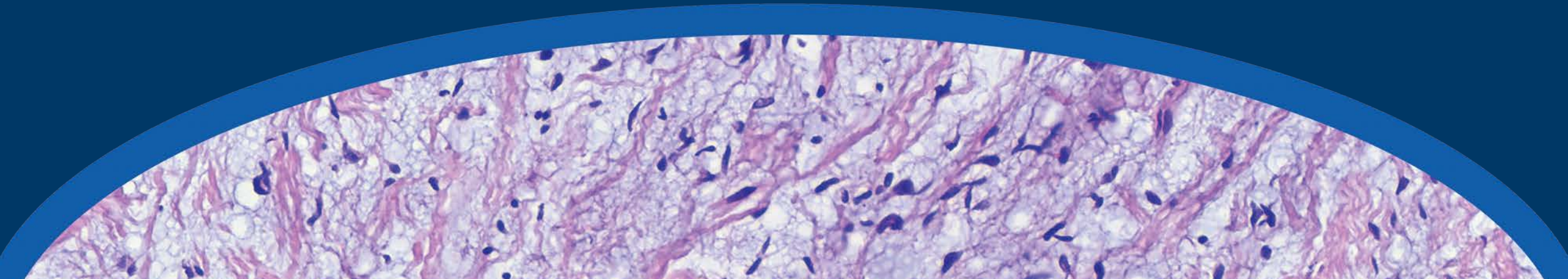
MDIC
MEDICAL DEVICE INNOVATION CONSORTIUM

Pathology Innovation Collaborative Community (PIcc)
Annual Meeting 2023

Unlocking the Potential of Digital Pathology and AI through Regulatory Science

Le Méridien Arlington

Day 1: June 27, 2023



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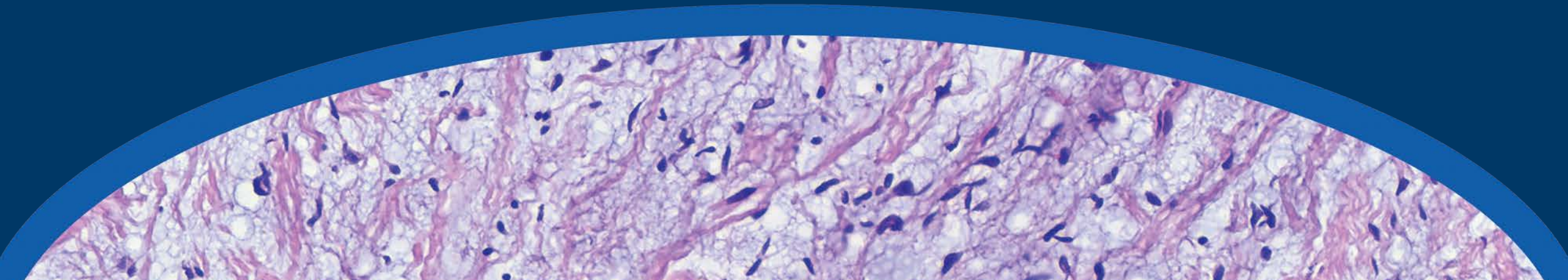
Annual Meeting 2023

Spread the message!

LinkedIn: @mdic

#PIcc #Cancer #Oncology #MedTech
#Innovation #patientsafety #regulation#FDA #biomarker
#oncology #digitalpathology #AI #CLIA #quality #technology



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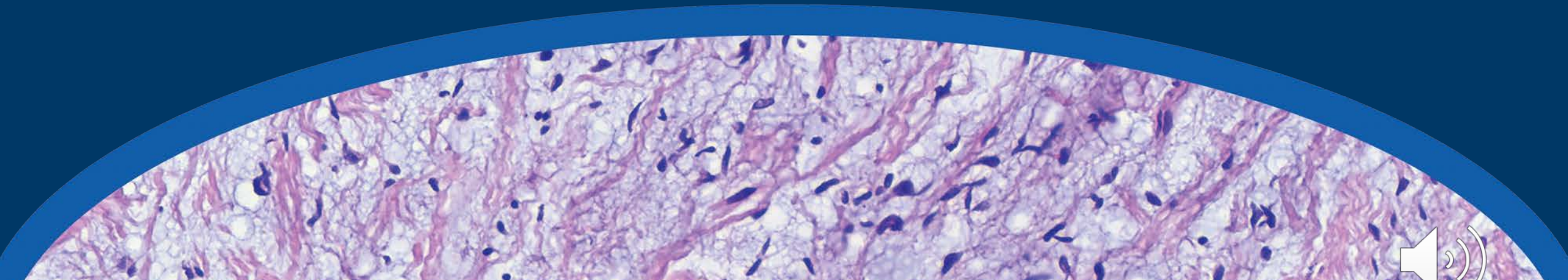
Welcome Remarks & Overview of MDIC

Andy Fish

President & CEO, MDIC



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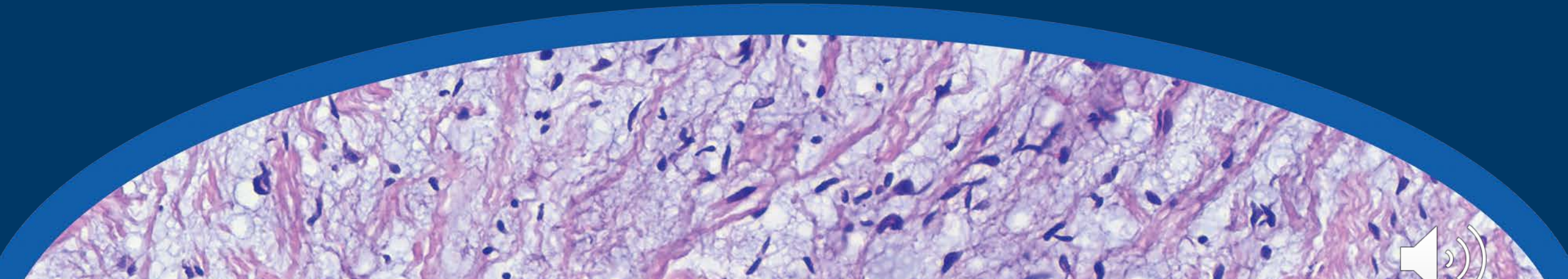
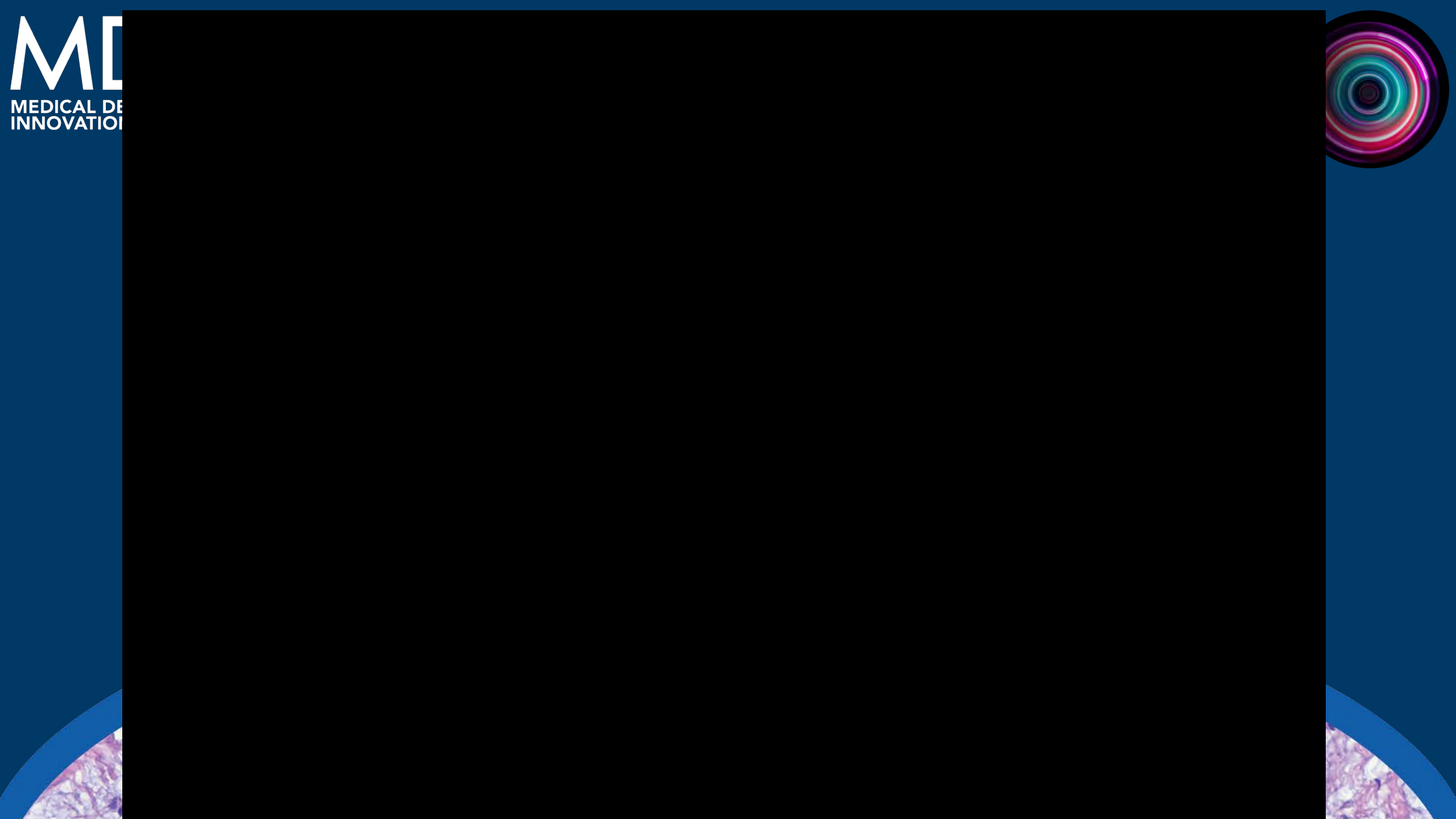
Welcome Remarks & Overview of PIcc

Jochen K. Lennerz, M.D., Ph.D.
Medical Director, Center for Integrated Diagnostics, MGH
&
Associate Professor, Harvard Medical School





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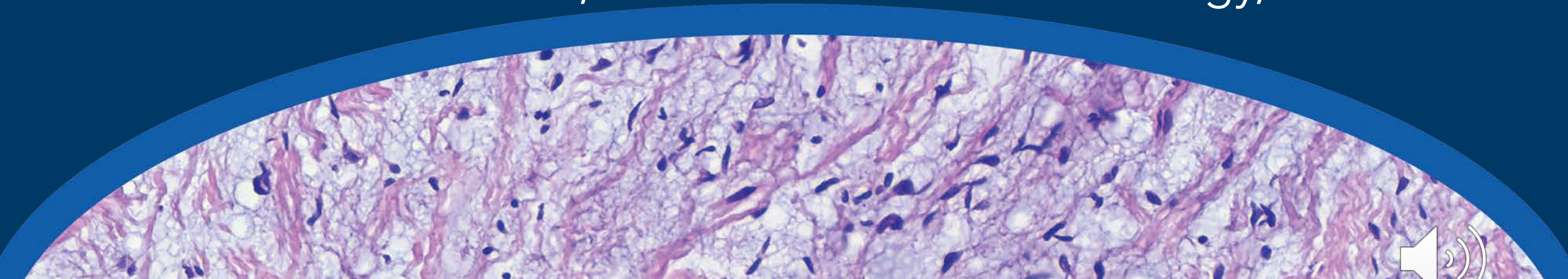
Session 1: Updates from Organizations and Initiatives related to DP/AI

Moderated by:

Joseph R Sapiente

Vice President, Clinical Science & Technology, MDIC



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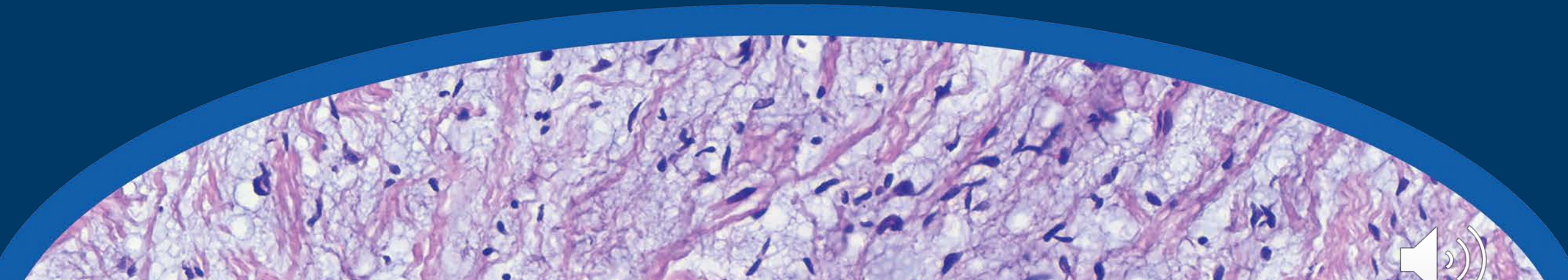

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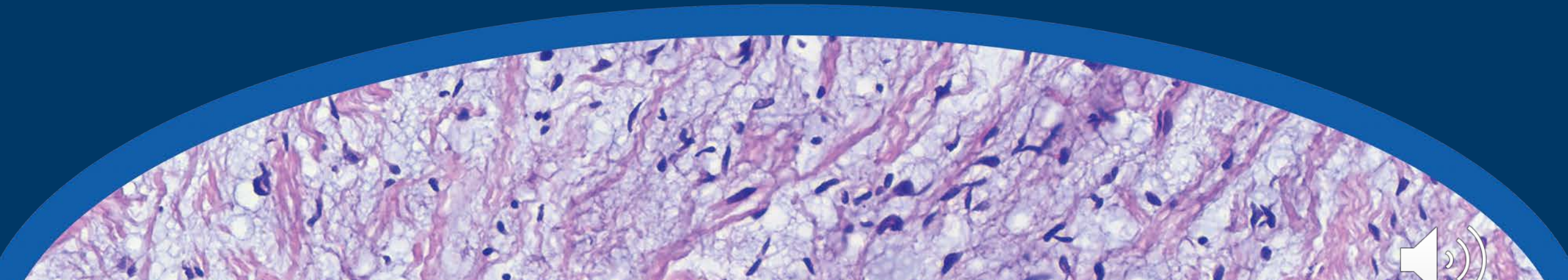
College of American Pathology (CAP): Pathology Innovation and Data Science

M. E. de Baca (Doc), MD
Sysmex VP for Medical Affairs &
CAP Board of Governors



COLLEGE of AMERICAN PATHOLOGISTS

CAP Update:

SHIELD
&
Council on Informatics and Pathology Innovation

M. E. de Baca, MD

June 27 2023

SHIELD

FDA SHIELD OBJECTIVES

The Food and Drug Administration (FDA) **Systemic Harmonization and Interoperability Enhancement for Laboratory Data (SHIELD)** is a public-private partnership that was assembled with a singular focus on improving the interoperability and utility of in-vitro diagnostic (IVD) test data.SHIELD provides the authoritative source of coding for COVID-19 testing and a wide variety of other assays.

** In vitro diagnostics are tests done on samples such as blood or tissue that have been taken from the human body. In vitro diagnostics can detect diseases or other conditions and can be used to monitor a person's overall health to help cure, treat, or prevent diseases.*

SHIELD

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FDA U.S. FOOD & DRUG ADMINISTRATION

Office of In Vitro Diagnostics and Radiological Health

SHIELD

SHIELD: laboratory data interoperability ***Describes the same test the same way, every time***

Benefits of FDA SHIELD

- **Eases burden** for stakeholder groups through unified approach
- **Advances standards based information exchange** across labs and healthcare institutions
- **Lays foundation for improved semantic interoperability**
  - Implementing infrastructure that harmonizes how lab data standards are applied practically to IVD testing

Issue

IVD/LAW

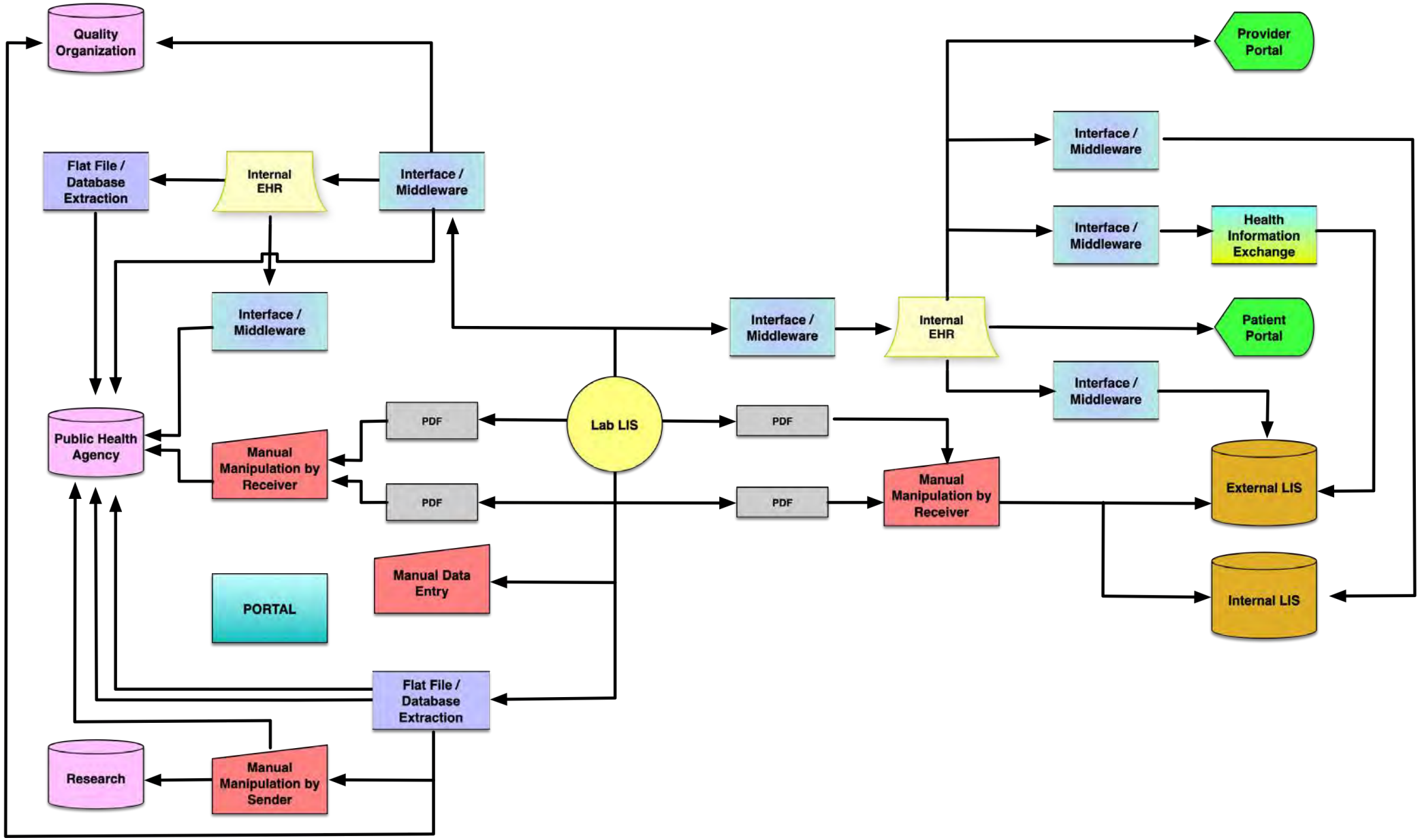
Approach

Impact

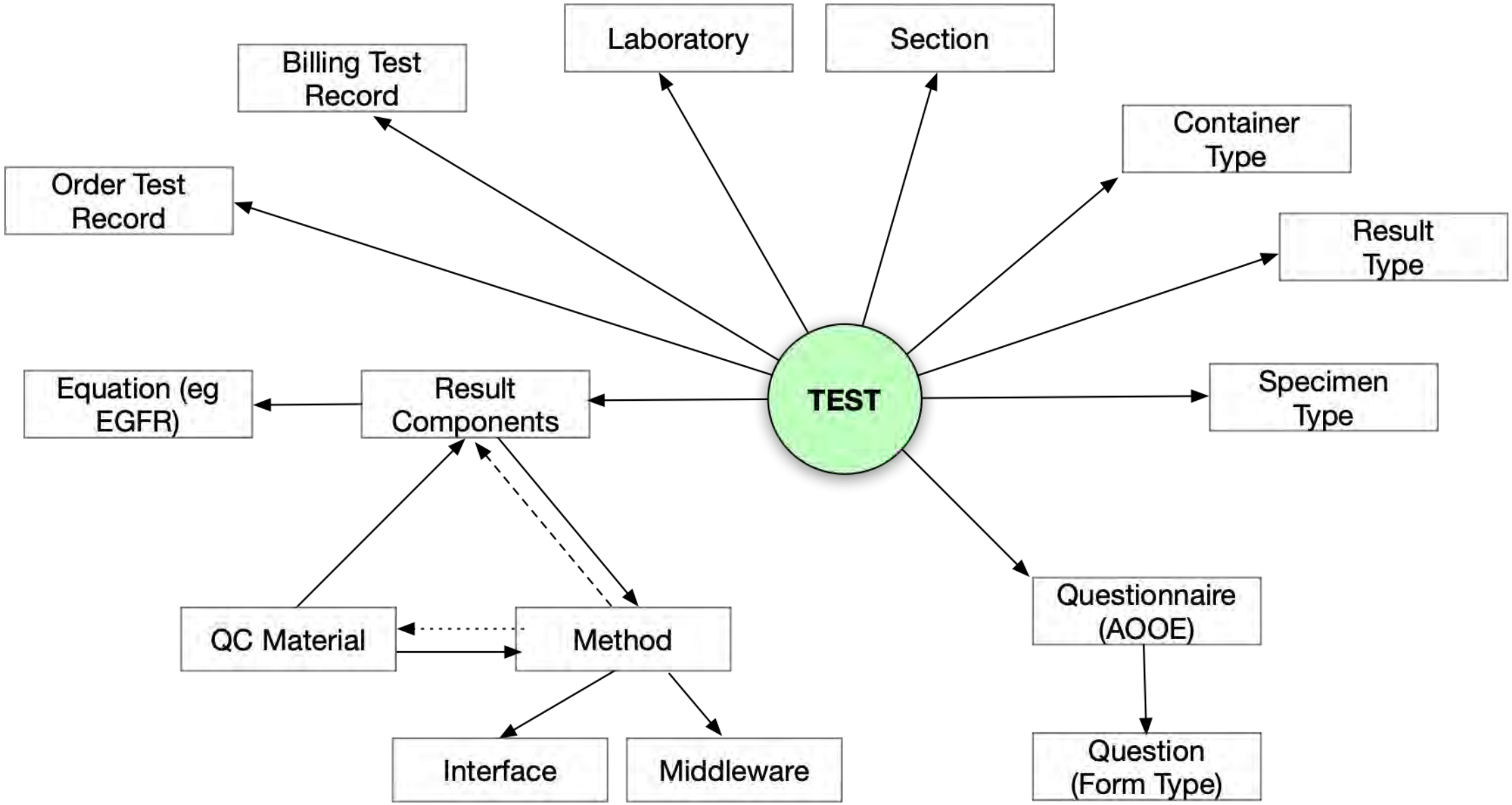
CAP:

We proposed the strategic design of a quality assurance program and supporting infrastructure to support in vitro diagnostic (IVD) test result data quality.

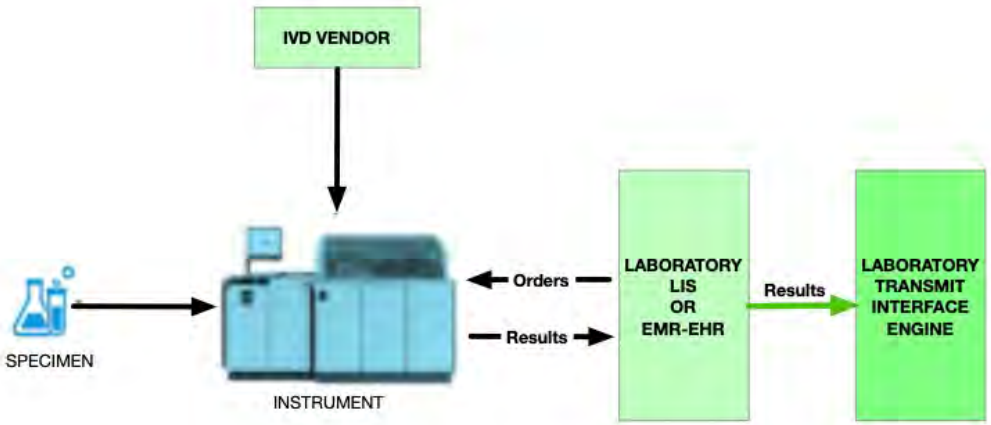
Current State of Laboratory Data



Current State of Laboratory Data



FUTURE STATE: DATA FLOW INFRASTRUCTURE



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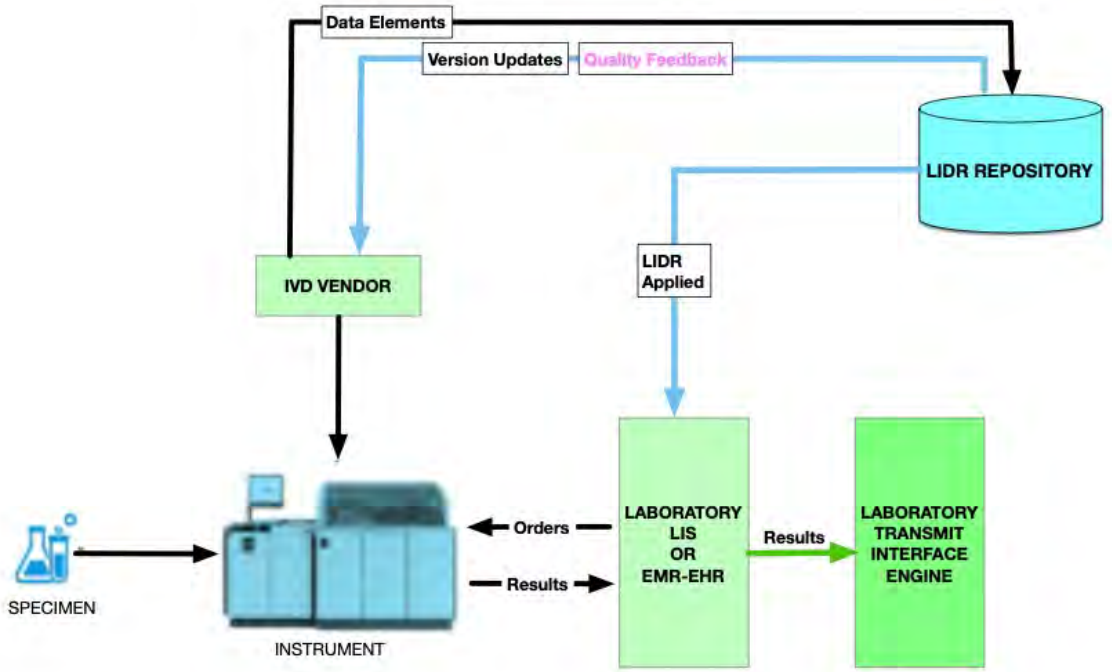

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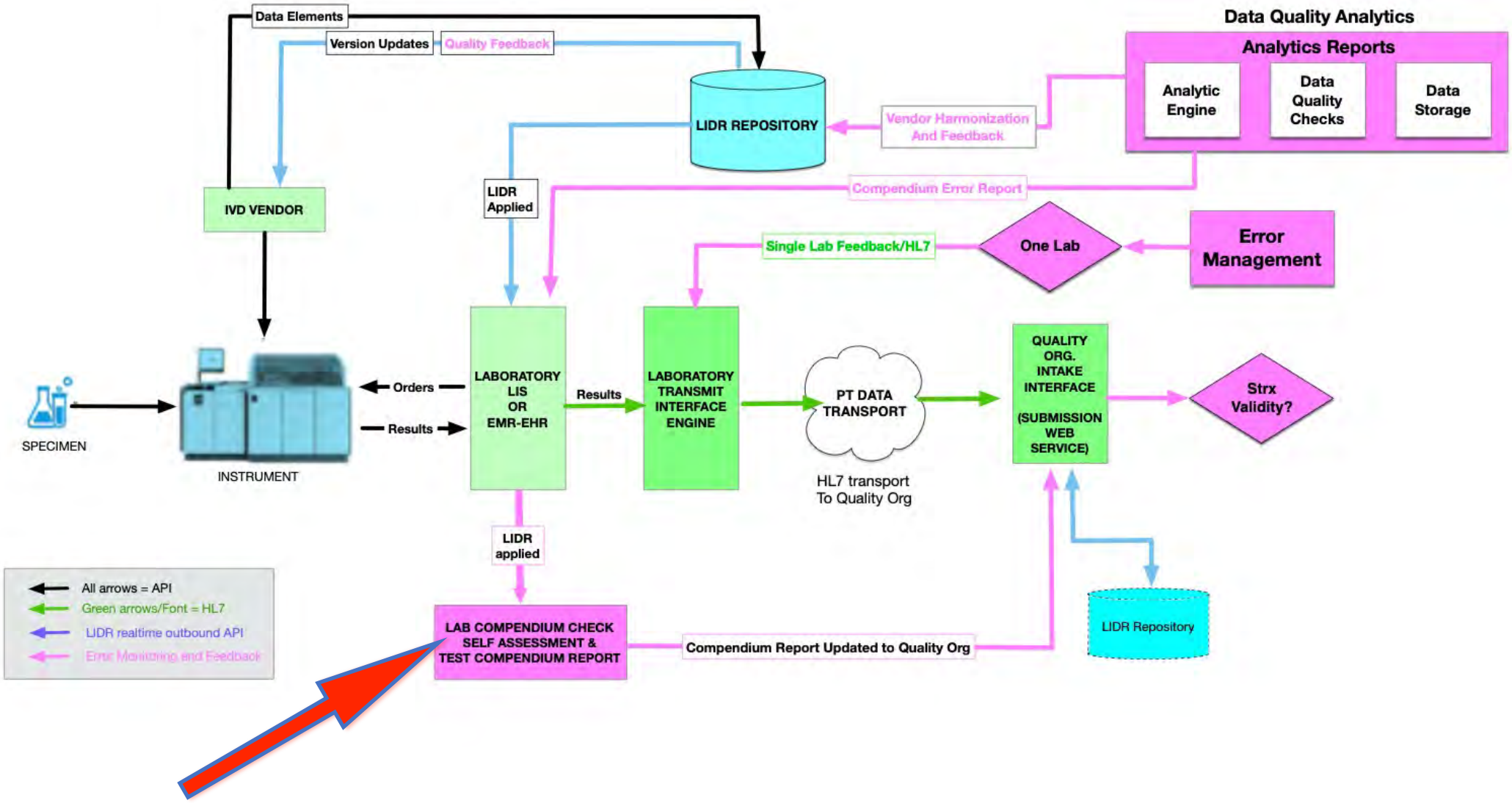
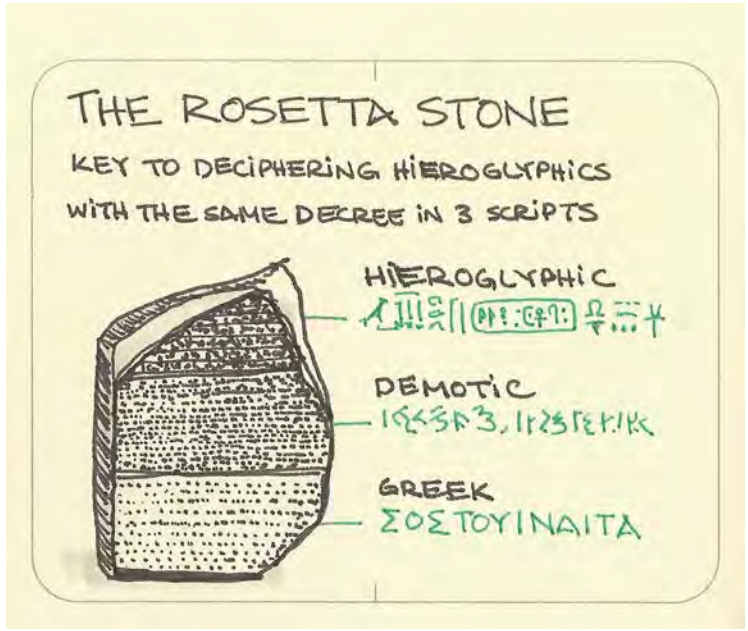
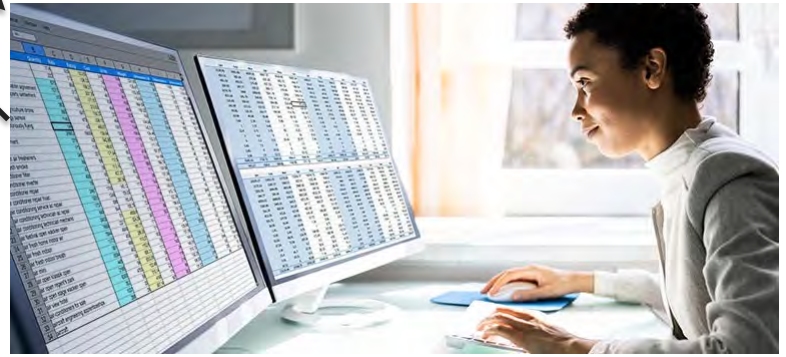


Self Assessment Toolkit



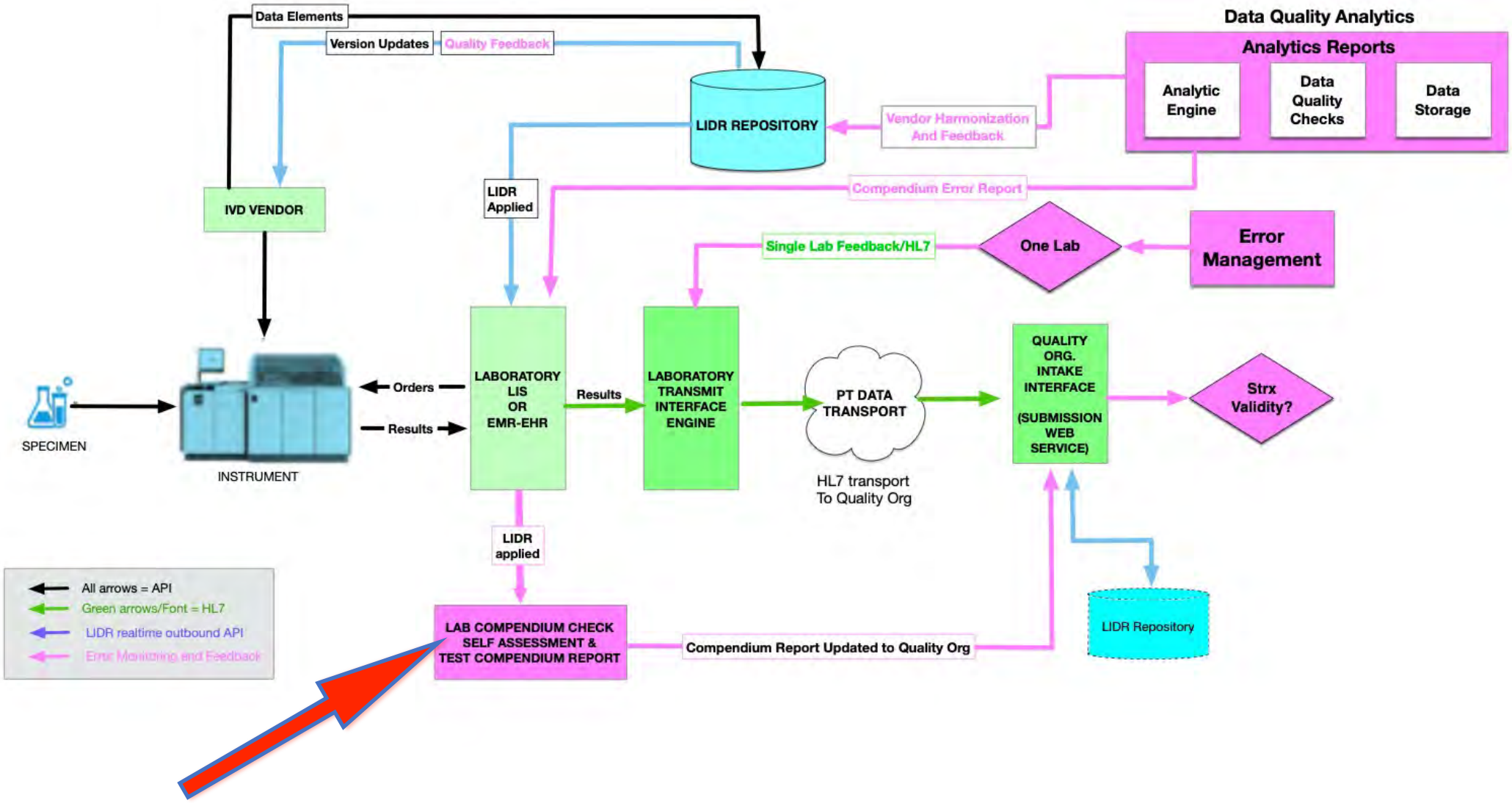


Laboratory Personnel

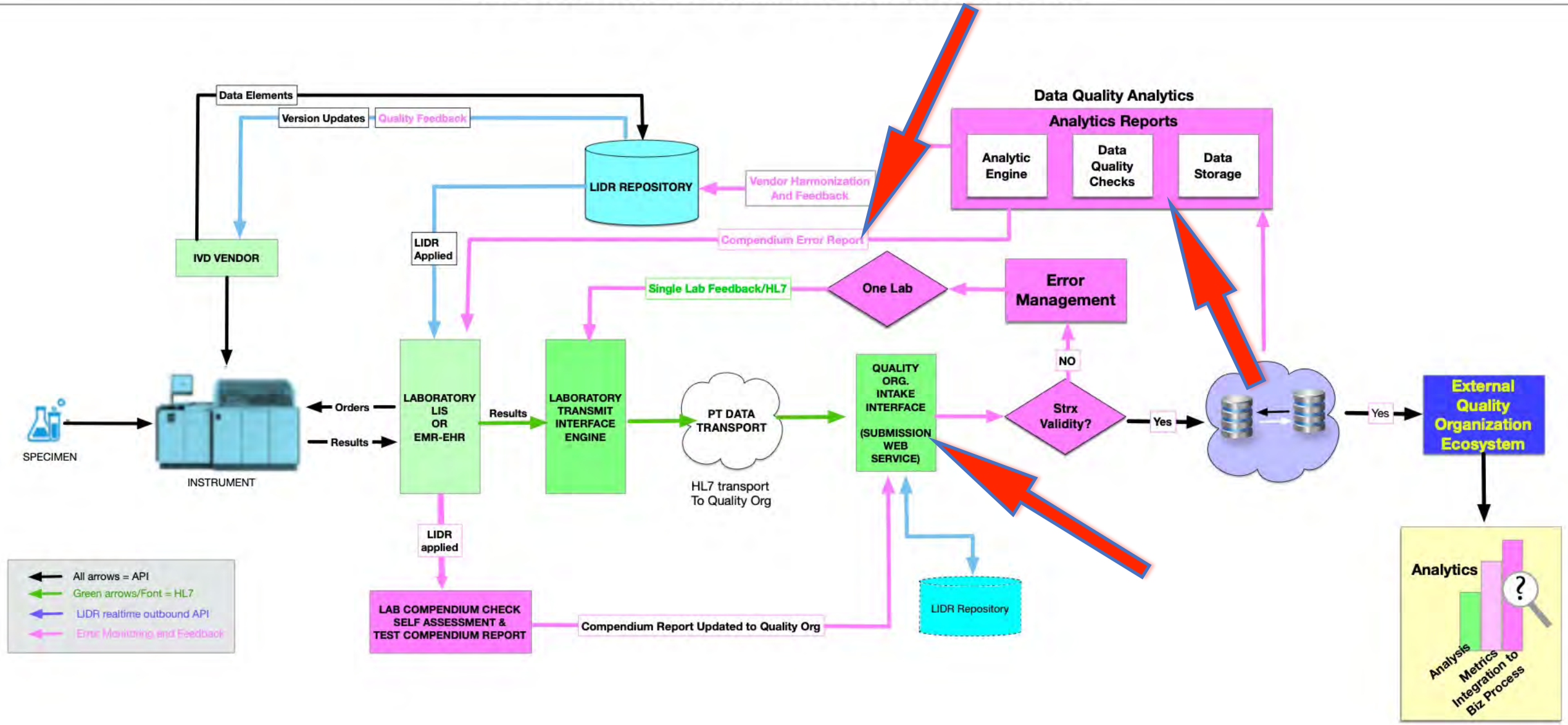
LIS/EHR Templates

LIS Analysts

FUTURE STATE: DATA FLOW INFRASTRUCTURE



FUTURE STATE: DATA FLOW INFRASTRUCTURE



Laboratory Data Quality External Assessment

Auswandererhallen der Hamburg-Amerika Linie, Hamburg.

Sanierungskarte.

Hapag

Befördernde Linie:

Akte No. 3955

Name des Passagiers: Fodit, Heinrich

Ankunftsdatum: 14/7 22

1. Desinfektion: 15. JUL 1922 Auswandererhallen HAMBURG

2. Desinfektion:

Tag der Impfung:

(Stempel des amerikanischen Arztes.) PUBLIC HEALTH SERVICE U.S. 1912

W. H. 6. 6. 22. 20 000.

HAMBURG-AMERIKA LINIE JOINT SERVICE WITH

UNITED AMERICAN LINES (INCORPORATED)

Inspection Card

(Third Class Passenger) (FROM EASTERN EUROPE.)

