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For Respiratory Testing, a Flexible Model Helps Laboratories Address the Reimbursement Responsibility

Customization of targets aligns with diagnostic stewardship goals and reins in healthcare costs

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The COVID-19 pandemic had an unexpected impact on respiratory testing: it stabilized what had previously been an uncertain landscape for syndromic panel reimbursement. Payers had long resisted routine coverage of these large panels, but with the new SARS-CoV-2 target needed alongside standard testing for influenza A, influenza B, and respiratory syncytial virus (RSV), suddenly, a syndromic panel for respiratory testing was considered useful and reasonable.

With the new reimbursement model, clinical laboratories may find it most straightforward to run syndromic panels for all respiratory infection cases. However, syndromic panels are not covered for all patients. Some medical policies only provide large panel coverage for patients who are immunocompromised or at high risk for complications. Additionally, syndromic panels may include targets considered inappropriate according to clinical testing guidelines, making them inconsistent with diagnostic stewardship goals. And in many—if not most—cases, they are not a cost-effective solution. The lack of flexibility in syndromic panels results in providers requiring multiple testing platforms or panels to meet the needs of their varied patient populations.

In an era of staffing shortages, there is a clear need for a single test that meets all respiratory infection testing. Now, the LIAISON PLEX® system offers the ease of use of a single assay, while providing the flexibility to match diagnostic stewardship goals. Clinicians and laboratorians are given the ability to customize targets based on appropriate clinical guidelines and those best suited to seasonality and unique patient populations. This option replaces the need for other syndromic panels, offering the ability to lower costs by running targeted panels with fewer targets while enabling users to opt for the full panel when needed. Flexible testing empowers providers to make testing decisions based on their expertise and clinical impression of the patient in front of them so they no longer have to rely on manufacturers to determine for which targets they test.

Key challenges in clinical testing

As clinical teams aim to identify the best fit for their respiratory testing needs, 3 relevant healthcare trends can help inform the selection process.

1. Clinical Laboratory Personnel Shortages.

Staffing shortages have always been common in clinical labs, but labor shortages have worsened since the pandemic. Because of this, laboratories may want to prioritize tests that are easy to use and require minimal hands-on time.

2. Rising healthcare costs.

As most aspects of healthcare are becoming more expensive, there has been increasing scrutiny about where and how money is spent. It is essential to find ways to be cost-effective—both in the interest of sustainability within each healthcare system and for the patients receiving bills for laboratory medicine.

3. Patients as consumers

Since the height of the COVID-19 pandemic, patients have become savvier than ever about diagnostic testing and the information they expect it to provide. In many cases, patients now have direct access to laboratory reports. Overall, patients are increasingly interested in learning about their test results, including the specific pathogen causing their infection.

The problem with one-size-fits-all testing

Real-world clinical data highlights that one-size-fits-all testing is not ideal for respiratory infections. In studies conducted at 6 geographically diverse clinical sites in the United States during the 2022-2023 respiratory season, test results illustrated the differences in pathogen prevalence by patient demographics (Table 1). Collectively, the studies encompassed 1,520 nasopharyngeal swabs analyzed as part of the FDA 510(k) submission for the Diasorin LIAISON PLEX® Respiratory *Flex* Assay, which has now been cleared by the FDA. The test includes 14 viral and 5 bacterial targets.

Traditional syndromic testing falls short in terms of both clinical efficiency and cost-effectiveness. During flu season, for example, running a targeted panel for influenza A/B testing is much more cost-effective than running a full syndromic panel for a patient with respiratory symptoms. Most testing platforms provide both small and large respiratory panels, assuming that the platform has sufficient ability to reflex from a targeted panel to a full syndromic panel. However, using a standard targeted panel provides a much lower detection rate than a custom targeted panel and forces providers to rely on a large syndromic panel far more often, resulting in significant target redundancy between panels, increased inefficiency, and higher costs of testing (Table 3). For example, in the clinical data for a pediatric population, a standard targeted panel captured the cause of disease just 24.9% of the time compared to a custom targeted panel that would have captured 85.3% of positives. This represents a 60.4% reduction in the need to reflex to a syndromic panel. Shifting testing volume from 789 syndromic tests to just 154 could represent significant cost savings—as much

as $88,265 in this small sample of 1,050 pediatric patients (Table 4).

