Landscape Assessment: Diagnostics Manufacturer Profiles

2020

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Section 1. Introduction

Diagnostics are a fundamental component of successful epidemic and pandemic control strategies. Ideally, the necessary diagnostic tools would be ready at the locations where they will be needed, the diagnostics industry could mount a rapid and flexible response to developing new products, and would be able to successfully scale up production and distribution of any new diagnostic tools that are needed.

In the past, there has been a lack of incentives for companies to develop the types of diagnostics that might be needed. The SARS-CoV-2 pandemic has highlighted on a grand scale the barriers to diagnostic preparedness that are common to all outbreaks, and perhaps has created a unique moment when the commercial, political and technological drive are sufficient to overcome some of these barriers for influenza diagnostics.

The landscape of diagnostic developers is enormous, complex, fragmented and constantly evolving, with a variety of players that each has their own mix of products relevant to influenza diagnostics. For instance, since the beginning of 2020, over 2000 different organizations have introduced new SARS-CoV-2 diagnostic tests, and quite a few are turning their attention to influenza testing as well. The aim of the report is to provide clarity around which key players may already have the diagnostic tools that are needed, and which may have innovative technologies, development expertise, or manufacturing and distribution capacity to be able serve as a key partner in ensuring pandemic preparedness. While reasonably comprehensive, this assessment is not meant to consider all diagnostics developers and manufacturers in the global landscape.

In order to identify promising companies that might serve specific unmet needs for influenza pandemic preparedness, we first identified a “long list” of companies that are involved in influenza diagnostics, or have interesting technologies that might be applied to influenza testing of one form or another. We then created a set of criteria for scoring the companies in order to identify those with characteristics that are relevant to IVPP. The scoring criteria were then applied to the long list of companies.

Out of this process, we selected companies to receive a full profile in this report, and others that would receive a briefer review. The criteria and the scoring process are described in Section 3. The profiles of the companies that were selected are presented in Section 4. A landscape assessment is presented in Section 5, which provides a perspective on how the companies compare relative to one another. In Section 6, comparisons across companies continues for several factors that would influence the selection of key potential partners for pandemic preparedness. Finally, in Section 7, we present our conclusions and recommendations.

In order to set the stage and provide background for one of the scoring criteria, we first review the highest priority Use Cases that were identified in the Halteres report entitled “Landscape Assessment: Current State and Future Trends in Technologies for Influenza Diagnostics,” (August 31, 2020, prepared for WHO). These Use Cases are presented in the following section.

Section 2. Priority Use Cases

Having the right diagnostic tools ready when they are needed to confront a pandemic first involves identifying what tools may be needed. A broad framework for defining the tools needed to address a new pandemic was produced in the report “Landscape Assessment: Current State and Future Trends in Technologies for Influenza Diagnostics,” and is based on specific Use Cases. The highest-priority Use Cases were identified, along with a few examples of specific settings where it would be valuable to be able to conduct that type of testing (**Table 1)**.

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Table 1. First Priority Use Cases for Tests Important to Influenza Pandemic Preparedness

Use Case	Intended Use	Example Settings	Importance of Rapid TTR	Importance of Ease-of-Use
1. Diagnosis	1A. Diagnose infection with the IVPP or pandemic virus in symptomatic individuals	• Centralized: Hospital labs, reference labs, clinics, urgent care, military • Decentralized: Primary care, urgent care, EDs, congregate living/working settings, potentially pharmacies	High	• Low in centralized locations • High in decentralized locations
	1B. Test of cure			
2. Differential Diagnosis	2A. Detect and distinguish infection with IVPP or pandemic virus and other causes of ILI in symptomatic individuals	• Centralized: Hospital labs, reference labs, clinics, urgent care, military • Decentralized: Primary care, urgent care, EDs, congregate living/working settings, pharmacies	High	• Low in centralized locations • High in decentralized locations
	2B. Detect and distinguish infection with IVPP or pandemic virus from other strains of flu			
3. Screening of Non-Symptomatic Individuals	3A. Determine if a non-symptomatic individual has a current infection with IVPP or pandemic virus	• Centralized: Hospital labs, reference labs, public health, military • Decentralized: Pharmacies, outreach programs, congregate living facilities	High	• Low in centralized locations • High in decentralized locations
	3B. Determine if an individual has been previously exposed to the IVPP or pandemic virus	• Centralized: Public health labs, reference labs, military • Decentralized: back-to-work, back-to-school, testing for travel and other activity clearances, community testing,	High	• Low in centralized locations • High in decentralized locations
4. Triage	4. Determine if an individual with ILI symptoms is likely to be infected with influenza and warrants temporary isolation or other treatment pending confirmatory testing	• Decentralized: Congregate living/working settings, hospitals, quarantine facilities, primary care, urgent care, EDs, military	Very high	• Very high
6. Confirmatory Testing	6. Confirm positive results (e.g. from triage testing) and to resolve discrepancies with prior testing	• Centralized: Hospital labs, commercial labs, public health labs, military	Moderate	• Moderate
7. Gold Standard (NAT)	7. Serve as a comparator assay for new non-gold standard testing methods and to verify periodically the continued IVPP or pandemic virus coverage of products on the market	• Centralized: Hospital and commercial reference labs, clinical study sites, military	Low	• Low
8. Surveillance	8A. Incidence: determine incidence of IVPP or pandemic virus	• Centralized: Public health labs, reference labs, military	Low	• Low
	8B. Prior exposure: determine fraction of a population has been exposed to the IVPP or pandemic virus			
	8C. Drug Resistance: determine the incidence of anti-viral resistance in the IVPP or pandemic virus			
	8D. Sentinel surveillance: detect re-emergence of prior strains or emergence of novel new strains			

Rows with grey fill indicate Use Cases not commonly performed today but that could be important in the future. Use Case number 5, "Health Surveys, Health Questionnaires and Health Checks" was not included because the tools usually used are simple questionnaires or devices such as thermometers, which are outside the scope of this report. Abbreviations: ED, emergency departments. Sens, sensitivity. Spec, specificity. TTR, time-to-result.

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Section 3. Selection of Companies

The landscape of diagnostic developers is large and diverse, with a much smaller number of players that are most likely to make a significant difference in pandemic preparedness. The aim of this report is to develop a "short list" of companies that hold the most promise as potential partners in efforts to improve global pandemic preparedness. We first collected a list of companies that currently have products related to influenza diagnostics or that have technologies that could be applied to influenza diagnostics and potentially offer something unique or fulfill the needs of an unmet Use Case. Fifty-eight representatives have been identified and are included in the "long list" of companies (see the accompanying Excel document). In order to focus on the companies that should receive an in-depth analysis, and others which were selected for a briefer summary review, we developed a set of six criteria to score them. The criteria and scoring rubric are presented below in **Table 2**. Data used to score each of the companies was gathered from publicly available information or provided non-confidentially by the company.

Table 2. Criteria for Scoring the Companies

Criteria	Weight	Score	Definition	Rationale for Inclusion
1. Use Case Fit	**2**	0	Company does not have commercialized products (assays) for any of the priority Use Cases	To be of interest, the commercialized technology offered must potentially address one or more Use Cases. A weighting of 2 is suggested to stress the importance of this criterion when considering companies that might best be prepared to respond to future pandemics.
		1	Company has commercialized products (assays) for 1-2 priority Use Cases	
		2	Company has commercialized products (assays) for 3+ priority Use Cases and / or product may meet a critical unmet need	
2. Commercial Presence	1	0	Company has no or limited presence in LMIC markets	The ideal partner company will have a large and growing presence in LMICs, with business sustainability further driven by significant market share in HICs
		1	Small to medium diagnostic company with growing international presence in HIC and LMIC countries	
		2	Top 10 diagnostic company with large international presence in many HICs and LMICs	
3. Annual Revenues from ILI Product Sales	1	0	Annual ILI diagnostic product sales estimated to be <$10M USD (Pre-COVID-19 pandemic)	To help ensure continued interest in developing and commercializing ILI products, the ideal company will already have appreciable revenues from sales of ILI-related products.
		1	Annual ILI diagnostic product sales estimated to be $10M–$50M USD (Pre-COVID-19 pandemic)	
		2	Annual ILI diagnostic product sales estimated to be >$50M USD (Pre-COVID-19 pandemic)	
4. FDA EUA for COVID-19 Test	1	0	No, or Yes, but company offers no other directly relevant assays	Once the COVID-19 pandemic wanes, companies with revenues from SARS-CoV-2 tests will seek to preserve their market presence. Combination SARS-CoV-2 + Flu (A/B/RSV) testing is one means of accomplishing this. EUA status was scored as of the time of preparation of this report and may change in ensuing months.
		1	Yes, company offers a COVID-19 assay and one or more other relevant assays on the same diagnostic instrument platform	
		2	Yes, and the company offers or has announced a multiplex influenza + COVID-19 assay	

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Criteria	Weight	Score	Definition	Rationale for Inclusion
5. Innovative/ Unique Technology with Potential IVPP Application	1	0	No publicly known novel technologies in development, or company technology may have application in ILI testing but feasibility data not available and value in still unknown	Many new, innovative technologies are under development. Technologies for which feasibility data shows promise in satisfying priority Use Cases should be identified and, at a minimum, included on a watch list.
		1	Company is developing a new technology that could potentially improve upon current tests used for flu; only limited preliminary feasibility data is available publicly	
		2	Company is developing a new technology with clear application in ILI testing, especially one that could address unmet Use Case needs, and where product feasibility has already been reported publicly.	
6. Company utilized GISRS materials	1	0	Company does not appear to have used GISRS materials	A main focus of this project is to identify companies already utilizing GISRS materials or who are benefiting directly from GISRS materials
		1	Company appears to have benefited from GISRS materials	
		2	Company directly contracted with GISRS	

These criteria were applied to the long list of companies in the diagnostics landscape in order to create the "Short List" of representative companies to investigate in depth. The results of this scoring are shown in **Table 3**, which presents individual criteria scores as well as the total score. The column titled Short List indicates which companies are considered in greater depth in this report. The symbol(s) present in the Short List column indicates the reason(s) that the company was included.

Companies with a total score of 9 or greater received a **green check** in the Short List column. In addition to being used to generate the total score, two of the criteria were also used to specifically "rule-in" companies to the Short List. The scoring for the first of these criterion is shown in the column labeled "5. Unique Technology for IVPP." This rule-in was created to ensure that the Short List included some companies with innovative or unique technologies that might fill gaps in the current landscape of products. Companies with a score greater than 0 for this criterion are included in the Short List, regardless of their total score. These companies have a **pink check** in the Short List column.

The scoring for the second "rule-in" criterion is in the column labeled "6. Listed in IVTM." This rule-in was created to ensure that information is provided on all the companies that have already engaged with the WHO IVTM process. Companies that scored greater than 0 for this criterion are included in the Short List, regardless of their total score, and have an **orange check** in the Short List column.

In total, 27 of the starting 58 companies (47%) were included in the Short List, and either a detailed company profile or a brief summary review for each of these companies is presented in Section 4.

Very small companies with undifferentiated products were either not listed or not scored. In the diagnostics landscape, there are many small companies that produce only immunochromatographic devices, but their influenza products are not particularly differentiated. While some of these companies are included in the long list, many were not scored because their scores would all be essentially the same, and the exercise would not have added to an understanding of the landscape. In a similar fashion, there are many companies that produce reagent kits for detecting influenza virus via RT-PCR that consist solely of tubes of reagents to be used on instruments of the user's choice (i.e., "open" platforms), and whose performance is not particularly differentiated. While some of these companies are included as examples in the long list, not all of them were scored. Companies that were not scored are listed in the footnote of Table 3.

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Table 3. Results of the Scoring Process

	Companies (That Were Scored)	Short List	Total Score (Out of 14)	1. Use Case Fit	2. LMIC Commercial Presence	3. ILI Revenue	4. SARS-CoV-2 EUA	5. RULE IN - Unique Technology for IVPP	6. RULE IN – Listed in IVTM
Top-Tier in Influenza Dx by Estimated ILI Revenue	Abbott	1	**12**	4	2	2	2	0	2
	BD (Becton Dickinson)	2	**12**	4	2	2	2	0	2
	Danaher/Cepheid	3	**14**	4	2	2	2	2	2
	Quidel	4	**11**	4	1	2	2	0	2
	Qiagen	5	**11**	4	2	1	2	0	2
	Roche	6	**11**	4	2	1	2	0	2
Other Leading Diagnostic Companies	Bio-Rad		**2**	0	1	0	1	0	0
	bioMerieux (Biofire/Idaho Technologies)	7	**12**	2	2	2	2	0	2
	Diasorin (Focus Diagnostics)	8	**9**	4	1	1	1	0	2
	Hologic	9	**11**	4	2	2	1	0	2
	Perkin-Elmer		**7**	4	1	1	1	0	0
	Siemens (Fast-Track)		**6**	4	1	0	1	0	0
	Thermo/Remel	10	**6**	2	1	2	0	1	0
Example Companies with Immunochromatographic Devices	Access Bio	11	**5**	0	2	0	0	1	2
	Bionote		**2**	2	0	0	0	0	0
	Chembio		**3**	0	1	0	0	0	0
	Denka		**4**	2	1	0	1	0	0
	Ellum (Qiagen partner)		**1**	0	0	0	1	0	0
	Fujirebio		**5**	2	1	1	1	0	0
	Meridian (PBM product)		**3**	2	1	0	0	0	0
	Orasure (PBM product)		**3**	2	1	0	0	0	0
	Princeton BioMeditech (PBM)	12	**5**	2	1	0	0	0	2
	Response Biomedical	13	**5**	2	1	0	0	0	2
	SD Biosensor		**4**	2	1	0	1	0	0
	TAUNS		**2**	2	0	0	0	0	0