Port of departure Hamburg Date of Departure 27. JULI 1922

Name of ship Mount Clay

Name of Immigrant: Emerik Fodit Last residence: Sztandras

Inspected and passed at ... Passed at quarantine, port of ... U. S. Passed by Immigration Bureau port of ...

Seat or Stamp of Consular or Medical Officer (Date) (Date)

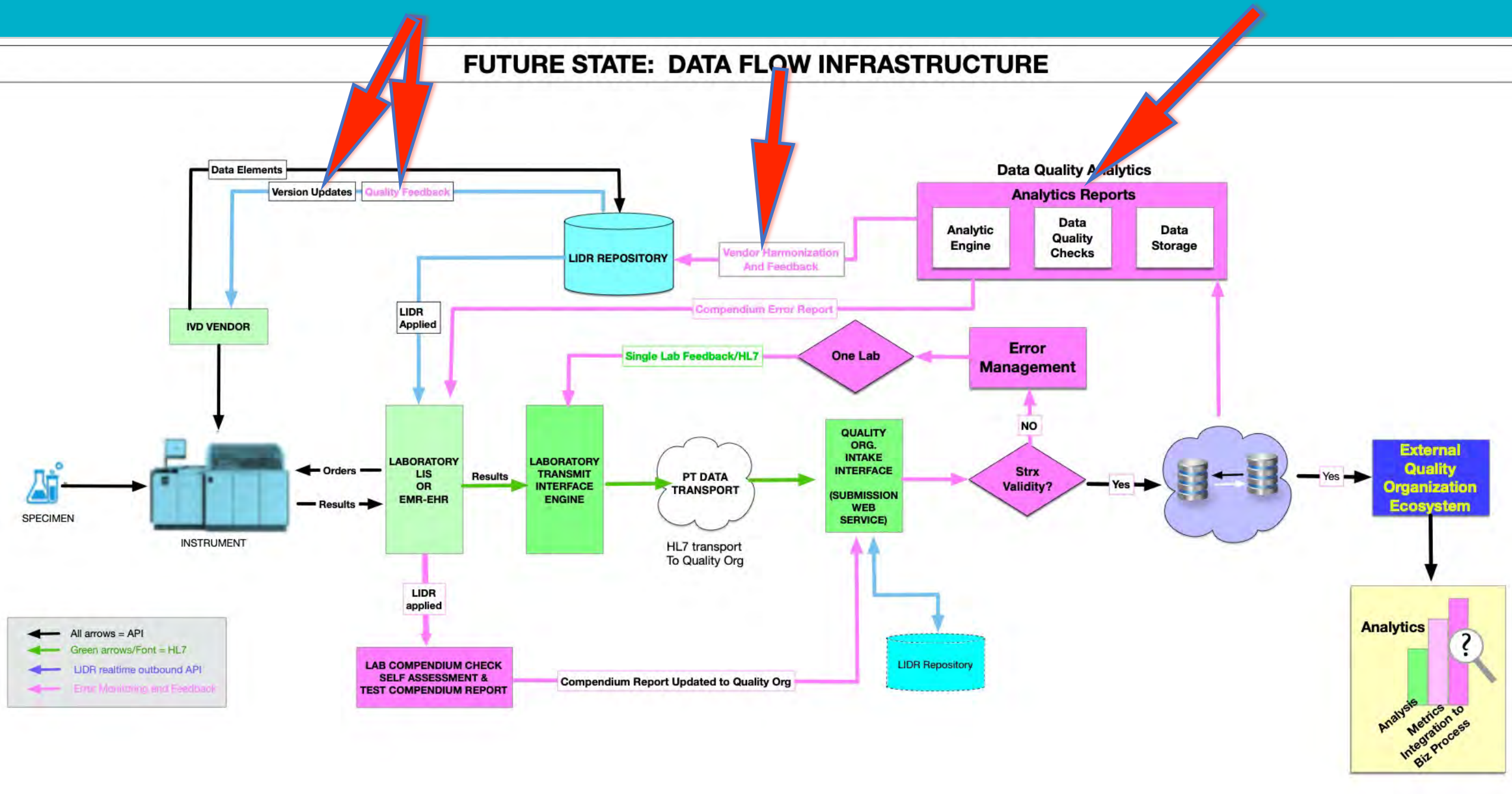
(The following to be filled in by ship's surgeon or agent prior to or after embarkation)

Ship's list or manifest 5 No. on ship's list or manifest 8

Berth No. | Steamship Inspection | 1st day 2 3 4 5 6 7 8 9 10 11 12 13 14 | To be punched by ship's surgeon at daily inspection

H. 6 Sch. 30. 3. 22. 5000.

FUTURE STATE: DATA FLOW INFRASTRUCTURE



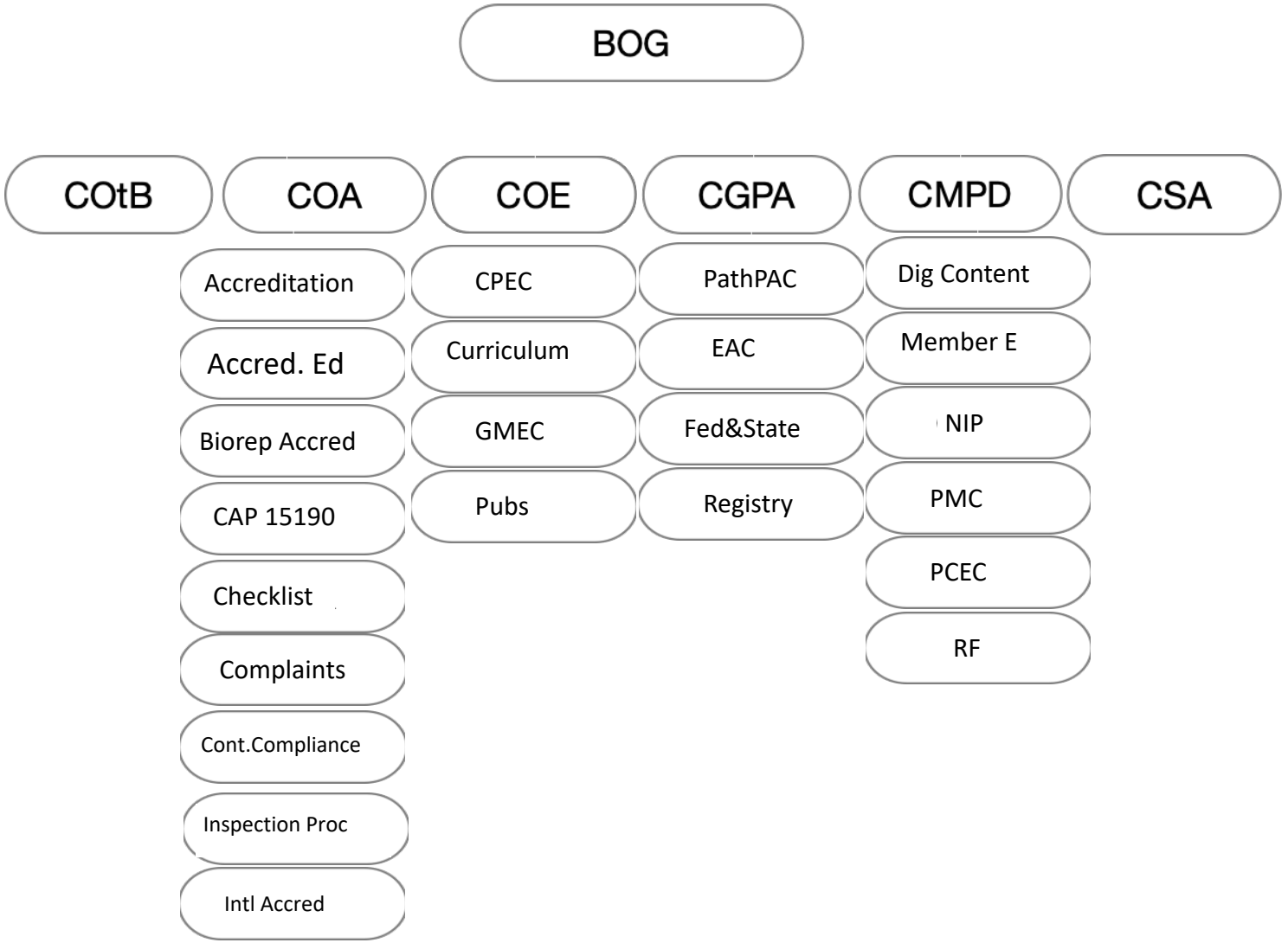
… Next Steps…

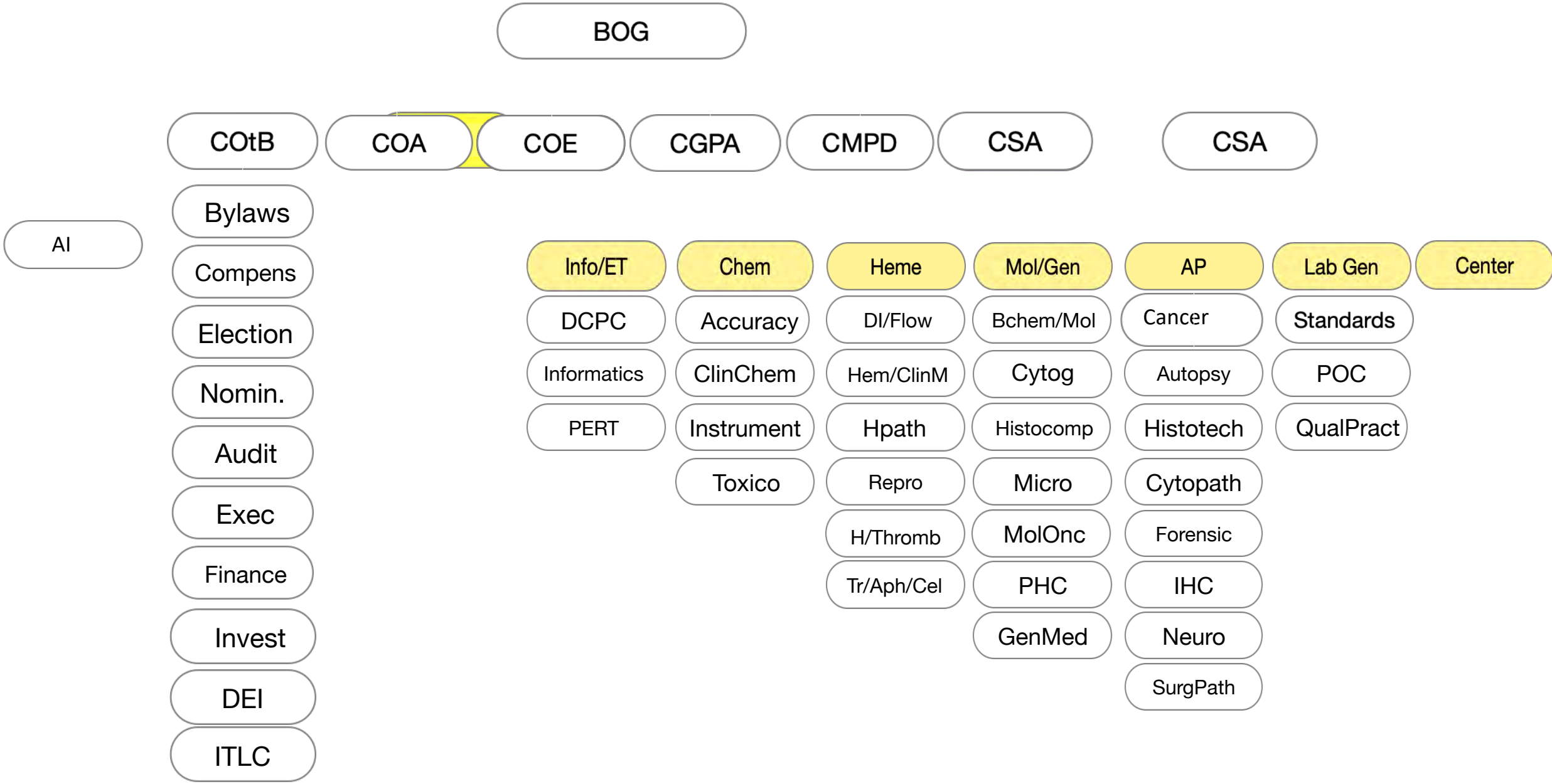
Year 2 Approved Objectives

1. Laboratory Coding Transmission Feasibility
2. Test Menu Coding Education & Training
3. Analysis Normal Form Clinical Narrative Development and Roundtrip Testing

Whew!

… (almost) Complete Pivot…


BOG
COtB
COA
COE
CGPA
CMPD
CSA
Accreditation
Accred. Ed
Biorep Accred
CAP 15190
Checklist
Complaints
Cont.Compliance
Inspection Proc
Intl Accred
CPEC
Curriculum
GMEC
Pubs
PathPAC
EAC
Fed&State
Registry
Dig Content
Member E
NIP
PMC
PCEC
RF


BOG
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CSA
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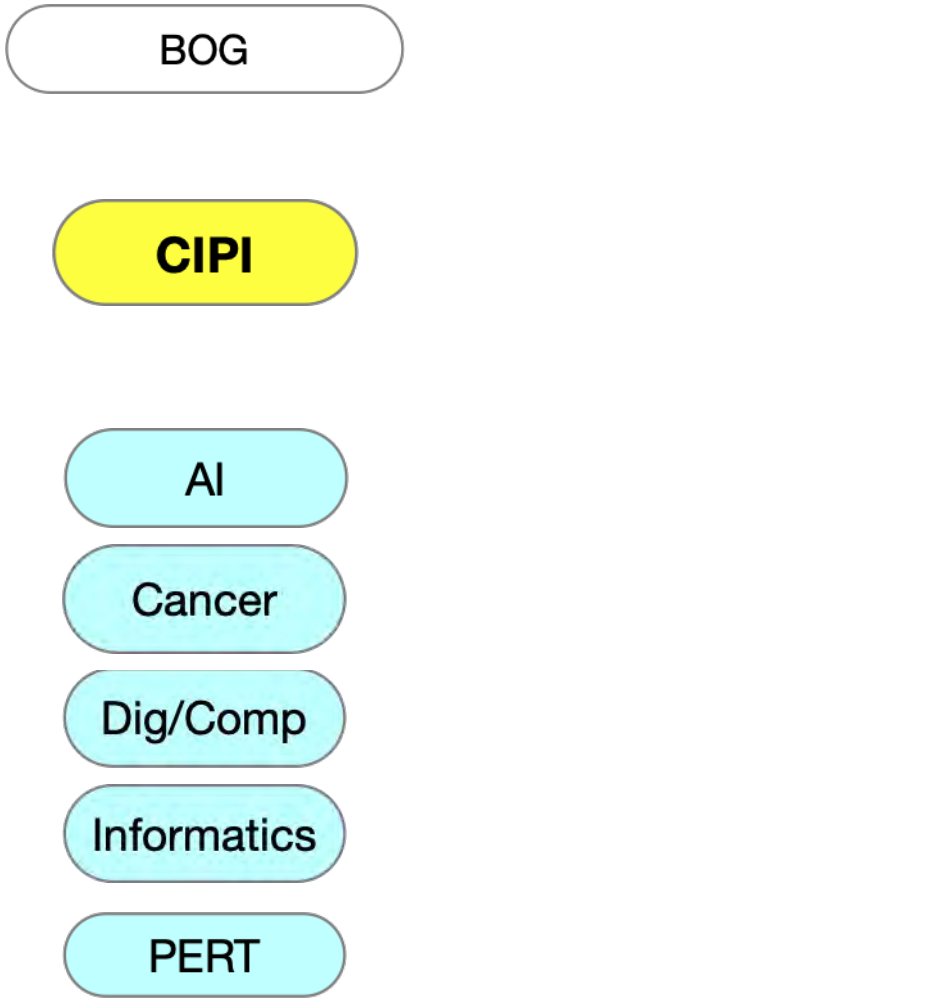
Compens
Election
Nomin.
Audit
Exec
Finance
Invest
DEI
ITLC
Info/ET
DCPC
Informatics
PERT
Chem
Accuracy
ClinChem
Instrument
Toxico
Heme
DI/Flow
Hem/ClinM
Hpath
Repro
H/Thromb
Tr/Aph/Cel
Mol/Gen
Bchem/Mol
Cytog
Histocomp
Micro
MolOnc
PHC
GenMed
AP
Cancer
Autopsy
Histotech
Cytopath
Forensic
IHC
Neuro
SurgPath
Lab Gen
Standards
POC
QualPract
Center


BOG
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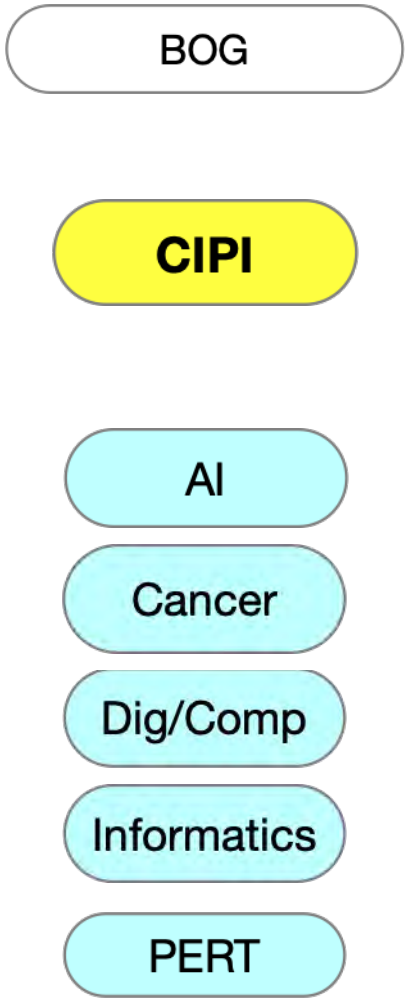
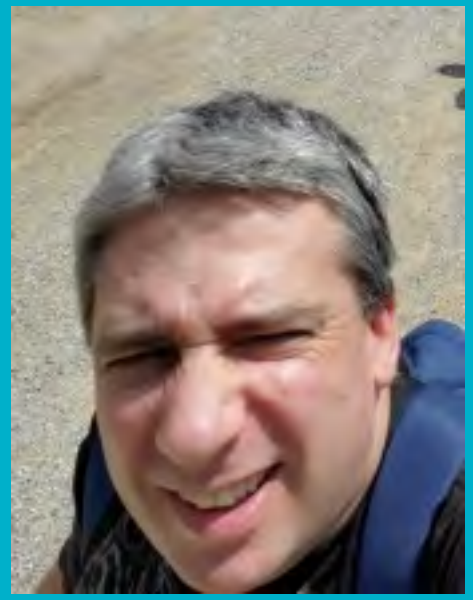
Informatics
PERT


BOG
CIPI
AI
Cancer
Dig/Comp
Informatics
PERT

1947

CAP Founded



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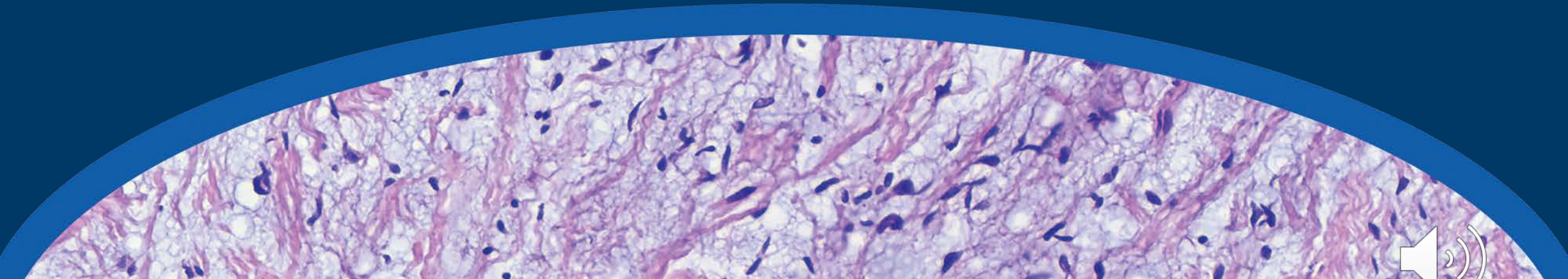
Digital Pathology Association (DPA) & DPA Foundation: Current scope of the work

Esther Abels

BioMedical Regulatory Health Science Expert

SolarisRTC LLC



Solaris
Research Trials Clinic

DPA and DPA Foundation

What do we do

SolarisRTC LLC
Esther Abels | BioMedical Regulatory Health Science Expert
info@solarisRTC.com
20230627

Solaris
Research Trials Clinic

? ? ? ? ?

Digital Pathology

Growth Opportunities

Precision medicine is rapidly changing

Budget, reimbursement and workforce are decreasing

Demand for personal approaches is growing

Increasing need for targeted Dx and Tx

Tx and Dx Paths need to be shortened

Acceleration through efficiency gains and showing effectiveness early on is needed

DIGITAL PATHOLOGY

DPA

ASSOCIATION

Mission: facilitate awareness, education and adoption of digital pathology and AI applications in healthcare and life sciences.

DPA fosters an exchange of ideas helping members understand, navigate, and influence the future of pathology.

Join our community & connect with **3,000+** digital pathology professionals!

digitalpathologyassociation.org

Going Global

Implementation: need for open agnostic digital platforms, understand and share of success

Consumers: knowing how to apply and actionable insights; reference sites

Serving Patients: Delivery of Care, share use cases, reimbursements, best practices, education

Footprint: Platform is to be integrated easily from research into clinic enabling easy integration of AI tools

General principles, harmonization, guidelines and connectathons

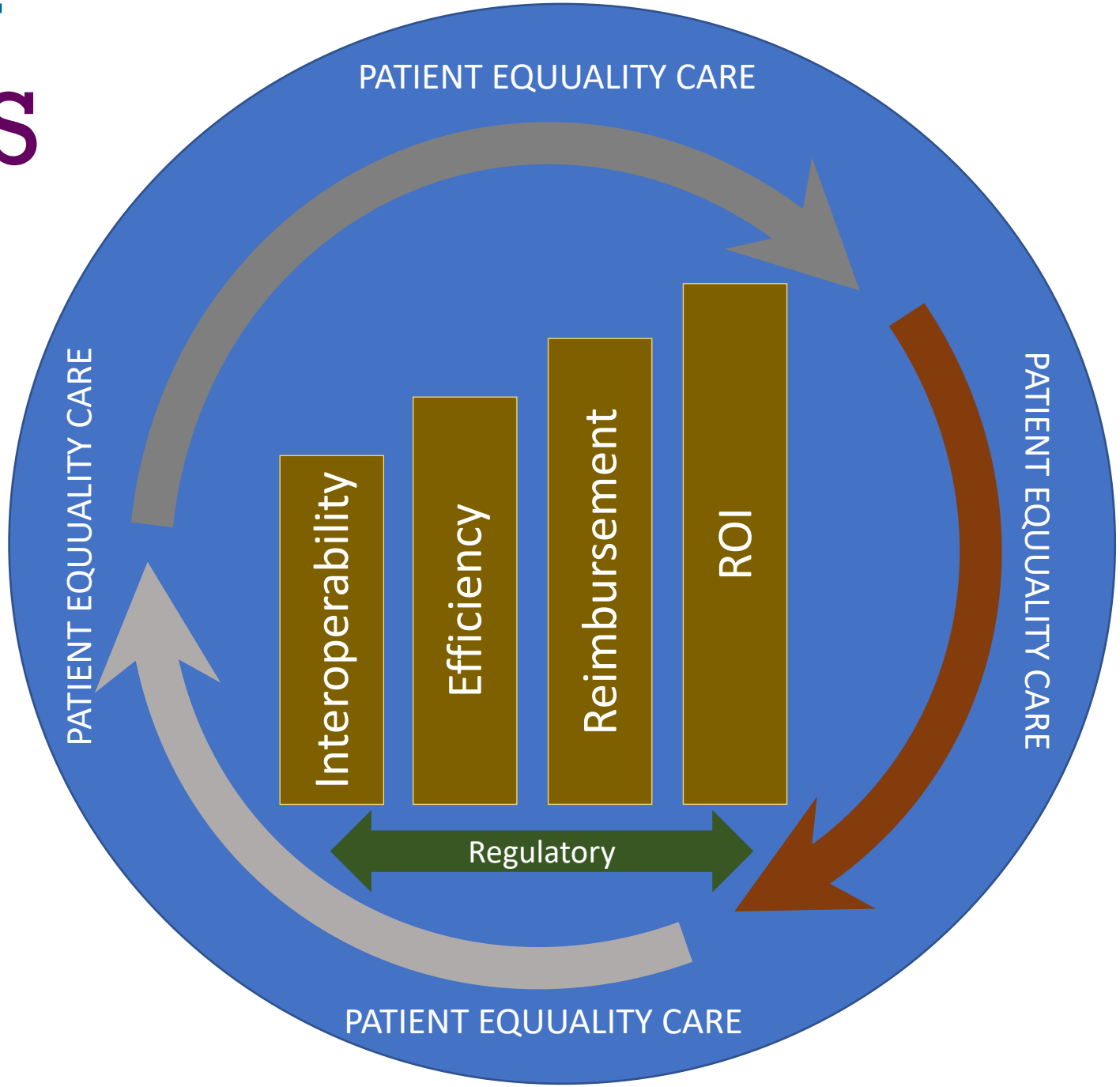
501(c)(3) organization established to raise philanthropic support to help realize the promise of digital pathology.

Our Vision: To bring digital pathology enabled precision medicine to every patient.

Our MISSION: Accelerate adoption of digital pathology to improve patient outcomes globally.

DIGITAL PATHOLOGY DPA ASSOCIATION FOUNDATION

Synergy of DRIVERS



Digital Pathology Effectiveness Study

PURPOSE:

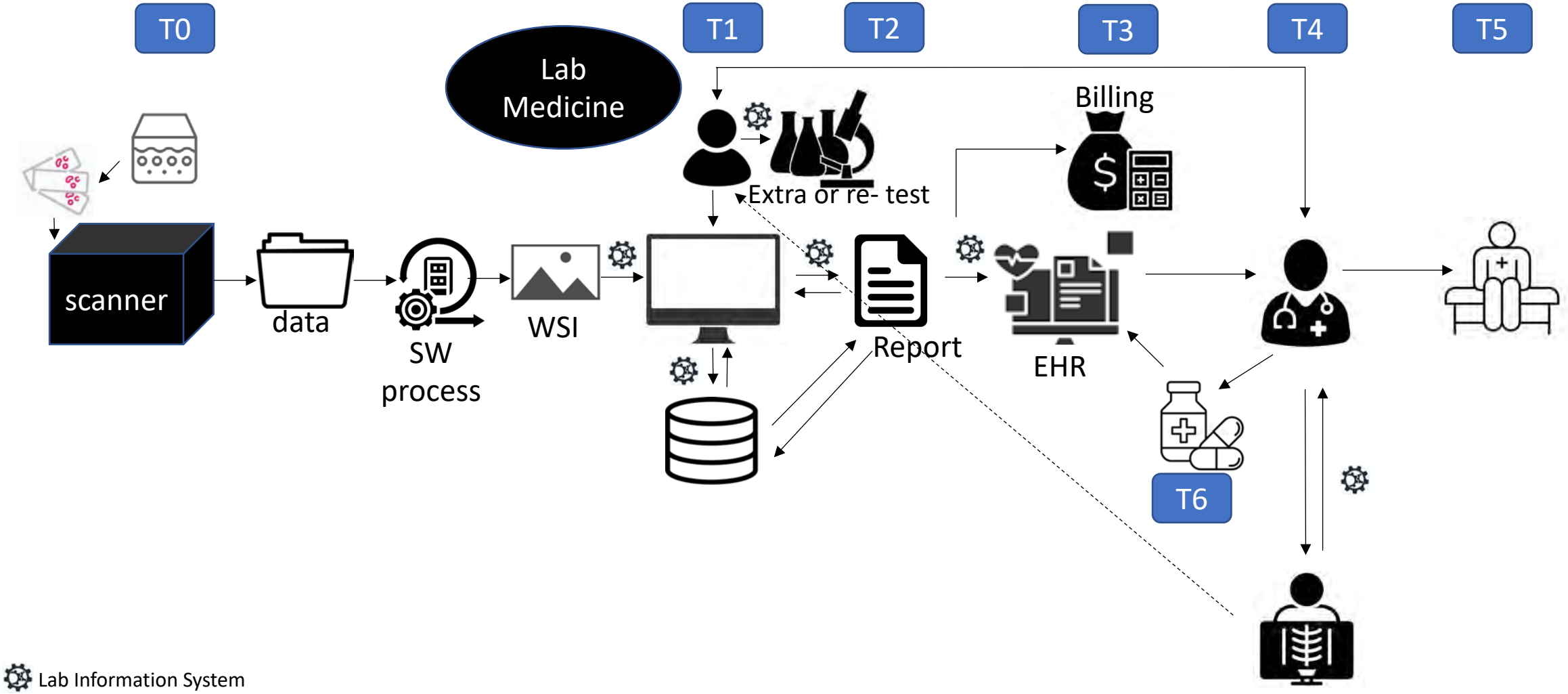
Document the impacts of adopting digital pathology for both patients and providers across a range of practice settings and community types.

ROADMAP

Timelines	Deliverables
Year 1	Effectiveness Study results Market Insights Optimization Stepping stone to unlock AI
Year 3	Best practices, Guidelines AI study driving for Regulatory Clarity, CPT codes, ROI Interoperability AI CPT application
Year 5	CPT Valuation Investigator Funded study Data as asset
>5yrs	Cyclic

Digital Pathology Performance

EFFECTIVENES STUDY



Lab Information System

Solaris

Research Trials Clinic

THANK YOU

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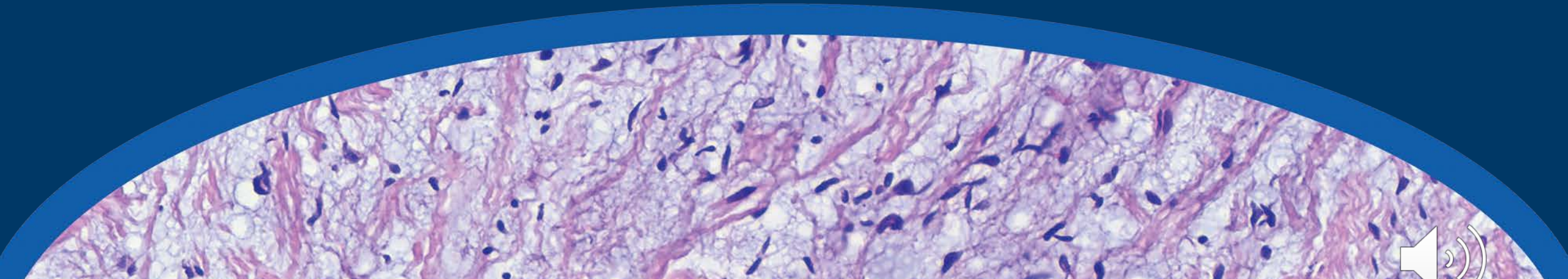
Association for Pathology Informatics (API) : Pathology Informatics – A Field or a New Practice?

Ji-Yeon Kim
Physician Director, Lab Informatics
Kaiser Permanente



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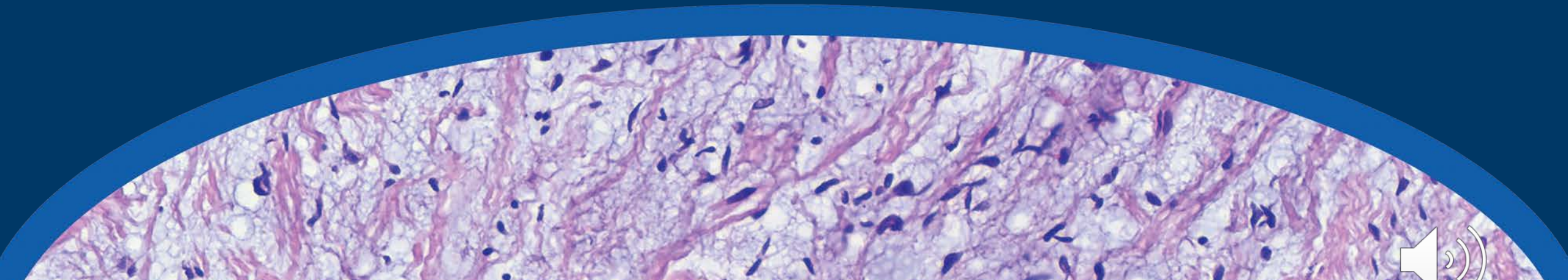
American Clinical Laboratory Association (ACLA)

Susan Van Meter
President, ACLA



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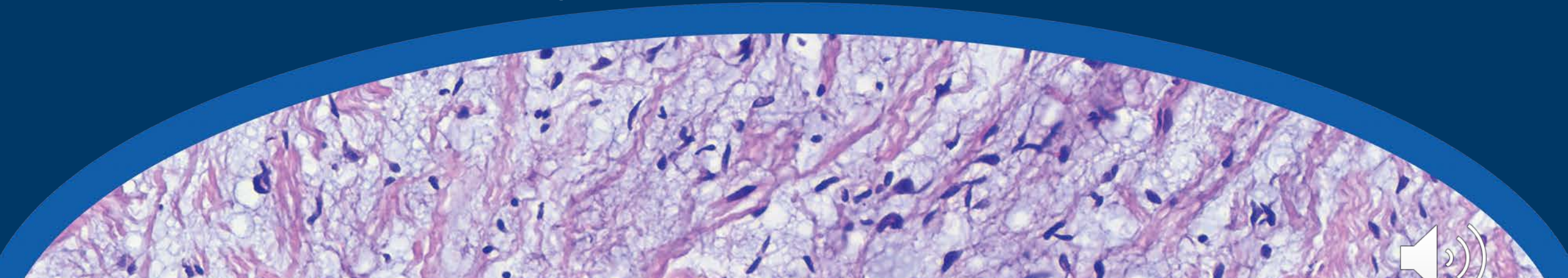
Association of Directors of Anatomic and Surgical Pathology (ADASP)

Alexandra Kalof, MD

Division Chief, CLIA Laboratory & Director of Anatomic Pathology

University of Vermont Medical Center



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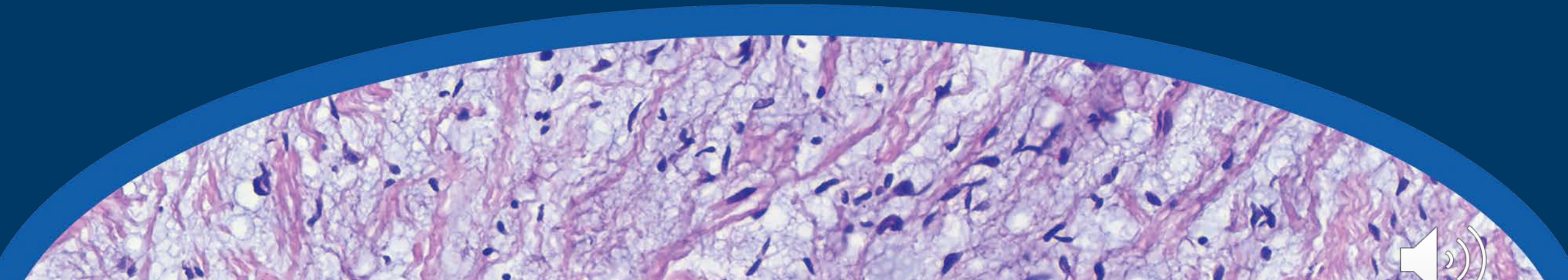
Panel Q&A



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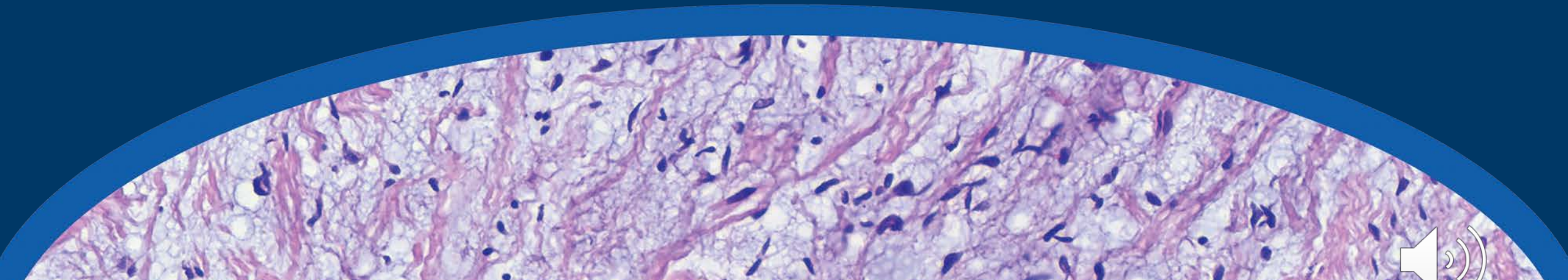
Coffee Break

Solaris
Research Trials Clinic



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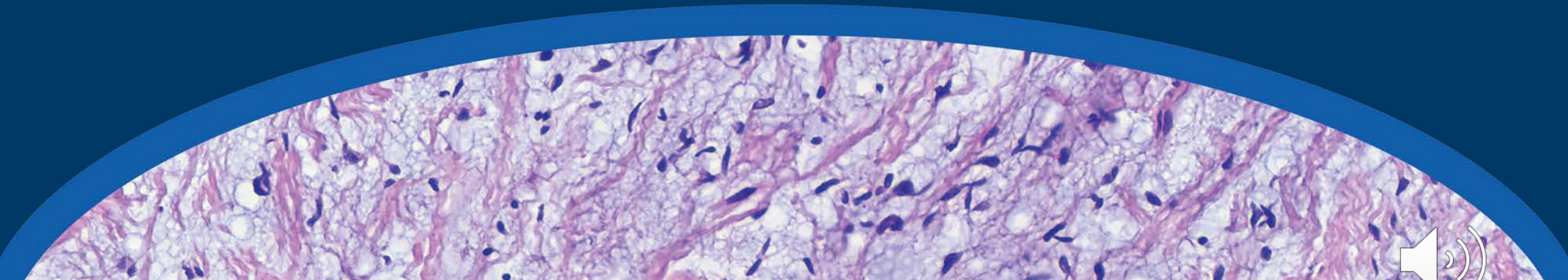
Q&A Session with Troy Tazbaz, Director, CDRH Digital Health Center of Excellence (DHCoE)

Moderated by

Jithesh Veetil, PhD

Senior Program Director, Digital Health & Technology (MDIC)



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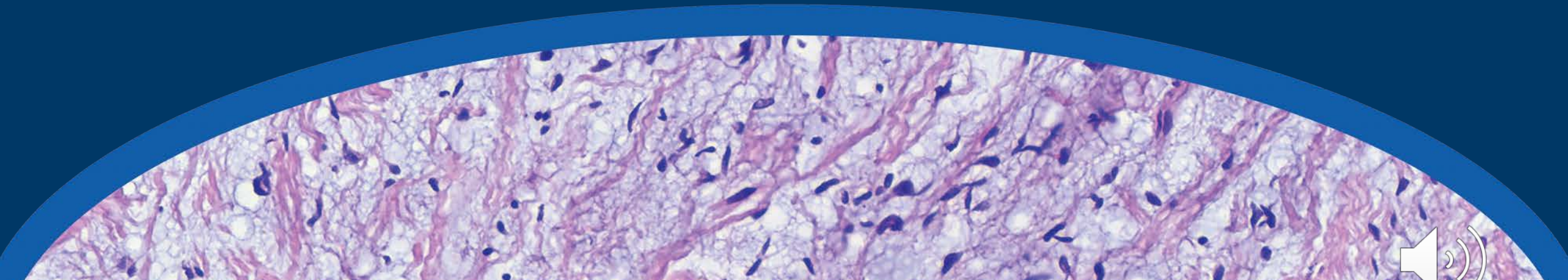
Session 2: From Regulatory Science to Patients

Moderated by
Mark Stewart & Brittany McKelvey



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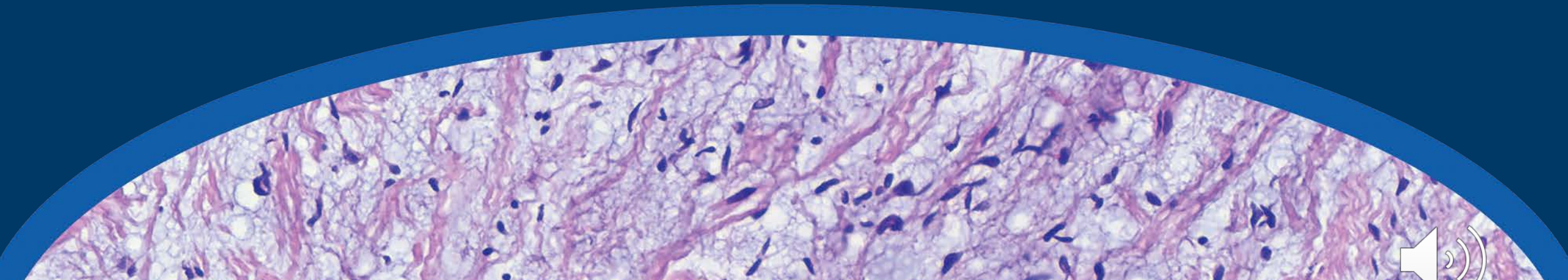
Friends of Cancer research (FOCR): Advancing Regulatory Science

Mark Stewart

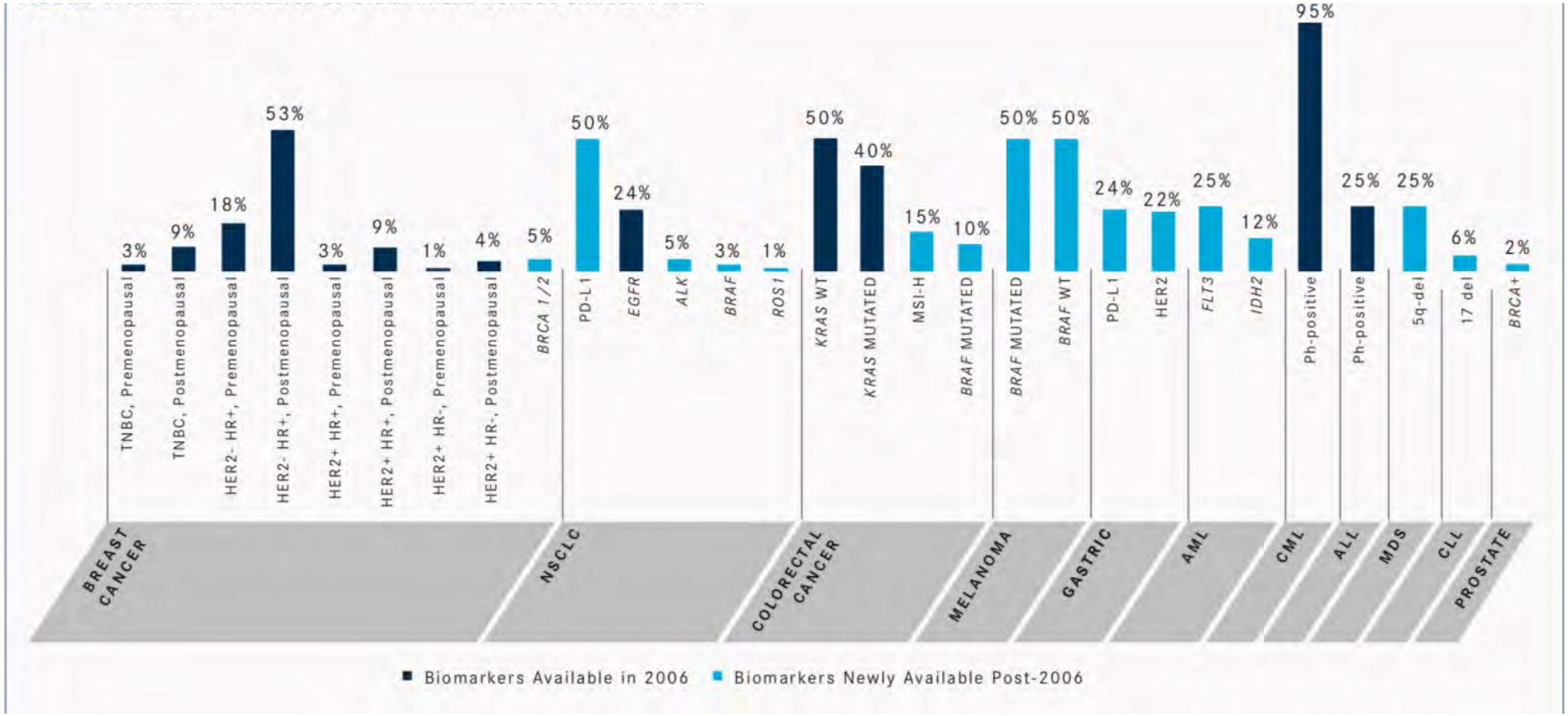
Vice President, Science Policy (FOCR)



Advancing Regulatory Science Through Collaboration

Mark Stewart, PhD
Vice President, Science Policy
mstewart@focr.org

Increasing use of biomarkers in cancer research and care

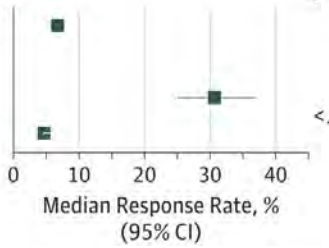


IQVIA. Global Oncology Trends 2019: Therapeutics, Clinical Development and Health System Implications.

