Billing and regulatory issues

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Medical Director, Center for Integrated Diagnostics
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Why care about billing and regulatory issues?

The final stages of *translational medicine* entail demonstration of clinical utility and achieving financial sustainability.

- Identify major challenges of integrating novel diagnostics into clinical practice
- Synthetize important elements of financial sustainability in diagnostic medicine

‘Failures’

Launching new tests ⇔ Time required to assess technology

Turn-around times + Clinical grade ⇔ High-complexity

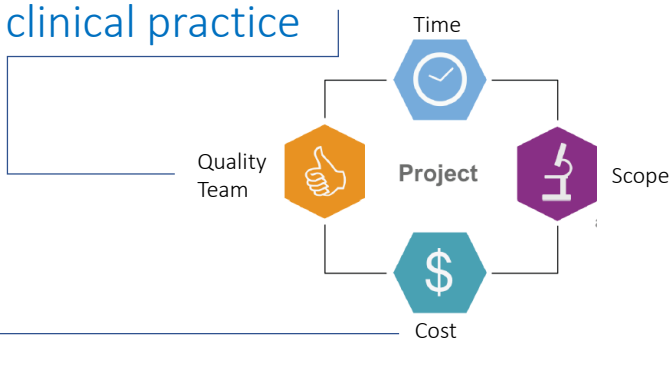
Novelty ⇔ Billing & Reimbursement

Internal vision ⇔ Stakeholder strategies

Data analytics ⇔ Resource requirements

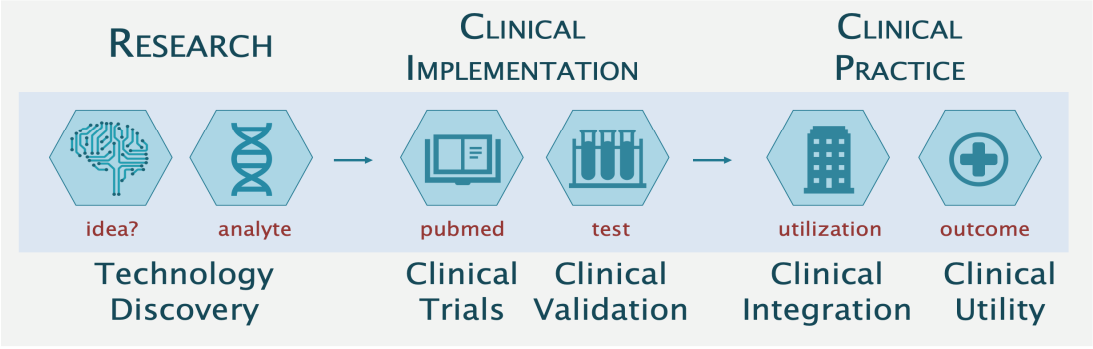
How to align these elements ?

Identify key challenges for integration of new diagnostic tools into routine clinical practice



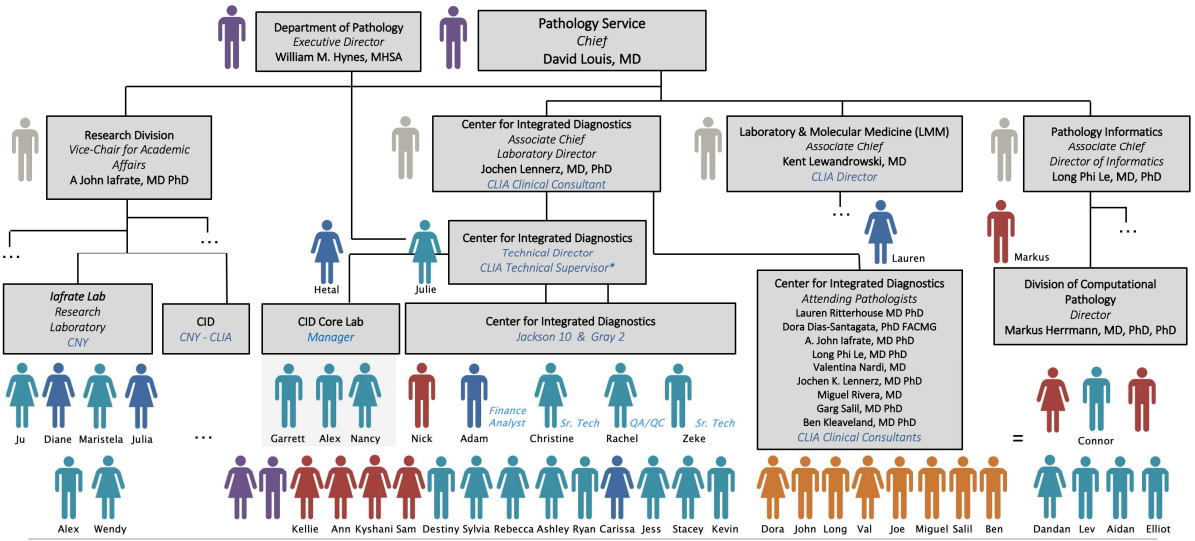
- How much? => Why? => strategy => alignment of initiative & funding source
- What ? => and in what order ? => what's first => operations
- Who => cross-functionality => interdisciplinary teams

