Counter Trends in Global Infectious Disease: To Decentralize Molecular Testing or Not

October, 2016

Market Diagnostics International

Consulting Services for Medical and Scientific Technologies

Counter Trends

The Competition is heating up!

Centralized Testing ⟵ ⟶ Decentralized Testing

- ✓ *New moderate- to high-volume laboratory platforms are available, or in development, from Roche (cobas 4800, 6800, 8800), Hologic (Panther Fusion), Abbott (Alinity m), and Beckman Coulter (DxN Veris).*

- ✓ *New, near-patient and point-of-care molecular tests are coming to market, both qualitative and quantitative, on systems such as Alere i and q, Roche LIAT, Cepheid GeneXpert Omni.*

- ✓ *The market for centralized hospital- or reference lab-based molecular infectious disease testing is well-established in the developed world for viral load monitoring, HAI and CT/NG tests, and growing for sepsis, respiratory, GI and other syndromic medicine panels.*
- ✓ *Also, some of the largest HIV viral load testing facilities in the world are in countries like Botswana.*

- ✓ *The market is moving to the clinic, physician's office, and pharmacy for flu, RSV, Strep A and other respiratory pathogens.*
- ✓ *By contrast, in low and middle income countries (LMICs) there is a significant unmet need for simplified, low-cost POC methods to effectively manage infectious disease, especially for MTB and HIV.*

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Session Goals

- ✓ *The continuum from centralized to decentralized testing*
- ✓ *The drivers of decentralized and POC testing and the related challenges*
  - *Global*
  - *Domestic*
- ✓ *The drivers of centralized testing and the related challenges*
- ✓ *Current market size for centralized and POC infectious disease testing*
- ✓ *Menus by testing venue and recent US market trends*
- ✓ *Examples of current and new POC and centralized testing technologies, as well as those in development*

What is the definition . . .

- ✓ *Centralized testing*

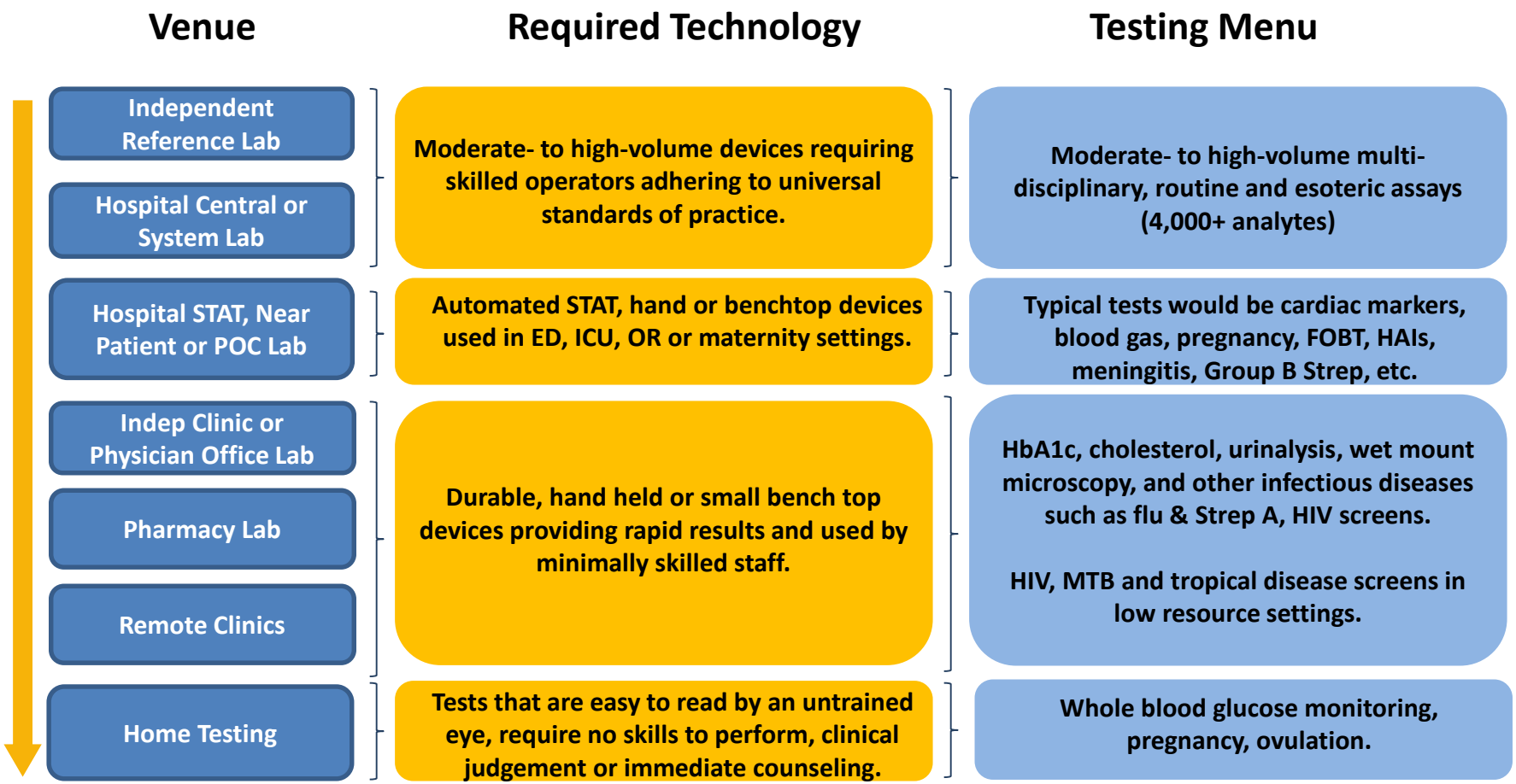
  The testing of patient specimens collected from multiple care venues at a locally, regionally, or nationally centralized laboratory, requiring the use of specimen transport and information management/reporting systems.