Personalized medicine improves outcomes for patients with cancer

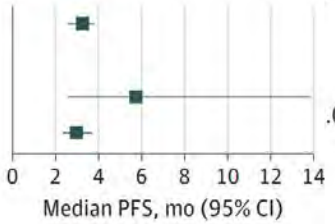
Response Rate

Variable	No. of Arms	Median Response Rate, % (95% CI)	*P* Value
Overall	351	6.56 (5.57-7.72)	
Used a personalized strategy			
Yes	58	30.62 (25.0-36.90)	<.001[a]
No	293	4.89 (4.22-5.66)	



Progression-Free Survival

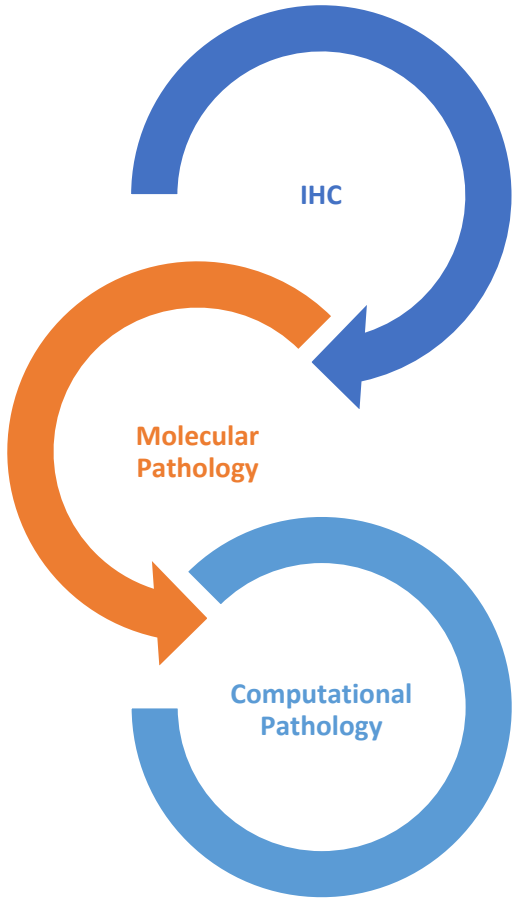
Variable	No. of Arms	Median PFS, mo (95% CI)	*P* Value
Overall	45	3.23 (2.56-3.80)	
Used a personalized strategy			
Yes	7	5.70 (2.56-13.78)	.049[a]
No	38	2.95 (2.30-3.70)	

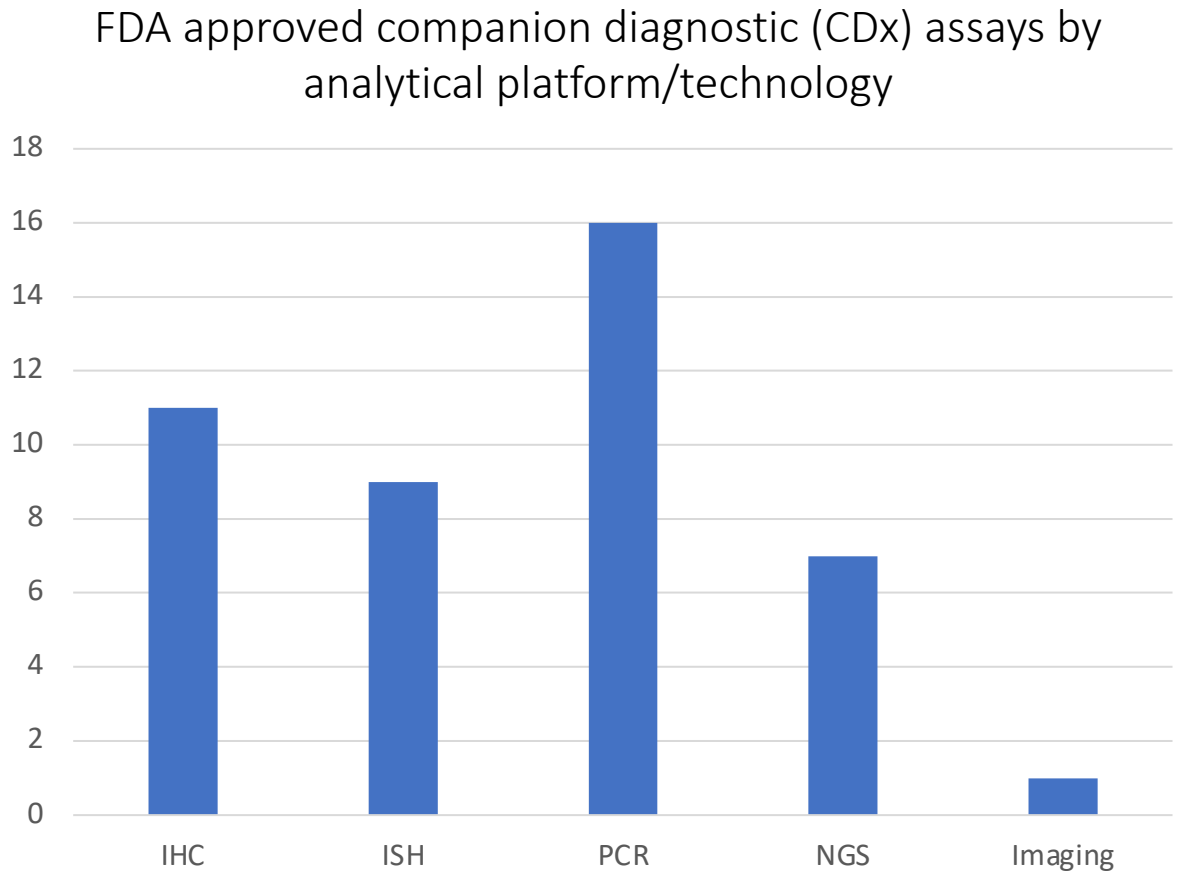


- Biomarkers that stratify patients likely to respond to therapy are now included in 39% of oncology trials, up from 25% in 2010
- Predictive biomarkers were associated with 60% of novel oncology therapeutics in 2018, and three were approved with a companion diagnostic.

Schwaederle M, et al. *JAMA Oncol.* 2016;2(11):1452–1459

Transformative technology enabling better patient selection and outcomes

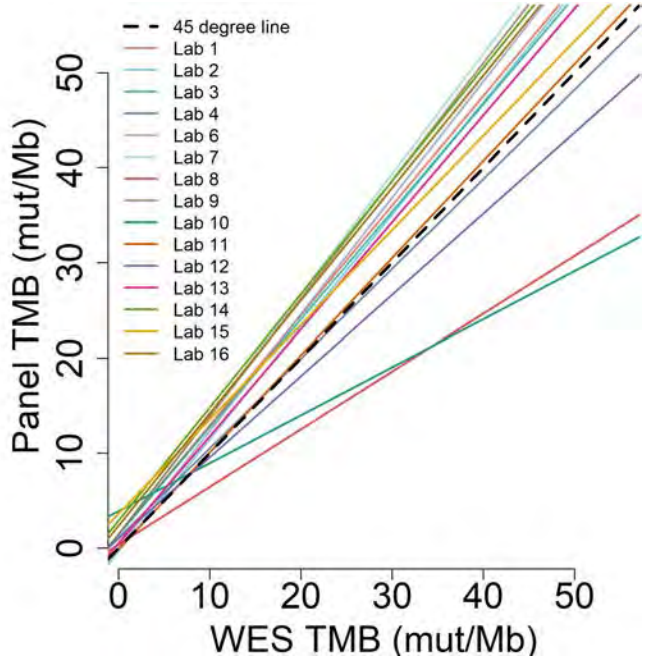




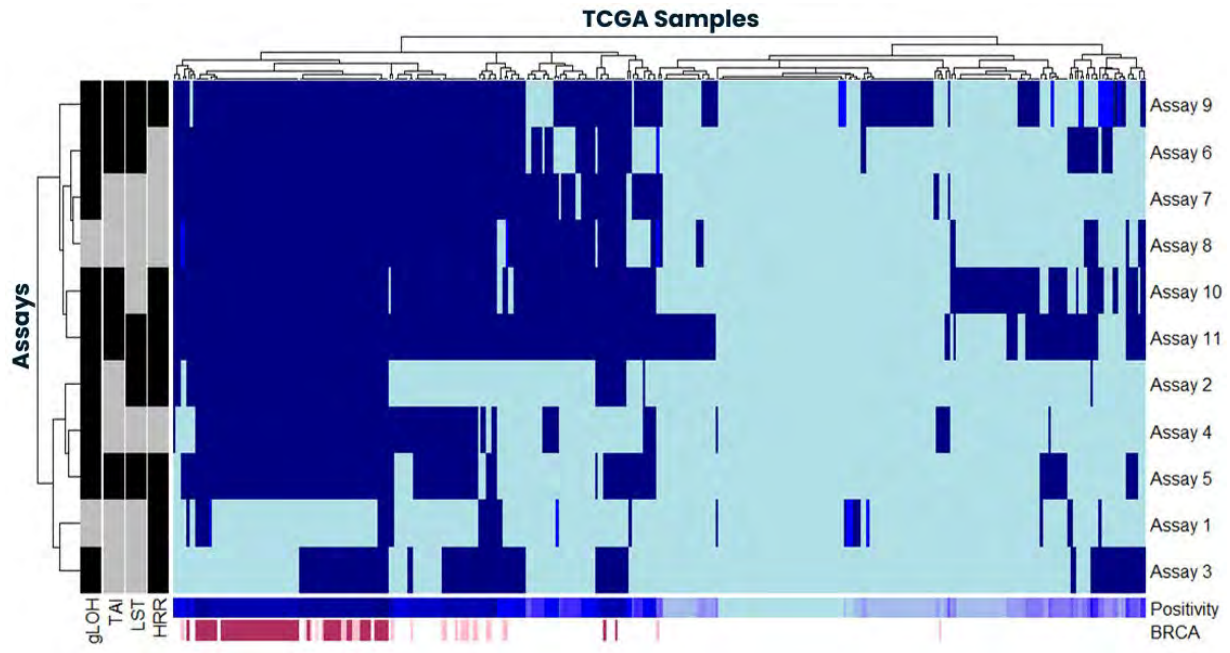
Jørgensen JT. Transl Oncol. 2021 Jun;14(6):101063.

Variation in diagnostic tests: harmonization project case study

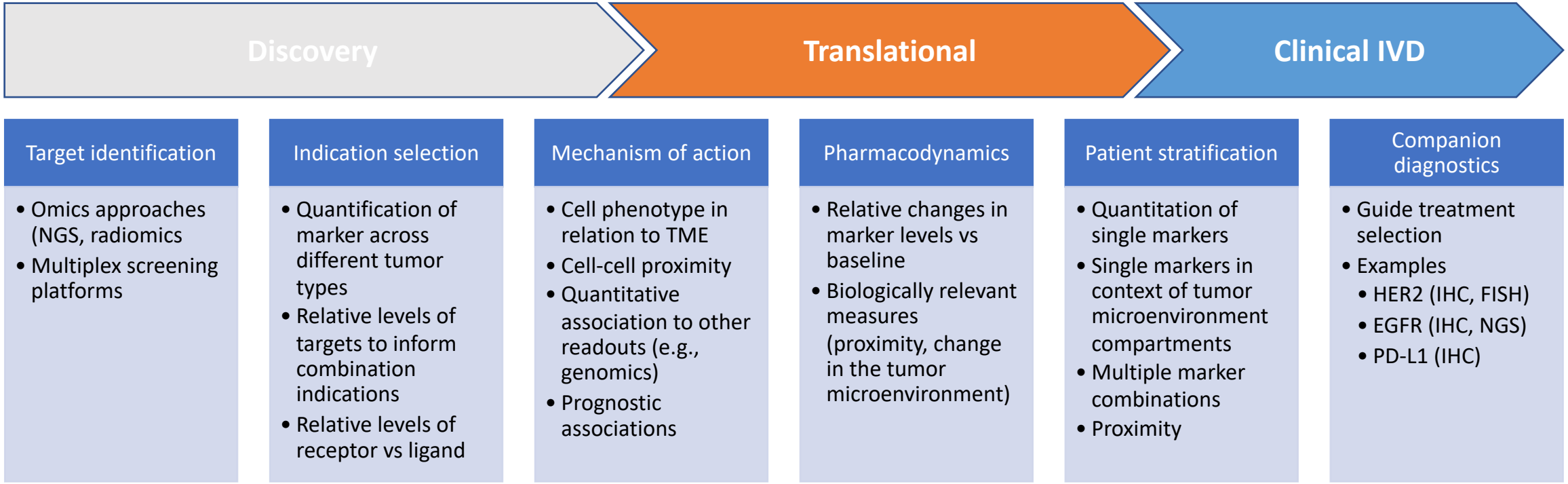
Tumor Mutational Burden



Homologous Recombination Deficiency

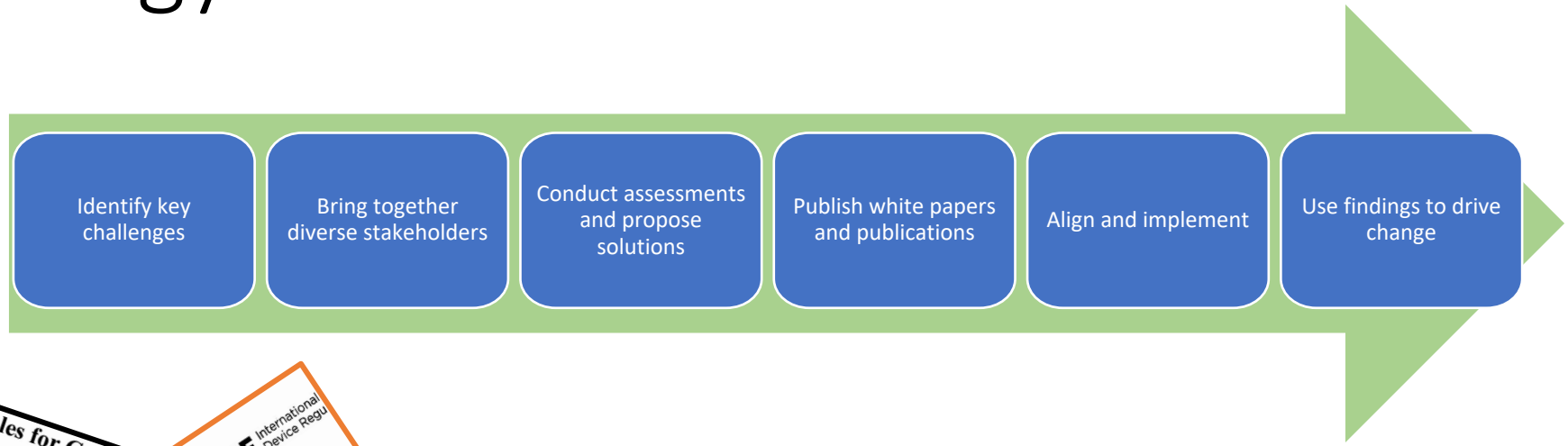


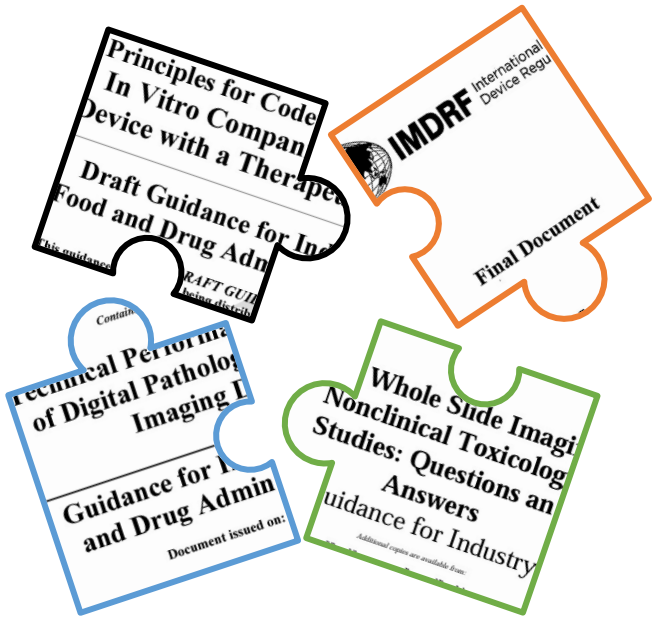
Digital pathology: from drug discovery to clinical diagnostics



Baxi V, et al. Mod Pathol. 2022 Jan;35(1):23-32.

Applying a collaborative model for digital pathology





Initial Opportunities:

- Outline potential use cases, considerations, and approaches for AI-driven digital pathology in oncology drug development
- Identify key challenges/opportunities for alignment of methodology

Emerging digital pathology harmonization effort

Use Case:

- Antibody-drug conjugates (ADCs) are an emerging drug class and often target cell surface receptors. IHC is used to identify the presence, location, and amount of the target.
  - Example: anti-HER2 ADCs

Objectives:

- Evaluate how comparable biomarker measurements are across digital pathology platforms, with or without comparison to manudl readings, with a common set of IHC slides.
  - Identify factors that may contribute to variability observed.
- Determine if a reference set can be used to standardize reporting of digital pathology measurements and performance.

Thank You

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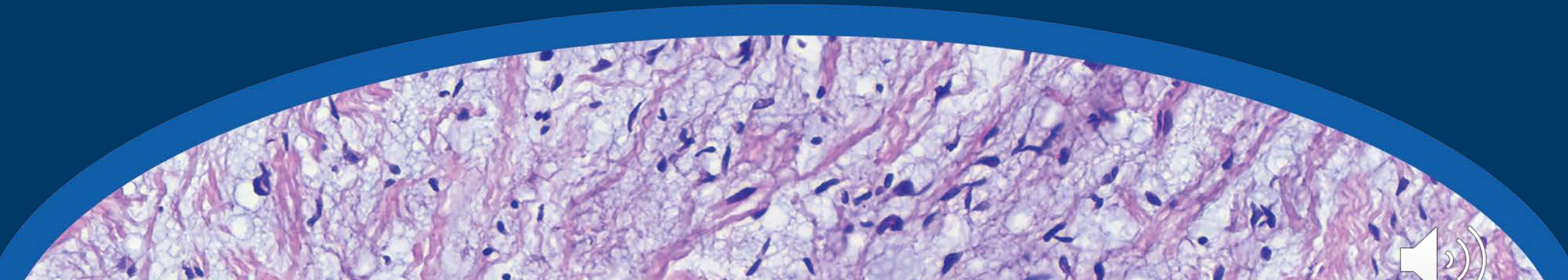
Value of Diagnostics in Healthcare

Hannah Mamuszka
CEO & Founder, Alva10



ALVA10

MOVING DIAGNOSTICS TO THE FOREFRONT OF PRECISION MEDICINE

PICC 2023

Hannah Mamuszka

Dismantling The Coding and Reimbursement Myths

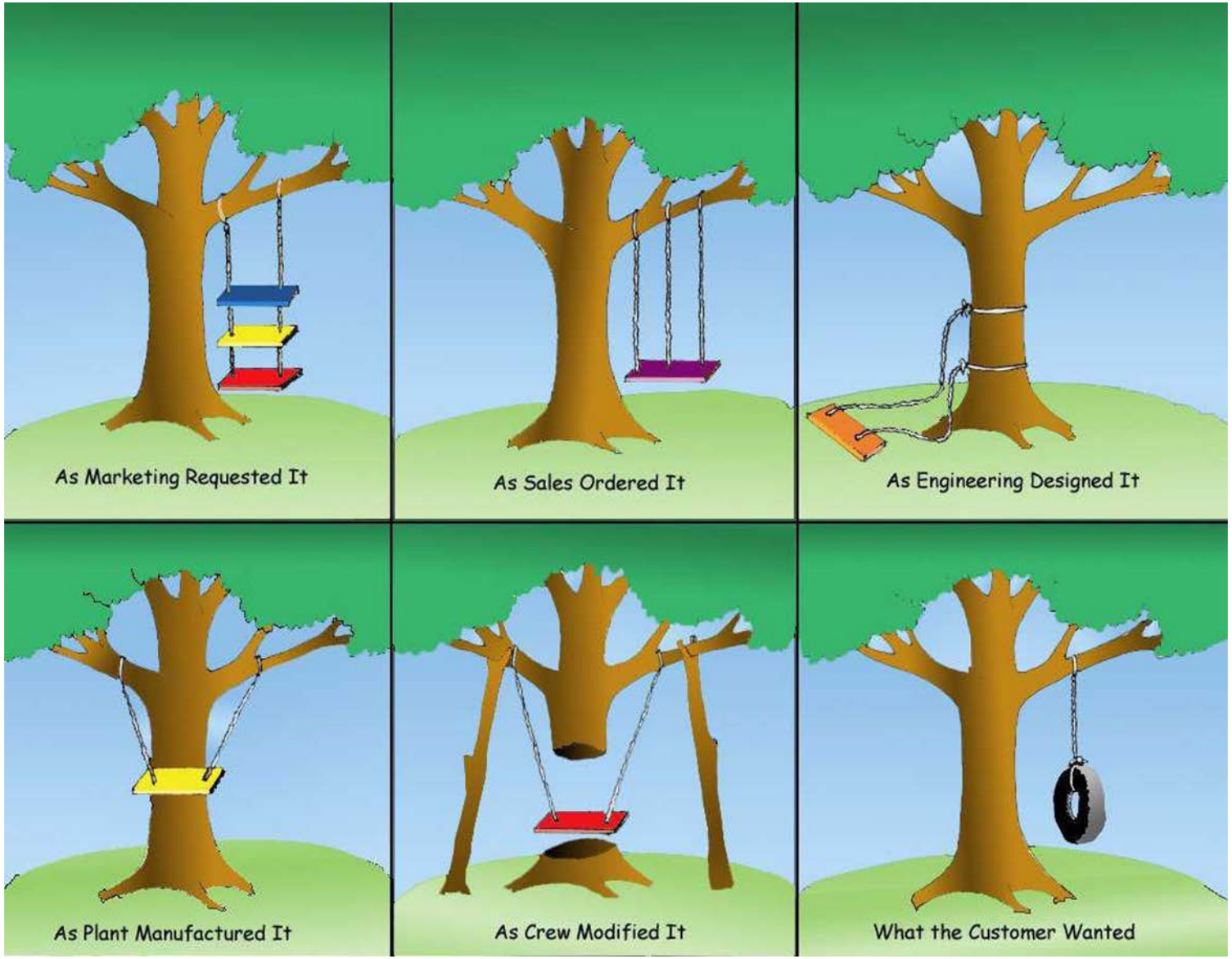
"Coding enables my test to get paid"

"As long as I have a code, I am all set"

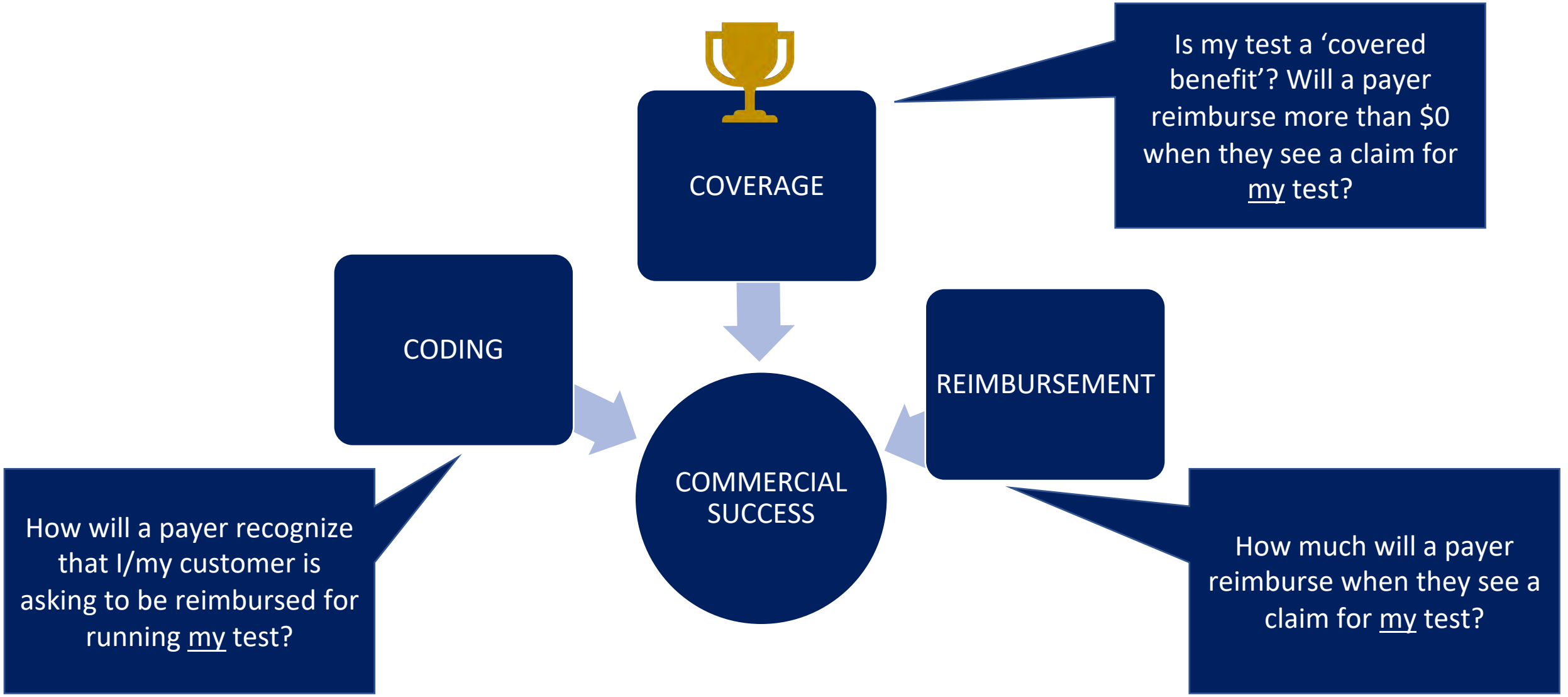
"Reimbursement is just a matter of getting the right code for my test"

Coding guarantees that your test claim will be processed by the insurance company administrative systems. It does NOT guarantee that the claim will be paid.

Acknowledging the payer (Medicare, commercial insurance, large employers, etc.) as the end customer of the lab and diagnostics industry



CODING – A PILLAR OF THE U.S. HEALTHCARE SYSTEM



STAKEHOLDERS OF REIMBURSEMENT ECOSYSTEM

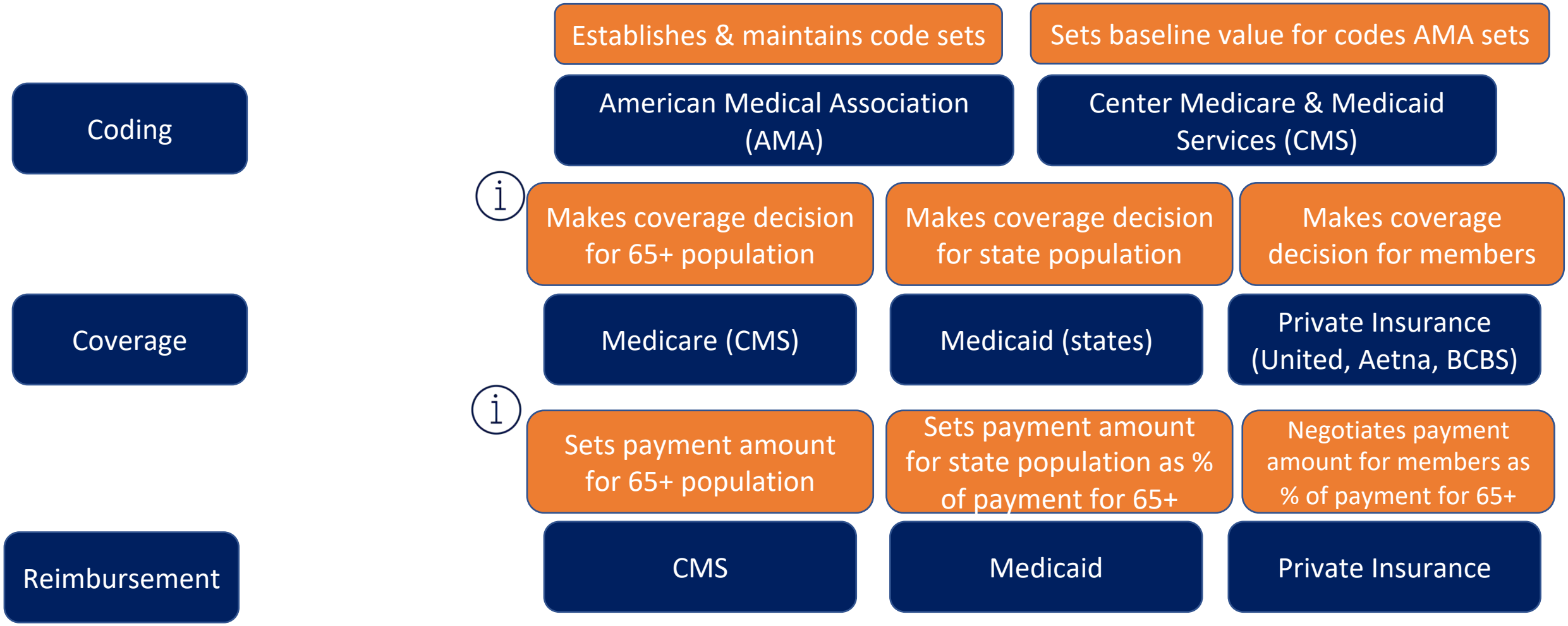
Coding	American Medical Association (AMA)	Center Medicare & Medicaid Services (CMS)	
Coverage	Medicare (CMS)	Medicaid (states)	Private Insurance (United, Aetna, BCBS)
Reimbursement	CMS	Medicaid	Private Insurance

INTERPLAYS BETWEEN STAKEHOLDERS

	Establishes & maintains code sets	Sets baseline value for codes AMA sets
Coding	American Medical Association (AMA)	Center Medicare & Medicaid Services (CMS)

Coverage	Medicare (CMS)	Medicaid (states)	Private Insurance (United, Aetna, BCBS)
Reimbursement	CMS	Medicaid	Private Insurance

INTERPLAYS BETWEEN STAKEHOLDERS



WHY DIAGNOSTICS STRUGGLE TO GAIN TRACTION

TOO OFTEN, DIAGNOSTIC COMPANIES:

- Don't understand economic impact of test to payers
- Don't confirm clinical utility with physicians
- Struggle with sample collection for development and validation
- Don't publish their data early enough
- Don't generate enough evidence to warrant coverage
- Assume early revenue before evidence is ready; don't raise enough money or allow enough time to generate evidence

Leading the payers to see

- Physicians who don't understand, don't agree with, or won't use the test
- Small data sets for validation
- Inaccurate economic assumptions
- Lacking or limited peer reviewed data
- Insufficient evidence for coverage
- An inability to generate more evidence to obtain coverage

Clinical Utility Confirmation

Do physicians agree there is a clinical problem?
Do physicians agree this test solves the problem?
Will physicians use this test?
Will using the test improve patient outcomes?

Payer Utility Agreement

Do payers agree there is a problem?
Do payers agree with the clinical utility of the test?
Do payers agree with the economic utility of the test?
How much data will payers need to see for pilot study engagement or coverage?

Commercial Planning

Is the company ready to deliver?
Coding timeline and planning
Billing logistics
Sales support and clinical training
Customer development and marketing support
Lab infrastructure (including reporting and TAT in clinical window)

Path to coverage and revenue

DESIGN WITH THE END IN MIND: ECONOMIC AND CLINICAL UTILITY

ECONOMIC UTILITY

- Allowing payers to appreciate downstream economic impact of implementation of test
- Empowering payers to enforce/waive Prior Auth when cost effective clinical pathways are clarified by diagnostic information
- Enabling payers to message improved patient outcomes and reduced employer costs to their customers for membership retention purposes

CLINICAL UTILITY

- Accurate diagnosis of disease
- Risk stratification
- Response prediction
- Patient adverse event profiles
- Payer costs of obtaining sample/diagnosis
- Critical junctions where lack of information leads to expensive interventions

ALVA10

MOVING DIAGNOSTICS TO THE FOREFRONT OF PRECISION MEDICINE

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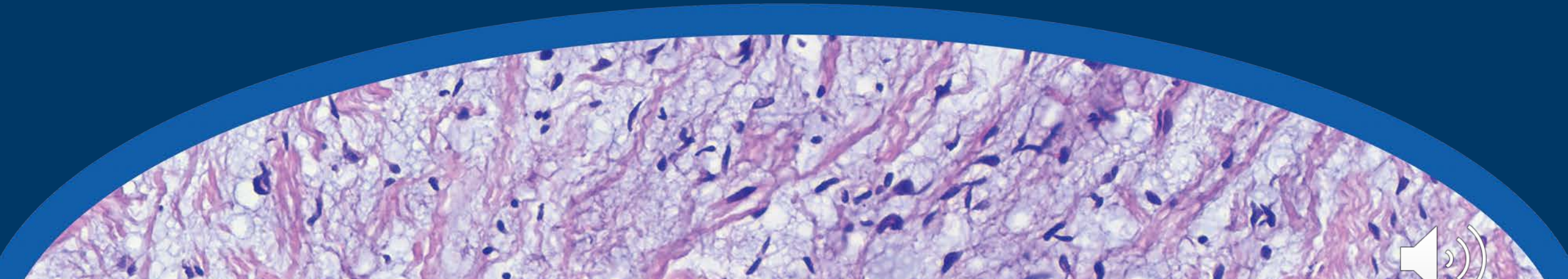
The Journey to Precision Pathology

Mariano de Socarraz
CEO, CorePlus



THE JOURNEY TO

PRECISION PATHOLOGY

BY MARIANO DE SOCARRAZ

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MEDICAL DEVICE INNOVATION CONSORTIUM


CORE
PLUS
Welcome to our world™

About us

welcome to our world

Total Cases

>125,083 WSI

>10,389 AI

Total Slides

>345,795 WSI

>124,882 AI

Tech-enabled

Since 1996

Established in
Carolina
Puerto Rico

Faculty

M.D.s, Ph.Ds, and
professionals with
vast field experience

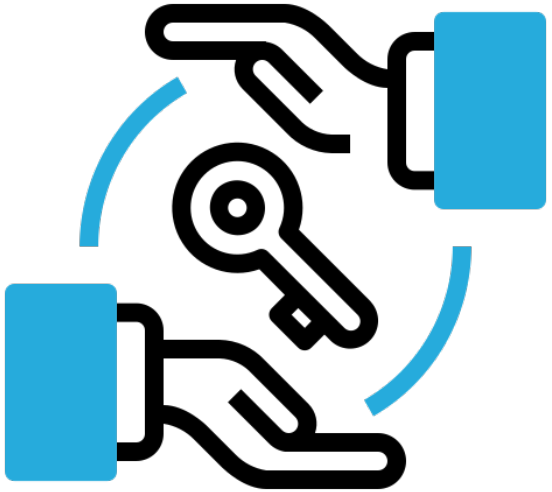
4 Years

In the
Digital Pathology
venture

Our Journey

To Digital Pathology & AI

Research



vs.

Our Journey

To Digital Pathology & AI

vs.

Research

Our Journey

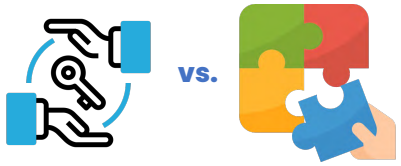
To Digital Pathology & AI

vs.

Research

Our Journey

To Digital Pathology & AI



Research

Our Journey

To Digital Pathology & AI

vs.

Research

Our Journey

To Digital Pathology & AI

vs.

Research

COLLEGE of AMERICAN PATHOLOGISTS

Validation guidelines

Our Journey

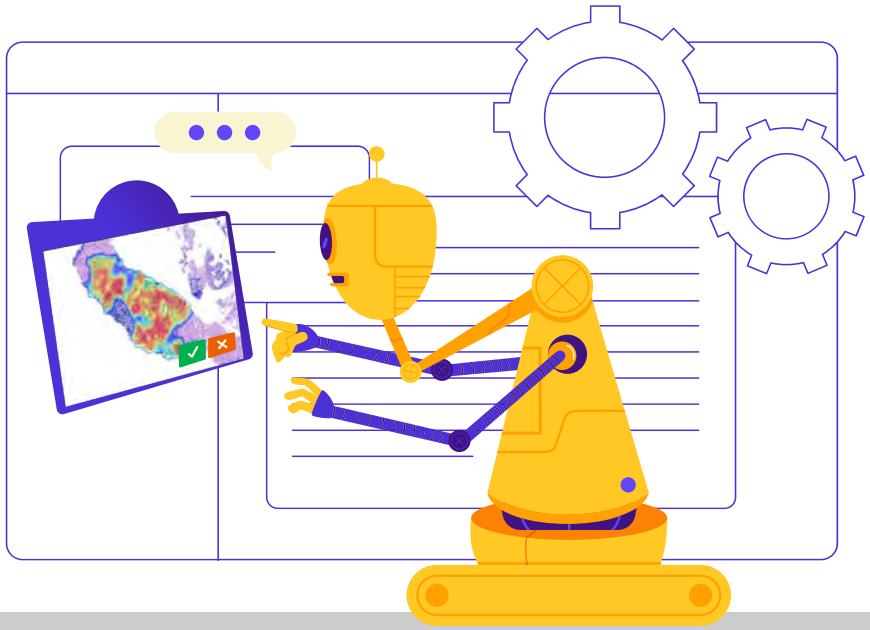
To Digital Pathology & AI

vs.