Center for Integrated Diagnostics - Concept

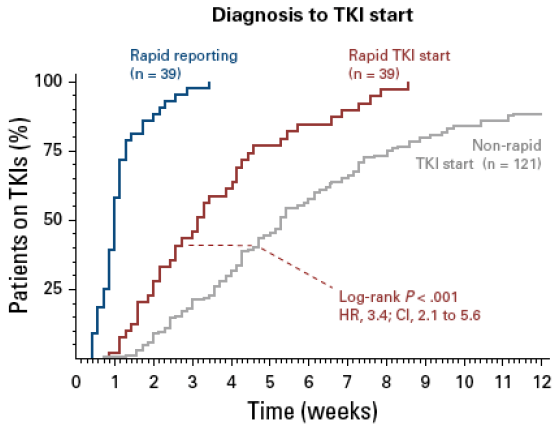


CENTER FOR INTEGRATED DIAGNOSTICS

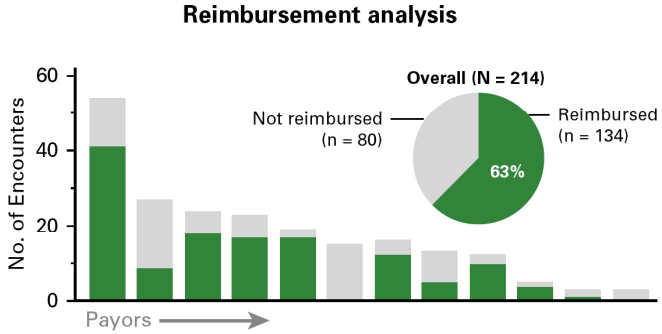
CID Organization



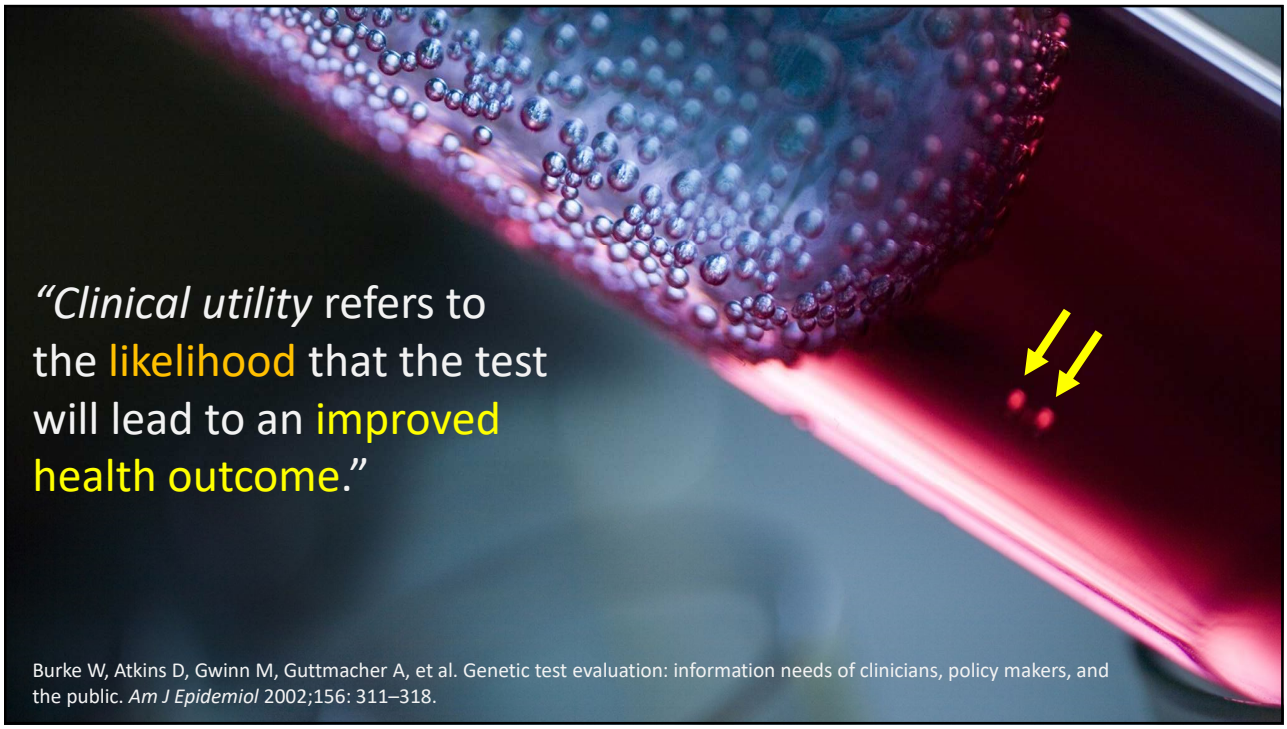
Rapid EGFR testing enables earlier initiation TKI therapy



Reimbursement analysis



Dagogo-Jack 2018 JCO PO



Plasma-based comprehensive somatic genomic profiling testing (CGP) using Guardant360® for patients with Stage IIIB/IV non-small cell lung cancer (NSCLC) is considered **MEDICALLY NECESSARY** when the following criteria have been met:

Diagnosis:

- When tissue-based CGP is infeasible (i.e., quantity not sufficient for tissue-based CGP or invasive biopsy is medically contraindicated), AND
- When prior results for ALL of the following tests are not available:
  - EGFR single nucleotide variants (SNVs) and insertions and deletions (indels)
  - ALK and ROS1 rearrangements
  - PDL1 expression.

Progression:

- Patients progressing on or after chemotherapy or immunotherapy who have never been tested for EGFR SNVs and indels, and ALK and ROS1 rearrangements, and for whom tissue-based CGP is infeasible (i.e., quantity not sufficient for tissue-based CGP), OR
- For patients progressing on EGFR tyrosine kinase inhibitors (TKIs).

If no genetic alteration is detected by Guardant360®, or if circulating tumor DNA (ctDNA) is insufficient/not detected, tissue-based genotyping should be considered.

www.bluecrossma.com/common/en_US/medical_policies/797Circulating_Tumor_DNA_For_Cancer.pdf