- ✓ *Decentralized testing*

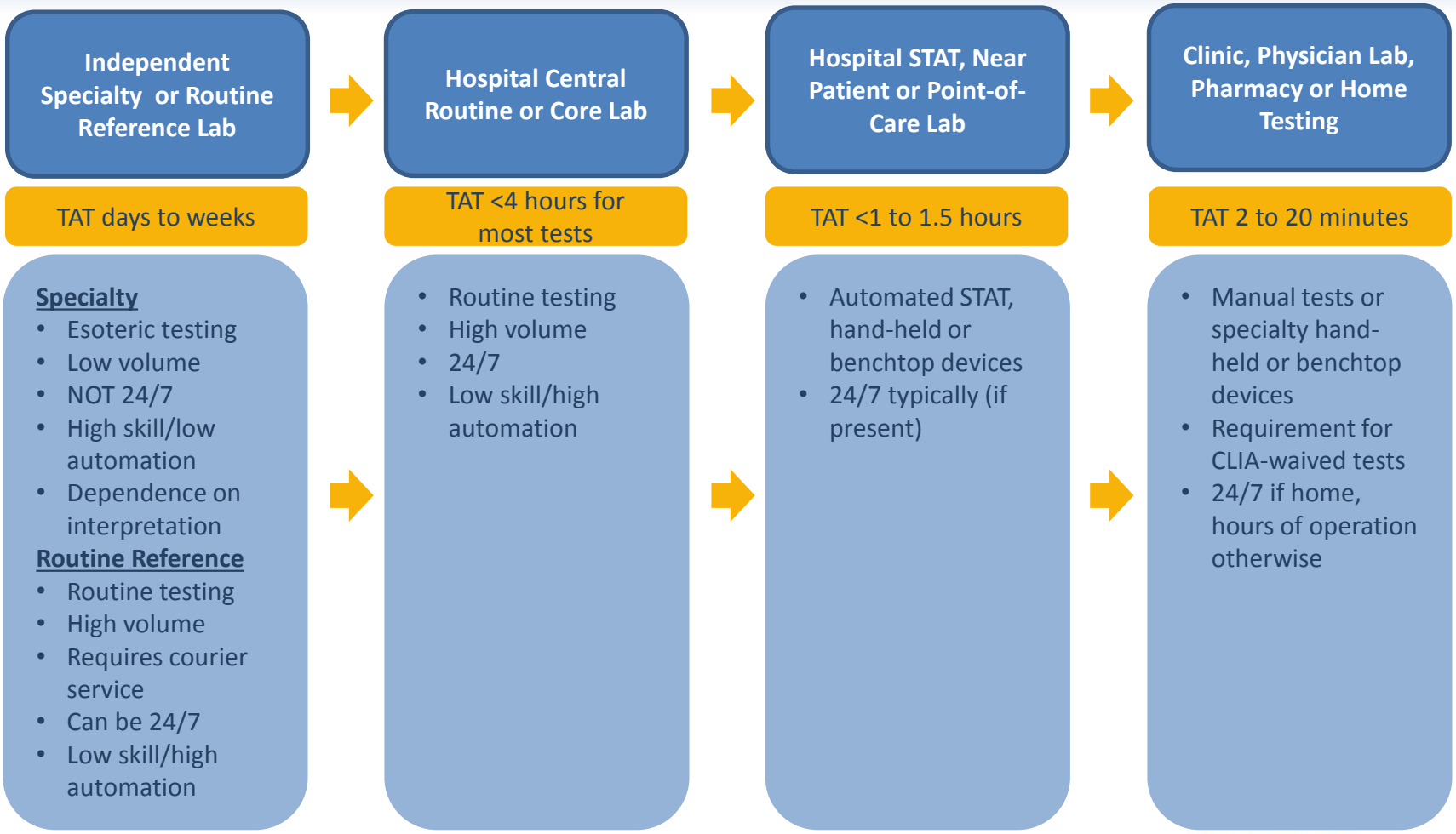
  The testing of patient specimens at or near the point-of-care with the assumption that test results will be available instantly or in a very short timeframe to assist caregivers with immediate diagnosis or clinical intervention[2].

[2]Adapted from Pablani, M. Does POCT induce the risk of error in laboratory testing? Clinica Chimica Acta, 2009: 404: 59-64

Continuum from Centralized to Decentralized Testing



Time Spectrum of Patient Testing



Global Drivers

Decentralized testing

- ✓ Global Health Emergencies (HIV, MTB, Ebola, Zika, etc.)

  Various organizations including the W.H.O., the Global Health Initiative, the Gates Foundation, F.I.N.D., etc. are encouraging, funding and establishing design goals for POC and near-patient technologies that bring infectious disease diagnosis and patient management tools to low- and middle-income countries (LMICs)

- ✓ Increasing Antimicrobial Resistance

  Growing antimicrobial stewardship programs and standards and recent landmark United Nations General Assembly declaration agreeing to combat antimicrobial resistance signed by 193 countries.

- ✓ Sustainable Development Goals (SDGs)

  Officially known as **Transforming our world: the 2030 Agenda for Sustainable Development**, this is an intergovernmental set of aspiration **goals** with 169 targets. The **Goals** are contained in paragraph 54 United Nations Resolution A/RES/70/1 of 25 September 2015.

