Bringing Personalized Medicine to the Clinic

CDx Partnerships: Keys to Success

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PrimeraDx

FDA's Definition of CDx

Definition and Use of an IVD Companion Diagnostic Device

An *IVD companion diagnostic device* is an **in vitro diagnostic device** that provides information that is **essential** for **the safe and effective use of a corresponding therapeutic product**. The use of an IVD companion diagnostic device with a particular therapeutic product is stipulated in the instructions for use in the labeling of both the diagnostic device and the corresponding therapeutic product, as well as in the labeling of any generic equivalents of the therapeutic product.

An IVD companion diagnostic device could be essential for the safe and effective use of a corresponding therapeutic product to:

- **Identify patients who are most likely to benefit from a particular therapeutic product**
- Identify patients likely to be at increased risk for serious adverse reactions as a result of treatment with a particular therapeutic product
- Monitor response to treatment for the purpose of adjusting treatment (e.g., schedule, dose, discontinuation) to achieve improved safety or effectiveness

FDA Draft Guidance – 14Jul11

PrimeraDx at a Glance

PrimeraDx is an IVD MDx Product Company

Next-generation qPCR diagnostic platform

- Assay 50-100 individual markers in one reaction
- Simultaneous quantitative and qualitative capabilities

High-value MDx IVD test kits

- Oncology and Infectious Disease
- Companion diagnostics

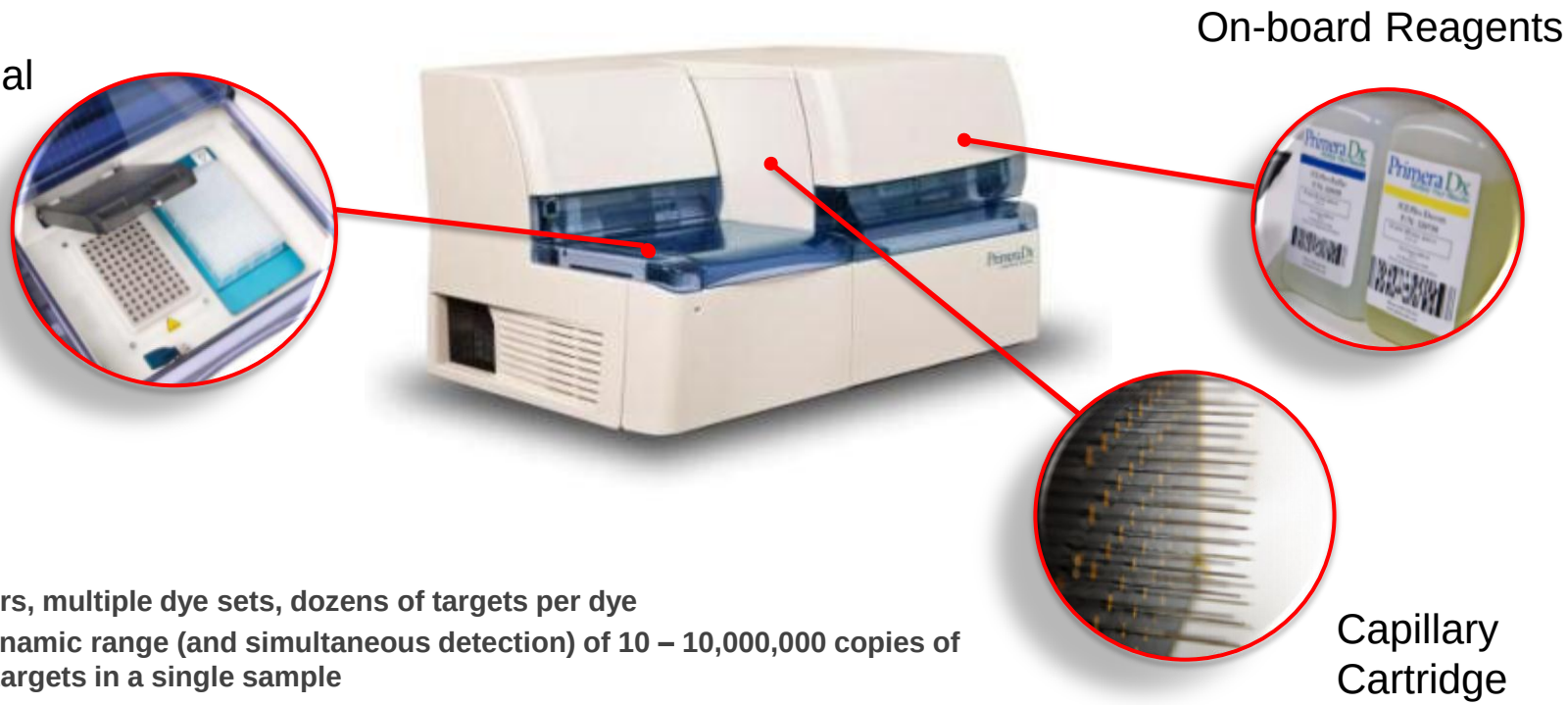
- End-point Qualitative Detection
- Real-time Quantification
- SNP
- Fusion Gene
- Gene copy #
- mRNA
- microRNA
- Controls

