

Gene Expression Testing System for Whole Blood Samples

ICD-10 Coordination and Management Committee Update
Spring 2025

EMERGENCY DEPARTMENT THROUGHPUT IS A MAJOR SYSTEMS ISSUE

25-40% of patients presenting to Emergency Departments have suspected infections¹

These patients are complex to diagnose and treat:

- Comorbid conditions and immunocompromise
- Borderline symptoms and lab results
- Complex diagnostic workups include multiple labs, imaging, and microbiology

Multiple metrics hinge on rapid decisions:

- Admission appropriateness
- SEP-1 compliance / finding 'occult sepsis'
- Emergency Department length-of-stay
- Antibiotic stewardship & bouncebacks for missed bacterial infections
- Patient and staff satisfaction

CURRENT ACUTE INFECTIONS DIAGNOSTIC SOLUTIONS FALL SHORT

<p>Traditional biomarkers Performance is suboptimal</p> 	<p>Microbiology is slow & misses deep infections</p> 	<p>'Sepsis' is more than a yes or no question</p> 
<p>WBC¹, PCT²⁻⁵, CRP³⁻⁵, lactate⁶ –</p> <p>Sub-optimal performance and not in guidelines</p>	<p>Full microbiology workups of radiographically confirmed pneumonias have a 60% false negative rate⁷</p>	<p>Most patients don't have sepsis, and 'not sepsis' leaves us at square one.</p> <p>What about:</p> <ul style="list-style-type: none"> • Non-severe infections • Non-infectious conditions • Sepsis mimics

1. Seigel TA, et al., Inadequacy of Temperature and White Blood Cell Count in Predicting Bacteremia in Patients with Suspected Infection, The Journal of Emergency Medicine, Volume 42, Issue 3, 2012, Pages 254-259, ISSN 0736-4679. 2. Goh KH, Wang L, Yeow AYK, et al. Artificial intelligence in sepsis early prediction and diagnosis using unstructured data in healthcare. Nat Commun. 2021;12(1):711. 3. Oliver Liesenfeld, et al., Rapid and Accurate Diagnosis and Prognosis of Acute Infections and Sepsis from Whole Blood Using Host Response mRNA amplification and Result Interpretation by Machine-Learning Classifiers, 10 October 2024, PREPRINT (Version 1) available at Research Square [https://doi.org/10.21203/rs.3.rs-5194992/v1]. 4. Severe Sepsis and Septic Shock: Management Bundle. National Quality Forum. January 5, 2015. Accessed December 7, 2023. 5. Christensen EE, et al. Diagnostic accuracy and added value of infection biomarkers in patients with possible sepsis in the emergency department. Shock. 2022;58(4):251-259. 6. Evans et al, Surviving Sepsis Campaign: International Guidelines for Management of Sepsis and Septic Shock 2021, Critical Care Medicine: November 2021 - Volume 49 - Issue 11. 5. Jain S, et al., Community-Acquired Pneumonia Requiring Hospitalization among U.S. Adults, N Engl J Med 2015;373:415-427.

BETTER INSIGHTS CAN LEAD TO BETTER OUTCOMES AND THROUGHPUT

Actionable clinical questions

Do I prescribe antibiotics?"



“What further tests do I order?”



“Does this patient have sepsis?”



“Should I admit or not?”



