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White Paper

Flexible Respiratory Pathogen Testing: Why Clinical Laboratories No Longer Have To Settle

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About St. Mary's

St. Mary's Hospital and Regional Medical Center is a 346-bed hospital in Grand Junction, Colorado, and is the largest hospital between Salt Lake City, Utah, and Denver, Colorado. St. Mary's is a Level II Trauma Center, Level III NICU, JC Accredited Stroke Center, and Certified Chest Pain Center, offering 24/7 OB Hospitalist Services, Brain and Spine Services, Heart and Vascular Services, Oncology Clinics, a full range of Imaging Services, Orthopedic Services and a Wound Clinic. In addition, St. Mary's hosts a Family Residency Program and two clinics for the underinsured or non-insured patients of Mesa County.

Executive Summary

The clinical microbiology laboratory is tasked with finding a testing solution that addresses the needs of the clinician and patient, and provides an optimal performance at the lowest cost and with the lowest workflow burden on the lab. This can be especially challenging for certain disease states, including respiratory tract infections. Until recently, none of the commercially available multiplex molecular tests for respiratory pathogens alone could provide the flexibility to satisfy the clinician's desire for both targeted and broad respiratory pathogen testing in a cost-effective manner for the lab and patient. The VERIGENE® Respiratory Pathogens *Flex* Test (RP *Flex*) is the first commercial test that allows the user to choose any combination of 16 viral and bacterial targets for an individual sample at the time of test ordering, based on the clinician and patient's needs and pay just for the targets reported. With RP *Flex*, clinical laboratories of all sizes can offer a respiratory pathogen testing algorithm that fully addresses clinician and patient needs in a format that minimizes the financial and resource burden on the laboratory.

Introduction

The clinical microbiology laboratory faces the challenging task of finding feasible diagnostic solutions that best satisfy the needs of the healthcare providers and the patients they serve. This can be especially challenging for certain disease states, including respiratory tract infections (RTIs). Considering the wide array of known respiratory pathogens, it is often difficult for a clinician to determine optimal patient management based on clinical presentation alone. Until recently, laboratories have not had access to diagnostics that allow them to sufficiently help clinicians with patient management decisions for suspected RTIs. Molecular diagnostics, specifically polymerase chain reaction (PCR) tests, have emerged as the first viable replacement to culture-based diagnostics because these tests can deliver accurate results for a broad array of respiratory pathogens in a more clinically meaningful turnaround. The adoption of PCR-based testing has increased significantly over the past decade as the complexity of these tests have reduced and as more and more publications have pointed to their ability to improve clinical and economic outcomes.

There is now an abundance of multiplex molecular options available for many infectious disease states, including RTIs. However, none of the currently available respiratory pathogen tests alone provide laboratories with a complete solution to address the full spectrum of provider, patient, and laboratory needs. Most labs are unable to purchase and support a combination of the commercially available tests to provide the optimal respiratory testing algorithm and are forced to settle for a sub-optimal testing algorithm. Ideally, a single respiratory pathogen test would meet the needs of the provider and the patient and provide both targeted and broad respiratory pathogen testing at a price point that is cost-effective for both types of testing. This would ultimately minimize unnecessary cost to the patient and provide a testing algorithm favorable to the public and private payers. In addition, this would minimize the resource investment required for the lab to implement an ideal testing algorithm.

Figure 1: Partial of the available non-flexible respiratory testing options

Background

There are a number of challenges specific to RTIs that can be addressed with different testing options provided by the laboratory. The lab has the difficult task of choosing a solution that best addresses the needs of the provider and patient using the resources available to the lab.

For the Clinician

- Clinician ordering patterns are impacted by a number of different factors, including seasonality, positivity, patient demographics, turnaround time, and patient history.
- For outpatients, clinician ordering patterns show that influenza and RSV are of greatest interest, as detection may impact patient management decisions, whereas detection of other viral pathogens may not.
- For inpatients, clinicians often order testing for a broader set of respiratory pathogens because positive identification of a pathogen could limit downstream testing, prevent unnecessary use of antibiotics, and impact patient cohorting.
- In order to keep healthcare costs down, clinicians want to be able to order only what is necessary to optimally treat each patient.

