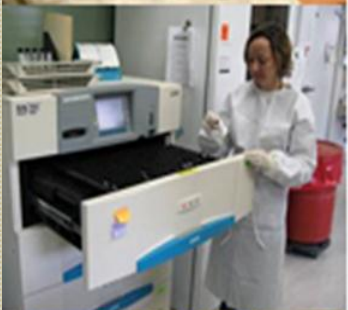
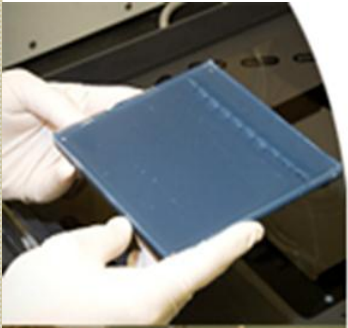




Performing Quality Molecular and Emerging Technology Testing Workshop

April 23, 2014





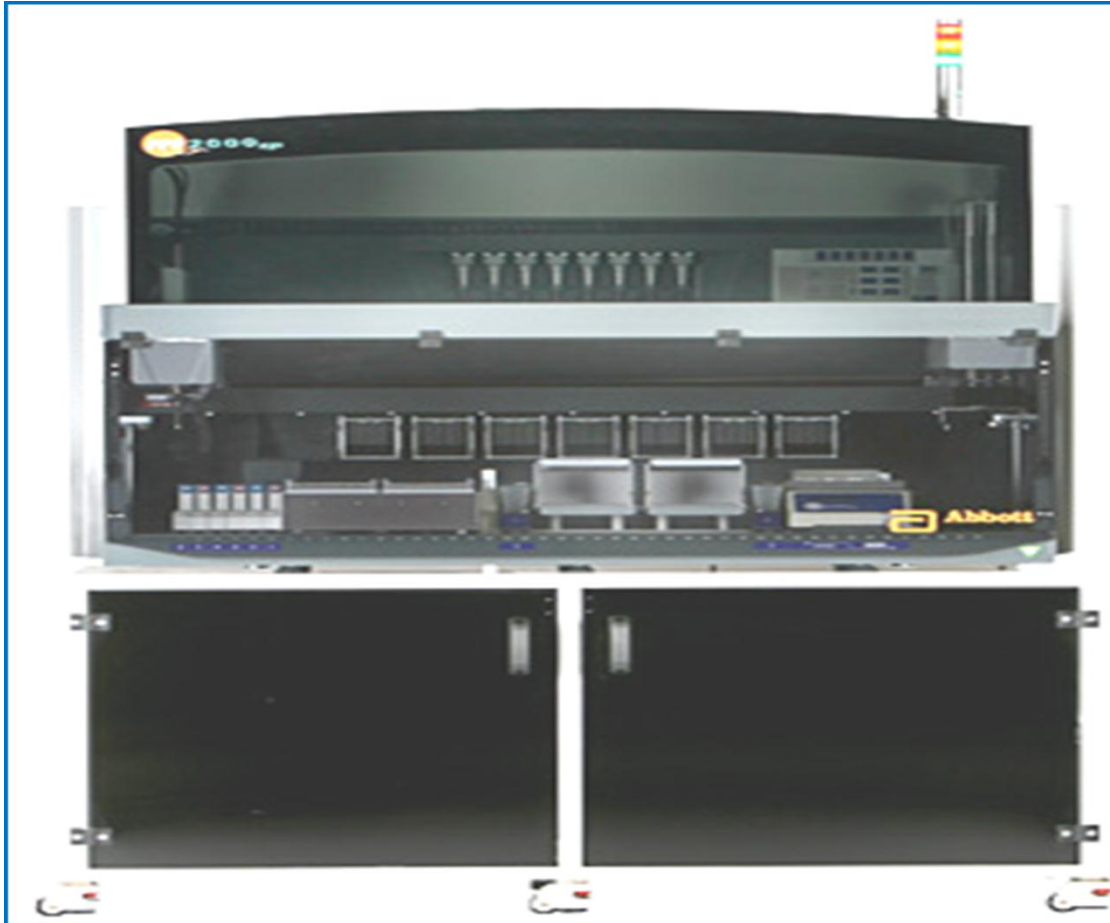
What's Available and How Do I Choose?

**A Moderated
Panel Discussion**

(Part 1)



Abbott Molecular, m2000 sp/rt System





Abbott Molecular, m2000 sp/rt System

■ PROs:

- ACL has been using Abbott technology for the last 7 years and have not found better replacement yet.
- Reagents are based on Celera and Promega IP chemistry – no issues with quality,
- Assays for HIV-1, HCV and HBV have the lowest LOD on the market
- QC have very low %CV (10-20%), stable standard curves, very good dynamic range of assays
- Open channel capability to develop LDT (CMV, EBV, BKV, VZV, HSV, RVP, Prodesse ProFlu)
- Flexible throughput of batches (high 96, medium 48-72, low 24)
- Flexible extraction protocols library (different sample matrix, sample volume and elution – DNA,RNA,TNA)
- LIS interface capable
- User friendly on-board interface (easy training)
- Automated quality checks and calibration , reagent expiration tracking

■ CONs:

- Instruments could have better reliability (ACL is using 2000sp over the limits about 70K per year)
- Large footprint
- Medium /High price of CE and service agreement
- Long TAT (extraction - 3.5-4.5 hours / amplification, detection~3 hours)
- Large volume of liquid and consumables waste



Abbott Molecular, m2000 Real Time System

- **What I really like:**
 - Open channel for LDT
 - Closed platform (low risk contamination)
 - Variable sizes of sample containers
 - Easy training
 - Good customer service
 - Very good quality of nucleic acid

- **Tips:**
 - Lab will benefit from having well trained super-user
 - Consider carefully if lab has enough test volume