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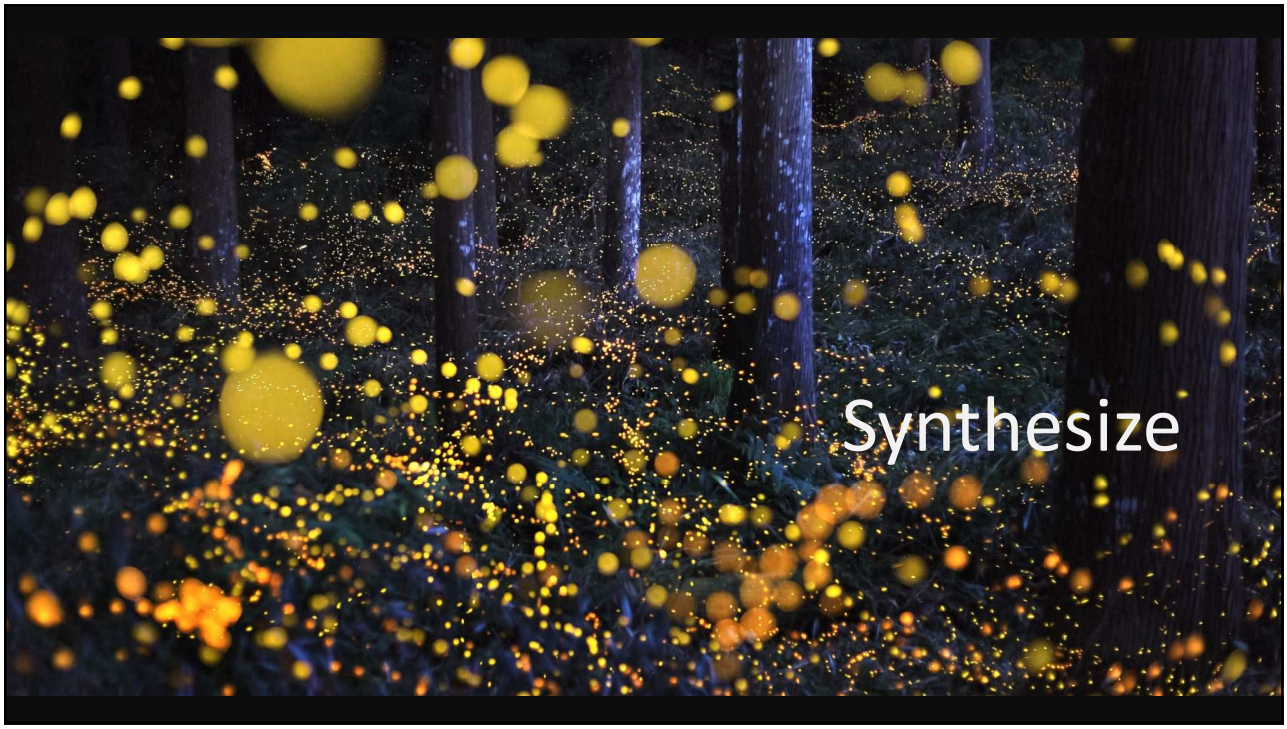
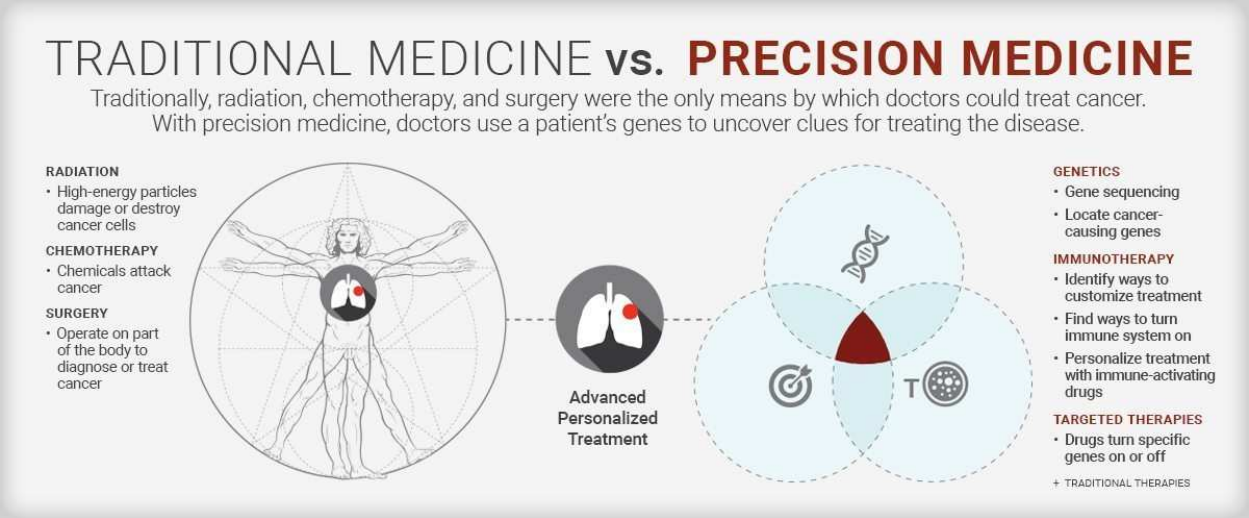




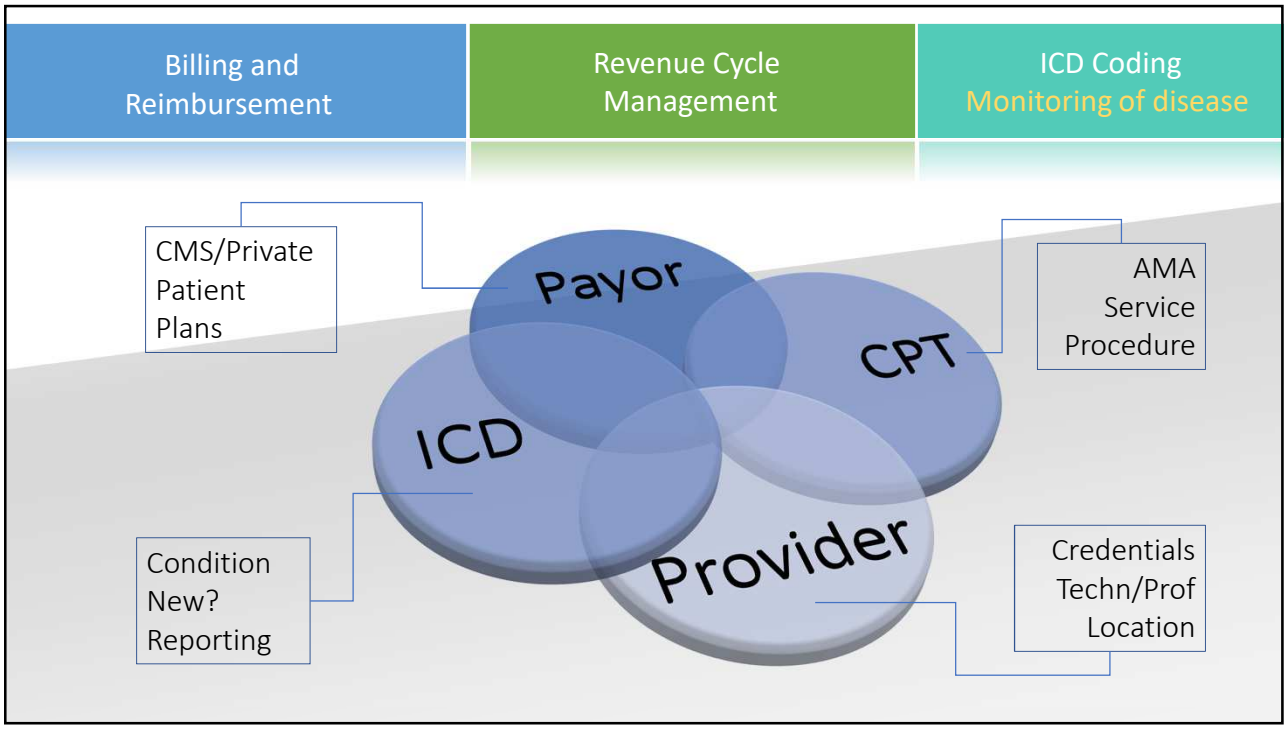
https://healthmatters.nyp.org/precision-medicine/