A retrospective analysis by Gonzalez and Amicarelli (2024)* revealed that viruses were overwhelmingly responsible for respiratory infections, with bacterial targets testing positive in less than 1% of all samples evaluated. However, there were significant statistical differences in the prevalence of pathogens among young, adult, and elderly patients. Patients younger than 21 years had the highest rate of rhinovirus/enterovirus at 27%; the same pathogens were positive in just 14% of adult samples and 9% of elderly patient samples. Meanwhile, influenza A was most common among the elderly, found in 33% of samples, but less prevalent in adults (25%) and in young patients (15%).

The data were even more striking for SARS-CoV-2, which was identified in 40% of elderly patient samples, 35% of adult samples, and just 8% of young patient samples. Age-related differences were also noted for adenovirus and human metapneumovirus.

*Gonzalez, K., & Amicarelli, G. (2024). Diagnostic Stewardship for Syndromic Respiratory Testing: Flexibility is the Name of the Game [White paper]. Diasorin.

	Pediatric (N=1050)			Adult (N=320)			Senior (N=150)		
	Tier	**N**	**%**	**Tier**	**N**	**%**	**Tier**	**N**	**%**
Adenovirus	1	157	15.0	2	11	3.4	2	0	0.0
Bordetella holmesii	3	0	0.0	3	0	0.0	3	0	0.0
Bordetella parapertussis	2	7	0.7	3	0	0.0	3	0	0.0
Bordetella pertussis	3	0	0.0	3	0	0.0	3	0	0.0
Chlamydia pneumoniae	3	0	0.0	3	0	0.0	3	0	0.0
Human coronavirus	1	94	9.0	1	24	7.5	1	7	4.7
Rhinovirus/enterovirus	1	284	27.3	1	46	14.4	1	14	9.3
Human metapneumovirus	1	106	10.1	1	20	6.3	2	5	3.3
Influenza A	1	79	7.5	1	41	12.8	1	25	16.7
Influenza A subtype H1	2	18	1.7	1	14	4.4	1	6	4.0
Influenza A subtype H3	2	63	6.0	1	26	8.1	1	19	12.7
Influenza B	3	6	0.6	2	2	0.6	2	0	0.0
Mycoplasma pneumoniae	3	0	0.0	3	0	0.0	3	0	0.0
Parainfluenza 1	2	10	1.0	2	1	0.3	2	0	0.0
Parainfluenza 2	2	6	0.6	2	5	1.6	2	1	0.7
Parainfluenza 3	2	36	3.4	2	6	1.9	2	0	0.0
Parainfluenza 4	2	8	0.8	3	1	0.4	3	0	0.0
RSV	1	94	9.0	2	11	3.4	1	13	8.7
SARS-CoV-2	1	82	7.8	1	112	35.0	1	60	40.0

Table 1: Example panel composition by age group, grouped into 3 tiers based on prevalence

While a syndromic panel deployed for each patient would likely have detected all of these pathogens, it would not have been clinically appropriate in light of the low prevalence of bacterial targets, for example. It would also have been far more expensive than necessary. A targeted approach would be more fiscally responsible, but this data clearly indicates that a different group of targets would be clinically appropriate for each category of patient as well (Table 1). The ability to customize testing by patient demographic factors and season would be quite valuable, both for the diagnostic stewardship goal of using the right test for the right patient and for the general goal of reducing healthcare costs.

	Population	Pediatrics (N=1050)		Adults (N=320)		Seniors (N=150)	
		N	%	N	%	N	%
With Multiple Systems	Targeted[a]	261	24.9	166	51.9	98	65.3
	Syndromic	789	75.1	154	48.1	52	34.7
Using LIAISON PLEX® System with *Flex*™ Testing	Tier 1[b]	896	85.3	283	88.4	144	96.0
	Tier 2[c]	142	13.5	36	11.3	6	4.0
	Tier 3[d]	12	1.1	1	0.3	0	0.0

Table 2: Reduction in syndromic testing shifted to smaller panels using the tiered testing approach

[a]Targeted testing assay: Influenza A, Influenza B, RSV A/B, SARS-CoV-2, reflexing all negatives to a syndromic respiratory panel
[b]Tier 1 assay including the 7 most prevalent targets by age group
[c]Tier 2 assay including the 5 next most prevalent targets by age group
[d]All Tier 1 and Tier 2 negatives reflexed to Tier 3, which included the remaining 7 targets on the panel