Domestic Drivers

Decentralized testing

- ✓ US healthcare reform and patient-centered care
- ✓ Technological advances
- ✓ Laboratory staffing shortages
- ✓ Rising incidence of lifestyle diseases (e.g., cardiac, diabetes)
- ✓ Increasing older population and chronic diseases
- ✓ Increased use of home-based POC
- ✓ Trend toward the decentralization of healthcare delivery

Global Challenges

Decentralized testing

- ✓ Cost vs. conventional POC methods or centralized testing
- ✓ Medical necessity/clinical urgency
- ✓ Need for clinical judgement and/or patient counseling
- ✓ Potential for error
- ✓ Regulatory concerns
- ✓ Management and oversight
- ✓ Impact of POCT on hospital lab operations
- ✓ Difficulty in linking test results to other clinical results and information systems
- ✓ Coverage restrictions by third-party payers/reimbursement uncertainty

Global Drivers

Centralized testing

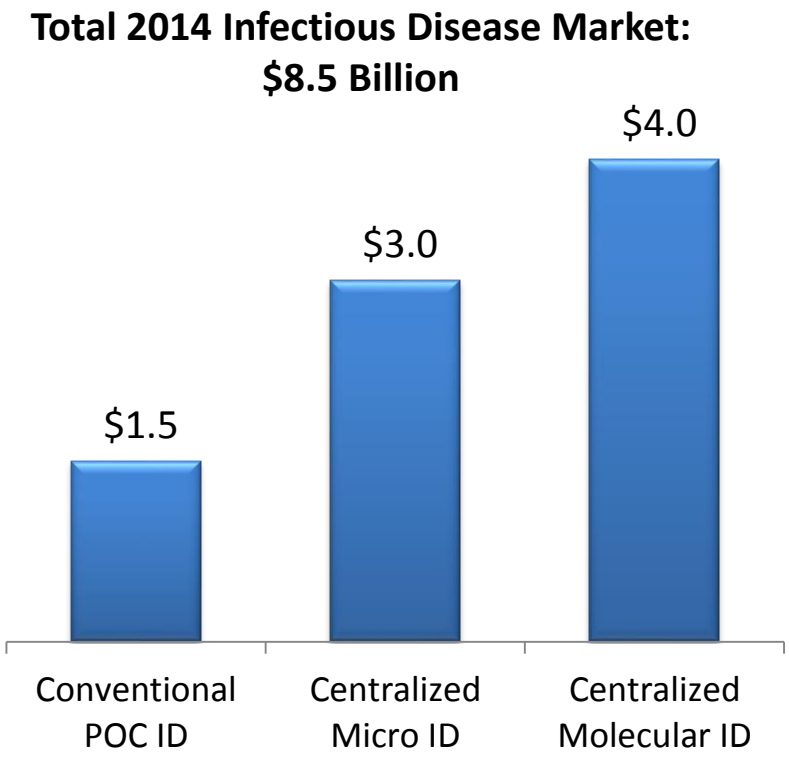
- ✓ Rapid evolution of laboratory automation solutions that reduce labor and reagent cost
- ✓ Funding/reimbursement reforms that favor economies of scale and low cost providers
- ✓ Private and public health system mandates to consolidate testing locations
- ✓ Need for highly skilled personnel for support the growth of complex, esoteric testing and technologies
- ✓ Sample consolidation to support clinical trials and test validation

Worldwide Infectious Disease Testing Market

The current conventional worldwide POC infectious disease market represents just 18% of the total $8.5B infectious disease testing market, but promises to grow at a higher rate as the technology moves to molecular methods.

Discipline	2014 ($ Billion)	CAGR
Conventional POC Infectious Disease Testing	**$1.5**	**5.9%**
Centralized Microbiology Testing	**$3.0**	**5.1%**
Molecular Infectious Disease Testing*	**$4.0**	**6.7%**
- Virology	$1.8	7.4%
- Bacteriology	$1.4	6.6%
- Blood Screening	$0.8	4.8%
TOTAL	**$8.5**	