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	Companies (That Were Scored)	Short List	Total Score (Out of 14)	1. Use Case Fit	2. LMIC Commercial Presence	3. ILI Revenue	4. SARS-CoV-2 EUA	5. RULE IN - Unique Technology for IVPP	6. RULE IN – Listed in IVTM
	WondFo Biotech		**4**	2	1	1	**0**	0	0
Other Example Companies with NAT Platforms (Small and Medium Companies)	Applied BioCode		**3**	2	0	0	1	0	0
	Atila		**5**	4	0	0	1	0	0
	Biocartis		**3**	2	0	0	1	0	0
	Cue	14 ✓	**2**	0	0	0	1	1 ✓	0
	Genmark		**6**	2	0	2	2	0	0
	Luminex		**6**	4	0	1	1	0	0
	Mesa Biotech	15 ✓	**4**	2	0	0	1	1 ✓	0
	Novacyt		**7**	4	0	1	2	0	0
	R-Biopharm	16 ✓	**6**	4	0	0	0	0	2 ✓
	Scope Fluidics	17 ✓	**1**	0	0	0	0	1 ✓	0
	Seegene		**8**	4	1	1	2	0	0
	Sekisui	18 ✓	**5**	2	1	0	0	0	2 ✓
	Visby Medical	19 ✓	**2**	0	0	0	1	1 ✓	0
Other Companies with Potentially Unique Technology Offerings for IVPP	Ativa	20 ✓	**2**	0	0	0	0	2 ✓	0
	Clear Labs	21 ✓	**3**	0	0	0	1	2 ✓	0
	Inflammatix	22 ✓	**1**	0	0	0	0	1 ✓	0
	LumiraDx	23 ✓	**2**	0	0	0	0	2 ✓	0
	Oxford Nanopore	24 ✓	**6**	2	1	0	2	1 ✓	0
	Pinpoint	25 ✓	**2**	0	0	0	0	2 ✓	0
	Quanterix	26 ✓	**2**	0	0	0	1	1 ✓	0
	Twist	27 ✓	**5**	2	0	0	1	2 ✓	0

Companies with a total score ≥ 9 received a green check in the Total Score and Short List columns. Companies with a score > 0 in column 5 (Unique offering for IVPP) received a pink check in column 5 and the Short List column. Companies with a score > 0 in column 6 (Listed in IVTM), received an orange check in column 6 and the Short List column. Companies included in the "Influenza top-tier Dx" based on estimated ILI-related revenue. Inclusion in "Other Leading Diagnostic Companies" is based on total reported revenue. Companies in the long list that were not scored: 1) InDevR was not scored because their testing products are RUO, and focused on vaccine development, not clinical Dx. 2) Companies that sell only immunochromatographic devices but do not manufacture or develop include Biosign, LABSCO, Lifesign, Polymedco, McKesson, 3M, BTNX. There are also likely to be other companies in China and elsewhere that do not market in English. 3) Companies with only NAT kits for open platforms: e.g., Altona, Primer Design, Lucira/Diassess. Companies in the immunochromatographic device category with "PBM" next to their name sell a product produced by Princeton BioMeditech. NGS, Next Generation Sequencing.

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For the total scores, nine companies received a score of 9 or greater out of a possible total score of 14, and a full comparison profile is presented for these companies in Section 4. Fifteen other companies have attributes that are potentially unique to contribute to influenza diagnostics, and a text summary of these companies and their potentially unique offering is presented in Section 4.

Aside from the high-scoring companies and those with potentially unique offerings for IVPP testing, an additional four companies are listed in the IVTM, and are included on the Short List for this reason. These companies are listed in **Table 4**, along with the reasons they did not score higher. Because these companies were "ruled-in" to the Short List, a text profile of these companies and their offerings are also presented in Section 4.

Table 4. IVD Companies Listed in IVTM With Scores Less Than 9

Company	Location	Total Score	Reasons for Lower Score
Princeton BioMeditech (PBM)	Monmouth Junction, USA	5	• Product(s) do not address > 2 Use Cases, • Estimated < $10M USD in ILI Dx revenue • No FDA EUA approved or announced SARS-CoV-2 • No publicly known unique technology offering
R-Biopharm	Darmstadt, Germany	6	• Unclear LMIC presence • Estimated < $10M USD in ILI Dx revenue • No FDA EUA approved or announced SARS-CoV-2 • No publicly known unique technology offering
Response Biomedical	Vancouver, Canada	5	• Product(s) do not address > 2 Use Cases • Estimated < $10M USD in ILI Dx revenue • No FDA EUA approved or announced SARS-CoV-2 • No publicly known unique technology offering
Sekisui	Osaka, Japan	5	• Product(s) do not address > 2 Use Cases • Estimated < $10M USD in ILI Dx revenue • No FDA EUA approved or announced SARS-CoV-2 • No publicly known unique offering (reseller of Accula platform)

A group of companies had intermediate scores in the 6 to 8 range, and therefore did not make the high-scoring cut-off of 9, and also did not get "ruled in" to the Short List by other criteria. These companies are listed in **Table 5**, along with the reasons they did not score higher.

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Table 5. Companies with Intermediate Scores and Reasons for Their Scores

Company	Location	Total Score	Reasons for Lower Score
Genmark	Carlsbad, CA, USA	6	• Product(s) do not address > 2 high-priority Use Cases • Estimated $30-$50M USD in ILI Dx revenue (pre-COVID-19) • Not known to have significant presence in LMIC • No publicly known uniquely differentiating technology offering • Not listed in IVTM
Luminex	Austin, TX, USA	6	• Not known to have significant LMIC presence • Estimated $10–50M USD in ILI Dx revenue (pre-COVID-19) • No FDA EUA approved or announced multiplex SARS-CoV-2 + influenza assay • No publicly known uniquely differentiating technology offering • Not listed on IVTM
Perkin-Elmer	Waltham, MA, USA	7	• Estimated $10–50M USD in ILI Dx revenue (pre-COVID-19; might be generous) • Presence in LMIC likely to be limited • No FDA EUA approved or announced multiplex SARS-CoV-2 + influenza assay • No publicly known unique technology offering • Not listed on IVTM
Novacyt	Vélizy-Villacoublay, France	7	• Unclear presence in LMIC • Estimated $10–50M USD in ILI Dx revenue • No publicly known unique technology offering • Not listed in IVTM
R-Biopharm	Darmstadt, Germany	6	• No known significant presence in LMIC • Estimated < $10M USD in ILI Dx revenue • No FDA EUA approved or announced multiplex SARS-CoV-2 + influenza assay • No publicly known unique technology offering
Seegene	Seoul, South Korea	8	• Estimated $10–50M USD in ILI Dx revenue (2019) • SARS-CoV-2 assay has EUA, but no EUA announced for multiplex with influenza • No publicly known unique technology offering • Not listed in IVTM
Siemens Healthineers	Boca Raton, FL, USA (parent company in Munich, Germany)	6	• Estimated < $10M USD in ILI Dx revenue • No FDA EUA approved or announced multiplex SARS-CoV-2 + influenza assay • No publicly known unique technology offering • Not listed on IVTM
Thermo Fisher	Waltham, Massachusetts, USA	6	• Products do not address > 2 high-priority Use Cases • No FDA EUA approved or announced multiplex SARS-CoV-2 + influenza assay • Not listed on IVTM

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Section 4. Company Profiles

In the following pages, detailed profiles are presented for the nine companies that received a total score of 9 or higher. These profiles have been standardized to the extent possible using publicly available information to better facilitate intercompany comparisons. After these profiles, briefer text summaries are presented for 18 other companies of interest.

Section 4A. Profiles of the Highest Scoring (Top Tier) Influenza Diagnostic Companies

<table>
<tr><td>Abbott</td><td colspan="2">Revenues (2019): $32B</td><td colspan="2">Overall market position</td></tr>
<tr><td rowspan="4">  </td><td colspan="2">HQ: Abbott Park, IL USA</td><td colspan="2">#3 diagnostic company ranking</td></tr>
<tr><td colspan="2">Year founded: 1890</td><td colspan="2">Influenza diagnostics market position</td></tr>
<tr><td colspan="2">Employees: 107,000</td><td colspan="2">Top 5</td></tr>
<tr><td>Name</td><td>Configuration</td><td>Description</td><td>Important Use Cases</td></tr>
<tr><td rowspan="3">Products related to Influenza diagnostics, or that could be applied</td><td colspan="2">ID Now</td><td>NAT isothermal POC.
Estimated install base: 18,000 in the US.
This automated assay qualitatively detects nucleic acid from viral RNA in nasal, nasopharyngeal, or throat swabs using isothermal nucleic acid amplification and returns results in less than 15 minutes.</td><td>POU Diagnosis</td></tr>
<tr><td colspan="2">BinaxNOW</td><td>Lateral flow Ag + reader.
Can provide results in 15 minutes from a nasal swab.
Appropriate for CLIA-waived point-of-care settings such as doctors' offices, emergency rooms, or schools.</td><td>POU Diagnosis</td></tr>
<tr><td colspan="2">M2000, Alinity m</td><td>RT-PCR Kits for closed platform.
The Alinity m system can run up to 1,080 tests in 24 hours, while the m2000 RealTime system can run up to 480 tests in 24 hours.</td><td>Diagnosis
Screening of Non-Symptomatic Individuals
Confirmatory diagnosis
Gold standard
Surveillance (infection)</td></tr>
</table>

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<table>
<tr><td>Corporate Structure</td><td>

4 major divisions: Nutrition, Medical Devices, Diagnostics, Pharmaceuticals
To meet the demand for COVID-19 testing, Abbott built two new manufacturing facilities in the US in 2020.

</td></tr>
<tr><td>Revenue breakdown by division/product</td><td>

$32B total 2019 revenue. Medical devices $12.2B, Diagnostics $7.7B, Pharmaceuticals $4.4B, Nutrition $74B.
2019 Diagnostics revenue: Core Lab $4.6B, Molecular $0.4B, POC $0.6B, Rapid Diagnostics $2.1B.
Q2 2020 $615M in COVID-19 Diagnostics revenue (6 assays)
Strong growth in the Diagnostics business in 2020 is being driven by demand for COVID-19 tests, including its immunoassay, molecular, and rapid point-of-care tests.

</td></tr>
<tr><td>Growth</td><td>

The BinaxNOW COVID-19 test is not currently configured to be used with the BinaxNOW reader. However, in the future, the installed base of readers may potentially support new versions of COVID-19 and other ILI tests.

<table>
<tr><th>Year</th><th>All Rev ($B)</th><th>Diagnostics Rev ($B)</th></tr>
<tr><td>2019</td><td>32.000</td><td>8.800</td></tr>
<tr><td>2018</td><td>30.580</td><td>7.500</td></tr>
<tr><td>2017</td><td>27.390</td><td>5.620</td></tr>
<tr><td>2016</td><td>20.850</td><td>4.810</td></tr>
</table>
</td></tr>
<tr><td>Organizational Characteristics</td><td>

Large scale manufacturing capacity (in-house and OEM)
Strong competence in design for manufacture

Product development process is often through acquisitions, but not exclusively, though response to need for COVID-19 was rapid

Strong technical competence
Large global presence in most countries (direct and distributors)
Capable of offering high-volume, low-cost products when it is to their competitive advantage
History of using low price to drive out competition

</td></tr>
<tr><td>Fraction of business in LMIC</td><td>

Sales in 106 countries.
The fraction of Diagnostics revenue in international markets: 75% of 2019 core Lab, 66% of 2019 Molecular, 22% of 2019 POC, and 41% of 2019 “Rapid Diagnostics” revenue

</td></tr>
<tr><td>Change in position changed over 3–5 years</td><td>

Total company revenues increased 62% (2016–2019)
Diagnostic revenues increased 83% (2016–2019)

</td></tr>
<tr><td>LMIC fit</td><td>

Decentralized Test Sites: The ID Now and BinaxNOW platforms could provide a strong base for assay menu expansion to meet future IVPP test demands if Abbott chooses to focus more on respiratory illnesses
Centralized labs: The Alinity and m2000 systems could be appropriate central lab systems if Abbott chooses to focus on respiratory illnesses. Many central labs already have the m2000 molecular platform installed, but other than COVID-19, the company does not currently offer any molecular respiratory assays.

</td></tr>
</table>

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BD (Becton Dickinson)	Revenues (2019): $17.3B	Overall market position	
	HQ: Franklin Lakes, NJ	#13 diagnostic company ranking	
	Year founded: 1906	Influenza diagnostics market position	
	Employees: 70,000	Small but growing presence with Veritor POC Flu A/B and now SARS-CoV-2 tests	
	Name	**Description**	**Important Use Cases**
Products related to Influenza diagnostics	BD Max	Realtime PCR assay and instrument	Diagnosis Differential diagnosis Confirmatory (potential)
	Veritor	Rapid Ag test and reader Estimated install base: 25,000	Diagnosis

Corporate Structure	• 3 divisions: BD Medical, BD Life Sciences (includes Diagnostics), BD Interventional
Revenue breakdown by division/product	• 2019 revenues: BD Medical: $9.1B, BD Life Sciences: $4.3B (Diagnostics : $1.5B), BD Interventional: $3.9B.
Growth (by division if possible)	

Year	All Rev ($B)	Diagnostics Rev ($B)
2019	17.290	1.550
2018	15.980	1.540
2017	12.090	1.380
2016	12.480	

Organizational Characteristics (especially those that enable sustained participation in pandemic preparedness)	• BD has a very significant presence in and support of LMIC markets, through the Global Health business inside of their Life Sciences Division, as well as through sales of their lancets, vacutainer tubes and other well-known laboratory consumables. For many years they have been a market leader in flow cytometry. The well-known Vacutainer line of blood tubes and similar consumables helps to solidify significant brand recognition and established market channels in many countries. Under their new CEO, the company is under significant financial pressure, in part due to the continued integration of several significant acquisitions since 2017, including C.R. Bard in 2017, NAT Diagnostics and Straub Medical in 2020, and others.
Fraction of business in LMIC	• Majority of sales in US. As of October 28, 2019, BD owned or leased 362 facilities in over 50 countries around the world for manufacturing, warehousing, administrative and research facilities. BD's emerging market revenues were $2.71B, $2.53B and $1.95B in 2019, 2018 and 2017, respectively, representing approximately 15% of total company revenues each year.
Change in position changed over 3–5 years	• Corporate revenues grew $4.81B, or 39% (2016–2019), largely due to acquisitions • Diagnostic revenues grew $0.17B, or 12%, (2017–2019), a reasonable growth rate relative to their main diagnostic competitors

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LMIC fit	• BD has built a strong LMIC presence around their flow cytometry (FACS) line of products. They have a good reputation for quality products and reliable customer support and have perennially supported many industry meetings in LMIC markets. They have a strong understanding of the procurement process. It will be interesting to see if they can continue this presence with the BD Max, a well-designed platform that has not had quite the market uptake of other molecular systems. The Veritor is a handheld device designed for POC testing locations but is not currently a focus of BD for expanded launch into LMIC markets.