Research

COLLEGE of AMERICAN PATHOLOGISTS

Validation guidelines



Our Journey

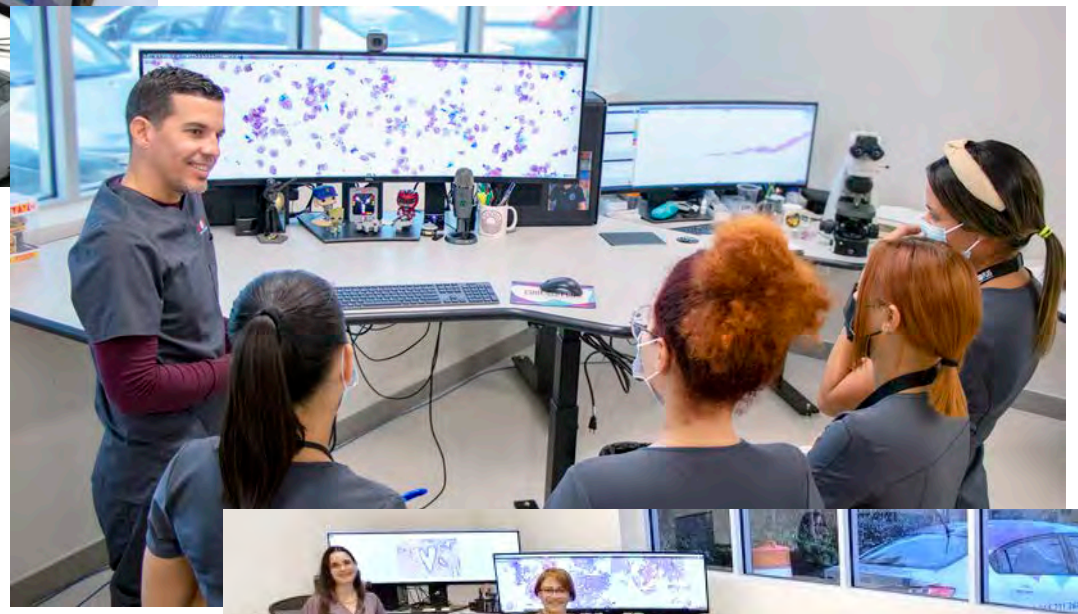
To Digital Pathology & AI

Research

Upgrades

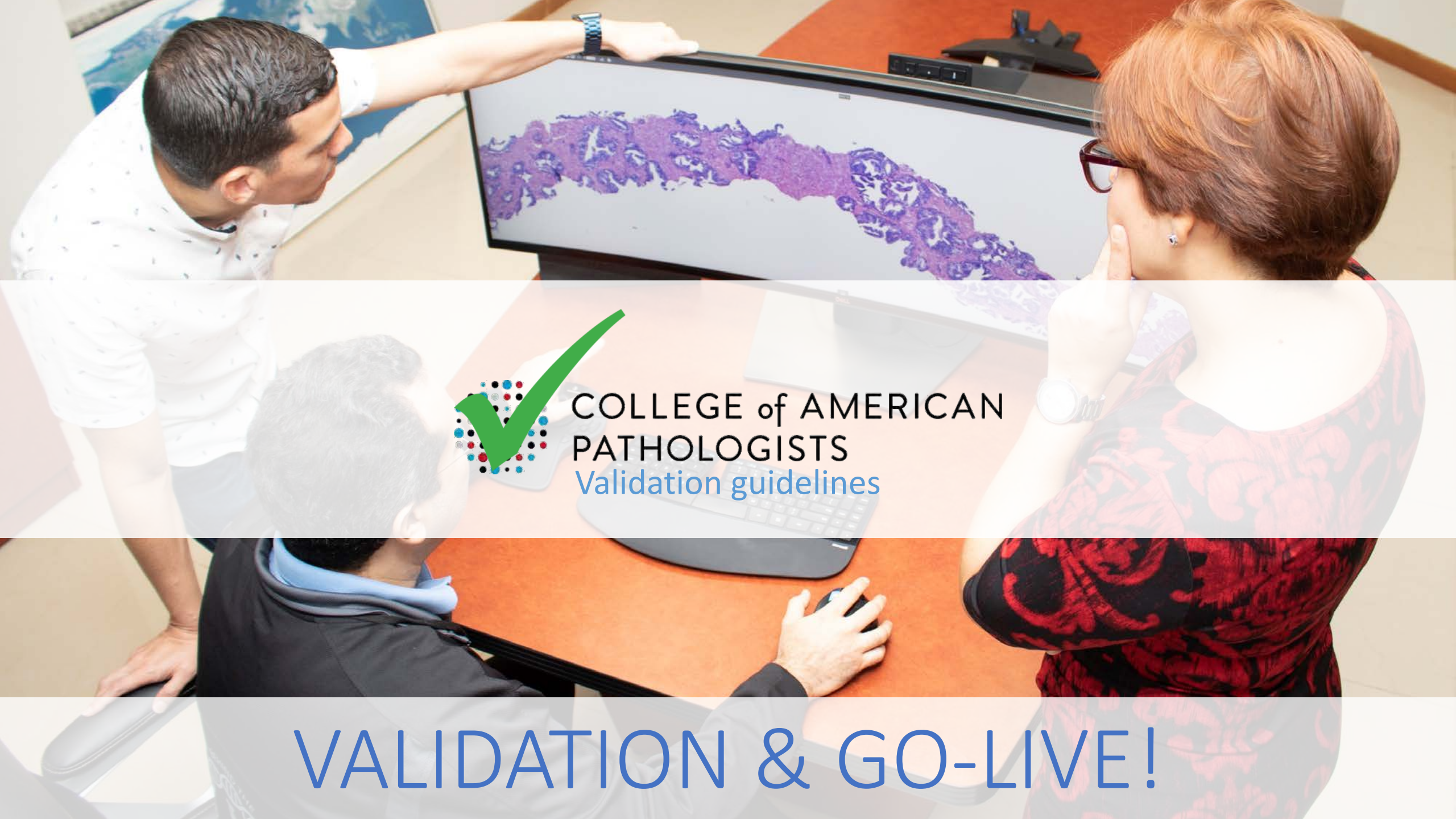
Our Journey

To Digital Pathology & AI



Research

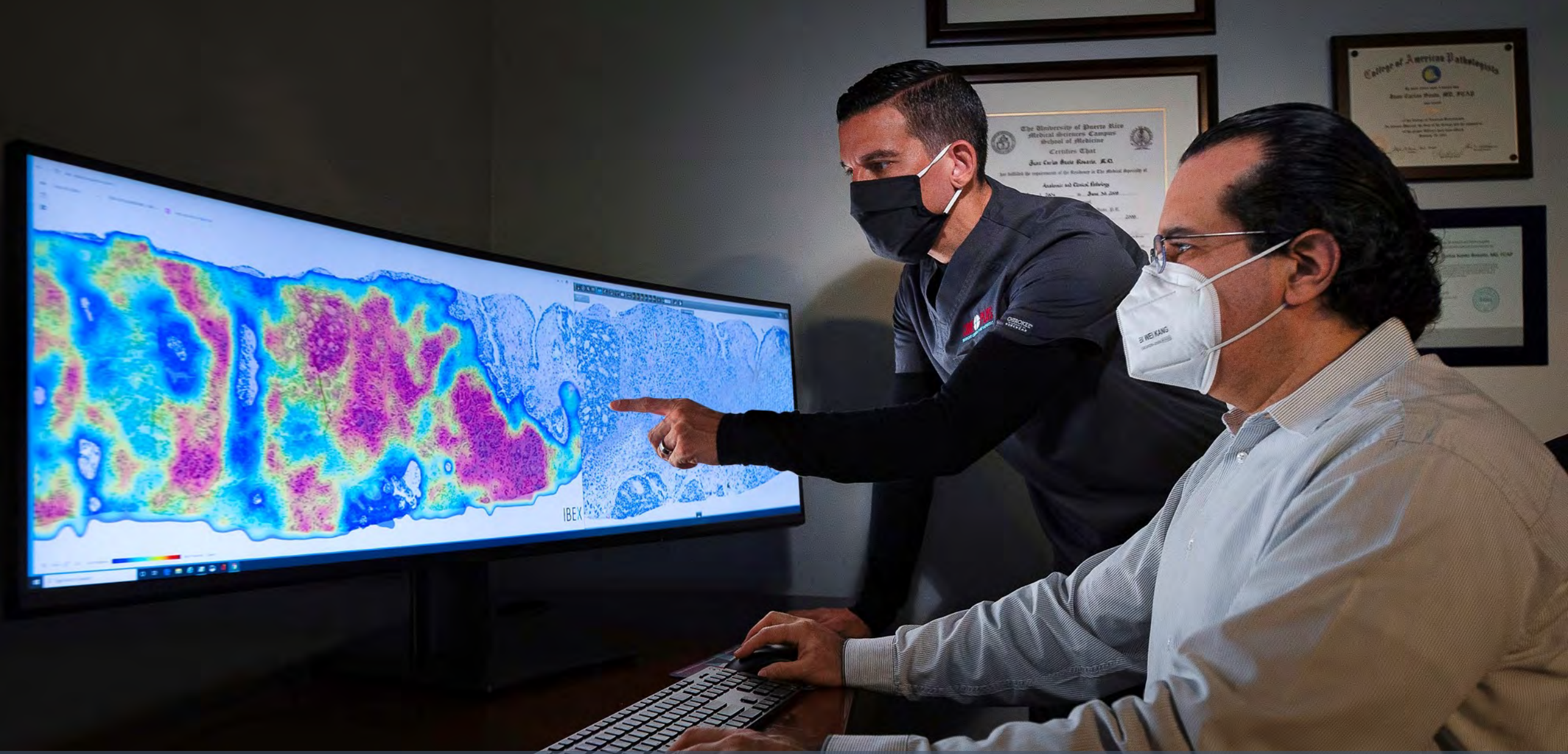
Upgrades



COLLEGE of AMERICAN PATHOLOGISTS

Validation guidelines

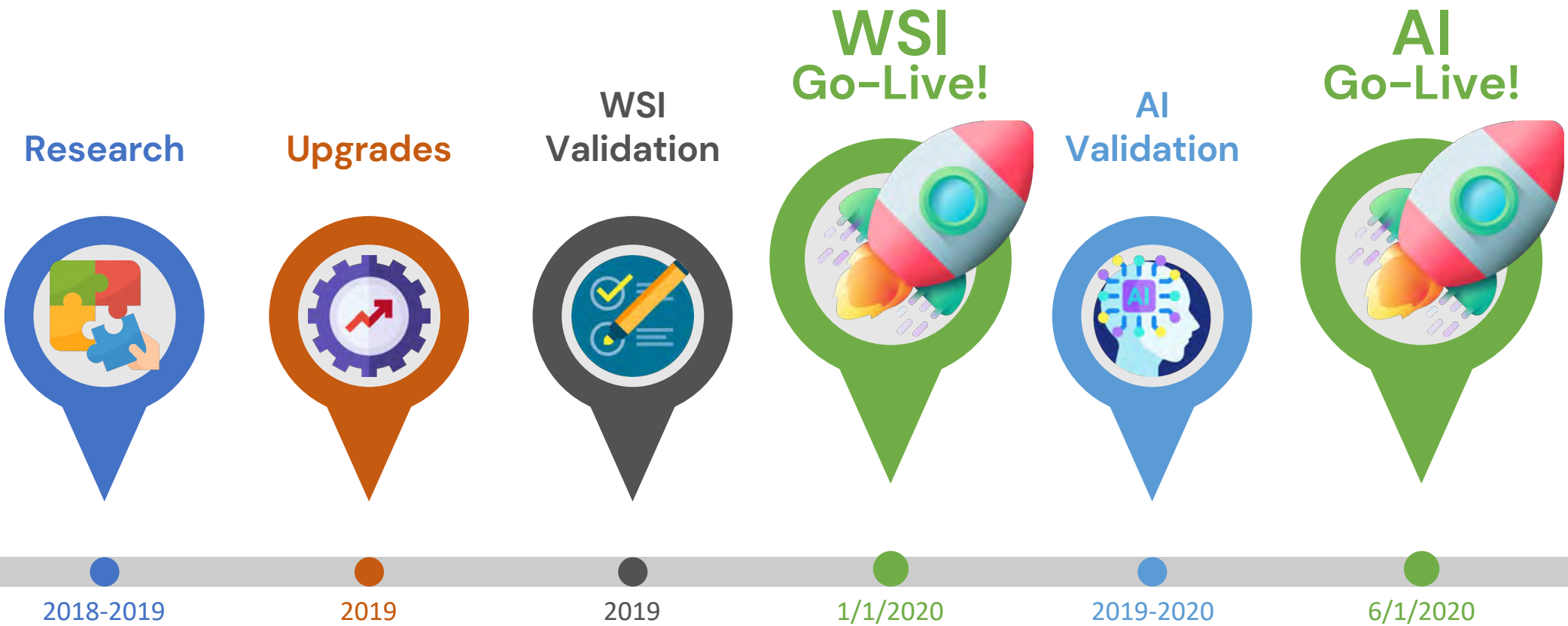
VALIDATION & GO-LIVE!



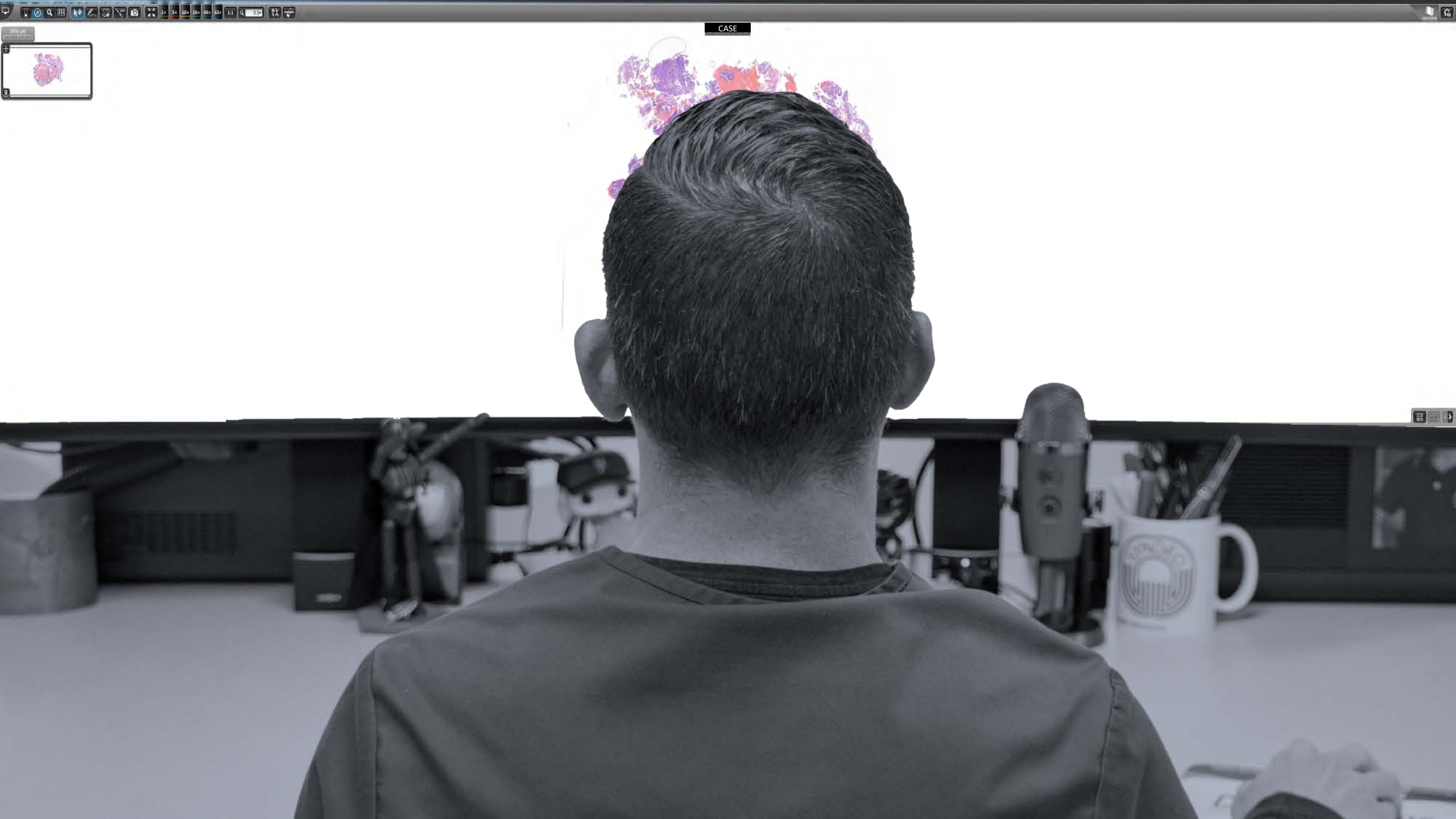
AI-ASSISTED DIAGNOSIS

Our Journey

To Digital Pathology & AI



So, how does **Pathology** look like in


CASE

Takeaways

Opportunities beyond the digital slide

ROI

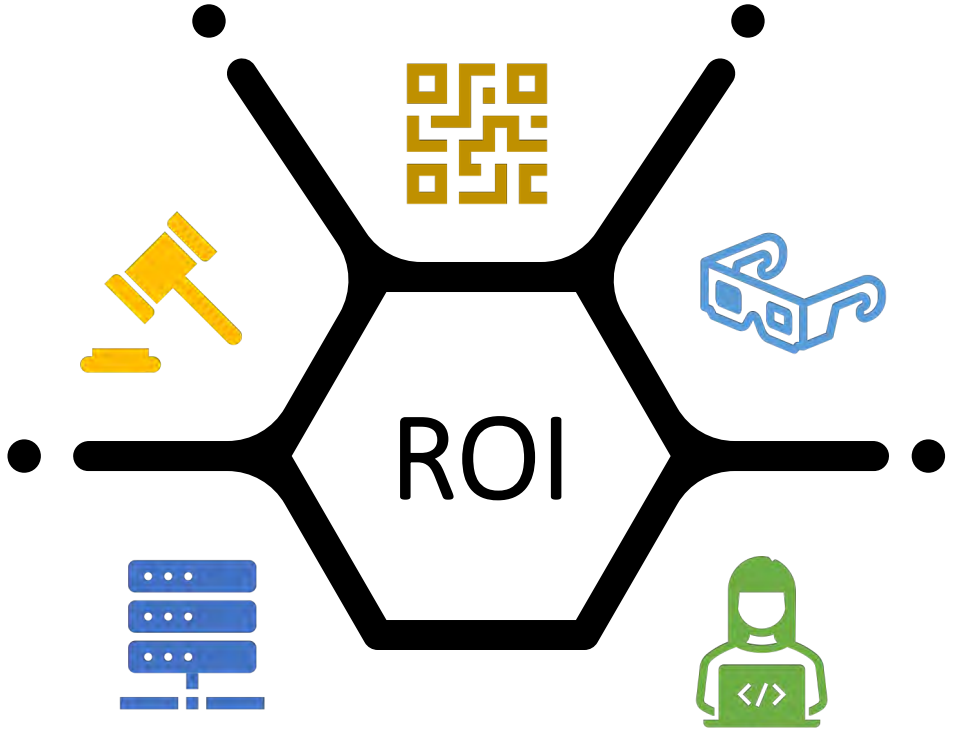
Return on Innovation is a metric used by CorePlus to understand the impact of innovation on the organization's measured operational performance, human resources development, life-enhancement for our staff, and the attainment of its mission and purpose.

Operational ROI

Safety (TPID)

Decrease Liability

Digital Workflow



Infrastructure & Interoperability

21st Century Toolkit

HUMAN RESOURCES ROI

Make a big impact with our professional slides and charts

1 PRACTICE SCALABILITY/ GROWTH

2 PROFESSIONAL GRATIFICATION

3 DEEP THOUGHT TIME

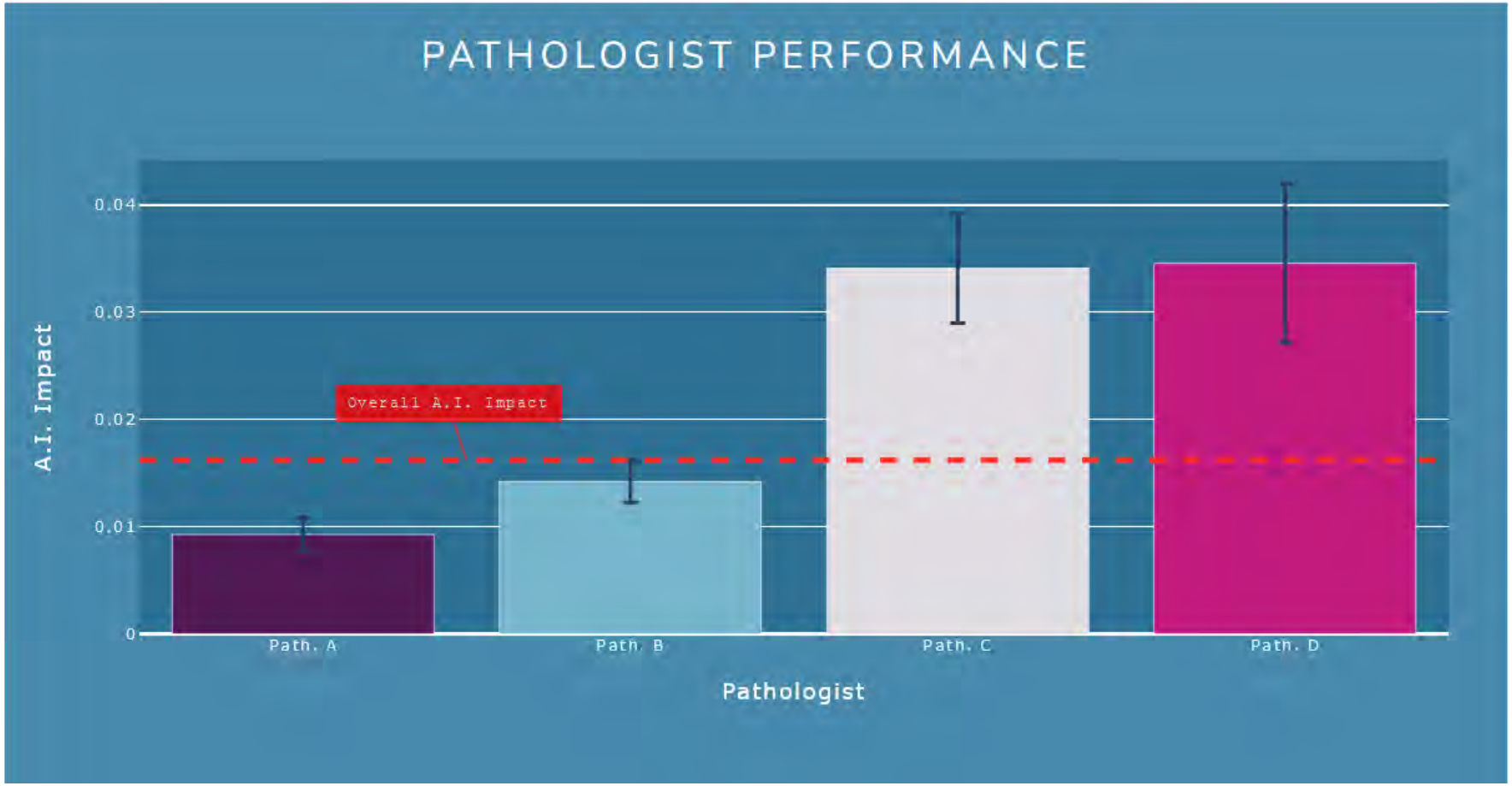
4 COGNITIVE FUEL REDISTRIBUTION

5 NEW SKILLSET ACQUISITION

6 TRANSFERRABLE SKILLSET

7 ERGONOMICS

Prostate AI Impact



9310

Total Cases

365,061

Tissue Sections

74

Men would not know they have cancer

THE VALUE IN ARTIFICIAL INTELLIGENCE

QALY = Quality Adjusted Life Years

1

~17,500 Fewer Undiagnosed Cases

Increased cancer detection

2

0.15 QALY Gained per Biopsy

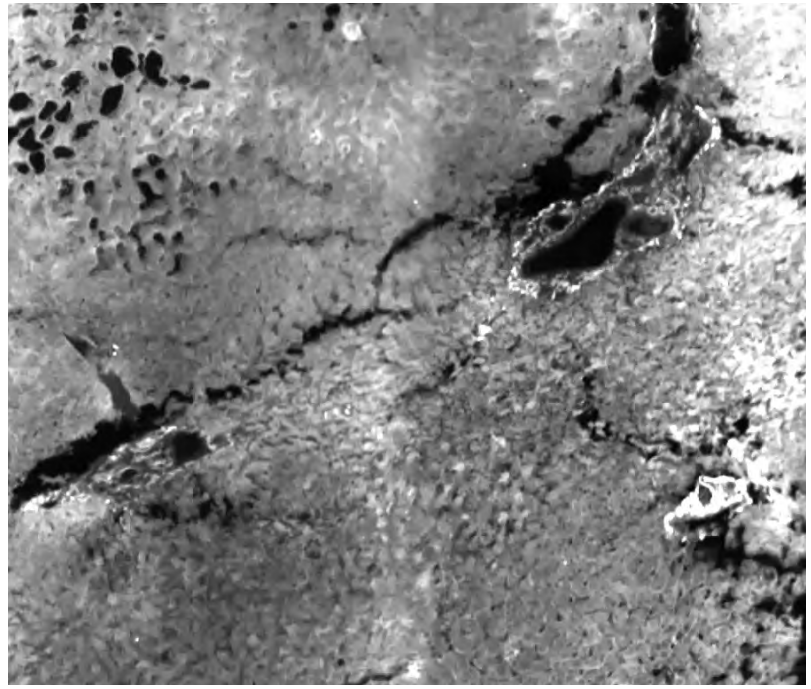
Higher quality of life

3

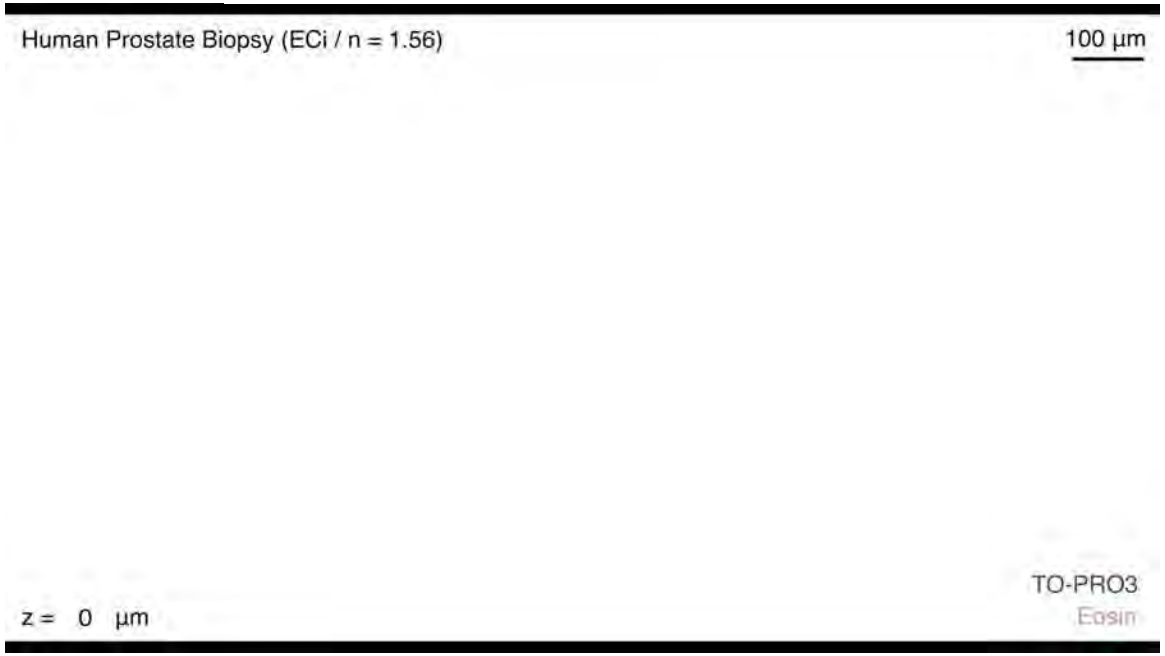
$7,500 More Value per Test

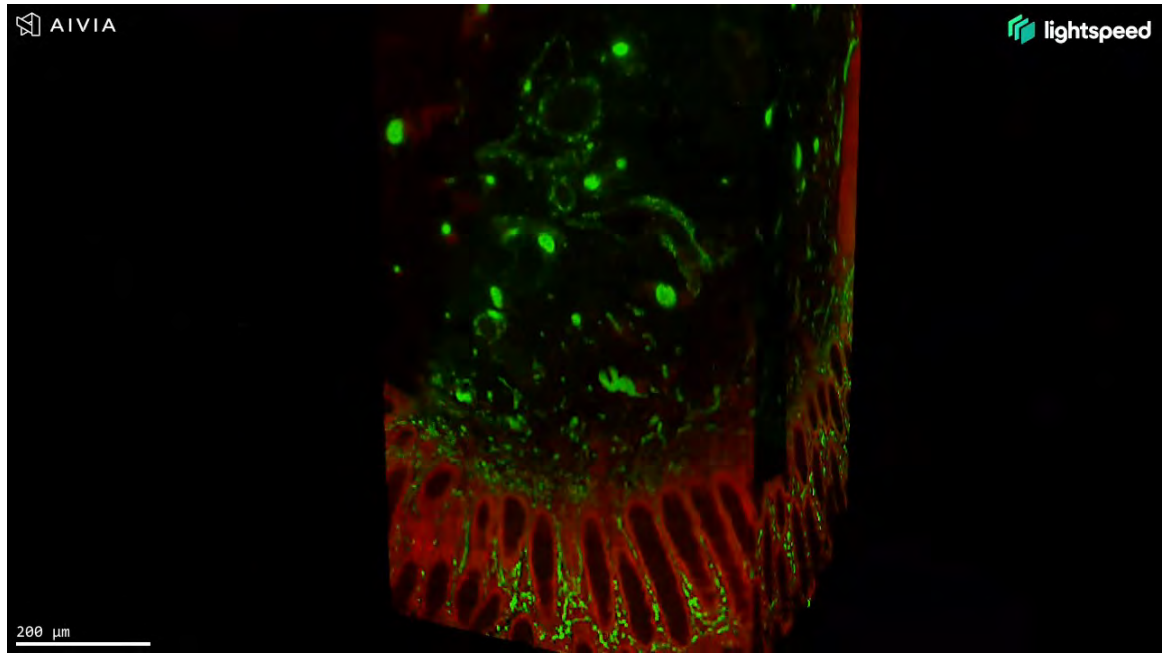
7.5% Increase in Value

… one more thing…



ALPENGLOW
BIOSCIENCES





"Once an AI technology has been validated and demonstrated to improve outcomes (and assuming the existence of high-quality evidence to support this), it raises the question of whether it would be unethical not to apply it in clinical practice."

Jackson B., et al, The Ethics of Artificial Intelligence in Pathology and Laboratory Medicine: Principles and Practice
Academic Pathology: Volume 8 2021, DOI: 10.1177/2374289521990784

CORE PLUS

THANK YOU!

GET IN TOUCH

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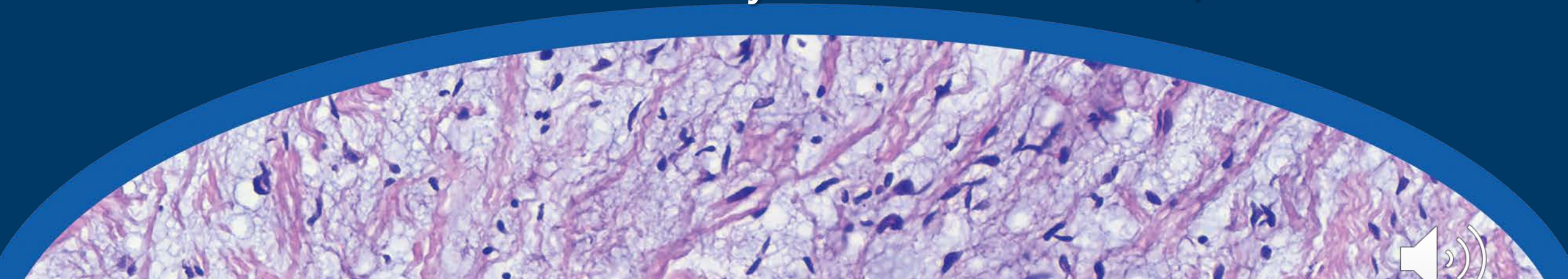
What We Can Learn From Other Technologies

P. "Mickey" Williams, Ph.D.
Director, Molecular Characterization Laboratory
Frederick National Laboratory for Cancer Research, NIH



Frederick National Laboratory for Cancer Research

Development, Validation and Harmonization of NGS Assays

Experiences from NCI-MATCH

P. Mickey Williams, PhD

Director of the Molecular Characterization Lab,
Frederick National Laboratory for Cancer Research

Jyune 27-28, 2023

MOCHA

SPONSORED BY THE NATIONAL CANCER INSTITUTE

Talk Overview

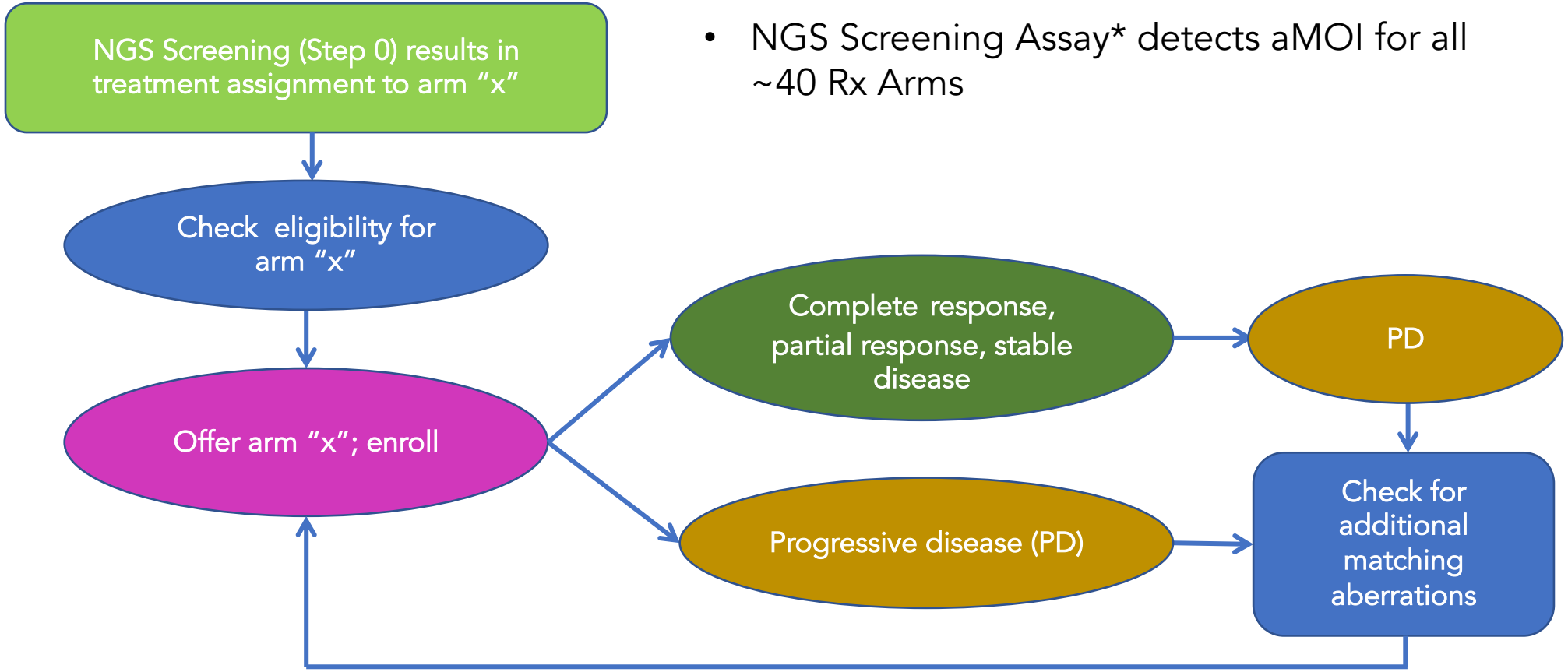
- High level overview of assay development & validation for the NCI-MATCH Trial
  - The NCI-MATCH Trial concept was developed in 2014-15
  - The trial launched prior to clinical NGS becoming a “routine” part of patient management AND prior to FDA clearance or approval of any NGS test
  - Concern about impact of uncontrolled pre-analytics; resulted in provision SOPs for core needle biopsy collection, shipping kits containing specimen vessels (formalin filled jars), overnight shipment to a pre-analytic processing lab (central specimen processing, blocking, macro-dissection and extraction)
  - Concern about cross assay & cross laboratory consistency of NGS, resulted in development of a central lab network, single assay platform and central data analysis pipeline
  - In my mind these concerns parallel similar concerns in the current state of AI driven digital pathology
- Finish with a snapshot of some community wide efforts, intending to ensure accuracy and consistency of critical clinical assays

Precision Medicine in Cancer Treatment

- Precision medicine is the tailoring of treatment for each individual based on molecular abnormalities found in tumors rather than the type of cancer
- Example:
  - *BRAFV600E* melanoma responds to BRAF inhibitors or BRAF inhibitors combined with MEK inhibitors but colorectal cancers with the same mutations appear not to respond
- We need to know more about which tumors will respond to agents targeted to "driver" mutations
- Most driver mutations are relatively rare across all tumor histologies
- A multi-arm treatment, precision medicine master screening protocol was developed

NCI-MATCH Schema (Single-Arm Phase II)

NCI-MATCH was the largest Precision Medicine Trial encompassing over 1,400 enrollment sites and 40 different treatment arms contained in 1 Master Protocol



- NGS Screening Assay* detects aMOI for all ~40 Rx Arms

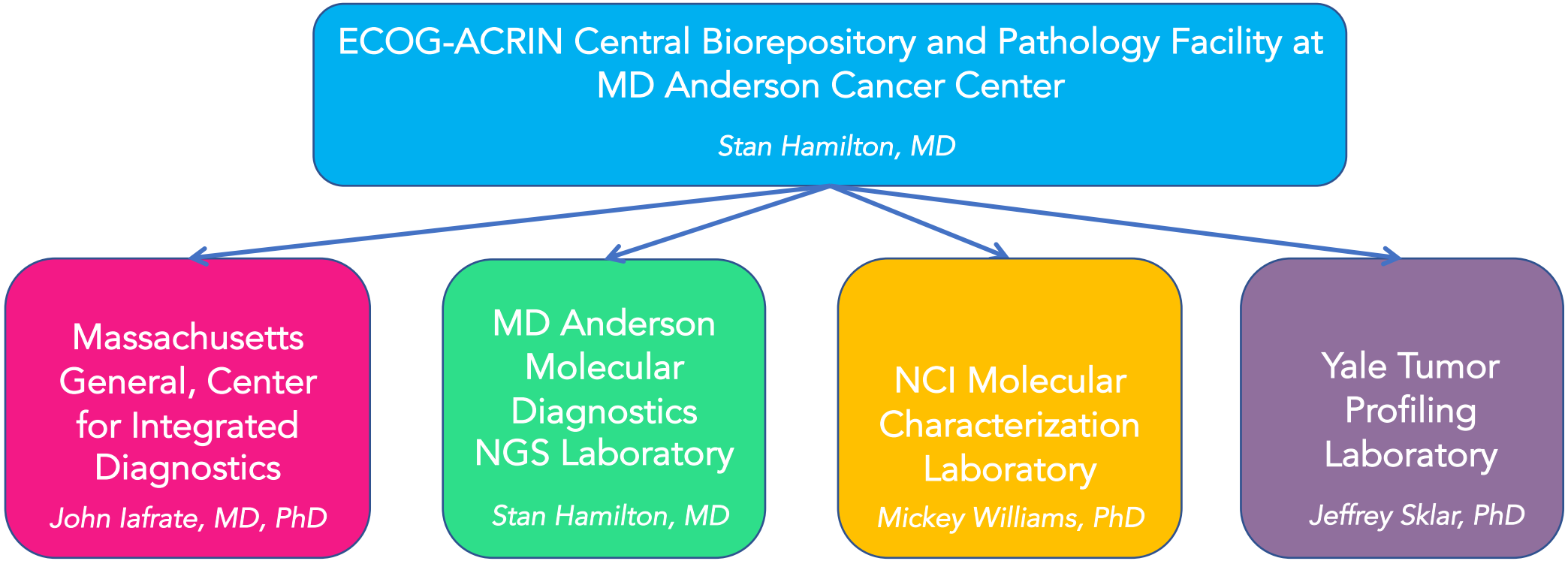
NGS Assay Requirements

- Required multi-analyte assay for screening for many treatment actionable somatic mutations
- Minimal tissue and nucleic acid input
  - Core needle biopsies, shipped overnight in formalin
- Acceptable performance with FFPET from all solid tumor histologies
- Cost efficiency for small specimen batch size
- Goal of 15-day turn-around-time
- Assay performance requires high specificity, acceptable sensitivity and reproducibility across labs, staff and instruments
- Based on the early state of clinical NGS, decision was made to use a central lab network, using the same analytically validated and harmonized NGS platform
- Input from many led to an assay platform selection; Oncomine Cancer Panel v1
- Details along with required analytical performance metrics were documented in "The Assay Intended Use Statement" and "Validation Plan"

Define the Assay System

- The assay system detailed via SOPs:
  - Sample acquisition
  - Shipment kits/instructions
  - Pre-analytic processing
  - Nucleic acid extraction
  - Shipment to assay laboratories
  - Receipt and accessioning
  - Assay protocols:
    - Reagents
    - Instruments
    - Assay controls
    - Assay QC acceptance criteria
  - Harmonized central data analysis and clinical report template

A Central Laboratory Network was Established



Tumor testing using validated single platform across central lab network of CLIA certified clinical laboratories

Pre-validation Activities and Analytical Validation(s)

- Laboratory groups met weekly to generate harmonized SOPs, assess pre-validation feasibility data and make tweaks, lock SOPs and data analysis pipeline
- Pre-submission meetings with CDRH to discuss “Intended Use” and “Validation Plan”
  - Intent to enroll patients across all solid tumors and lymphoma, patients will have progressed after treatment with standard of care
  - The use of NGS for patient enrollment screening and treatment assignment led to a nonsignificant risk assessment, requiring an Abbreviated IDE operation
  - The meetings proved very helpful input prior to moving into Analytical Validation
    - Need to demonstrate accurate performance in potentially difficult tissues (brain, pancreas, bone, blood, etc.)
    - Demonstration of harmonization
- All lab staff trained together with locked SOPs prior to initiating Analytical Validation
- Trained staff performed independent analytical validations in their respective labs

NCI-MATCH Assay Proved Fit for Intended Use

"…the assay tailored for this trial is highly sensitive for detecting genetic mutations from a variety of tumor tissue and, for the first time, has been reproduced with accuracy by multiple clinical laboratories, laying the groundwork for future clinical utility."

