

Drive More Efficient Clinical Action by Streamlining the Interpretation of Test Results

Background

The availability of rapid, multiplexed technologies for the comprehensive detection of infectious diseases is creating a paradigm shift regarding the role of the laboratory in impacting patient outcomes, infection control and antimicrobial stewardship. The drastically improved turnaround time from test order to reported result removes the laboratory as a bottleneck in patient care. However, this new capability has created the need for enhanced synergy between the laboratory, nurses, physicians, pharmacy, and antimicrobial stewardship programs (ASP)¹.

One area where this is particularly relevant is in the diagnosis and treatment of sepsis. While rapid, multiplex molecular tests can identify the potential causative agent and associated resistance genes nearly 1-2 days sooner than traditional methods^{2,3}, the rapid report may not drive rapid clinical decisions such as modification of antimicrobial therapy. Some healthcare providers have challenges linking a rapid diagnostic result to a patient treatment action. Again, in the example of sepsis diagnosis, the positive identification of the potential causative organism and resistance gene may be provided within 3 hours after gram-stain, but the physician may be unable to act on the result without guidance from pharmacy, infection control, or an ASP. In the most extreme case, if the result is provided at 4 PM, but pharmacy consultation and action is delayed until 7 AM the next day then the benefit of a <3 hour diagnostic result is negated by a treatment bottleneck of 15 hours.

The ePlex instrument delivers several key solutions designed for the patient and

optimized for the lab. Given the prior examples, ePlex instrument software can offer a novel solution for Patient Centered Care and Sample-to-Answer benefits with the ePlex Templated Comments (TC) module. The ePlex TC module delivers the capability to match an assay detection result with user-customizable algorithms which can drive patient treatment immediately without the need for further consult or delay. Throughout this white paper, we will demonstrate the capability and unique benefits the ePlex TC module can deliver to healthcare providers.

Templated Comments Module

The ePlex TC module provides a rules-based engine which enables users to create customizable conditions based on ePlex panel results to communicate interpretive comments on the result report and through to the laboratory information system (LIS). Users can define rules in a logical IF, THEN, ELSE structure. In the following example of using the ruled-based engine to enable automation of the local antibiogram and related treatment algorithm, the ePlex TC module could be customized as follows:

- IF: Enterococcus, Detected, AND (vanA Detected or vanB Detected)
- THEN add comment: Vancomycin-resistant Enterococcus, semi-urgent result, implement contact precautions, preferred therapy ampicillin, consult ID if require alternative drug of choice.

The goal of including templated comments directly on the results report is to drive more efficient clinical action by streamlining the interpretation of results. While the ePlex TC

module can have multiple applications, the most obvious impact is to enable laboratories to automate collaboration with infectious disease clinicians, infection control and pharmacy services to guide clinicians with crucial information to make more rapid clinical assessment and optimize patient care.

Implementation of Templated Comments

As part of GenMark's commitment to Long-Term Partnership, we provide hands-on training and tools to configure and implement the ePlex TC module. We will help facilitate engagement with Pharmacy, Infectious Disease and Antimicrobial Stewardship teams regarding the functional capability of Templated Comments and what that may provide for your institution. Each institution can align the antibiogram to specific targets with a recommended clinical action plan. The outcome of these discussions will be a blood culture identification recommended action plan which we can then load directly into the ePlex TC module. GenMark will train your team on how to enter and edit this information directly in the ePlex TC module and will assist with educating patient care staff on the implementation, utilization and benefits of templated comments.

Impact of Templated Comments in the Hospital

The addition of templated comments onto the results report can streamline patient management and provide greater synergy between the laboratory, treating physician, pharmacy, and antimicrobial stewardship team. Instead of receiving just an organism and resistance gene identification, the physician will now see how these other key stakeholders would interpret and provide direction on the result immediately upon receiving the report via the LIS. Typically, without this type of result driven action plan on the report, the physician would consult other groups (pharmacy, infectious disease) or await direction from pharmacy and others

leading to delays to optimal therapy for the patient. ePlex Templated Comments removes that potential bottleneck and enhances the overall management of sepsis patients.