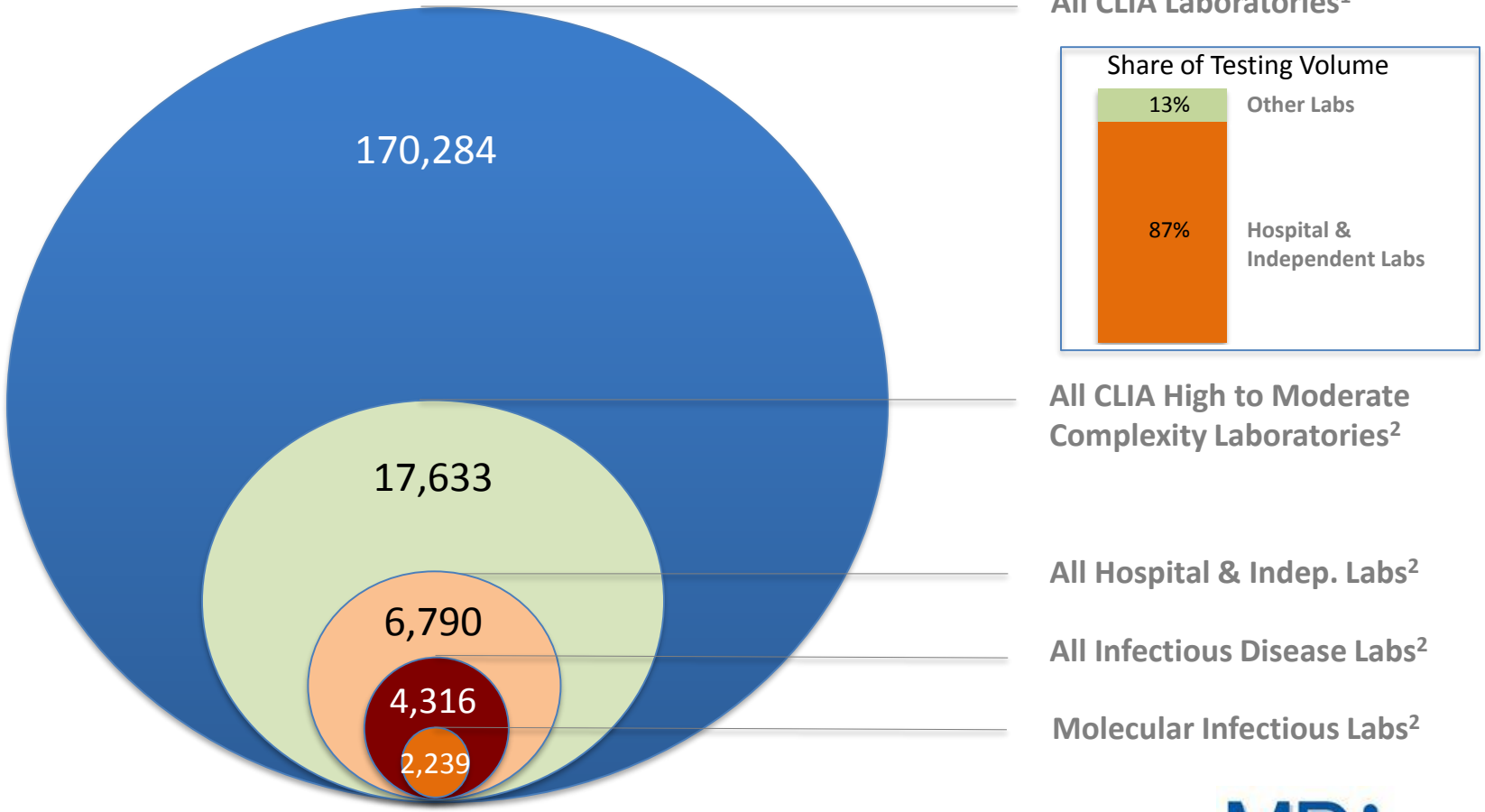
*Only centralized testing in 2014



Source: Company reports, EAC 2014 WW IVD Market estimates, Alere Analyst Day presentation at AACC 2015, MDxI estimates

US Clinical Laboratory Universe

An estimated 25% of the 17,633 US high to moderate complexity clinical laboratories currently perform infectious disease tests. Hospital and Independent labs comprise 87% of all test volume.



[1]SOURCE: Lewin Group, *Laboratory Medicine*, pp. 69-80. IOM, *Medicare Laboratory Payment Policy,* Appendix D, pp. 215-223. Numbers represent the number of licenses issued under CLIA regulations. A recent review of these numbers by MDxI indicates that many laboratory locations operate under multiple licenses.

[2]SOURCE: MDxI IVD Insights LabFile, January 2015

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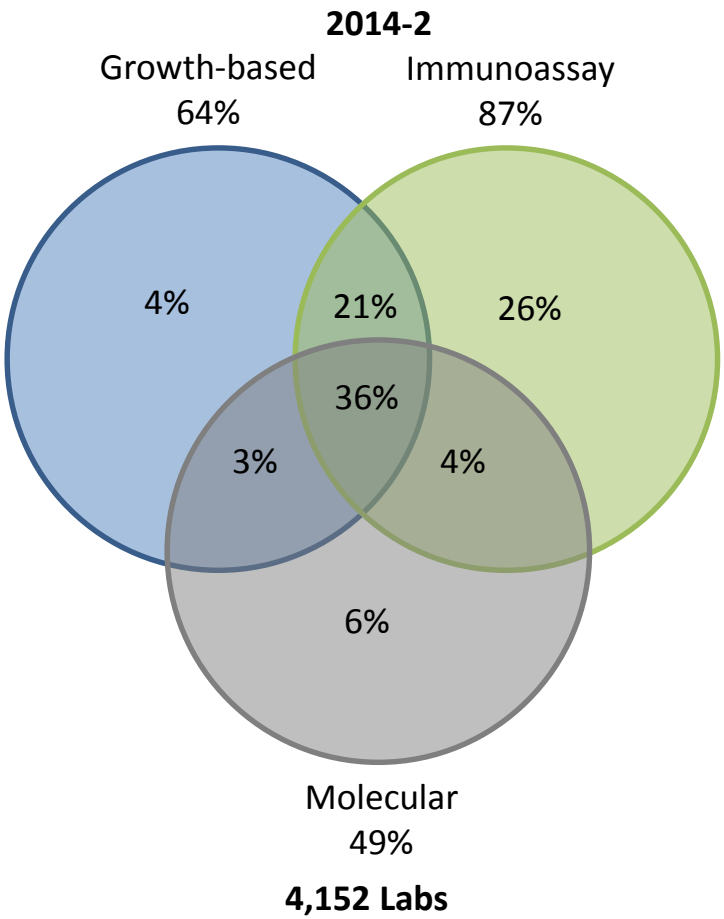
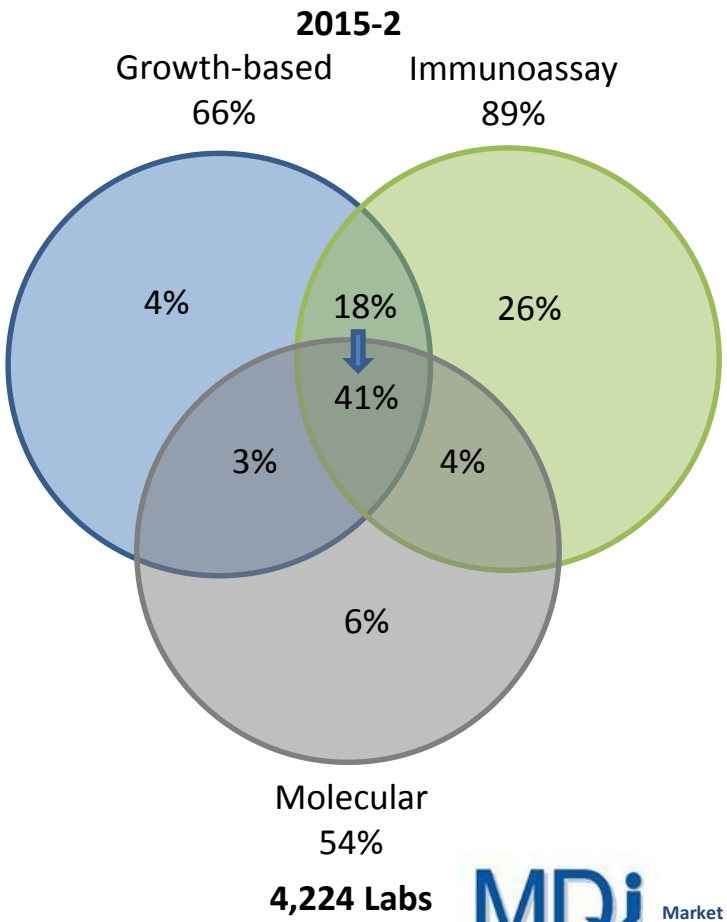
US Infectious Disease Testing Universe

The primary trend for the past few years has been the migration of testing from growth-based tests and immunoassays to molecular methods.