Chih-Jian Lih et al, *The Journal of Molecular Diagnostics,* Vol 19, Issue 2, March 2017

Evolution of NCI-MATCH NGS Assays

- During the course of NCI-MATCH several NGS assays received FDA approval/clearance
- Routine NGS testing with both FDA approved/cleared and LDT's became more accessible
- Insurance coverage was more reliable for certain tests/indications
- Several NCI-MATCH Treatment Arms remained open due to low aMOI hit-rate
- A designated lab network was established to continue screening
  - 29 labs were vetted via assay validation reports & a blinded concordance test
  - Central lab verification was required for first pass clinical outcome assessment

Community Efforts Addressing Assay Accuracy and Comparability

- FOCR TMB Harmonization Project
- FOCR ctMONITOR
- FOCR HRD Harmonization
- FNIH QCM for Predictive ctDNA Assays
- FNIH AML MRD Harmonization
- MDIC Somatic Reference Samples
- AMP
- CAP
- Is there a need for AI Digital Pathology “Reference Materials” and “Cross Assay/Lab Harmonization” efforts?

Thanks for Your Attention!

- AND THANKS TO:
- The PI's of NCI-MATCH and Laboratory and Supporting Staff
- All the enrollment site PIs and Essential site staff
- Most Importantly, All the PATIENTS and their FAMILIES

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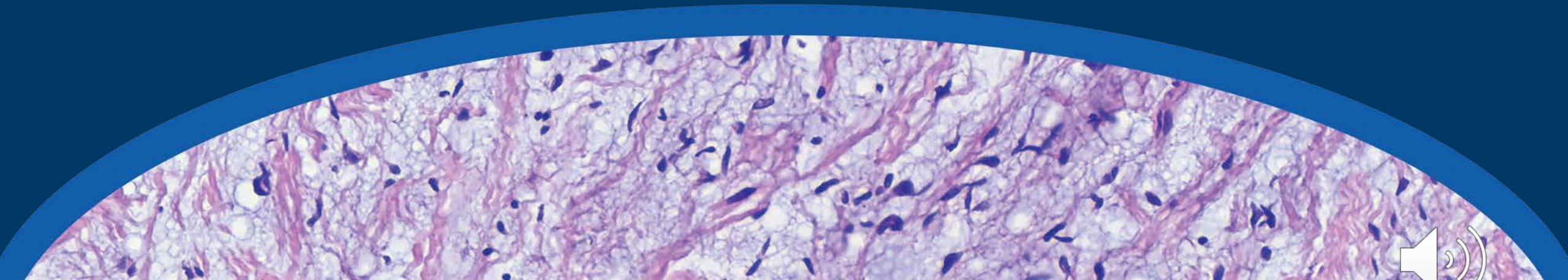
Pathology Innovation Collaborative Community (PIcc)
Annual Meeting 2023

Pre-Analytics & APPIA

Joshua Greenlee, MBA

Senior Product Manager & Laboratory Workflow/ Productivity Strategist

Sakura Finetek USA, Inc



APPIA

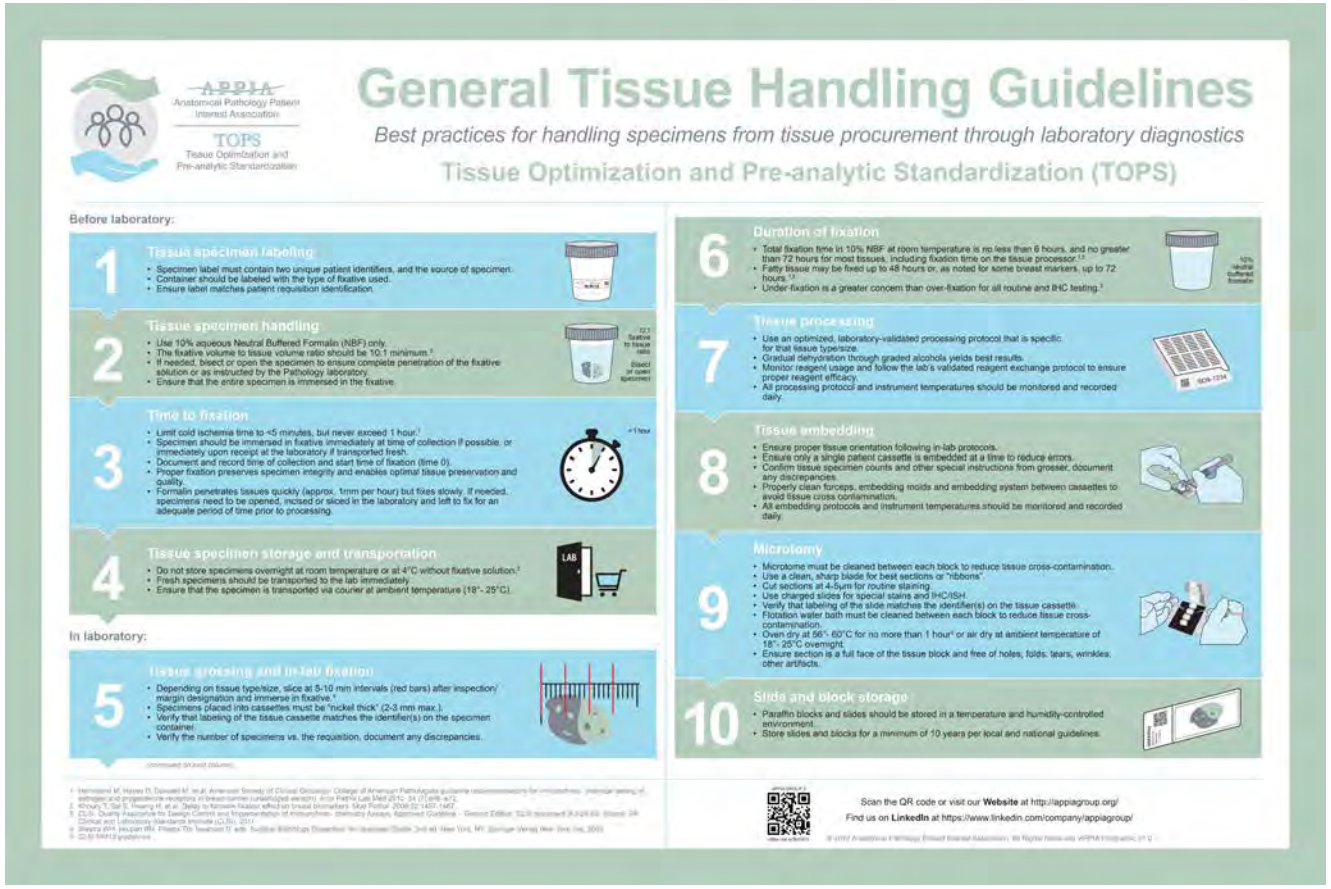
Anatomical Pathology Patient Interest Association

- The Anatomical Pathology Patient Interest Association (APPIA) was founded and incorporated in 2016.
- APPIA is an organization formed by industry partners actively engaged across all phases of anatomical pathology from specimen acquisition, preparation, and examination.
- APPIA's mission is cooperative industry partners dedicated to advancing anatomical pathology to benefit patient care by advocating and fostering quality, education, and best practices.
- APPIA is a resource to those who contribute to quality patient outcomes

APPIA
Anatomical Pathology Patient Interest Association

TOPS
Tissue Optimization and Pre-analytic Standardization

- The Tissue Optimization and Pre-analytic Standardization (TOPS) program was APPIA's first education initiative.
- TOPS provides best practice suggestions and guidelines on tissue handling and pre-analytics collected from notable resources in the industry.
- Guidelines are displayed in an easy-to-read infographic for laboratories and education programs.
- Training materials are available focusing on audiences from laboratory personnel to nurses and surgeons.
- Presentations have been given at the National Society of Histotechnology and other society meetings to support continuing education.



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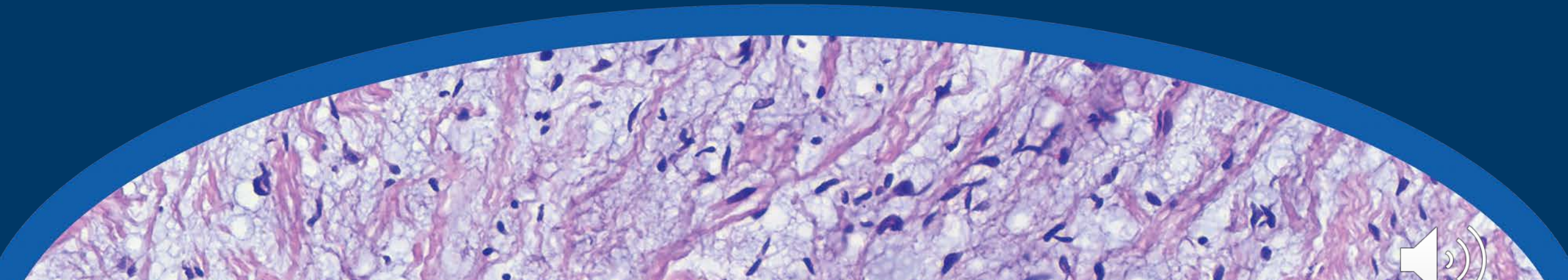
Panel Discussion/ Q&A

Moderated by: Mark Stewart



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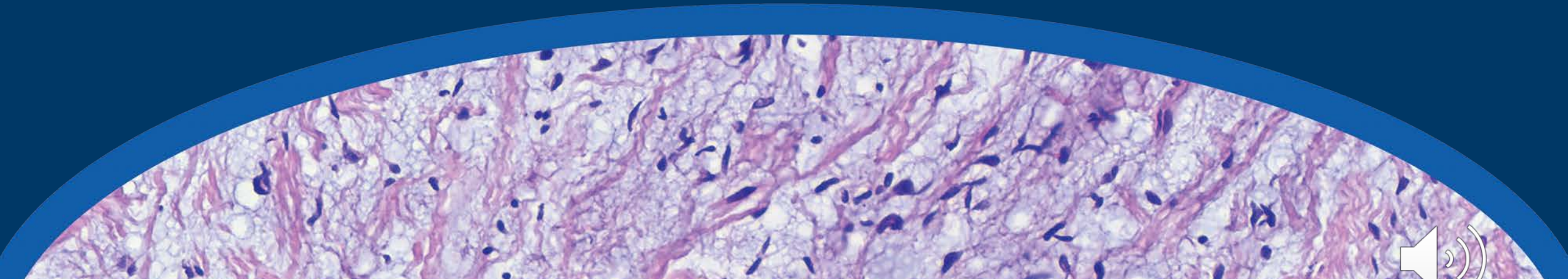
Lunch Break

Sponsored by:

Roche



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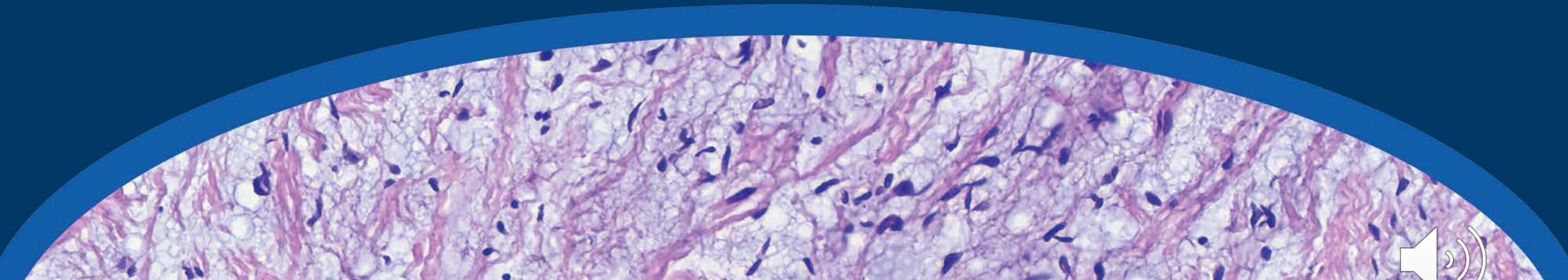
Key Note 1:
A Vision for Digital Pathology and AI

Thomas Fuchs

Founder and Chief Scientist, Paige



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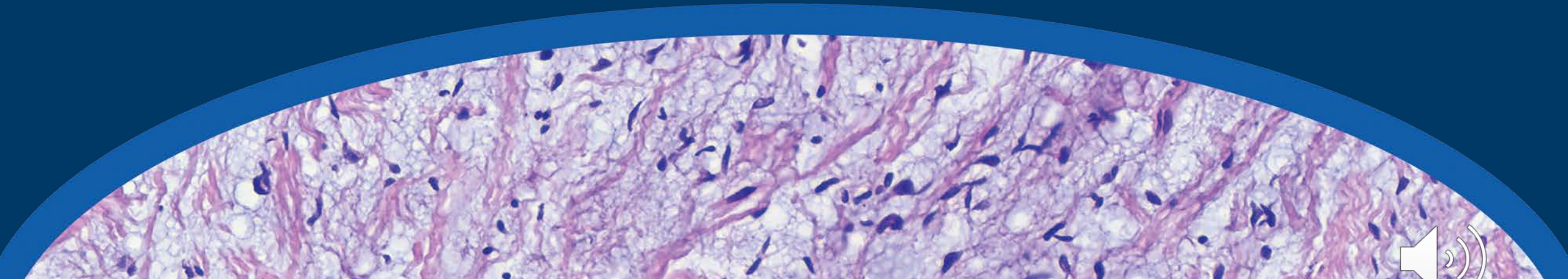
The Journey to Precision Pathology

Mariano de Socarraz
CEO, CorePlus



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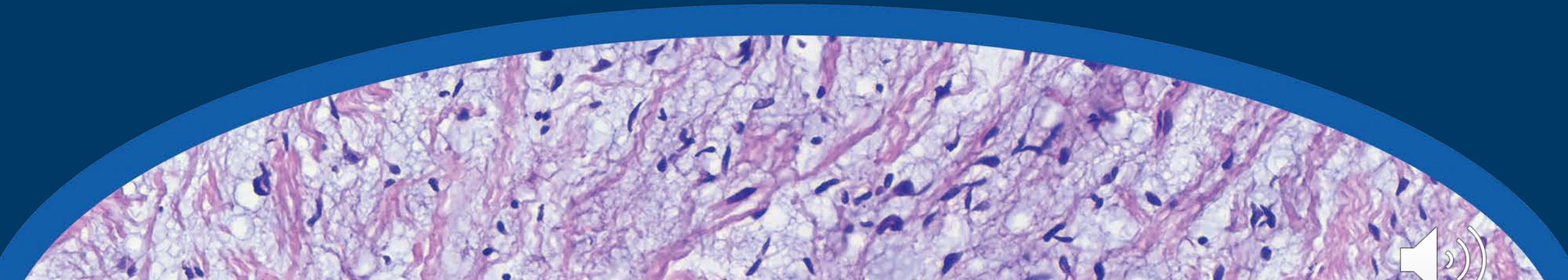
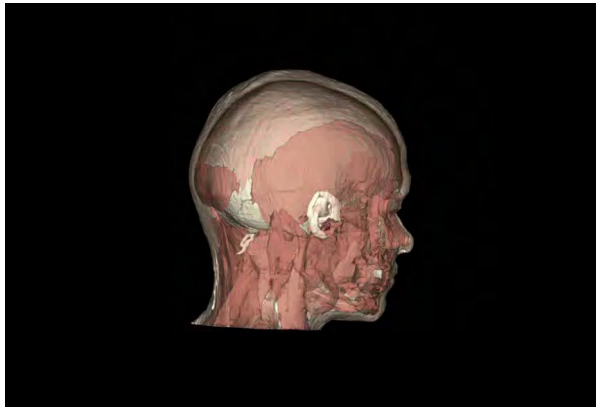
Session 3:
FDA Research at OSEL & Update on PCCP from DHCoE

Moderated by:
Ed Margerrison





U.S. FOOD & DRUG ADMINISTRATION

Accelerating Medical Device Innovation with Regulatory Science Tools

Office of Science and Engineering Labs (OSEL)

Center for Devices and Radiological Health (CDRH)

U.S. Food and Drug Administration (FDA)

CDRH's Office of Science and Engineering Labs

165
FEDERAL EMPLOYEES
Up to 180 visiting scientists

140 Research Projects
In 20 Program Areas

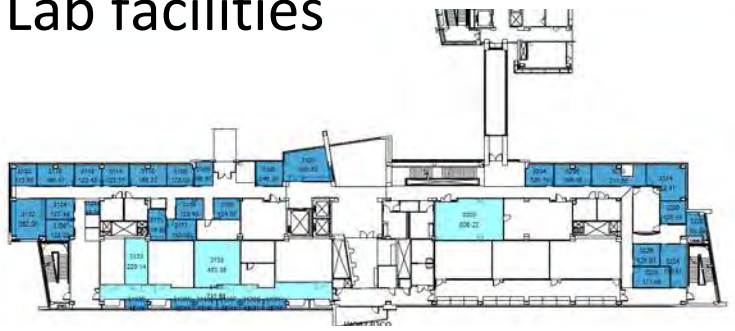
400/year
Peer-reviewed presentations, articles, and other public disclosures

> 3,000/year
Premarket regulatory reviews

75
Standards and conformity assessment committees

70%
Staff with a graduate degree

55,000 ft²
Lab facilities



OSEL Regulatory Science Program Areas

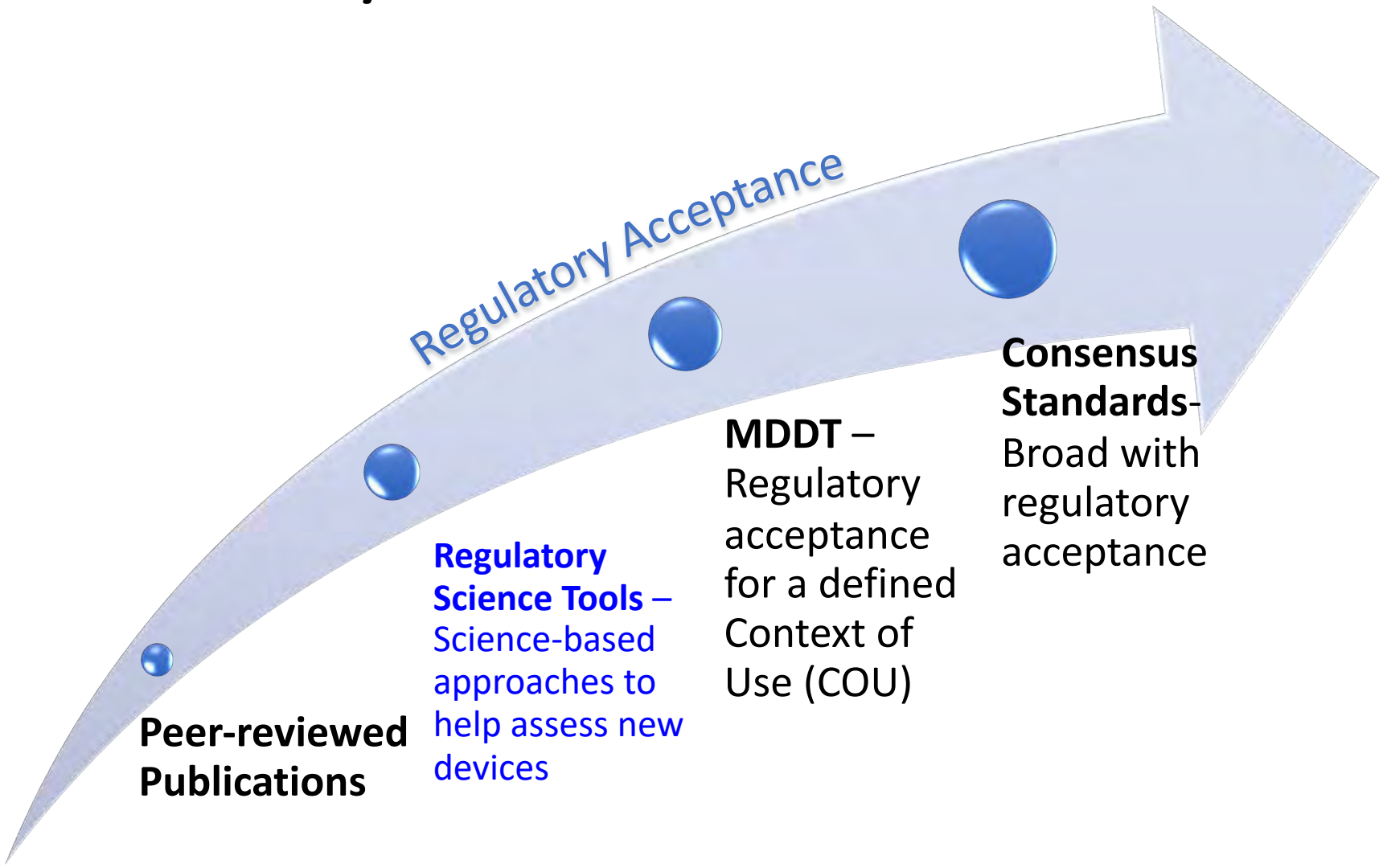
- Advanced Patient Monitoring and Control
- AR/VR - extended reality (XR)
- Artificial Intelligence (AI) / Machine Learning
- Biocompatibility/Toxicology
- Cardiovascular
- Computer Modeling and Simulation
- Digital Pathology
- Electromagnetic and Electrical Safety
- Emergency Preparedness
- Human Device Interaction
- Materials Performance
- Medical Imaging and Diagnostics
- Microfluidics
- ~~Nanotechnology~~
- Neurology
- Ophthalmology
- Orthopedic Devices and Additive Manufacturing
- Post Market Signal Response
- Sterility and Infection Control
- Therapeutic Ultrasound

OSEL's Focus on Regulatory Science Tools

- OSEL develops Regulatory Science Tools (RSTs), which are innovative, peer-reviewed approach or methodology to help assess the safety or effectiveness of a medical device or emerging technology
  - Brought into the public domain as early as possible before standards may be available

- We have identified a number of types
  - Virtual and physical phantoms
  - CM&S and related datasets
  - Lab methodologies
  - Best practices

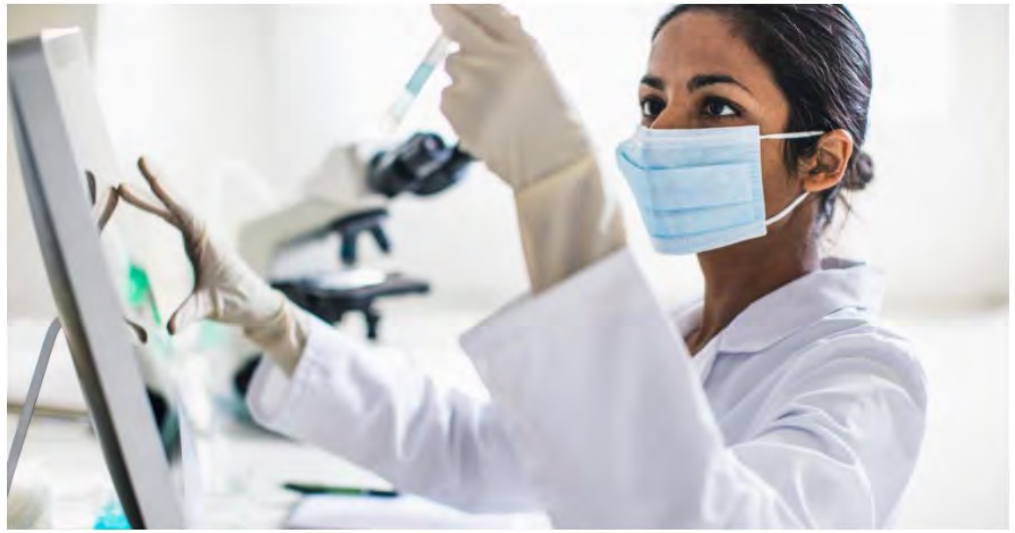
The Family of Device Assessment Tools



More than 140 RSTs published

Catalog of Regulatory Science Tools to Help Assess New Medical Devices

Share | Tweet | Linkedin | Email | Print



https://www.fda.gov/medical-devices/science-and-research-medical-devices/catalog-regulatory-science-tools-help-assess-new-medical-devices

Phantoms

Search: Export Excel

Phantom Name	Description	Type	Areas	Reference
3D printed phantom material and design with tissue-relevant Raman signature	A tool for performing Raman spectroscopy measurements on a well-characterized 3D printed sample that has tissue-simulating	Physical	Medical imaging	Article
Blood Mimicking Fluid for High I Focused Ultrasound				
Digital models of retinal vascula a clinical fundus camera image				
Microcalcification templates				
Nanostructured Virus-simulating Evaluating Optical Biosensing M				
Parchment breast phantom				
Phantom for assessing performa infrared hematoma detectors				

Methods

Search: Export Excel

Method Name	Description	Type	Areas	Reference
Approach to Validate Simulation-Based Distributions	A method to validate simulation data using meaningful agreement metrics which offer a natural way to visually localize	Lab Method	Credibility assessment in modeling	Article
Assessing texture reproduction of camera-phone-based medical devices				
Automated Rapid Accelerated Aging (Automated RAA)				
Battery of image quality test methods for evaluation of fluorescence imaging systems				
Benchmark problems for verifying cardiac electrophysiological models				
Confocal Laser Methods (CLM) for quantitative evaluation of dioptric power characteristics of intraocular lens (IOL) implants				
Considerations for Accelerated Wear Durability Testing for Transcatheter Heart Valves				

Computational Models and Simulations

Search: Export Excel

Model or Simulation Name	Description	Type	Areas	Reference
Benchmark Datasets for Validation of Computational Fluid Dynamics Models	Experimental datasets of velocity and pressure on simplified medical devices used to validate computational fluid dynamic (CFD) models	Dataset	Cardiovascular	Wiki
Benchmark PIV Dataset for Laminar Flow in an Anatomically Realistic IVC	Velocity and hemolysis datasets to improve the predictive capability of CFD simulations in the evaluation of medical devices.	Dataset	Cardiovascular	Article Article
CFD/6DOF Model of Clot Transport and Capture in an IVC Filter	A computer simulation for prediction of the capture efficiency of IVC filters	Model	Cardiovascular	Article Article
CHRIS: Color Hazard and Risk Calculator	Rapid (screening level) risk assessments of color additives in medical devices	Model	Biocompatibility/toxicology Orthopedics	Article
Color Scale Study Data	Color scale study repository for Cardiac CT and Prostrate MRI Studies	Model	Artificial intelligence/machine learning	GitHub
Computational model of the human cardiac action potential	Model and software of the human action potential appropriate for simulating arrhythmia initiation in human hearts	Model	Cardiovascular	Article Code
Computational model of the rabbit cardiac action potential	Parsimonious (reduced complexity) model and software of the rabbit action potential amenable to large scale simulations of arrhythmias	Model	Cardiovascular	Article Code
Computational modeling comparisons of ASTM F2182 test	Technical considerations when using the modeling analog of the ASTM F2182	Model	Electromagnetic and electrical safety	Article

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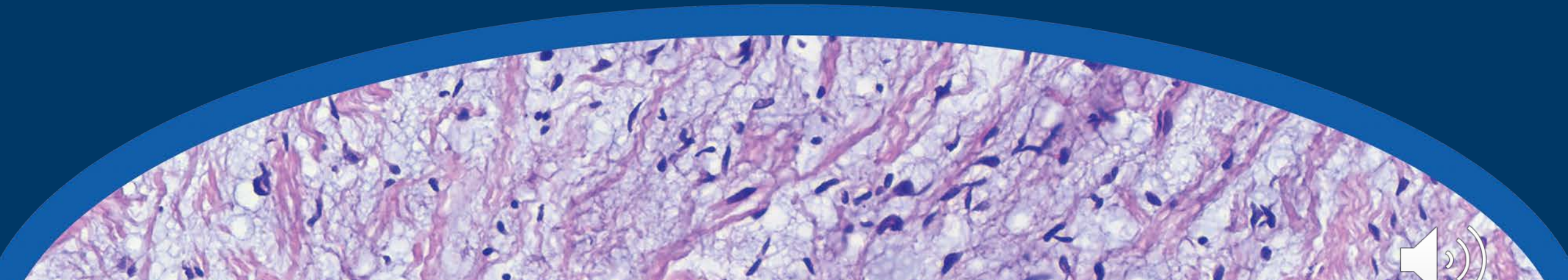
FDA Talk 2: Regulatory Science Projects In OSEL's Digital Pathology Program

Brandon Gallas
OSEL/CDRH



Regulatory Science Projects in OSEL's Digital Pathology Program

Brandon D. Gallas

FDA liaison to PIcc!

Division of Imaging, Diagnostics, Software Reliability (DIDSR)

Office of Science and Engineering Laboratories (OSEL)

Center for Devices and Radiological Health (CDRH)

U.S. Food and Drug Administration (FDA)

Disclaimers

- The mention of commercial products, their sources, or their use in connection with material reported herein is not to be construed as either an actual or implied endorsement of such products by the Department of Health and Human Services. This is a contribution of the U.S. Food and Drug Administration and is not subject to copyright.
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Introduction

- Introduce
  - DIDSR digital pathology program
  - Digital pathology landscape
- Digital pathology gaps and efforts
  - Technical performance
  - Computational pathology
  - Role of the pathologist
- Hidden slides offer more details for Q&A

OSEL Digital Pathology Team

- Anant Agrawal
- Arian Arab
- Aldo Badano
- Kenny Cha




- Wei-Chung Cheng
- Weijie Chen
- Katherine Elfer
- Brandon Gallas



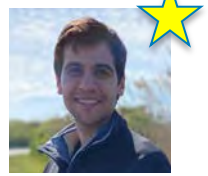

21 Research Fellows
+ 13 Summer Fellows

- Alexej Gossmann
- Seyed Kahaki
- Nicholas Petrick
- Berkman Sahiner
- Ravi Samala
- Frank Samuelson
- Si Wen
- Victor Garcia







OSEL Digital Pathology Team

- **Research projects**
- **Regulatory support**

- Anant Agrawal
- Arian Arab


- Seyed Kahaki

- Wei-Chung Cheng
- Weijie Chen


- Brandon Gallas

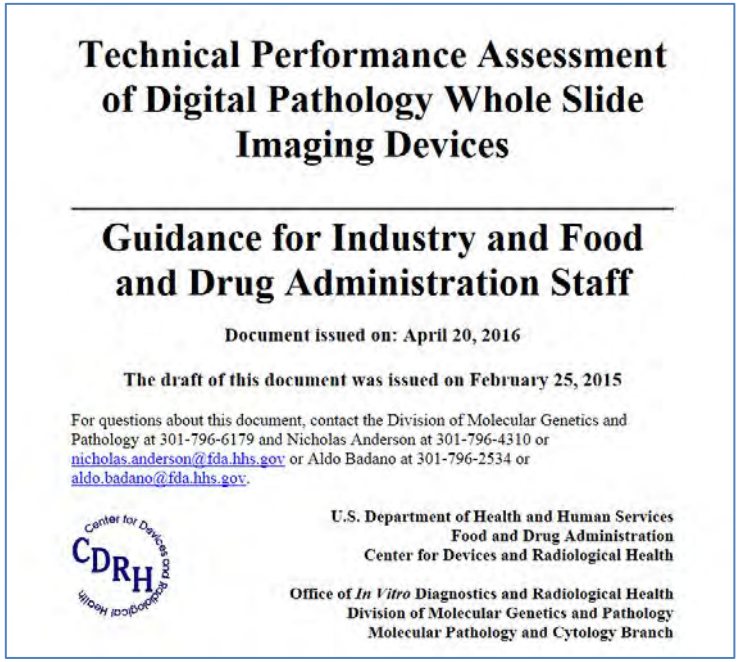
- Si Wen
- Victor Garcia


Regulatory Landscape

- **Technical Performance Assessment**
  - TPA Guidance issued 2016
  - Increase clarity and performance requirements

Digital Pathology is in its infancy (2017)

- Clearance required clinical studies with thousands of cases plus analytical studies and bench tests
- Clearance covered end-to-end system
- Components cleared as separate products
  - PSY: Whole slide imaging system
  - QKQ: Digital pathology image viewing and management software
  - PZZ: Digital Pathology Display



Technical Performance Assessment of Digital Pathology Whole Slide Imaging Devices

Guidance for Industry and Food and Drug Administration Staff

Document issued on: April 20, 2016

The draft of this document was issued on February 25, 2015

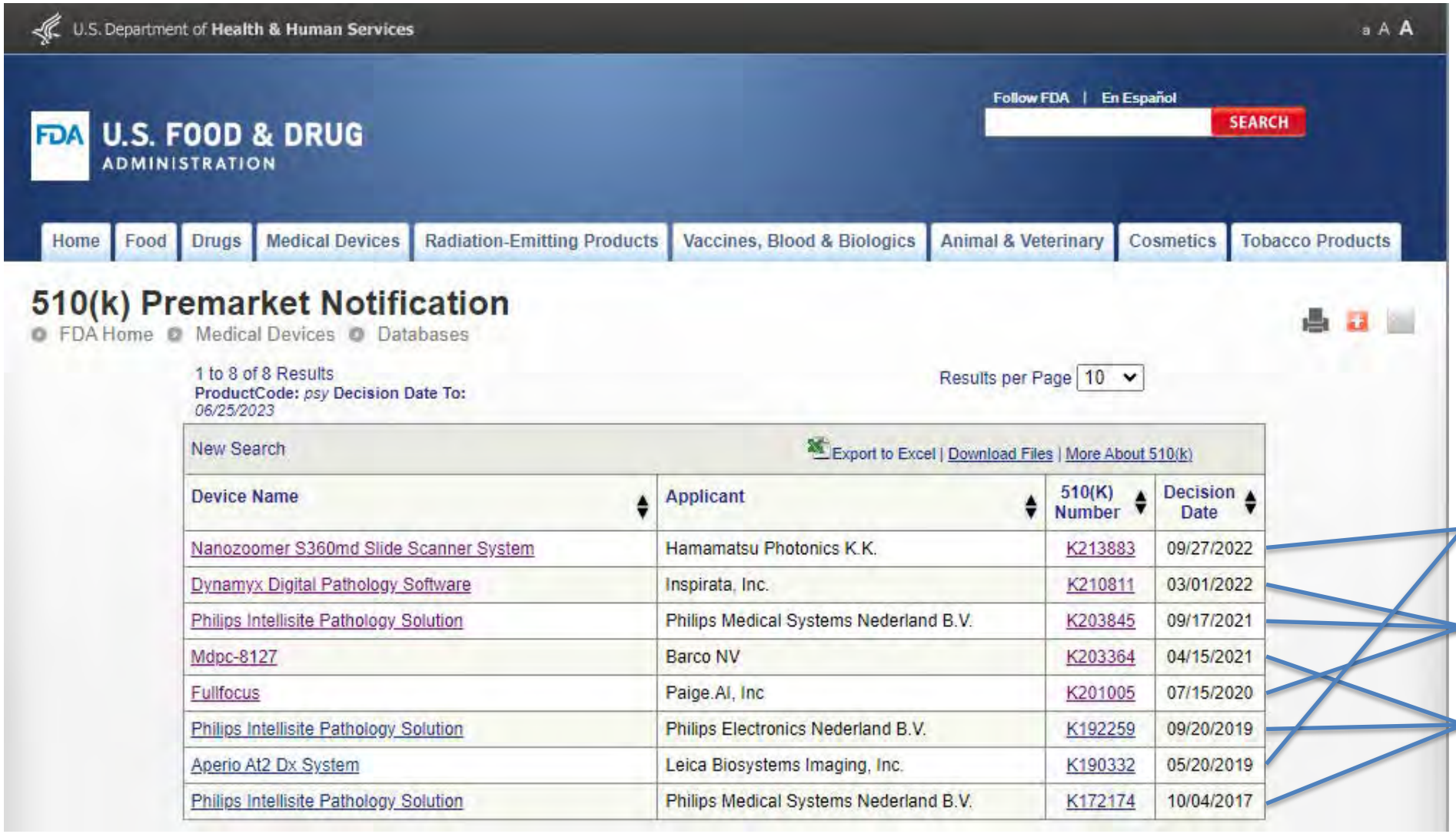
For questions about this document, contact the Division of Molecular Genetics and Pathology at 301-796-6179 and Nicholas Anderson at 301-796-4310 or nicholas.anderson@fda.hhs.gov or Aldo Badano at 301-796-2534 or aldo.badano@fda.hhs.gov.