For the Patient

- The lab must focus on choosing a respiratory testing algorithm that is cost-effective for the patient, as the recent shift to high-deductible healthcare plans now requires patients, rather than insurance companies, to pay for more of the laboratory-based diagnostic charges.

For the Laboratory

- Labs must equip themselves with the appropriate diagnostics to support the decision-making process of the clinician in order to minimize the inappropriate or unnecessary use of antimicrobials and unnecessary cost to the patient.
- In many labs, the current solution for respiratory pathogen testing is to choose between utilizing multiple platforms, combining an abbreviated panel with send out testing, or running a one-size-fits-all panel for all patients.
- With a constant downward pressure on reimbursement, none of these options offer a sustainable, long-term solution.

Table 1: Examples of respiratory testing algorithms used prior to availability of flexible panels

Testing Algorithm	Pros	Cons
Send out all respiratory tests to reference lab	• Labs with very limited resources can execute this algorithm	• Turnaround time (2-3 days) not clinically meaningful • Expensive for the clinical value provided
Rapid flu & RSV in-house, send out remaining tests to reference lab	• Reduced turnaround time (TAT) for flu & RSV testing • Satisfy Emergency Department's (ED) desire for < 60 minute TAT • Provide some testing closer to patient to impact clinical management decisions	• Turnaround time (2-3 days) not clinically meaningful • Expensive for the clinical value provided • Sensitivity of rapid tests not ideal for optimal patient management
Molecular flu +/- RSV in-house, send out remaining tests to reference lab	• Reduced TAT for flu & RSV testing • Highly sensitive molecular testing for flu +/- RSV • Provide flu +/- RSV testing with strong sensitivity closer to the patient	• Turnaround time (2-3 days) not clinically meaningful for send out tests • Expensive for the clinical value provided
Broad molecular panel for all patients	• Reduced TAT for all respiratory pathogen testing • Highly sensitive molecular testing for flu +/- RSV	• Expensive cost of testing to lab and patient • Testing is often times too broad for a patient
Molecular flu +/- RSV and broad molecular panel	• Reduced TAT for all respiratory pathogen testing • Highly sensitive molecular testing for all pathogens • Minimizes unnecessary testing cost to patient	• Expensive to acquire multiple molecular platforms • Extra quality control testing, proficiency testing, lab technician training, and inventory management of reagents

Solution

The VERIGENE Respiratory Pathogens *Flex* Test (RP *Flex*) is a sample to result respiratory panel for 16 of the most common viral and bacterial respiratory pathogens, and is designed in a way that provides laboratories with the flexibility to dictate how the test can be used to address the specific needs of a lab's provider network and patient population.

Table 2: Viral and bacterial targets included on VERIGENE® RP *Flex*

VERIGENE® RP *Flex*	
Viruses	
Adenovirus	Parainfluenza 2
Human Metapneumovirus	Parainfluenza 3
Influenza A	Parainfluenza 4
Influenza A (subtype H1)	Rhinovirus
Influenza A (subtype H3)	RSV A
Influenza B	RSV B
Parainfluenza 1	
Bacteria	
Bordetella pertussis	*Bordetella parapertussis/ bronchiseptica*
Bordetella holmesii	

VERIGENE RP *Flex* Design Features

- Each RP *Flex* cartridge contains a broad panel of 16 viral and bacterial targets.
- Any combination of targets can be selected for an individual sample at the time of test ordering.
- Additional results not originally reported can be reflexed instantly without having to run an additional test.
- The lab pays only for the targets selected for reporting.
- By consolidating all respiratory testing need on to one platform, labs can minimize quality control testing, proficiency testing, technician training, and inventory management time.

Advantages for the Clinician

- Sensitive and cost-effective targeted and broad molecular testing for respiratory pathogens for all patients.
- Instant reflexing capabilities allow clinicians the ability to start with a targeted test and instantly reflex to a broader test if initial results are negative.
- ED clinicians can continue ordering rapid immunoassays for outpatient influenza and RSV testing.