Tangible clinical outcomes

Improve outcomes in sepsis and readmits

Reduce diagnostic testing and errors

Improved SEP-1 bundle compliance

Reduce unneeded hospital care

TRIVERITY TEST SYSTEM OVERVIEW

No sample prep required
< 1-minute hands on time
~30-minute turnaround time

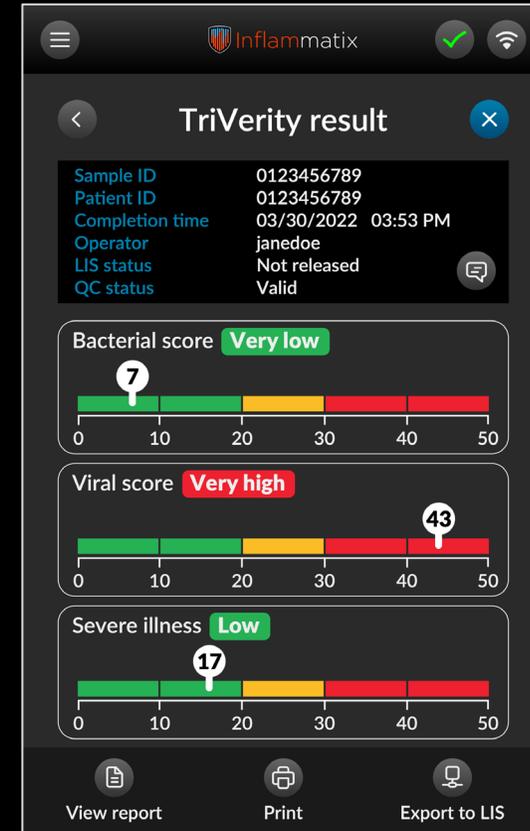
Cartridge accepts
sample directly:
no pipetting



Instrument could be placed in:

1. Central (stat) lab
2. ED satellite lab
3. ED POC station

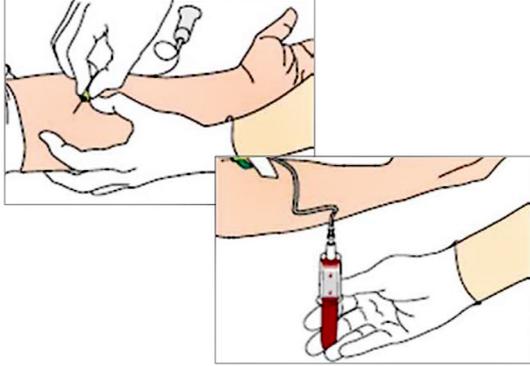
Example TriVerity Test Result:
A “Very low” bacterial, “Very high” viral and “Low” severity*
scores imply a non-severe viral infection



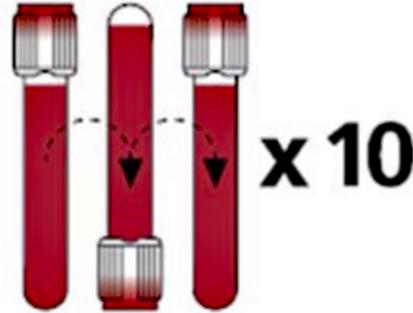
Severe Illness Score defined as need for mechanical ventilation, vasopressors or renal replacement therapy in the next seven days.

TRIVERITY SIMPLE CLINICAL WORKFLOW

- 1 Whole blood sample is collected using a PAXgene® Blood RNA Tube



- 2 Sample is inverted 10 times to ensure adequate mixing of RNA stabilizer



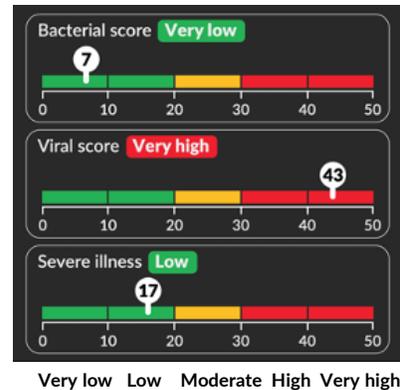
- 3 Obtain new TriVerity Cartridge from room temperature storage



- 4 PAXgene® tube is inserted into cartridge. Cartridge is then inserted into system. Test run time is ~30 minutes



