FEP 2.04.127 Multitarget Polymerase Chain Reaction Testing for Diagnosis of Bacterial Vaginosis

**Effective Date:** April 1, 2019

**Related Policies:**
- 2.04.10 Identification of Microorganisms Using Nucleic Acid Probes

**Multitarget Polymerase Chain Reaction Testing for Diagnosis of Bacterial Vaginosis**

**Description**

Bacterial vaginosis (BV) is a common medical condition resulting from an imbalance in the normal vaginal flora. Although identification of *Gardnerella vaginalis* has traditionally been associated with BV, there is no single etiologic agent. Most cases are asymptomatic, and most symptomatic cases can be diagnosed using clinical and microscopic evaluation. Multitarget polymerase chain reaction (PCR) testing is proposed as an alternative to currently available laboratory tests to diagnose BV. This test may improve outcomes if it is a more accurate and reliable method to diagnose BV.

Examples of commercially available multitarget PCR tests and the organisms in the panels are shown in Table 1; this may not be an exhaustive list of all commercially available tests.

**Table 1. Components of Commercially Available Multitarget PCR Tests**

<table>
<thead>
<tr>
<th>Organism</th>
<th>SureSwab</th>
<th>BD Max</th>
<th>MDL Panel</th>
<th>NuSwab</th>
<th>GenPath BV Test</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Atopobium vaginae</em></td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td><em>Gardnerella vaginalis</em></td>
<td>X</td>
<td>X</td>
<td>X</td>
<td></td>
<td>X</td>
</tr>
<tr>
<td><em>Lactobacillus</em> species</td>
<td>X&lt;sup&gt;a&lt;/sup&gt;</td>
<td>X</td>
<td>X</td>
<td></td>
<td></td>
</tr>
<tr>
<td><em>Megasphaera</em> (type 1, type 2, and/or species)</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td><em>BVAB</em> (type 1 and/or type 2)</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td></td>
<td>X</td>
</tr>
</tbody>
</table>

BVAB: bacterial vaginosis-associated bacteria; MDL: Medical Diagnostics Laboratory; PCR: polymerase chain reaction.

<sup>a</sup> *Lactobacillus crispatus* and *Lactobacillus jensenii*.

The SureSwab Total (Quest Diagnostics) test involves obtaining vaginal swab specimens, extracting total DNA, and quantitating the four types of bacteria using PCR. Results are reported as log cells per milliliter for each organism and concentrations of all *Lactobacilli* species are reported together then classified into one of the following three categories: not supportive, equivocal, and supportive.
A classification of *not supportive* of BV diagnosis is based on:

- The presence of *Lactobacillus* species, *G. vaginalis* levels <6.0 log cells/mL, and absence of *Atopobium vaginae* and *Megasphaera* species; or
- The absence of *Lactobacillus* species, *G. vaginalis* levels <6.0 log cells/mL, and absence of *A. vaginae* and *Megasphaera* species; or
- The absence of all targeted organisms.

A classification of equivocal is based on:

- The presence of *Lactobacillus* species, plus *G. vaginalis* at least 6.0 log cells/mL, and/or presence of *A. vaginae* and/or *Megasphaera* species.

A classification of supportive of BV diagnosis is based on the absence of *Lactobacillus* species, and presence of *G. vaginalis* levels of at least 6.0 log cells/mL, and presence of *A. vaginae* and/or *Megasphaera* species.

Another product, the BD Max (Becton, Dickinson), tests for markers of BV and vaginitis. The test uses a similar process to that described for SureSwab. Vaginal swab specimens are collected, DNA is extracted, and real-time PCR is used to quantitate targeted organisms. Results of BV marker tests are not reported for individual organisms. Instead, qualitative BV results are reported as positive or negative for BV based on the relative quantity of the various organisms.

Medical Diagnostics Laboratory offers a Bacterial Vaginosis Panel. Markers are shown above in Table 1 and are assessed using real-time PCR and *Lactobacillus* is profiled using quantitative PCR. GenPath Diagnostics also offers a bacterial vaginosis test.

The NuSwab® Select BV test (Laboratory Corporation of American) uses semiquantitative PCR analysis of three predictive marker organisms of vaginal dysbiosis to generate a total score that is associated with the presence or absence of BV. In this test system, samples with a total score of 0 to 1 are considered negative for BV, samples with a score of 3 to 6 are positive for BV, and samples with a score of 2 are indeterminate for BV.

Several of the manufacturers of the BV tests also have extensions that include other causes of vaginitis such as *Trichomonas vaginalis* and *Candidiasis* species.

**OBJECTIVE**

The objective of this evidence review is to evaluate the technical performance, diagnostic accuracy, and clinical utility of multitarget polymerase chain reaction testing in patients with signs or symptoms of bacterial vaginosis.

