: Stable at room temperature

436 Heartland virus (Phlebovirus) by Real-Time PCR

Clinical significance: On August 30, 2012, a new tick-borne viral pathogen was reported in the New England Journal of Medicine called the Heartland virus. The Heartland virus is a phlebovirus of the Bunyaviridiae family. It is a single-stranded, negative-sense RNA virus. Infection with Phleboviridiae result in diverse pathologies, many associated with fever such as Rift Valley Fever. Although there is no available epidemiologic data, a potential vector may be Amblyoma americanum (the Lone Star tick). The clinical presentation closely resembles infection with Human Granulocytic Anaplasmosis and STFSV including fever, fatigue, thrombocytopenia, and diarrhea. Recognition may be important to differentiate it from infection with Human Granulocytic Anaplasmosis due to the similar clinical presentation. In this assay, DNA is extracted from the specimen and subjected to Real-Time PCR amplification.

Method: Real-Time PCR

Specimen: Whole blood yellow top tube (ACD solution A), tick

Transport: Stable at room temperature

262 Hepatitis A virus (HAV) by Real-Time PCR

Clinical significance: Hepatitis A virus (HAV) is an enterovirus transmitted by the orofecal route. It causes an acute form of hepatitis but does not have a chronic stage and will not cause any permanent damage to the liver. Only three out of four people with HAV have symptoms, which include jaundice, nausea, fatigue, and vomiting. In 1991, the Centers for Disease Control and Prevention (CDC) reported a low mortality rate of 0.004% for the general population. For those aged 50 and over, the rate jumps to 0.0175%. There is no specific treatment for HAV. The best preventions against HAV are the commercially available vaccines, as well as good hygiene and sanitary conditions. In order to facilitate an accurate diagnosis of this disease, a reverse transcriptase-polymerase chain reaction (RT-PCR) test capable of detecting HAV has been developed. In this assay, RNA is extracted from the specimen and subjected to PCR amplification.

Method: Real-Time PCR

Specimen: Whole blood yellow top tube (ACD solution A)

Transport: Stable at room temperature

268 Hepatitis B virus (HBV) Genotyping by Pyrosequencing

Only performed after test #260 is positive.
Charges will be the total of tests #260 + #268.

Clinical significance: The Hepatitis B virus is the most common cause of serious liver infection. The virus is transmitted through blood and infected bodily fluids. 90% of healthy adults will develop antibodies against the virus and recover. Unfortunately, 90% of babies, and 50% of young children are unable to get rid of the virus and may become chronically infected. Chronic Hepatitis B infection can lead to cirrhosis or liver cancer. Despite the availability of anti-HBV drugs, it has become increasingly difficult to effectively treat patients due to the development of drug resistant strains. Drug resistance arises from mutations in the viral genome, specifically in the regions that encode the molecular targets of therapy. These mutations alter the viral enzymes in such a way that the enzyme's function is no longer inhibited by a drug, leaving the virus to replicate freely. The SeqHepB system has identified novel mutations in HBV associated with resistance to individual drugs. Genetic sequencing of the Reverse Transcriptase (RT) region can identify each of these mutations and thereby help determine a drug's effectiveness.

Method: Pyrosequencing

Specimen: Whole blood yellow top tube (ACD solution A)

Transport: Stable at room temperature

267 Hepatitis B virus (HBV) Subtyping by Pyrosequencing

Clinical significance: The Hepatitis B virus is the most common cause of serious liver infection. The virus is transmitted through blood and infected bodily fluids. Ninety percent of healthy adults will develop antibodies against the virus and recover. Unfortunately, 90% of babies, and 50% of young children are unable to get rid of the virus and may become chronically infected. Chronic Hepatitis B infection can lead to cirrhosis or liver cancer. Determining which subtype of HBV a patient has may help predict disease progression and/or a patient's response to anti-viral therapy. In this assay, DNA is extracted from the specimen and subjected to PCR amplification.

Method: Pyrosequencing

Specimen: Whole blood yellow top tube (ACD solution A)

Transport: Stable at room temperature

260 Hepatitis B virus (HBV) viral load by Real-Time PCR

Clinical significance: Hepatitis B virus (HBV) is implicated in hepatocellular carcinoma and cirrhosis. HBV infections represent a major public health problem because of the ability of HBV to cause a chronic carrier state. The spectrum of infection can range from a primary, self-limiting infection that resolves, to a persistent, chronic infection that may remain throughout a person's lifetime. Current diagnostic methods rely on serum HBV antigen or direct visualization of the virus in serum by electron microscopy. These techniques, however, lack the sensitivity to detect low levels of viremia. The Real-Time PCR amplification method is used to detect HBV in serum/plasma with a marked increase in sensitivity. Real-Time PCR is an ultra sensitive assay that utilizes intermolecular controls, which coincide with the tested specimen. Quantifying the presence of HBV aids the clinician in patient stratification and therapeutic monitoring. A positive result should be considered in conjunction with clinical presentation and additional established clinical tests. In this assay, DNA is extracted from the specimen and subjected to PCR amplification.

Method: Real-Time PCR

Specimen: Whole blood yellow top tube (ACD solution A)

Transport: Stable at room temperature

252 Hepatitis C virus (HCV) Subtyping by Pyrosequencing

Only performed after test #250 is positive.
Charges will be the total of tests #250 + #252.

Clinical significance: Hepatitis C virus (HCV) causes liver disease and is passed through contact with infected blood or blood products. HCV is the leading cause of cirrhosis, increased risk of hepatic cancer, and the most common reason for liver transplants in the United States. HCV pyrosequencing is useful in determining the genotype of a patient sample. Determination of the viral genotype serves as a useful prognosticator of both the interferon response and disease progression, information which in turn aids the physician in determining the most suitable and efficacious treatment method. In this assay, RNA is extracted from the specimen and subjected to reverse transcriptase PCR amplification followed by Pyrosequencing to determine subtype.

Method: Pyrosequencing

Specimen: Whole blood yellow top tube (ACD solution A)

Transport: Stable at room temperature

250 Hepatitis C virus (HCV) viral load by Real-Time PCR

Clinical significance: Hepatitis C virus (HCV) causes liver disease and is passed through contact with infected blood or blood products. HCV is the leading cause of cirrhosis, increased risk of hepatic cancer, and the most common reason for liver transplants in the United States. This assay is useful in determining the viral load of a patient sample, which can assist clinicians by serving as both a confirmatory assay following a positive result in a first-tier assay and a means to monitor the suitability and length of antiviral HCV drug treatment. In this assay, RNA is extracted from the specimen and subjected to reverse transcriptase PCR amplification.

Method: Real-Time PCR

Specimen: Whole blood yellow top tube (ACD solution A)

Transport: Stable at room temperature

261 Hepatitis G virus (HGV) by Real-Time PCR

Clinical significance: Hepatitis G virus (HGV) has been identified recently as a possible causative agent for non-A, non-B and non-C hepatitis. HGV is related to the Hepatitis C virus (HCV). Like HCV, it is transmissible by blood transfusion and has a tendency to develop a chronic carrier state. Initially, several studies reported that HGV is associated with acute, chronic non-A-E hepatitis, fulminant hepatitis, and aplastic anemia. Recently, its clinical significance in cases of human hepatitis in adults has become increasingly controversial. In this assay, RNA is extracted from the specimen and subjected to reverse transcriptase PCR amplification.

Method: Real-Time PCR

Specimen: Whole blood yellow top tube (ACD solution A)

Transport: Stable at room temperature

257 Herpes simplex virus 1 (HSV-1) IgG by ELISA

Serum required

Clinical significance: HSV-1 classically presents as herpes gingivostomatitis, an infection of the oral mucosa. It can also cause conjunctivitis, keratitis, and herpetic whitlow. Almost all recurrent cold sores or fever blisters are due to HSV-1. However, genital herpes also can be caused by HSV-1. HSV has been isolated from virtually all visceral or mucocutaneous sites. HSV infections can affect the central nervous system causing aseptic meningitis, HSV encephalitis, and autonomic radiculopathy. Visceral HSV infections include esophagitis, pneumonitis, and disseminated infection. Definitive diagnosis of herpes infections is fundamental to the management of patients and the development of strategies to prevent transmission to partners and neonates. Detection of antibodies allows diagnosis of an infection when other methods such as culture or antigen detection are impractical or yield negative results. In this assay, patient serum is analyzed by ELISA for the presence of HSV-1-specific IgG antibodies.