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Devices and Radiological Health

Office of *In Vitro* Diagnostics and Radiological Health
Division of Molecular Genetics and Pathology
Molecular Pathology and Cytology Branch

510(k) database – PSY

https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpmn/pmn.cfm



PSY: WSI system

QKQ: WSI Viewer

PZZ: WSI Display

Regulatory Landscape

- **Paige Prostate**
  - DEN200080, authorized 09/21/2021
  - first AI-based software for identifying an area of interest on the prostate biopsy image with the highest likelihood of harboring cancer so it can be reviewed further by the pathologist.
  - Analytical device performance
    - Bench testing: standalone performance
    - Precision study: intra-site and inter-site agreement
  - Clinical reader study
    - 16 readers, 190 Ca + 420 benign cases

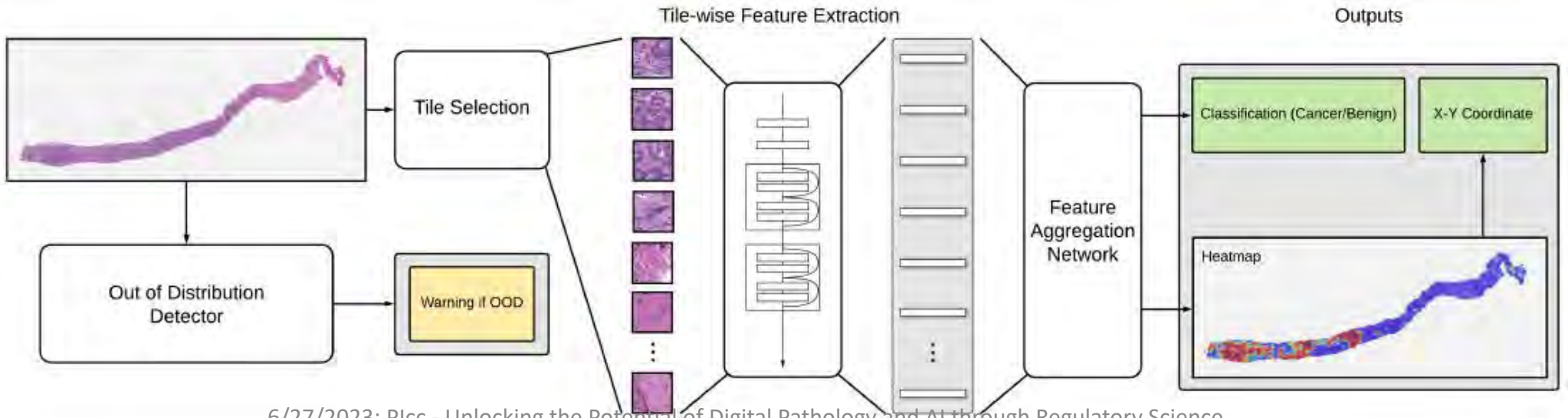
https://www.fda.gov/news-events/press-announcements/fda-authorizes-software-can-help-identify-prostate-cancer

FDA NEWS RELEASE

FDA Authorizes Software that Can Help Identify Prostate Cancer

Share Tweet LinkedIn Email Print

For Immediate Release: September 21, 2021



Hot Off the Press

JMI Journal of Medical Imaging

https://doi.org/10.1117/1.JMI.10.5.051804

REVIEW

Regulatory considerations for medical imaging AI/ML devices in the United States: concepts and challenges

Nicholas Petrick,[a,*] Weijie Chen,[a] Jana G. Delfino,[a] Brandon D. Gallas,[a] Yanna Kang,[b] Daniel Krainak,[b] Berkman Sahiner,[a] and Ravi K. Samala[a]

[a]U.S. Food and Drug Administration, Center for Devices and Radiological Health, Office of Science and Engineering Labs, Silver Spring, Maryland, United States

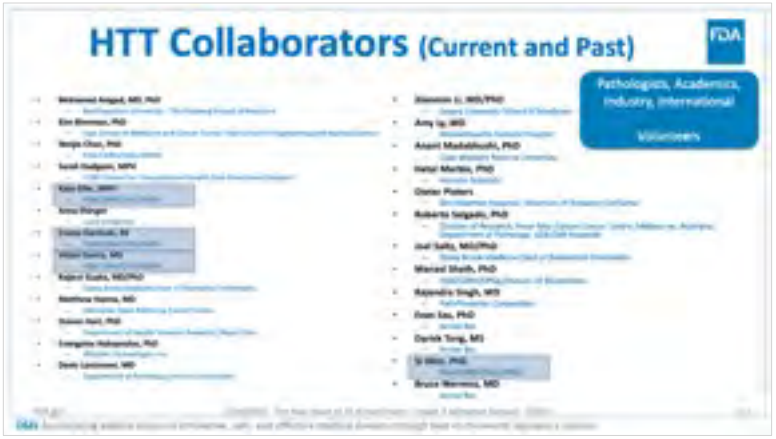
[b]U.S. Food and Drug Administration, Center for Devices and Radiological Health, Office of Product Evaluation and Quality, Silver Spring, Maryland, United States


Collaborations With Academia
Research Collaboration Agreements
Collaborators from academia
HARVARD
EMORY
Yale University


External Collaborations - Standards
DICOM
Activity: WG26 Digital Pathology
Supplement: Sup145, Sup222
IEC TC62/SC62B
Activity: WG51 Evaluation methods for colour displays
Standard: IEC 62563 Medical image display systems
DICOM
IEC
International Electrotechnical Commission


External Collaborations
Pathology Innovation Collaborative Community
Activity: Monthly meetings with exchange and discussions about regulatory pathways, programs, and research
International Immuno-Oncology Working Group
Roberto Salgado's "TILs in Breast Cancer" experts
W.H.O. - IC3R
International Collaboration for Cancer Classification and Research
Share and receive feedback on projects, including clinical expertise
TILS BREAST CANCER
IC R


External Collaborations
Friends of Cancer Research
White Paper: Digital Pathology and AI/ML in Drug Development
BigPicture
A central repository of digital pathology slides to boost the development of artificial intelligence
Imaging Data Commons
Enabling access, visualization, and analysis in multi-modal imaging data science
FRIENDS of CANCER RESEARCH
bigpicture
Imaging Data Commons


HTT Collaborators (Current and Past)
Pathologists, Academics, Industry, International
Volunteers

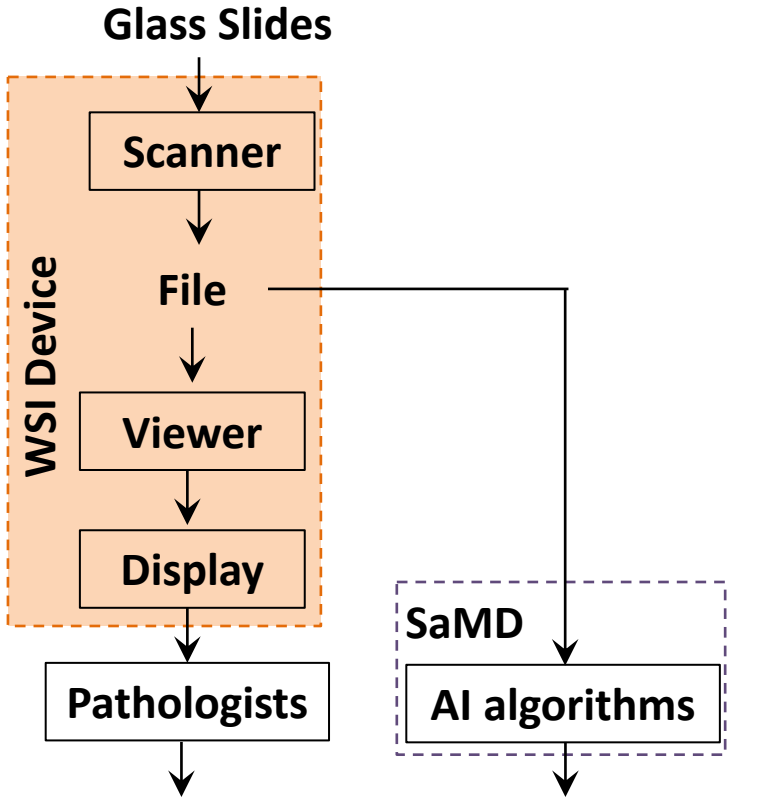
Primary Digital Pathology Research Areas

- Technical performance assessment
- Computational pathology
- Role of the pathologist

Technical Performance Assessment

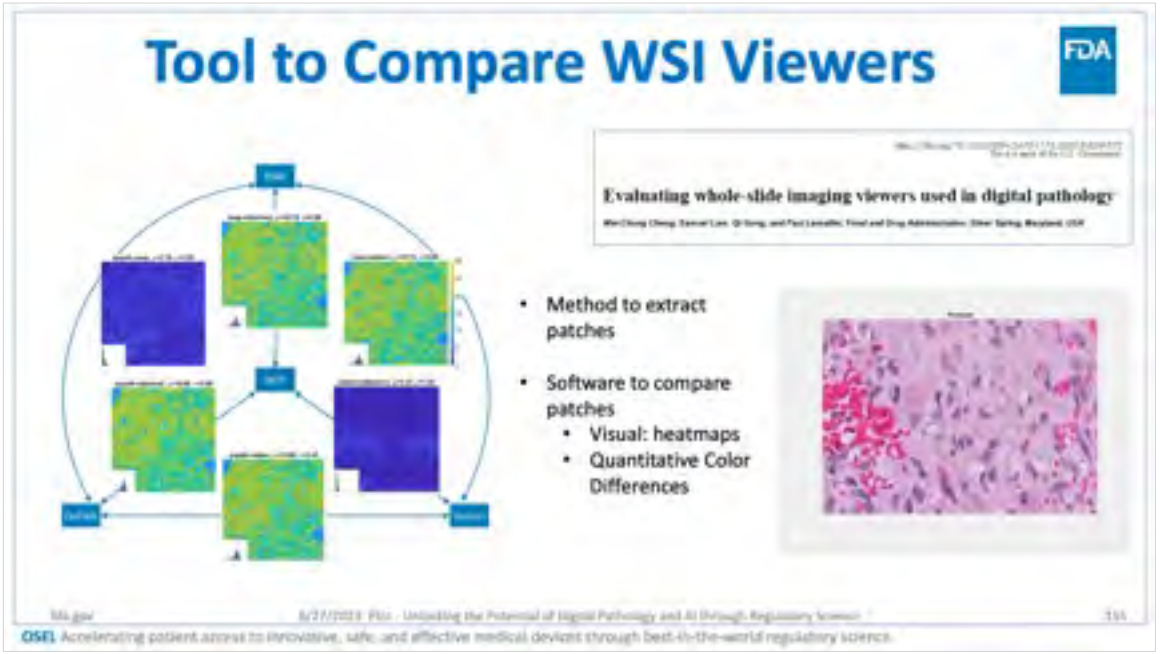
Gaps

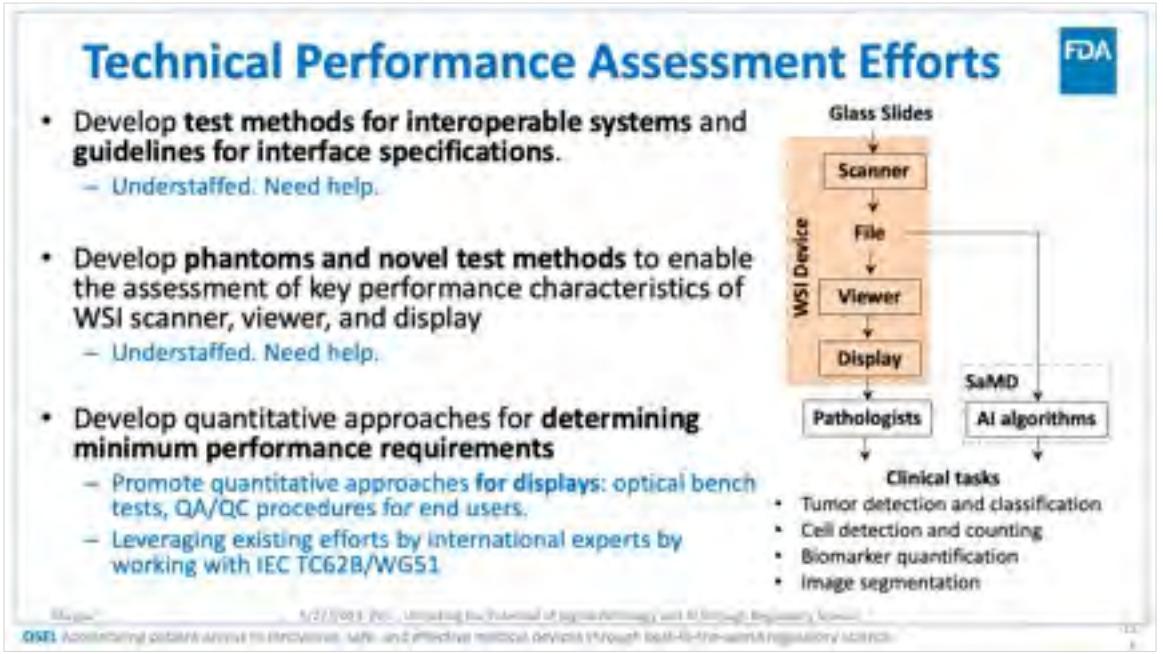
- Need methods to demonstrate interoperability between scanners and viewers
- Need to understand image quality along the pipeline
- Need data demonstrating correlation between technical performance and clinical performance (scanning and display)



Technical Performance Assessment

Wei-Chung Cheng

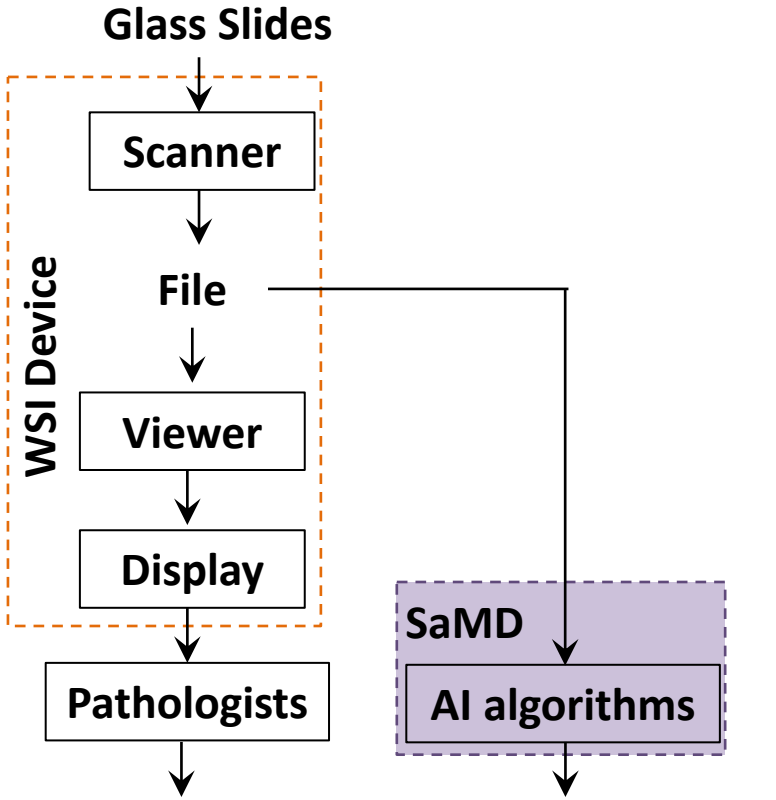




Computational pathology

Gaps

- Need standardized statistical methods to assess AI/ML models
- Need methods to treat noisy and incomplete reference standard labels
- Need to understand generalizability of AI/ML models
  - Sites, slide prep, scanners/imaging
  - Standardized datasets
- Need template to report AI/ML architecture and development elements



Clinical tasks

- Tumor detection and classification
- Cell detection and counting
- Biomarker quantification
- Image segmentation

Computational pathology

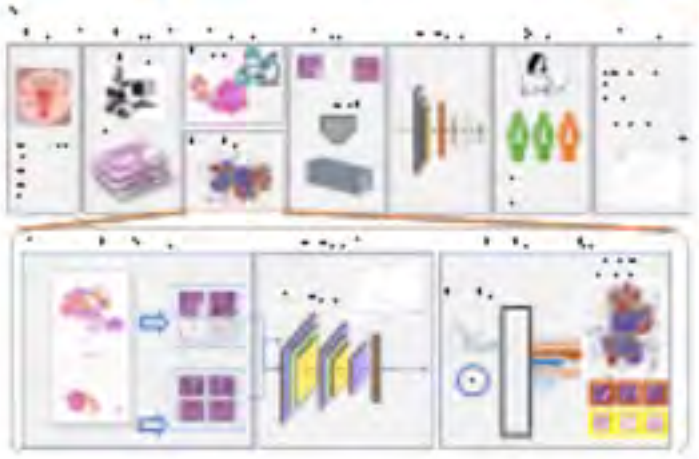
Seyed Kahaki

Weijie Chen

Arian Arab

Use case for regulatory science research

- Histopathology Image Transformation for Predicting the Response to Hormonal Treatment (Endometriosis)
- Data collection:
  - Washington University: 91 slides, two scanners, pathologist annotation, clinical data
  - University of Oklahoma
- Development pipeline and model are tools that permit research on
  - Weakly labeled training data
  - Generalizability across scanners and clinical sites
- Tool: Checklist to report AI/ML architecture and development elements
- Tool: Performance assessment software



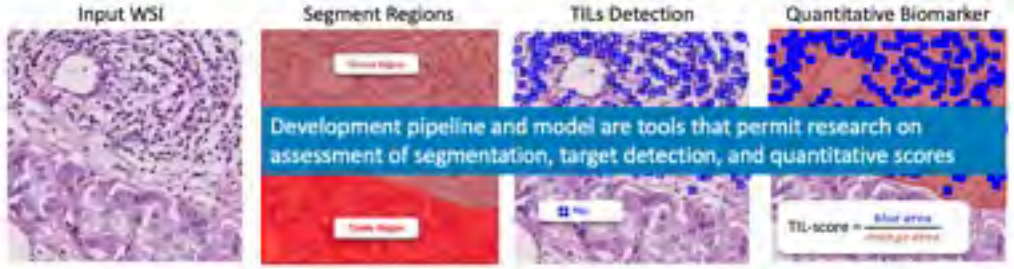
OSEL Accelerating patient access to innovative, safe, and effective medical devices through best-in-the-world regulatory science

Seyed Kahaki

Use case for regulatory science research

TiGER

- Tumor-infiltrating lymphocytes (TILs) are a potentially useful **quantitative biomarker**.
- TiGER: first public challenge to evaluate computer algorithms for the automated assessment of TILs
  - H&E WSIs of HER2+ and triple-negative breast cancer (TNBC) patients.



OSEL Accelerating patient access to innovative, safe, and effective medical devices through best-in-the-world regulatory science

Use case for regulatory science research

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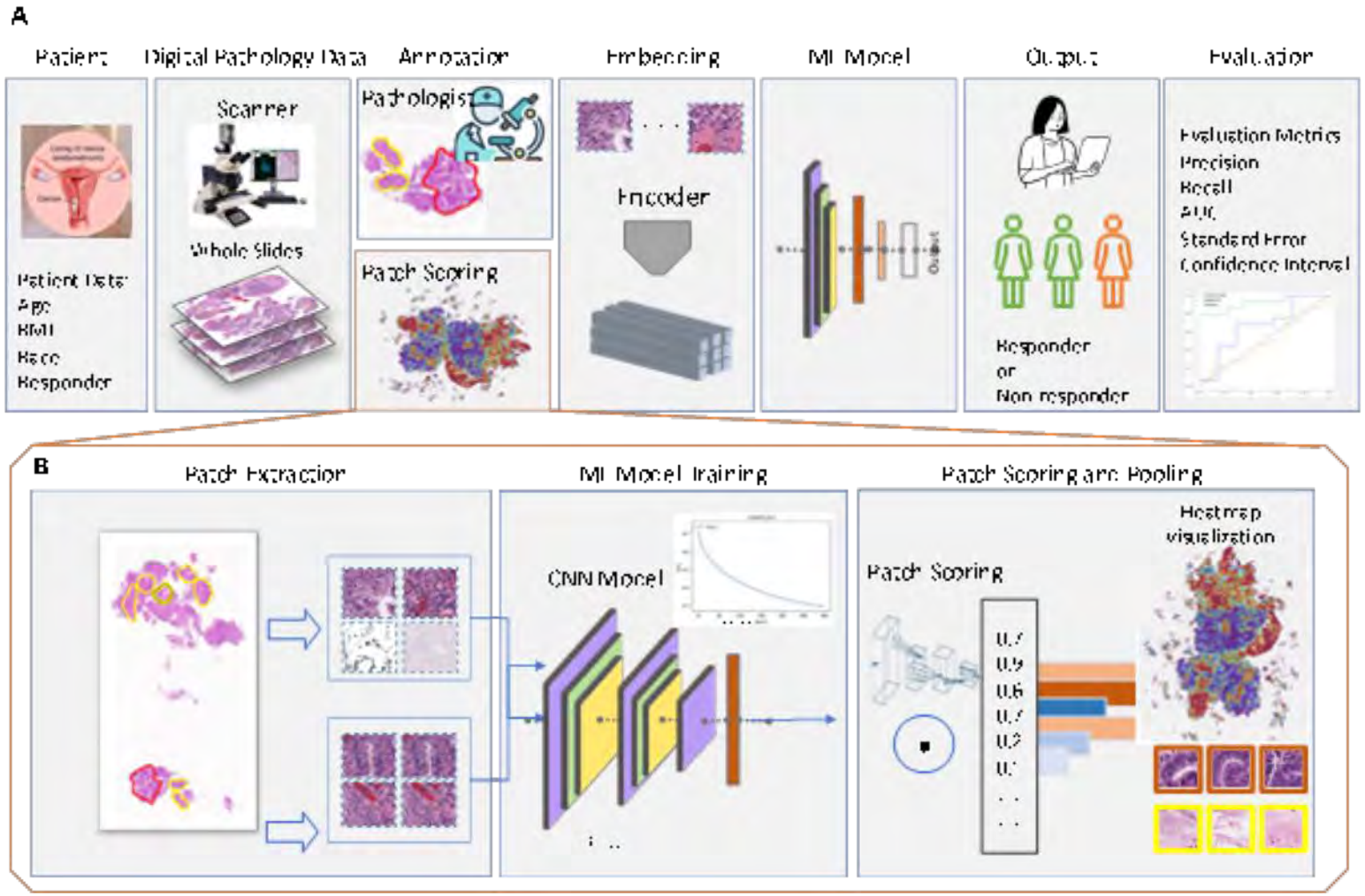
- Tool: Checklist to report AI/ML architecture and development elements
- Tool: Performance assessment software

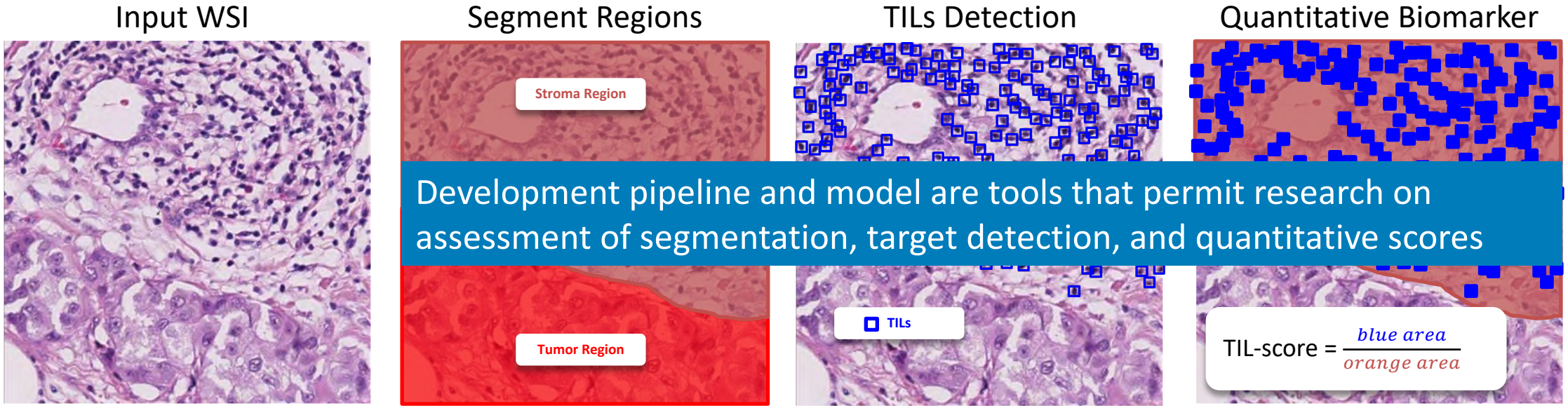


Use case for regulatory science research

TiGER

Tumor InfiltratinG lymphocytes in breast cancER

- Tumor-infiltrating lymphocytes (TILs) are a potentially useful **quantitative biomarker**.
- TiGER: first public challenge to evaluate computer algorithms for the automated assessment of TILs
  - H&E WSIs of HER2+ and triple-negative breast cancer (TNBC) patients.

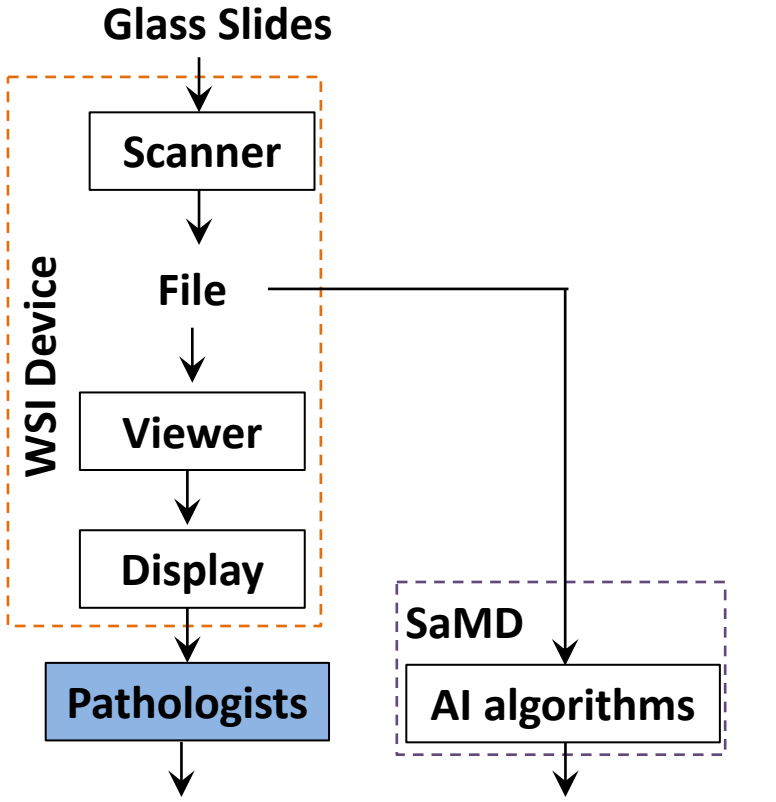


*C. Denkert et al., "Tumour-infiltrating lymphocytes and prognosis in different subtypes of breast cancer: a pooled analysis of 3771 patients treated with neoadjuvant therapy", The Lancet Oncology, 19, 2018, 40-50.

Role of the pathologist

Gaps

- Need methods to account for variability from pathologists
  - End users and reference standard
  - Detection/classification, quantitative measurements, segmentations
- Need template to report methods to determine the reference standard by panel of pathologists
- Need software and performance report templates



High-Throughput Truthing Project (HTT)


Brandon Gallas


Si Wen


Victor Garcia


Kate Elfer

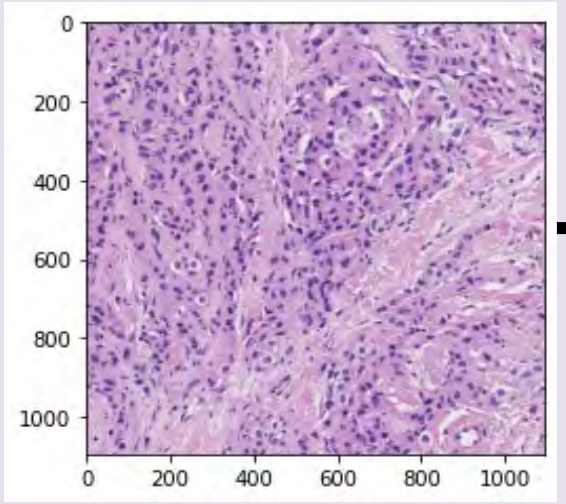

Emma Gardecki


Ryan Birmingham

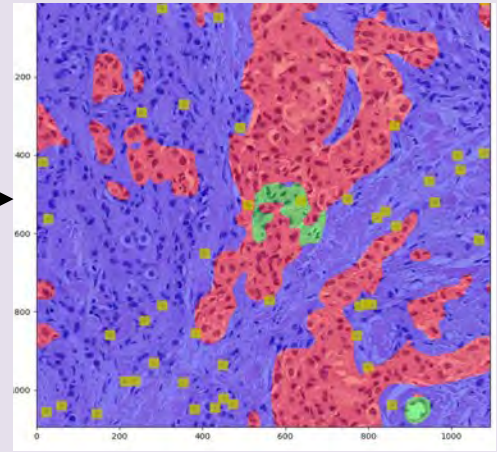
Reference-Standard Dataset

Slides, Images, Pathologist Annotations

Pivotal Study -> Validate AI/ML Models



AI/ML

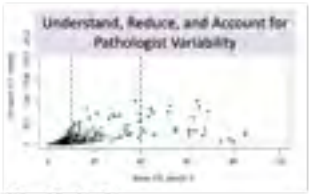


HTT Pivotal Study is LIVE!

- Help get the word out to pathologists that specialize in breast cancer and other stakeholders
  - Contact Brandon.Gallas@fda.hhs.gov

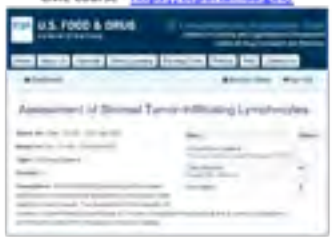
HTT data-collection tools and data

Pilot study: Data and Analysis Methods Publicly Shared

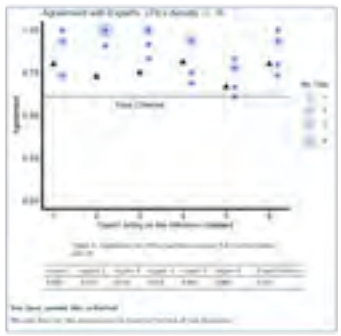


HTT Pathologist Training

CME course - https://reportal.fda.gov/



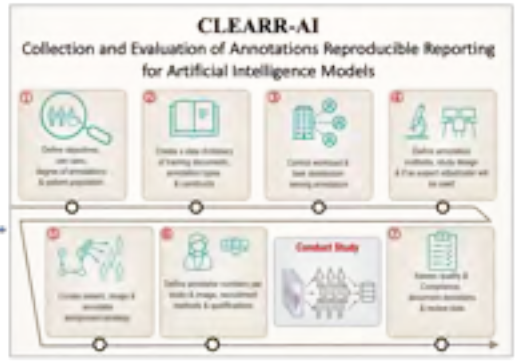
Interactive Training: Feedback and Proficiency Tests



- Each pathologist gets performance report
  - Feedback and proficiency tests
  - Must pass proficiency test to participate in pivotal study
  - Basis for statistical analysis plan
  - Model-expert agreement vs. expert-expert agreement

HTT Protocols

- Clinical metadata paper (chart review)
- ROI selection and batch creation protocols
  - Study population – Clinical population
  - Demographics, disease severity, biomarker range
- CLEARR-AI
  - Demonstrate report with HTT study specifics
- Statistical analysis plan
  - Under development



Summary

- Introduce
  - DIDSR digital pathology program
  - Digital pathology landscape
- Digital pathology gaps and efforts
  - Technical performance
  - Computational pathology
  - Role of the pathologist

- Lots of opportunities to address gaps.
- We are here to discuss and collaborate

- Q&A: Visit hidden slides?

- **What is Regulatory Science?**

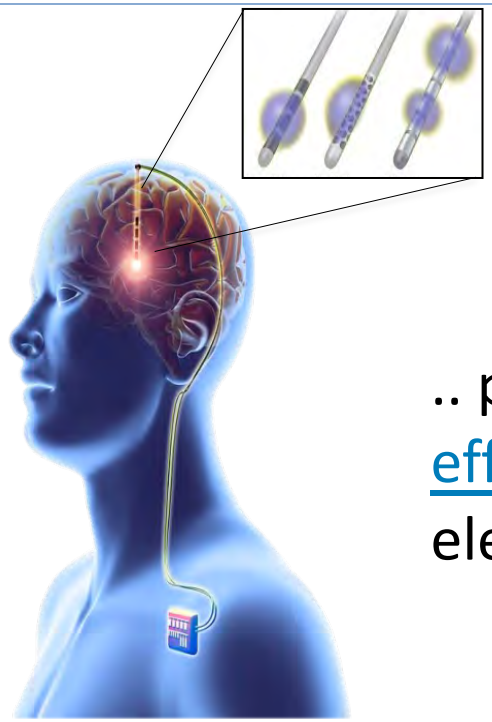
  The science of developing new tools, standards, and approaches to assess the safety, efficacy, quality, and performance of all FDA-regulated products.
  https://www.fda.gov/science-research/science-and-research-special-topics/advancing-regulatory-science

- Unofficial: Development and **standardization** of data, tools and methods that **generalize** across biomarkers, devices, and diseases

Tools

- Accelerating Medical Device Innovation with Regulatory Science Tools
  - https://www.fda.gov/news-events/fda-voices/accelerating-medical-device-innovation-regulatory-science-tools
  - https://cdrhhome.fda.gov/spaces/1/cdrh-news/articles/feature/4158/regulatory-science-tools-to-accelerate-medical-device-innovation
- Medical Device Development Tools (MDDT)
  - https://www.fda.gov/medical-devices/medical-device-development-tools-mddt
- Catalog of Regulatory Science Tools
  - https://www.fda.gov/medical-devices/science-and-research-medical-devices/catalog-regulatory-science-tools-help-assess-new-medical-devices

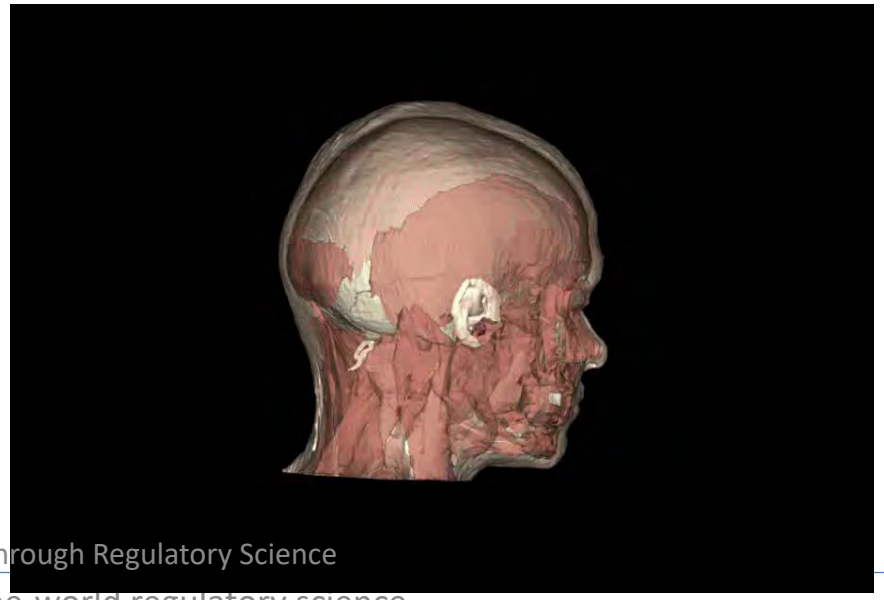
Title and content (black background)



CDRH Mission

.. protect and promote the health of the public by ensuring the safety and effectiveness of **medical devices** and the safety of radiation-emitting electronic products…

We facilitate medical device innovation by advancing regulatory science, providing industry with predictable, consistent, transparent, and efficient regulatory pathways, and assuring consumer confidence in devices marketed in the U.S.



CDRH in Perspective

1900
EMPLOYEES

18k
Medical Device Manufacturers

183k
Medical Devices
On the U.S. Market

22k/year
Premarket Submissions
includes supplements and amendments

570k
Proprietary Brands

25k
Medical Device Facilities Worldwide

1.4 MILLION/year
Reports on medical device adverse events and malfunctions

Office of Science and Engineering Laboratories (OSEL)

- Conduct laboratory-based regulatory research to facilitate development and innovation of safe and effective medical devices and radiation emitting products
- Provide scientific and engineering expertise, data, and analyses to support regulatory processes
- Collaborate with colleagues in academia, industry, government, and standards development organizations to develop, translate, and disseminate science and engineering-based information regarding regulated products
- https://www.fda.gov/about-fda/cdrh-offices/office-science-and-engineering-laboratories

OSEL in Perspective

183
FEDERAL EMPLOYEES
Up to 180 visiting scientists

140 Projects
In 27 Laboratories and Program Areas

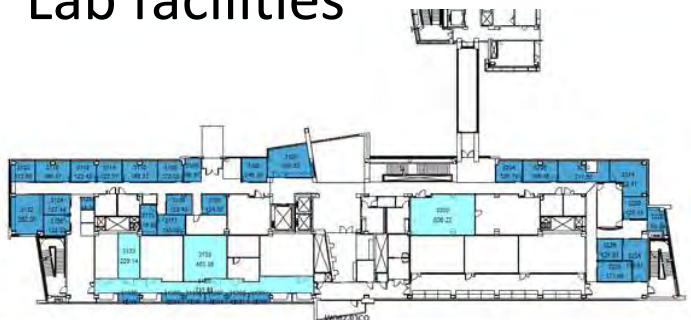
400/year
Peer reviewed presentations, articles, and other public disclosures

2,500k/year
Premarket Regulatory consults

75
Standards and conformity assessment committees

70%
Staff with post graduate degree

55,000 ft²
Lab facilities



Division of Imaging, Diagnostics and Software Reliability (DIDSR)

- Develop least burdensome approaches for regulatory evaluation of imaging and big-data devices
  - Efficient clinical trials accounting for reader variability, simulation tools, in silico phantoms and imaging trials, addressing issues related to imperfect / missing reference standards, and limited data for training/testing of machine classifiers
- Develop measures of technical effectiveness of imaging and big-data technologies
  - Phantoms, laboratory measurements, computational models

DIDSR in Perspective

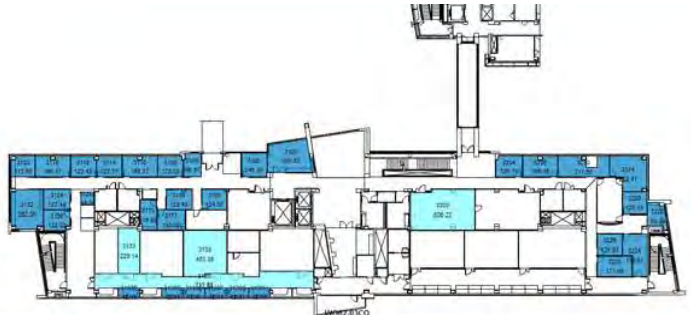
35
FEDERAL EMPLOYEES
14 Fellows/Students
3 Open Staff Positions

145/year
Peer reviewed articles, code and presentations

4 Program Areas
- AI/ML
- Medical Imaging and Diagnostics
- Digital Pathology
- Mixed Reality (AR/VR/XR)

550/year
Premarket
Regulatory consults

~15,000 ft²
DIDSR Lab and facilities

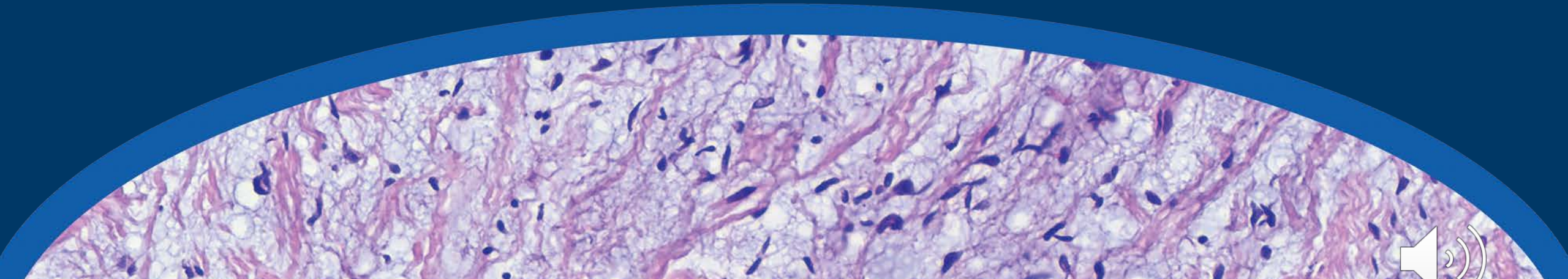


MDIC
MEDICAL DEVICE INNOVATION CONSORTIUM

Pathology Innovation Collaborative Community (PIcc)
Annual Meeting 2023

FDA Talk 3: DIDSR AI/ML Research Program And Gaps

Alexej Gossmann
OSEL/CDRH, FDA



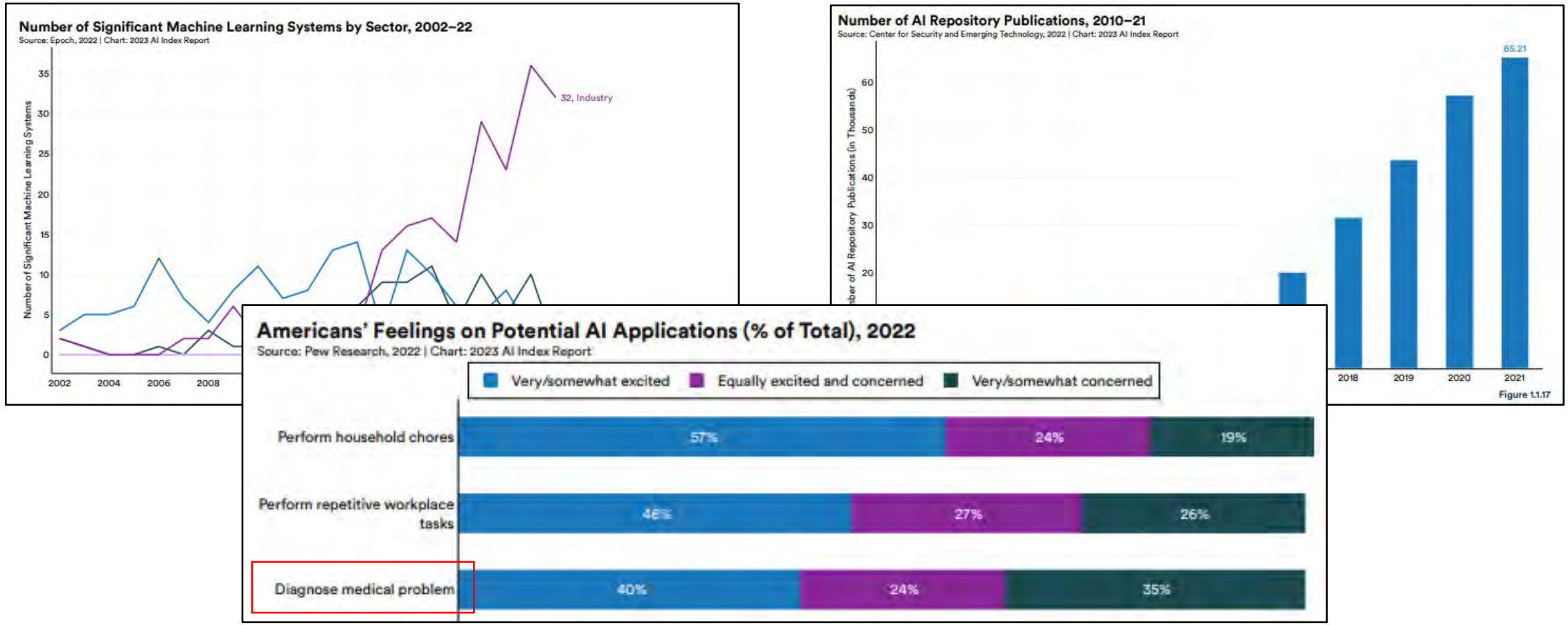
FDA/CDRH/OSEL Artificial Intelligence (AI) / Machine Learning (ML) Research Program, and Regulatory Science Gaps

Pathology Innovation Collaborative Community Annual Meeting (PIcc23)

June 27, 2023

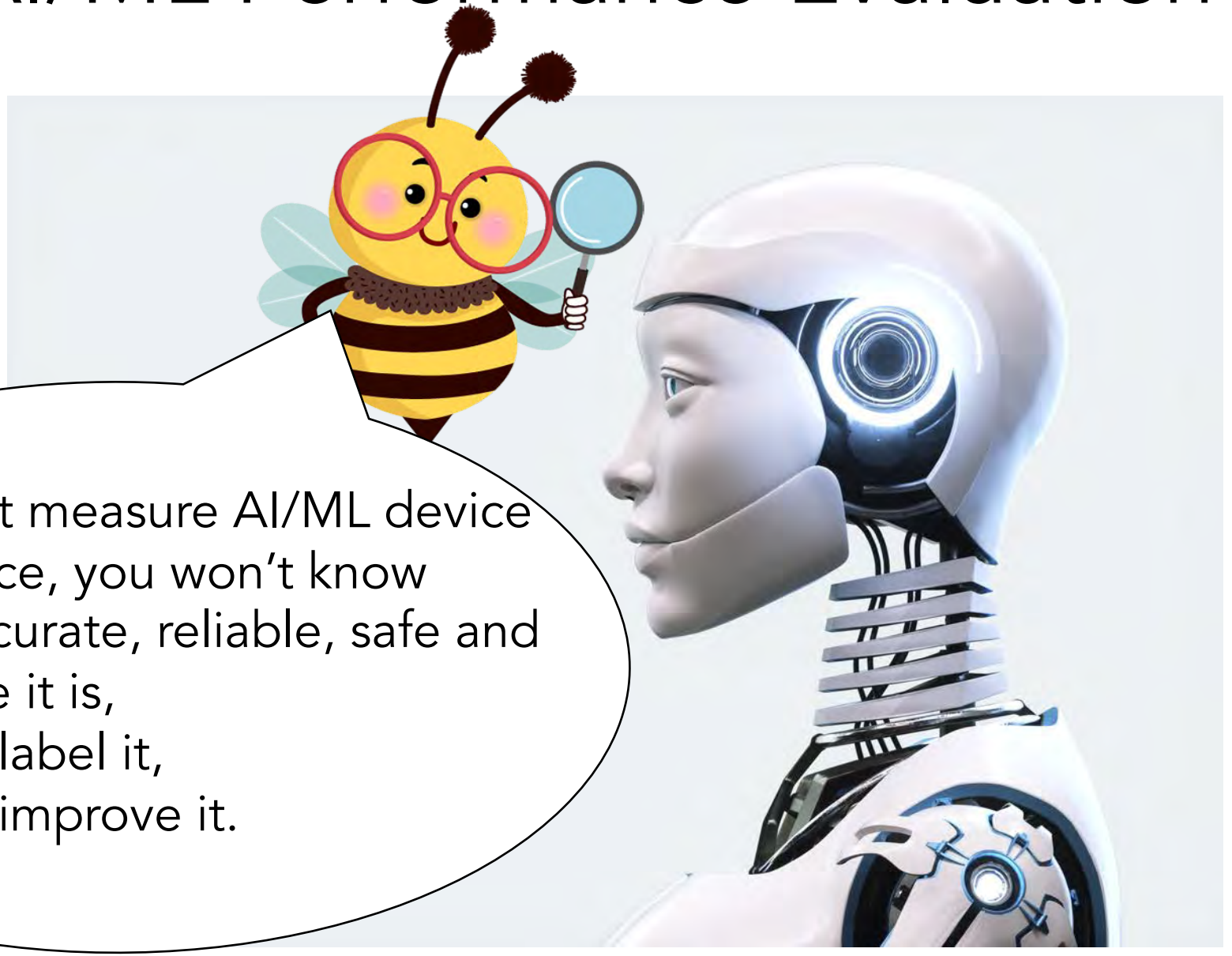
Alexej Gossmann
Staff Fellow
Division of Imaging, Diagnostics and Software Reliability
Office of Science and Engineering Labs
Center for Devices and Radiological Health
U.S. Food and Drug Administration

AI/ML is taking the world by storm!