SOURCE: MDxI IVD Insights, 2014-2 and 2015-2

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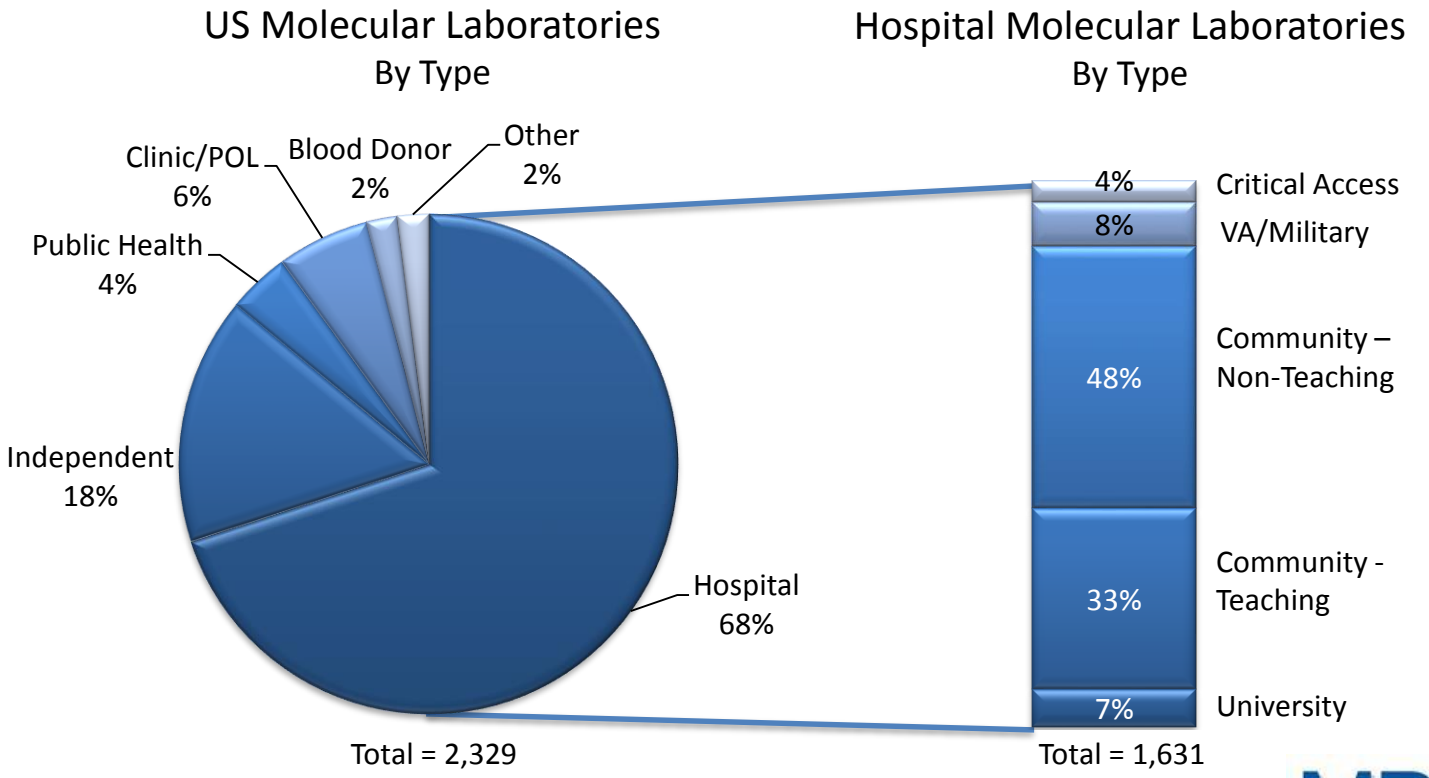
US Molecular Infectious Disease Testing Universe

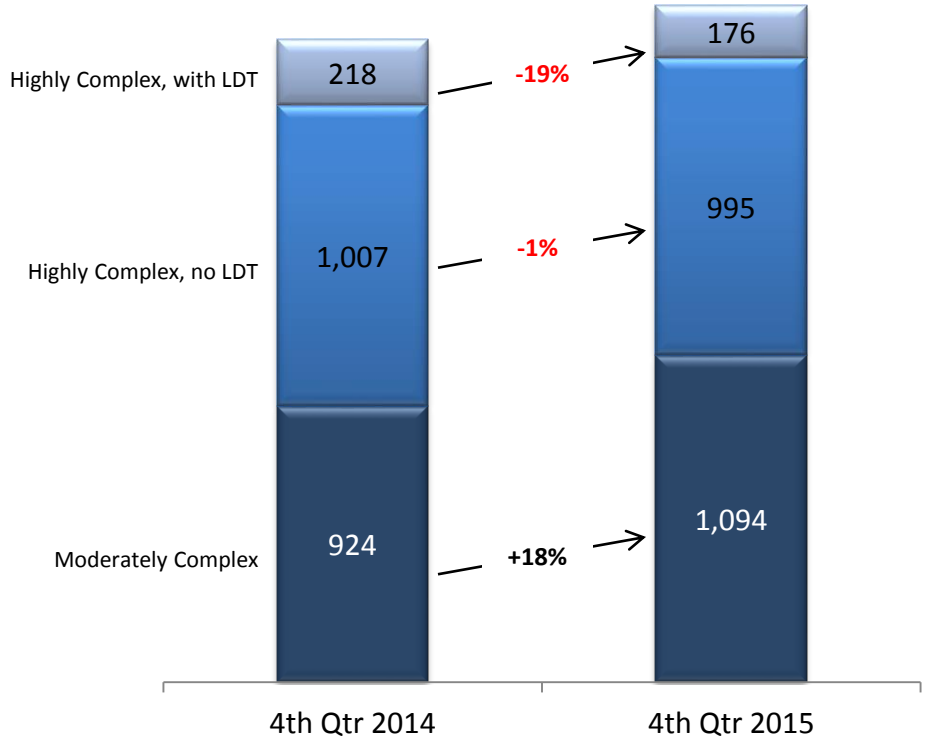
MDxI currently tracks a total of 2,329 laboratories that perform molecular infectious disease testing. Over two-thirds are associated with a hospital.