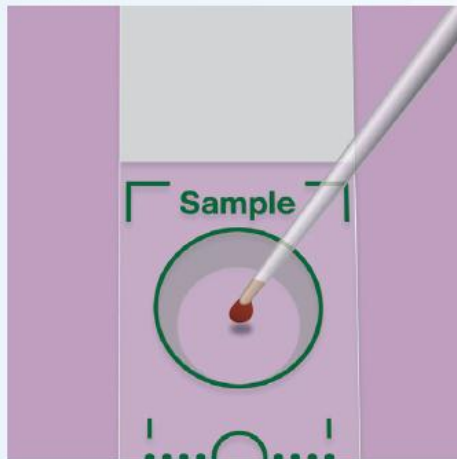


AdvanDx, QuickFISH



3 Easy Steps: Fix Sample, Hybridize Probes and View Results.
5 Min. Hands-on Time. 20 Min. Turn-around Time.

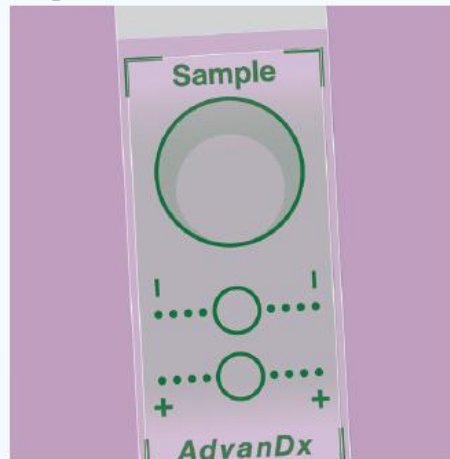
Fix



5 Min.

Fix 10 μ L of Blood Culture Sample to QuickFISH Slide.

Hybridize



15 Min.

Add PNA Reagents. Hybridize for 15 Min. at 55°C.

Examine



View Results

Examine on Fluorescence Microscope (60x or 100x Oil Objective).



AdvanDx, QuickFISH

- **PROs:**

- Just minutes of hands on time
- Little hardware to buy
- Easy to perform
- Done in 20 minutes

- **CONs:**

- Requires fluorescent microscope
- Not walk-away automation
- Cost of reagents
- No resistance genes targeted

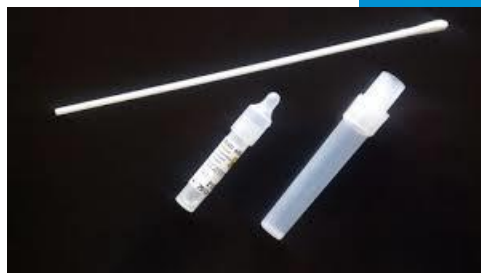
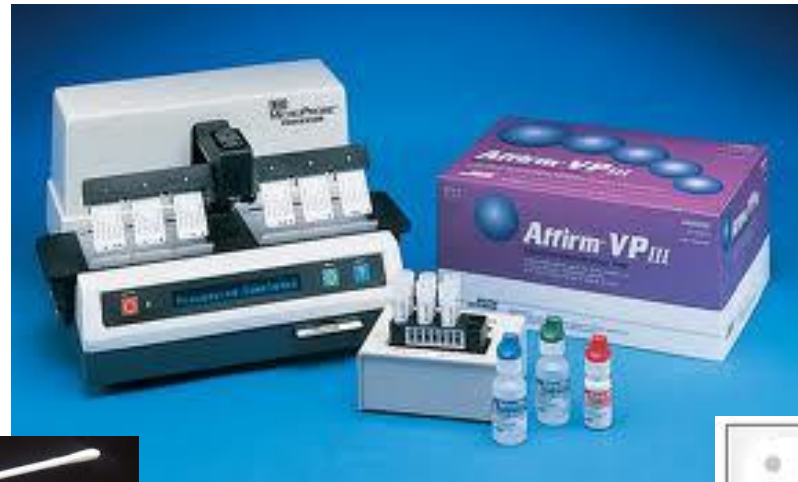


AdvanDx, QuickFISH

- **What I really like:**
 - Everything on one slide
 - Targets 3 most common GNRs in our patient population
- **Tips:**
 - Get the fluorescent microscope filter from AdvanDx



BD Diagnostic Systems, Affirm VPIII Microprocessor





BD Diagnostic Systems, Affirm VPIII Microprocessor

- **PROs:**
 - Sensitivity
 - Ease of use
 - Does not rely on *Trichomonas* motility
- **CONs:**
 - Higher cost than wet prep
 - Absolute 72h limit on transport when using the optional Ambient Temperature Transport System
 - Unlubricated speculum recommended during collection: not acceptable to many patients