Stanford HAI. 2023 AI Index Report: Measuring Trends in Artificial intelligence. Retrieved 4 April 2023.
https://aiindex.stanford.edu/report/

AI/ML Performance Evaluation



If you don't measure AI/ML device performance, you won't know

- How accurate, reliable, safe and effective it is,
- How to label it,
- How to improve it.

Overview of this talk

- OSEL, DIDSR: Explain who we are
- Describe regulatory science challenges and gaps in medical AI/ML
- Describe OSEL AI/ML research program activities to address these gaps

Office of Science and Engineering Labs (OSEL)

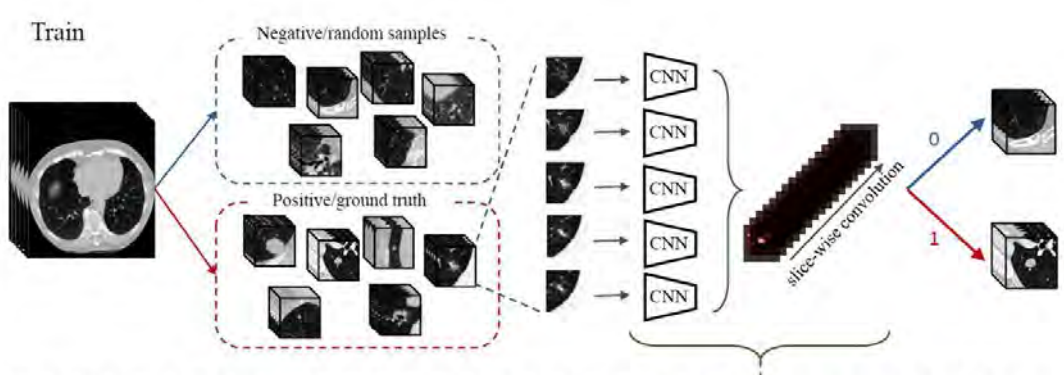
Mission Statement

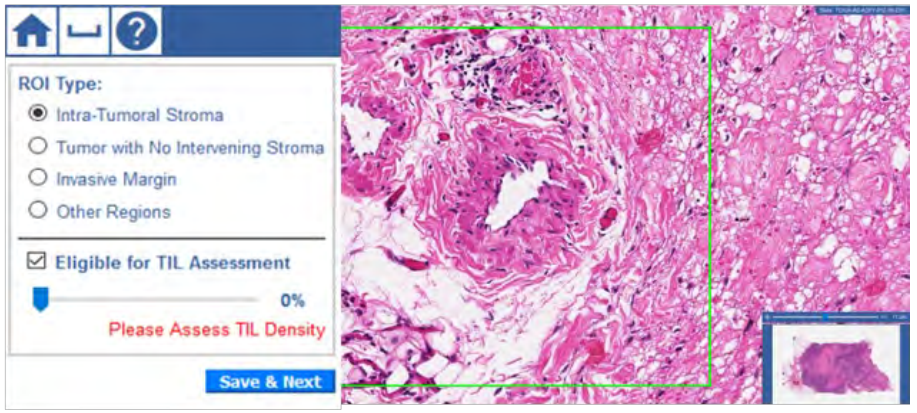
Accelerating patient access to innovative, safe and effective medical devices through best-in-the-world regulatory science.

An OSEL employee

What OSEL/DIDSR Does

- Division of Imaging, Diagnostics, and Software Reliability (DIDSR)
- Conduct regulatory science research for a variety of imaging, AI/ML, MXR, and diagnostic devices.
- Develop approaches for assessing imaging and big-data technologies.





OSEL AI/ML Program

- AI/ML program
  - Regulatory science research
  - Developing robust AI/ML test methods
  - Evaluating methodologies for assessing AI/ML
- AI/ML team identified regulatory gaps
  - Not all AI/ML knowledge gaps
  - Important ones to support FDA regulatory mission

Regulatory Science Gaps and Challenges

- Limited labeled training and test data
- Bias, equity, and generalizability
- Ground truth and metrics for performance estimation
- Evolving algorithms – How to maintain safety and effectiveness for devices with a predetermined change control plan (PCCP)
- Emerging clinical application of AI/ML
- Data Drift and Postmarket AI/ML Performance Monitoring

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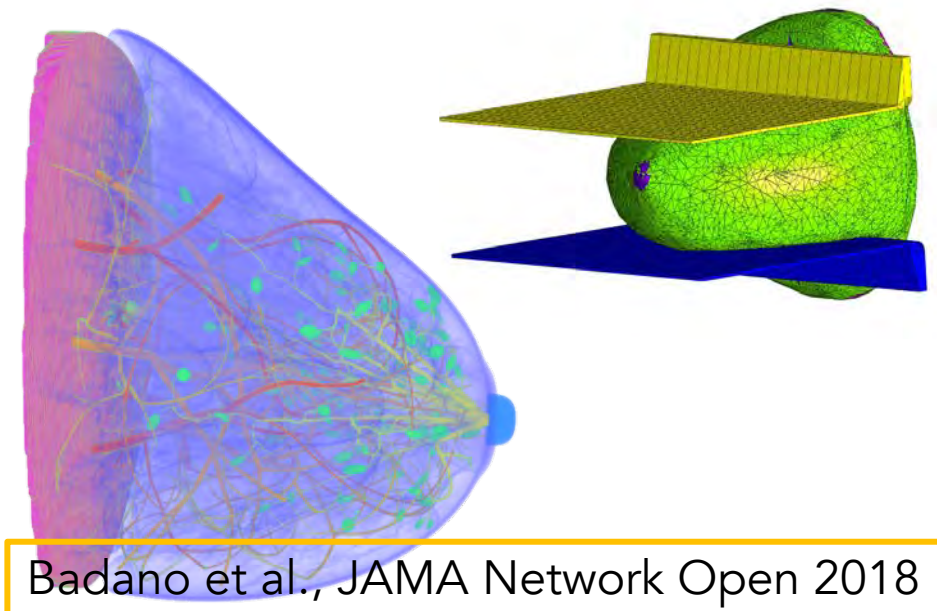
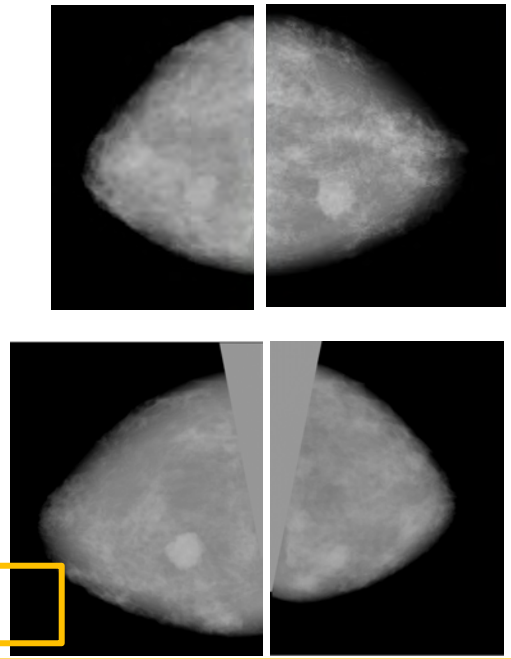
Limited labeled training and test data

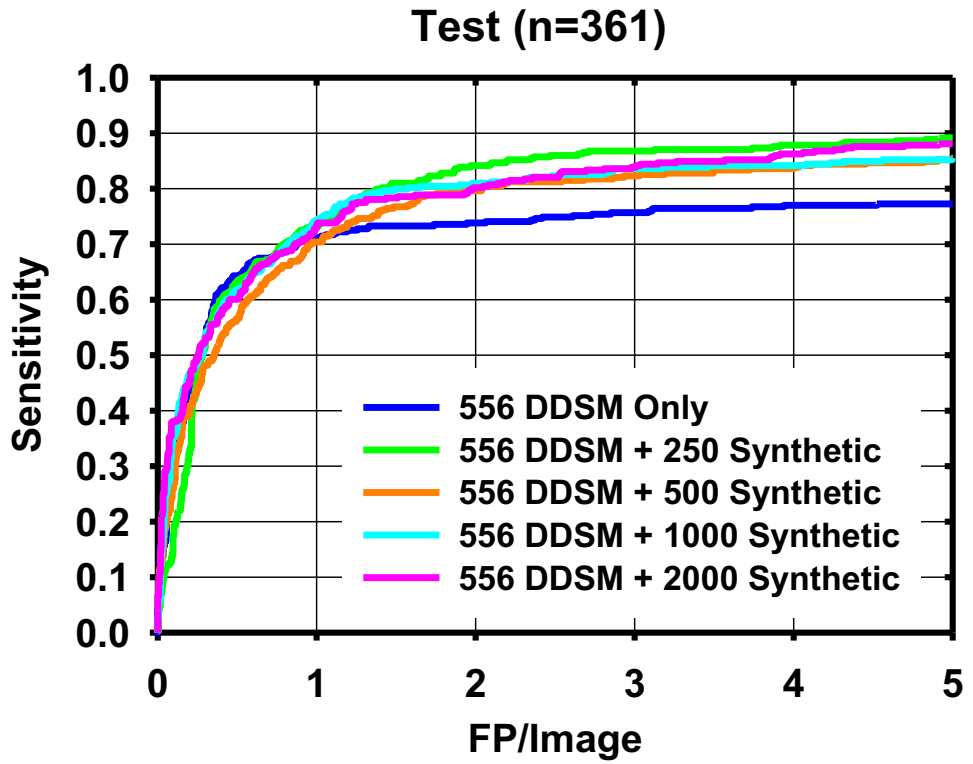
- There is a need for
  - Fundamental understanding of the limitations of smaller datasets and
  - Novel techniques to enhance AI/ML algorithm training and testing when the real-world datasets are limited in size

Use of synthetic data for AI training and testing

- AI algorithms require large training data sets for high performance
- Limited annotated data sets for medical images
- In-silico images may help







Badano et al., JAMA Network Open 2018

RST: [VICTRE: In Silico Breast Imaging Pipeline | FDA]

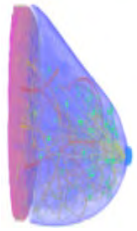
Cha et al., "Evaluation of data augmentation via synthetic images for improved breast mass detection on mammograms using deep learning," Journal of Medical Imaging 2020

REALYSM: Simulations-based testing for AI devices

Goal: Generate realistic simulated data where real patient examples are unavailable

Badano et al. The stochastic digital human … ArXiv preprint 2023.

(a) Data Simulation: Sample simulation parameters



Breast Phantom Generation

Lesion Insertion

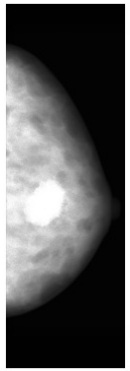
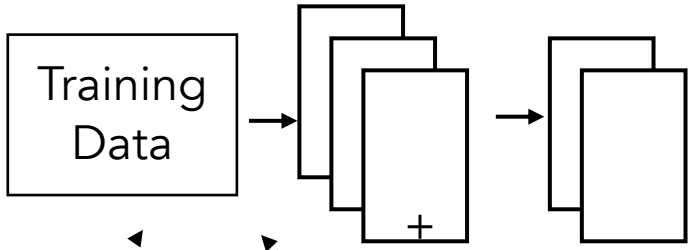


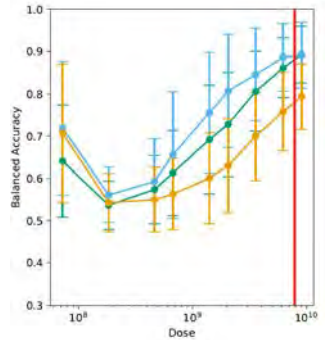
Image Generated Using Acquisition Simulation

(b) AI Model

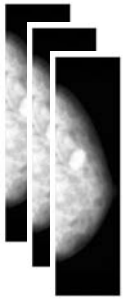


Model Decision

(c) AI Evaluation



197



Option 1: Generate Simulated Training Data

Option 2: External Training Data

Sizikova et al. Fully-Detailed, Physics-based In Silico Approach for Evaluating … 2023 (in review)

Regulatory Science Gaps and Challenges

- Limited labeled training and test data
- **Bias, equity, and generalizability**
- Ground truth and metrics for performance estimation
- Evolving algorithms – How to maintain safety and effectiveness for devices with a predetermined change control plan (PCCP)
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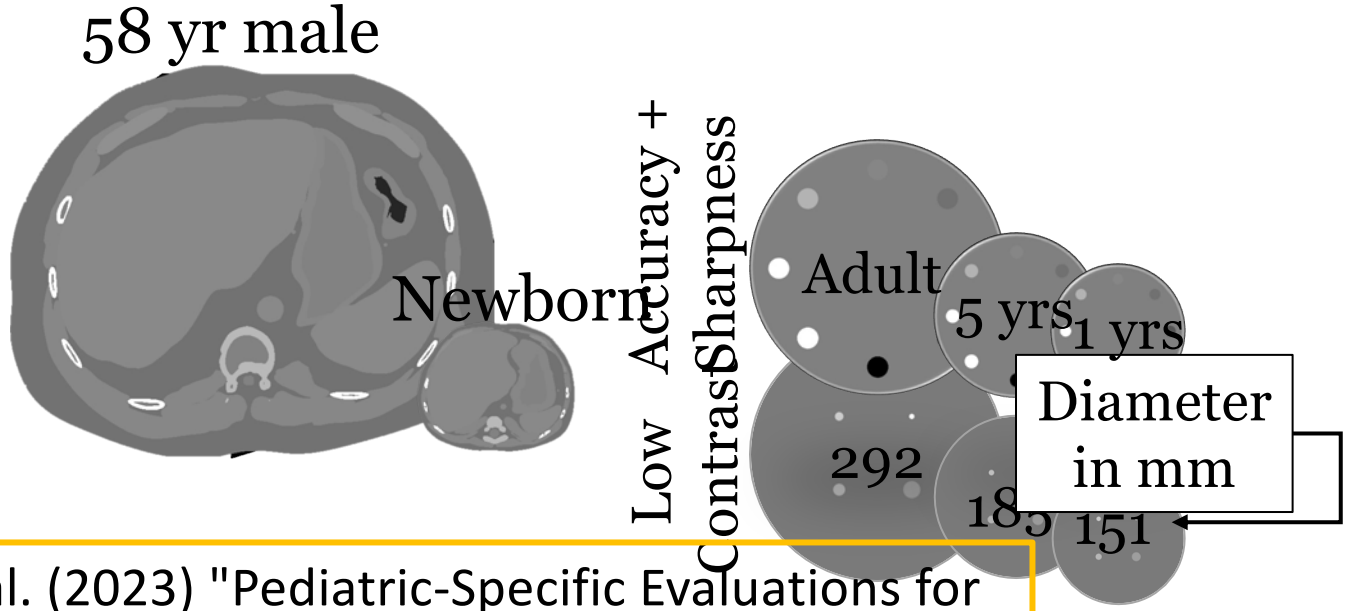
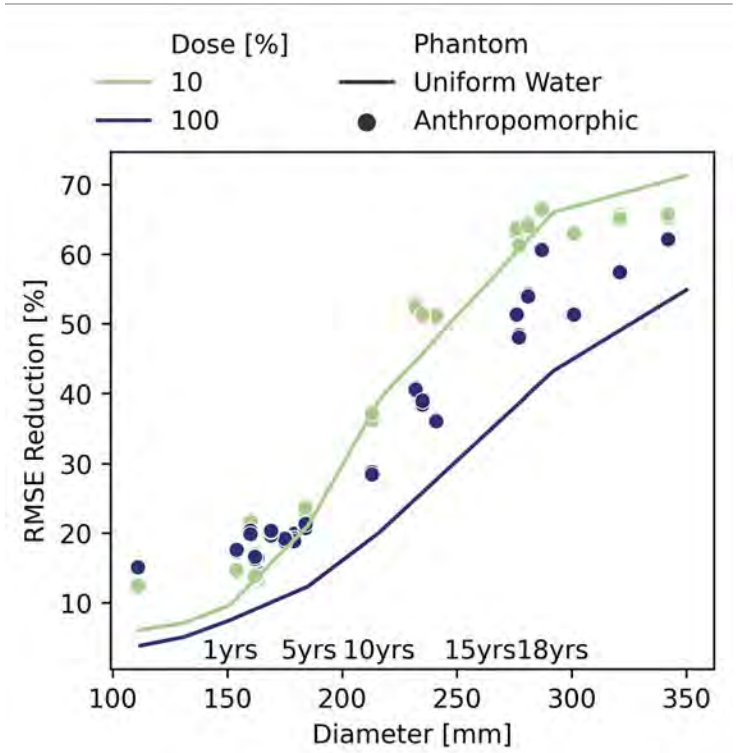
Bias, equity, and generalizability

- There is a need for methods to understand, analyze and minimize performance differences of AI/ML-enabled devices among subgroups

Pediatric-Specific Evaluations for Deep Learning CT Image Reconstruction and Denoising

- Deep learning image reconstruction (DLIR) models primarily trained on adults.
- Do pediatric patients benefit equally from adult-trained DLIR models?
- **PEDiatric CT Evaluation ToolKit (PED-ETK)**





Nelson et al. (2023) "Pediatric-Specific Evaluations for Deep Learning CT Image Reconstruction and Denoising Techniques" - under review

https://github.com/DIDSR/PED-ETK

Pediatric-Specific Evaluations for Deep Learning CT Image Reconstruction and Denoising

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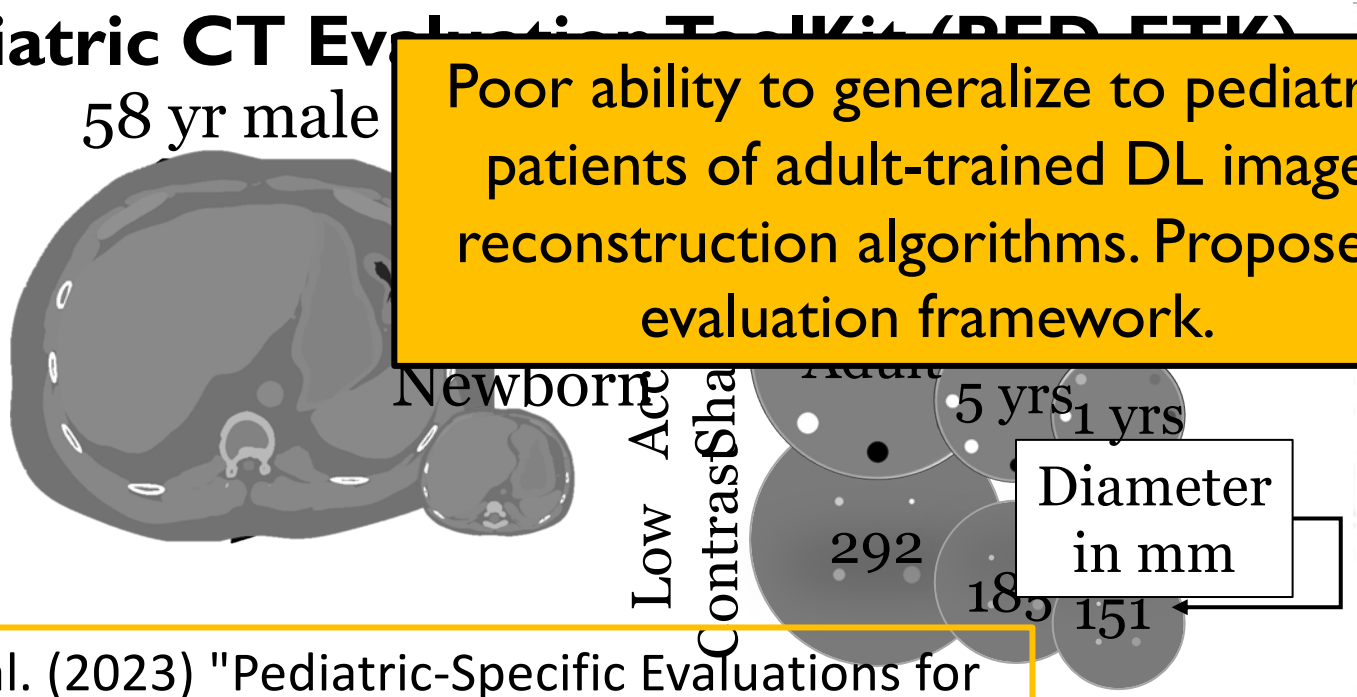
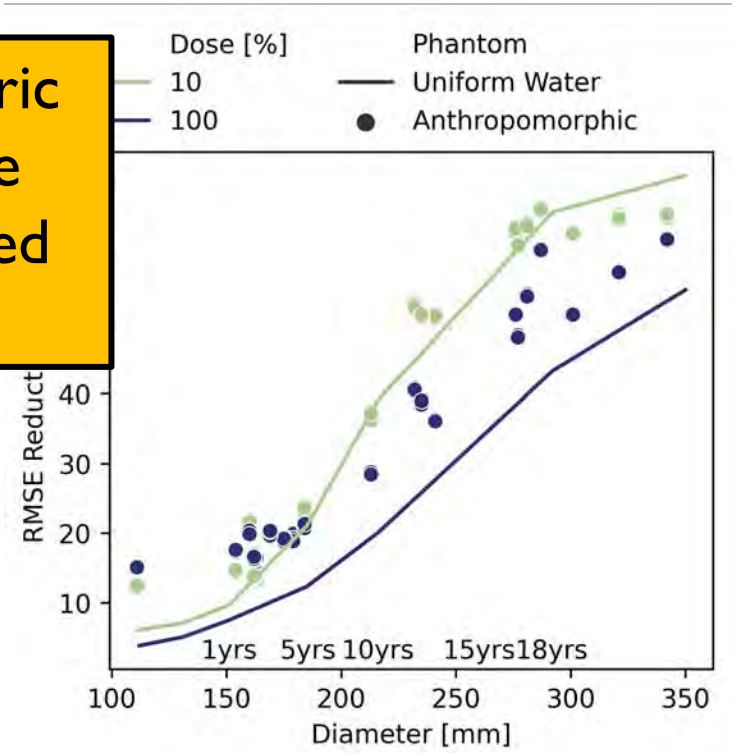


Poor ability to generalize to pediatric patients of adult-trained DL image reconstruction algorithms. Proposed evaluation framework.



Nelson et al. (2023) "Pediatric-Specific Evaluations for Deep Learning CT Image Reconstruction and Denoising Techniques" - under review

https://github.com/DIDSR/PED-ETK

Regulatory Science Gaps and Challenges

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- Bias, equity, and generalizability
- **Ground truth and metrics for performance estimation**
- Evolving algorithms – How to maintain safety and effectiveness for devices with a predetermined change control plan (PCCP)
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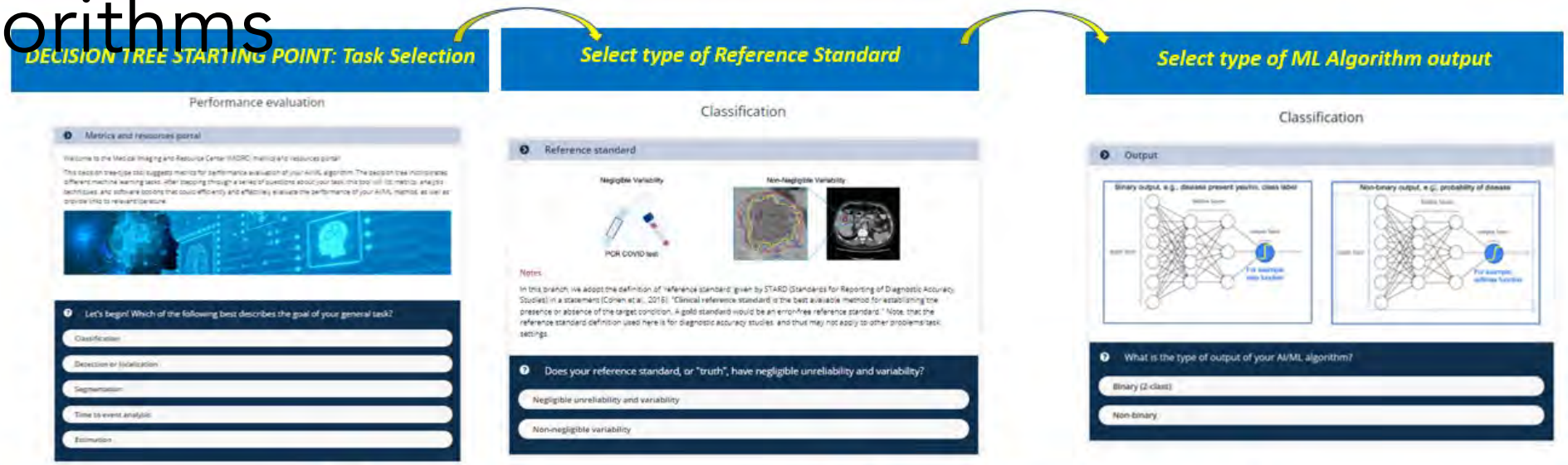
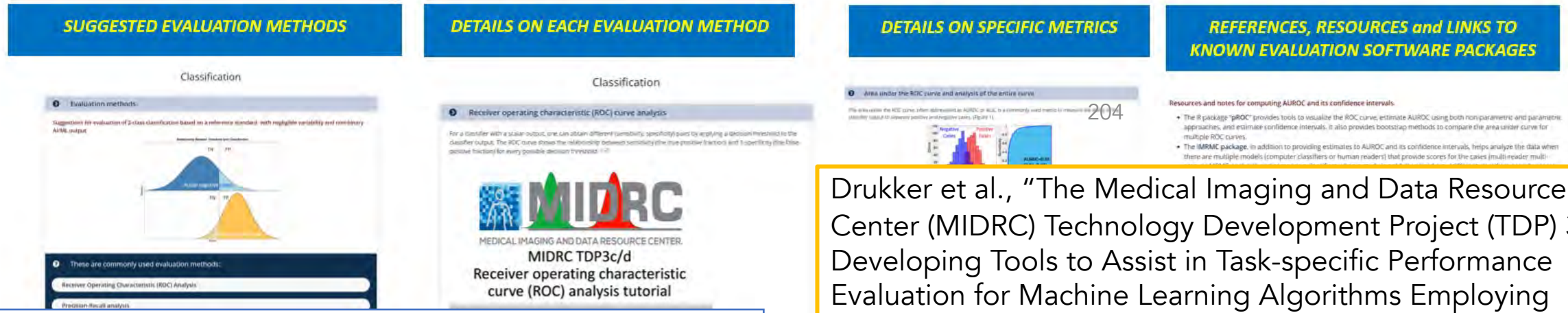
Ground truth and metrics for performance estimation

- A need to understand how to determine the level of truth needed to evaluate AI-enabled devices in a least burdensome fashion
- The metrics used to determine AI/ML performance
- Determination of acceptable performance criteria

MIDRC: Task-specific Performance Evaluation Metric Selection Tools for Machine Learning Algorithms





https://www.midrc.org/performance-metrics-decision-tree

Drukker et al., "The Medical Imaging and Data Resource Center (MIDRC) Technology Development Project (TDP) 3c: Developing Tools to Assist in Task-specific Performance Evaluation for Machine Learning Algorithms Employing MIDRC Data," AAPM 2022

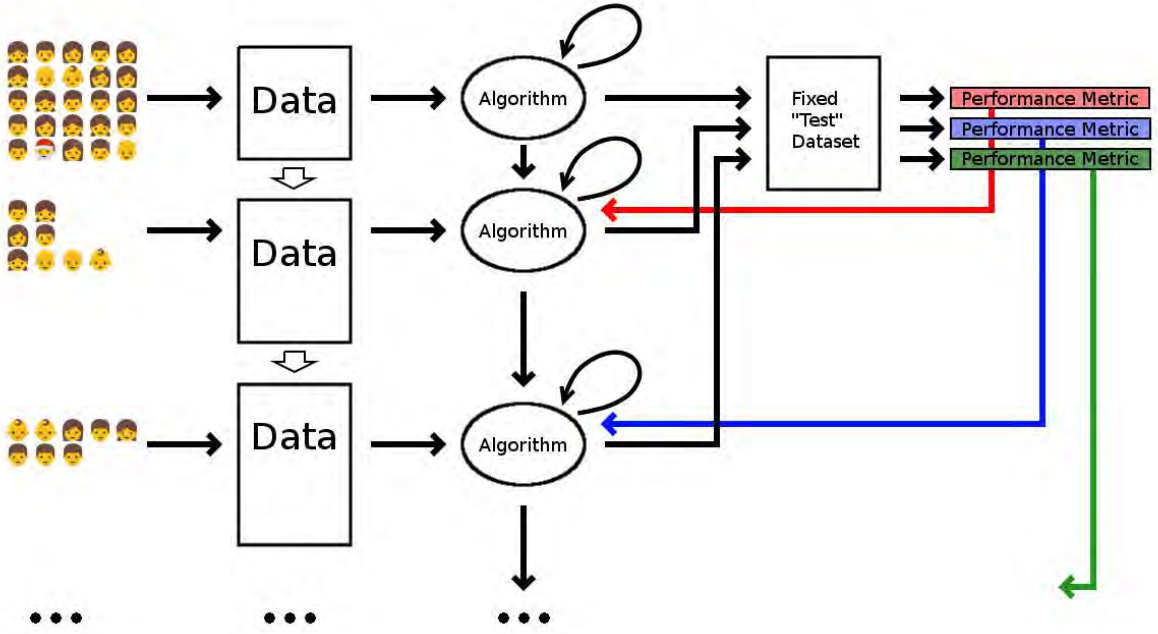
Regulatory Science Gaps and Challenges

- Limited labeled training and test data
- Bias, equity, and generalizability
- Ground truth and metrics for performance estimation
- **Evolving algorithms – How to maintain safety and effectiveness for devices with a predetermined change control plan (PCCP)**
- Emerging clinical application of AI/ML
- Data Drift and Postmarket AI/ML Performance Monitoring

Evolving algorithms

- How to maintain safety and effectiveness for devices with a predetermined change control plan (PCCP)
- Our stakeholders would like a more flexible pre-market regulatory process to allow for periodic modifications of AI/ML algorithms over time and evolving AI algorithms without the need for a new regulatory submission.
- There are many open questions related to the regulation of such devices.

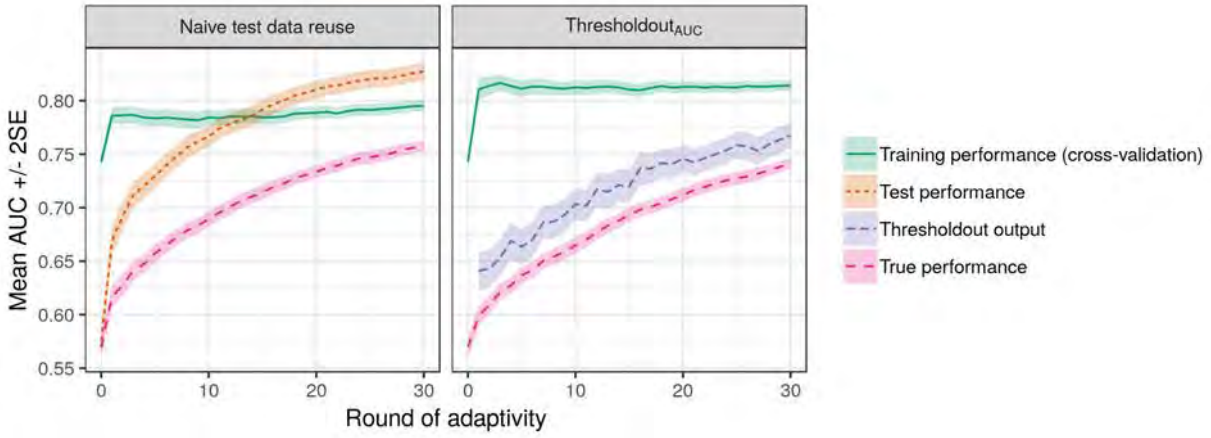
How can we reuse an existing test dataset to validate sequential algorithmic modifications?



Methods that allow for valid test data reuse restrict the amount of information leaked with each query by

(a) perturbing the query result with random noise → differential privacy

(b) restricting the number of bits of information returned.