Method: ELISA

Specimen: Serum

Transport: Stable at room temperature

258 Herpes simplex virus 2 (HSV-2) IgG by ELISA

Serum required

Clinical significance: The most painful and annoying recurrent genital herpes cases are due to HSV-2. It can also cause conjunctivitis, keratitis, herpetic whitlow and herpes gingivostomatitis, an infection of the oral mucosa. HSV has been isolated from virtually all visceral or mucocutaneous sites. HSV infections can affect the central nervous system causing aseptic meningitis, HSV encephalitis, and autonomic radiculopathy. Visceral HSV infections include esophagitis, pneumonitis and disseminated infection. Definitive diagnosis of herpes infections is fundamental to the management of patients and the development of strategies to prevent transmission to partners and neonates. Detection of antibodies allows diagnosis of an infection when other methods, such as culture or antigen detection, are impractical or yield negative results. In this assay, patient serum is analyzed by ELISA for the presence of HSV-2-specific IgG antibodies.

Method: ELISA

Specimen: Serum

Transport: Stable at room temperature

126 Herpes subtype (HSV-1 & HSV-2) by Real-Time PCR

When sampling a crusted over lesion, moisten the swab with sterile saline solution prior to swabbing.

Clinical significance: HSV infections are epidemic in the United States. Genital herpes is the most common cause of genital ulcer disease in the developed world. HSV-2 is the most common cause of genital ulcers in the United States and is the cause of more than 90% of recurrent disease. Most painful and annoying recurrent genital herpes is due to HSV-2 and almost all recurrent cold sores or fever blisters are due to HSV-1. HSV-1 classically presents as herpes gingivostomatitis, an infection of the oral mucosa. It can also cause conjunctivitis, keratitis, and herpetic whitlow. However, genital herpes also can be caused by HSV-1. It has been documented that as many as one third of herpes infections are due to HSV-1, particularly in adolescents and young adults. This type of genital herpes is much less frequently recurrent and each recurrence usually lasts only a few days. The main application for HSV subtyping is with regard to the clinical issue of recurrent infection. Although antigen detection systems for HSV can be specific and sensitive when applied to the evaluation of clinical genital lesions, the titer of HSV present during asymptomatic reactivations is 10- to 100-fold less than the titer present during symptomatic episodes. Therefore, methods based on the detection of viral proteins in such cases are less sensitive than DNA amplification assays. In this assay, DNA is extracted from the specimen and subjected to PCR amplification.

Method: Real-Time PCR

Specimen: ***OneSwab***®, whole blood yellow top tube (ACD solution A)

Transport: Stable at room temperature

238 Human herpes virus 6 (HHV-6) IgG by ELISA

Serum required

Clinical significance: Human herpes virus 6 (HHV-6) is a member of the Herpesviridae family. HHV-6 isolates are classified into two variants, A and B. Although the two variants are very closely related, they have distinct differences in immunologic, biologic, epidemiologic, and molecular properties. Studies indicate that HHV-6 infects nearly all humans by 2 years of age, causing mild disease that often resolves on its own. However, HHV-6 reactivation or new infections within immunocompromised populations, particularly HIV positive individuals and organ transplant recipients, are now viewed as common opportunistic infections that could result in organ rejection or death. More recently, a link has been made between HHV-6 and the pathogenesis of Multiple Sclerosis (MS). As a result, HHV-6 is now deemed an emerging pathogen. Serological testing, although incapable of differentiating among the viral variants, serves as a useful clinical tool for the monitoring of at-risk populations. In this assay, patient serum is analyzed by ELISA for the presence of HHV-6-specific IgG antibodies.

Method: ELISA

Specimen: Serum

Transport: Stable at room temperature

219 Human herpes virus 6 (variant A and B) by Real-Time PCR

Clinical significance: Human herpes virus 6 (HHV-6) is a member of the Herpesviridae family. HHV-6 isolates are classified into two variants, A and B. Although the two variants are very closely related, they have distinct differences in immunologic, biologic, epidemiologic, and molecular properties. HHV-6 variant B is the causative agent of the common childhood illness Roseola and, more recently, has also been associated with Multiple Sclerosis (MS) and other neurological disorders. Variant A is implicated in patients suffering from mononucleosis, HIV and organ transplant recipients. A subset of individuals with chronic fatigue syndrome exhibit HHV-6 variant A infection. In this assay, DNA is extracted from the specimen and subjected to PCR amplification.

Method: Real-Time PCR

Specimen: Whole blood yellow top tube (ACD solution A), CSF

Transport: Stable at room temperature

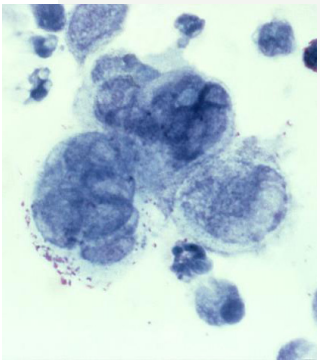
263 Human herpes virus 7 (HHV-7) by Real-Time PCR

Clinical significance: Human herpes virus 7 (HHV-7) is a member of the T-lymphotropic beta herpesviruses and is closely related to HHV-6 and Cytomegalovirus (CMV). Roseola infantum occurs within infant and young children populations as a result of primary infection. Infections typically last approximately six days and are typified by a rash on the neck and trunk, mild upper respiratory infection and swollen glands. A common infection, typically occurring in 95% of the population by the age of five, HHV-7 lies in a latent state, reemerging when the host immune system is compromised. Reemergence levels have been reported to be as high as 45% in liver transplant recipients and elevated in bone marrow transplant recipients. A report by Osman et al. in 1996 revealed active HHV-7 infections correlated with increased risk of developing CMV disease, evidence that is further bolstered by the study that linked HHV-6 and HHV-7 reactivation within transplant recipients through their interaction with CMV. Clinical manifestations of reactivated virus have only been linked with the development of encephalitis in bone marrow transplant recipients and with hepatitis in liver transplant recipients. Due to the high prevalence of infection, serological testing is not a useful means of determining reactivation status. Viral culturing is discouraged due to the length of time required for completion of the procedure, which increases the likelihood of a possible HHV-7-mediated CMV reactivation. Real-Time PCR assays are considered to be the most appropriate diagnostic tool as it is a fast and reliable method that can also serve as a means of determining viral load. In this assay, DNA is extracted from the specimen and subjected to PCR amplification.

Method: Real-Time PCR

Specimen: Whole blood yellow top tube (ACD solution A)

Transport: Stable at room temperature



221 Human herpes virus 8 (HHV-8) by Real-Time PCR

Clinical significance: Human herpes virus 8 (HHV-8), also known as Kaposi's Sarcoma-associated Herpes virus (KSHV), is the most recently discovered human tumor virus. Virtually all Kaposi's sarcoma lesions are HHV-8 positive. It is associated with HIV infection, immunosuppressed patients, as well as endemic Kaposi's sarcoma areas in Africa, Eastern Europe, and the Mediterranean basin. HHV-8 encodes genes that can modulate cellular growth properties and possibly play a role in disease progression. In this assay, DNA is extracted from the specimen and subjected to PCR amplification.

Method: Real-Time PCR

Specimen: Whole blood yellow top tube (ACD solution A)

Transport: Stable at room temperature

203 Human T-lymphotropic virus-I (HTLV-I) by Real-Time PCR

Clinical significance: HTLV was the first human oncogenic retrovirus to be identified. It is the causative agent of adult T-cell leukemia-lymphoma and tropical spastic paraparesis, or HTLV-I associated myelopathy (HAM/TSP). HTLV infection is endemic to the islands of southwestern Japan, the Caribbean basin, including the West Indies, northern South America, the southeastern US, Central and west Africa, Melanesia, the Middle East, and India. HTLV is thought to be transmitted sexually, through contact with blood, vertically from mothers to their fetus, and through breast milk. Available evidence indicates that infection is probably life long and asymptomatic in most individuals. The HTLV viruses potentiate and activate the expression of HIV *in vitro* and in human populations and may accelerate disease progression. In this assay, RNA is extracted from the specimen and subjected to reverse transcriptase PCR amplification.