US Molecular ID Lab Universe by CLIA Complexity

The increasing number of molecular laboratories is driven by adoption of moderately complex molecular tests.

For the first time, we are seeing a significant drop in the number of labs performing LDTs, likely due to an increasing number of commercially available tests and the anticipated regulation of LDTs by FDA.



SOURCE: MDxI IVD Insights, 2014-2 and 2015-2

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Most Commonly Performed Molecular Tests in the US Market

The most common molecular assays offered by infectious disease labs are for hospital-associated infections, followed by respiratory and sexually transmitted infections.

On average, these labs perform four to five different molecular assays.

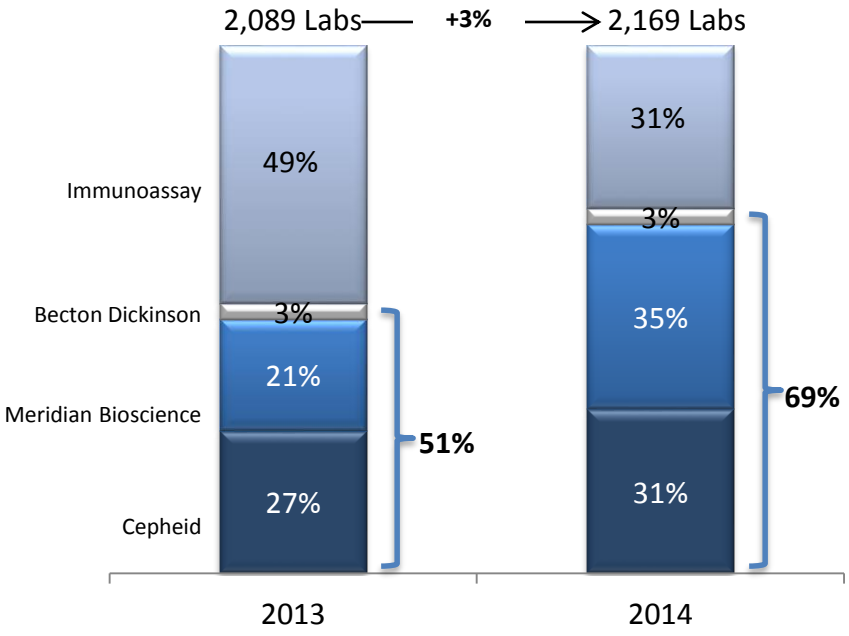
Assay	Percent of MDx Inf Disease Labs Performing
1. C. difficile	61%
2. CT/NG	53%
3. MRSA	40%
5. Influenza A/B, qualitative	36%
6. T. vaginalis	32%
7. High Risk HPV	31%
8. G. vaginalis	24%
9. Candida sp.	24%
10. RSV	23%
11. Respiratory Panel	19%

SOURCE: MDxI IVD Insights, 2015-2

The Adoption of Moderately Complex Tests – C. difficile

In the past few years, an increase in the number of molecular labs has been driven by the adoption of simple, moderately complex test by molecular-naive labs, exemplified by the rapid movement from ELISA to molecular C. difficile methods.

Share of Labs Performing Each Brand/Method



	2013	2014	Net Change
Total Sites*	**2,031**	**2,053**	**+22**
Total Molecular Methods	**1,085**	**1,193**	**+108**
- Cepheid	575	674	+99
- Meridian Bioscience	435	748	+313
- Becton Dickinson	70	69	-1
- Hologic	4	2	-2
- Quidel	1	6	+5
Total Immunoassay Methods	**1,049**	**860**	**-189**
Total Cell Culture Methods	**2**	**2**	**0**
Total Methods	**2,136**	**2,169**	**+33**
Methods per Site	**1.05**	**1.1**	**+0.06**

*does not include approximately 1,150 small hospital (<25 beds) and other low volume labs performing C. difficile tests but reporting proficiency data through the American Proficiency Institute.

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Point of Care Testing Market Segments
Typical Molecular Testing Menu

Category	Menu	Hospital			Dr's Office			Pharmacy	Public Health Clinic	
		ED	ICU	Maternity	OB/GYN	Family Practice	HIV/ID		OECD Country	Developing Country
Hospital Acquired Infections	MRSA	X	X							
	VRE	X	X							
	C. Diff	X	X							
	VAP		X							
Diagnostic Panels	Sepsis	X	X							
	Meningitis/ Encephalitis	X	X							
	Respiratory panel	X	X							
	GI panel	X	X							
	Vaginitis panel			X	X				X	
Group B Strep				X	X					
HPV					X	X			X	X
Respiratory Infections	Flu A/B					X	X	X		
	RSV					X	X	X		
	Strep A					X	X	X		
	TB						X		X	X
	Drug resistant TB						X		X	X

