Start With the End in Mind – A Diagnostic Company’s Perspective on Companion Diagnostic Development

Dr Bob Holt
Disclaimer

• This presentation contains my personal views and research and does not necessarily reflect the policies or endorsement of Hologic Inc.
• This presentation contains forward-looking information that involves risks and uncertainties, including statements that are based upon assumptions made by market research which are subject to known and unknown risks and uncertainties that could cause actual results to differ materially from those anticipated.
Hologic Overview

• 5,500 employees, offices in 15 countries
• $2.5 billion annual revenue
• Developer, manufacturer and supplier of diagnostic products
• Proprietary automated molecular diagnostic systems and kits
• 73 FDA approved/cleared products on the market
• Products sold in 111 countries
• Manufacture 80 million diagnostic tests a year in three ISO13485 certified manufacturing facilities

Hologic provides its CDx development service through its Contract Research Organisation brand Tepnel Pharma Services
“Traditional” Companion Diagnostic Development Workflow

Pre-Clinical  Phase I  Phase II  Phase III  Launch

Biomarker Discovery and Verification  Companion Diagnostic Development

Product Development  Analytical and Clinical Validation  Regulatory
“Traditional” Companion Diagnostic Development Workflow
Our Companion Diagnostic Development Service

- Concept and Feasibility
- Product Definition and Planning
- Development and Verification
- Validation and Launch Prep
- Post Market Support
# Timelines

<table>
<thead>
<tr>
<th>Approval Process</th>
<th>Number of Products on the Market</th>
<th>Examples</th>
<th>Development Times</th>
</tr>
</thead>
<tbody>
<tr>
<td>CE-Mark</td>
<td>54</td>
<td>APTIMA® HPV and PROGENSA® PCA3</td>
<td>8-12 months</td>
</tr>
<tr>
<td>510k</td>
<td>29</td>
<td>APTIMA® Combo 2</td>
<td>1-2 years</td>
</tr>
<tr>
<td>BLA</td>
<td>5</td>
<td>Aptima® HIV-1 RNA qualitative assay</td>
<td>1-2 years</td>
</tr>
<tr>
<td>PMA</td>
<td>8</td>
<td>Aptima HPV 16 18/45 genotype assay</td>
<td>2 years+</td>
</tr>
</tbody>
</table>
Our Companion Diagnostic Development Service

Concept and Feasibility
Our Companion Diagnostic Development Service

- Concept and Feasibility
- Product Definition and Planning
- Development and Verification
- Validation and Launch Prep
- Post Market Support

Decisions that are made here

End up here
Concept and Feasibility

• Driven by Pharma and Dx company - multiple stop/go’s before design control
• When should I engage with a Dx partner and regulatory authorities?
• The sooner the better:
  – Biomarker discovery and proof of concept studies
  – R&D assay development
  – Platform/technology choice
  – Legal agreements and IP searches
  – Regulatory assessment of clinical trial design
  – Market research
  – Risk analysis
  – **Define Product Requirements** – this feeds directly into the product design
Product Requirements

- Key to the success of a CDx development product – multi stage process
- As much information as possible is required - as early as possible
- Gathered from multiple sources and stakeholders by both Pharma and Dx companies
Product Requirements

Please contact robert.holt@Hologic.com if you would like a copy of the full requirement list and Product Development workflow.

Http://Hologic.com
http://tepnelpharmaservices.com
Cost of Correcting a Requirements Error

Repeat Design – Pre Market Bridging Studies – Post Market Bridging Studies
Our Companion Diagnostic Development Service
Project Plan and Schedule

• High level project plan covering the whole development process
• Identifies processes, deliverables, milestones and timelines
• Product Scope (from Product Requirements)
• Project Team and Responsibilities
• Supplemented by individual plans from each functional area:
Extended Team Structure

Pharma Team Leader

Dx Team Leader

R&D  Operations  Clinical  Regulatory  Quality  QC  BD/Marketing

Drug Development  Biomarker Development  Clinical  Regulatory  Quality  Assay Development  BD/Marketing
Design Control

- Design Control is a formal documentation procedure applied to product development
- It is an FDA requirement for medical devices
- Runs alongside and throughout the product development process
Requirements and Design Inputs

- User and Design Requirements - from Product Requirements and Project Plan
- Design Inputs (What?) are formed from User and Design Requirements - these are quantifiable verifiable specifications
Requirements and Design Inputs

- User and Design Requirements - from Product Requirements and Project Plan
- Design Inputs (What?) are formed from User and Design Requirements - these are quantifiable verifiable specifications
Requirements and Design Inputs

- User and Design Requirements - from Product Requirements and Project Plan
- Design Inputs (What?) are formed from User and Design Requirements - these are quantifiable verifiable specifications
Design Outputs and V&V

- Specify how the product will be tested during Verification and Validation
- Design Verification: Did you design the device right? Outputs = Inputs?
- Design Validation: Did you design the right device?
Design Outputs and V&V

- Trace Matrix
- Design History File
- Device Master Record - procedures and specifications for a finished device
Our Companion Diagnostic Development Service

Concept and Feasibility

Product Definition and Planning

Design and Stage Reviews
Design and Stage Reviews

Design Reviews:

- Formal technical reviews conducted by Core Team and an independent technical experts (Pharma and/or Dx)
- Ensure design inputs are addressed by outputs to meet design requirements
- Move project to next stage

Stage Reviews:

- Gate meeting to make business decision on continuation of the project.
- Review progress against Project Plan and Schedule
- Go/Kill/Hold/Recycle
Our Companion Diagnostic Development Service

- Concept and Feasibility
- Product Definition and Planning
- Development and Verification
Development and Verification

- Implementation of product design and the systems required to manufacture them
- Verification testing to ensure all components of the product are ready for validation
Development and Verification

• QC method development and validation

• Manufacturing:
  – Vendor identification and qualification
  – Manufacturing equipment IQ/OQ/PQ
  – Packaging, manuals, labelling and shipping
  – Assay formulation
  – Development lots – small scale
  – IUO pilot lots – large scale

• Regulatory preparation

• Clinical Trial preparation

Ready for Validation
Our Companion Diagnostic Development Service

- Concept and Feasibility
- Product Definition and Planning
- Development and Verification
- Validation and Launch Prep
Validation and Regulatory Submission

• **Analytical Validation**
  – Carried out prior to clinical validation
  – Demonstrate the fitness of the assay (e.g. repeatability, reproducibility)

• **Clinical Validation**
  – Clinical utility of both the CDx test and the drug
  – Store samples that are consented for use in bridging studies
  – The sooner you engage with a Dx partner the sooner we can look at your trial design

• **Regulatory Submission**
  – Regulatory guidance is required throughout the entire product development process
  – Timelines and requirements vary depending on factors including; 510k/PMA/CE, US/ex-US
Regulatory Approval!
Our Companion Diagnostic Development Service

- Concept and Feasibility
- Product Definition and Planning
- Development and Verification
- Validation and Launch Prep
- Post Market Support
Post Approval

• cGMP full scale IVD manufacturing production lots
• Post Launch Surveillance
• Marketing
• Manuals and IFU
• Technical Support
• Customer Support
• Reimbursement
• Bridging studies
Start with the End in Mind....