One Size Does Not Fit All: Unique study management challenges for diagnostic companies

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For today's discussion

Diagnostic test development and regulatory pathways – a primer

How are diagnostic companies different?

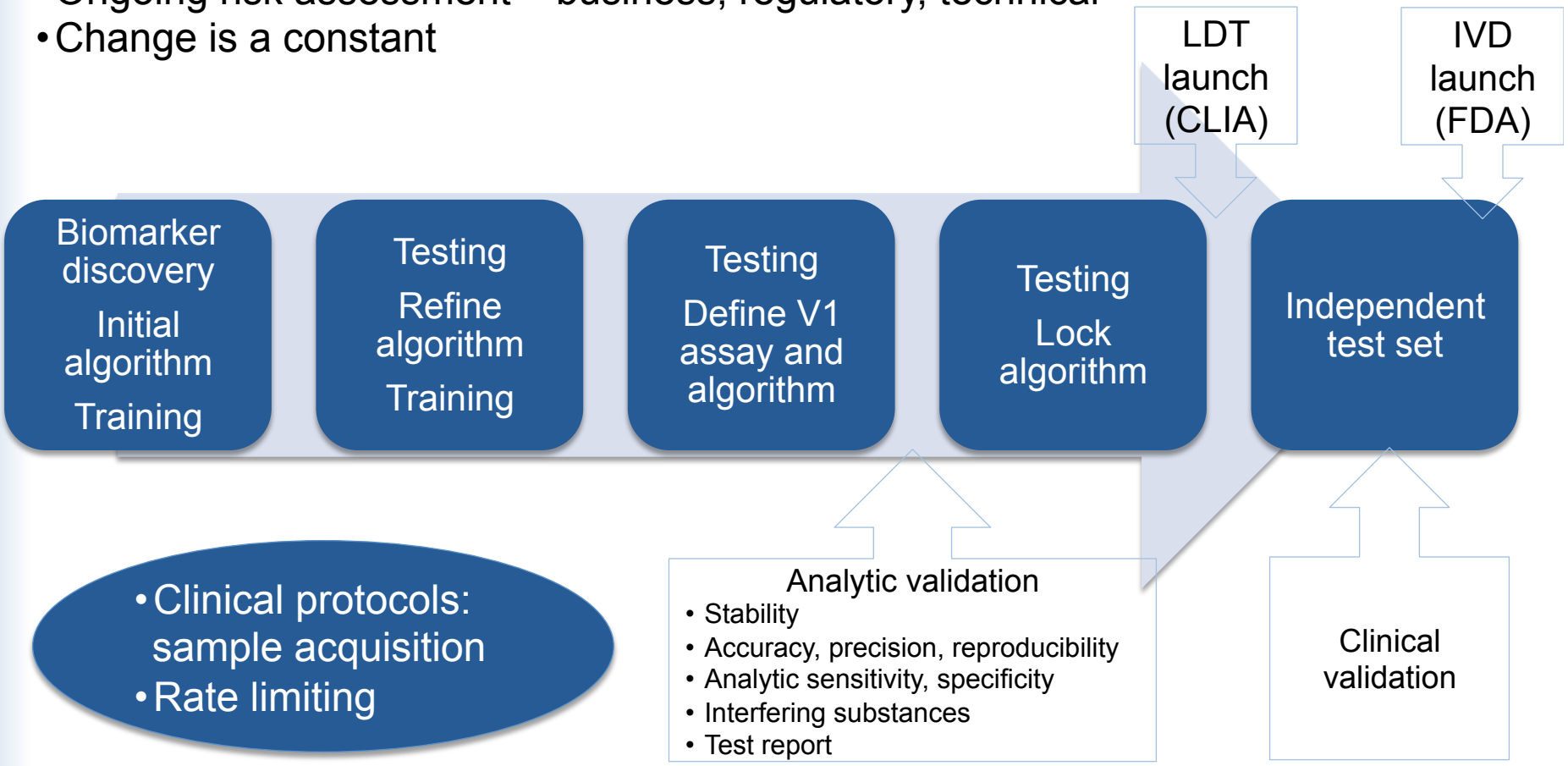
Diagnostic study design

What do diagnostic companies need from our CRO partners?