Point of Care Testing Market Segments
Typical Molecular Testing Menu

Category	Menu	Hospital			Dr's Office			Pharmacy	Public Health Clinic	
		ED	ICU	Maternity	OB/GYN	Family Practice	HIV/ID		OECD Country	Developing Country
Sexually Transmitted Infections	HIV viral load & EID			X			X		X	X
	HCV viral load						X		X	X
	HBV viral load						X		X	X
	CT/NG				X	X			X	X
	HSV				X	X			X	X
	Trichomonas				X	X			X	X
	Syphilis								X	X
Tropical Diseases	Ebola virus								X	X
	Zika virus								X	X
	Dengue fever									X
	Chikungunya									X
	Marburg									X
	Malaria									X

Pricing vs. Reimbursement and Funding Challenges

US HIV Viral Load Testing

Reimbursement: $115.92[1]

Per Test Cost Reagents by Vol Segment[2]

<3,600	$65.00 - $90.00
3,600 to 10,000	$45.00 - $65.00
10,000 to 40,000	$25.00 - $45.00
40,000 to 100,000	$20.00 - $25.00
>100,000	~$20.00
Weighted Ave Price	$32.24

US CT/NG Testing

Reimbursement: $47.80[1]

Per Test Cost Reagents by Vol Segment[2]

<3,600 test per year	$18.83
3,600 to 10,000	$13.18
10,000 to 40,000	$15.69
40,000 to 100,000	$13.15
100,000+	$7.50
Weighted Ave Price	$12.87

LMIC HIV Viral Load Testing

Funding Target: $10.00 to $15.00

Per Test Cost Reagents by Vendor[3]

Alere q™ HIV 1/2 Detect	$14.95 to $25.00
Cepheid Xpert Viral Load	$19.10
SAMBRA II HIV-1 Viral Load	$20.28
Molbio Trunat HIV Viral Load	$14.00
Quidel Savannah Realtime HIV	$11.00
Hologic Aptima HIV Quant	$10.00 - $25.00

[1]CMS 2016 Laboratory Fee Schedule

[2]US pricing for central labs, not point-of-care, based on internal proprietary research and market experience

[3]Putting HIV and HCV to the Test: A Product Guide for Point-of-Care CD4 and Laboratory-Based and Point-of-Care Virological HIV and HCV Tests, July 2015, Medecins Sans Frontieres Access Campaign (some prices conditional on large volume orders of >800,000 to 1.5 million tests)

Technology Example: Viral Load

Cepheid GeneXpert®

System Components:

- Instrument comes in modular format available with 1, 2, 4 or 16 modules
- Assay cartridges capable of fully integrated PCR reaction

Key Features:

Throughput:	~ 4 - 5 tests per module per 8 hour shift
Time to result:	~ 90 - 105 minutes depending on the assay
Hands on time:	< 2 minutes
Sample types:	Whole blood/DBS for EID, EDTA plasma or serum depending on the assay
Capacity:	1, 2, 6 or 16 tests at a time. No built in memory
Power supply:	Mains only. No battery.
Connectivity:	No internal printer. Ethernet, WiFi and USB ports

Virology Test Menu:

US FDA Approved:	HIV Qual, HIV-1 viral load, HCV viral load
CE Marked:	HIV-1 & 2 Qualitative test for early infant diagnosis
WHO Pre-qualified:	HIV Qual
In development:	HIV viral load, Ebola/Marburg virus assay

Pricing:

Instruments:	GeneXpert II	$11,530 with 2 ports
	GeneXpert IV	$17,000 with 4 ports
	GeneXpert XVI	$71,000 with 16 ports
Assays:	HIV Qual test	$17.35 - $19.90/test*
	HIV-1 viral load	$14.20 - $19.10/test*
	HCV viral load	$15.05 - $19.20/test*

* Volume dependent

References:
MSF: Putting HIV and HCV to the Test. (July 2015)
UNITAID: HIV/AIDS Diagnostics Technology Landscape (October 2015)
www.Cepheid.com

Technology Example: Viral Load

Cepheid GeneXpert® Omni

System Components:

- Small, portable instrument that takes a single cartridge
- Assay cartridges capable of fully integrated PCR reaction

Key Features:

Throughput:	~ 4 - 5 tests per user per 8 hour shift
Time to result:	~ 90 - 105 minutes depending on the assay
Hands on time:	< 2 minutes
Sample types:	Whole blood/DBS for EID, EDTA plasma or serum depending on the assay
Capacity:	1 test at a time. No built in memory
Power supply:	Mains or built in rechargeable & supplemental batteries providing total off mains operating time of up to 16 hours.
Connectivity:	Wireless and web enabled

Virology Test Menu: See previous slide. Cartridges for all GeneXpert platforms are the same.

Pricing:

Instruments:	GeneXpert Omni $3,000
Assays:	See previous slide.

References:
MSF: Putting HIV and HCV to the Test. (July 2015)
UNITAID: HIV/AIDS Diagnostics Technology Landscape (October 2015)

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Technology Example: Viral Load

Alere™ q

System components:

- Small, portable instrument with touch screen display
- Assay cartridges with fully integrated PCR assay procedure

Key Features:

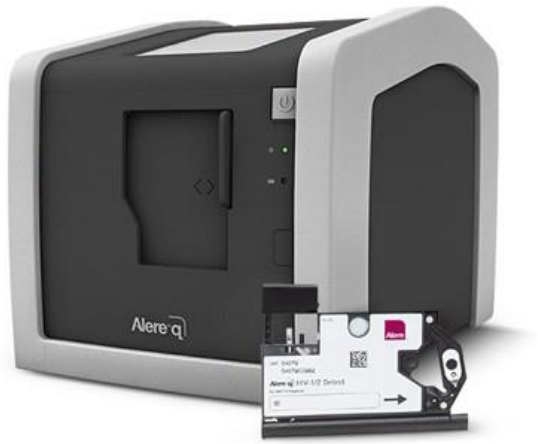
Throughput:	8 tests per user per 8 hour shift
Time to result:	52 minutes
Hands on time:	~ 3 minutes including blood draw
Sample type:	Whole blood from finger stick, heel prick or venipuncture
Capacity:	1 test at a time. Can store up to 1,000 results
Power supply:	Built in UPS. Works from mains or battery (8 hours life)
Connectivity:	Results can be printed, stored, exported to a USB drive or to a remote server via GSM mobile phone network