**POLICY STATEMENT**

Multitarget polymerase chain reaction testing for the diagnosis of bacterial vaginosis is considered investigational.

**BENEFIT APPLICATION**

Screening (other than the preventive services listed in the brochure) is not covered. Please see Section 6 General exclusions.

Benefits are available for specialized diagnostic genetic testing when it is medically necessary to diagnose and/or manage a patient’s existing medical condition. Benefits are not provided for genetic panels when some or all of the tests included in the panel are not covered, are experimental or investigational, or are not medically necessary.
Multitarget Polymerase Chain Reaction Testing for Diagnosis of Bacterial Vaginosis

Experimental or investigational procedures, treatments, drugs, or devices are not covered (See General Exclusion Section of brochure).

**FDA REGULATORY STATUS**

In October 2016, the Food and Drug Administration completed a review of a de novo request for classification of the BD Max™ Vaginal Panel (Becton, Dickinson). The test was granted class II designation, marketing authorization, and is indicated for the direct detection of DNA targets from bacteria associated with bacterial vaginosis (DEN160001).

Clinical laboratories may develop and validate tests in-house and market them as a laboratory service; laboratory-developed tests must meet the general regulatory standards of the Clinical Laboratory Improvement Amendments. Laboratories that offer laboratory-developed tests must be licensed by the Clinical Laboratory Improvement Amendments for high-complexity testing.

**RATIONALE**

**Summary of Evidence**

In individuals who have signs or symptoms of BV who receive multitarget PCR testing, the evidence includes several prospective studies on technical performance and diagnostic accuracy. The relevant outcomes are test validity, symptoms, and change in disease status. Several studies have evaluated the diagnostic accuracy of multitarget PCR tests for BV, including two studies evaluating commercially available tests. The studies found sensitivities between 90% and 95% and specificities between 85% and 90% compared with standard methods of diagnosis. Most studies used a combination of the Amsel criteria and Nugent scoring as the reference standard. There is a lack of direct evidence on the clinical utility of PCR testing for BV (ie, studies showing that testing leads to better patient management decisions and/or better health outcomes than current approaches). Moreover, a chain of evidence does not currently support multitarget testing because most symptomatic women can be diagnosed with a standard workup. The evidence is insufficient to determine the effects of the technology on health outcomes.

**SUPPLEMENTAL INFORMATION**

**Practice Guidelines and Position Statements**

**Centers for Disease Control and Prevention**

The Centers for Disease Control and Prevention (2015) updated its guidelines on sexually transmitted diseases. Regarding the diagnosis of bacterial vaginosis (BV), the guidelines stated: “BV can be diagnosed by … clinical criteria (i.e., Amsel's Diagnostic Criteria) or Gram stain. A Gram stain (considered the gold standard laboratory method for diagnosing BV) is used to determine the relative concentration of lactobacilli … PCR [polymerase chain reaction] has been used in research settings for the detection of … organisms associated with BV, but evaluation of its clinical utility is still underway. Detection of specific organisms might be predictive of BV by PCR. Additional validation is needed…..”

**American College of Obstetricians and Gynecologists**

Published in 2012 and reaffirmed in 2018, the American College of Obstetricians and Gynecologists has produced a practice bulletin on the prediction of preterm birth. The bulletin stated that BV testing is not recommended as a screening strategy in asymptomatic pregnant women at increased risk of preterm birth.
U.S. Preventive Services Task Force Recommendations

The USPSTF (2008) recommendations on screening for BV in pregnancy have stated that:

“The USPSTF recommends against screening for bacterial vaginosis in asymptomatic pregnant women at low risk for preterm delivery.” (Grade D recommendation)

“The USPSTF concludes that the current evidence is insufficient to assess the balance of benefits and harms of screening for bacterial vaginosis in asymptomatic pregnant women at high risk for preterm delivery.” (I statement)

These recommendations are currently in revision.

Medicare National Coverage

There is no national coverage determination (NCD). In the absence of an NCD, coverage decisions are left to the discretion of local Medicare carriers.

REFERENCES

FEP 2.040.127 Multitarget Polymerase Chain Reaction Testing for Diagnosis of Bacterial Vaginosis


POLICY HISTORY

<table>
<thead>
<tr>
<th>Date</th>
<th>Action</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>December 2014</td>
<td>New Policy</td>
<td>Policy created with literature review. Multitarget polymerase chain reaction (PCR) testing for diagnosis of bacterial vaginosis is considered investigational.</td>
</tr>
<tr>
<td>March 2019</td>
<td>Update Policy</td>
<td>Policy updated with literature review through October 1, 2018; references 3-7, 9-10 and 15-16 added; reference 18 updated. Policy statement unchanged.</td>
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