Method: Real-Time PCR

Specimen: Whole blood yellow top tube (ACD solution A)

Transport: Stable at room temperature

266 La Crosse Encephalitis virus by Real-Time PCR

Clinical significance: La Crosse virus (LAC) is the causative agent of La Crosse encephalitis. This vector-borne disease is transmitted through the bite of an infected *Aedes triseriatus* tree hole mosquito. Laboratory confirmed cases of La Crosse virus occur with decreasing frequencies from North to South and the vast majority of infections occur within the eastern half of the United States. LAC is traditionally active in the upper Midwest and Great Lakes areas; however, in recent years there has been an increase in frequency in the Mid-Atlantic States. Most LAC infections are subclinical; however, when symptoms are evident, the onset is abrupt. LAC virus produces an acute encephalitis that begins with a mild fever and illness lasting on average 1 to 3 days and sometimes persisting for up to one week. Patients typically present with fever, chills, abdominal pain, and headache with or without photophobia. One can also experience upper respiratory symptoms with or without sore throat as well as cough. More serious illness can occur, characterized by vomiting, nuchal rigidity, lethargy and coma. In this assay, RNA is extracted from the specimen and subjected to reverse transcriptase PCR amplification.

Method: Real-Time PCR

Specimen: Whole blood yellow top tube (ACD solution A)

Transport: Stable at room temperature

223 Parvovirus by Real-Time PCR

Clinical significance: Human Parvovirus B19, first recognized in 1975, causes a variety of disease syndromes determined by the age and hematological status of the host. In healthy individuals, it causes erythema infectiosum, also known as fifth disease. In women, in particular, the rash illness is accompanied by arthritis. In subjects with hemolytic anemia, a more profound anemic episode occurs, with transient loss of erythrocyte precursors from the bone marrow. It is commonly associated with immunocompromised individuals. B19 infection should be considered as part of the differential diagnosis in any patient presenting with an acute polyarthritis. In contrast to rheumatoid arthritis, B19 infection is not associated with joint destruction. However, differentiation between early rheumatoid arthritis and B19 arthropathy is important because the immunosuppressive therapy prescribed for rheumatoid arthritis is not indicated in Parvovirus B19 infection. In this assay, DNA is extracted from the specimen and subjected to PCR amplification.

Method: Real-Time PCR

Specimen: Whole blood yellow top tube (ACD solution A)

Transport: Stable at room temperature

138 Polyomavirus BK by Real-Time PCR

Clinical significance: Polyomavirus BK is a member of the Papovavirus family and infects up to 90% of the general population. After primary infection, which generally occurs in childhood without evident symptoms, the virus can remain latent in the urinary tract. Reactivation can be enhanced by immunosuppressive conditions, leading to overt clinical disease. Renal allograft recipients are particularly sensitive to reactivation as Polyomavirus BK has been implicated widely in dysfunction of the allograft. In this assay, DNA is extracted from the specimen and subjected to PCR amplification.

Method: Real-Time PCR

Specimen: ***UroSwab***®, whole blood yellow top tube (ACD solution A)

Transport: Stable at room temperature

139 Polyomavirus JC by Real-Time PCR

Clinical significance: Polyomavirus JC is a double-stranded DNA virus belonging to the Papovavirus family. It is estimated that 60% to 80% of adults in Europe and the United States have antibodies to JC virus, suggesting infectivity rates are quite high. It is proposed that JC virus establishes a latent infection in the kidney after a primary infection. JC virus has been linked to the development of hemorrhagic cystitis, ureteral stenosis and allograft dysfunction in renal transplant recipients. It is also believed to be the primary causative agent of both nephropathies after transplantation and progressive multifocal leukoencephalopathy. In this assay, DNA is extracted from the specimen and subjected to PCR amplification.

Method: Real-Time PCR

Specimen: ***UroSwab***®, whole blood yellow top tube (ACD solution A), biopsy (fresh), biopsy (paraffin),

Transport: Stable at room temperature

264 St. Louis Encephalitis virus by Real-Time PCR

Clinical significance: St. Louis Encephalitis virus (SLE) is a flavivirus capable of inducing aseptic meningitis or encephalitis in infected individuals. Transmission is via a bite from an infected mosquito and can occur anywhere within the continental United States, although the CDC reports the highest prevalence in Indiana, Illinois, Mississippi, Ohio and Texas. The incubation period is typically from five to fifteen days. Symptoms range from mild, limited to fever and headache, to severe, marked by headache, high fever, disorientation, stupor, neck stiffness and occasional convulsion and paralysis. Hospitalization for CNS infection occurs for 95% of recognized cases with a reported 3% to 30% mortality rate. There is no specific treatment for SLE and no available vaccine. In this assay, RNA is extracted from the patient specimen and subjected to PCR amplification.

Method: Real-Time PCR

Specimen: Whole blood yellow top tube (ACD solution A)

Transport: Stable at room temperature

215 Varicella-zoster virus (VZV) by Real-Time PCR

When sampling a crusted over lesion, moisten the swab with sterile saline solution prior to swabbing.

Clinical significance: Varicella-Zoster Virus (VZV), also known as HHV3, is a member of the neurotrophic alpha herpesvirus family, which is considered to be the most infectious of the human herpes viruses. The alpha herpesviruses' possess factors that increase their infectivity, including short reproductive cycles, the ability to replicate in multiple cell types and the ability to induce high levels of host cell tissue destruction quite rapidly. Humans serve as the alpha herpesviruses' only natural reservoir, which means transmission is person-to-person through either the aerosolization of virus in nasopharyngeal secretions or more directly by contact with vesicle fluids or respiratory secretions. Primary infections result in chickenpox and 95% occur during childhood. Presenting symptoms include rash, low-grade fever, headaches and malaise. Patients with chickenpox remain infective until the last skin lesion has dried and crusted over. Those who are infected during adulthood experience a greater number of complications and account for nearly half of all chickenpox-related deaths. Neonates and pregnant women are particularly susceptible to severe primary VZV infections. Complications associated with VZV infection include bacterial superinfections of the skin and lower respiratory tract. Diagnosis is typically based on clinical presentation, but in some instances, particularly immunocompromised individuals, clinical evaluation is necessary. Because VZV is capable of establishing a latent state within the sensory ganglia, infection is life-long and viral reactivation in the form of shingles or Ramsay Hunt Syndrome is possible at any age. Shingles occur in approximately 20% of the adult population at least once in their lives, with 1% experiencing multiple reactivations. Vaccination with the live attenuated Oka strain of VZV, Varivax, is available and recommended for adults over the age of sixty for the prevention of shingles. In this assay, DNA is extracted from the specimen and subjected to PCR amplification.

Method: Real-Time PCR

Specimen: ***OneSwab***®, ***UroSwab***®, whole blood yellow top tube (ACD solution A), CSF

Transport: Stable at room temperature

243 West Nile virus by Real-Time PCR

Clinical significance: West Nile virus (WNV) is spread most often by infected mosquitoes. In 1999, the CDC reported that there were 62 human cases of WNV infection in New York State. Since then, this flavivirus has rapidly spread throughout the continental United States. Although about 80% of infected people show no symptoms upon infection, the remaining 20% exhibit mild symptoms such as fever, headache, body aches, nausea and vomiting. Symptoms typically present 3 to 14 days post infection. In about 1 out of 150 infected people, symptoms are much more severe and range from high fever, neck stiffness, stupor and disorientation to coma, tremors, convulsions, muscle weakness, vision loss, numbness, and even paralysis. Real-Time PCR is most successful for detection when utilized immediately after infection. Subsequently, serological assays are available to determine exposure to WNV.

Method: Real-Time PCR

Specimen: Whole blood yellow top tube (ACD solution A), biopsy (fresh), biopsy (paraffin), CSF

Transport: Stable at room temperature

244 West Nile virus IgG/IgM by ELISA

Serum required

Clinical significance: Diagnosis of WNV infection relies on high clinical suspicion. Virus isolation is rarely a viable option because this technique is laborious, time-consuming, and requires expensive facilities. The IgM antibody-capture enzyme-linked immunosorbent assay (ELISA) is currently the most efficient diagnostic method. MDL has developed a convenient and specific serology test for the detection of antibodies against WNV; this ELISA-based assay represents an advancement over currently available diagnostic tests because it is designed to eliminate antigenic cross-reactivity with other flaviviruses.

Method: ELISA

Specimen: Serum

Transport: Stable at room temperature

265 Western Equine Encephalitis virus by Real-Time PCR

Clinical significance: Western Equine Encephalitis virus is a mosquito-transmitted disease that affects both humans and horses. A member of the Togoviridae family, it is one of several mosquito-borne viruses that induce serious, sometimes fatal, infections that affect the central nervous system. Symptoms range from mild, with few or no overt symptoms, to severe and possibly fatal and may take five to ten days to manifest following a mosquito bite. The more severe cases can be distinguished from the less severe by the presence of a high fever with sudden onset, drowsiness, nausea, vomiting and irritability that is followed by weakness, confusion and coma. Infections in young infants often present with seizures. While there is no specific treatment, medical intervention is necessary to limit complications, which include brain damage in 13% of cases and are fatal in 3% of persons exhibiting severe symptoms. Seasonality within the United States is primarily during June and July. Prevention consists of limiting exposure to mosquitoes, covering exposed flesh and the use of insect repellents. In this assay, DNA is extracted from the patient specimen and subjected to PCR amplification.