- 5 Machine-learning derived algorithms generate three scores

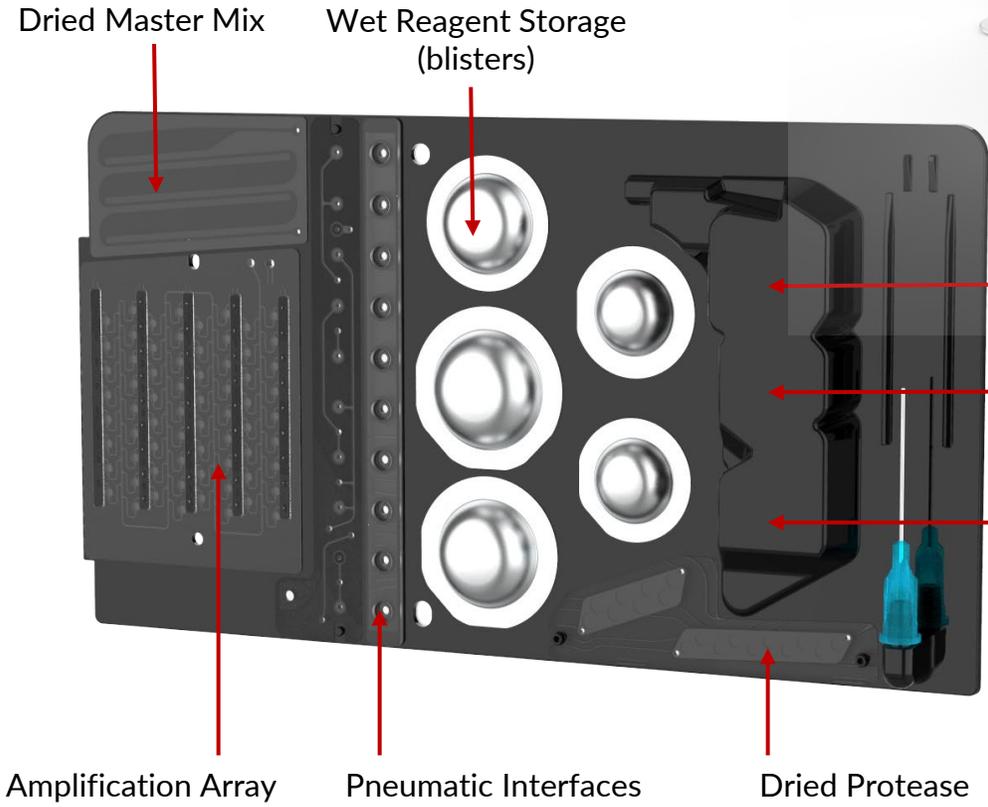


- 6 Results can be delivered to a patient's electronic medical record (or viewed on screen or printed) and are accessible in a patient's laboratory results section.