Virology Test Menu:

US FDA Approved:	None
CE Marked:	HIV-1 & 2 Qualitative test for early infant diagnosis
WHO Pre-qualified:	HIV-1 & 2 Qual (EID)
In development:	HIV & HCV viral load, TB & Ebola/Marburg virus assay

Pricing:

Instrument:	$25,000
HIV Qual test:	$14.95 - $25.00/test depending on volume



References:
Alere analyst report 2015
MSF: Putting HIV and HCV to the Test. (July 2015)
UNITAID: HIV/AIDS Diagnostics Technology Landscape (October 2015)

Technology Example: Viral Load

Alere™ i

System components:

- Small, portable instrument with touch screen display
- Assay cartridges with fully integrated PCR assay procedure
- NEAR Technology – Isothermal molecular amplification technology called Nicking Enzyme Amplification Reaction

Key Features:

Throughput:	
Time to result:	"In minutes". Most targets in 5 – 10 minutes
Hands on time:	
Sample type:	Assay dependent
Capacity:	
Power supply:	Mains only
Connectivity:	Results can be exported to an LIS

Virology Test Menu:

US FDA Approved:	None. Currently only Flu A/B and Strep A
CLIA Waived:	Yes
CE Marked:	As above for FDA
In development:	Focused on Respiratory, HAI, STD. Planning HBV Instrument targeted mainly at US market

Pricing:

Instrument:	~ $8,000
Assays:	Not disclosed

References:
1. www.alere.com
2. www.devinemedical.com

Technology Example: Viral Load

Roche cobas LIAT ™

System components:

- Small instrument for fully automated PCR sample prep, amplification and detection
- Assays performed in reaction tubes

Key Features:

Throughput:	24 tests in an 8 hour shift
Time to result:	Under 20 minutes
Hands on time:	< 2 minutes
Sample types:	Assay dependent
Capacity:	1 test at a time
Power supply:	Battery and mains
Connectivity:	HL7 enabled
Other:	Barcoded data entry, strong quality control features, capability to test multiple targets in a single sample

Virology Test Menu:

US FDA Approved:	Flu A/B, Strep A (Also CLIA waived)
CE Marked:	Flu A/B, Strep A
WHO Pre-Qualified:	None
In development:	HIV & HCV viral load planned

Pricing:

Instrument:	Not available
Tests:	Not available

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Technology Example: Viral Load

Diagnostics for the Real World SAMBA II System

System components:

- Tablet Module and Assay Module linked via Bluetooth
- Each Tablet Module can control up to 8 Assay Modules
- SAMBA reaction takes place in a hermetically sealed cartridge

Key Features:

Throughput:	~ 4 runs per assay module per 8 hour shift
Time to result:	90 minutes
Hands on time:	
Sample types:	Whole blood (Capillary and venous)
Capacity:	1 test at a time.
Power supply:	Mains only. No battery
Connectivity:	Built in ethernet and USB ports

Virology Test Menu:

US FDA Approved:	None
CE Marked:	HIV Qual from whole blood HIV viral load from plasma

Pricing:

Instrument:	$25,000 - $30,000 (For 200 instruments)
Tests:	$20 - $28/test (For > 500,000 tests)

Key Questions

- ✓ *Can available resources and reimbursement levels support the wholesale decentralization of molecular tests at a time when the options for centralized testing are expanding and the cost of that testing is likely to come down?*
- ✓ *How will the movement of molecular testing from CLIA highly complex to CLIA moderately complex and CLIA waived technologies impact the US market?*
- ✓ *Are there synergistic opportunities for diagnostic product manufacturers in LMICs and the developed world?*

One Conclusion (US) . . .

"Clinical laboratories are in the midst of a technological revolution that is likely to continue during the twenty-first century . . . Whether new technologies are implemented may depend on their impact on laboratory costs and, if they are more costly, on payers' willingness to pay for them.

While efforts to automate central laboratories are likely to continue, trends appear to indicate that:

- ✓ *Much routine testing in the future could be delivered through POCT and home-based testing*
- ✓ *Centralized laboratories are likely to concentrate more on esoteric testing*
- ✓ *Automation and shifts in the sites where laboratory services are delivered will result in major shifts in laboratory staffing needs.*
  - *Demand for skilled IT professionals, experts to monitor and service robotic equipment, and allied health professionals is likely to grow.*
  - *Overall decreases in labor costs, however, will likely lead to decreases in the cost per test."*

Source: The National Academies Press, Medicare Laboratory Payment Policy: Now and in the Future (2000)

Upcoming Forum at AMP . . .

DxMA
For Diagnostics Market Professionals

Counter Trends in Global Infectious Disease: To Decentralize Molecular Testing or Not?

DoubleTree by Hilton Charlotte
8:00 am to 11:00 am | November 10, 2016
Charlotte, NC

Moderator: Bob McGonnagle, Publisher, CAP Today

Panelist:
Mickey Urdea
Founder and Partner, Halteres Associates
Chairman, Catalysis Foundation for Health

Panelist:
Chris Parkhouse
Director, Virology and TB Global Marketing, Cepheid

Panelist:
Lucy Hattingh
Senior Consultant, MDxI
Principal, IDM Consulting
(former Global Marketing Director at Roche Molecular and Hologic)

Panelist:
Invited
Director of Business Development, Roche Molecular Diagnostics

Panelist:
Invited
Key Laboratory Opinion Leader, Point of Care Diagnostics

For more information or to register, go to: http://dxma.org

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Thank You!

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