Converting Ideas into Commercially Viable Products

Vivian Jonas, M.S.
Associate Director, Development
Gen-Probe
Vivian.Jonas@gen-probe.com

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Basic Steps

- Define customer needs
- Set product requirements
- Determine technology and platform to be used to meet requirements
- Develop assay on platform
- Transfer to Manufacturing
- Analytical Verification and Validation
- Clinical Trials
- Commercialization

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Intellectual Property

- Do you own the intellectual property (IP)?
- Can you license the IP?
  - Cost?
  - Royalities?
- U.S. and other countries

Funding

It costs a lot to develop high quality products

- Modes of funding
  - Small business grants
  - Government grants
  - Venture capital
  - Self-funding

- Cost/Benefit analysis for obtaining capital
- Comparison with other opportunities

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Who is the customer?

- Patient
- Labs
  - Reference Lab
  - Hospital Lab
- Physician
- Public Health
- Epidemiologists
- Clinical Research

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Define Customer Needs

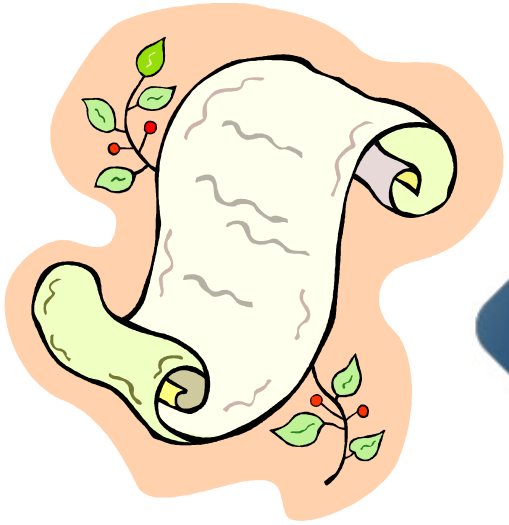
- Intended Use
  - What information does the physician need to treat the patient?
  - Will the results be used in conjunction with other tests?
  - Is the test going to be used for screening?

Define Customer Needs

- How does the test fit into the laboratory workflow?
  - Manual assay
  - Instrumentation
  - Timing

Define Customer Needs

- Guidance documents
  - CDC recommendations
  - WHO recommendations
- Regulatory Agencies
  - ISO 13485
  - U.S. FDA
  - Other regulatory agencies
- Professional Organizations
  - ATS, AMA, ACOG, etc



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Level of Regulation Required

- Lab developed tests
- Analyte Specific Reagents (ASR)
- Research Use Only (RUO)
- *In vitro* Diagnostic (IVD)
  - 510k/self-certification
  - PMA

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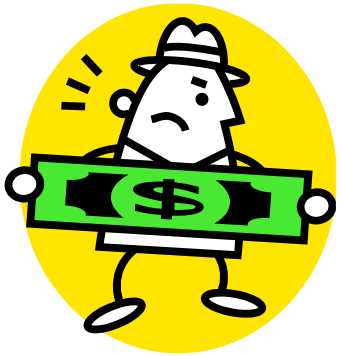
Pricing

- Pricing sensitivity
  - Trade-offs with respect to value of result
    - Payers/Insurance
    - Lab cost
    - Reimbursement
    - CPT codes



Examples

- Technology Driving the Product
  - Multiplexing
    - Results affect treatment?
    - Reimbursement

Set Product Specifications

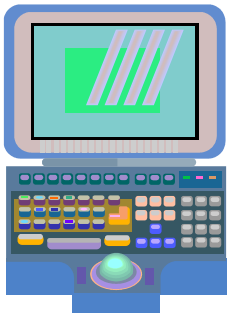
- Intended Use
  - Sample Types
    - Handling
  - Reagent Expiration Dating
  - Compliance with Regulations

Set Product Specifications

- Analytical Performance
  - Sensitivity and Specificity
  - Reproducibility
  - Interference
  - Cross reactivity
- Clinical Performance
  - Sensitivity and Specificity
  - Positive Predictive Value
  - Negative Predictive Value