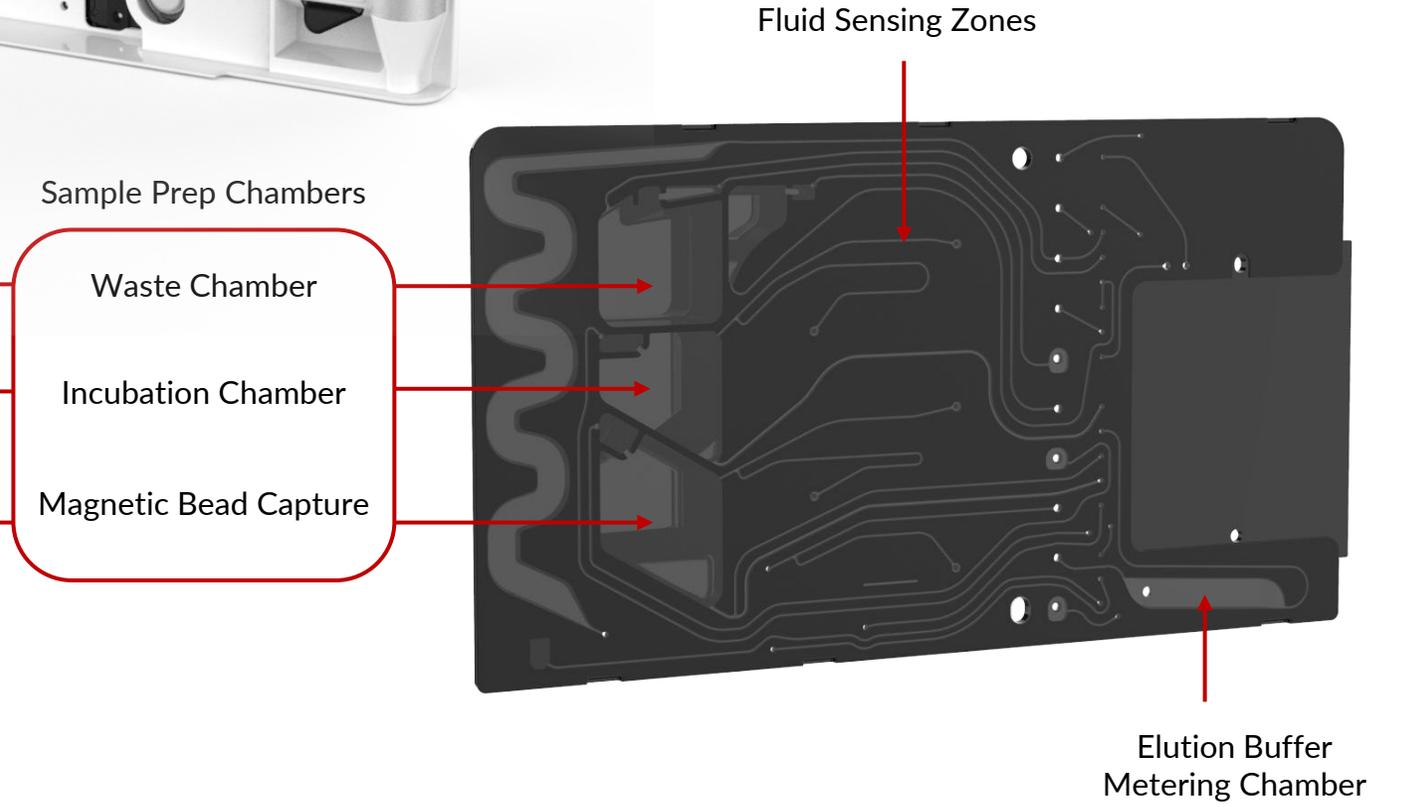


TRIVERITY CARTRIDGE OVERVIEW

Front View



Rear View



29 HOST RESPONSE mRNA MARKERS IN THE TRIVERITY TEST¹⁻⁶

The genes in the test are associated with relevant inflammatory pathways

Relevant genes by pathways:

Cellular metabolism and homeostasis	Intracellular signaling and antiviral response	Immune receptors	Inflammatory mediators	Immune cell interaction
<ul style="list-style-type: none">• ANKRD22• XAF1• ZDHHC19• ARG1• RSAD2• CTSL1• PSMB9• KCNJ2• TDRD9	<ul style="list-style-type: none">• IFI44L• HERC5• BATF• OLFM4• IFI127• OASL• IFI44	<ul style="list-style-type: none">• LY86• C3AR1• CD163• IL1R2• IL18R1	<ul style="list-style-type: none">• TGFB1• DEFA4• S100A12• 1SG15	<ul style="list-style-type: none">• HLA-DMB• CEACAM1• JUP• CLEC5A

TRIVERITY ACCURACY ESTABLISHED IN MULTICENTER STUDY

The genes in the test are associated with relevant inflammatory pathways

Clinical performance by interpretation band
(Particularly high accuracy in 0-10, the “very low”
and 40-50, the “very high” bands)