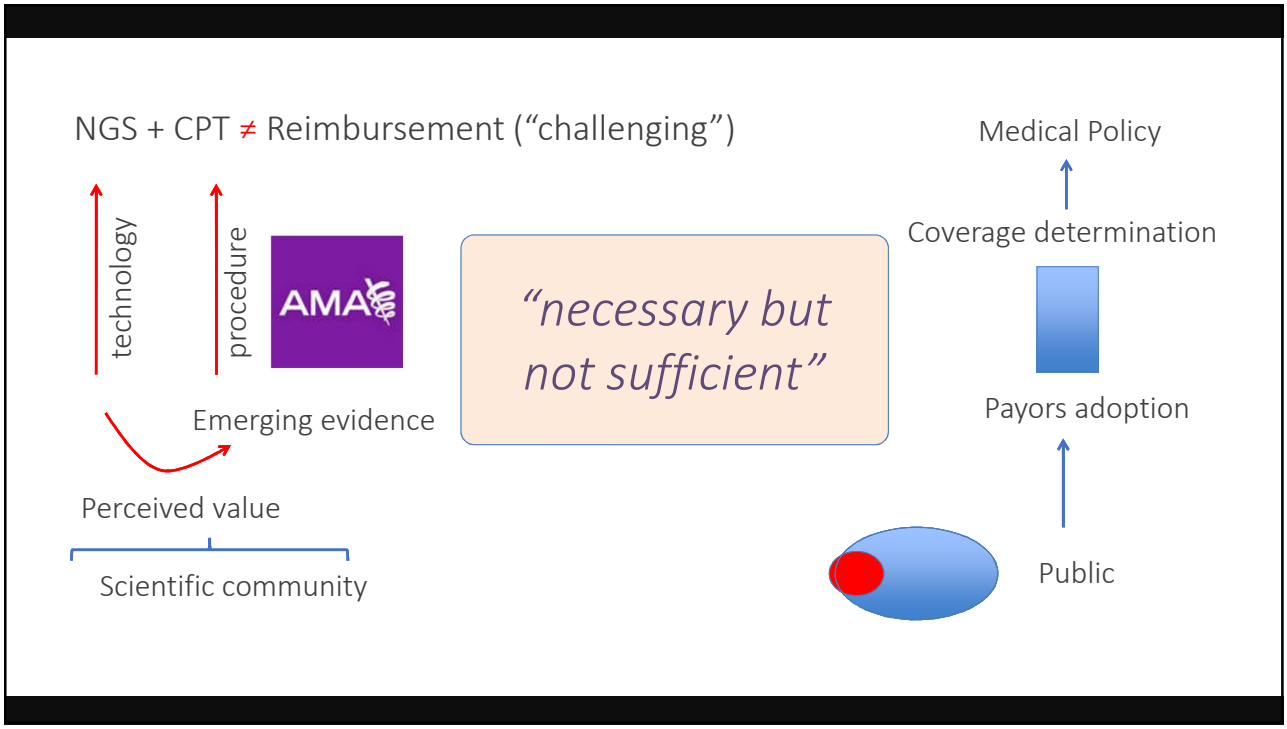
The AMA Has Established Several CPT Code Sets for Molecular Diagnostic Tests

Molecular Diagnostic CPT Codes

MoPath Codes

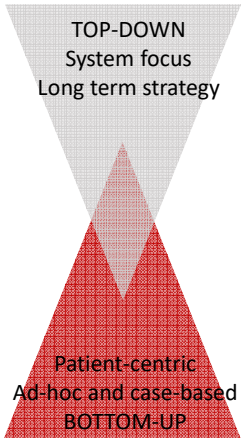
Tier 1 Codes	Tier 2 Codes	MAAA Codes	NGS Codes
Codes for commonly-performed gene-specific and genomics procedures, where a single test or procedure corresponds to a single CPT code	Codes for less-commonly performed single-gene tests, organized into nine ascending levels of technical resources and interpretative work performed by the clinician	Codes for Multianalyte Assays with Algorithmic Analyses (MAAAs), or assays that analyze multiple biomarkers with application of a proprietary algorithm to obtain a risk score	Codes for tests using next-generation sequencing (NGS) technologies, specified by methodology (e.g., whole genome vs. whole exome) and indication (scheduled for implementation in 2015)
81210 BRAF 81235 EGFR	81400 = L1 81401 … 81408 = L9		81445 = 5-50 solid 81450 = 5-50 heme 81455 = 51+


Billing and Reimbursement
Revenue Cycle Management
ICD Coding
Monitoring of disease
CMS/Private Patient Plans
Payor
CPT
ICD
Provider
AMA Service Procedure
Condition New? Reporting
Credentials Techn/Prof Location

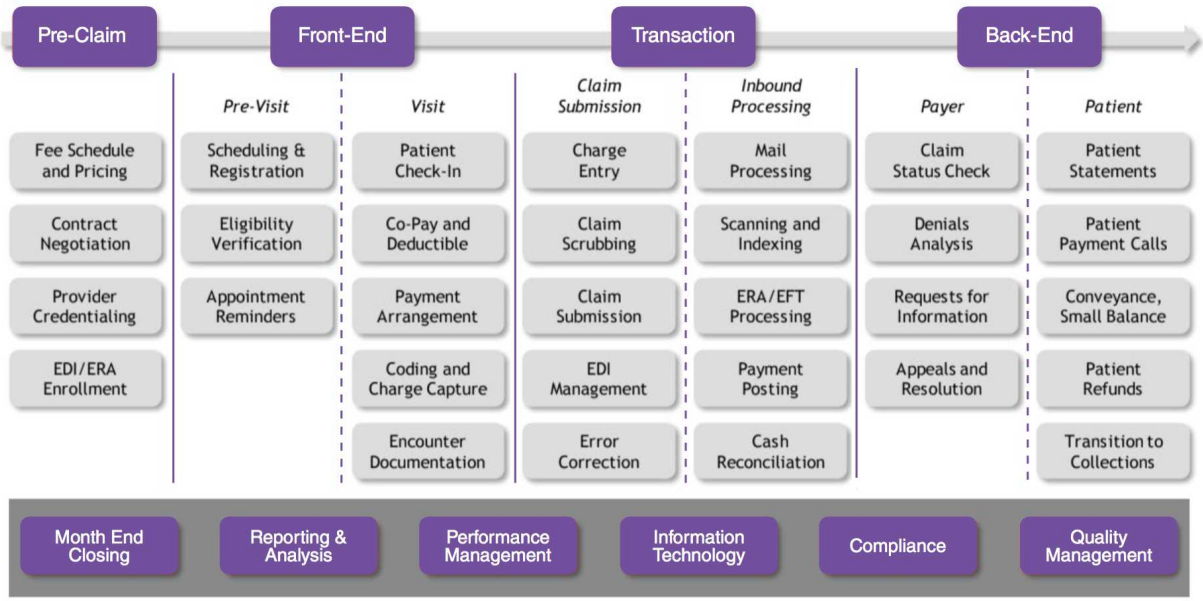

NGS + CPT ≠ Reimbursement ("challenging")
technology
procedure
AMA
Emerging evidence
Perceived value
Scientific community
"necessary but not sufficient"
Medical Policy
Coverage determination
Payors adoption
Public