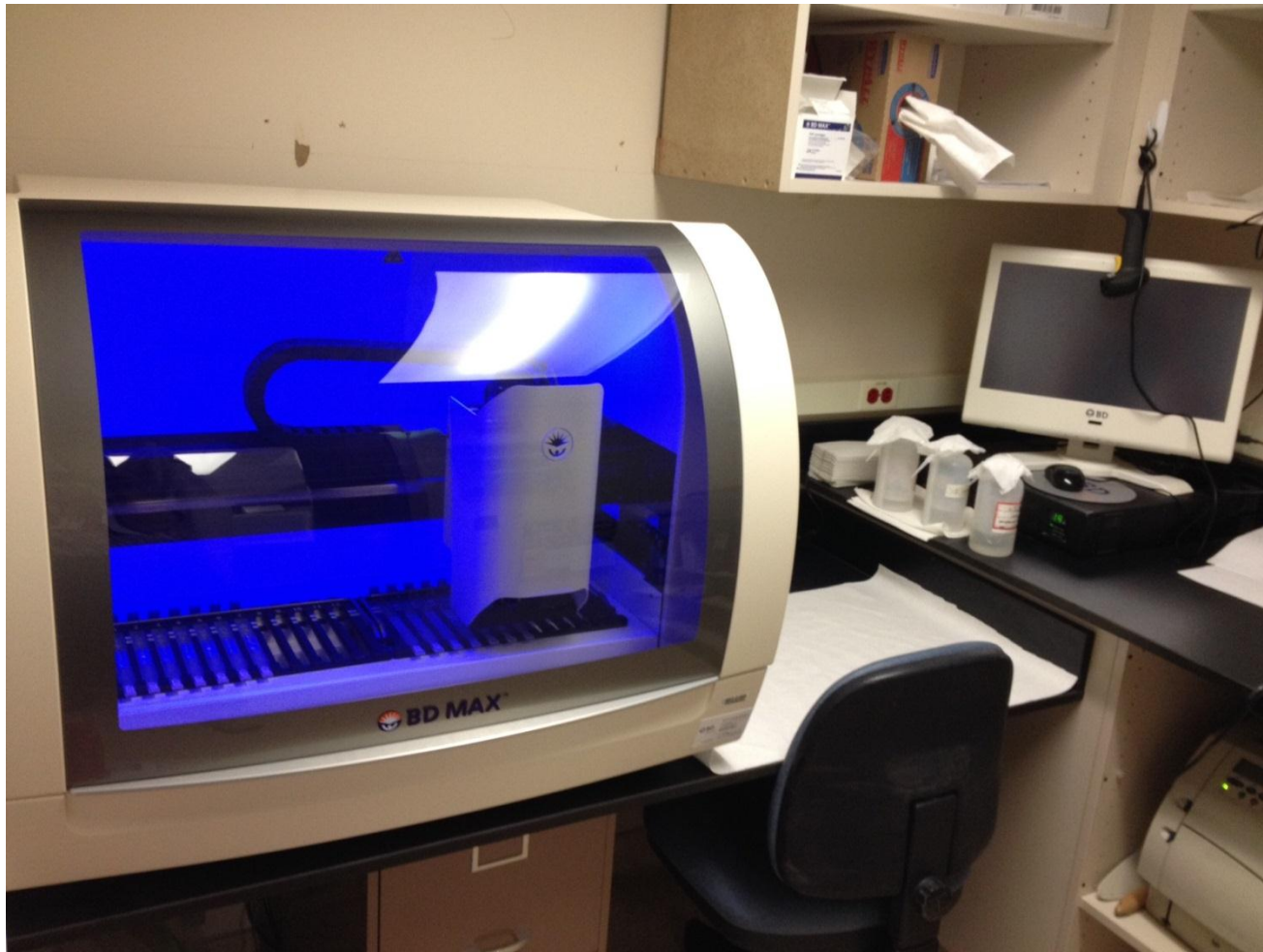


BD Diagnostic Systems, Affirm VPIII Microprocessor

- **What I really like:**
 - 72h transport time vs. 1/2h for wet prep
 - Assay is controlled, sensitive
 - Assay is more reproducible (but still depends on the tech's eyeball reading of the developed slide)
 - Assay does not rely on tech's microscopy skills
- **Tips:**
 - Low room temperature, or Reagent B not at room temperature can cause non-specific binding seen as light blue coloration of the slide
 - Slide must be read against a white sheet of paper; any blue seen is read as Positive



BD Diagnostic Systems, BD MAX





BD Diagnostic Systems, BD MAX

- **PROs:**
 - Walkaway to an extent
 - Runs up to 24 samples at once
 - Minimal maintenance
 - Some assays run simultaneously
 - Open platform
- **CONs:**
 - Storage considerations
 - Peculiarities in pipetting (repeats)
 - Redundancy
 - GBS assay can “hog the instrument”
 - Less analytical freedom in IVD form

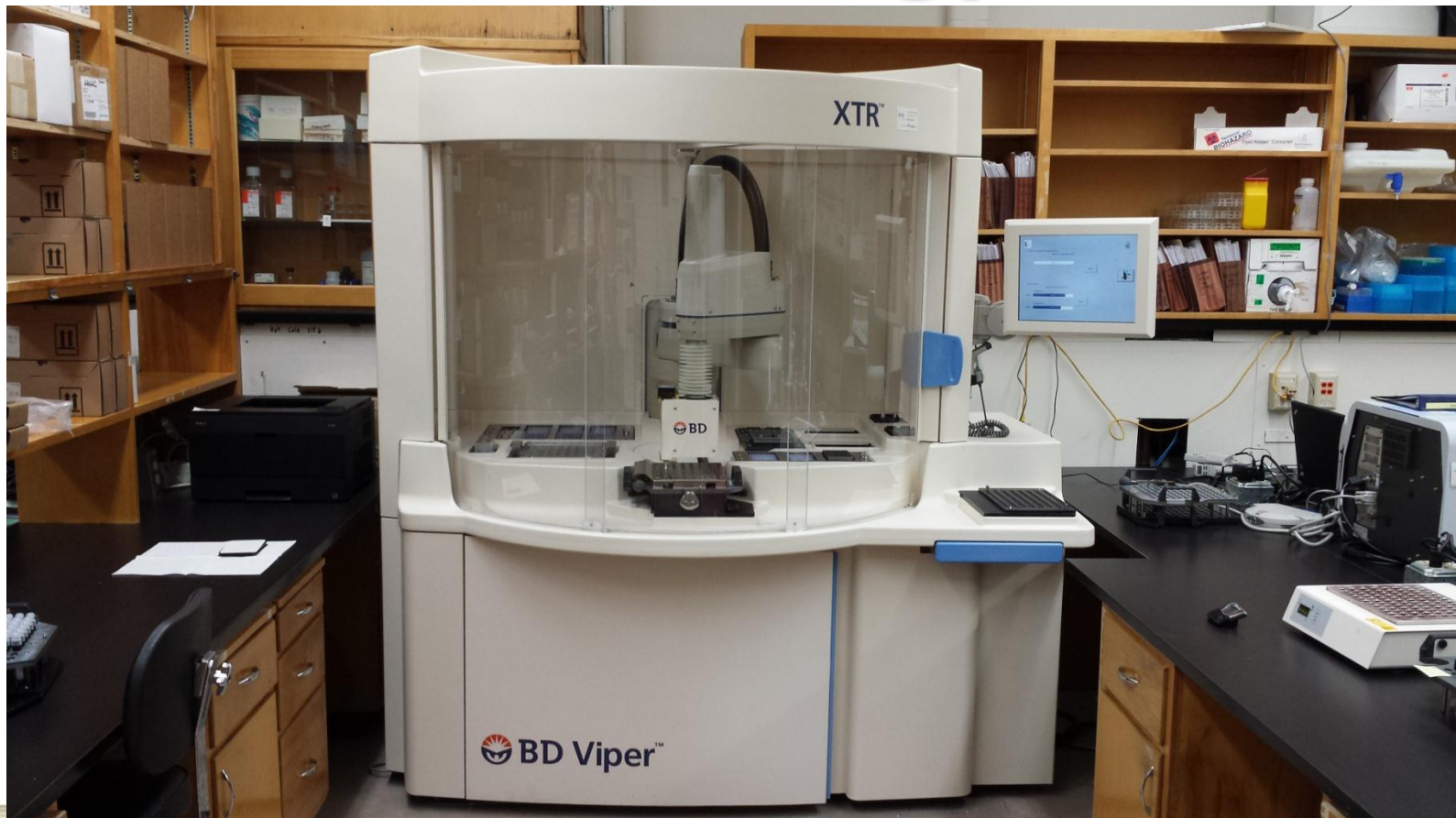


BD Diagnostic Systems, BD MAX

- **What I really like:**
 - Performance of MRSA and *Clostridium difficile* testing at same time has improved turnaround time versus batching
- **Tips:**
 - Game planning
 - Get started early in shift
 - May need a devoted technologist