Several studies have highlighted the importance and impact of combining rapid multiplex molecular BCID testing with an effective antimicrobial stewardship program (ASP) and rapid action plan. One such study highlighted reduction in time to effective therapy and higher rates of de-escalation when results were coupled with ASP³. Another study concluded rapid molecular results are more impactful at influencing clinical decision making when delivered with an action plan or automated antimicrobial stewardship program in real-time². The rapid detection of the organism and antimicrobial resistance genes when applied with local epidemiology of antimicrobial resistance, agreed 100% with subsequent phenotypic susceptibility testing⁴, thus, allowing for targeted therapy recommendations directly in the results report to the clinician.

Given the increasing threat of antimicrobial resistance, many countries are instituting new standards regarding Antimicrobial Stewardship. In the US, the Joint Commission standards for medication management and Antimicrobial Stewardship is just one example of increasingly stringent requirements⁵.

The ePlex BCID Panel* with the ePlex TC module can:

- Provide rapid detection of >95% of the organisms responsible for sepsis and BSI, saving days compared to conventional culture methods
- Automate the interpretation of the local antibiogram to guide the choice of appropriate antimicrobial therapy based on ePlex Panel results
- Integrate rapid results with automated ePlex Templated Comments to fast-track treatment intervention improving Antimicrobial Stewardship Programs and Infection Control

*ePlex BCID Panels are CE-IVD. Not available for sale in the US.

Case Study Examples:

The following two theoretical cases illustrate the impact of ePlex BCID Panels with the ePlex TC module compared to alternative approaches to blood culture identification testing for sepsis. In both theoretical cases, ePlex BCID Panels led to more rapid identification of both the causative organism and resistance gene than the alternative

algorithms. The use of a prepared templated comment action plan led to more rapid physician action, Infectious Disease physician consult and off-hour clinical intervention. In the case study examples, the combination of the rapid and comprehensive ePlex BCID Panel with prepared templated comments led to 10-12x reduction in time from test order to physician report and clinical intervention.

Case Study #1: ePlex BCID Panel compared to Traditional Culture and AST

Patient arrives to emergency department with suspected sepsis at 07:00 and blood bottles are collected and incubated at 08:00 and patient is started on broad spectrum antibiotics. Blood bottles ring positive at 15:00 (7 hours after incubation) beginning the diagnostic synopsis and timeline below:

	Blood Bottle Positive	Gram Stain	Organism ID ¹	Resistance / Susceptibility	Antibiogram Based Action Plan to Physician	Physician Clinical Intervention	Summary
ePlex BCID result	N/A	Gram-positive cocci	<i>E. faecalis</i>	<i>vanA</i> detected	Vancomycin-resistant <i>Enterococcus</i> , implement contact precautions, preferred therapy Ampicillin	Removed broad spectrum Piperacillin-Tazobactam + Vancomycin, started Ampicillin	Administered targeted therapy at 10.5 hours after patient blood draw
ePlex BCID timeline 00:00 hr, [T=hr:min]	15:00 [T=0]	15:30 [T=0:30]	17:20 [T=2:20]	17:20 [T=2:20]	17:50 [T=2:50]	18:20 [T=3:20]	Identification & ASP driven action in <3.5 hours
Traditional Culture & AST²	N/A	Gram-positive cocci	<i>E. faecalis</i>	Ampicillin MIC=1 Imipenem MIC=2 Meropenem MIC=8	Ampicillin 99% susceptible, MIC≤8	Removed broad spectrum Piperacillin-Tazobactam + Vancomycin, started Ampicillin	Administered targeted therapy at 52 hours after patient blood draw.
Traditional timeline 00:00 hr, [T=hr:min]	15:00 [T=0]	15:30 [T=0:30]	+1 day 09:30 [T=18:30]	+2 day 09:30 [T=42:30]	+2 day 11:30 [T=44:30]	+2 day 12:00 [T=45:0]	Identification and AST driven action in 45 hours