Levels of Approaching Financial Sustainability

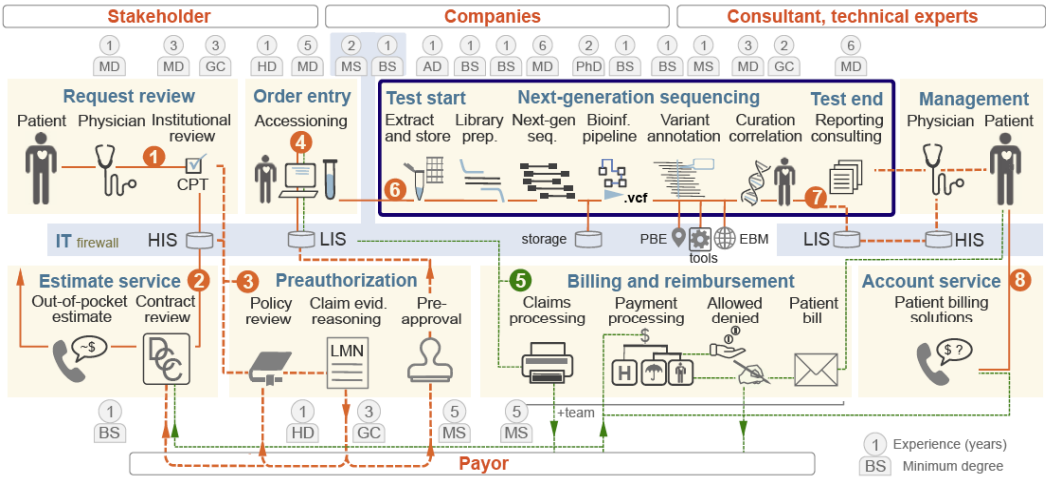
Global or International level
National or US-level
State level
Region
Local
System
Institutional
Departmental
Divisional
Patient Level
Procedure(s)
Test(s) ordering
Out of pocket estimate



- VALID
- FDA
- Insurance – coverage policies
- Strong clinical utility
- Robust coding strategy
- Prior authorization
- Appeals
- Cost estimation service



Synthetize the healthcare infrastructure for financially-sustainable genomics



Lennerz et al., 2016 JMD

Erdafitinib (BALVERSA®)

12.1 Mechanism of Action

Erdafitinib is a kinase inhibitor that binds to and inhibits enzymatic activity of FGFR1, FGFR2, FGFR3 and FGFR4 based on *in vitro* data. Erdafitinib also binds to RET, CSF1R, PDGFRA, PDGFRB, FLT4, KIT, and VEGFR2. Erdafitinib inhibited FGFR phosphorylation and signaling and decreased cell viability in cell lines expressing FGFR genetic alterations, including point mutations, amplifications, and fusions. Erdafitinib demonstrated antitumor activity in FGFR-expressing cell lines and xenograft models derived from tumor types, including bladder cancer.

- The efficacy population consists of a cohort of 87 patients who were enrolled in this study with disease that had progressed on or **after at least one prior chemotherapy** and that had at least 1 of the following genetic alterations:
- FGFR3 gene mutations (R248C, S249C, G370C, Y373C) or
- FGFR gene fusions (FGFR3-TACC3, FGFR3 BAIAP2L1, FGFR2-BICC1, FGFR2-CASP7)

All covered

FGFR3 mutations are covered by SNaPshot assay
R248C and S249C map to exon 7
G370C and Y373C map to exon 9
We cover the following exons (in parenthesis)
FGFR1 (4,7-8,13,15,17),
FGFR2 (7,9,12,14),
FGFR3 (7-9,14-16,18),

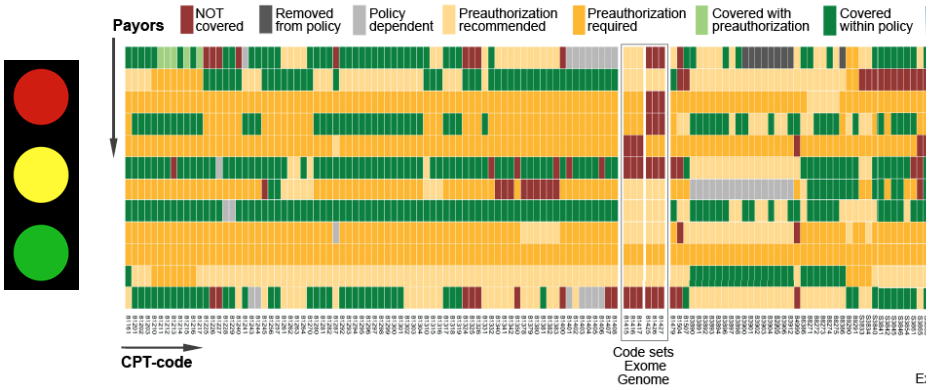
FGFR fusions are covered by solid fusion assay
We cover the following exons (in parenthesis)
FGFR1 (2, 8-10, 17)
FGFR2 (2, 8-10, 17)
FGFR3 (8-10, 17, intron 17)

Insurance coverage?

Table 1a. Conditions for which Solid Tumor NGS Panel Testing is MEDICALLY NECESSARY

Disease for Which Test is Covered	Additional Requirements
B-Cell NHL	Diagnostic, Prognostic, Monitoring
Bladder Urothelial Carcinoma	Stage IV or recurrent or unresectable
Breast	Stage IV or refractory or recurrent
Cholangiocarcinoma	Stage IV or recurrent or unresectable
Colorectal Cancer	Stage IV or recurrent or unresectable
Endometrial Carcinoma	Stage IV or recurrent or unresectable
GI Stromal Tumor	Any stage
Glioma	Diagnostic, Prognostic, Monitoring
Medulloblastoma	Diagnostic, Prognostic, Monitoring
Melanoma	Stage IIIB, IIIC, IV or recurrent or unresectable
Meningioma	Grade 2 to 4 (only recurrent or unresectable)
Neuroblastoma	Any stage
Non-Small Cell Lung Cancer	Stage IIIB, IV or recurrent
Ovarian	Relapsed or refractory advanced (stage II or higher), non-mucinous ovarian cancer being considered for PARP inhibitor therapy
Pancreatic Tumors	Diagnostic, Prognostic
Pediatric Tumors	Patient age under 21 years
Prostate	Metastatic castration-resistant
Rare Tumors	Less than 5,000/year in US; Metastatic or recurrent or unresectable
Stomach/Esophageal Cancer	Stage IV or recurrent or unresectable
T-Cell NHL	Diagnostic, Prognostic
Thyroid Cancer	Stage IV or recurrent or unresectable
Unknown Primary	May be used for Diagnosis or Therapeutic Decision Making

Payor Rules by CPT-codes of Selected Molecular-Genetic Tests

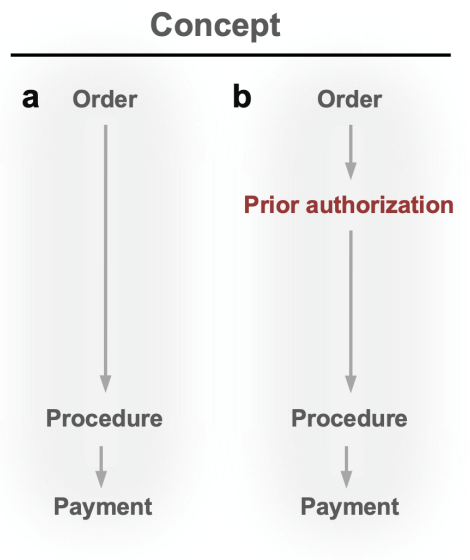


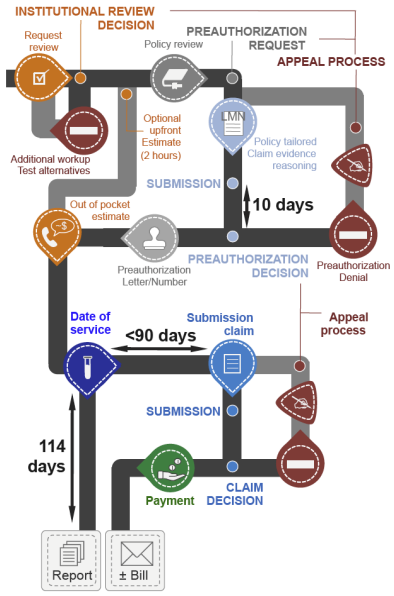
"Policy-tailored claim evidence reasoning"