DIAGNOSTIC TEST DEVELOPMENT AND REGULATORY PATHWAYS

Diagnostic test development

- Continuous feedback loop due to ongoing training and testing results
- Assay and algorithm characteristics in flux until "locked"
- Ongoing risk assessment – business, regulatory, technical
- Change is a constant



LDT: Laboratory Developed Test; CLIA: Clinical Laboratory Improvement Act; CMS: IVD: In Vitro Diagnostic; FDA: Food and Drug Administration

Regulatory Pathways:
Laboratory Developed Test (LDT)
In Vitro Diagnostic (IVD)

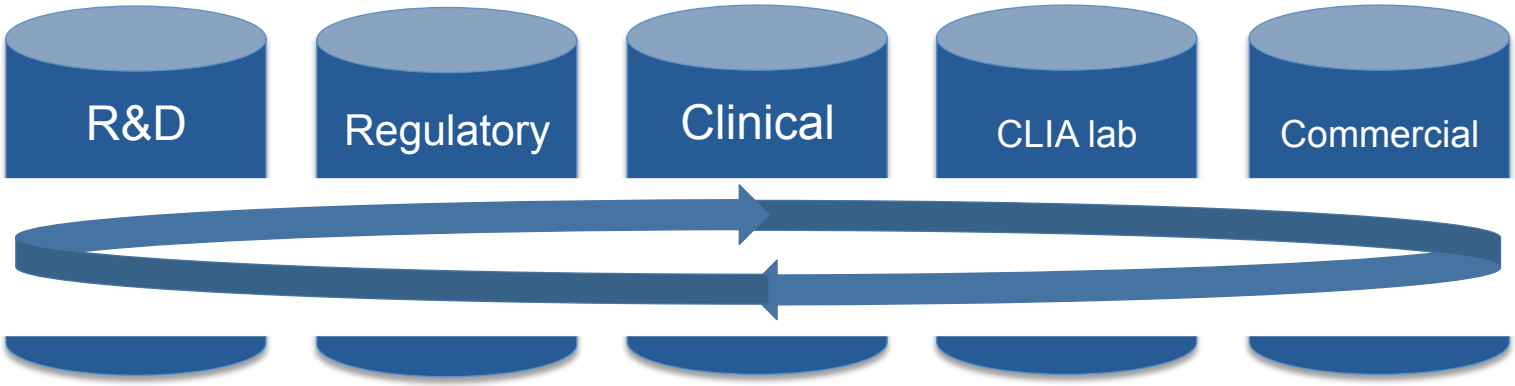
	LDT	IVD
Testing performed	Design, manufactured and used in single lab	Single lab Kit for sale to other labs Health care setting Point of care – home, clinic Companion diagnostic
Regulatory body	CLIA, via CMS FDA: enforcement authority	FDA (PMA or 510k)
Documentation	GCP if applicable GLP, GMP CLIA SOPs/quality system	QSR GCP if applicable GLP, GMP CLIA SOPs/quality system if applicable
Analytic validation	Required	Required
Clinical validation	Optional	Required

CLIA: Clinical Laboratory Improvement Act; CMS: Centers for Medicare & Medicaid Services; GCP: Good Clinical Practices; GLP: Good Laboratory Practices; GMP: Good Manufacturing Practices; PMA: Premarket Approval; QSR: Quality System Regulation

HOW ARE DIAGNOSTIC COMPANIES DIFFERENT?

