

Xpert® Xpress MVP (US-IVD*)

Target Selection for Bacterial Vaginosis

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Bacterial vaginosis (BV) is a polymicrobial syndrome in which the normal vaginal flora, mostly *Lactobacillus* sp., is replaced by an overgrowth of anaerobic bacteria. This state of dysbiosis is a continuum that presents unique diagnostic challenges in terms of identifying optimal bacterial targets for molecular detection to enable laboratory diagnosis. The Xpert Xpress MVP test was designed to target DNA from anaerobic bacteria that are strongly associated with BV, i.e., *Atopobium* sp., Bacterial Vaginosis-Associated Bacterium 2 (BVAB2) and *Megasphaera* Type 1 (*Megasphaera*-1).¹⁻³ The rationale for selecting these organisms as BV targets is based on the scientific literature and in consultation with thought leaders.

Using taxon-directed 16S rRNA gene PCR, Fredricks et al.¹ showed that *Megasphaera* sp., BVAB2 and *Atopobium* sp., are highly associated with and are excellent markers for BV. Alone or in combination, these organisms provide high sensitivity and specificity for BV compared to Amsel's criteria and Nugent Score.¹ Although *Gardnerella vaginalis*, a gram-negative bacillus that has long been associated with BV, showed high sensitivity as a target organism, and was detected in 96% of women with BV, it was also detected in 70% of women without BV.¹ Due to its poor specificity, *G. vaginalis* alone is not reliable as an indicator of BV either by molecular detection¹ or by culture.⁴ Cartwright et al.² developed a semi-quantitative multiplex PCR assay based on *A. vaginae*, BVAB2, and *Megasphaera*-1 as BV targets and demonstrated a sensitivity of 95.4% and specificity of 90.2% and a high diagnostic accuracy for BV in symptomatic women compared to Amsel's criteria and Nugent Score. Several studies assessing various BV marker combinations that included *G. vaginalis* showed a lower sensitivity or specificity than a combination of either *A. vaginae* and BVAB2,³ or *A. vaginae*, BVAB2, and *Megasphaera*-1.² Notably, several nucleic acid amplification tests (NAATs) based on multi-organism BV algorithms have provided more accurate results than DNA probe hybridization tests that only target *G. vaginalis* for BV, such as the BD Affirm VPIII Microbial Identification Test.⁵⁻⁷

Lactobacillus sp. are mainly associated with normal or healthy vaginal flora and the Xpert Xpress MVP test focuses on the detection of BV flora. The type and distribution of *Lactobacillus* sp. may vary across diverse populations¹ and organisms such as *L. iners* can be found in high numbers in both BV and healthy vaginal flora.³ In their study, Hilbert et al. showed that even in combination, *Lactobacillus* sp. only had a 70% sensitivity and 74% specificity, highlighting their limited utility as negative indicators of BV.³

Based on these findings and in order to maximize the sensitivity, specificity and accuracy of the test, *Atopobium* sp. (*Atopobium vaginae*, *Atopobium* novel species CCUG 55226), BVAB2 and *Megasphaera*-1, were selected as the BV targets for the Xpert Xpress MVP test, while *G. vaginalis* and *Lactobacillus* sp. were excluded.

Table 1. Xpert Xpress MVP — Target Organisms for Bacterial Vaginosis

Organism	BV Target	Rationale
<i>Atopobium</i> sp. (<i>A. vaginae</i> , <i>Atopobium</i> novel species CCUG 55226)	✓	• Strong association with BV • Combination offers optimal sensitivity, specificity, and accuracy for BV
Bacterial Vaginosis-Associated Bacterium (BVAB2)	✓	
<i>Megasphaera</i> -1	✓	
<i>Gardnerella vaginalis</i>	X	• Sensitive but not specific for BV • Found in 70% of women without BV
<i>Lactobacillus</i> sp.	X	• Mostly found in healthy vaginal flora • Species type and distribution varies • <i>L. iners</i> found equally in BV and non-BV flora • Limited utility as negative predictors of BV

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0930-04