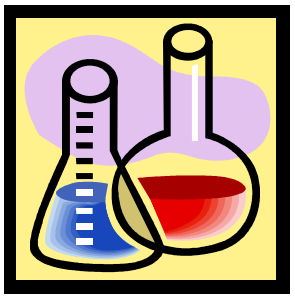
Set Specifications

- Workflow Specifications
  - Instrument Platform
    - Time to Result?
    - Manual Steps Allowed?
- Instrument Specifications
  - Hardware
  - Software
- Controls and Calibrators



Development

- Reagents
  - New product?
    - Controls
    - Reagents needed
    - Containers needed
    - Packaging needed
    - Platform
    - Software
  - Product line extension?
    - Verify existing reagent formulations
    - Software



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Development

- Reagent Optimization
  - Initial formulae
  - DOEs
  - Instrument System
  - Software
  - System and Assay Integration
    - Sequence files
    - Data interpretation algorithms
    - LIMS system compatibility

Development

- Preliminary formulations
- Optimize Formulations
  - DOEs
- Analytical studies
  - Sensitivity
  - Specificity
  - Stability studies
  - Determine preliminary performance

Development

- Assay Integration
  - Test using clinical samples
  - Reagent stability studies
- Determine preliminary assay performance characteristics
- **Software Transfer Review**

Development

- Finalize formulation
  - **Formulation Review Document**
- Transfer formulations to Manufacturing
  - Development Lots/Process Development
  - **Process Review**

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Quality Control

- Develop quality control methods for components and kits
  - Analytical methods
    - *E.g.* oligomer purity, pH
  - Use testing
    - Kit release testing
- Develop specifications
  - Raw materials
  - Labeled reagents
  - Kits
- **Quality Transfer Review**

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Performance Verification

- Build GMP Lots
  - Pre-clinical studies internally and externally
  - Verify performance on instrument with final assay software
  - Test material against the specifications
  - Assay verification studies
  - Clinical Trials
  - Prepare Regulatory Submissions
    - PMA submission to U.S. FDA $250,000
    - Canada – Class III device submission $8600

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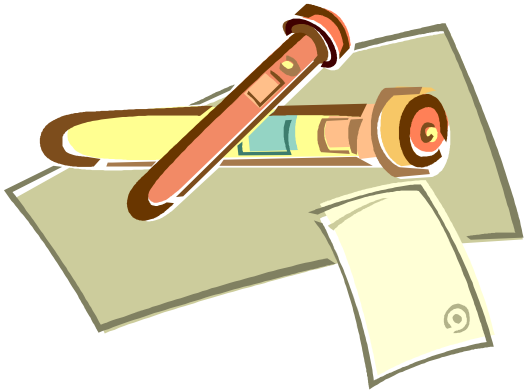
Clinical Trials

- Trial design is critical to support claims
  - Statistical Analysis Plan
    - Statistically relevant number of samples
  - IRB approval
  - Site Contracts



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Clinical Trials

- Trial Design
  - Comparator methods
  - Prevalence of disease at sites
  - Intended Use Samples
    - Remnant samples?
    - Prospectively collected?
    - Informed consent required?
- Protocol
- IUO Package Insert
- Training and Start

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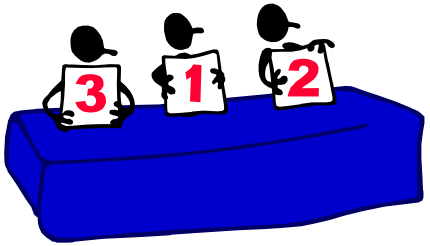
MTD Trial Design

- Novel trial design for diagnostic product
  - Compared patient diagnosis, including signs and symptoms, with MTD results
  - Physician expert panel to adjudicate discrepants
- Multi-center study
  - Range of disease prevalence
  - One ex-US site



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Regulatory Submissions

- Description of device
- Data to support claims
  - Performance Data
    - Sensitivity, specificity, PPV, NPV
  - Analytical Data
    - *E.g.* interference, recovery, reproducibility
  - Labelling
    - Directions for use
    - Labels

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Time to Approval Varies

- U.S.
  - 510k – 150 days
  - PMA average review time over 5 years was 288 days
- Japan
  - ~1 year
- Canada
  - 12-178 days depending on Class of device over a 4 year period