A real-time, multiplex, multi-modal "All in one well" MDx solution

Only PrimeraDx Can Do This

The ICEPlex System – Fully Automated, Real-Time, Multiplex qPCR

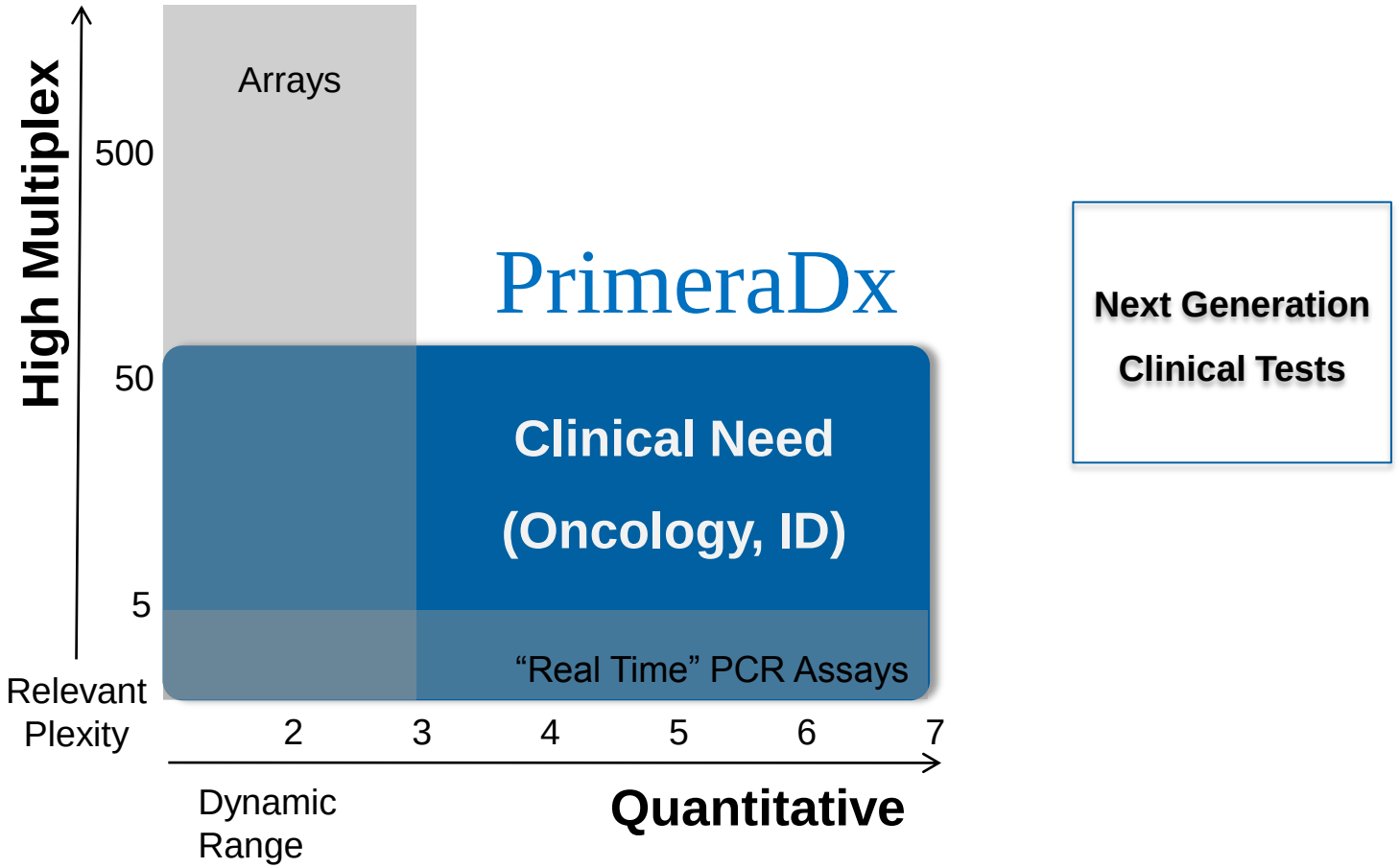
Walk-away Workflow with Automated Reporting of Assay Results