Method: Real-Time PCR

Specimen: Whole blood yellow top tube (ACD solution A)

Transport: Stable at room temperature

1301 Liquid Pap

Clinical significance: Pap testing is valuable for the early detection and prevention of cervical cancer. Traditional Pap smear techniques involve collecting cells from the cervix and smearing them onto a glass slide followed by microscopic examination by a laboratory professional to look for abnormal cells. Liquid-based Pap test technology involves placing cervical samples into a vial of liquid preservative. The liquid in the vial preserves the delicate cell detail and eliminates issues of the conventional pap smear such as drying and clumping of cells during the action of "smearing" the cervical cells onto a glass slide. Advantages of this liquid–based technology include preservation of the cells with minimal interference due to cell overlap or the presence of blood, mucus, and inflammation. Therefore cervical cytology is enhanced as epithelial cells, diagnostically relevant cells, and infectious organisms are more clearly visible resulting in a reduction of unsatisfactory slides.

Method: Cervical Cytology

Specimen: *ThinPrep*®

Transport: Stable at room temperature

1401 Biopsy (H&E Stain)

Clinical significance: Hematoxylin and eosin (H&E) stains are essential for recognizing various tissue types and the morphologic changes that form the basis of contemporary cancer diagnosis. It works well with a variety of fixatives and displays a broad range of cytoplasmic, nuclear, and extracellular matrix features. It is the most universal and traditional method for the examination of formalin-fixed tissue sections of all tissues.

Method: Histology

Specimen: Tissue in buffered formalin

Transport: Stable at room temperature

1222 *BRCA1/2*: Ashkenazi Jewish 3-site Mutation Analysis

Clinical significance: Breast cancer is the second most common newly diagnosed cancer and second leading cause of cancer death among women in the United States. The American Cancer Society's estimate for the United States is about 231,840 new cases of women breast cancer in 2015. Based upon today's statistical model, about 7 out of 100 women (or 7%) will get breast cancer by age 70 and about 1 out of 100 women (or 1%) will get ovarian cancer by age 70. For women who have mutations in their BRCA1 and/or BRCA2 genes, the risk for early breast and ovarian cancer is greatly increased: their life-time risk can reach up to 65%-80% for breast cancer and 45%-56% for ovarian cancer by the age of 70. Approximately one in 400 to 800 individuals in the general population may carry a pathogenic germline mutation in their BRCA1 or BRCA2 genes. The prevalence of the BRCA1/2 mutations in the Ashkenazi Jewish population is higher (one in 40 individuals), and are mostly presented as the following three founder-specific mutations: 187delAG, 5385insC and 6174delT. Cancer epidemiological studies have reported that 78%-96% of Ashkenazi Jews with detectable mutations carry one of these founder mutations. Based on the National Comprehensive Cancer Network (NCCN) Guidelines Version 2.2014 for Hereditary Breast and/or Ovarian Cancer Testing, testing for Ashkenazi Jewish founder-specific mutation(s) should be performed first. Full sequencing may be considered if ancestry also includes non-Ashkenazi Jewish relatives or other hereditary breast and/or ovarian cancer syndrome criteria has been met.

Method:	Next Generation Sequencing, MLPA, DNA sequencing
Specimen:	Saliva, whole blood yellow top tube (ACD solution A)
Transport:	Stable at room temperature
Turnaround Time:	Following typical billing authorization, 14-21 days.

1236 *BRCA1/2*: Ashkenazi Jewish 3-site Mutation Analysis (Reflex to Breast Cancer High Risk Extended Panel Plus)

If the Ashkenazi Jewish 3-site Mutation Analysis is negative, reflex to 1235.

Clinical significance: The Ashkenazi Jewish population has been found to have two particular "founder mutation" variants in the BRCA1 gene (185delAG and 5382insC) and one founder mutation in the BRCA2 gene (6174delT). Cancer epidemiological studies have reported that 78% to 96% of Ashkenazi Jews with detectable variants carry one of these. Sanger DNA sequencing is performed to analyze these specific genetic locations. For a description of all genes identified in this panel, please refer to the Hereditary Breast and Ovarian Cancer (HBOC) syndrome Technical Bulletin.

Method:	Next Generation Sequencing
Specimen:	Saliva, whole blood yellow top tube (ACD solution A)
Transport:	Stable at room temperature
Turnaround Time:	Following typical billing authorization, 14-21 days.

1224 Specific Site Analysis: *BRCA1* and *BRCA2*

Clinical significance: Breast cancer is the second most common newly diagnosed cancer and second leading cause of cancer death among women in the United States. The American Cancer Society's estimate for the United States is about 231,840 new cases of women breast cancer in 2015. Based upon today's statistical model, about 7 out of 100 women (or 7%) will get breast cancer by age 70 and about 1 out of 100 women (or 1%) will get ovarian cancer by age 70. For women who have mutations in their BRCA1 and/or BRCA2 genes, the risk for early breast and ovarian cancer is greatly increased: their life-time risk can reach up to 65%-80% for breast cancer and 45%-56% for ovarian cancer by the age of 70. Approximately one in 400 to 800 individuals in the general population may carry a pathogenic germline mutation in their BRCA1 or BRCA2 genes. For known familial BRCA1 and BRCA2 mutations, MDL performs targeted DNA sequencing detection for a specified BRCA1 and/or BRCA2 variants (based on the family BRCA testing results).

Method:	Next Generation Sequencing, MLPA, DNA sequencing
Specimen:	Saliva, whole blood yellow top tube (ACD solution A)
Transport:	Stable at room temperature
Turnaround Time:	Following typical billing authorization, 14-21 days.

1279 Lynch Syndrome Gene Panel: 5 Genes (EPCAM, MLH1, MSH2, MSH6, PMS2) by Gene Sequencing with Deletion/Duplication Analysis

Clinical significance: Lynch syndrome is a tumor predisposition syndrome characterized by an increased risk of developing colorectal, ovarian, uterine, and other cancers. This test detects genes associated with a hereditary predisposition to Lynch syndrome.

Method:	Gene Sequencing with Deletion/Duplication Analysis
Specimen:	Saliva, whole blood yellow top (ACD solution A)
Transport:	Stable at room temperature
Turnaround Time:	Following typical billing authorization, 14-21 days.

2600 Breast Cancer High Risk Extended Panel Plus: 15 genes (BRCA1, BRCA2, CDH1, PTEN, TP53, STK11, ATM, CHEK2, PALB2, BARD1, BRIP1, RAD51C, RAD51D, NF1, NBN) by Gene Sequencing with BRCA1/2 Deletion/Duplication Analysis

Clinical significance: The most common hereditary cause of breast cancer is Hereditary Breast and Ovarian Cancer (HBOC) syndrome, which is caused by a germline variation in the genes BRCA1 and BRCA2. The diagnosis of HBOC is suspected in families with early-onset breast cancer, certain ethnic backgrounds (e.g. Ashkenazi Jewish), male breast cancer, and multiple family cases of breast, ovarian, prostate or pancreatic cancers. Other hereditary cancer syndromes associated with certain gene variants also increase the risk for developing breast, ovarian and other cancers. Variants in the BRCA1, BRCA2, PTEN, and TP53 genes are associated with a lifetime breast cancer risk of 40% to 85%. Variants in the ATM, CHEK2, CDH1, PALB2 and other genes are associated with a lifetime breast cancer risk of 20% to 40%. Panel testing of high risk genes may have greater sensitivity in identifying patients with potentially pathogenic genetic variants and greater efficiency in the evaluation of hereditary cancer syndromes. An accurate and comprehensive family history of cancer is essential for the identification of patients with a risk for hereditary breast and ovarian cancer and should include a three generation family history with information on both maternal and paternal lineages.

Method:	Next Generation Sequencing
Specimen:	Saliva, whole blood yellow top tube (ACD solution A)
Transport:	Stable at room temperature
Turnaround Time:	Following typical billing authorization, 14-21 days.