¹ ID identification

²AST antimicrobial susceptibility test

Case Study #2: ePlex BCID Panel compared to other multiplex molecular methods and traditional AST

A hospital patient's condition worsens to suspected sepsis at 18:00 and blood bottles are collected and incubated at 19:00 and patient is started on broad spectrum antibiotics. Blood

*ePlex BCID Panels are CE-IVD. Not available for sale in the US.

bottles ring positive at 07:00 the next day (12 hours after start) beginning the diagnostic synopsis and timeline below:

	Blood Bottle Positive	Gram Stain	Organism ID	Resistance / Susceptibility	Antibiogram Based Action Plan to Physician	Physician Clinical Intervention	Summary
ePlex BCID result	N/A	Gram-negative rod	<i>P. aeruginosa</i>	IMP detected	Organism resistant to carbapenems and other beta-lactams, implement contact precautions, consult Infectious Disease for colistin-polymyxin B + carbapenem	Removed broad spectrum Piperacillin-Tazobactam + Tobramycin + Vancomycin, started colistin-polymyxin B + meropenem	Isolation & administered targeted therapy at 16 hours after patient blood draw
ePlex BCID timeline 00:00 hr, [T=hr:min]	07:00 [T=0]	07:30 [T=0:30]	09:20 [T=2:20]	9:20 [T=2:20]	9:50 [T=2:50]	11:00 [T=4:00]	Identification & ASP driven action in 4 hours
Other Multiplex Molecular & Traditional Methods	N/A	Gram-negative rod	<i>P. aeruginosa</i>	KPC negative ¹ ; Reflex to culture/AST ² Imipenem MIC=64 Meropenem MIC=32 Ceftriaxone=64	Ceftazidime/avibactam >95% susceptible, MIC<1	Removed broad spectrum Piperacillin-Tazobactam + Tobramycin + Vancomycin, started colistin-polymyxin B + meropenem	Delayed isolation & administered targeted therapy at 59 hours after patient blood draw
mMDx + Traditional Timeline 00:00 hr, [T=hr:min]	07:00 [T=0]	07:30 [T=0:30]	09:00 [T=2:00]	+1 day 21:00 [T=38:00]	+2 day 05:00 [T=46:00]	+2 day 06:00 [T=47:00]	Identification and AST driven action in 47 hours

¹ID identification

²only carbapenem resistance marker on panel

³AST antimicrobial susceptibility test

Conclusion:

GenMark is dedicated to Patient Centered Care and, with ePlex BCID Panels combined with the ePlex TC module, we deliver the only solution for rapid, comprehensive routine blood culture identification and clinical decision making for suspected sepsis patients. Getting results quickly removes the laboratory from being a bottleneck in executing more effective Antimicrobial Stewardship Programs and driving rapid clinical action. However, rapid BCID results are most effective when all stakeholders in the

hospital work to automate the local antibiogram and design an action plan to help treating physicians utilize these rapid results to improve patient treatment.

GenMark is ready to help educate your hospital patient care staff regarding ePlex solutions for sepsis. We can also deliver a complete implementation plan to deliver a more effective way to manage sepsis in your hospital. Contact us for more information and details at www.genmarkdx.com/ePlexsepsissolutions.

References:

1. Sullivan, Kaede V. (2017) Clin Micro Newsletter 39 (16):125-129.
2. Banerjee, et. al., (2015) Clin Infect Dis. 61 (7):1071-80
3. MacVane, S. et al., (2016) J Clin Micro 54 (10):2455-2463.
4. Rodel, et. al., (2016), Diag Micro and Inf Dis, 84:252-257.
5. Joint Commission Perspectives®, July 2016, Volume 36, Issue 7