- **Dual lasers, multiple dye sets, dozens of targets per dye**
- **Assay dynamic range (and simultaneous detection) of 10 – 10,000,000 copies of multiple targets in a single sample**
- **Innovative software to track, analyze and report results**
- **Proven reliability – customer experience**
- **Manufactured under QSR, ISO and GMP standards**
- **Flexible software: User-definable assay conditions for LDT capabilities, company-developed assay design software speeds assay/product development**

There is No Comparable Technology Available

ICEPlex Enables Real-time Multi-modal, Multiplex, Quantitative Tests



Rx-CDx Regulatory

FDA's Expectations

- FDA requires IVD approval prior to or simultaneous with NDA approval…
- …so drug developer contracts with diagnostic manufacturer to develop an approvable IVD
- CDx-IVD is no different than any other PMA *EXCEPT* device label reflects Rx

GOAL : Contemporaneous approval of Rx and Dx

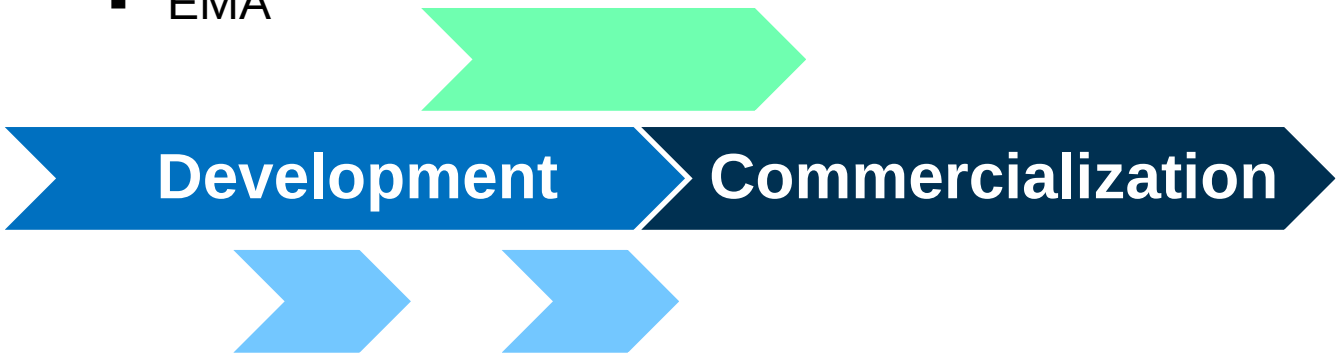
- "Copy-cat" CDx IVD now an option

Rx & Dx Are Different Industries

Rx

- Ph I > II > III
- IND > NDA / BLA
- CDER / CBER
- EMA

- Detail ordering physician
  - Oncologist
- Negotiate reimbursement



CDx

- Design Control
- Verification & Validation
- Pre-IDE > IDE > PMA
- CDRH / OIVD
- CE Mark

- Detail lab directors
  - Pathologist
- Labs sell to ordering physicians (Onco / Heme Path)
- Labs are reimbursed and can negotiate

Rx & Dx Have Different Concerns About CDx

Rx

- Incomplete understanding of IVD development
- Unfamiliar with CDRH
- CDx must finish first