Different company structure

Classic



Small diagnostics Company

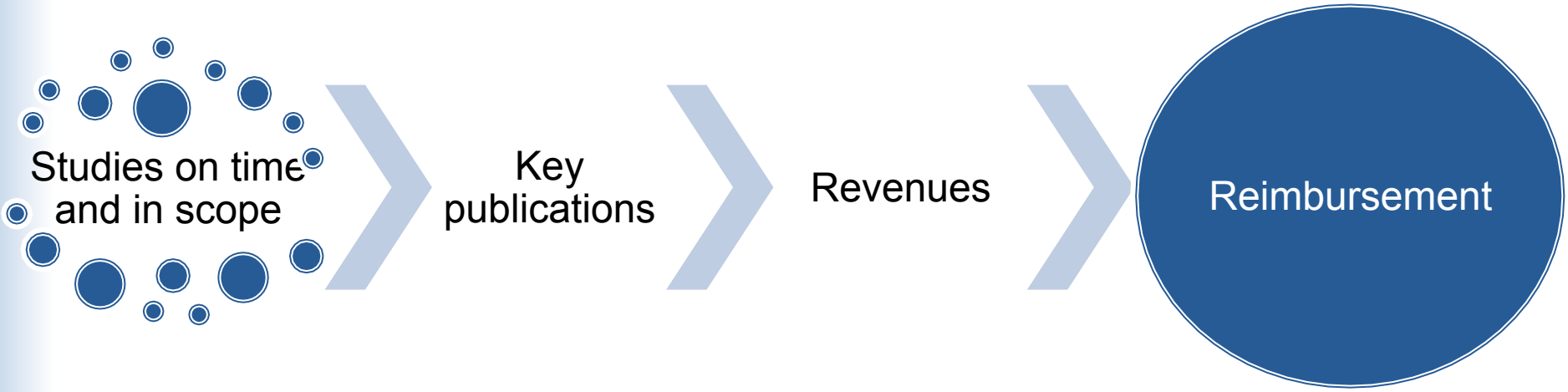
- Silos without walls
- Iterative learning
- Cross-functional communication

Different business drivers and operational realities

Rapid path to market	→	Speed Sample quality and quantity Own physician/KOL relationships
Low cost to market	→	Low budget Eliminate unnecessary processes
R&D drives product development	→	Clinical operations responsive to new information, changing requirements
May not be FDA-regulated	→	Flexible documentation and SOPs
Plan likely to change frequently	→	Flexible plan

Different study goals

Study goals = company goals



DIAGNOSTIC DEVELOPMENT STUDY DESIGN

The Three Priorities of Diagnostic Studies

1. The sample
2. The sample
3. The sample

Different studies at different phases of development

	Analytic Validation	Clinical Validation	Health Economics	Clinical Utility	Patient Outcomes
Shows product	Is robust and reproducible	Delivers a consistent, valid clinical result based on a Gold Standard	Has an effect on the overall payer market	Changes the real-world clinical setting Physician behavior	Changes the real-world clinical setting Patient outcomes
Achieves	CLIA launch	FDA submission OUS regulatory strategy	Payer dossier	Payer dossier	Payer dossier
Types of studies	• **Sample collection**	• **Sample collection**	• Economic and payer modeling	• Questionnaires • Retrospective chart reviews • Patient registries	• Patient registries • Randomized controlled trials
CRO opportunity	✓	✓	✓	✓	✓

Sample collection study design

Either single visit or longitudinal sample collection

Retrospective chart review for applicable clinical data

Target patient population

Defined gold standard

Sample collected and handled per protocol

Sample collection studies are not clinical trials

Changes during study are expected and acceptable

- Patient population
- Sample collection and handling

Can enrich for diseased population

Can use multiple cohorts, including retrospective, to complete test development

Site selection: balance high-volume with early engagement of KOLs and target customers

- Early-stage studies may lack sufficient scientific rigor for academic approval

Sample collection studies differ from pharma/device studies

No FDA Form 1572

No phase 1, 2, 3 testing

No patient intervention

No “First in Man”

No randomized control trial

No patient results or outcomes

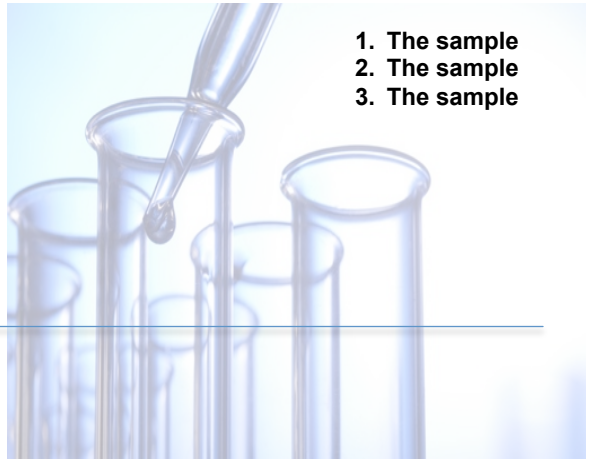
No requirement to post on clinicaltrials.gov

Minimally-invasive and non-invasive studies (venipuncture, urine/saliva) eligible for expedited IRB review

No AE/SAE reporting (with some exceptions)