BD Diagnostic Systems, BD Viper System with XTR Technology





BD Diagnostic Systems, BD Viper System with XTR Technology

■ **PROs:**

- Reliable
- Fully automated
- Menu---CT, GT, HSV1, HSV2, T. vaginalis
- Different agents can be run simultaneously
- Multiple specimen types including cyto preservatives
- Up to 4 96-well plates /8.5 hr shift
- Less than 20 minutes hands on time per run
- Reasonable cost
- Room temp reagent storage

■ **CONS:**

- No Backup
- Large footprint
- Need to bleach carriers—Can use H₂O₂ on instrument
- Slow to develop new assays

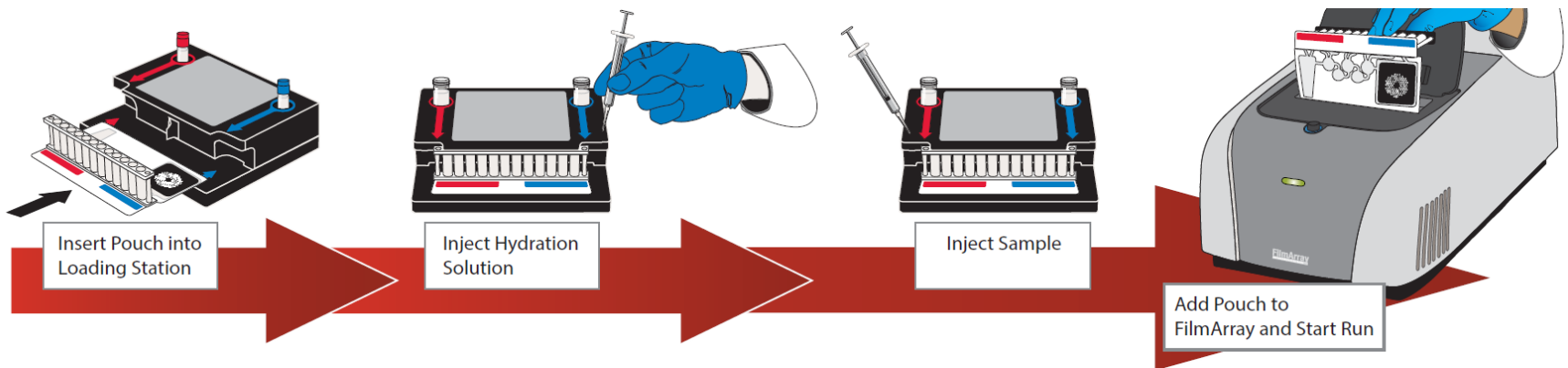


BD Diagnostic Systems, BD Viper System with XTR Technology

- **What I really like:**
 - Reduced labor from 2 FTEs to 1
 - Minimal training required
 - Robotics reduces variability
 - Ready to use reagents
 - Minimal fluid waste
 - No separate room required
- **Tips:**
 - Make sure you have room



Biofire Diagnostics, FilmArray





Biofire Diagnostics, FilmArray

- **PROs:**
 - Sensitive, fast (~1.5H)
 - Covers the 'other' respiratory viruses
 - Also detects 3 atypical bacterial pathogens
 - Currently has favorable reimbursement
- **CONs:**
 - Expensive
 - Very low throughput
 - Covers the 'other' respiratory viruses (relevance, and in which settings?)



Biofire Diagnostics, FilmArray

- **What I really like:**
 - Fast, random access format
 - Sensitivity
 - Answers the question 'Is it a virus other than flu or RSV?'
 - Can be run in a non-molecular lab setting
- **Tips:**
 - Closed system still needs consideration of linear workflow, amplicon contamination
 - Handle pouches carefully – they can tear!
 - Pay close attention to pouch filling – may not fully fill, leading to erroneous results
 - Manufacturer says external controls aren't needed; I disagree



Cepheid, GeneXpert



eneXpert[®]
Module



GX-I



GX-II



GX-IV



GX-XVI



GeneXpert
Infinity-48





Cepheid, GeneXpert

■ PROs:

- Self-contained PCR test device
- TAT
- Reagent/cartridge storage
- Efficient/LEAN workflow
- Ideal system for any size lab

■ CONs:

- Balancing TAT with justified analyzer capacity during peak testing times
- Xpert software
- Minimized need for highly skilled technologists
- Monthly maintenance
- Reagent storage/logistics
- Assay expense
- Limited Test Menu
- Customer Service
- A word on MRSA, from our perspective



Cepheid, GeneXpert

- **What I really like:**
 - Efficient/LEAN system
 - Tech satisfaction
 - Rapid, accurate test results and improved patient care
 - Walk-away time
- **Tips:**
 - Supply ordering
 - Avoid lab-developed changes, if possible
 - QC
 - LIS interfacing & auto-verification
 - TAT



Cepheid, GeneXpert Infinity-48



Cepheid, GeneXpert Infinity-48

- **PROs:**

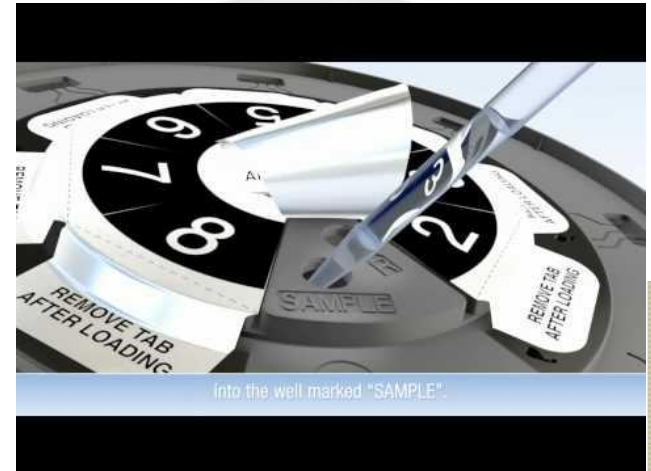
- **CONs:**



Focus Diagnostics, 3M Integrated Cyclor



12 in deep x 8 in wide x 12 in high





Focus Diagnostics, 3M Integrated Cyclor

- **PROs:**
 - **Scalable**
 - Universal disk with up 96 sample capability
 - Direct disk with 8 sample capability - All in one reaction mix in single use vials
 - **Flexible**
 - Perform multiple assays simultaneously as well as multiplex (4 channel capability)
 - FDA-cleared, ASRs -Extensive menu including internal control reagent and primer set, Laboratory developed tests
 - **Qualitative and Quantitative software**
 - **Bidirectional connectivity**
 - **Small footprint**
 - **Results in 1 hour**
- **CONs:**
 - **Quality control software rudimentary - No editing capability**
 - **Universal disk wells tiny and close together**