- CDx access
- LDT vs IVD

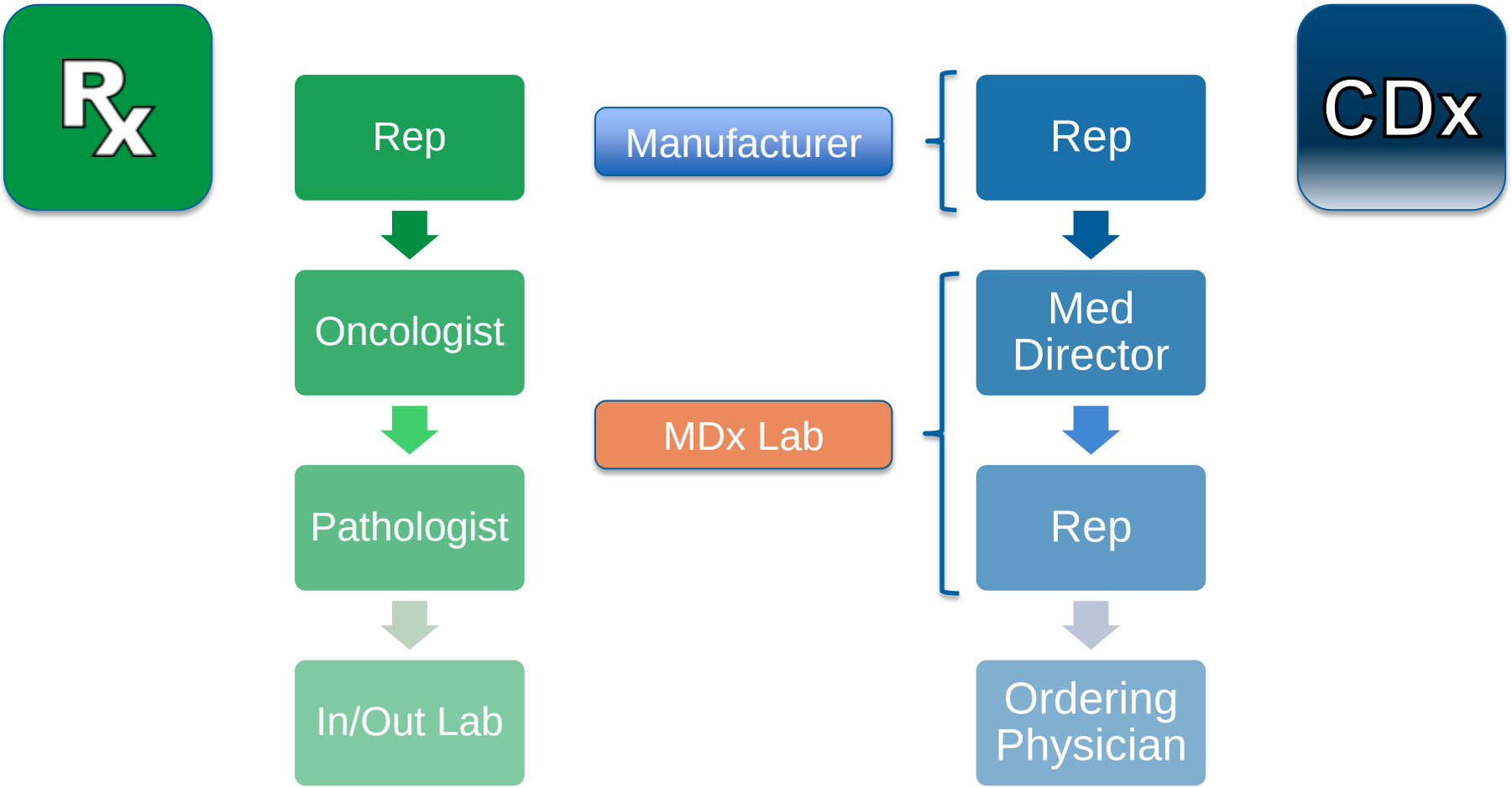
Development → **Commercialization**

CDx

- Designated CRO lab
- No control over clinical module of PMA

- LDT vs IVD
- Lab / Rx messaging
- Reimbursement

Rx-CDx Commercial Differences



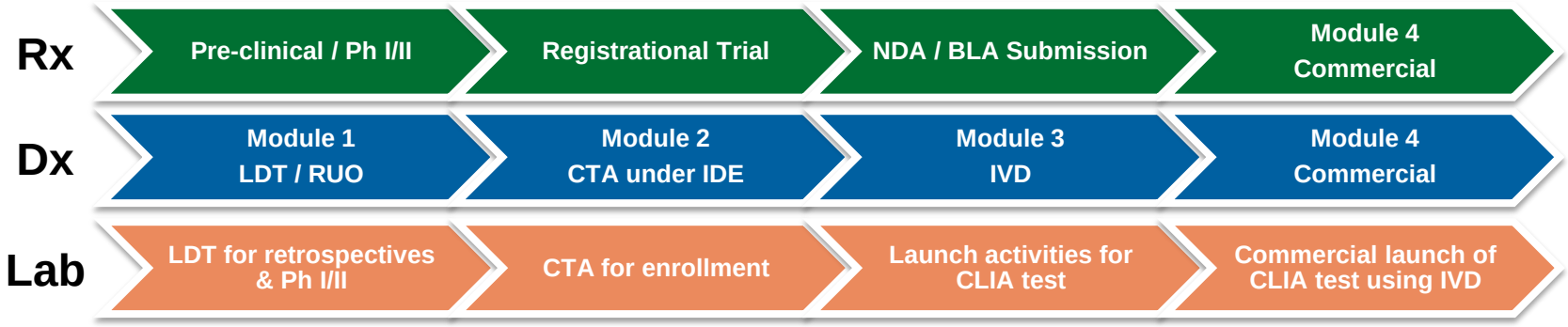
PrimeraDx

Modular CDx Program Structure

Features	• Assay design • Assay development • Under Design Control • Tissue-specific	• Final robustness testing • Transfer to manufacturing • cGMP production lots • IDE negotiation, approval • CE Mark	• Trial support to CLIA CROs • V&V studies • Concordance analyses • PMA preparation and submission • XUS registrations	• Pre-launch conversion from CROs to commercial lab • Facilitate lab partner reimbursement • Support post-approval surveillance trial
Deliverables	IVD-track assay for use in CLIA or R&D setting	IVD-track IUO for use in registrational trial	• PMA submission • Global registrations	Global distribution
Benefits	• Identical formulation • Design History File established • Risk of discordance very low • Remains flexible to iterations • Smooth tech transfer	• cGMP lots identical to IVD • Risk of discordance extremely low • Can be deployed at CRO labs in parallel to V&V studies • IDE in place for patient selection	• Eliminates risk of off-protocol use of IUO • Risk of discordance extremely low • Discordance tie-breaker not required • PMA submission ahead of NDA	• Use of CROs that also have large lab network commercial capabilities allows smooth conversion at launch • Reimbursement in major territories more streamlined