SEPSIS-SHIELD
Study (NCT04094818)
Results¹

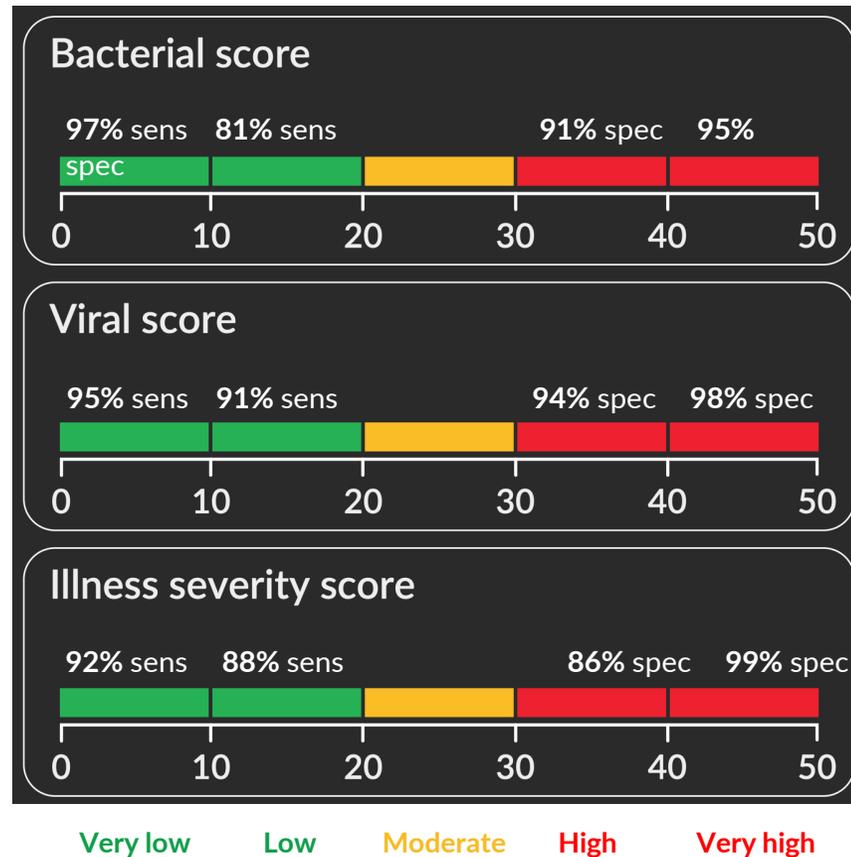
N=1,222 patients from
22 sites (21 in the US)

Broad inclusion criteria:

ED presentation with: Suspected
infection and 1+ VS abnormal

OR

Blood culture order and 2+ VS
abnormal



Comparator

Physician-adjudicated
infection (consensus)

Need for mechanical
ventilation, vasopressors or
renal replacement therapy in
the next seven days.

SUMMARY

- Patients frequent the Emergency Department suspected of acute infections and sepsis
- Today, improvement is needed with respect (1) antimicrobial stewardship, (2) diagnostic stewardship, (3) patient disposition decisions (admit vs discharge) (4) SEP-1 bundle compliance
- The TriVerity Test is an in-vitro diagnostic that measures 29 host response genes and applies machine learning-derived algorithms to inform on the likelihood of a bacterial infection, viral infection and illness severity (defined as need for mechanical ventilation, vasopressors or renal replacement therapy in the next seven days). The TriVerity™ test received 510(k) clearance on January 10, 2025
- The TriVerity test is performed on a whole blood sample in the TriVerity Cartridge using the Myrna Instrument in approximately 30 minutes
- The TriVerity Test is indicated for adult patients presenting to the emergency department suspected of an acute infection and one abnormal vital sign or suspected sepsis and two abnormal vital signs
- In a 22-center, 1,222 patient study, the TriVerity Test demonstrated excellent clinical performance, with sensitivity and specificity of over 90% in outer bands across its three scores
- There is no existing code that accurately describes the TriVerity Test. Thus, we request the creation of a new ICD-10-PCS code that describes this type of test