Focus Diagnostics, 3M Integrated Cyclor

- **What I really like:**
 - ASRs are designed to run using the same conditions so multiple assays can be run simultaneously
 - Results in about an hour
 - Upload sample identification
 - Auto build assays to include and require controls
- **Tips:**
 - For quantitative assay, each instrument requires its own calibration curve with 4 – 8 data points per calibrator
 - Pipetting small volumes into tiny wells can be difficult



GenMark Diagnostics, eSensor XT-8



Multiplex PCR test for the detection of 16 respiratory viruses including: Influenza A (H1,H3 & pdmH1), Influenza B, RSV A, RSV B, Parainfluenza 1, Parainfluenza 2, Parainfluenza 3, Parainfluenza 4, Human metapneumovirus, rhinovirus/enterovirus, Coronavirus NL63, Coronavirus OC43, Coronavirus 229E, Adenovirus subgroup B, Adenovirus subgroup C and Adenovirus subgroup E



GenMark Diagnostics, eSensor XT-8

- **PROs:**
 - No equipment maintenance
 - Superior performance characteristics
 - Includes all the major viral respiratory pathogens (IVD)
 - Influenza subtyping capability
 - Co-infection detections
 - Can be completed in less than one day
 - Batch 1 to 24 specimens per test run
 - LIMS interface
 - Long expiration date
- **CONs:**
 - High cost \$\$\$
 - Extraction step required
 - New instrument in development...
 - Rhinovirus-centric probe design
 - Does not include respiratory bacterial pathogens



GenMark Diagnostics, eSensor XT-8

- **What I really like:**
 - No instrument maintenance (e.g. no fluidics to maintain)
 - No instrument calibrators
 - Superior performance characteristics
 - Ease of use
 - Good customer support 😊
- **Tips:**
 - Open amplification platform so must have good contamination prevention strategies in place
 - Purchase large lots to manage QC costs



Great Basin Corporation, Portrait PA500 Benchtop Analyzer



21.4" Deep





Great Basin Corporation, Portrait PA500 Benchtop Analyzer

- **PROs:**
 - Fairly simple to operate
 - Result interpretation is simple (pos/neg)
 - Can be used "On-demand"
 - No instrument costs
- **CONs:**
 - The caps can be tricky to close
 - The blister packs occasionally pop
 - 2 hour test; 20 min setup time



Great Basin Corporation, Portrait PA500 Benchtop Analyzer

- **What I really like:**
 - The instrument is easy to use
- **Tips:**
 - Each instrument requires its own computer so include that in footprint when calculating space



Hologic/Gen-Probe, PANTHER System

PANTHER INSTRUMENT





Hologic/Gen-Probe, PANTHER System

- **PROs:**
 - Easy to operate instrument
 - Very little daily maintenance
 - Low risk of cross-contamination
 - Easy to incorporate into most labs
 - Good for smaller labs with lower test volumes

- **CONs:**
 - Reagent preparation
 - Reagent expiration date only 72 hours on the instrument.
 - Need to unload and refrigerate reagents everyday if test volumes low.



Hologic/Gen-Probe, PANTHER System

- **What I really like:**

- PANTHER instrument is very easy to operate
- The reagents and specimens are easy to load and unload
- The instrument has random access capability
- Testing is contained in one instrument – no need to transfer tubes during testing to another instrument.

- **Tips:**

- Take the time to train techs well who will be operating the instrument. We started with a limited number until comfortable with the operation.
- Make sure to read package insert for each test added to the instrument. Reagent preparation and storage not the same for all tests.



Hologic/Gen-Probe, TIGRIS DTS Analyzer





Hologic/Gen-Probe, TIGRIS DTS Analyzer

- **PROs:**
 - Performance characteristics of TMA
 - Large-volume batch analyzer
 - Direct tube sampling (no uncapping)
 - Walkaway to an extent
 - Minimal daily, weekly maintenance
- **CONs:**
 - Lots of consumables (storage)
 - Instrument tied until end of runs
 - Decontamination and care
 - Extensive monthly maintenance
 - Redundancy



Hologic/Gen-Probe, TIGRIS DTS Analyzer

- **What I really like:**
 - High-throughput, battle axe
 - Vendor (including engineers)
 - Laboratory-developed assays
- **Tips:**
 - Game planning
 - Allow proper reagent warm-up
 - Ensure homogeneity of reagents
 - Keep an eye on waste volume



Luminex, xTAG



Multiplex PCR test for the detection of 14 gastrointestinal pathogens including: Adenovirus 40/41, Campylobacter (*C. jejuni*, *C. coli* and *C. lari*), Cryptosporidium (*C. parvum* and *C. hominis*), *E. histolytica*, *E. Coli* 0157, Enterotoxigenic *E. coli* (ETEC), *Giardia lamblia*, Norovirus (GI & GII), Rotavirus A, *Salmonella*, Shiga toxin producing *E. coli* (STEC), *Shigella* (*S. boydii*, *S. sonnei*, *S. flexneri* and *S. dysenteriae*), *V. cholerae* (toxigenic) and *Y. enterocolitica*



Luminex, xTAG

■ PROs:

- Multiple assays available (IVD) including GPP, RVP, & Cystic Fibrosis
- Customizable panels available
- High throughput..up to 96 per test run
- Low multiplex panel costs
- Good customer support 😊

■ CONs:

- High instrument maintenance
- Instrument calibrators and controls with each run
- Extraction required
- Not as robust as other assays
- Short expiration dates



Luminex, xTAG

- **What I really like:**
 - Customizable panels
 - Ease of use
 - Spreadsheet output of MFI data
- **Tips:**
 - Carefully evaluate MFI cut-off values and verify internally
 - Open amplification platform so must have good contamination prevention strategies in place
 - Purchase service contract
 - Avoid long idle times



Meridian Bioscience, Illumipro-10





Meridian Bioscience, Illumipro-10

- **Pros:**
 - Unit is small
 - Flexible for stat or batch runs
 - Walk away capability once sample prep is completed

- **Cons:**
 - Crucial 10 minute incubation
 - Once the door is closed and testing started 40 min wait.