Danaher	Revenues (2019): $17.91B	Overall market position	
DANAHER	HQ: Washington, DC, USA	#4 diagnostic company ranking	
	Year founded: 1969 (1984 for manufacturing)	Influenza diagnostics market position	
	Employees: 59,000	Key competitor with Cepheid's Flu A/B/RSV and now SARS-CoV-2 testing	
	Name	**Description**	**Important Use Cases**
Products related to Influenza diagnostics	Cepheid GeneXpert™	Real time RT-PCR assay cartridges with instrument. Estimated installed base: 23,000 global, 5,000 in the US. 1-80 GeneXpert tests can be run at the same time, depending on the instrument configuration. Typical test times are under 60 minutes.	Diagnosis Differential diagnosis
	Beckman Coulter Access 2	SARS-CoV-2 IgG and IgM tests. Lower volume immunoassay analyzer.	Screening of Non-Symptomatic Individuals
	Beckman Coulter Unicel Dxl 600/800	SARS-CoV-2 IgG and IgM tests. Mid (600 series) and High (800 series) volume immunoassay analyzers	Screening of Non-Symptomatic Individuals

Corporate Structure	• 3 Divisions: Diagnostics, Life Sciences, Environmental and Applied Solutions, incorporating ~20 operating companies. • Danaher acquired Cepheid in 2016. Past acquisitions include other well-known names, such as Beckman Coulter, Radiometer, Pall, GE Biopharma and Leica Biosystems, among others
Revenue breakdown by division/product	• $17.91B 2019 Revenues: Diagnostics $6.6B (Cepheid >$1B, Beckman Coulter >$1B), Life Sciences $7.0B, Environmental and Applied Solutions $4.4B.

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<table>
<tr><td>Growth (by division if possible)</td><td>
<table>
<tr><th>Year</th><th>All Rev ($B)</th><th>Diagnostics Rev ($B)</th></tr>
<tr><td>2019</td><td>17.910</td><td>6.560</td></tr>
<tr><td>2018</td><td>17.050</td><td>6.260</td></tr>
<tr><td>2017</td><td>18.330</td><td>5.840</td></tr>
<tr><td>2016</td><td>16.880</td><td>5.040</td></tr>
</table>
Annual compound growth at Cepheid since acquired by Danaher has exceeded 20% (very favorable relative to their diagnostics competitors)
</td></tr>
<tr><td>Organizational Characteristics (especially those that enable sustained participation in pandemic preparedness)</td><td>Danaher follows a federated-like business model, whereby they identify, acquire and continue to operate high value companies, typically retaining their facilities, research and manufacturing operations while consolidating corporate functions where practical. Danaher brings advantages of scale to their family of companies, demanding improved efficiency demands in return. While Danaher has a stable of high value companies with well-accepted technologies and presence in global markets (e.g., Cepheid, Beckman-Coulter and Radiometer), they will likely not be low-cost providers in LMIC markets.</td></tr>
<tr><td>Fraction of business in LMIC</td><td>Facilities in more than 60 countries.
Sales by region: North America 39% (37% US), Western Europe 23%, Other developed markets 6%, high growth markets 32%. High growth markets are defined as developing markets which are experiencing extended periods of accelerated growth in GDP and infrastructure (e.g. Eastern Europe, Middle East, Africa, Latin America, Asia, (excluding Japan, Australia and New Zealand))
Diagnostics sales by region: North America 39%, Western Europe 17%, other developed markets 6%, high growth markets 38%.</td></tr>
<tr><td>Change in position changed over 3–5 years</td><td>Danaher corporate revenue growth was only 6% (2016–2019), relatively lower vs. their key competitors.
Diagnostic revenues, however, grew an impressive ~30% over this same time period, driven largely by the acquisition of Cepheid.</td></tr>
<tr><td>LMIC fit</td><td>The Danaher presence in LMIC markets is through the companies it has acquired, e.g., Cepheid, Beckman Coulter and Radiometer. The Cepheid GeneXpert™ system is the leading molecular platform in LMIC markets for decentralized testing (primarily Level II and Level III settings) as well as in centralized laboratories (Infiniti system). GeneXpert is the benchmark against which other molecular diagnostic platforms are frequently judged. The platform is best known for its HIV, TB, Flu A/B/RSV, MRSA, C. diff. and hepatitis menu of tests, but the company also has a few dozen other assays in various markets or under development, including SARS-CoV-2 alone or with flu and RSV. The Beckman platform is best-known for its clinical chemistry menu offered on large central laboratory analyzers while the Radiometer platform is well-suited for POC hematology testing with expanding immunoassay and clinical chemistry assays. Danaher is a strong contender for providing existing or development new IVPP tests, especially on the Cepheid platforms (GeneXpert™).</td></tr>
</table>

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Quidel	Revenues (2019): $535M (~50% US)	Overall market position	
	HQ: San Diego, USA	In the top 20 diagnostic companies	
	Year founded: 1979	Influenza diagnostics market position	
	Employees: 1250	26% of 2019 revenue = $139 M	
	Name	**Description**	**Important Use Cases**
Products related to Influenza diagnostics	Sofia (DIA)	Rapid fluorescent immunoassay with reader. Estimated installed base: 50,000[1]	Diagnosis Differential diagnosis in development
	Quickvue Influenza A + B	Dipstick format	Diagnosis Differential diagnosis in development
	Lyra (open NAT)	Kits of tubes (high complexity). Validated on 7 cyclers[2]	Diagnosis Screening of Non-Symptomatic Individuals Confirmatory diagnosis Surveillance (infection)
	Solana MDx	Estimated install base: est. 1100 Instrument offers mid-complexity automation of nucleic acid detection using helicase-dependent amplification and fluorescence detection.	Diagnosis

Corporate Structure	• 3 manufacturing facilities (2 in San Diego, 1 in Ohio) • The company is organized in 4 divisions: Rapid Immunoassays, Cardiac Immunoassays, Specialized Diagnostics, Molecular Diagnostics
Revenue breakdown by division/product	• $535M 2019 revenues: Rapid Immunoassays $191M, Cardiac Immunoassays $266M, Specialized Diagnostics $55M, Molecular $22M. • $139M in Influenza diagnostics revenue, likely # 1 or 2 in the influenza testing market • The company expects that the Solana platform will be a driver of growth in 2020 (pre-COVID-19 impact).
Growth (by division if possible)	• Relatively low 2.5% total revenue growth 2018–2019. Rapid Immunoassays 5%, Cardiac Immunoassays 0% (still integrating the Alere acquisition), Specialized Diagnostics 3%, Molecular Diagnostics 12%. • Q2 2020 : > $100M in COVID-19 product revenue; representing >50% of 2019 total year sales, putting this division on track to double sales in 2020.

Year	All Rev ($B)
2019	0.535
2018	0.522
2017	0.278
2016	0.192

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Organizational Characteristics (especially those that enable sustained participation in pandemic preparedness)	• Quidel has a very strong manufacturing capacity, capable of producing ~100 million or more high-quality tests, with attractive cost of goods, per year. As a relatively nimble company, given top management support, the company can mobilize and address new market demands with impressive speed (see COVID-19 response for example). However, if the demand is not apparent or well-understood, or top management has not endorsed resource allocations for rapid response, the company will not be quick to respond.
Fraction of business in LMIC	• LATAM 3% ($16M), EMEA 11% ($58M), China 13% ($68M), Asia 5% ($27M). A significant fraction of this is sales of the Triage cardiac product line acquired in 2017 from Alere. • Core Quidel products: LATAM $7M, EMEA $14M, China $7M, Asia $12M. Sales & marketing support: 50 employees in China, 20 in India
Change in position changed over 3–5 years	• Corporate revenues rose 178% (2016–2019), largely due to the addition of cardiac sales from the acquisition of the Alere Triage system and assays.
LMIC fit	• The Sofia (FIA) and Quickview platforms offer CLIA waiver for influenza tests. These are good platforms for antibody and antigen testing where appropriate. Quidel has earmarked continued funding to improve assay performance and to expand the menu. The company was one of the first to meet FDA's demands that marketed POC assays offer improved assay performance at the cut-off or face removal from market. They are also developing a new lower cost, smaller version of this platform. • The Savanna (sample-to-result) NAT platform in development is designed for "potentially CLIA-waived settings" (cartridge cost < $5, instrument cost ~$ 10,000). This platform has been in development for several years, with slowed completion dates presumably due to insufficient allocation of development resources by the company. This system could be appropriate for low-plex IVPP tests if Quidel chooses to focus on these products. Alternatively, if existing flu products react with new IVPP they will be in a position to address the market with existing products. • For Quidel to be able to sustainably expand their business in LMIC markets, they will need to add significant local headcount for sales, marketing, market development and customer support, either directly through hiring Quidel personnel or indirectly through local distributors or other partnerships. Quidel is spending significant resources to expand their local operations in India and China and may be in a position to complement these efforts in other regions of the world in the near future. The company could benefit from engaging assistance with local registrational studies and regulatory activities.

Qiagen	Revenues (2019): $1.53B		Overall market position	
	HQ: Hilden, Germany		In the top 20 diagnostic companies	
	Year founded: 1984		Influenza diagnostics market position	
	Employees: 3,600		Not a top competitor in ILI markets	
	Name	**Configuration**	**Description**	**Important Use Cases**
Products related to	QIAstat Dx		Realtime PCR assay cartridges and small instrument, with SARS-CoV-2 panel	Diagnosis Differential diagnosis (possible)

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Influenza diagnostics		and respiratory virus panel 1,000 instruments placed at end of 2019	
	Artus	RT-qPCR reagent kits	Differential diagnosis
	QIAsymphony	Centralized lab instrument can be used to perform LDTs and other OEM molecular assays as well as the QIAreach anti-SARS-CoV02 system and test	Diagnosis Differential diagnosis (possible)

Corporate Structure	• Headquartered outside Dusseldorf, Germany. 2 Divisions: Molecular Diagnostics and Life Sciences. The company operates four primary manufacturing sites (Sweden, Germany, and US (Beverly, MA and Germantown, MD). Traditionally, Qiagen has grown through acquisition, often leaving acquired companies to operate in pre-existing facilities. They have a very diverse portfolio of diagnostic consumables necessary to support diagnostic testing (e.g., specialized sample collection and processing tubes), assays and instrument systems designed to support a wide variety of assay technologies, including molecular, sequencing, POC and other.
Revenue breakdown by division/product	• $1.53B 2019 Revenue: Molecular Diagnostics $737M, Life Sciences $789M. • 2019 Molecular Diagnostics revenues reflected lower companion diagnostic sales of $42M, a 28% year-over-year drop. • QIAsymphony drove Molecular Diagnostics growth in 2019.
Growth (by division if possible)	<table><tr><th>Year</th><th>All Rev ($B)</th><th>Diagnostics Rev ($B)</th></tr><tr><td>2019</td><td>1.530</td><td>0.737</td></tr><tr><td>2018</td><td>1.500</td><td>0.732</td></tr><tr><td>2017</td><td>1.420</td><td></td></tr><tr><td>2016</td><td>1.340</td><td>0.663</td></tr></table>
Organizational Characteristics (especially those that enable sustained participation in pandemic preparedness)	• Under their former CEO, Per Schatz, Qiagen was frequently a go-to company with new technologies addressing new market demands, outbreak testing needs, etc. The company was open to innovative business arrangements and interested in learning about, supporting or acquiring new technologies. Under the current leadership, the company is under increased financial pressure and has been consumed with fending off a takeover bid from Thermo Fisher. It is not clear to what extent Qiagen will maintain the level of interest in new technologies and market opportunities they have shown in the past but they should remain on a short list of potentially impactful companies in IVPP. If existing tests show acceptable performance with IVPP they will be in a position to address the IVPP market.
Fraction of business in LMIC	• Qiagen markets products in more than 130 countries but country sales figures are not broken out.
Change in position changed over 3–5 years	• Corporate revenues grew 14% (2016–2019), representing relatively modest growth vs. the leading companies • Diagnostic revenues grew 11% (2016–2019)

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LMIC fit	• Qiagen has a market presence in many LMIC markets. The company has a wide variety of instrument platforms available for use with lab developed tests as well as their own assay products. For decentralized testing locations, the QIAstat would be a reasonable option, but is currently lacking in menu. The Rotor-Gene and QIAamplifier platforms are other options for decentralized labs. For centralized laboratories, the company offers the QIAsymphony workhorse, QIAquant and other platforms, with available reagent kits specially designed to support assay developers. Qiagen also offers a menu of Artus kits for use on various qualified analyzers. • Qiagen would be a good company to approach to discuss development preparedness for new ILI tests.