2601 BRCAcare 1/2 Comprehensive BRCA Analysis by Gene Sequencing with Deletion / Duplication Analysis

Clinical significance: The most common hereditary cause of breast cancer is Hereditary Breast and Ovarian Cancer (HBOC) syndrome, which is caused by a germline variation in the genes BRCA1 and BRCA2. The diagnosis of HBOC is suspected in families with early-onset breast cancer, certain ethnic backgrounds (e.g. Ashkenazi Jewish), male breast cancer, and multiple family cases of breast, ovarian, prostate or pancreatic cancers. Other hereditary cancer syndromes associated with certain gene variants also increase the risk for developing breast, ovarian and other cancers. Variants in the BRCA1, BRCA2, PTEN, and TP53 genes are associated with a lifetime breast cancer risk of 40% to 85%. Variants in the ATM, CHEK2, CDH1, PALB2 and other genes are associated with a lifetime breast cancer risk of 20% to 40%. Panel testing of high risk genes may have greater sensitivity in identifying patients with potentially pathogenic genetic variants and greater efficiency in the evaluation of hereditary cancer syndromes. An accurate and comprehensive family history of cancer is essential for the identification of patients with a risk for hereditary breast and ovarian cancer and should include a three generation family history with information on both maternal and paternal lineages.

Method:	Next Generation Sequencing
Specimen:	Saliva, whole blood yellow top tube (ACD solution A)
Transport:	Stable at room temperature
Turnaround Time:	Following typical billing authorization, 14-21 days.

1267 Long QT Syndrome by Next Generation Sequencing (KCNQ1, KCNH2, SCN5A, KCNE1, KCNE2, KCNJ2, CACNA1C, CAV3, SCN4B, AKAP9, SNTA1, ANK2, CALM1, CALM2, KCNJ5)

Clinical significance: Long QT Syndrome (LQTS) is a cardiac disorder resulting from abnormal ion-channel functions leading to prolonged repolarization of cardiac muscle characterized by long QT interval and T-wave abnormalities on the electrocardiogram (ECG) and the ventricular tachycardia *torsade de pointes* (TdP). The most common symptom in individuals with LQTS is unexpected fainting (syncope). The panel includes 15 genes that are definitively associated with LQTS or other inherited arrhythmia disorders that may present with clinical features similar to LQTS. Many of these genes code for ion channel proteins of the heart muscle that help regulate the movement of sodium, potassium and calcium ions in and out of cardiac cells, as well as their associated regulatory factors and interacting proteins.

Method: Next Generation Sequencing

Specimen: Whole blood yellow top (ACD solution A)

Transport: Stable at room temperature

Turnaround Time: 5-10 days

1263 Thrombophilia Panel

1264 Factor II (F2 20210 G>A)
1265 Factor V Leiden (F5 1601 G>A)
1266 MTHFR Mutations (MTHFR 677 C>T, MTHFR 1298 A>C)

Clinical significance: The Thrombophilia Panel analyzes genes that are associated with an increased risk for the development of venous thromboembolism (VTE). Individuals who have inherited a pathogenic variant in one of these genes have a predisposition to excessive blood clot formation. However, not all patients with a genetic predisposition to thrombosis will develop VTE. The presence of inherited thrombophilia may interact with other VTE risk factors to determine a patient's VTE risk. It can be helpful to identify individuals who have a genetic predisposition to blood clots in order to establish or confirm a diagnosis, help predict risk of future thrombotic events, or guide treatment and management decisions.

Method: Next Generation Sequencing

Specimen: Whole blood yellow top (ACD solution A)

Transport: Stable at room temperature

Turnaround Time: 5-10 days

1231 Cystic Fibrosis Core Test by Sanger Sequencing

23 major CFTR mutations approved by ACOG/ACMG

Clinical significance: Cystic Fibrosis (CF) is an autosomal recessive inheritable disease that afflicts approximately 30,000 people within the United States and 70,000 worldwide, with 1,000 new cases diagnosed each year. Due to its recessive inheritable pattern, people may be carriers of the disease, having inherited a defective gene but not exhibiting symptoms. It is estimated that an additional ten million, or one in every thirty-one Americans, are carriers. Carrier status occurs more frequently within Ashkenazi Jewish and Caucasians of European descent populations, each of which has a one in twenty-nine carrier risk rate. The defective gene responsible for CF was identified in 1989 as the Cystic Fibrosis Transmembrane Conductance Regulator (CFTR) gene. The CFTR protein serves as a chloride channel within epithelial cells; disruption of its function induces an electrolyte imbalance that results in excess sodium chloride levels in sweat, a hallmark and diagnostic indicator of disease, and is believed to cause the thickening of fluids in the lungs and digestive tract. Since its discovery, more than 1,500 mutations have been defined within the CFTR gene. Both the American College of Obstetricians and Gynecologists (ACOG) and the American College of Medical Genetics (ACMG) have developed guidelines for genetic testing to include twenty-three of the most common CFTR mutations. The MDL Cystic Fibrosis Core Test is a next generation sequencing (NGS)-based CFTR gene analysis screen for the 23 major mutations recommended by the American College of Obstetricians and Gynecologists (ACOG) and the American College of Medical Genetics (ACMG) for Cystic Fibrosis screening. The complete list of mutations analyzed consists of: ΔF508, ΔI507, A455E, G85E, G542X, G551D, N1303K, R117H, R334W, R347P, R553X, R560T, R1162X, W1282X, 621+1G>T, 711+1G>T, 1717-1G>A, 1898+1G>A, 2184delA, 2789+5G>A, 3120+1G>A, 33659delC, and 849+10kbC>T. When a mutation from this list is detected, it is confirmed by PCR amplification followed by Sanger DNA Sequencing prior to reporting.

Method: Sanger Sequencing

Specimen: ***OneSwab***® (cervicovaginal), whole blood yellow top (ACD solution A)

Transport: Stable at room temperature

Turnaround Time: 5-10 days

1232 Cystic Fibrosis Comprehensive Test by Next Generation Sequencing

191 variants of the CFTR gene including the 23 major mutations approved by ACOG/ACMG

Clinical significance: The MDL Cystic Fibrosis Comprehensive Test is a next generation sequencing (NGS)-based CFTR gene analysis screen for 191 gene variants, including the 23 major mutations recommended by ACOG/ACMG for Cystic Fibrosis screening and 9 genes approved by the FDA for determining Ivacaftor treatment effectiveness. When a mutation from this list is detected, it is confirmed PCR amplification followed by Sanger DNA Sequencing prior to reporting. CF-causing mutation detected by this assay can be found at: www.cftr2.org. To view the full list of mutations detected by this assay, please refer to the Cystic Fibrosis technical bulletin. This assay cannot detect mutations affecting gene regions not examined by this assay. The 191 CFTR gene variants do not represent the complete list of possible CF-causing mutations. The prevalence of particular CF-causing mutations varies based upon the ethnic background of the patient

Method: Next Generation Sequencing

Specimen: ***OneSwab***® (cervicovaginal), whole blood yellow top (ACD solution A)

Transport: Stable at room temperature

Turnaround Time: 5-10 days

1233 Cystic Fibrosis Site Specific Analysis by DNA Sequencing

Must specify variant (mutation)

Clinical significance: Cystic Fibrosis (CF) is an autosomal recessive inheritable disease that afflicts approximately 30,000 people within the United States and 70,000 worldwide, with 1,000 new cases diagnosed each year. Due to its recessive inheritable pattern, people may be carriers of the disease, having inherited a defective gene but not exhibiting symptoms. It is estimated that an additional ten million, or one in every thirty-one Americans, are carriers. Carrier status occurs more frequently within Ashkenazi Jewish and Caucasians of European descent populations, each of which has a one in twenty-nine carrier risk rate. The defective gene responsible for CF was identified in 1989 as the Cystic Fibrosis Transmembrane Conductance Regulator (CFTR) gene. The CFTR protein serves as a chloride channel within epithelial cells; disruption of its function induces an electrolyte imbalance that results in excess sodium chloride levels in sweat, a hallmark and diagnostic indicator of disease, and is believed to cause the thickening of fluids in the lungs and digestive tract. Since its discovery, more than 1,500 mutations have been defined within the CFTR gene. Both the American College of Obstetricians and Gynecologists (ACOG) and the American College of Medical Genetics (ACMG) have developed guidelines for genetic testing to include twenty-three of the most common CFTR mutations. The ΔF508 mutation accounts for approximately two-thirds of all mutant CF alleles worldwide and 70% of the CF cases within the United States, while the W1282X mutation predominates within the Ashkenazi Jewish population. The MDL Cystic Fibrosis Site Specific Anaylsis by DNA Sequencing test can be utilized for family known CFTR gene mutations.

