

## Clinical Bulletin: DxWound *mecA* Test

### Description

Antibiotic resistance is considered by the CDC to be a major public health threat in the United States.<sup>1</sup> Patients with antibiotic resistant infections have higher morbidity and mortality, including longer hospital stays with increased costs to the healthcare system.<sup>1</sup> To help mitigate the consequences of antibiotic resistance, the CDC has called for improved antibiotic stewardship and the development of new diagnostic tests.<sup>1</sup>

Since the introduction of methicillin into clinical use, methicillin-resistant *Staphylococcus aureus* (MRSA) strains have emerged worldwide as important nosocomial pathogens with substantially increasing occurrences in the community.<sup>2,3</sup> MRSA is categorized as a serious threat by the CDC with more than 80,000 severe MRSA infections per year, leading to over 11,000 deaths.<sup>1</sup> *mecA*, a gene detected by DxWound, is an antibiotic resistance gene associated with *Staphylococcus* species, including *Staphylococcus aureus*, *Staphylococcus lugdunensis*, *Staphylococcus epidermidis* and other Coagulase-Negative staphylococci (CoNS).<sup>4,5</sup> The *mecA* gene mediates oxacillin/methicillin resistance.<sup>4,5</sup> DxWound tests for both *mecA* and *Staphylococcus aureus*, and when both are detected, MRSA may be present.

### Indications for Ordering

The DxWound *mecA* test can be useful for any patient suspected of having a methicillin-resistant *Staphylococcal* skin and soft tissue infection (SSTI) based on the clinician's determination of medical necessity. The DxWound test can identify *S. aureus* directly from a wound sample without the need for culture enrichment. The presence of *mecA* may indicate resistance to oxacillin/methicillin and all beta-lactams with the exception of cephalosporins with anti-MRSA activity.<sup>5</sup> When *S. aureus* and *mecA* are both detected, then MRSA may be present. In a patient with clinical signs and symptoms of infection, these *Staphylococcal* and *mecA* tests may help clinicians quickly target antibiotic therapy.

### Methodology

DxWound tests analyze DNA using real-time polymerase chain reaction (PCR) technology. The tests are performed on a swab sample taken directly from the site of infection without need for bacterial growth. The swab sample is collected in a solution that kills microorganisms at the same time as protecting microbial DNA, essentially preserving the wound microbiome in time at the point of specimen collection. DNA is detected directly from the patient specimen without culture enrichment. All DxWound tests have  $\geq 95\%$  accuracy and  $\geq 99\%$  reproducibility. The accuracy and reproducibility of DxWound tests were defined by either comparison to culture reports for wound samples and/or by correct identification of known organisms or antibiotic resistance genes in reference samples obtained from the FDA-CDC antimicrobial resistance isolate bank, commercial vendors, and research laboratories. For more information, please refer to the Technical Specifications bulletin.

### Clinical Use

*Staphylococcus* species have an endogenous penicillin binding protein (PBP), which is vital to peptidoglycan synthesis and cell wall formation.<sup>6-8</sup> Beta-lactams, such as methicillin or oxacillin, specifically target PBP and irreversibly inactivate the enzyme, leading to defective cell wall formation and eventually cell death.<sup>6-8</sup> When the *mecA* gene is active in *Staphylococcus* species, it encodes a new PBP, termed penicillin binding protein 2a (PBP2a), which results in a reduced affinity and less accessibility for beta-lactams, as well as a reduced rate of beta-lactam-mediated enzyme acylation, thus contributing to bacterial beta-lactam resistance.<sup>6-8</sup>

A study of samples from complicated skin and skin structure infections showed that 50.9% of *S. aureus* isolates in North America (U.S. and Canada) encoded and expressed the *mecA* gene.<sup>9</sup> Multiple studies have shown that MRSA is associated with longer lengths of stay, and often with poorer outcomes, compared with methicillin-susceptible *S. aureus* (MSSA) or non-MRSA infections.<sup>10,11</sup> Beta-lactam antibiotics may be used to treat infections cause by various *Staphylococcus* species. However, since *mecA* has been associated with resistance to these antibiotics, testing for this gene can help clinicians identify potential antibiotic resistant *Staphylococcus* species to rapidly target antibiotic therapy.

### Test Interpretation

The DxWound report provides specific information about the *mecA* gene and its association with resistance to oxacillin/methicillin and all beta-lactams with the exception of cephalosporins with anti-MRSA activity.<sup>5</sup> See Table 1 for additional information regarding *mecA* test interpretation.

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Table 1. DxWound mecA Test Interpretation<sup>12,13</sup>

DxWound Test Results	Potential Organism Present	Common Antibiotic Coverage	
		Oral	IV
<i>Staphylococcus aureus</i> or <i>Staphylococcus lugdunensis</i> + <i>mecA</i>	Methicillin-Resistant <i>Staphylococcus aureus</i> (MRSA) or <i>Staphylococcus lugdunensis</i>	Clindamycin, Doxycycline, Linezolid, Minocycline, TMP-SMX	Daptomycin, Linezolid, Vancomycin
<i>Staphylococcus aureus</i> or <i>Staphylococcus lugdunensis</i> (No <i>mecA</i> )	Methicillin-Sensitive <i>Staphylococcus aureus</i> (MSSA) or <i>Staphylococcus lugdunensis</i>	Cephalexin, Dicloxacillin, any MRSA active agent*	Cefazolin, Nafcillin, Oxacillin, any MRSA active agent*

\* Possible alternative if patient has true penicillin allergy

## Limitations

- These tests detect the presence of genes and do not detect whether the genes are expressed
- These tests do not detect all known antibiotic resistance mechanisms, nor do they identify with which *Staphylococcal* species *mecA* is associated
- In addition to *Staphylococcus aureus* and *Staphylococcus lugdunensis*, it is possible that *mecA* can also be associated with other CoNS species that are not included in these tests, such as *S. epidermidis*, which is commonly found in normal skin flora.<sup>14</sup> More than 70% of opportunistic *S. epidermidis* are resistant to oxacillin/methicillin.<sup>15,16</sup>
- The use of PCR to test *S. aureus* isolates for the presence of the *mecA* gene can result in a small percentage of strains (3%) testing positive for *mecA*, but being highly susceptible to methicillin-like antibiotics.<sup>17,18</sup>
- The DxWound Genetic Analysis Report does not make recommendations for treatment. All test results should be evaluated in the context of the patient's individual clinical presentation.

## Technical Assistance

For technical assistance with interpretation or to speak with one of our clinical support specialists, scientists or clinical pharmacists, please call Client Services at 877-866-0603, Monday–Friday 5:00am to 5:00 pm (Pacific Time).

## Reporting

All test results are reported, generally, within 1 business day of specimen receipt. These results are available in the VIRA online portal as a DxWound Report.

## References

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## How to Order

Using the VIRA online portal, medically necessary tests are ordered by individual test based on patient-specific elements identified during the clinical assessment and documented in the patient's medical record by the provider. Submit swab specimen in the collection device provided according to the directions in the Specimen Collection Manual. A completed Documentation of Medical Necessity Form is required with each order.



Contact CogenDx to learn more.  
Client Services: 877.866.0603  
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