Meridian Bioscience, Illumipro-10

- **What I really like:**
 - Simple easy to follow procedures
 - Clean up is quick
 - Maintenance is simple
 - Results in about one hour.

- **Tips:**
 - Run a negative control every batch
 - Do not rush
 - Keep the area clean.



Nanosphere, Verigene Processor SP with Verigene Reader





Nanosphere, Verigine Processor SP with Verigene Reader

- **PROs:**
 - Just minutes of hands on time
 - Several assays available and more coming
 - Almost totally automated
- **CONs:**
 - Cost of reagents
 - Requires 2 – 2.5 hours on the instrument
 - Intervention required for detection



Nanosphere, Verigine Processor SP with Verigene Reader

- **What I really like:**
 - Easy to perform
 - Growing number of assays
 - Good sensitivity and specificity
- **Tips:**
 - Use tools provided with cartridges



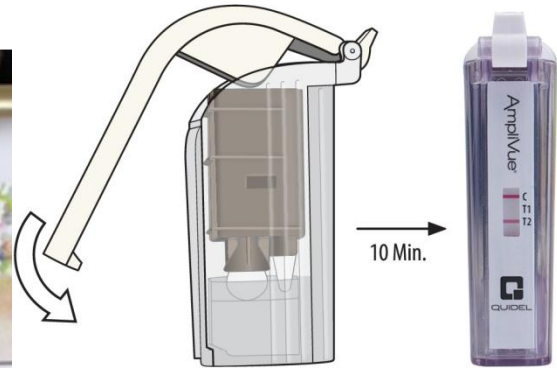
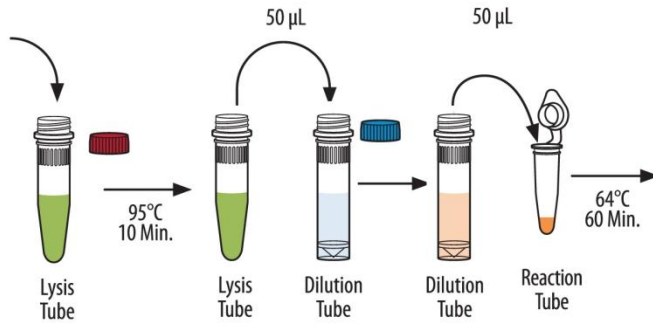
Quidel AmpliVue

Sample Preparation

Amplification

Detection

Result





Quidel AmpliVue

- **PROs:**
 - No capital expenditure, low cost
 - Moderate complexity
 - No need to batch, high throughput
 - Very sensitive
- **CONs:**
 - Critical timing between incubation steps
 - Must read between 10-30 min
 - No printed result

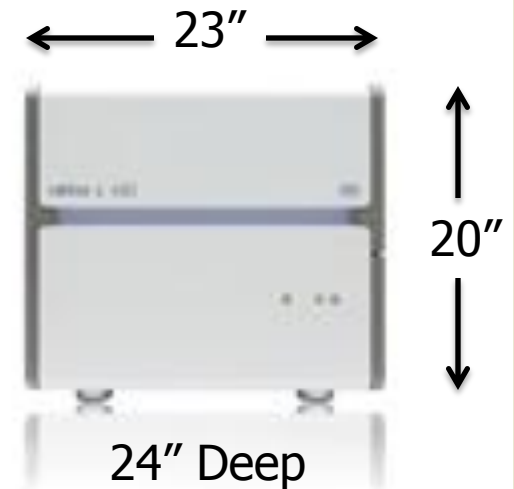
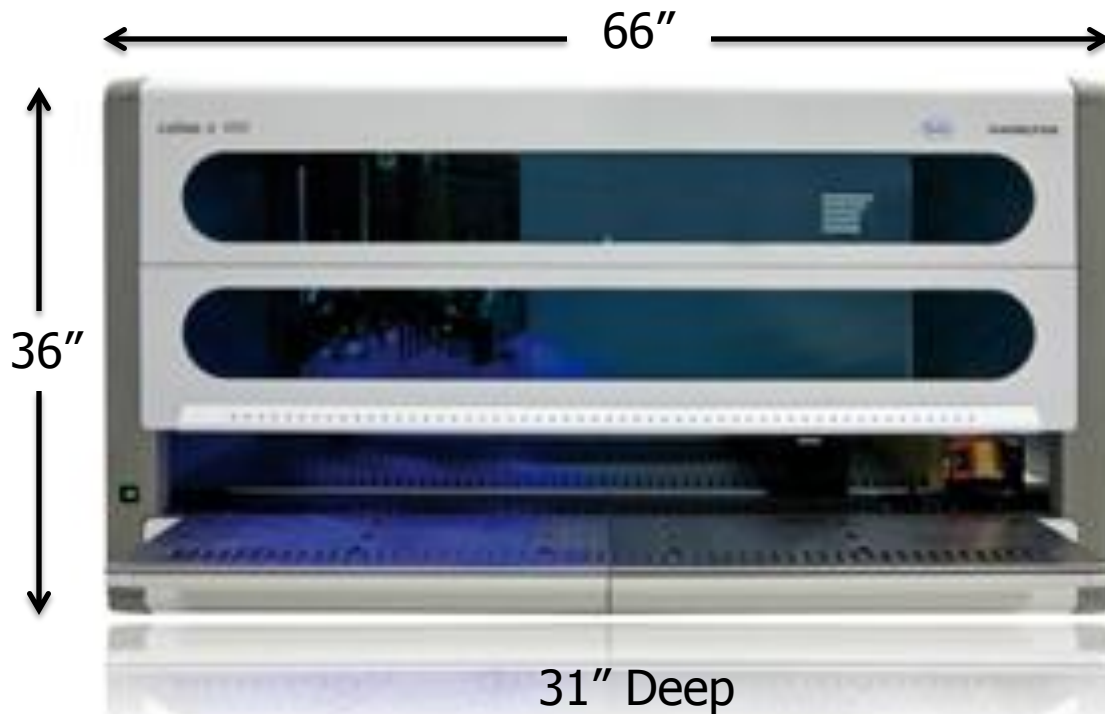