Method: Next Generation Sequencing
Specimen: ***OneSwab***® (cervicovaginal), whole blood yellow top (ACD solution A)
Transport: Stable at room temperature
Turnaround Time: 5-10 days

1274 Genetic Carrier Screening Panel (2 genes)

Cystic Fibrosis Core Test (23 major CFTR variants approved by ACOG/ACMG) (CFTR)
Spinal Muscular Atrophy (SMN1)

Method: Next Generation Sequencing
Specimen: Whole blood yellow top (ACD solution A)
Transport: Stable at room temperature
Turnaround Time: 5-10 days

1216 Sickle Cell Anemia by SNP Genotyping with Pyrosequencing

Clinical Significance: Sickle Cell Anemia is the most common inherited blood disorder in the United States, affecting approximately 72,000 Americans or 1 in 500 African Americans. This autosomal recessive hemoglobinopathy is characterized by sickle-shaped red blood cells that obstruct blood flow, leading to episodes of pain, chronic hemolytic anemia, and severe infections. Usually beginning in early childhood, Sickle Cell Anemia is caused by a single nucleotide polymorphism (SNP) in codon 6 of the hemoglobin beta (HBB) gene. A second SNP in HBB codon 6 results in Hemoglobin C Disease, an autosomal recessive disorder causing a mild hemolytic anemia. This assay uses conventional PCR in conjunction with pyrosequencing technology to detect both SNPs.

Method: Pyrosequencing
Specimen: ***OneSwab***® (cervicovaginal)
Transport: Stable at room temperature
Turnaround Time: 5-10 days

1224 Site Specific Analysis (specify variant)

Method: Next Generation Sequencing
Specimen: Saliva, ***OneSwab***® (cervicovaginal), *ThinPrep*®, whole blood yellow top (ACD solution A)
Transport: Stable at room temperature
Turnaround Time: 5-10 days

1273 Spinal Muscular Atrophy (SMN1)

Clinical significance: Spinal Muscular Atrophy (SMA) is an autosomal recessive neurodegenerative disease that results from the degeneration of spinal cord motor neurons leading to atrophy of skeletal muscle and overall weakness. Affected children have a deficiency in movement, possibly requiring wheelchair assistance. A frequent cause of death of patients with SMA is respiratory failure. There is no effective treatment for the disease. The disorder is caused by a variation in the survival motor neuron gene (SMN1), which is responsible for the production of a protein essential to motor neurons. More than 98% of patients with SMA have an abnormality in both copies of the SMN1 gene, causing a deletion or other pathogenic variation. The occurrence of SMA is approximately 1 in 10,000 live births and it is reported to be the leading genetic cause of infant death.

Method: Next Generation Sequencing
Specimen: Whole blood yellow top (ACD solution A)
Transport: Stable at room temperature
Turnaround Time: 5-10 days

1215 Torsion Dystonia by Real-Time PCR

Clinical Significance: Dystonia is a movement disorder involving sustained muscle contractions and abnormal posturing with a strong hereditary predisposition and without a distinct neuropathology. Torsion dystonia is a form of dystonia known as early-onset dystonia (also called idiopathic or generalized torsion dystonia) that begins in childhood around the age of twelve. Torsion dystonia is an autosomal dominant condition, which means that dystonia appears when a person is heterozygous, having one copy of a mutated gene and one copy of a normal gene. Torsion dystonia has a 30% to 40% penetrance, meaning 30% to 40% of people who have a mutated gene develop symptoms. This disorder has been estimated to occur at rates approximately 5 to 10 fold greater in the Ashkenazi Jewish community, as compared to non-Jewish and non-Ashkenazi populations. A 3-bp (CAG) deletion in the coding region of the TOR1A (DYT1) gene, located on chromosome 9q34, accounts for the majority of cases with this form of dystonia, especially in individuals of Ashkenazi Jewish descent. A second mutation, 18-bp deletion (Phe323_Tyr328del) has recently been identified. The TOR1A gene, which encodes the protein, torsinA, is a member of a gene family with three homologous members in humans, encoding torsinB, torp2 (torp2a), and torp3 (torp3a). The precise function of torsinA is not known. The Torsion Dystonia test screens for two mutations in the TOR1A gene: delGAG and del18bp. This assay is performed in a Real-Time PCR format utilizing two separate PCR reactions.

Method: Real-Time PCR
Specimen: ***OneSwab***® (cervicovaginal)
Transport: Stable at room temperature
Turnaround Time: 5-10 days

Pharmacogenomics

Clinical significance: Pharmacogenomics can be thought of as a combination of pharmacology and genomics. It is the science of how an individual's genetic makeup can influence the way they metabolize drugs; and therefore, how long a drug stays effective in their system. A person's genetic makeup not only determines eye and hair color and disease susceptibilities, it also predicts how an individual will respond to drugs based on their genetic variability. Understanding this, and using Pharmacogenomics information as part of a prescribing decision, can help achieve a more personalized solution for patients.

Method: Next Generation Sequencing

Specimen: Saliva, Whole blood yellow top (ACD solution A)

Transport: Stable at room temperature

Turnaround Time: 5-10 days

CARDIOLOGY:

3101 **Antiplatelet Agents** - Aspirin, Cilostazol, Clopidogrel, Prasugrel, Ticagrelor (ABCB1, CYP1A2, CYP2B6, CYP2C9, CYP2C19, CYP2D6, CYP3A4, CYP3A5, ITGB3, SLOC1B1)

3102 **Statins** - Atorvastatin, Fluvastatin, Lovastatin, Pitavastatin, Pravastatin, Rosuvastatin, Simvastatin (ABCB1, ABCG2, APOE, CYP2C9, CYP2D6, CYP3A4, CYP3A5, KIF6, SLCO1B1)

3103 **Anticlotting Agents** - Acenocoumarol, Coumarol, Fluindione, Phenprocoumon,Warfarin (CYP2C9, CYP2C19, CYP2D6, VKORC1)

3104 **Thrombophilia** - Susceptibility to Factor II, Factor V Leiden (F2, F5, MTHFR)*

If only Test 3104 is ordered from the Drug-Based Pharmacogenomics section, equivalent Test 1263 will be substituted. If Test 1263 is ordered in conjunction with other Drug-Based Pharmacogenomics tests, equivalent Test 3104 will be substituted.

3105 **Calcium Channel Blockers** - Amlodipine, Nifedipine (CYP3A4, CYP3A5)

3106 **Beta Blockers** - Bufuralol, Carvedilol, Metoprolol, Propranalol, Talinolol, Timolol (ABCB1, CYP2D6, UGT1A1)

3107 **Congestive Heart Failure** - Digoxin (ABCB1)

3108 **Antiarrhythmics** - Flecainide, Propafenone (CYP2D6)

3109 **Antihypertensives** - Benazepril, Debrisoquine, Enalapril, Irbesartan, Losartan, Olmesartan, Verapamil (ABCB1, CYP2D6, CYP2C9, MTHFR, SLOC1B1)

PAIN MANAGEMENT

3201 **Pain Management - General** - Alfentanil, Buprenorphine Codeine, Fentanyl, Hydrocodone, Ketamine, Lornoxicam, Methadone, Morphine, Opioids, Oxycodone, Sumatriptan, Tramadol (ABCB1, COMT, CYP2B6, CYP2C9, CYP2D6, CYP3A4, DBH, OPRD1, OPRM1)

3202 **Sedatives and Relaxants, including muscle relaxants** - Carisoprodol, Dextromethorphan, Midazolam, Propofol, Rocuronium, Tolperisone (CYP2B6, CYP2C19, CYP2C9, CYP2D6, CYP3A4, CYP3A5, SLCO1B1)

MALIGNANT DISEASE

3301 **Alkaloids** – Vincristine (ABCB1)

3302 **Alkylating Agents** - Cyclophosphamide (CYP2B6, CYP2C19, CYP3A4, MTHFR, SLCO1B1, TMPT)

3303 **Antimetabolites -** Cytarabine, Fludarabine, Mercaptopurine, Methotrexate, Silibinin (ABCB1, ABCG2, MTHFR, SLCO1B1, TPMT)

3304 **Anthracyclines** - Anthracyclines (gen), Doxorubicin, Epirubicin, Idarubicin (ABCB1, CYP2B6, CYP2C19, SLCO1B1)

3305 **Kinase Inhibitors -** Gefitinib, Icotinib, Imatinib, Sorafenib, Sunitinib (ABCB1, ABCG2, CYP2B6, CYP2C19, CYP2D6, CYP3A4, CYP3A5, SLCO1B1)

3306 **Platinum Derivatives** - Carboplatin, Cisplatin, Oxaliplatin, Platinum Compounds (gen) (ABCB1, ABCG2, CYP3A5, MTHFR, TPMT)