Roche	Revenues (2019): $61.9B	Overall market position	
	HQ: Basel, Switzerland	#1 diagnostic company ranking	
	Year founded: 1896	Influenza diagnostics market position	
	Employees: 98,000	Not a top competitor in respiratory testing, but were very fast to market with SARS-CoV-2 tests	
	Name	**Description**	**Important Use Cases**
Products related to Influenza diagnostics	Cobas 6800/8800	SARS-CoV-2 + Influenza A/B test Fully integrated, lab based, high throughput One 8800 system can run up to 20,000 tests per week. Significant installed base in LMIC national reference and central labs.	Diagnosis Differential diagnosis
	Cobas Liat	POC PCR cartridge and instrument	Diagnosis Differential diagnosis

Corporate Structure	• Two overall areas of the company: Pharmaceuticals and Diagnostics. Diagnostics is divided into Diabetes Care, Molecular Diagnostics, Centralized Diagnostics and Tissue Diagnostics
Revenue breakdown by division/product	• $61.9B 2019 Revenue: Diagnostics $12.99B • Diagnostics revenue by division: Diabetes Care $1.93B, Molecular Diagnostics $2.12B, Centralized Diagnostics $7.87B, Tissue Diagnostics $1.1B.
Growth (by division if possible)	

Year	All Rev ($B)	Diagnostics Rev ($B)
2019	61.91	12.99
2018	58.13	13.17
2017	54.17	12.28
2016	51.35	11.65

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Organizational Characteristics (especially those that enable sustained participation in pandemic preparedness)	• Flu drug Xofluza approved by US FDA in 2019 • Despite being #1 or #2 in global diagnostics, Roche is a conservative company, typically preferring to wait to move into new market segments until the market and revenue opportunities are reasonably well-understood. This conservatism makes them relatively late to enter new markets, only entering once the market size can justify the diversion of resources from other internal programs. Having said this, as a global health care company, the board of directors and top management can and will move very quickly if faced with a global crisis which they believe Roche might help to address. Examples include their recent rapid response to developing and introducing SARS-CoV-2 tests, and in the past, their rapid responses to West Nile Virus and Ebola. If existing products detect IVPP sufficiently, their existing market could be expanded rapidly.
Fraction of business in LMIC	• Represented in over 100 countries but country sales figures are not broken out.
Change in position changed over 3–5 years	• Corporate revenues grew a respectable $10.92B or 22% (2016–2019) • Combined diagnostic sales, including diabetes, grew $1.43B or 12.5% (2016–2019)
LMIC fit	• Roche has a reasonably strong installed base of cobas systems in Level III/IV laboratories, positioned primarily for HIV viral load and diagnostic testing. They have struggled with penetrating into decentralized settings. The Liat platform is meant to help them here but has been slow to be adopted outside the US and Europe, in part due to its limited menu.

bioMerieux	Revenues (2019): $3.0B	Overall market position	
	HQ: Marcy-l'Etoile, France	#10 diagnostic company ranking	
	Year founded: 1963	Influenza diagnostics market position	
	Employees: 12,000	A market leader in respiratory virus panel testing	
	Name	**Description**	**Important Use Cases**
Products related to Influenza diagnostics	BIOFIRE® Respiratory Panel 2.1 *plus*	Fully automated BIOFIRE FilmArray® 2.0 and TORCH. Detects 23 viruses (including SARS-CoV-2) and 4 bacteria. Estimated install base: 15,900 placements by Q3 2020 vs 10,400 total at end of 2019.[3] 45 minute run time. CE Marked.	Diagnosis Differential diagnosis
	VIDAS	Immunoassay platform with an install base of >26,000. SARS-CoV-2 assays detects IgG or IgM.[4]	Screening of Non-Symptomatic Individuals

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<table>
<tr><td>Corporate Structure</td><td>• bioMerieux is a family-run global diagnostic company with two main operating divisions: Clinical and Industrial. The Clinical division generated 83% of sales in 2019, while Industrial Microbiology generated 17%.
• bioMerieux is present in 44 countries, serves more than 160 countries with the support of a large network of distributors, and has 18 production sites around the world.</td></tr>
<tr><td>Revenue breakdown by division/product</td><td>• $3.0B 2019 Revenue: Clinical $2.475B, Industrial $525M.
• The Clinical division, including immunoassay, microbiology and molecular biology, was up 11% year over year. Total molecular biology sales were $752M. FilmArray sales exceeded $672M, with international revenues making up 19%.
• By Q3 2020, molecular biology sales were up vs. Q3 2019 by 120%, due to FilmArray Respiratory Panel 2.1 plus (includes SARS-CoV-2) sales</td></tr>
<tr><td>Growth (by division if possible)</td><td><table><tr><th>Year</th><th>All Rev ($B)</th><th>Diagnostics Rev ($B)</th></tr><tr><td>2019</td><td>3.001</td><td>2.475</td></tr><tr><td>2018</td><td>2.858</td><td>2.350</td></tr><tr><td>2017</td><td>2.589</td><td>2.125</td></tr><tr><td>2016</td><td>2.324</td><td>1.859</td></tr></table></td></tr>
<tr><td>Organizational Characteristics (especially those that enable sustained participation in pandemic preparedness)</td><td>• bioMerieux is very well known for its expertise and global leadership position in culture-based diagnostics. They have established programs in genetics, cancer, immunoassay, molecular and point of care with varying degrees of success. Their molecular business was acquired through the acquisition of Idaho Technologies and has been the predominant focus of internal investment outside of their core culture businesses. bioMerieux is a well-known mid-sized diagnostic company, with strong brand awareness in most countries around the world, especially the Francophile countries.</td></tr>
<tr><td>Fraction of business in LMIC</td><td>• Over 90% of total corporate sales are from international markets. bioMerieux has a strong presence in many LMIC markets, especially Francophile countries</td></tr>
<tr><td>Change in position changed over 3–5 years</td><td>• Total corporate revenues were up $0.68B, or 27% (2016–2019)
• Diagnostic Unit sales were up $0.62B, or 32% (2016–2019), driven by sales of FilmArray Respiratory Panel</td></tr>
<tr><td>LMIC fit</td><td>• bioMerieux acquired the well-known Idaho Technology FilmArray platform in 2013. Though the system is a market leader in mid-plex molecular testing in the US and EU, the company has struggled with market penetration in other markets, due notably to the high price of the instrument and assay cartridges. If the system and assay price could be reduced, bioMerieux could use its brand awareness and market presence in many LMIC countries, and its familiarity with local country registration and procurement processes, to drive sales. Due to its presence in so many markets, bioMerieux is a cosmopolitan, international company with strong understanding of diverse cultures and practices. They are a market leader in cell culture and microbiology, have very deep knowledge of biological organisms and are frequent supporters of local healthcare-related initiatives. The company would be a good potential partner in the IVPP space if they could achieve lower product pricing. If the existing assays for flu show good performance for IVPP they could provide a differential diagnostic test quickly</td></tr>
</table>

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Diasorin	Revenues (2019): $0.79B	Overall market position	
DiaSorin	HQ: Saluggia, Italy	#18 diagnostic company ranking	
	Year founded: 2000	Influenza diagnostics market position	
	Employees: 2,000	Not a market leader in this space	
	Name	**Description**	**Important Use Cases**
Products related to Influenza diagnostics	Liaison MDX Simplexa Influenza A H1N1 (2009) Kit Simplexa Flu A/B & RSV Direct Gen II Kit	Liaison MDX is a thermocycler for real time PCR applications. The MDX technology was acquired by DiaSorin S.p.A. in 2016 from 3M Inc. (Focus Diagnostics). Estimated installed base exceeds 800 systems in the US and Europe	Diagnosis Differential diagnosis Triage

Corporate Structure	• DiaSorin Molecular is a company of DiaSorin S.p.A. The DiaSorin S.p.A. is made up of 25 companies, 4 branches, 6 manufacturing facilities (Saluggia (Italy), Dietzenbach (Germany), Stillwater, Minnesota (US), Cypress, California (US), Dartford (UK), and Kyalami (South Africa)), and 5 research facilities. They produce and distribute in vitro diagnostics reagent kits for immune and molecular diagnostics.
Revenue breakdown by division/product	• $790M 2019 revenue for DiaSorin S.p.A. DiaSorin Molecular $71M
Growth (by division if possible)	Year: All Rev ($B) 2019: 0.791 2018: 0.790 2017: 0.721 2016: 0.630
Organizational Characteristics (especially those that enable sustained participation in pandemic preparedness)	• The company has sought to establish a significant presence in molecular testing and they are only a mid-sized company overall. They are not known for fast development of new technologies and have been slow to complete menu expansion. Their sales are driven primarily by high complexity CLIA immunoassay tests. Molecular testing represents less than 10% of sales.
Fraction of business in LMIC	• DiaSorin distributes tests to Europe, Israel, US, Canada, Mexico, Brazil, China, India and Australia, and sells test in other countries through distributors. • Revenue by region: Europe and Africa $364M, Asia Pacific $150M, Latin America $46M, US and Canada $230M.
Change in position changed over 3–5 years	• Corporate revenues increased 24% (2016–2019)
LMIC fit	• The company sells primarily in the US and Europe. It has only a small presence in LMIC markets (Latam and Africa).

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Hologic	Revenues (2019): $3.4B	Overall market position	
HOLOGIC®	HQ: Marlborough, MA, US	#15 diagnostic company ranking	
	Year founded:	Influenza diagnostics market position	
	Employees: 6,500	A mid-sized player in respiratory virus testing today	
	Name	**Description**	**Important Use Cases**
Products related to Influenza diagnostics	Prodesse Pro Flu + Assay	PCR Reagent kits	Diagnosis
	Panther Fusion Flu A/B/RSV assay	Fully automated, high throughput, instrument. Smaller footprint than Abbott or Roche systems. Estimated installed base: 1,700 systems (increase of 200 in 2019, 45% of all units are placed outside of US).	Diagnosis Differential diagnosis (influenza A, influenza B and RSV)

Corporate Structure	• Hologic is primarily focused on improving women's health and well-being through early detection and treatment of disease. • 5 Divisions: Diagnostics, Breast Health, Medical Aesthetics, GYN Surgical and Skeletal Health. • Diagnostics headquartered in San Diego, CA (former Gen-Probe facility acquired by Hologic). Manufacturing facilities in US, Germany, UK, and Costa Rica. Presence in Belgium, Spain, and China.
Revenue breakdown by division/product	• $3.37B 2019 revenues: Diagnostics $1.180M (Molecular Diagnostics $665M), Breast Health $837M, Medical Aesthetics $252M, Gyn Surgical $436M, Skeletal Health $65M, Service revenue $596M.[5] • Molecular diagnostics revenue increase driven by Aptima family of assays on the Panther and the larger Tigris instrument systems.
Growth (by division if possible)	**Year** / **All Rev ($B)** / **Diagnostics Rev ($B)** 2019 / 3.367 / 0.290 2018 / 3.218 / 0.276 2017 / 3.059 / 0.274 2016 / 2.830 / 0.255
Organizational Characteristics (especially those that enable sustained participation in pandemic preparedness)	• Hologic has gained significant brand awareness and market presence over the years, primarily through acquisition of other well-known brands. Though much of their M&A focus lies outside of the IVD sector, two very large notable exceptions include Cytec and Gen-Probe. Their Panther line of molecular instrument systems is designed to serve the needs of medium to large laboratories. The company is not typically a fast mover, preferring to move into more mature markets via partnerships and acquisitions.

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Fraction of business in LMIC	• 25% of their business is from sales outside the US. • International revenue: $671M, $634M, $539M and $492M (2019, 2018, 107 and 2016, respectively) • Europe 11.8%, Asia-Pacific 8.5%, rest of world 4.4%
Change in position changed over 3–5 years	• Corporate revenues grew $0.57B or 20% (2016–2019) • Diagnostics revenues grew $35M or 14% (2016–2019)
LMIC fit	• Hologic does not have a large presence in decentralized testing. Their strength is in moderate to high throughput systems, especially for virus testing, in centralized labs. Despite their rapid move into SARS-COV-2 testing in the US, they may not presently be an ideal go-to company for development of new IVPP-directed assays. However, if existing tests are useful for IVPP their installed base could be rapidly utilized

Section 4B. Summaries of Other Notable Companies

More Sensitive Antigen Tests

Several companies were identified that have potentially innovative products that could serve an unmet need for more sensitive and/or rapid detection tests, including antigen and NAT. These are of particular interest because of their appropriateness for diagnostic Use Cases in decentralized settings that require rapid, low cost and low complexity tests, such as in LMICs.

One company that stands out in this category is **LumiraDx**. LumiraDx was founded in 2014 by individuals formerly with the companies Medisense, Inverness Medical and Alere. The company has raised approximately $600M through debt and equity from institutional and strategic investors including the Bill & Melinda Gates Foundation, Morningside Ventures and U.S. Boston Capital Corporation. For a relatively new company, they have very strong corporate competence in product development, manufacturing, and commercialization. They aim to commercialize cloud-enabled platforms that integrate health system networks to improve both individual's health and population-wide outcomes. They are based in London, UK and Waltham, MA, USA, with manufacturing in Stirling, Scotland, and currently have more than 600 employees. Their point-of-care platform consists of a small portable instrument, low-cost microfluidic cards and seamless digital connectivity. The instrument can perform both fluorescence and electrochemistry measurements. They currently sell an immunofluorescence assay for SARS-CoV-2 antigen detection with EUA CLIA-waiver with the current good sensitivity and a TTR of 12 minutes. A news release from August 2020 indicates that the company will produce 2 million tests in September 2020, and up to 10 million tests in December. No information has been found publicly on their current install base of instruments, or how they plan to scale this, though it was recently announced that the system would be submitted for WHO EUL review in anticipation of procurement through various agencies for SARS-C0V-2 antigen testing, primarily for placement in sub-Saharan Africa.

Lumira also sells a rapid nucleic acid amplification assay to detect SARS-CoV-2 for open platforms. An anti-SARS-CoV-2 antibody test to launch in the near future is also planned. The future menu for their point-of-care platform has not been published on their website, though their News page mentions tests for coagulation monitoring.

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Overall, LumiraDx is a newly emerging contender in the point-of-care diagnostics scene that is currently commercializing a next generation point-of-care SARS-CoV-2 antigen test. A multiplex SARS-CoV-2 + influenza test is in development. If this test also performs well, this company has the funding and commercialization expertise, and will soon have a significant installed base of instruments, to make a significant impact in the influenza diagnostics space.

A second notable company in the area of higher-sensitivity point-of-care antigen tests is **Pinpoint Sciences**. Pinpoint was founded in 2016, currently has less than 10 employees, is in the venture funding phase, and is based in San Francisco, CA, USA. Pinpoint has developed a novel biosensor technology that performs label-free electrical detection of specific biomolecules with great precision and at low cost. This technology was spun out of University of California, Santa Cruz, US. Their cartridge-based platform is easy-to-use, and was designed to require no reagents, no cold chain or sample preparation. The multichannel nanosensors have molecular probes (binders) immobilized on to the tip, and current spectroscopy is used to detect the binding of antigen in a quantitative fashion. The technology performs multiplex assays, and results are displayed within 30 seconds. The hand-held battery-powered reader device is expected to cost ~ $100 in high volumes. They are developing a SARS-CoV-2 assay with a four-channel nanosensor. Initial data for the detection of influenza virus using an aptamer binder appears promising, and was able to detect as low as 500 femtograms per mL (~1,000 times more sensitive than current antigen tests) though data using real clinical samples has not been made public. Pinpoint believes that its platform has potential for the broad application to a wide range of markets, including human and animal health, food safety, water contamination, and environmental surveillance.

Overall, Pinpoint has a potentially transformative technology that could address some very challenging settings, such as screening at social gathering and other congregation spots , educational facilities and workplaces. They should be kept on the watch list to follow the technology's performance capabilities, how successful they are at scaling production, and how they aim to commercialize their platform.

Another company in the area of higher-sensitivity point-of-care antigen tests is **Quanterix**. Quanterix was founded in 2007, currently has ~ 250 employees, generated $57M in revenue in 2019, and is based in Billerica, MA, USA. They have developed an ultrasensitive single-molecule array immunoassay technology called Simoa on an automated platform called HD-X. Initial performance for detecting SARS-CoV-2 antigen in blood showed promising clinical sensitivity and specificity, as well as an LOD that is reported to be 2000 times more sensitive than current EUA approved antigen tests. If this performance using a capillary blood sample can be validated, their technology might be able to resolve some of the challenges that have emerged for SARS-CoV-2 testing which has so far required swab or oral fluid/saliva-based sampling.