Commercialization

- Finalize Instructions for Use
- Training manuals
- Technical support plans
- Customer complaint processes
- Plan for product improvements

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Post-Launch Surveillance

- Customer Feedback
- Required post-launch studies
- Review independent reports of product performance
- Customar Complaints
  - Trend and track data received

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Improvements

- Customer input drove MTD1 to MTD2
  - Sensitivity improvement
    - Increased volume of sample
    - Smear negative claim in the U.S.
  - Ease of Use
    - Elimination of Hybridization Controls
  - Addtion of Specimen Processing Controls
    - Provides control on reagents used by lab to process sputum

Marketing Studies

- Conduct studies in high/low prevalence sites
- Evaluate multiple sample types – even those that are not part of the package insert claims
- Approach testing from different angles
  - Physician versus laboratorian spin
    - Lab tests comparisons
    - Comparisons to patient diagnosis

Get the Word Out

- Peer-reviewed journal articles
- Poster presentations at appropriate conferences
- Discussions with thought leaders
  - WHO, FIND, CDC, BMGF, etc.
  - Physicians
  - Laboratorians

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Get the Word Out

- Multiple publications in a short time on Cepheid Xpert® MTB/RIF

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Barriers to Introduction

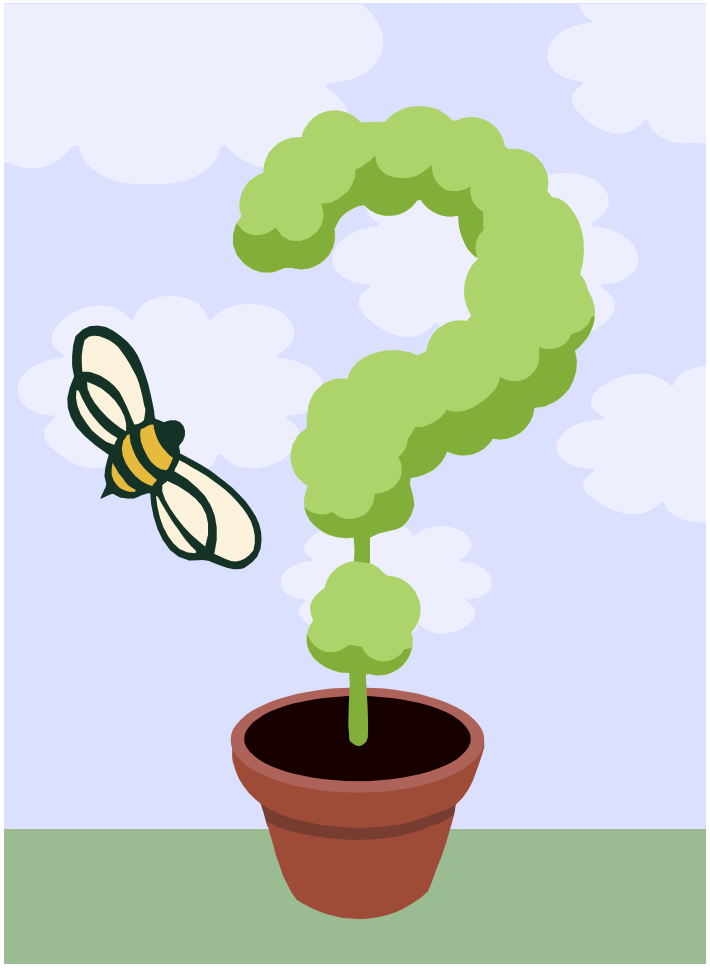
- Regulatory
- Emotional/Cost
  - Smear is good enough
  - Culture is the gold standard
  - Technology and value not well understood

Barriers to Introduction - MTD

- Conservative approach to public health
  - New technology
    - Amplfication versus culture
  - Expectations of performance
    - Oversell of sensitivity
- Cost
  - More expensive than culture
    - Decreased cost to public health system/hospital, but higher lab costs

The Holy Grail:

- Low cost
- Near patient
- Simple sample processing
- Easy to use
- Includes drug susceptibilty



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