Infectious Disease Diagnostics

Tackling Infectious Diseases

Uppsala Health Summit - October 10th, 2017

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## When to tackle infectious diseases

*Prevention & action – contribution from Diagnostic solutions*

<table>
<thead>
<tr>
<th>Surveillance</th>
<th><strong>Track &amp; prevent:</strong> find outbreaks – pathogens – resistances – in hospital/globally – blood screening</th>
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</thead>
<tbody>
<tr>
<td>Screening</td>
<td><strong>Identify infections:</strong> patient screening – population at risk</td>
</tr>
<tr>
<td>Diagnosis</td>
<td><strong>What’s the bug / patient response:</strong> bacteria/viruses/fungi/parasites – resistances – severity of infection – risk for sepsis – sepsis</td>
</tr>
<tr>
<td>Treatment decision</td>
<td><strong>Act precisely &amp; with impact:</strong> which therapy – broad/narrow spectrum antibiotics – avoid antibiotic resistance – isolate patient – intensive care – closely monitoring</td>
</tr>
<tr>
<td>Monitoring</td>
<td><strong>React:</strong> monitoring therapy response – change treatment – treatment duration</td>
</tr>
</tbody>
</table>
How to tackle Infectious Diseases

Diagnostic technologies

Infectious Diseases

Traditional

Culture

Proteomics
(Proteins)

ELISA

Mass Spec

Molecular

Genomics
(DNA/RNA)

NAAT

NGS

Live Cell Molecular
(Bio-response)

Optical
(Morphokinetic, digit, fluorescence)

Others

Accelerate Dx, First Light, QuantaMatrix

Detection of Live Bacteria
Phenotypic Test
Direct from Clinical Samples
Diagnostic Solutions

* A test result depends on four elements

- Assay specific Reagents
- Core Reagents
- Test Result
- Assay Specific Software / calibration data
- Instrument
Instruments and software

Customers need solutions from point of care to high throughput lab

- Research Lab / Academia
- Physician’s office
- ER / ICU
- Microbiology Lab
- Hospital / Commercial Lab

Provide Dx solution as customer need

Point of Care | Central Lab | Bloodscreening

- cobas® Liat® System
- cobas® 4800 System
- cobas® 6800 System
- cobas® 8800 System

- User Defined Functionality (UDF)
- cobas omni Utility Channel

- cobas® 4000 System
- cobas® 6000 System
- cobas® 8000 System
Infectious Disease assay portfolio strategy
Rapidly increase menu across instruments

Genomics
- Influenza A/B
- Influenza A/B + RSV
- HIV-1
- HIV-2
- HBV
- HCV
- HCV GT
- HSV-1/2
- HPV
- CMV
- WNV
- DPX
- HEV
- Zika (IND)
- 'chikV/denV*
- MRSA/SA
- CT/NG
- C. diff
- MAI*
- TV/MG*
- MTB*
- RIF/INH*
- Strep A
- Babesia

Proteomics
- HAV
- HBV
- HCV
- HIV-1
- HTLV 1+2
- HSV-1
- HSV-2
- CMV
- Rubella
- HIV-2*
- Syphilis
- Toxo
- Chagas

>10 assay other pathogens in development or planned

* In development or under discussion
IVD Assay development requires extensive performance validation

The usual assay development pathway in blood screening

<table>
<thead>
<tr>
<th>Need</th>
<th>• Public health need &amp; market demand</th>
</tr>
</thead>
<tbody>
<tr>
<td>Develop</td>
<td>• Test Development</td>
</tr>
<tr>
<td></td>
<td>- Extensive in vitro performance verification testing</td>
</tr>
<tr>
<td></td>
<td>- CE review/approval</td>
</tr>
<tr>
<td>Develop</td>
<td>• US Clinical Trials</td>
</tr>
<tr>
<td></td>
<td>- 10,000 individual donations &amp; 10,000 pools; reproducibility and other studies</td>
</tr>
<tr>
<td></td>
<td>- FDA review/approval (BLA)</td>
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</table>

Available in CE and U.S.
Emerging pathogens may require a different approach
Donor screening tests for use under IND

Need
- Potential public health threat
- No current market demand

Develop
- Test Development
  - Limited performance verification testing

Prepare
- Test available for potential use under investigational new drug (IND) protocol

Extend
- If public health need develops
  - Donors can be tested under cost recovery IND
  - Test can be further validated with additional studies for BLA
Agile assay design software identifies primers and probes

Designed to work with cobas omni reagents

- Agile assay design software is an *in silico* method to identify best candidate detection set for target pathogen RNA or DNA

- Uses standardized chemistries of cobas omni reagents and system thermocycling conditions to quickly winnow potential primers and probes to best choice.

- **cobas** omni reagents and standardized conditions facilitate rapid test design.
From A to cobas® Zika in 10 weeks
Response to an emergent public health need

- Zika virus may be spread by blood transfusion.
- An apparent link between microcephaly and Zika in Brazil in late 2015 sparked global concern.
- First Zika cases reported in Puerto Rico in December 2015
- In early 2016, FDA reached out to test manufacturers for help with Zika screening test under IND
- February 2016: FDA issued Guidance that prohibited use of blood collected in “Zika active areas”
  - IMPACT: Puerto Rico forced to halt blood collections & rely on import from U.S. states
  - Raised concern for spread to Gulf Coast and other states
- Concern and surveillance for the spread of Zika to U.S. states continued
  - Some blood centers and testing laboratories initiated screening in late spring and summer 2016
- First locally-acquired Zika cases detected in Miami, Florida in late July 2016
  - Blood screening results used to surveil and help direct vector control efforts
- On August 26, 2016, FDA revised its Guidance to mandate all U.S. donations be screened with NAT test or pathogen-reduction technology
From A to cobas® Zika in 10 weeks
Design, development & deployment in 10 weeks

Collections in Puerto Rico resume April 2, 2016

Align Zika GenBank sequences

2,336 primers & probes
1,139 assay candidates
117 after additional scoring
3 selected for wet lab testing
1 test + 1 reference method

April 3, 2016
cobas® Zika is used at 12 U.S. testing laboratories

More than 4 million donations screened with cobas® Zika

<table>
<thead>
<tr>
<th></th>
<th>Number of Donations screened with cobas® Zika</th>
<th>Number of Donations with Evidence of Zika virus</th>
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<tbody>
<tr>
<td>Puerto Rico</td>
<td>111,842</td>
<td>356</td>
</tr>
<tr>
<td>United States*</td>
<td>4,154,192</td>
<td>27</td>
</tr>
<tr>
<td>Total</td>
<td>4,265,665</td>
<td>383</td>
</tr>
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</table>

*Includes donations collected in the 50 U.S. states or at U.S. military facilities around the world.

- BLA submitted to FDA in April 2017
- Currently under FDA review
Thoughts for the workshop

Market:
- market need and demand -> actionable result
- point of care vs. central lab; especially in low income countries

Assay development and validation
- access to samples, especially for new infectious threats
- pathogen and resistance information (e.g. sequences, resistances, mutations)
- variety of relevant specimen (blood, saliva, stool, sputum, BAL, nasal / nasopharyngeal / throat swab, urine, vaginal swab, …)
- time is critical, but assays have to be safe and effective, high validation efforts
Doing now what patients need next