There are a number of unanswered questions related to whether Quanterix might have something to contribute to the influenza diagnostics landscape. The first is whether influenza virus proteins are also present in the blood of most patients (or whether their technology could be applied to swab or other sample types). Secondly, most of Quanterix's business in the past has been in detecting cytokine panels for clinical trials run by the pharmaceutical industry, and their platform has been used to characterize the "cytokine storm" generated in some COVID-19 patients. They do not have an influenza diagnostics product, nor have they produced any IVD products in the past, but they recently received an NIH RADx

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(Rapid Acceleration of Diagnostics) grant to commercialize their platform for the detection of SARS-CoV-2. Up to this point, there have been no announcements regarding the release of a multiplex SARS-CoV-2 + influenza assay, though their technology is capable of large multiplexes. They have also not announced the format, time to result or level of resources required for the diagnostics instrument that will conduct their Simoa assay, though press releases indicate that it is intended for laboratory use. Also, the HD-X system is large and best used in a high complexity laboratory setting. No POC-type device using Simoa assay technology has been reported.

Overall Quanterix has a potentially transformative technology for use in laboratory settings. With recently announced license agreements such as one with Abbott Diagnostics (October 2020), it is likely the company will continue to have adequate resources to continue technology development.

Another company that has successfully developed sensitive point-of-care antigen detection assays is **Access Bio**, though this technology has not been applied to their influenza tests. Access Bio was founded in 2001, currently has an estimated 60 employees, has an estimated $36M in revenues. It is estimated that their ILI-related revenue is only a small fraction of this total, making them a minor player in the influenza diagnostics market. The company has its headquarters in Somerset, New Jersey and manufacturing facilities in the US, Ethiopia (assembly only), and South Korea. Access Bio has a comprehensive line of diagnostic platforms, including rapid immunoassays (e.g., malaria, HIV, HPV), biosensors (e.g., glucose, HbA1c, bilirubin, hemoglobin, G6PD), and nucleic acid-based tests for “open” platforms (e.g., Zika, Dengue). Of note, the company has been the leading global supplier of malaria immunochromatographic tests, annually producing more than 130 million tests. Their website claims they can produce more than 170 million rapid diagnostic tests per year, and that they distribute products to more than 120 different countries.

They successfully developed (in collaboration with Global Good) and recently launched an ultra-sensitive *P. falciparum* malaria immunochromatographic device that is 5 times more sensitive than other currently available products. They have lateral flow cartridges for influenza, and for malaria.

Though Access Bio is a smaller company, and their influenza product is not well-differentiated from others on the market, they have a large manufacturing capacity for lateral flow tests, especially outside the US, as well as distribution channels in to many LMICs. With their growing global presence and expanded manufacturing capacity, the company remains a leading contender for manufacturing low cost, high quality rapid diagnostic tests. They are open to contract manufacturing relationships.

Low-Multiplex, Lower-Resource POC NAT Platforms

Four companies were identified as having NAT instrument platforms that were purpose-built for lower-resource and other POC settings. This category of products is of particular interest because there is still an unmet need for lower-cost, lower-complexity, more rapid and highly sensitive detection methods for diagnostic and screening Use Cases in decentralized settings, particularly in LMICs. The platforms expected to excel in these settings might be called “low-multiplex,” in that they focus on test menu for the detection of single pathogens or small panels of two or three pathogens. It is not anticipated that

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NAT platforms that focus on high-multiplex test menus will excel in these settings, as they focus commercially on capturing greater value through a high-multiplex test.

The company **Mesa Biotech** sells a platform called Accula that uses RT-PCR to generate a visual read-out and is both CLIA-waived and CE Marked. The company claims that the platform was specifically designed to be used outside of the laboratory in decentralized settings. The Accula platform has several potentially incremental improvements over certain features of other competing point-of-care influenza NAT platforms (e.g., Cepheid GeneXpert, Abbott ID Now) including its very small size (implying a potentially very low cost) and more rapid result (30 minutes for influenza, which is faster than Cepheid's 45 minutes, but not faster than the ID Now's 15 minutes).

Mesa was founded in 2015 and currently has ~30–50 employees, and is based in San Diego, CA. Mesa is privately held with an estimated revenue of $5M,[6] making them a very minor player in the current influenza testing market. Their influenza A+B assay was the first assay launched for the Accula platform. This assay was launched in mid-2019, and it is disappointing to find no published performance data. Mesa has also launched an EUA POC SARS-CoV-2 assay with a 30 minute time to result. Unfortunately, a performance evaluation of the SARS-CoV-2 assay suggests that the assay lacks clinical sensitivity.[7] In July 2020 they received a $15M award through the NIH RADx program for scale-up and deployment of their SARS-CoV-2 test. The web site does not indicate what the installed base is for their instrument, or whether a multiplex SARS-CoV-2 + influenza test might be in development.

Overall, Mesa Biotech's platform has some potentially incremental improvements over competing products for priority Use Cases in the underserved decentralized Use Settings. They are worth watching to determine whether the resources they have recently marshalled to scale up their installed base and manufacturing capacity will be sufficient for them to become a more important player in the influenza diagnostic market.

The company **Cue** sells a platform called the Cue Health Monitoring system which consists of single-use disposable cartridges and the Cue Cartridge Reader. The cartridges use an isothermal amplification chemistry and electrochemical detection, and the company recently received an EUA for a SARS-CoV-2 assay. The company claims that the platform was specifically designed for both healthcare settings and home use, suggesting it will be suitable for decentralized settings. The Cue Health Monitoring system has several potentially incremental improvements over certain features of other competing point-of-use NAT platforms (e.g., Cepheid GeneXpert, Abbott ID Now) including its very small size, portability and more rapid result (20 minutes for SARS-CoV-2, which is faster than Cepheid's 45 minutes, but not faster than the ID Now's 15 minutes). The reader will reportedly cost several hundred dollars, and each cartridge will cost "tens of dollars."[8]

Cue is a well-funded start-up which was founded in 2010 and has raised more than $150M USD in venture funding. The company is based in San Diego, CA, USA. They are not currently a player in the influenza testing market. However, prior to the SARS-CoV-2 pandemic, Cue was working on an influenza A+B test with $30M in support from BARDA, which apparently is undergoing validation now.[9] An image on their website shows a rendering of cartridges for other tests, some of which would be NATs and some immunoassays, including several which may be envisioned for healthcare settings (RSV, "Strep"),

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and others which may be envisioned for home use (vitamin D, HbA1c, cholesterol, testosterone, pregnancy and "fertility").

Importantly, Cue recently announced that they have received a $481M award from the Department of Defense, which they will use to build-out a manufacturing facility in San Diego, USA, and scale up production of their SARS-CoV-2 cartridge to 100,000 cartridges per day by March 2021. Recent announcements have not indicated whether a multiplex SARS-CoV-2 + influenza assay is in development.[8]

Overall, Cue's platform has some potentially incremental improvements over competing products for priority Use Cases in the underserved decentralized Use Settings. Their platform is also notable in its apparent capability to perform immunoassays as well. They are worth watching, to determine whether they can match the performance of other NAT platforms on the market, whether their platform can successfully perform immunoassays as well, and whether the enormous resources they have recently obtained to scale up their install base and manufacturing capacity will be sufficient for them to become a more important player in the influenza diagnostic market.

Scope Fluidics is based in Warsaw, Poland and was founded in 2010 in the Institute of Physical Chemistry at the Polish Academy of Sciences. The number of employees is not known, and the company is not known to currently have any revenues. Scope appears to function as a technology incubator involved in various product development efforts related to diagnostics and healthcare. One of their projects, which has been spun out into the company Curiosity Diagnostics, is a fully integrated and automated POC NAT platform called PCR|ONE. The platform uses an infrared temperature cycling capability to perform an "ultra-fast" PCR cycling. The platform is capable of performing up to 64 separate PCR reactions in separate microwells. The platform is designed for use in laboratories and appears to have a single cartridge bay. The company has already obtained a CE-IVD certificate for the device. They claim a cartridge COGS of $5, and plan on reagent rental agreements for the instrument to result in per-cartridge price of $20–25.[10]

The company has developed a SARS-CoV-2 assay with a time-to-result of 15 minutes. The website indicates that clinical evaluations for this assay are underway in October 2020 and they plan to submit for an FDA EUA by the end of 2020. They also plan to follow-up this up within a relatively short time frame with an application for approval for a multiplex SARS-CoV-2 + influenza + RSV assay. This assay will reportedly distinguish influenza A, B and two H1N1 targets.

Earlier development efforts before the SARS-CoV-2 pandemic were focused on a multiplex assay for *S. aureus* and MRSA, and the firm will start a clinical trial for this indication in October 2020.

Overall, Scope/Curiosity Diagnostics has some incremental improvements in time to result, and possibly in multiplex capacity, compared to other NAT POU platforms, though they do not appear to be aiming for decentralization in very low-resource settings and have not announced intentions to pursue a CLIA waiver. It will be interesting to watch if they can demonstrate equivalent performance on real-world samples with their best-in-class time-to-result for a PCR-based test.

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Visby Medical is a start-up company based in San Jose, CA, USA which was previously known as Click Diagnostics. It was founded in 2012, is privately held, and the current number of employees is not known.

Visby has developed an instrument-free, portable, fully disposable cartridge called the Personal PCR device that performs an automated RT-PCR reaction with a time-to-result in 30 minutes. They developed a test for detecting *N. gonorrhoeae* and drug resistance mutations and applied for FDA authorization in March 2020. In August 2020, they received $19M in prize money for this test in the US government-sponsored Antimicrobial Resistance (AMR) Diagnostic Challenge. They have also developed a device for the diagnosis of SARS-CoV-2 infection, which also has a time to result of 30 minutes. In September 2020, they announced that they had been awarded the first phase of the NIH RADx program to accelerate the development of this device, and in October 2020 received the second phase of RADx funding of $9.6M, which they are using to secure their supplier base and scale up manufacturing.[11]

Visby received EUA for this SARS-CoV-2 device in September 2020, for use in moderate-complexity CLIA certified laboratories. There are several manual sample and reagent preparation steps required before the PCR amplification, making the workflow for this device more complex than other platforms being positioned for very low resource settings, such as lateral flow devices. Pricing for the device has not been announced. Current production is reported to be in the tens of thousands of devices per week, with plans to scale further.

No announcement has been made about plans to develop a multiplex SARS-CoV-2 + influenza device, though their technology has the multiplex capabilities to do so.

Overall Visby has an innovative product, which if proven to have performance similar to other PCR-based tests on the market, could truly bring high-sensitivity testing with very rapid results to some low-resource settings. It will be worth watching to see if they develop tests that include influenza, what their pricing will be, and how this might affect the influenza testing landscape.

NGS Platforms to Improve Accessibility for Lower-Resource Settings

While determining high-resolution strain information was not classified as among the highest priority Use Cases for influenza pandemic preparedness, it is clear that technologies that provide greater accessibility (i.e., less centralized) to high-throughput sequencing of individual influenza strains would contribute to a better understanding of strain evolution, and perhaps help identify the circulation of IVPP more rapidly. In addition, companies with next-generation sequencing (NGS) technologies are beginning to leverage the extreme multiplexing capabilities of these technologies to develop true diagnostic assays that are capable of very high-throughput at a low cost-per-sample. Three companies were identified that could potentially contribute unique approaches towards greater accessibility to high-throughput sequencing.

The first of these companies is **Oxford Nanopore Technology** (ONT). ONT was founded in 2005 and currently has about 500 employees. They are a small but unique player in the next-generation sequencing (NGS) space. They have headquarters and manufacturing in Oxford, UK, a commercial presence in seven other countries, and sales into nearly 100 countries. They have raised more than

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£600M since inception and are privately held, with estimated revenues of £32M in 2018, though essentially none of this to date is related to ILI diagnostics.[12] They specialize in a variety of NGS called nanopore sequencing, which permits smaller, less-costly instrumentation than other types of NGS, and longer read lengths, though base-calling may not be as accurate relative to other NGS chemistries. Their traditional markets have been in research and applied markets, though a limited number of organizations have used their platforms to develop Lab Developed Tests (LDTs) or sample-to-answer NGS platforms for applied markets (such as food safety testing, see the next company profiled — Clear Labs). Because of the small size and low cost of some of their instruments, relatively simple workflows, and reagent kits that do not require cold chain, they have been able to apply their platforms in point-of-use ("near-sample") settings. The installed base for ONT instruments is not known, though the vast majority will be in research labs, not in diagnostic laboratories.

In their first foray into the diagnostics space, ONT just received a CE Mark for a high-throughput, low-cost SARS-CoV-2 diagnostic assay called the LamPORE COVID-19 assay. The assay targets the sequence of three conserved genes, along with the human actin gene as a control for sample adequacy. This high-complexity test requires a laboratory to isolate RNA from patient samples. The time-to-result is two hours, and when run on their GridION platform with five random-access bays in pools of 24 to 480 samples, over 9000 samples could be processed in 24 hours. Initial data on the LOD and clinical sensitivity and specificity look strong. Press releases indicate they are also pursuing an EUA for this assay. Their website indicates that a respiratory virus panel assay is in development, which will include influenza A, B and RSV.

Due to the scalability of their platform and its potentially low cost per test, it would certainly provide some advantages in surveillance applications. However, at lower pooling levels, the price-per-test may be too high to be practical. It will be interesting to watch the market's reactions to the complexity of the assay, time-to-result and data analysis issues for pure diagnostic or screening Use Cases, and how many testing locations have the sample throughput needs to take advantage of its scale capabilities, which will be critical to keeping the cost-per-test low.

Interestingly, ONT recently announced a 4-year, $100M initiative with the BMGF, Africa CDC, Microsoft and Illumina called the Africa Pathogen Genomics Initiative (Africa PGI). This initiative aims to rapidly expand access to NGS tools across Africa and will catalyze the placement of an installed base of platforms that could greatly expand influenza surveillance and molecular epidemiology into a geographic area that has been underserved.

Overall, ONT is an interesting new player to watch in the landscape of influenza diagnostics, whose technology could be potentially transformative for surveillance Use Cases, and which might also contribute to diagnostic, differential diagnostic, and screening Use Cases.