Advantages for the Patient

- Patients bear a lower cost burden, since clinicians can optimize patient management without having to order unnecessary testing.
- This is especially critical at hospitals like St. Mary's, where we serve a diverse patient population that includes underinsured or uninsured patients.

Advantages for the Laboratory

For St. Mary's, the RP *Flex* algorithm is a comprehensive, clinically meaningful, and cost-effective solution for respiratory pathogen testing.

Impact at St. Mary's:

At St. Mary's, RP *Flex* has allowed the lab to provide an optimal respiratory pathogen testing algorithm for the clinicians, patients, and laboratory.

Table 3: Current respiratory testing algorithm at St. Mary's

Test Orderables	Testing Platform	Targets Reported
Rapid – Flu	BD Veritor	Influenza A, Influenza B
Rapid - RSV	BD Veritor	RSV
PCR – Flu	VERIGENE® RP *Flex*	Influenza A, Influenza A/H1, Influenza A/H3, Influenza B
PCR – RSV	VERIGENE® RP *Flex*	RSV A, RSV B
PCR – Flu & RSV	VERIGENE® RP *Flex*	Influenza A, Influenza A/H1, Influenza A/H3, Influenza B, RSV A, RSV B
PCR - Bordetella	VERIGENE® RP *Flex*	*Bordetella pertussis, Bordetella parapertussis / bronchiseptica, Bordetella holmesii*
PCR – Full Respiratory Panel	VERIGENE® RP *Flex*	All RP *Flex* viral and bacterial targets

It would not be possible with the resources we have at St. Mary's to provide this diagnostic value if we could only choose from the fixed-panel, fixed-cost multiplex respiratory pathogen panels available. With the testing algorithm now in place, we are still able to impact ED clinician management decisions through use of rapid flu and RSV tests for lower-risk outpatients and then provide targeted and broad respiratory pathogen molecular testing using RP *Flex* for the remainder of our patient population. We do not restrict test ordering of either the rapid or molecular testing options to our clinicians. As expected, we do see distinct ordering patterns representative of the varying needs of the patient population we serve.

Based on the 2013 test volumes for molecular respiratory pathogen test orders, use of VERIGENE RP *Flex* will provide an $83,017 annual cost savings compared to running a molecular influenza and RSV test in-house and sending out all other respiratory tests to a reference laboratory. Compared to running a broad respiratory pathogens panel for all respiratory work-ups, RP *Flex* will provide a $131,350 annual cost savings. By performing both targeted and broad respiratory pathogen testing using just one test on one molecular

Table 4: Cost analysis of the respiratory pathogen diagnostic testing algorithms considered for implementation at St. Mary's

Test Algorithm Considered	Flu PCR	RSV PCR	Flu/RSV PCR	Adv PCR	EV PCR	*Pertussis* PCR	Broad RVP	Total
# of tests/year	1,244	232	2	135	37	2	77	1,729
Flu/RSV PCR in-house + send out	$65			$230	$174	$72	$555	$176,437
Broad RVP only in-house	$130							$224,770
VERIGENE® RP *Flex* in-house	$50	$50	$70	$50	$50	$50	$130	$92,650

platform, the burden on the lab is minimized, reducing the amount of time and resources that would have to be devoted to quality control testing, proficiency testing, technician training, and inventory management.

Conclusion

Given the wide range of viruses and bacteria that can cause respiratory infections, the varying seasonality of these pathogens, and the diverse needs and preferences of clinicians and patients, clinical laboratories have sought testing algorithms that offer as much flexibility as possible. The ability to meet clinicians' needs by pre-defining multiple orderables from a single test on a single platform is advantageous to clinicians, patients, and the laboratory. Clinicians can choose from a variety of test orderables, all of which provide accurate results in a timely manner. Patients do not have to pay for unnecessary testing. And the laboratory can offer a number of different testing options without having to maintain multiple platforms and manage multiple tests. VERIGENE RP *Flex* has allowed community hospitals like St. Mary's to offer a full range of rapid, molecular, respiratory testing options to its clinicians and patients that would not have been possible before. With RP *Flex*, each institution can adopt the respiratory testing solution that best fits its clinicians' needs, while keeping costs lower for the patient and efficiently utilizing limited resources in the laboratory.