Systems			Age Group					
	Test		Pediatrics		Adults		Seniors	
		Cost per Test[a]	N	Total Cost	N	Total Cost	N	Total Cost
Multiple Systems	Targeted	$60	261	$15,660	166	$9,960	98	$5,880
	Syndromic	$139	789	$109,671	154	$21,406	52	$7,228

Table 3: Example cost(s) incurred relying on targeted testing reflexing to syndromic

[a]Mordor Intelligence - Global Infectious Disease Diagnostics Market Report; DeciBio ID DxBook 2024

System	Age Group									Cost Saved
	Pediatrics (N=1050)			Adults (N=320)			Seniors (N=150)			
	N	Cost	Savings	N	Cost	Savings	N	Cost	Savings	Total Savings
Tiered	154	$21,406	$88,265	37	$5,143	$16,263	6	$834	$6,394	$110,922

Table 4: Example cost(s) savings resulting from shifting to tiered testing and reducing syndromic testing volumes

Flex™ Testing is the answer

A novel approach to syndromic panel testing can help clinical labs respond to all of these challenges. *Flex*™ Testing is designed to streamline workflows with a single, easy-to-use assay while allowing lab staff to customize the results they view.

Here's how it works: clinical labs implement and verify a single syndromic panel for respiratory infections that covers the most common viral and bacterial targets. Each patient sample is processed and run on the entire panel. However, lab users choose the targets they want to view for each sample and pay based on the number of targets reported. Labs can choose target subsets, grouping them into pre-defined panels that can be run repeatedly (for example, a custom panel of the most likely pathogens for a healthy adult patient). In addition to the ability to select custom sub-panels from the broader panel, the other value in *Flex* Testing lies in what happens when initial testing occurs. If the results from a custom panel come back negative, lab members can use the test software to report other findings from the full panel without needing to run the assay again or collect another sample from the patient. Reporting more groups of targets will increase the cost for that particular sample, but overall, this approach will pave the way for significant savings compared to running standard syndromic panels for all patients.

Flex Testing brings about the next generation of respiratory diagnostics by providing laboratories with complete control over target selection and panel design. Panels can be selected at any time, allowing for customization based on seasonal variation, response to local outbreaks, and other changes in demand. Custom panels can be pre-defined for all lab users or selected ad hoc as needed. The more targeted the panel, the lower the cost of reporting results. Routinely available customizable panels might include selections such as a "first-tier winter panel," "reflex winter panel," or "persistent cough panel," among other groupings.

Flex Testing addresses key goals and challenges in clinical labs:

- A single, standard assay run on an automated, sample-to-answer system minimizes the need for technical manual intervention, complex training, or verification of multiple assays, responding to challenges associated with staff shortages.

- The ability to easily customize subsets of targets makes it possible to align with clinical guidelines, testing only the targets that are appropriate for each patient's circumstances and demographics.

- The *Flex* Testing model allows users to pay only for the targets they choose to have reported, addressing the constant issue of reining in costs.

- Easy customization of targets allows laboratories to adapt to rapidly changing reimbursement guidelines.

- Having ready access to other results from the full syndromic panel if the initial selection of targets comes back negative significantly reduces turnaround time by eliminating the need to run follow-up testing. This makes reporting relevant results in a clinically actionable time frame possible.

Try *Flex* Testing now

Flex Testing is not just an interesting concept; it's a readily available model that can now be implemented in clinical laboratories for respiratory infection testing. The sample-to-answer LIAISON PLEX® Respiratory *Flex* Assay from Diasorin run on the LIAISON PLEX® system has been cleared by the FDA for clinical laboratory use.

REFERENCES

1. Berry GJ, Jhaveri TA, Larkin PMK, Mostafa H, Babady NE. ADLM guidance document on laboratory diagnosis of respiratory viruses. [Epub] J Appl Lab Med May 2, 2024, as doi: 10.1093/jalm/jfae010. https://www.myadlm.org/science-and-research/academyguidance/laboratory-diagnosis-of-respiratory-viruses **2.** Gonzalez, K., & Amicarelli, G. (2024). Diagnostic Stewardship for Syndromic Respiratory Testing: Flexibility is the Name of the Game [White paper]. Diasorin.

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