Minimal monitoring

Target patient population



Represents commercial population

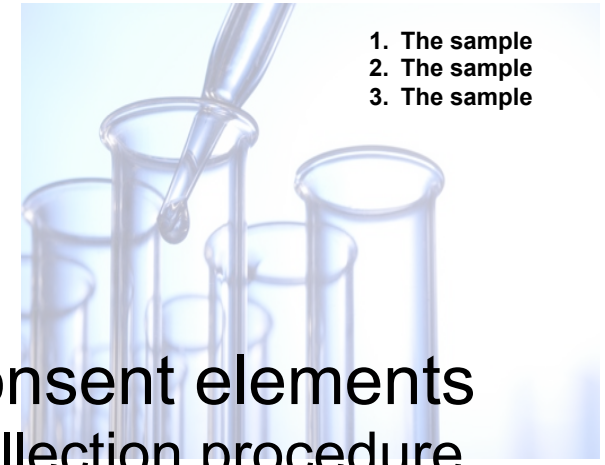
Includes diseased and not diseased

May enrich for diseased samples

Relevant clinical data is collected and verified

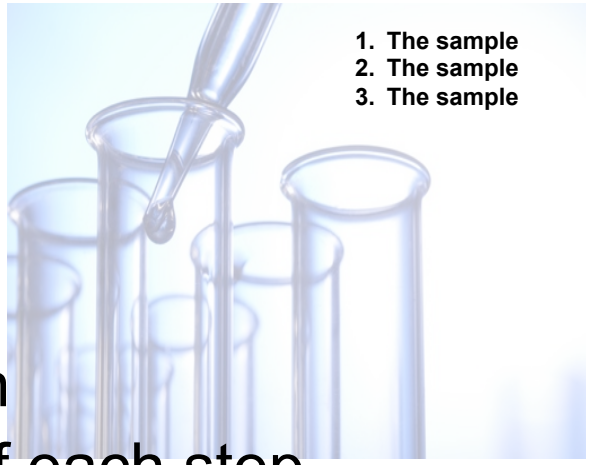
Gold standard is supported by literature, guidelines and community

Good Clinical Practices
Informed consent



- GCP
  - IRB oversight
  - Subject informed consent
  - Investigator qualifications
  - Site training includes sample management
  - Minimal monitoring
- Informed consent elements
  - Sample collection procedure
  - Volume/number of sample(s) collected
  - Duration of participation
    - Single or multiple visits
    - Time to obtain relevant clinical data
  - No patient results provided
  - Long-term sample storage for future research
  - Patient compensation
  - Optional posting on clinicaltrials.gov

Sample requirements



- Sample type
- Collection
  - Method
  - Timing
  - Tube/ampule
  - Media
- Processing
- Storage conditions
- Shipping materials
- Shipping methods
- Days/hours/minutes between steps

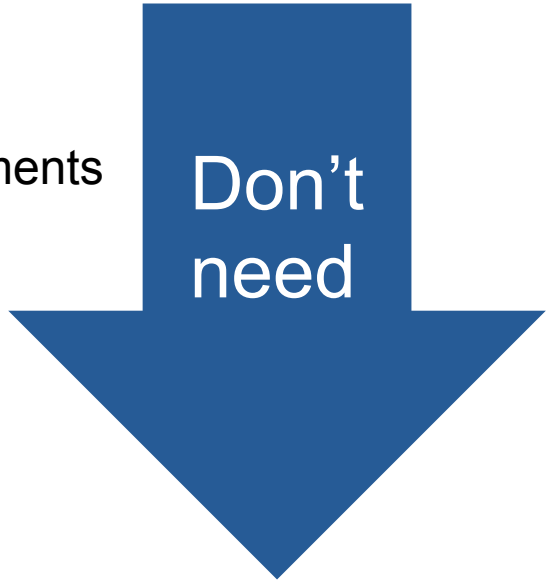
- Documentation
  - Date/time of each step
  - Collection method
  - Processing method
  - Volume or other metric
  - Refrigerator/freezer logs
  - Shipping records
  - Chain of custody

WHAT DO DIAGNOSTIC COMPANIES NEED?

Diagnostics companies

- High-volume sites
- Regulatory literacy
- Flexible operational plans
- Ownership of key relationships
- Core competency: biosample management
- Budget moderation
- Speed

- Complex processes
- Misaligned regulatory requirements
- Excess clinical data
- Extra oversight
- Expense



Diagnostics companies need