Lennerz et al., J Mol Diagnostics, 2016

"Realization of Personalized Medicine requires Personalized Medical and Financial Clearance Processes"

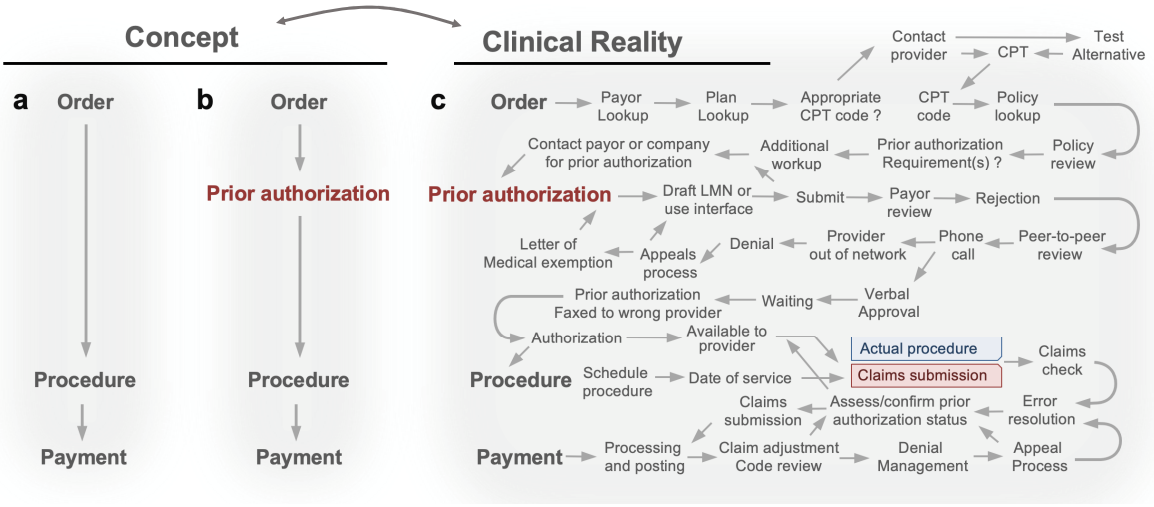
I will try to convince you of this statement





Center for Integrated Diagnostics, internal – Lennerz et al., unpublished

Lennerz et al., 2016 JMD



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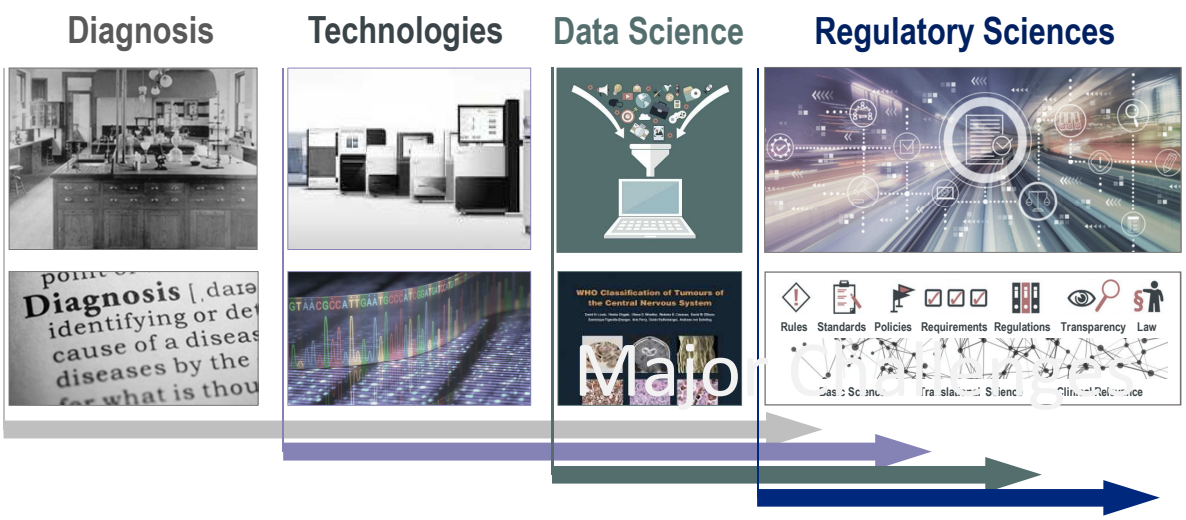
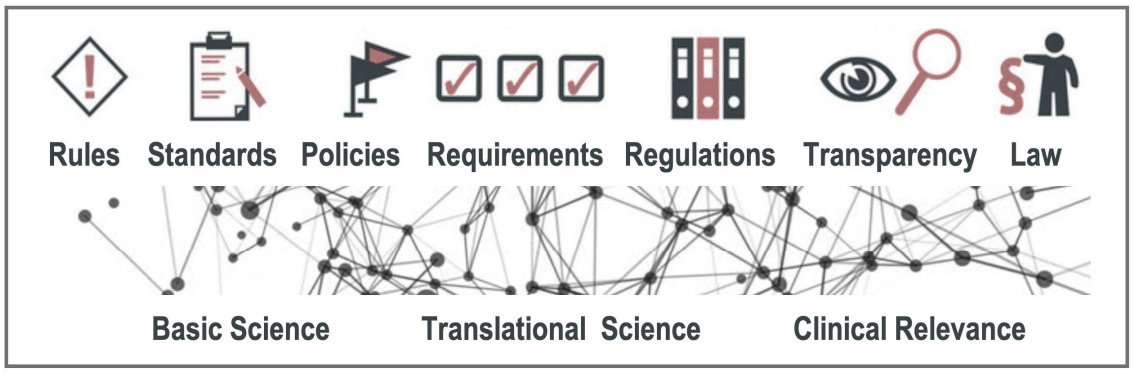
What's next in Diagnostic Pathology



