MEDICAL/SCIENTIFIC AFFAIRS BULLETIN

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).[1,2,3] 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 detection[1] 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 96.7% and specificity of 92.2% 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.[5,6,7]

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

* US-IVD. *In Vitro* Diagnostic Medical Device.

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

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