A second company with a unique approach in terms of improving accessibility to NGS for sequencing influenza virus is **Clear Labs**. Clear Labs was founded in 2014, has ~ 50 employees, is based in San Carlos, CA, USA, and is privately held.[13] Their initial product, launched in 2015, was a fully automated sample-to-answer platform to perform NGS analysis in the food safety sector. The platform integrates liquid handling automation and a GridION nanopore sequencing instrument from Oxford Nanopore, along with

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a fully automated data analysis pipeline. This platform has been successfully deployed to very low complexity food production facilities

The company has developed a diagnostic assay for SARS-CoV-2, which generates sequence from about half of the virus' genome, with an 8-hour time-to-result.[14] This assay generates both a presence or absence "call" for a sample, as well as the sequence for the virus and annotation of strain variants that are identified, a potential leading competitive advantage of this technology. The assay is highly scalable and could process many samples at once, which would keep the cost per assay lower, but the pool limits and anticipated price-per-assay have not been announced. The FDA EUA for this assay was announced in September 2020. Clear Labs has not announced the development of a multiplex SARS-CoV-2 + influenza test, but their technology could easily perform such an assay with essentially no change in the cost of goods.

Overall, Clear Labs has taken the valuable step of fully integrating both the wet-lab and bioinformatics analysis for an NGS assay that could be applied to influenza. This could greatly enhance its ability to move to less-centralized settings that are capable of only medium-complexity testing. It will be interesting to see which market sub-sectors they have the most success in, and whether they develop a multiplex SARS-CoV-2 + influenza assay.

Another company that has something potentially unique to offer in terms of improving accessibility to NGS for influenza viruses is **Thermo Fisher Scientific**. They offer a kit called the PathAmp FluA Reagents for the Ion Torrent semiconductor NGS platform, which is the only commercially available kit that has been identified for NGS of influenza viruses. It is approved for veterinary use only. Up to 10 viruses can be pooled for analysis on a single Ion 314 chip (for the PGM instrument).[15] The high-complexity workflow can be completed in approximately 24 hours. Illumina is widely believed to dominate the clinical NGS market, though the precise fraction of labs that have an Ion Torrent instrument, and the size of the installed base for the Ion Torrent PGM are not known. Up until 2020, the application emphasis for the Ion Torrent clinical NGS has been in the oncology arena, and it is likely that many of the instrument placements are in labs that perform specialty oncology diagnostics, rather than infectious disease testing or surveillance.

No announcements have been identified which indicate that there are any plans to develop clinical diagnostics assays related to SARS-CoV-2 or a multiplex SARS-CoV-2 + influenza.

Thermo Fisher Scientific has $24B in revenue and approximately 70,000 employees. Despite their enormous size, only 2% of their revenue is in their "specialty diagnostics" business segment, and only 11% of their revenue is in their "Life Science Solutions" business segment, where the Ion Torrent revenue is recognized. They are not one of major diagnostics companies in terms of assay production. Though they also have other products for influenza testing, including the Xpect Flu A & B lateral flow cartridge, reagents for neuraminidase inhibition assays (for phenotypic drug resistance testing), and RUO and veterinary-use PCR kits to detect AIV strains such as H7N9, and none of their ILI-related diagnostic products are known to generate significant revenue.

Overall, though Thermo Fisher is a large player in molecular diagnostics, they have not been a major player in the influenza diagnostics market. It is not clear that its NGS offering has significant advantages

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(in pooling, time to result, or complexity) over the ONT or Clear Labs offerings, nor that their existing install base would provide them with any advantage in the high-throughput influenza sequencing arena. However, their market presence and installed base could be beneficial for rapid deployment of IVPP testing capacity versus smaller players.

Twist Bioscience is a leader in synthetic DNA production that has branched out over the years to providing high multiplex oligo pools and kits for NGS library construction, as well as synthetic controls for nucleic acid tests, libraries of gene variants, and other products. The company was founded in 2013, is based in San Francisco, U.S., they have 400 employees and revenues of $54M in 2019.

Their proprietary methods for synthesizing large numbers of unique oligos on a silicon wafer platform allows them to produce more than 20 million oligos per month at a disruptive price point. Their need for quality assessment of their oligos led them to implement industrial-scale NGS on Illumina platforms. They have commercialized products for targeted NGS library construction. In 2015, in response to the Ebola outbreak, they developed a pan-viral oligo pool with over 600,000 oligos to capture the sequences for more than 1000 human viruses. They have published a protocol to use this pool to detect all viruses in a human clinical sample. They helped implement the instrumentation (MiSeq) and protocols for NGS at both the Pasteur Institute in Dakar, Senegal and the Liberian Institute for Biomedical Research in Liberia, that was used to analyze samples from suspected Ebola cases, and which identified many other viruses as well as Ebola. The pan-viral oligo pool is capable of detecting influenza viruses, though the amount of strain typing information that it provides is not known, and a performance evaluation of its clinical performance remains to be demonstrated. They have also shown that it is straightforward (e.g., no additional training was required) for these labs in LMICs to swap out the oligo set and perform other assays (e.g., for Lassa virus and Monkeypox). Recently, they have launched a research-use-only oligo set for sequencing human respiratory viruses in clinical samples. While the protocols and instrumentation described are for high-complexity laboratories, the demonstration of their success and flexibility in LMIC is worthy of note.

Overall, Twist has developed some potentially valuable tools that could be applied to the high-throughput surveillance of influenza along with other viruses, and has demonstrated that they can be operationalized on one of the world's most commonly-used NGS platforms in high-complexity labs in LMIC. It will be important to follow the use and success of tools like these as the pandemic preparedness community develops an NGS strategy for influenza surveillance.

Platforms for Influenza Triage Use Cases

Two companies were identified that have potentially unique products in the category of point-of-care triage tests for influenza or ILI. This category of products is of particular interest because there is still an unmet need for very low-cost, rapid, and low complexity tests for triage Use Cases. Solutions for this Use Case could be critical in a pandemic situation, to relieve some of the burden for higher-cost and potentially slower diagnostic and screening tests, particularly in LMIC.

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The first company in this category is **Ativa**, which is a privately-held start-up in Minneapolis that was founded in 2008, and has less than 20 employees. They have raised ~ $36M in funding since their inception.

Ativa is developing a point-of-care blood cell analyzer called the Diagnostic Work Station (DWS) based on miniaturized flow cytometry technology. The goal of their platform is to detect the body's earliest immune responses to specific pathogens, possibly before symptoms appear. Their platform uses a low-cost disposable cassette which analyzes a small sample of capillary blood, and provide results within 5 minutes. The company is developing what they refer to as an infectious disease card which, when combined with different machine-learned algorithms under development, will potentially distinguish and diagnose a wide-variety of infectious diseases and other chronic health conditions. They are developing an algorithm for sepsis triage, and in addition, for SARS-CoV-2 triage. In theory, an algorithm could be developed for influenza triage as well. No announcements have been made regarding when these tests might be launched. Their goal for the platform is to develop tests for a wider range of indications, including those that might use urine as a sample type.

Overall Ativa has a unique flow cytometry-based technology that could potentially be applied to influenza diagnostic to serve triage Use Cases, which have been underserved in all Use Settings. They have a potentially unique path to business (revenue) sustainability because the DWS can also perform routine general health panels such as a 5-part CBC and a basic metabolic panel, which are some of the most frequently performed test panels in the world.

A second company that is developing a platform that might be used in triage Use Cases for influenza is **Inflammatix**. They are a privately held start up in Burlingame, CA, USA that was founded in 2016, and has approximately 60 employees. They received a BARDA grant for $75M for the development of their platform. Their platform, called Myrna, analyzes the host's immune response by detecting specific mRNA patterns expressed by cells in the blood. The time-to-result is expected to be 30 minutes, and the cost somewhere in the $50 range. They are developing tests for sepsis triage (29 mRNAs, in pivotal studies), fever triage (7 mRNAs, in product development), influenza triage (15 mRNAs, in clinical validation), immunotherapy response for sepsis (33 mRNAs, in clinical validation), and "tropical fever" (discovery phase, to distinguish bacteria vs. viral vs. malarial vs. TB infection), and recently, for COVID severity (5 mRNAs). They recently received a $1M award from DARPA for their COVID severity test.

Overall, Inflammatix is an interesting new player in the influenza diagnostics arena with the potential to address triage Use Cases, which have been underserved in all Use Settings. They will be worth watching, to see the performance of their influenza test, and whether the price point and time to result make them a viable option for triage Use Cases.

Other Companies Listed on the IVTM

Four companies are listed on the IVTM that did not score high enough to be considered a top tier player in the influenza diagnostic landscape, nor do they appear to have a potentially unique technology to offer. These companies are Princeton BioMeditech, R-biopharm, Response Biomedical, and Sekisui.

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However, because they are listed in the IVTM, brief summaries of them are presented here to provide some perspective on their place within the landscape.

Princeton BioMeditech is an interesting player in the immunochromatography space. They are a small company, reportedly having 175 employees and generate $35M in revenue.[16] They are specialists in immunochromatography devices, selling only test cartridges and reader instruments for the human health, veterinary, and food safety markets. They are a self-described world leader in "rapid, point-of-care diagnostics" and have introduced over 70 immunochromatographic tests into the market. They manufacture an influenza antigen lateral flow test which appears to be sold under their own brand name and also under the brand names of other diagnostic companies, including Meridian, Orasure, Biosign, LABSCO Lifesign, Polymedco and McKesson. Their manufacturing capacity for immunochromatographic devices is one of the largest in the world. Overall, Princeton BioMeditech is a capable OE partner for higher volume lateral flow test strip manufacturing.

R-Biopharm is a medium-sized company based in Darmstadt, Germany that produces products for a variety of clinical diagnostic assay types, including ELISAs (traditional and array-based formats), lateral flow, immunoblots, and PCR (kits consisting of tubes of reagents for open platforms) for both the human health and "food and feed" analysis markets. They also produce a range of control products that can be used to emulate patient samples. The company was founded in 1988, and the web site indicates that they have almost 1000 employees world-wide (~500 in Germany and ~ 500 abroad). It is privately held and revenue information is not available, though the number of employees suggests that it may in the range of $200–300M. They sell a lateral flow device for influenza virus + RSV, as well as one for SARS-CoV-2. Their products do not appear to be significantly differentiated from others on the market. R-Biopharm is represented by subsidiaries in the USA, UK, Italy, France, Latin America, Brazil, Spain, Belgium, Australia, India, China and the Netherlands, as well as by a worldwide extensive network of more than 120 distributors. Overall, R-Biopharm is not a major player in the influenza diagnostics market, nor does it appear to have any uniquely differentiating technologies or products for IVPP.

Response Biomedical is a small diagnostics company that specializes in reader-based immunochromatographic tests. They were founded in 1992 are based in Vancouver, Canada. They reportedly have ~ 65 employees and $12M in revenue.[17] They sell an influenza A+B assay, as well as a SARS-CoV-2 assay. The company has been in existence for many years but has been unable to sufficiently distinguish their products from their competitors, leaving them with a relatively small market presence.

Sekisui Diagnostics is a subsidiary of Sekisui Chemical Company of Tokyo, Japan. Sekisui Diagnostics was founded in 1985, is headquartered in Burlington, MA, USA, has annual revenue of $200M, and 450 employees worldwide. Their ILI-related diagnostic systems (influenza OSOM lateral flow, Acucy digital immunoassay system (DIA), and distribution of Mesa's POC NAT platform, are a very small part of their overall business, which includes the production of enzymes and specialty biochemicals, clinical chemistry diagnostics, immunochromatographic tests for other infectious diseases, and pre-analytic systems.

Though Sekisui Diagnostics has several platforms for influenza diagnostics, and they are a subsidiary of a very large company with a global customer base and distribution, they are a minor player in the

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influenza diagnostics landscape that does not appear to focus their development or commercial efforts on infectious disease diagnostics.

Section 5. Market Landscape

In the previous section, information was presented about the individual companies and some of their products. In this section, we provide a landscape perspective that aids in understanding who the major players are relative to one another, and which companies and platforms compete in which sectors. This landscape view is shown in **Figure 1**.

In this figure, companies with platforms that are more suited for laboratory environments are shown on the left, companies with platforms that are more suited for point-of-care or point-of-use are shown on the right (though there is no black and white line that divides the two), and companies in the center have platforms for both types of settings. Estimated Influenza-or ILI-related revenues for each platform are indicated by the colored circles. It is important to note that this figure represents the situation before the SARS-CoV-2 pandemic, and before the launch of any multiplex SARS-CoV-2 + influenza assays. These events are changing the landscape dramatically, and it will be worth revisiting the landscape once a few additional quarters of revenue are reported, and the new multiplex assays have progressed further in their commercialization.

Eight major players are shown in the center of the concentric rings, including Abbott, Quidel, Danaher, Roche, Becton Dickinson, Hologic, Qiagen and bioMerieux. Minor players are shown outside of the inner ring. Companies which have not yet commercialized products are shown outside the outer-most ring.

A legend for the sizes of the colored circles is shown in the lower left, with the smallest size of colored circle indicating platforms or companies estimated to have < $10M in influenza-related revenues, the intermediate size-colored circles indicating platforms estimated to have between $10M and $50M in influenza-related revenue, and the largest size circles indicated platforms estimated to have > $ 50M in influenza-related revenue, with all estimates based on publicly available information.

The colors help to identify which platforms compete with each other – for instance, the dark green circles indicate point-of-use immunoassay platforms with a reader, and that Quidel's Sofia, Abbott's BINAX Now and BD's Veritor dominate this market sub-sector (by having the largest estimated influenza-related revenues), while the platforms from Sekisui and SD Biosensor are minor players, and that of LumiraDx is just being commercialized, while Quanterix has yet to be commercialized.

Similarly, it is possible to see that relatively few players have a light blue circle which indicates a low-multiplex point-of-use NAT platform for single-pathogen tests (or small panels of two or three pathogens). Cepheid's GeneXpert, Abbott's ID Now and Roche's Liat dominate this market, while the platforms from Mesa Biotech/Sekisui and Quidel are minor players.