3307 **Steroid Hormone Inhibitors -** Exemestane, Mitotane, Tamoxifen (ABCB1, CYP2B6, CYP2C19, CYP2D6, CYP3A4)

3308 **Taxanes** - Docetaxel, Paclitaxel, Taxanes (gen) (ABCB1, CYP2C8, CYP3A4, CYP3A5, SLCO1B1)

3309 **Topoisomerase Inhibitors** - Etoposide, Irinotecan (ABCB1, SLOC1B1, UGT1A1)

3310 **Uracil Derivatives** - Capecitabine, Fluorouracil, Folfox, Folox, Leucovorin, Tegafur, Xelox (ABCB1, ABCG2, DPYD, MTHFR, SLCO1B1)

3311 **Antiemetics** - Dolasetron, Granisetron, Ondansetron (ABCB1, CYP2D6, CYP3A5)

PSYCHIATRIC DISORDERS (INCLUDING ADDICTION)

3401 **Addiction to Alcohol, Cocaine, Heroin, Opioids, Tobacco** - Anti-addiction (Nicotine), Anti-addiction (Opioids), Buprenorphine, Bupropion, Ethanol, Disulfiram, Heroin, Levodopa, Methadone, Naloxone, Naltrexone, Nicotine, Suboxone (ABCB1, ANKK1, COMT, CYP2B6, CYP2C19, CYP2D6, CYP3A4, DBH, MTHFR, OPRM1)

3402 **ADD/ADHD -** Atomoxetine, Bupropion, Dextroamphetamine, Imipramine, Methylphenidate, Modafinil, Nortriptyline (ANKK1, ABCB1, ADRA2A, CYP2B6, CYP2C19, CYP2D6, DRD1)

3403 **Alzheimer's Disease** - Donepezil, Galantamine, Olanzapine, Risperidone (ABCB1, ANKK1, CYP1A2, CYP2C9, CYP2D6, CYP3A5, HTR2A, MTHFR)

3404 **Anxiety, Insomnia, Severe Agitation** - Bupropion, Dexmedetomidine, Duloxetine, Escitalopram, Lorazepam, Midazolam, Oxazepam, Venlafaxine (ABCB1, ADRA2A, ANKK1, COMT, CYP1A2, CYP2B6, CYP2C19, CYP2D6, CYP3A4, CYP3A5, GABRP, HTR2A, UGT2B15)

3405 **Autism Spectrum Disorders** - Aripiprazole, Quetiapine, Risperidone (ABCB1, ANKK1, COMT, CYP2D6, CYP3A4, CYP3A5, HTR2A)

3406 **Bipolar Disorder** - Aripiprazole, Lamotrigine, Lithium, Olanzapine, Oxcarbazepine, Quetiapine, Valproic acid (ABCB1, ABCG2, ANKK1, CYP1A2, CYP2C9, CYP2D6, CYP3A4, CYP3A5, COMT, DRD1, GABRA6, HTR2A, MTHFR, UGT2B7)

3407 **Depressive Disorder and Major Depressive Disorder** - Amitriptyline, Antidepressants (gen), Antipsychotics (gen), Aripiprazole, Bupropion, Citalopram, Clomipramine, Desipramine, Diazepam, Doxepin, Duloxetine, Escitalopram, Fluoxetine, Fluvoxamine, Imipramine, Maprotiline, Mirtazapine, Nortriptyline, Olanzapine, Opipramol, Paroxetine, Quetiapine, Sertraline, SSRIs (gen), Trimipramine, Venlafaxine, Vortioxetine (ABCB1, ADRA2A, ANKK1, COMT, CYP1A2, CYP2B6, CYP2C19, CYP2C9, CYP2D6, CYP3A4, CYP3A5, DRD4, GABRP, GRIK4, HTR2A, HTR2C, MTHFR)

3408 **Epilepsy** - Antiepileptics (gen), Brivaracetam, Carbamazepine, Clobazam, Lamotrigine, Mephenytoin, Oxcarbazepine, Phenobarbital, Phenytoin, Valproic acid (ABCB1, ABCG2, ANKK1, CYP1A2, CYP2C19, CYP2C9, CYP3A4, CYP3A5, GABRA6, UGT2B7)

3409 **Parkinson's Disease** - Entacapone (COMT)

3410 **Schizophrenia** - Antipsychotics (gen), Aripiprazole, Chlorpromazine, Clozapine, Fluphenazine, Haloperidol, Iloperidone, Nemonapride, Olanzapine, Quetiapine, Risperidone, Thioridazine, Trifluoperazine, Zuclopenthixol (ABCB1, ANKK1, COMT, CYP1A2, CYP2C9, CYP2D6, CYP3A4, CYP3A5, DRD1, HTR2A, HTR2C, MTHFR)

3411 **Fibromyalgia** - Amitryptyline, Atomoxetine, Buproprion, Carbamazepine, Carisoprodol, Codeine, Desipramine, Dextromethorphan, Duloxetine, Escitalopram, Fluoxetine, Milnacipran, Naltrexone, Nortriptyline, Prednisone, Quetiapine, Tramadol, Venlafaxine (ABCB1, ADRA2A, ANKK1, COMT, CYP1A2, CYP2B6, CYP2C19, CYP2D6, CYP3A4, CYP3A5, DBH, GABRP, HTR2A, OPRM1, UGT2B7)

PSYCHOTROPIC

3412 Post-Traumatic Stress Disorder (PTSD) Aripiprazole, Bupropion, Buspirone, Desvenlafaxine, Dronabinol, Duloxetine, Fluoxetine, Fluvoxamine, Guanfacine, Hydroxyzine, Ketamine, Lamotrigine, Mirtazapine, Nefazodone, Paroxetine, Propranolol, Quetiapine, Risperidone, Sertraline, Trazodone, Valproic Acid, Venlafaxine, Vilazodone, Zolpidem (ABCB1, ABCG2, ANKK1, COMT, CYP1A2, CYP2B6, CYP2C19, CYP2C9, CYP2D6, CYP3A4, CYP3A5, DRD1, GABRP, HTR2A, UGT1A1, UGT2B7)

INFECTIOUS DISEASE

3501 HIV/AIDS - Antivirals (HIV), Atazanavir, Dolutegravir, Efavirenz, Etravirine, Indinavir, Lamivudine, Lopinavir, Nelfi navir, Nevirapine, Ritonavir, Tenofovir, Zidovudine (ABCB1, ABCG2, APOE, CYP2B6, CYP2C19, CYP2D6, CYP3A4, CYP3A5, UGT1A1)

3502 Antifungals and Antibiotics - Daptomycin, Dicloxacillin, Erythromycin, Rifampicin, Sulfonamides (gen), Voriconazole (ABCB1, CYP2B6, CYP2C9, CYP2C19, CYP3A4, SLCO1B1)

3503 Anti-Mycobacterials - Anti-Mycobacterials (TB), Ethambutol, Isoniazid, Pyrazinamide, Rifampicin (ABCB1, CYP2B6, SLCO1B1)

IMMUNOLOGY / IMMUNE MODULATION

3601 Transplantation - Busulfan, Cyclophosphamide, Cyclosporine, Everolimus, Methylprednisone, Prednisone/Prednisolone, Sirolimus, Tacrolimus (ABCB1, CYP2B6, CYP2C19, CYP2C9, CYP3A4, CYP3A5, MTHFR, SLCO1B1, TMPT)

3602 Rheumatoid Arthritis - Leflunomide, Methotrexate, Sulfasalazine (ABCB1, ABCG2, CYP1A2, MTHFR, SLCO1B1)

3603 Type-II Diabetes - Repaglinide, Sulfoureas (gen), Urea Derivatives (gen) (CYP2C8, CYP2C9, SLCO1B1)

3604 Gastritis and Colitis - Esomeprazole, Lansoprazole, Loperamide, Omeprazole, Pantoprazole, Rabeprazole, Tacrolimus (ABCB1, CYP2C19, CYP3A4, CYP3A5)

3605 Inflammation - Anti-inflammatories (gen), Celecoxib, Dexamethasone, Diclofenac, Flurbiprofen, Lornoxicam, Meloxicam, Prednisone/ Prednisolone (ABCB1, CYP2C9, COMT, DBH, OPRM1)