What's next in Molecular Diagnostics: Regulatory Science



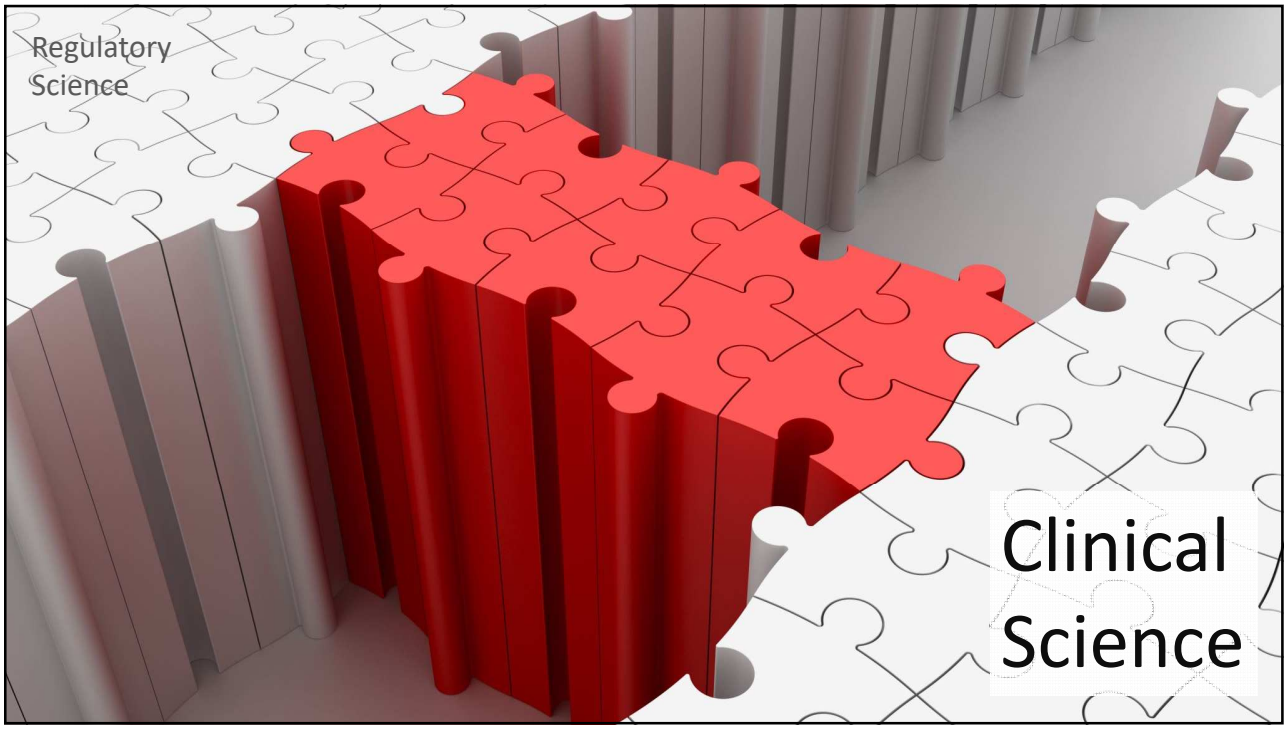
"Immediate" Result Release Rule

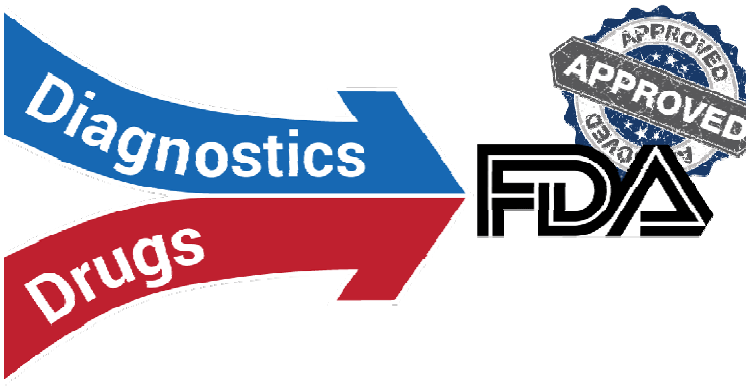
Missed, Misunderstood Test Results Harm Patients

The medical profession must end its refusal to allow direct reporting of significant test results to patients from pathologists and radiologists.

By **Vinita Parkash, MBBS, MPH**, Contributor Sept. 15, 2020, at 11:21 a.m.

Misdiagnosis due to miscommunication is not uncommon. As many as 62% of laboratory and 36% of imaging results are overlooked by care providers. (GETTY STOCK IMAGES)





Benefits of CDx

- A one-stop shop where everything gets done together. The drug and device may be developed in collaboration removing problems with sample availability and/or the need for additional device trials.
- A reduced time to market for the drug by coordinating better communication between divisions of the FDA, providing clarity on optimal use of drug, and ensuring drug approval is not delayed by the lack of a companion diagnostic.
- Providing clarity on optimal use of a drug as well as the potential for differentiation in an increasingly crowded market.

Proposed legislation to revise LDT landscape via "Technology certification" =the VALID Act

LDT => perceived concerns about "validity" and reproducibility of results

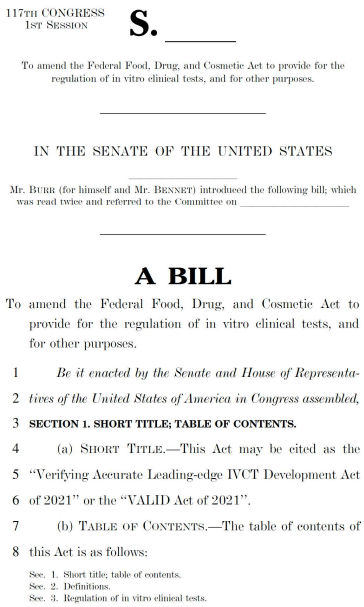
Representatives Larry Bucshon (R-IN) and Diana DeGette (D-CO), members of the House Energy & Commerce Committee, have been working to advance a draft of the so-called **Diagnostic Accuracy and Innovation Act (DAIA)** that they penned with extensive input from lab and diagnostic industry players.

Senate Committee on Health, Education, Labor, and Pensions, Michael Bennet (D-CO) and Orrin Hatch (R-UT), have incorporated the agency's ideas into a discussion draft of a bill, called the **Verifying Accurate, Leading-edge IVCT Development (VALID) Act**

The FDA has historically exercised enforcement discretion over LDTs, leaving the Centers for Medicare & Medicaid Services to oversee them under the Clinical Laboratory Improvement Amendments. But, in recent years the FDA has wanted to end its enforcement discretion, which the lab industry and pathologists have fought against, challenging the agency's authority to regulate lab processes and maintaining that such a move would hinder innovation and harm patients.

The centerpiece of FDA's regulatory reform proposal is precertification, which has intrigued lab industry players as well. In its technical assistance to DAIA, the agency described precertification as a process through which diagnostic developers could garner premarket approval or clearance for one test representative of a group of tests using the same technology and have other elements in common. Approval of that representative test would precertify other tests in the group and allow the lab to launch them without premarket review.