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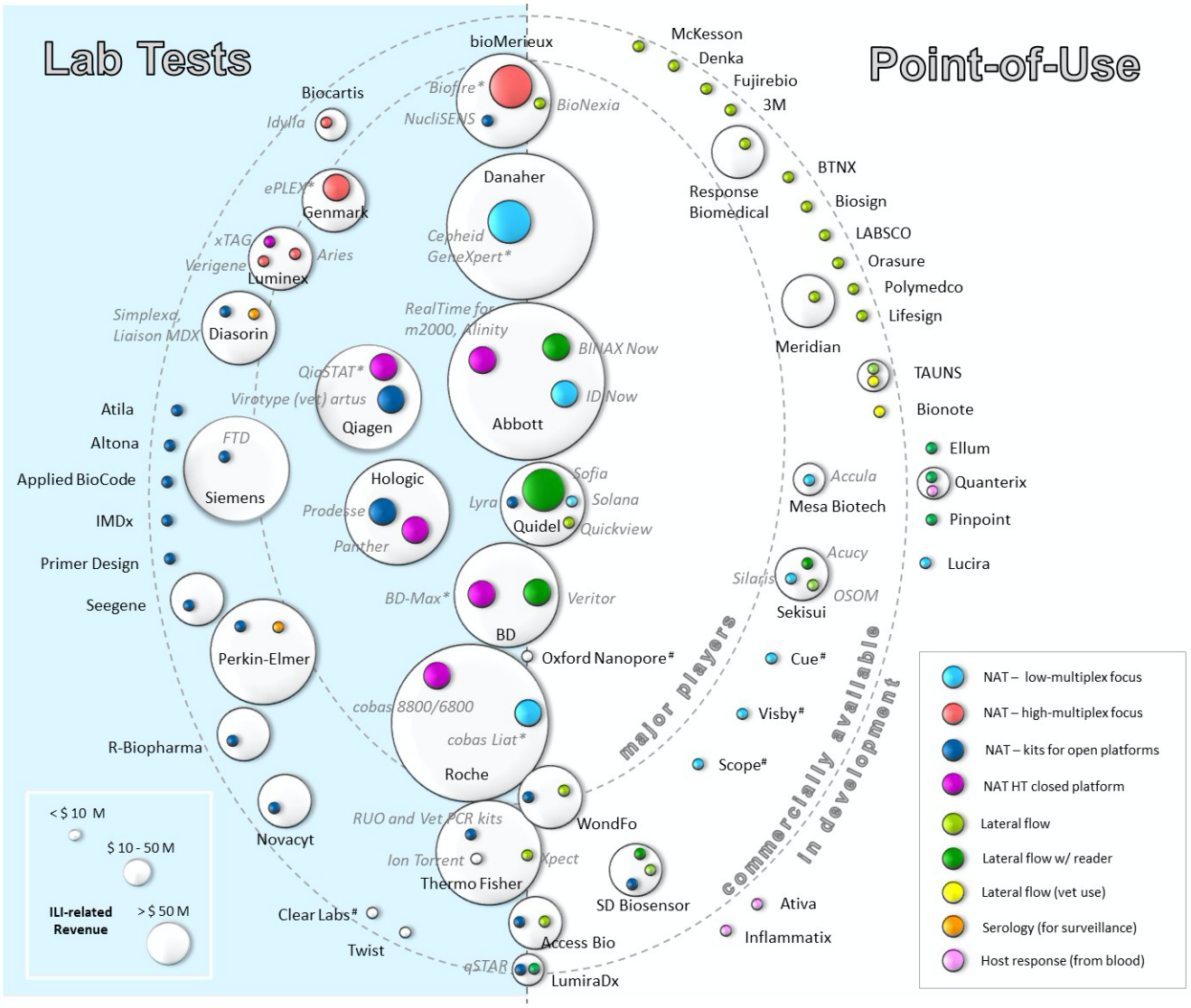
Figure 1. Market Landscape of Influenza Diagnostic Companies



Company names are shown in black, and their platform names are shown in gray italics. *Company has EUA for Influenza + SARS-CoV-2 test. #Company has commercialized a platform and assay for SARS-CoV-2, but not yet for influenza. BD: Becton Dickinson. Diasorin Liaison MDX is not HT. Oxford Nanopore's platforms could be in lab or point-of-use. Vet = product for veterinary use. Major diagnostic company not shown: Bio-Rad. The company iCubate has a sample-to-answer platform (2 instruments), with 2 FDA cleared assays, though their respiratory panels and GI panel assays are RUO, and therefore they are not shown.

There are also a limited number of specialty players who focus on fully automated systems to perform high-multiplex panel assays (shown by the rose-colored circles). While a few have obtained some traction, they still constitute a minority fraction of the influenza testing market due to price and reimbursement challenges, and the preferences of clinical decision makers who have questioned the actionability vs. price of large respiratory panel tests.

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With this landscape view, the important players become apparent, both in total size as well as in the revenue generated by their influenza-related tests. It is easier to discern that relatively few companies are offering a spectrum of platforms that spans the divide between NAT and immunoassay testing, and that most of these are the very large players that have substantial resources to develop and support multiple platforms, such as Abbott, BD and Quidel. However, several major players in the influenza test market have only one platform, such as Danaher and bioMerieux.

Quidel stands out for having a broad spectrum of platforms (though not all generate substantial revenue), as well as the major player where influenza-related testing constitutes the largest part of its business. In addition, influenza-related testing (in the form of high-multiplex respiratory panels) is also a major portion of bioMerieux's and GenMark's revenues.

The relatively few low-multiplex platforms designed for lower-resource and lower-complexity settings is perhaps not surprising, given the challenges in their development, the regulatory environment, and in the business cases for performing these assays at the point-of-use. This type of platform is critical for certain settings, and it will be important to carefully consider which may be the potential best long-term partners for pandemic preparedness, especially for LMIC (see Figure 2 below on menu for low-multiplex POC platforms for lower-resource settings).

There are a very large number of players with fairly undifferentiated lateral flow devices for antigen detection and many are not shown in the figure, including a number from Asia (see for instance Sakai-Tagawa et al. 2017) and other regions of the world. To understand where the landscape could be headed in the future, it is more useful to focus on several emerging and innovative players, reviewed in Section 4, who are developing products with much higher sensitivity and which could radically transform this part of the landscape in the near future.

There are also a large number of players with fairly undifferentiated kits for NATs for lab-based open platforms, including major players such as Qiagen, but also many small players. It is possible that the need for more rapid time-to-result for diagnostic (and potentially screening) Use Cases, and the enormous innovation and resources that have been unleashed by the SARS-CoV-2 pandemic to develop and commercialize POU NAT platforms and multiplex assay that include influenza, will radically transform this part of the landscape as well.

Some nuances in the landscape are not apparent given the high-level perspective taken and the reliance of historical data to generate the figure. For instance, the figure likely underestimates the potential impact of some companies for which there is very little public information, but who could end up being important players, such as the previously mentioned LumiraDx, Pinpoint, or Visby. Another nuance which does not come out in the figure is how the landscape would be altered by the emergence of an IVPP or pandemic virus that is detected by some existing platforms but not others. The impact of changes brought to the diagnostic industry due to the COVID-19 pandemic, and the potential for their lasting impact in the post-pandemic world, also bears watching.

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Section 6. Readiness to Respond in the Face of a New Pathogen

Pandemic preparedness should include a plan for the rapid development, manufacturing scale up, and distribution of the critical tests, which are likely to include immunochromatographic tests (generally lateral flow cassettes) for antigen detection for Diagnosis Use Cases. It is therefore interesting to examine which companies have the largest manufacturing capacities for these types of products. Examples of companies with annual production capacities exceeding 100 million test strips include Abbott, AccessBio, Quidel, SD Biosensor and Wondfo, with BD well under that volume range but expanding.

If an instrumented diagnostic platform is to be widely deployed in decentralized settings (including LMIC), its initial deployment (before a pandemic) and its sustained utilization will depend on the platform having a menu that is of high interest and utility in these decentralized settings, along with per-assay prices that can be accommodated in those settings. We therefore looked at what other menu items are available for the low-multiplex point-of-use NAT platforms designed for lower-resource and low-complexity settings within the influenza virus diagnostic landscape. **Figure 2** shows only these companies and platforms and lists the assay menu available for that platform, other than influenza virus or influenza virus + RSV assays. In the figure, menu items that are of possible interest to LMICs are shown in bold, while menu items that are likely to be of lesser interest to LMICs are shown in regular font.

All of the platforms that are focused on low-multiplex NATs have extremely limited menus except for Danaher's GeneXpert. Even the big companies like Abbott and Roche, who have the resources, have not developed big menus for their platforms, which is likely a reflection of many factors, including pricing and reimbursement issues combined with operational and workflow challenges at the POU, which ultimately drive the commercial attractiveness for a platform manufacturer. Outside of the current pandemic situation, this could limit the appeal of these platforms, especially in LMIC.

However, the current pandemic is driving the placement of many low-multiplex NAT platforms to a much wider array of lower-resource and lower-complexity settings. Some fraction of the installed bases of these platforms will then presumably be used for performing SARS-CoV-2 + influenza assays. It will be important to observe over time whether any of them will receive substantial placements in LMICs over several years, and which of these platforms look likely to sustain their installations afterwards.

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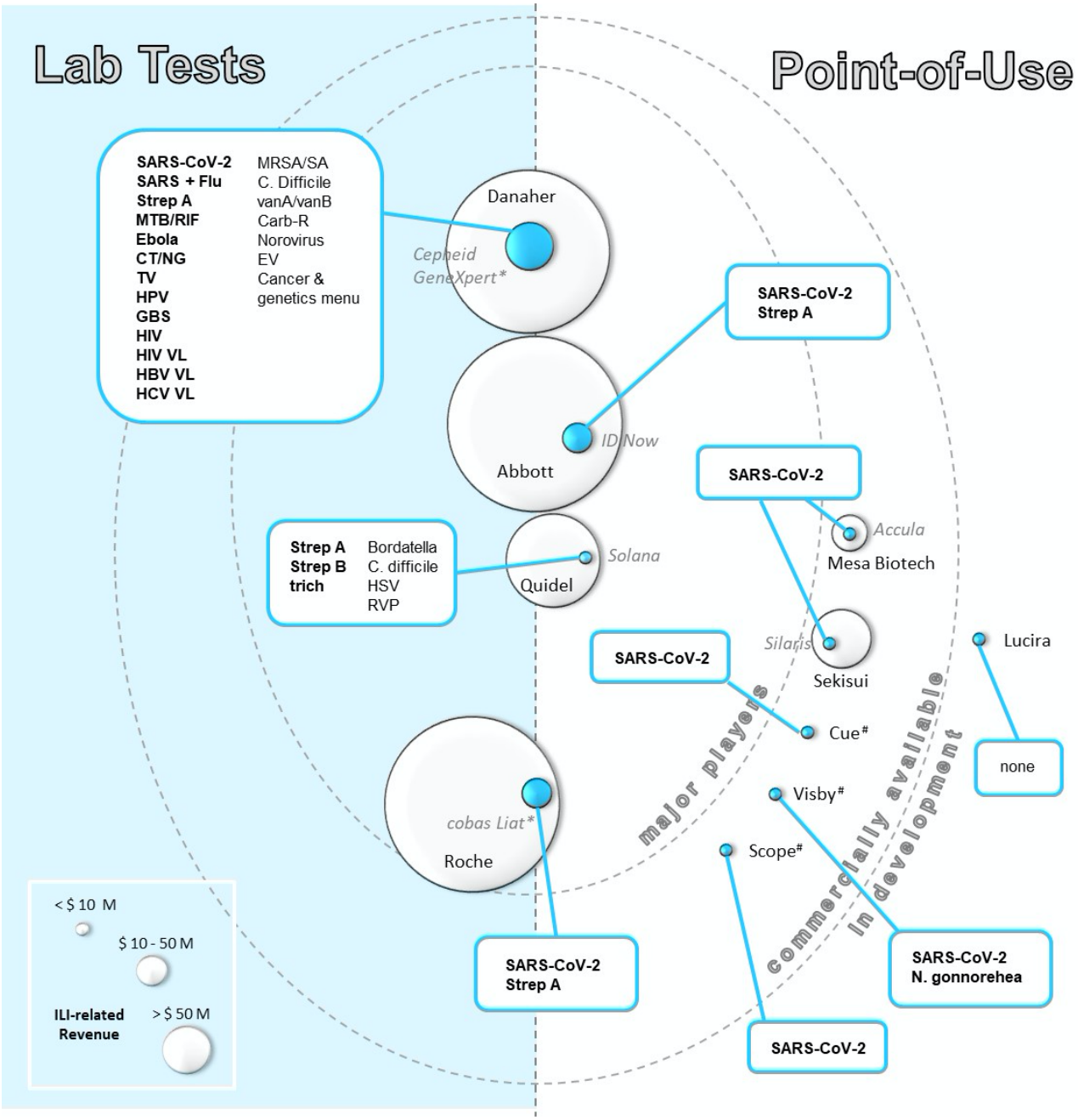
Figure 2. Low-Multiplex Point-Of-Use NAT Platforms and Their Menu Other than Influenza



Not shown are companies with high-multiplex platforms and much higher price points per assay that are unlikely to be feasible for low-resource settings. #These companies have only a SARS-CoV-2 assay, they do not have an influenza assay at this time. Not shown: assays alluded to in images on Cue's website, which include some immunoassays as well as NATs (influenza, RSV, HbA1c, cholesterol, vit D, pregnancy, "fertility," "inflammation")

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Section 7. Discussion

Because diagnostic tools are such a critical component in pandemic detection, assessment and control strategies, significant planning and preparation are necessary to ensure that the right tools are available at the locations where they will be needed in the event of a pandemic. This advance planning is especially needed because in the absence of a pandemic, the existing landscape of diagnostic manufacturers has not had the incentives necessary to develop and manufacture all of the types of diagnostic tools that might be needed. In this report, the landscape of companies involved in influenza diagnostics is reviewed with the aim of providing clarity around which key players may already have the diagnostic tools that are needed, and which may have innovative technologies, development expertise, or manufacturing and distribution capacity to be able serve as key partners in ensuring pandemic preparedness.

The organizing framework for this analysis is a set of high priority Use Cases for influenza tests and the specific settings in which they need to occur. These Use Cases and settings help define the user needs in specific situations, and from these needs, we can determine which products or technologies can meet those needs. In the Halteres report entitled "Landscape Assessment: Current State and Future Trends in Technologies for Influenza Diagnostics," dated August 31, 2020, which was prepared for the WHO we saw that some settings where influenza testing occurs are already fairly well-served by the technologies and products that exist today. These settings are the high-complexity and well-resourced labs that perform testing for diagnosis, differential diagnosis, and surveillance Use Cases. Remaining challenges for these types of settings include streamlining or simplifying processes and building resiliency into their supply chains.