3606 Systemic Lupus Erythematosus - Cyclophosphamide (CYP2B6, CYP2C19, CYP3A4, MTHFR, SLCO1B1, TMPT)

3607 Gout - Allopurinol (ABCG2)

3608 Antihistamines - Fexofenadine (ABCB1)

3609 Antiasthmatics - Zafirlukast (CYP2C9)

OTHER

3701 Anesthesiology - Nitrous Oxide (MTHFR)

3702 Beta Thalassemia - Deferasirox (CYP1A2, UGT1A1)

3703 Narcolepsy - Modafinil (ABCB1)

3704 Contraception - Oral Contraceptives (gen) (CYP2C9, F2, F5, MTHFR)

3705 Erectile Dysfunction - Sildenafil, Vardenafil (CYP3A4, CYP3A5)

3706 Bladder Control - Tolterodine (CYP2D6)

ALPHABETCAL LISTING BY DRUG NAME:

3801 Acenocoumarol
3803 Alfentanil
3804 Allopurinol
3805 Amitriptyline
3806 Amlodipine
3807 Anthracyclines (gen)
4001 Antiaddiction -Nicotine
4002 Antiaddiction -Opioids
4003 Antidepressants (gen)
3808 Antiepileptics (gen)
4004 Anti-inflammatories (gen)
4005 Antimycobacterials - TB
3809 Antipsychotics (gen)
4006 Antivirals - HIV
3810 Aripiprazole
3811 Aspirin
3812 Atazanavir
3813 Atomoxetine
3814 Atorvastatin
3815 Benazepril
4007 Brivaracetam
3816 Bufuralol
4008 Buprenorphine
3817 Bupropion
3818 Busulfan
3819 Capecitabine
3820 Carbamazepine
3821 Carboplatin
3822 Carisoprodol
3823 Carvedilol
3824 Celecoxib
3826 Chlorpromazine
3827 Cilostazol
3828 Cisplatin
3829 Citalopram
3830 Clobazam
3831 Clomipramine
3832 Clopidogrel
3833 Clozapine
3834 Codeine
3836 Cyclophosphamide
3837 Cyclosporine
3838 Cytarabine
3840 Daptomycin
3841 Debrisoquine
3842 Deferasirox
3843 Desipramine
3844 Dexamethasone
3845 Dexmedetomidine
3846 Dextroamphetamine
4009 Dextromethorphan
3847 Diazepam
3848 Diclofenac
3849 Dicloxacillin
3850 Digoxin
3851 Disulfiram
3852 Docetaxel
3853 Dolasetron
4010 Dolutegravir
3854 Donepezil
3855 Doxepin
3856 Doxorubicin
4011 Duloxetine
3857 Efavirenz
3858 Enalapril
3859 Entacapone
3860 Epirubicin
3861 Erythromycin
3862 Escitalopram
3863 Esomeprazole
4012 Ethambutol
4013 Ethanol
3864 Etoposide
3865 Etravirine
3866 Everolimus
4014 Exemestane
3867 Fentanyl
3868 Fexofenadine
3869 Flecainide
3870 Fludarabine
3871 Fluindione
3872 Fluorouracil
3873 Fluoxetine
3874 Fluphenazine
3875 Flurbiprofen
3876 Fluvastatin
3877 Fluvoxamine
3878 Folfox
3879 Folox
3880 Galantamine
3881 Gefitinib
3882 Granisetron
3883 Haloperidol
4015 Heroin
3884 Hydrocodone
3885 Icotinib
3886 Idarubicin
3887 Iloperidone
3888 Imatinib
3889 Imipramine
3890 Indinavir
3891 Irbesartan
3892 Irinotecan
4016 Isoniazid
3893 Ketamine
3894 Lamivudine
3895 Lamotrigine
3896 Lansoprazole
3897 Leflunomide
3898 Leucovorin
3899 Levodopa
3900 Lithium
4018 Loperamide
3901 Lopinavir
3902 Lorazepam
3903 Lornoxicam
3904 Losartan
3905 Lovastatin
3906 Maprotiline
4019 Meloxicam
3907 Mephenytoin
3908 Mercaptopurine
3909 Methadone
3910 Methotrexate
3911 Methylphenidate
3912 Methylprednisone
3913 Metoprolol
3915 Midazolam
3916 Milnacipran
3917 Mirtazapine
3918 Mitotane
3919 Modafinil
3920 Morphine
3921 Naloxone
3922 Naltrexone
3923 Nelfinavir
3924 Nemonapride
3925 Nevirapine
3926 Nicotine
3927 Nifedipine
3928 Nitrous oxide
3929 Nortriptyline
3930 Olanzapine
3931 Olmesartan
3932 Omeprazole
3933 Ondansetron
3934 Opioids (gen)
3935 Opipramol
3936 Oral Contraceptives (gen)
3937 Oxaliplatin
3938 Oxazepam
4020 Oxcarbazepine
3939 Oxycodone
3940 Paclitaxel
3941 Pantoprazole
3942 Paroxetine
3943 Phenobarbital
3944 Phenprocoumon
3945 Phenytoin
3946 Pitavastatin
3947 Platinum Compounds (gen)
3948 Prasugrel
3949 Pravastatin
3950 Prednisolone
3950 Prednisone
3951 Propafenone
3952 Propranalol
3953 Propofol
4021 Pyrazinamide
3954 Quetiapine
3955 Rabeprazole
3956 Repaglinide
3957 Rifampicin
3958 Risperidone
3959 Ritonavir
3960 Rocuronium
3962 Rosuvastatin
3963 Sertraline
4022 Sildenafil
3964 Silibinin
3965 Simvastatin
3966 Sirolimus
3967 Sorafenib
3968 SSRIs (gen)
4023 Suboxone
3969 Sulfasalazine
3970 Sulfonamides (gen)
3971 Sulfoureas (gen)
3972 Sumatriptan
3973 Sunitinib
3974 Tacrolimus
3975 Talinolol
3976 Tamoxifen
3977 Taxanes (gen)
3978 Tegafur
4024 Tenofovir
3979 Thioridazine
3980 Ticagrelor
3981 Timolol
3982 Tolperisone
3983 Tolterodine
3984 Tramadol
3985 Trifluoperazine
3986 Trimipramine
3987 Urea Derivatives (gen)
3988 Valproic acid
3989 Vardenafil
3990 Venlafaxine
3991 Verapamil
3992 Vincristine
3993 Voriconazole
3994 Vortioxetine
3995 Warfarin
3996 Xelox
3997 Zafirlukast
3998 Zidovudine
3999 Zuclopenthixol

Food Intolerance Testing

2001 Comprehensive Food Sensitivity Test (Reactivity to 204 foods) IgG by Immunoblot

Clinical significance: Non-IgE mediated, or non-allergic, food hypersensitivities are on the rise. Food intolerances may present as non-immunologic adverse reactions in gastrointestinal-related disorders, such as lactase deficiency, dietary protein-induced enterocolitis syndromes, and eosinophilic gastrointestinal disease, as well as in autoimmunity disorders, inflammatory skin diseases, migraine headaches, chronic fatigue syndrome, asthma, and even autism. As such, these conditions often resolve when the offending food is avoided. This multi-parameter test contains optimized combinations of **204** relevant foods and their respective additives for detecting food-specific IgG antibodies in serum via Immunoblot.

Method: Immunoblot
Specimen: Serum
Transport: Stable at room temperature

2002 Expanded Food Sensitivity Test (Reactivity to 108 foods) IgG by Immunoblot

Clinical significance: Non-IgE mediated, or non-allergic, food hypersensitivities are on the rise. Food intolerances may present as non-immunologic adverse reactions in gastrointestinal-related disorders, such as lactase deficiency, dietary protein-induced enterocolitis syndromes, and eosinophilic gastrointestinal disease, as well as in autoimmunity disorders, inflammatory skin diseases, migraine headaches, chronic fatigue syndrome, asthma, and even autism. As such, these conditions often resolve when the offending food is avoided. This multi-parameter test contains optimized combinations of **108** relevant foods and their respective additives for detecting food-specific IgG antibodies in serum via Immunoblot.

Method: Immunoblot
Specimen: Serum
Transport: Stable at room temperature

2003 Food Sensitivity Test (Reactivity to 96 Foods) IgG by Immunoblot

Clinical significance: Non-IgE mediated, or non-allergic, food hypersensitivities are on the rise. Food intolerances may present as non-immunologic adverse reactions in gastrointestinal-related disorders, such as lactase deficiency, dietary protein-induced enterocolitis syndromes, and eosinophilic gastrointestinal disease, as well as in autoimmunity disorders, inflammatory skin diseases, migraine headaches, chronic fatigue syndrome, asthma, and even autism. As such, these conditions often resolve when the offending food is avoided. This multi-parameter test contains optimized combinations of **204** relevant foods and their respective additives for detecting food-specific IgG antibodies in serum via Immunoblot.

Method: Immunoblot
Specimen: Serum
Transport: Stable at room temperature

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