Concern: Places LDTs into the existing device framework



117TH CONGRESS
1ST SESSION

S. _____

To amend the Federal Food, Drug, and Cosmetic Act to provide for the regulation of in vitro clinical tests, and for other purposes.

IN THE SENATE OF THE UNITED STATES

Mr. BURR (for himself and Mr. BENNET) introduced the following bill; which was read twice and referred to the Committee on _____

A BILL

To amend the Federal Food, Drug, and Cosmetic Act to provide for the regulation of in vitro clinical tests, and for other purposes.

Be it enacted by the Senate and House of Representatives of the United States of America in Congress assembled,

SECTION 1. SHORT TITLE; TABLE OF CONTENTS.

(a) SHORT TITLE.—This Act may be cited as the "Verifying Accurate Leading-edge IVCT Development Act of 2021" or the "VALID Act of 2021".

(b) TABLE OF CONTENTS.—The table of contents of this Act is as follows:

Sec. 1. Short title; table of contents.
Sec. 2. Definitions.
Sec. 3. Regulation of in vitro clinical tests.

Why Regulatory Sciences?

- New high-complexity tests (e.g. NGS + machine learning) are entering the market
- ML/AI tools have the potential to unlock the potential of computational pathology; ?how are we assessing benefits and risks to patients in clinical practice?
- **How will the FDA receive (scientific) input for reasonable guidance?**
- There is a (missed) opportunity to provide scientific input into regulatory science.

Collaborative Communities with CDRH Participation

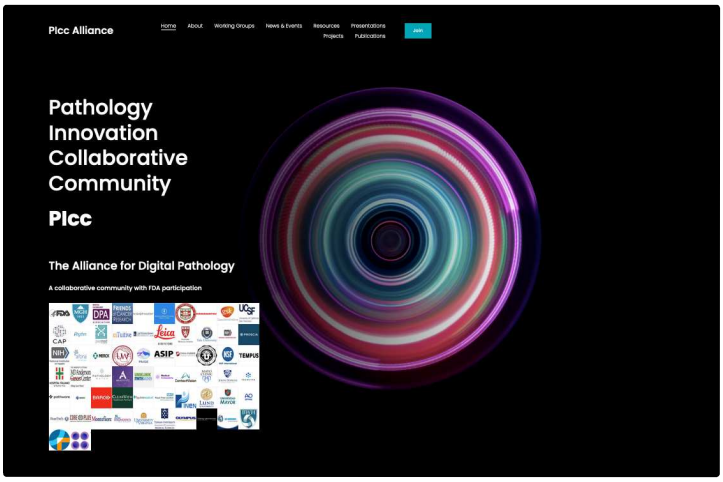
The FDA currently participates as a member of these collaborative communities, which have been established and are managed and controlled by external stakeholders.

- Collaborative Community on Ophthalmic Imaging
- National Evaluation System for health Technology Coordinating Center (NESTcc) Collaborative Community
- Standardizing Laboratory Practices in Pharmacogenomics Initiative (STRIPE) Collaborative Community
- International Liquid Biopsy Standardization Alliance (ILSA)
- Xavier Artificial Intelligence (AI) World Consortium
- Case for Quality Collaborative Community
- Heart Valve Collaboratory (HVC)
- Wound Care Collaborative Community
- Pathology Innovation Collaborative Community (PICC)
- RESCUE (REducing SuiCide Rates Amongst IndividUals with DiabEtes) Collaborative Community)
- MedTech Color Collaborative Community
- Digital Health Measurement Collaborative Community (DATAcc)

www.pathologyinnovationcc.org

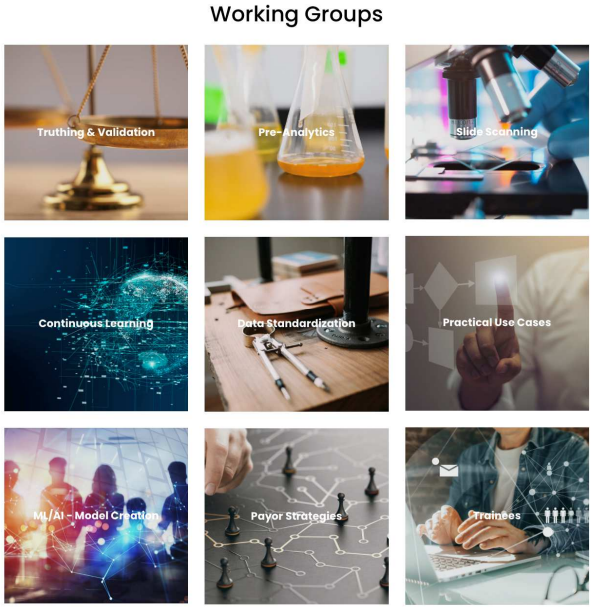
Objectives:

- Tackle large-scale projects in pre-competitive space
- Develop evaluation tools, methods, and standards
- Clarify and improve regulatory pathways



How we operate

- PICC is providing the infrastructure and platform for individual projects
- Currently >20 projects
- Aggregation into 9 workgroups (when applicable)

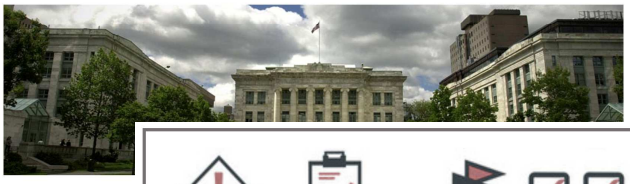


Molecular Diagnostics:
Current Roles in Cancer Diagnosis and Patient Management

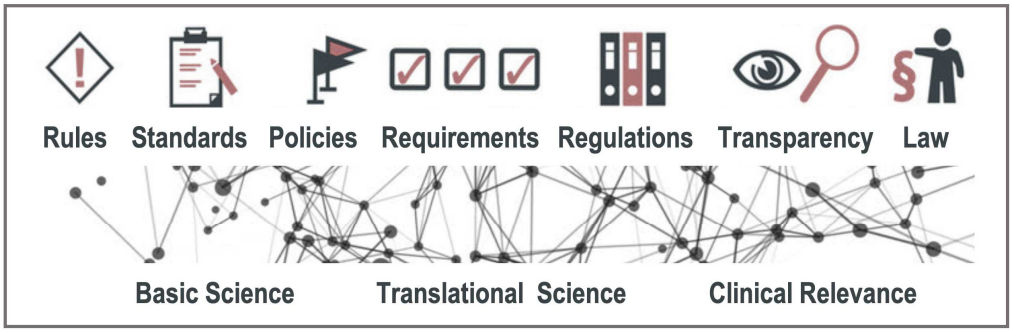
HARVARD MEDICAL SCHOOL

Live Stream

Monday, September 13, 2021 - Friday, September 17, 2021



Navigate regulatory waters



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Thank you
What's next?
CENTER FOR INTEGRATED DIAGNOSTICS
Interested?
Jlennerz@partners.org