Quidel AmpliVue

- **What I really like:**
 - Moderate complexity
 - No capital/low cost
 - Scalability

- **Tips:**
 - Stress with techs the potential for amplicon contamination
 - Keep unidirectional flow

Roche Diagnostic Corporation, cobas 4800 system



Roche Diagnostic Corporation, cobas 4800 system



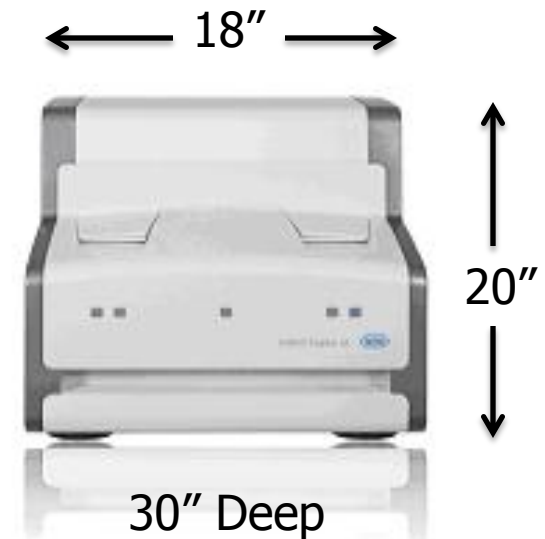
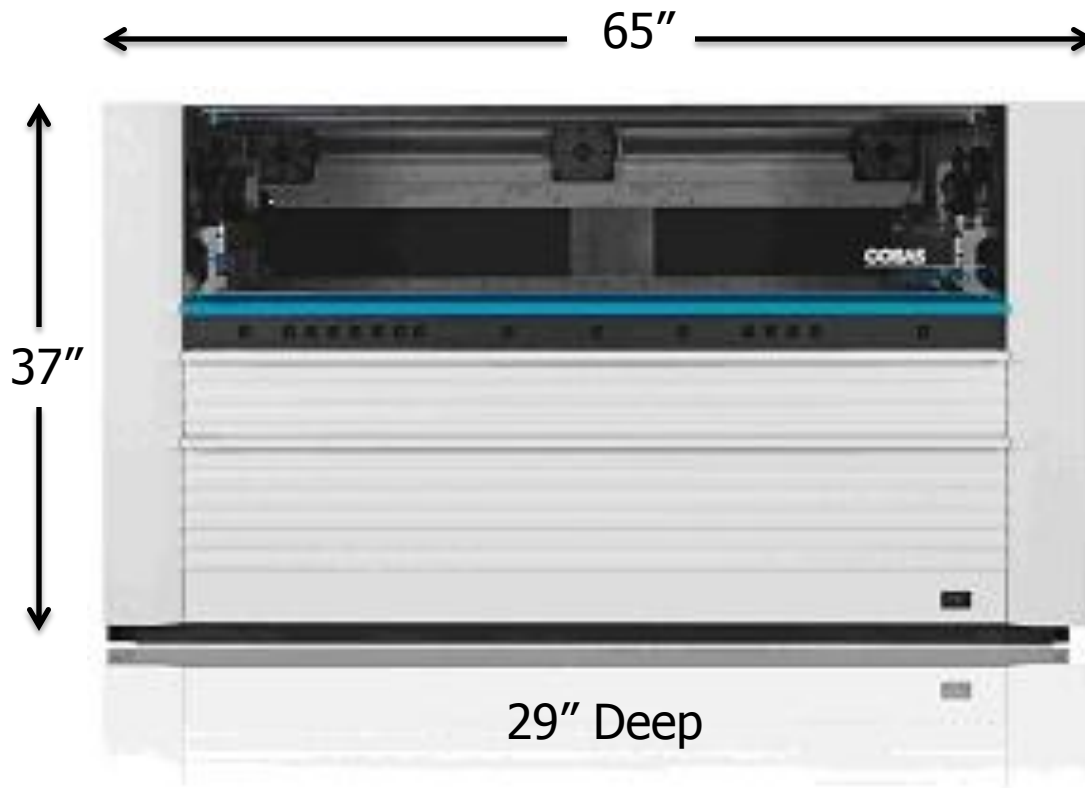
- **PROs:**
 - Minimal hands on time
 - Bi-Directional interface
 - Four IVD Real-Time Assays (HPV, CT/NG, EGFR, BRAF v600)
 - z480 can be used as an open platform real-time thermocycler
- **CONs:**
 - Reagent available in 24 or 96 test kits and are one time use
 - Stand alone z480 can't run FDA approved assays
 - There are a lot of disposables required