However, other settings where influenza testing occurs, or should be occurring, still do not have their needs completely met. These include decentralized and lower resource settings in both HIC and LMIC markets, where diagnosis, differential diagnosis, and surveillance Use Cases should be occurring. For these settings, the existing tests on the market still do not fully serve one or more needs related to sensitivity, time-to-result, ease-of-use and/or price point. In this report, special attention is paid to preparedness for these decentralized settings as there are fewer appropriate test options, and the technological, regulatory, and commercial challenges are greater for the types of platforms that serve these settings. This is particularly important for pandemic influenza testing since time-to-results will be more critical than for seasonal flu if antiviral drug distribution is to be employed; for example, Tamiflu is most effective in the first one to two days after symptoms begin.

Given the needs of all the Use Cases and settings for tests, and the landscape of players that might fill specific roles in diagnostic preparedness, what should be done to ensure widespread access to the diagnostic tools that will be needed for global pandemic preparedness? Success in improving preparedness will hinge on selecting and supporting the best players to fulfill specific roles in preparedness. This will include tests that exist today and are likely to react sufficiently with IVPP and pandemic strains and new tests that cannot be developed until an outbreak begins. When considering what should be done, and which companies can do it, it is helpful to categorize the issues to be

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addressed into those that should be completed before a new pandemic emerges, and those that need to be completed after an IVPP or pandemic influenza virus emerges.

Preparedness Before a New Pandemic

A number of improvements to influenza diagnostic testing access and capabilities would ideally be made before a new pandemic emerges. These include a) catalyzing the adoption of appropriate testing platforms, especially those with broader menu capabilities, to underserved settings and geographic areas, b) enabling the development and commercialization of potentially transformative new technologies and products, and c) mitigating supply chain risks through testing diversification, simplification, stockpiling, or other strategies.

Expanding the installed base of existing test platforms to underserved settings and geographic areas would ideally be undertaken before a new pandemic emerges. Selection, procurement, installation and training for a new platform are all time consuming, and the scale-up of manufacturing for instrument systems can also be a significant challenge. The underserved settings today include primarily low-resource settings, which will require very low complexity (potentially fully-automated) testing systems. The manufacturers with the largest current revenues and installed bases for low-complexity platforms include Abbott, Quidel, Cepheid and Becton Dickinson (see the individual profiles for these companies as well as Figure 1). These companies have the product development capabilities, commercial maturity, manufacturing and distribution capabilities, and commercial commitment to the influenza testing market that makes them capable of sustaining participation in influenza pandemic preparedness. However, they are likely to require incentives to broaden their reach. New generations of systems are being developed that could potentially challenge these industry leaders; e.g., LumiraDx, Mesa Biotech, Cue, Visby and others, as described elsewhere in this report.

Another category of underserved settings are the labs which should be performing higher-throughput influenza surveillance in LMICs, which ideally would be able to perform sequencing-based testing.

Efforts to broaden the installed bases of important low-complexity platforms would be greatly aided by a map of the current installed bases of existing platforms, the assay menu offered, and their associated catchment areas, which would help to identify the gaps in availability. In addition, ongoing updates to the test availability map, which would include changes impacting flu testing driven by the SARS-CoV-2 pandemic, would provide additional insight into the future installed base trends, including the entry of potentially significant new players such as LumiraDx, Cue and Visby. Strategies and mechanisms (e.g., funding and training) to drive adoption of appropriate platforms into underserved settings should be undertaken before a new pandemic emerges. As parenthetically mentioned here, adoption may only be commercially viable and sustainable in lower-resource settings if a wider test menu is developed for a particular platform that is of local value and interest during non-pandemic periods. It may therefore be important to incentivize platform developers to consider the broader diagnostic needs of underserved areas. These could include advanced market commitments, guaranteed minimal sales even in low flu incidence years, assistance with manufacturing scale up, development costs, access to appropriate sample panels, partnerships with procurers and NGOs, and introductions to policy makers and distributers.

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Enabling the development of potentially transformative new technologies and products is critical to meeting the testing needs of specific settings that are underserved by today's products. In particular, new technologies and/or products maybe be the only way to meet all the performance, speed, ease-of-use and price needs for low-resource settings where testing for diagnosis and differential diagnosis Use Cases should be occurring today but is not. There are also significant tail winds in these efforts due to the enormous resources that are being devoted to the development and commercialization of innovative tests and products for SARS-CoV-2.

Supply chain risks can be mitigated through a variety of strategies, which should be undertaken before a pandemic begins, if possible. One straightforward approach which has been used extensively in response to the SARS-CoV-2 pandemic is to diversify the vendors from which supplies, reagents, components and consumables are obtained. These efforts took labs several months after the SARS-CoV-2 pandemic was declared, which set testing back in many locations. These experiences highlight the benefits of employing this strategy before a pandemic begins. Test manufacturers and procurers should be encouraged to analyze their supply chain risks and address these issues before the next pandemic, though this strategy can be difficult to implement if pricing disparity arises or persists across alternative vendors. Another strategy that has been seen in 2020 in response to the explosion in demand for SARS-CoV-2 testing is to simplify or streamline protocols to reduce the required reagent and consumable needs. For instance, many labs and some product developers devised and validated "extraction-free" sample preparation methods that did not require RNA extraction reagents when these products became impossible to procure in the world markets. The ability of manufacturers to adopt or transition to such streamlined methods before the next pandemic could be a criterion for selecting favored partners and will reduce the supply chain risks when demand for testing escalates rapidly.

Supply chain risks can be mitigated by stockpiling key reagents, consumables, components, cartridges or even instruments. Stockpiling of generic reagents, consumables and critical components with demonstrated shelf-lives is a clear opportunity to prepare for a pandemic. Stockpiling of other items whose shelf-life is shorter or has not been demonstrated, or for which there is some doubt regarding their performance for an IVPP, may need a more formal cost-benefit-risk analysis. Creating a stockpile over a number of years, and maintaining it with regular replenishment of new products as old products expire, could also help manufacturers deal with the significant variation in demand for influenza tests from year to year, which has historically been a commercial challenge for manufacturers. The global health community could make funds available to scale up the production and stockpiling of tests that are likely to function well for an IVPP or new pandemic strain, and then continuously replenish the supply when needed based on lot stability studies. This type of strategy is already used in the U.S. and other countries for national stockpiles of the influenza antivirals Tamiflu (oseltamivir) and Relenza (zanamivir), where the existing supplies can be used to treat new outbreaks. In the U.S. there has been an active program to study extended shelf lives for both drugs, which have now been shown to be stable for an additional 15 and 10 years beyond the historical manufactures' expiration dates, respectively.[18] Similarly, programs to extend diagnostic test shelf life should be possible.

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Activities After an IVPP or Pandemic Emerges

It is clear that some responses to the emergence of an IVPP or pandemic influenza virus can only be undertaken after it has been identified. However, specific infrastructure and processes can be put in place ahead of time to ensure that these responses can occur rapidly and smoothly. The responses include a) evaluating whether existing tests adequately detect the new virus, b) if needed, enabling the development, approval and commercialization of new tests that are capable of detecting the new virus and/or distinguishing it from other pathogens, and c) supporting the manufacturing scale-up and distribution of appropriate tests.

Rapidly evaluating the capabilities of existing commercialized tests to detect and discriminate a new virus is critical for rapid containment of an outbreak. Each manufacturer must undertake this effort for their own products, however, it would be beneficial for there to be a mechanism to provide assistance to companies that need it (e.g., in the form of patient samples, controls and standards), as well as a mechanism in place to implement independent, unbiased evaluation(s) to be conducted by third party(ies) as early as possible in an outbreak and on an as-needed basis

WHO should enable these evaluation efforts at the manufacturers' sites by rapidly providing panels of samples for test development and validation. The companies will need a few samples in substantial volume for development (which can be contrived samples), as well as a larger set of more distinct samples in small volumes for validation. Currently, each manufacturer tries to find solutions for themselves. Larger companies with the money and experience are very good at creating their own materials or contracting partners to do it for them; however, smaller companies (perhaps with innovative technologies) are more likely to struggle with these efforts. The supply of influenza viral isolates by WHO is important, but seems to be little known within the diagnostics manufacturing community. As best we can tell from interviews with four of the major flu diagnostics manufacturers for both the 2009 H1N1 pandemic and the recent SARS-CoV-2 pandemic, each company found their own path to the viral materials they required to develop and validate their tests.

In order to enable the efforts to evaluate existing products against an IVPP or pandemic influenza virus, the WHO, either on their own or in partnership with one or more reagent suppliers such as ATCC, Sino Biologicals, BEI or SeraCare, might provide deactivated viral isolates broadly (careful to recognize the different needs for NAT and immunoassays), and standardize the quantification with agencies like NIST in the U.S.

An additional resource which would be valuable is a set of clones for antigen production in at least three vectors (e.g., *E. coli*, baculovirus, yeast) so that the manufacturers can compare the benefits of one versus another (e.g., reactivity with host flu viral antibodies, posttranslational modifications, cross reaction with human anti-vector antibodies), as well as develop antibodies against the viral isolates and cloned antigens. Some reagent providers will eventually do this themselves, but it can take many weeks to months. It is likely (but not guaranteed) that many of the existing lateral flow tests will provide adequate detection of a new IVPP or pandemic strain, and the companies need to demonstrate this as soon as possible after an IVPP or pandemic strain is identified in order to assure that the tests can be used without modification. Most companies conducted such studies successfully with the H1N1

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outbreak in 2009. Many of the existing nucleic-acid-based tests should detect new strains as well, but it's more likely that NGS assays will be able to cover all variants with their existing tests. To improve the rate at which the existing RNA tests can be evaluated and, if necessary, modified, WHO should provide early sequence information broadly and consider creating or supporting a sequence data base center like the Shafer Lab at Stanford University has for HIV resistance mutations.

Once evaluations have been performed to test the ability of existing commercial tests to detect an IVPP or new pandemic strain, it could be concluded that new tests are required to detect and/or distinguish this virus from other pathogens. If this conclusion is reached, then the infrastructure and resources to enable the development, approval and commercialization of new tests should be in place to support these efforts. Well-positioned manufacturers who have a track record of rapidly developing high-performing tests should be identified ahead of time. Relationships should be established ahead of time to lay path to market.

It is also possible that entirely new technologies and products will provide great advantages to confront a new pandemic, such as very fast or sensitive antigen tests. The development of new technologies in smaller companies has its own challenges and complexities to deal with, so assistance with regulatory submissions, manufacturing and commercial issues will be beneficial if rapid development and implementation is the goal. Smaller companies will need assistance and incentives to complete the development of influenza products, especially in light of the current economic incentives to focus solely on the COVID-19 pandemic. Several of the companies in this report with innovative products in development had been pursuing influenza tests but changed their focus once the COVID-19 pandemic began (e.g., Pinpoint, Cue, Ativa, LumiraDx and others). The global health community should be encouraged to assist small companies. WHO in particular could provide assistance by accelerating the process of evaluating pre-qualification and emergency use submissions to as short a time as possible. Other assistance that could benefit companies might consist of:

- Brokering deals (financing) for implementation in LMICs
- Financing the completion of product development
- Assistance with the WHO Pre-Qualification and/or EUL submissions
- Assistance in arranging manufacturing scale-up and commercialization
- Brokering relationships with test procurers, distributors and Ministries of Health in many countries.

For example, if WHO could support incentives for the biggest manufacturers of influenza tests to partner with smaller technology companies whose products can fill unmet needs for particular settings, it could greatly enhance the rate at which new tests get to the market.

Regardless of whether existing tests or new tests are needed for a new IVPP or pandemic strain, preparation for scaling up the manufacture of reagents, consumables and possibly instruments could be critical for meeting test demand on a global scale. Stockpiles may function to alleviate some of the pressure, but they should not be seen as a replacement for the ability to rapidly scale production to meet the testing demands if existing products are shown to be insufficient. Agreements should be forged in advance with the companies with the larger manufacturing capacities and those with diverse

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geographic manufacturing options, to hedge against the risk that a single high-production site is severely affected early in a pandemic. During 2020, significant investments have been made in scaling the manufacturing capacity for single-use cartridges by companies like Cue, LumiraDx and Quidel due to the SARS-CoV-2 pandemic. LumiraDx and Cue both have influenza tests in development, while Quidel already has a EUA for a combination SARS-CoV-2 and flu A/B antigen test. These investments will have changed the landscape significantly and could be leveraged when an IVPP or new influenza pandemic emerges. Where manufacturers do not have distribution today, procurer or other NGO assistance could be essential.

It is clear that diagnostic tests are of enormous importance to epidemic and pandemic preparedness. Understanding the landscape of companies involved in influenza diagnostics provides a foundation upon which to build a plan to address the current shortcomings in accessibility to the diagnostic tools needed for influenza pandemic preparedness. Information about the capabilities of each company allows the identification of those that are best positioned to address specific unmet needs in the market. The landscape is evolving and dynamic and should be monitored for significant changes over the next year or two. Addressing these shortcomings in preparedness will allow a more rapid assessment and containment of future pandemics, and potentially reduce the healthcare, economic and social burdens that can be caused by a pandemic.

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Abbreviations

ABBREVIATION	EXTENSION
RNA	Ribonucleic acid
Ag	Antigen
AIV	Avian influenza virus
BARDA	US Biomedical Advanced Research and Development Authority
CDC	US Center for Disease Control
CE	Conformité Européenne, conformity with European standards
CLIA	Clinical Laboratory Improvement Amendments (US regulatory standards)
COVID-19	Coronavirus disease 2019
Dx	Diagnostics
ED	Emergency Department
EMEA	Europe, Middle East, Asia
EUA	Emergency Use Authorization (U.S. FDA)
EUL	Emergency Use Listing (WHO)
FDA	US Food and Drug Administration
Flu	Influenza
HIC	High-income countries
ILI	Influenza-like symptoms
IVD	In vitro diagnostic
IVPP	Influenza virus with pandemic potential
IVTM	Influenza Virus Traceability Mechanism
LATAM	Latin America
LDT	Lab developed test
LMIC	Low- and middle-income countries
LOD	Limit of detection
MRSA	Methicillin-resistant Staphylococcus aureus
NAT	Nucleic Acid Test
NGO	Non-governmental organization
NGS	Next generation sequencing
NIH	US National Institutes of Health
OEM	Original equipment manufacturer
PCR	Polymerase Chain Reaction
POC	Point of Care
POU	Point of Use
RSV	Respiratory syncytial virus
RT-PCR	Reverse transcriptase polymerase chain reaction
SARS-CoV-2	Severe acute respiratory syndrome coronavirus 2
TTR	Time to Result
UK	United Kingdom
US	United States
USD	United States dollar
WHO	World Health Organization

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