Broad benefits to pharma:
- Modules align with therapeutic asset clinical development, risks, commitments
- Transactions appropriate to near-term needs

Rx-Dx-Lab Solution to CDx Development & Commercialization

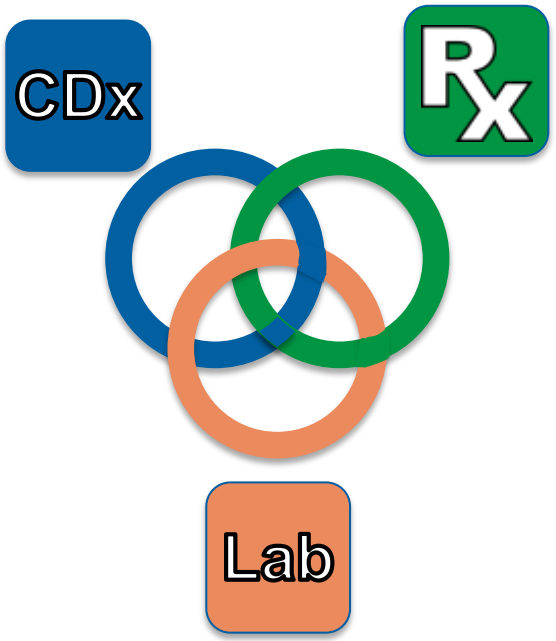


Features	• LDT / RUO on platform and on protocol for using in early work	• CTA under IDE at designated lab	• Lab prepares for IVD and drug launch during FDA review period	• Lab launches full commercial activities simultaneous with Rx/CDx
Benefits	• LDT / RUO approximates the proper test so low risk of discordance • Relationship between PDx and Lab independent of Pharma	• Conversion from LDT to CTA is seamless and low risk	• Lab has transparency with Rx/CDx timelines and commercial strategies • Allows reimbursement to be in place at CDx launch	• Launch of Rx/CDx has missing partner to seamlessly migrate from CTA to CLIA • Option to share commercial data and incorporate into strategy

Broad benefits to pharma clients:
- Reduces deal time and tech transfer risk to Lab
- Reduces platform adoption risk for CTA deployment
- Provides ready CDx access solution at commercial launch

PrimeraDx 3-Way Partnership Structure

- ✓ Aligned with Rx development
- ✓ Aligned with Rx budgetary constraints
- ✓ Aligned with Rx commercialization
- ✓ Addresses commercial path
- ✓ Mitigates Rx *AND* Dx risk



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The Multiplex PCR Company