Roche Diagnostic Corporation, cobas 4800 system



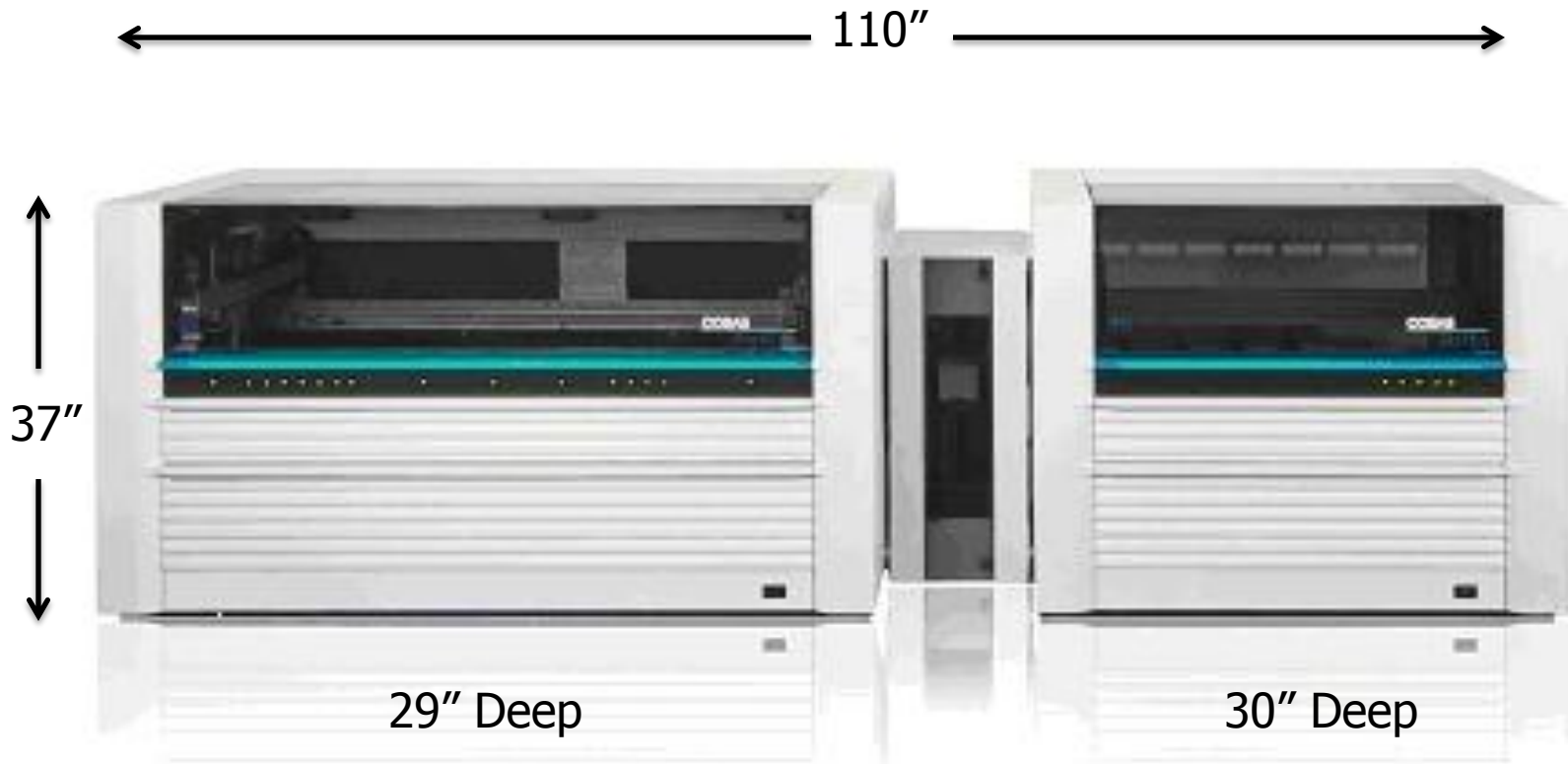
- **What I really like:**
 - Instrument setup and maintenance is very easy
 - The actual test reagents take up only a small amount of refrigerator space
 - The instrument can run cytology specimens directly from the vial
- **Tips:**
 - Workflow must account for testing volume to minimize reagent waste

Roche Diagnostic Corporation, cobas Taqman 48 Analyzer





Roche Diagnostic Corporation, cobas Taqman 96 Analyzer



Roche Diagnostic Corporation, cobas Taqman Analyzer



■ PROs:

- Can load test cartridges on instrument multiple times (unlike COBAS 4800)
- Extraction, amplification, detection are fully automated
- Multiple assays all utilizing very similar assay setup
- Can be used as an automated nucleic acid extractor

■ CONs:

- Significant amount of daily maintenance
- PCR tube transfer device doesn't always lock; can lead to dropped tubes

Roche Diagnostic Corporation, cobas Taqman Analyzer



- **What I really like:**
 - The assay setup is very similar so it is easy to train techs on multiple assays
 - The system is almost fully automated so it can be run during times of limited staffing
 - Tech support can login to your system to help with troubleshooting
- **Tips:**
 - Need to be aware that there is a manual transfer step and PCR reactions must be transferred in a timely fashion
 - This instrument has a significant footprint and requires a very clean environment



Roche/Iquum Laboratory-in-a-tube (Liat™) Analyzer



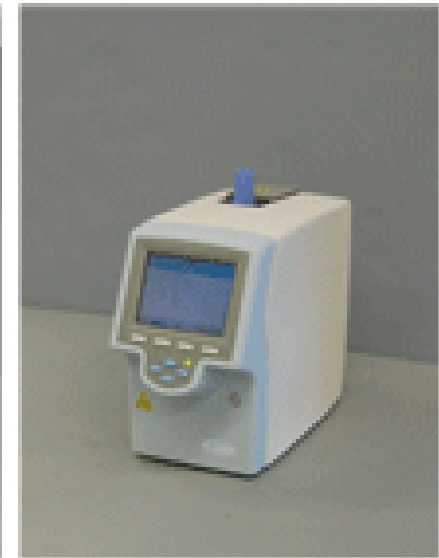
STEP 1.
Add sample



STEP 2.
Scan barcode



STEP 3.
Insert tube



Done!
Results in 20 minutes



Roche/Iquum Laboratory-in-a-tube (Liat™) Analyzer

- **PROs:**
 - Designed to perform rapid molecular diagnostic testing in a point of care setting
 - Automated sample-to-result multiplex real-time RT-PCR assay FDA approved for the detection and discrimination of influenza A and influenza B in approximately 20 minutes
 - Intended for use in laboratories certified to perform "moderate complexity" tests
 - Simple 3 step test process:
 - Collect a raw biological sample into a Liat Tube
 - Scan the tube's barcode to identify the test and track the patient sample
 - Insert the tube into the Liat Analyzer.
- **CONs:**



Roche/Iquum Laboratory-in-a-tube (Liat™) Analyzer

- **What I really like:**
 - Hands-on time of less than 1 minute and a total time-to-result of approximately 20 minutes
 - Very small footprint
 - Integrates multiple intelligent features, such as sample volume metering, on-board internal control, advanced error diagnostics, and automated data interpretation to ensure the quality of results when operated by minimally trained users
 - Completely closed system eliminates contamination
- **Tips:**



What's Available and How Do I Choose?

**A Moderated
Panel Discussion**

(Part 2)



Checklist for Selecting New Equipment/Assays

- **Determining Need**
 - Demand Present
 - Cost Effective
 - Compatible and/or Adaptable with Current LIS
 - Location
- **Research and Analysis**
 - Form a Research Team
 - Establish Timeline/Goals
 - Costs/Reimbursement/Billing Codes
 - Instrument Availability and Intended Use
- **Making a Decision**
 - Create Pros and Cons Table
 - Cost/benefit Analysis
 - Balancing Priorities