Gossmann et al., "Test Data Reuse for the Evaluation …," SIAM J Math Data Science, 2021

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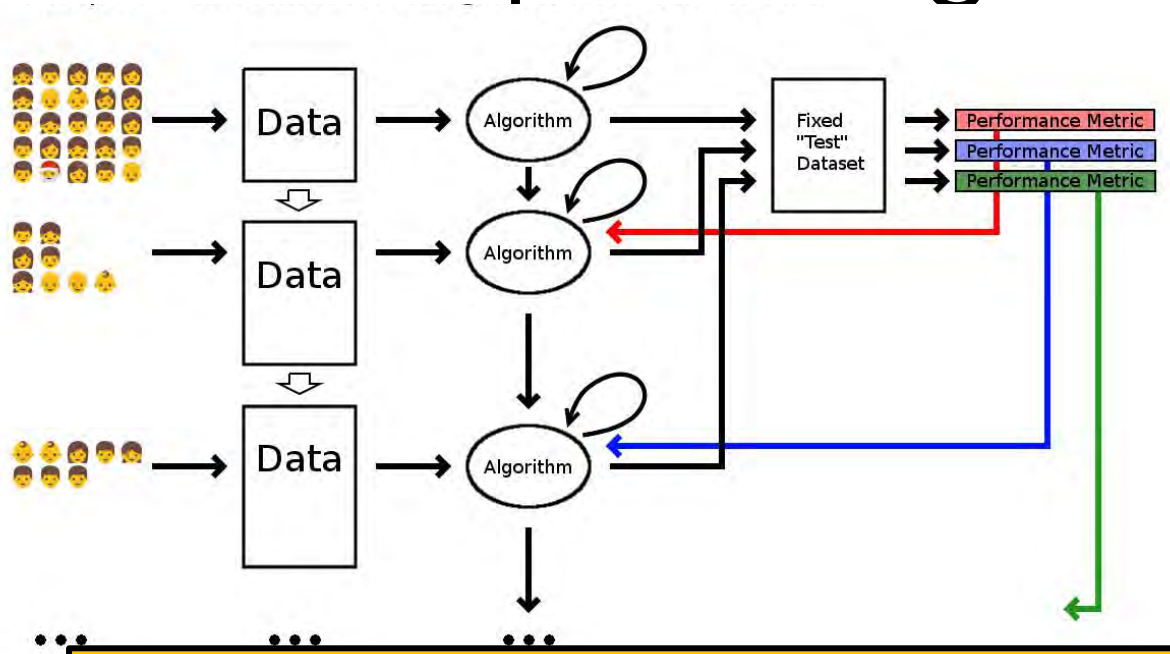

Methods that allow for valid test data reuse restrict the amount of information leaked with each query by

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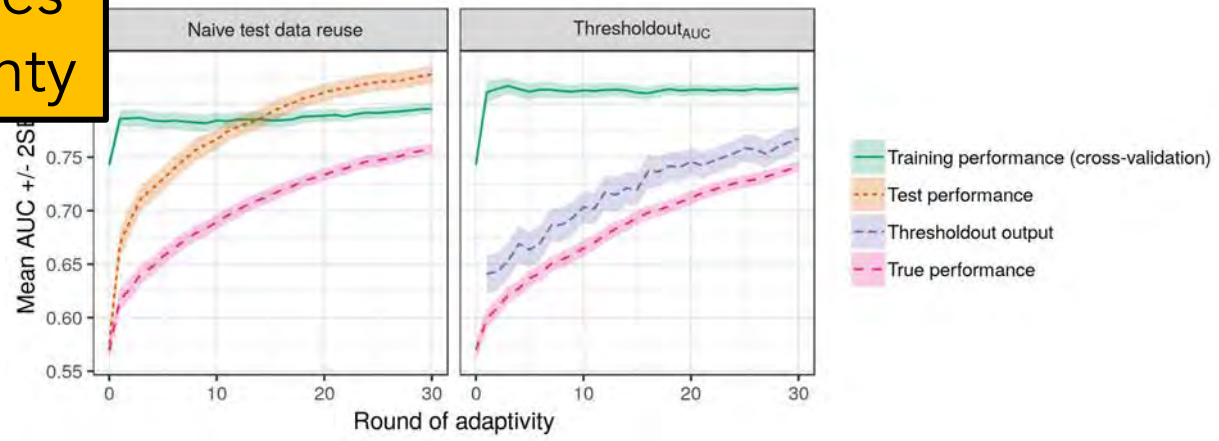
Accuracy of reported performance values improves at the cost of higher uncertainty

Gossmann et al., "Test Data Reuse for the Evaluation …," SIAM J Math Data Science, 2021



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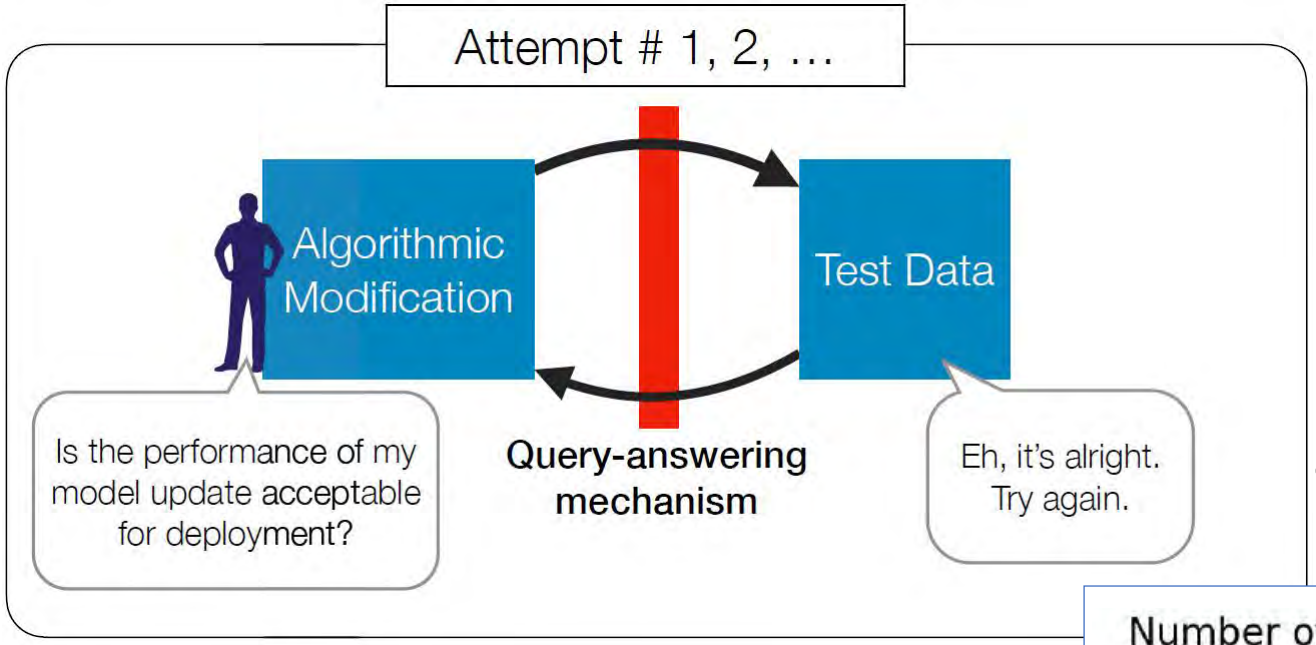

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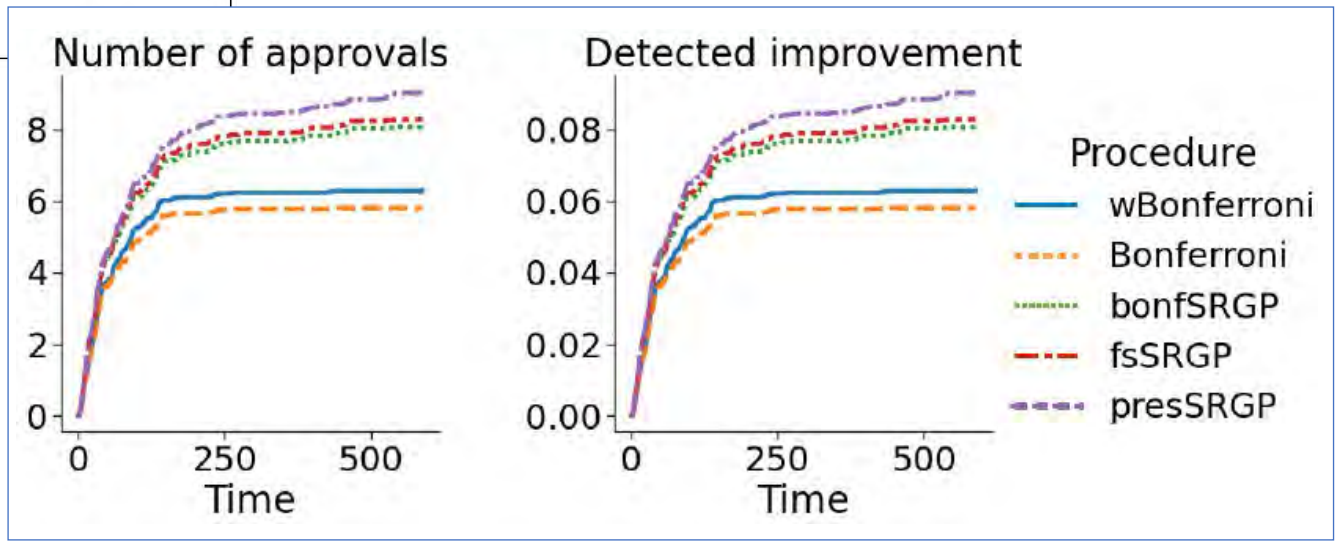

Feng et al., "Sequential algorithmic modification with test data reuse," UAI, 2022

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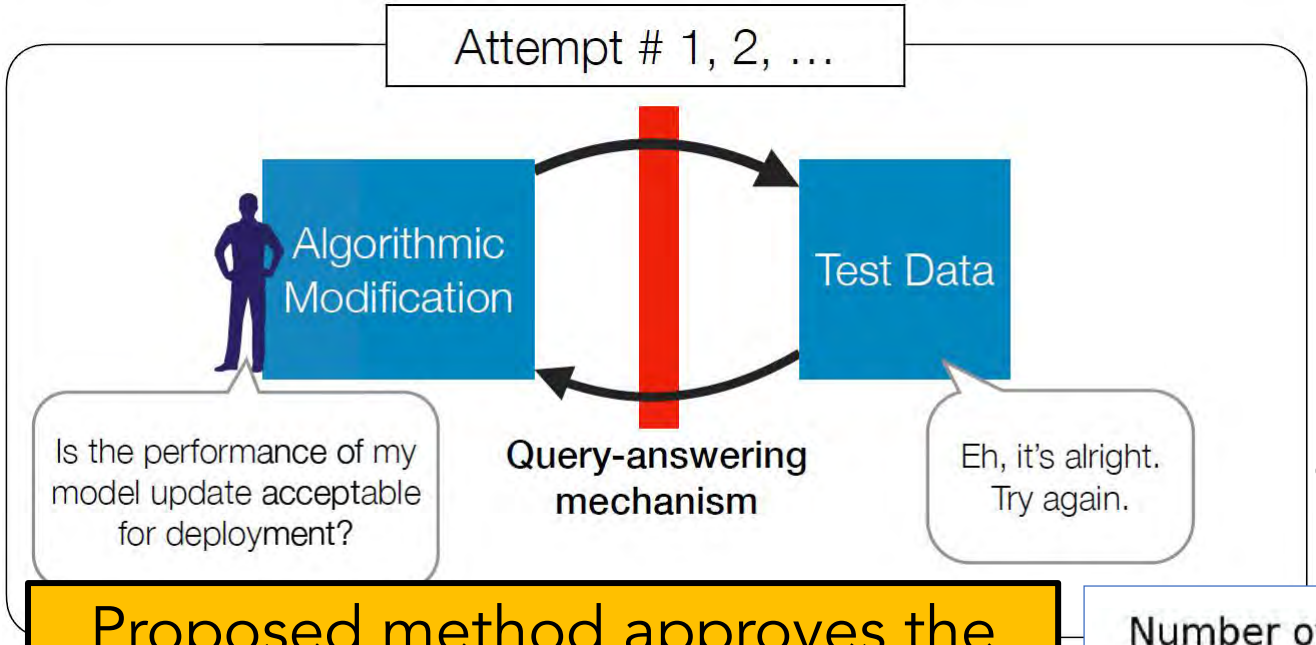

Methods that allow for valid test data reuse restrict the amount of information leaked with each query by

(a) perturbing the query result with random noise → differential privacy

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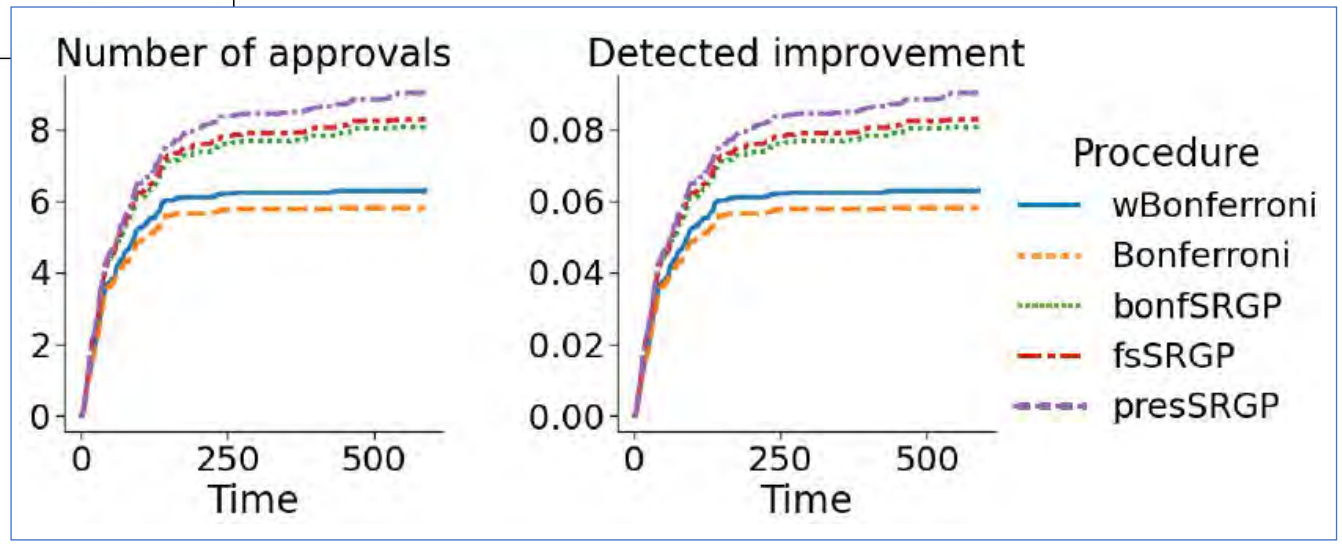
Proposed method approves the most model updates and achieves the best performance, while controlling the rate of bad approvals.



algorithmic modification with test data reuse," UAI, 2022

Regulatory Science Gaps and Challenges

- Limited labeled training and test data
- Bias, equity, and generalizability
- Ground truth and metrics for performance estimation
- Evolving algorithms – How to maintain safety and effectiveness for devices with a predetermined change control plan (PCCP)
- **Emerging clinical application of AI/ML**
- Data Drift and Postmarket AI/ML Performance Monitoring

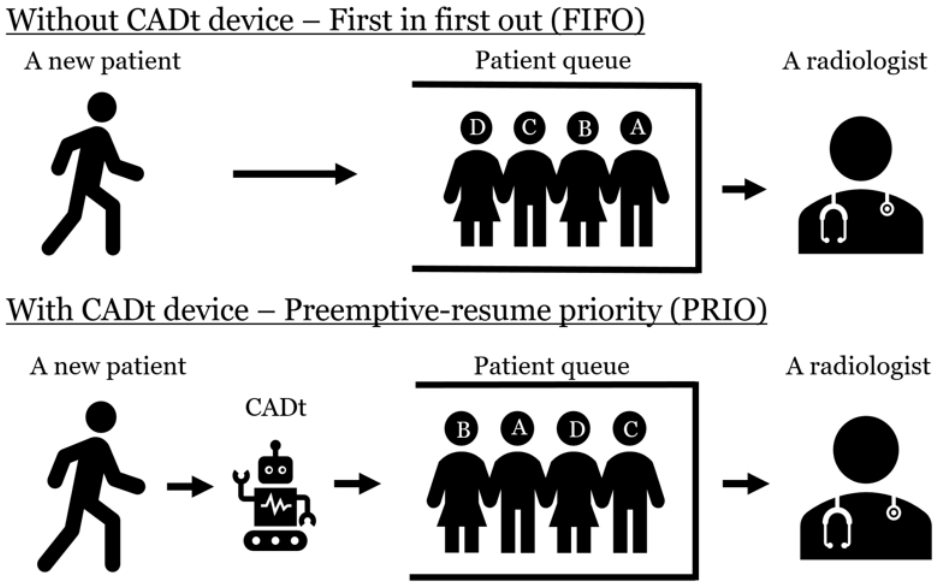
Emerging clinical application of AI/ML

- Device sponsors continue to think of new ways to utilize AI/ML in medical practice, including
  - Automating patient referrals,
  - Triaging patients,
  - Reading images autonomously,
  - Large language models (LLMs) applied to medical records,
  - Etc.
- We need methods for evaluating these new and different uses of AI.

A Modeling Tool for Streamlined Assessment of Emerging Radiological Computer-Assisted Triage (CADt) and Notification Software

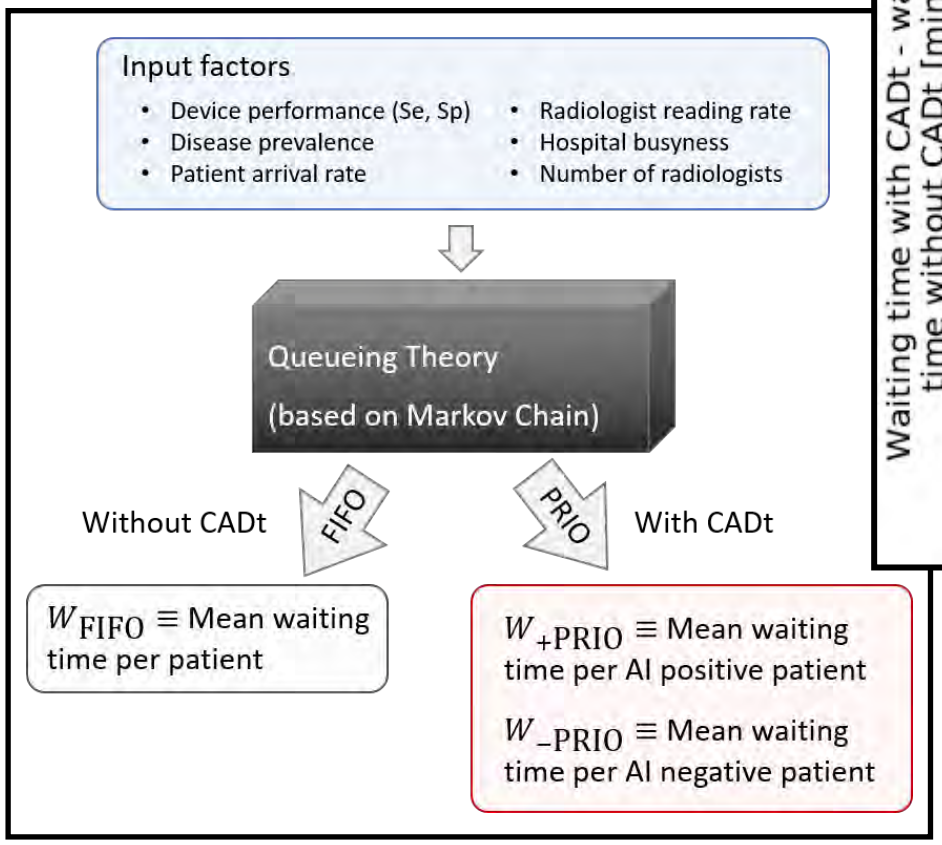
- 30+ FDA-approved CADt devices since 2018
- Why CADt devices?
    - Faster diagnosis and treatment for time sensitive diseases e.g. stroke
- How effective is a CADt device?

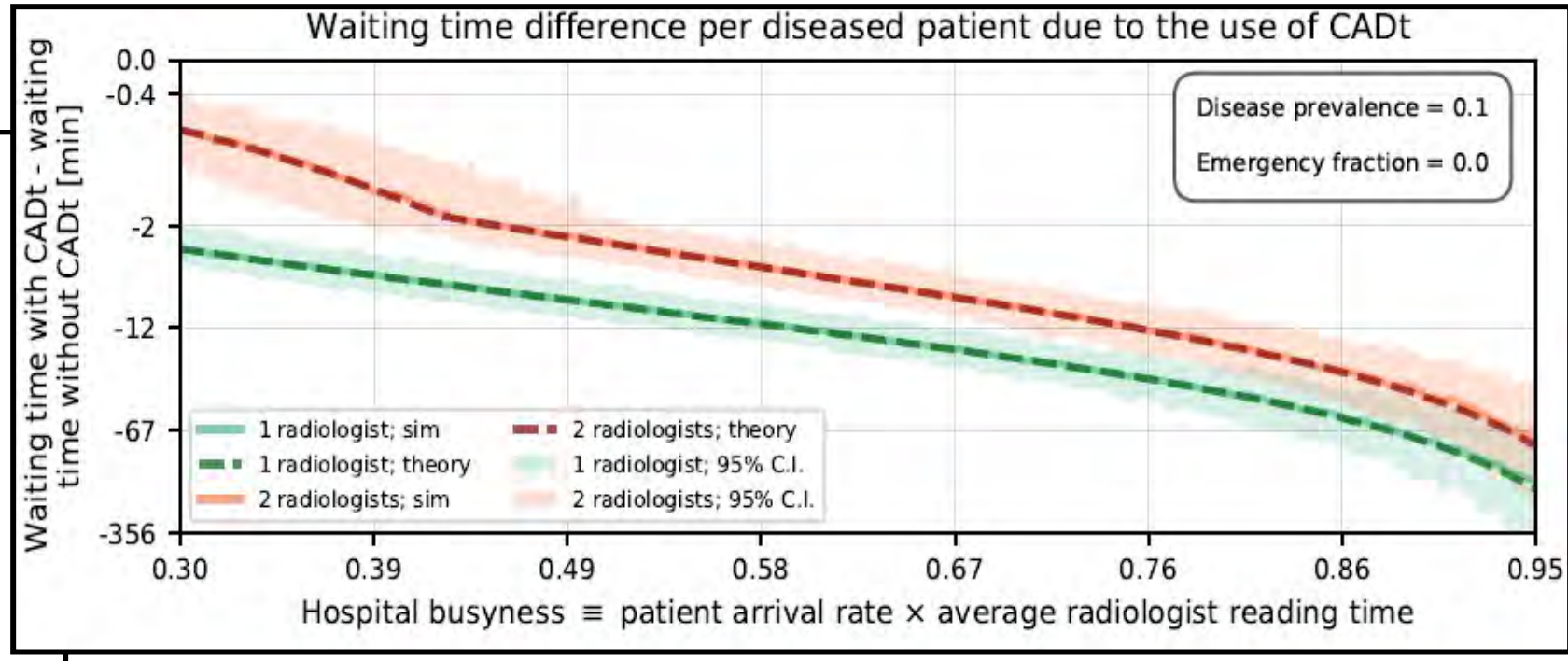
  → Use queueing theory to quantify the amount of time savings



Thompson et al., "Wait-Time-Saving Analysis and …," SPIE MI, 2022

A Modeling Tool for Streamlined Assessment of Emerging Radiological Computer-Assisted Triage (CADt) and Notification Software





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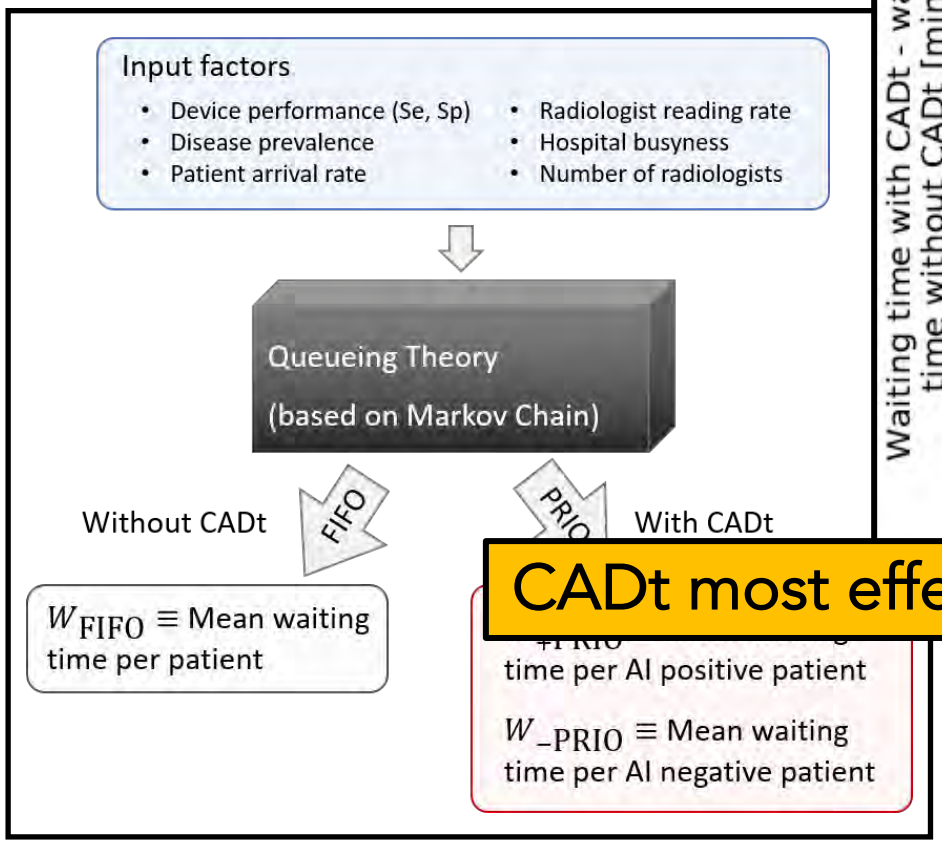
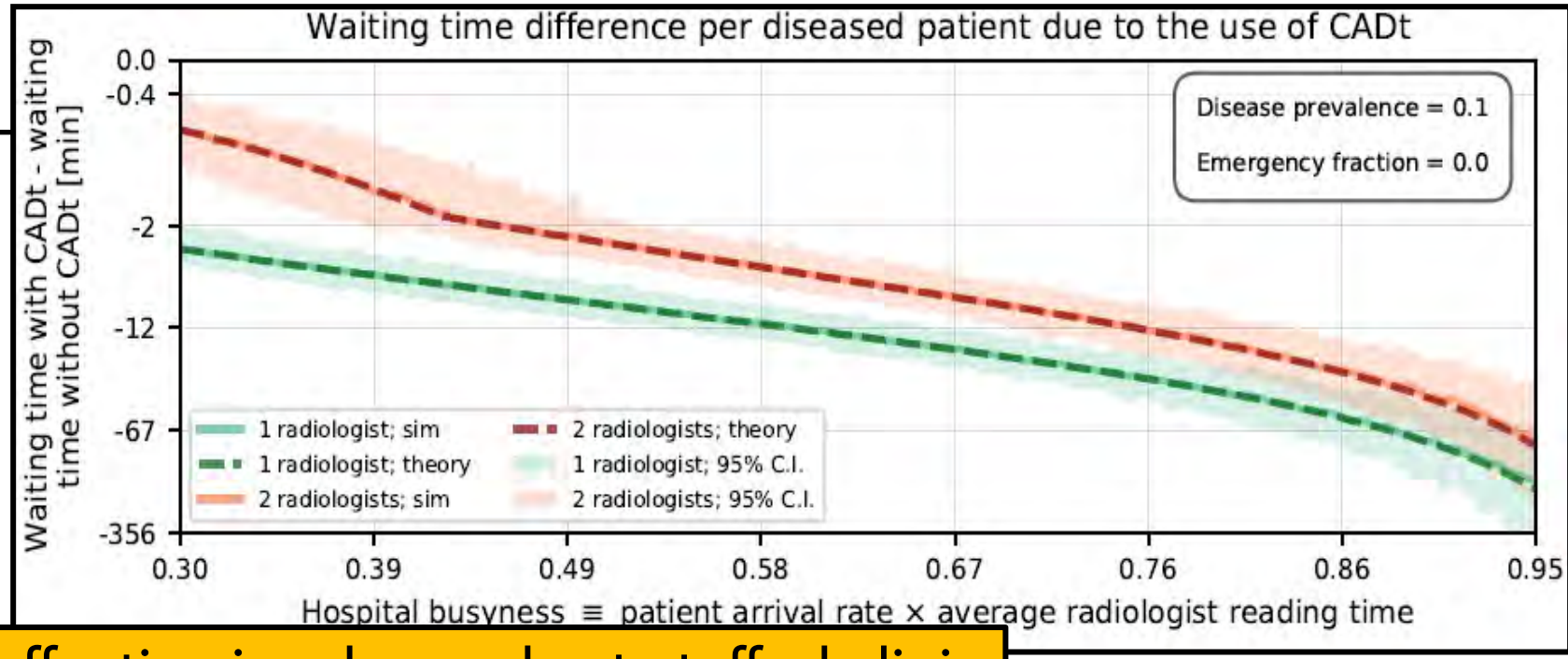
A Modeling Tool for Streamlined Assessment of Emerging Radiological Computer-Assisted Triage (CADt) and Notification Software





CADt most effective in a busy, short-staffed clinic

Thompson et al., "Wait-Time-Saving Analysis and …," SPIE MI, 2022

Regulatory Science Gaps and Challenges

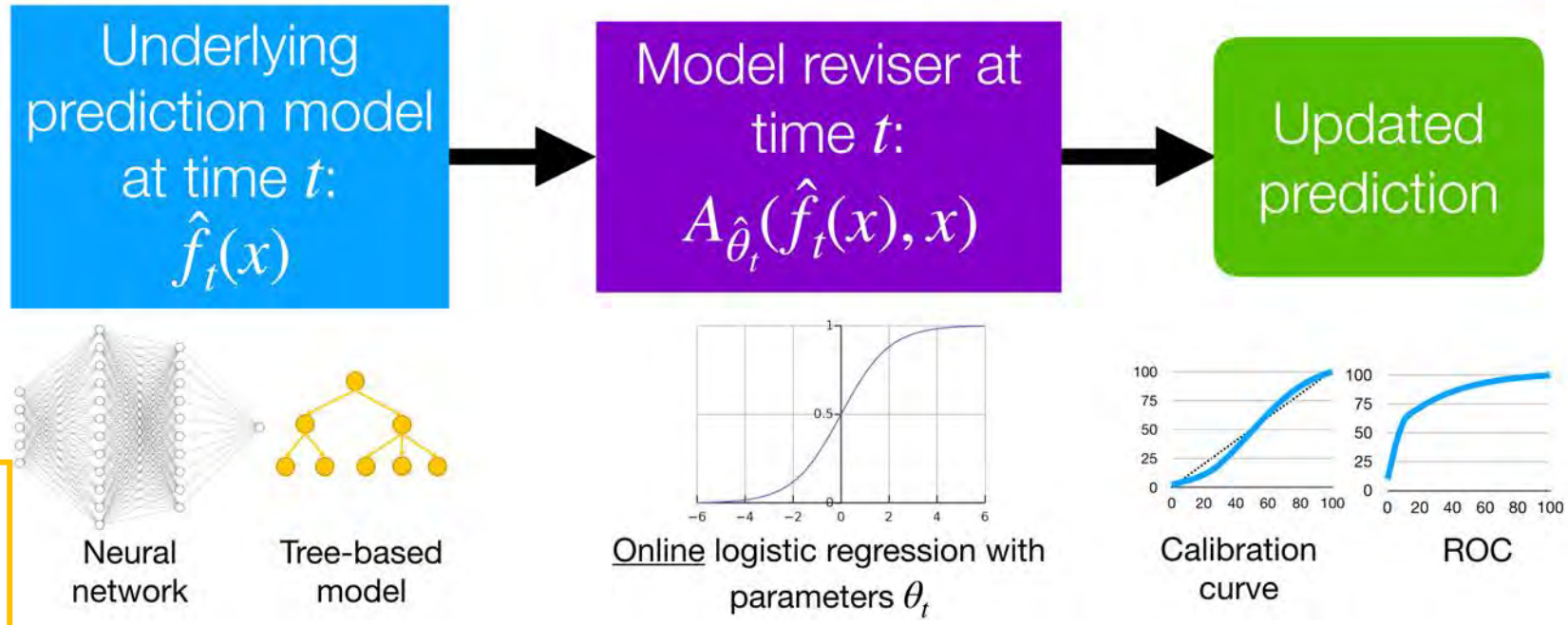
- Limited labeled training and test data
- Bias, equity, and generalizability
- Ground truth and metrics for performance estimation
- Evolving algorithms – How to maintain safety and effectiveness for devices with a predetermined change control plan (PCCP)
- Emerging clinical application of AI/ML
- **Data Drift and Postmarket AI/ML Performance Monitoring**

Data Drift and Postmarket AI/ML Performance Monitoring

- Data acquisition systems and protocols, and patient populations change over time and by site.
- AI/ML device users, such as radiologists, and patients want to know that the AI products they are using will be accurate and reliable even as practice and patient populations change.
- We need planned and standardized methods for detecting changes to the inputs of AI devices, monitoring the accuracy of their outputs, and mitigating effects of those drifts.

Online Recalibration

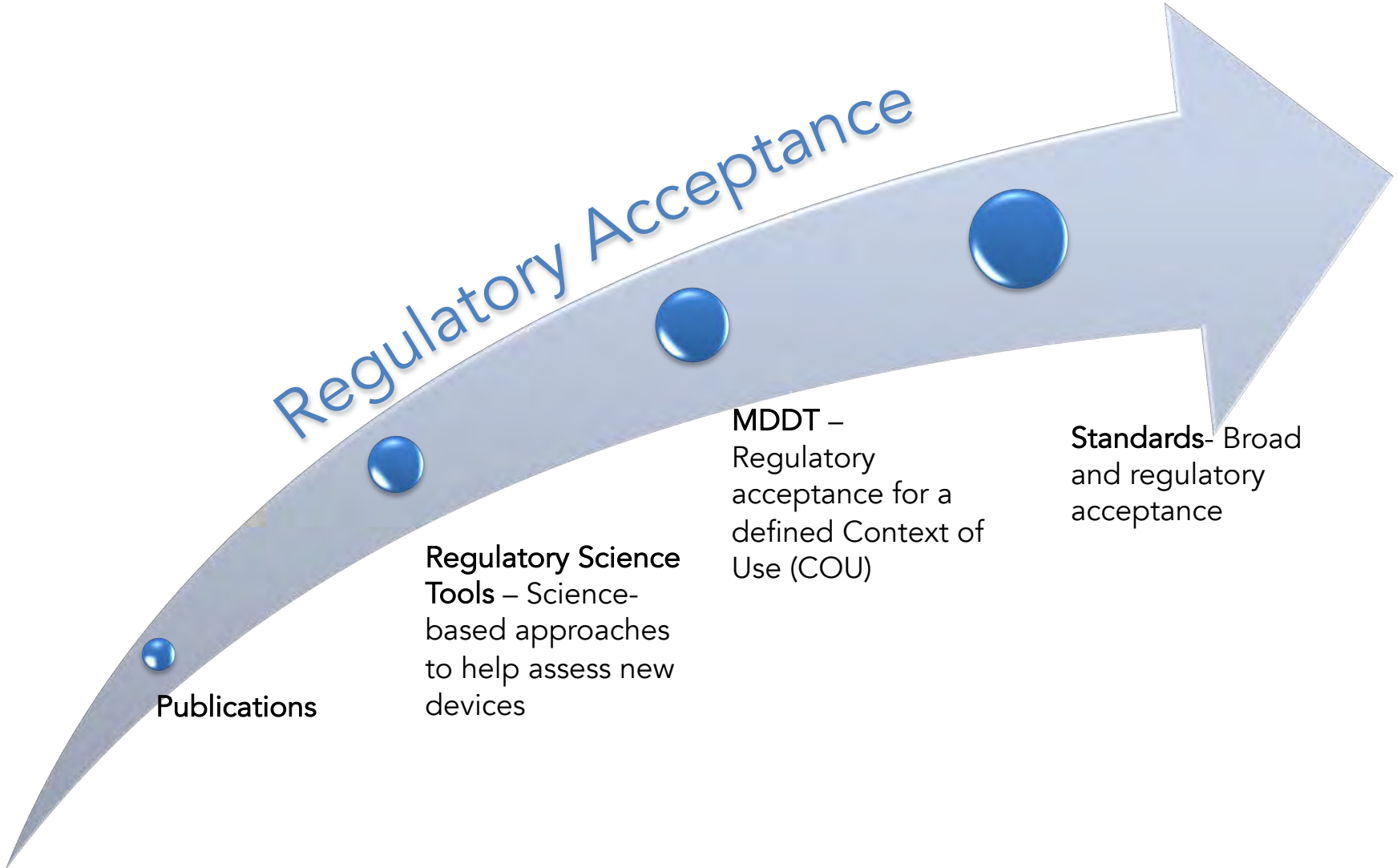
- Model updates can protect against changes in the environment, and learn from accumulating data.
- However, algorithmic modifications also carry the risk of deteriorating model performance.
- We design an online logistic recalibration and revision procedure that provides performance guarantees.



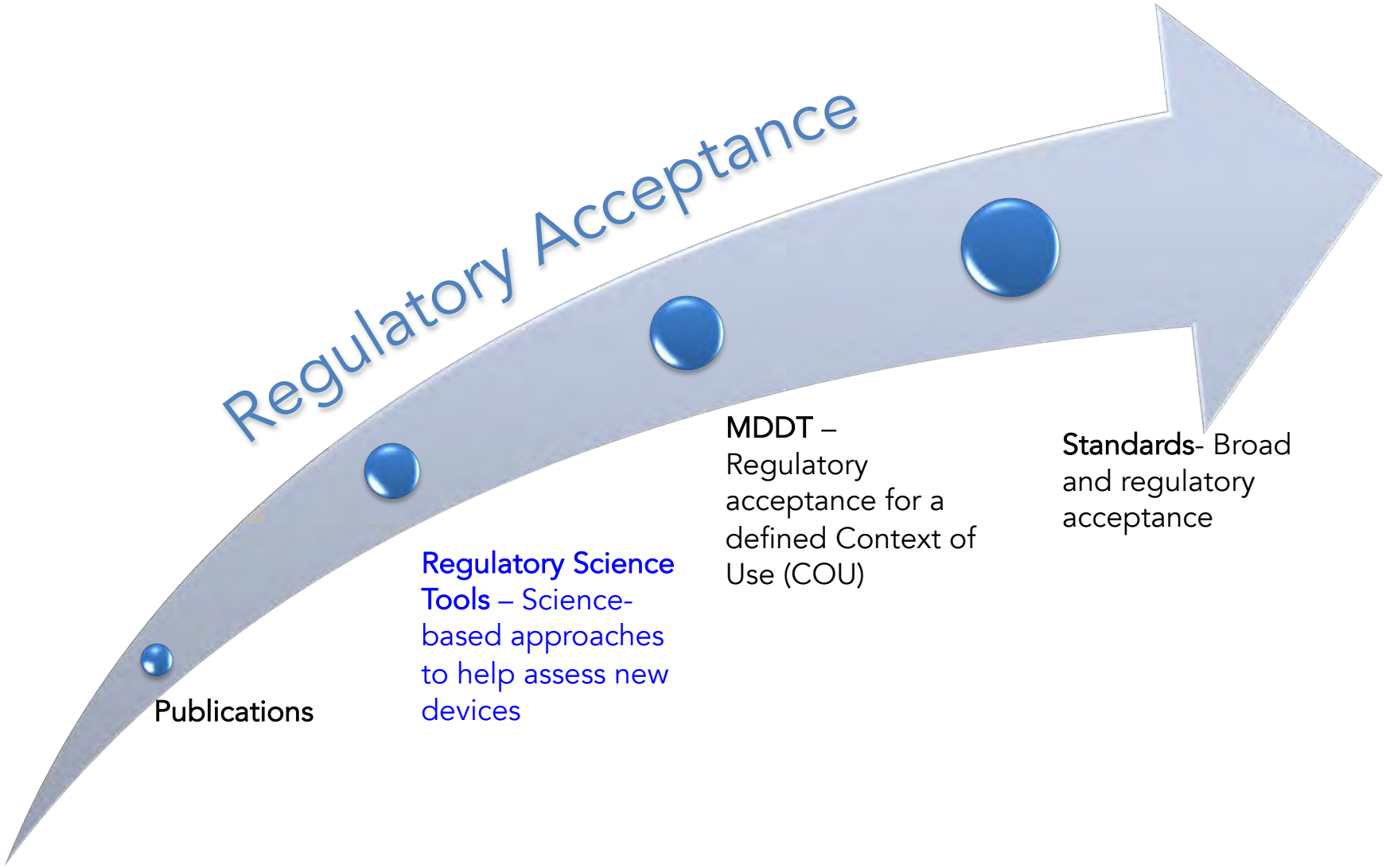
Feng et al., "Bayesian logistic regression for online recalibration and revision …," JAMIA 2022.

Putting tools in the hands of stakeholders

Regulatory Science Tools (RST)



Regulatory Science Tools (RST)



AI/ML Relevant RSTs

iMRMC: Multi-Reader Multi-Case Reader Studies	Statistical tools (java GUI and R package) to analyze, size, and simulate multi-reader multi-case (MRMC) reader studies	Model	Imaging reader studies, Artificial intelligence/machine learning	GitHub
iRoeMetz Application	A java application used to simulate reader scores for multi-reader multi-case (MRMC) reader studies	Model	Imaging reader studies, Artificial intelligence/machine learning	GitHub

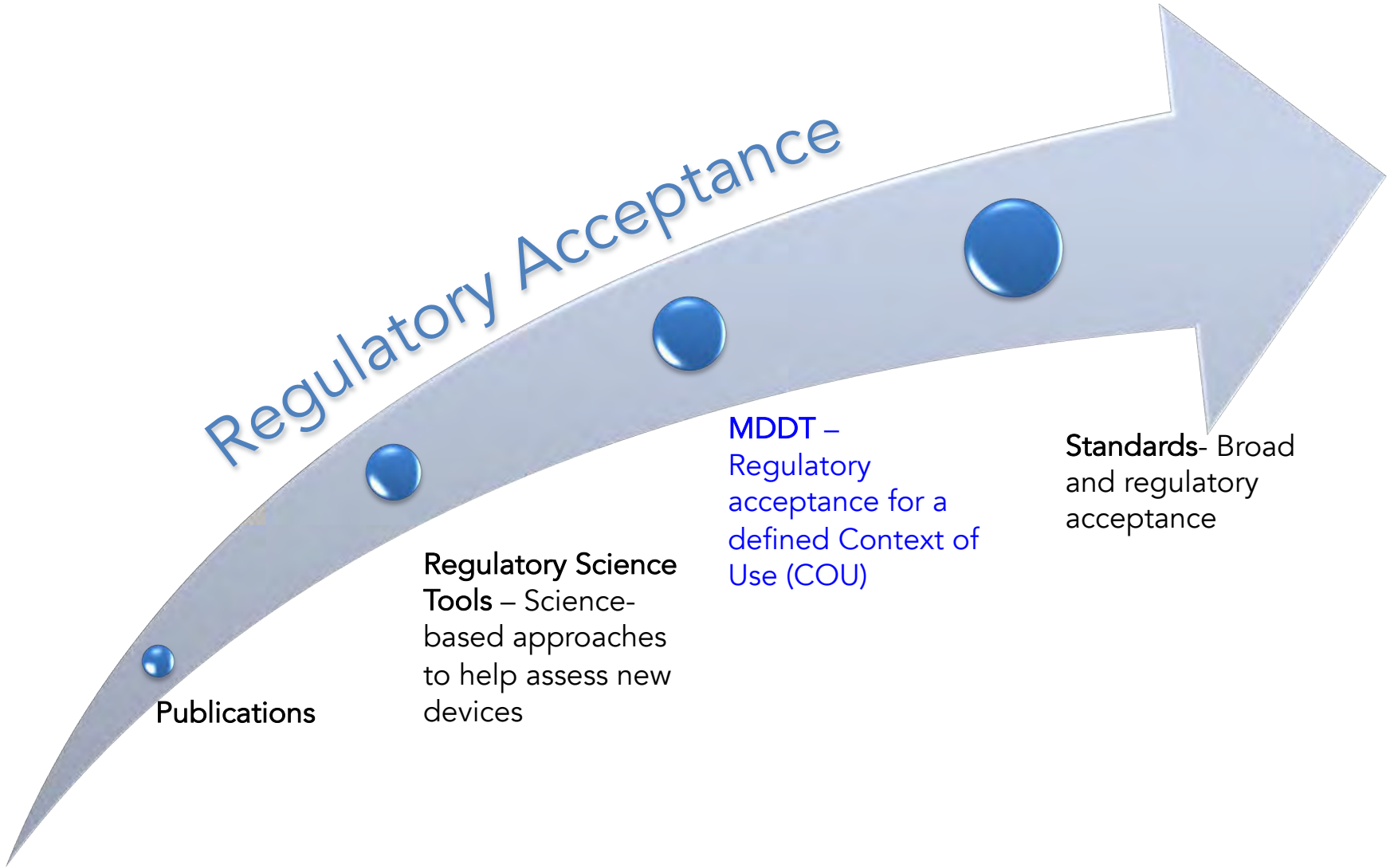
Catalog of Regulatory Science Tools to Help Assess New Medical Devices

Share Tweet Email

https://www.fda.gov/medical-devices/science-and-research-medical-devices/catalog-regulatory-science-tools-help-assess-new-medical-devices

VICTRE: Breast Mass Generation Software	A modeling software that randomly generates main body of breast masses including random branching spicules grown out from the mass surface	Model	Medical imaging and diagnostics	GitHub
VICTRE: Digital Mammography Regions of Interest (ROIs)	VICTRE ROI patches for digital mammography of breast density categories with microcalcification cluster and spiculated mass inserted signals.	Dataset	Medical imaging and diagnostics	GitHub
VICTRE: Model Observers (MO)	Computer model observer functions to perform location-known lesion detection tasks	Model	Medical imaging and diagnostics	GitHub
VICTRE: Virtual Imaging Clinical Trials for Regulatory Evaluation	An entirely in-silico imaging clinical trial replicating a premarket study.	Model	Medical imaging and diagnostics	GitHub Article
VICTRE: Multi-modality Anthropomorphic Breast Phantom	A digital breast phantom with modifiable parameters including phantom voxel size (resolution) and breast density	Phantom, Virtual	Medical imaging and diagnostics	GitHub Document
VICTRE_MCGPU: Pivotal Study Simulations	A simulation tool that replicates a Siemens Mammomat Inspiration system for VICTRE	Model	Medical imaging and diagnostics	GitHub

Regulatory Science Tools (RST)



Medical Device Development Tools (MDDTs)

Qualification of Medical Device Development Tools

Guidance for Industry, Tool Developers, and Food and Drug Administration Staff

Document issued on: August 10, 2017

The draft of this guidance document was issued on November 14, 2013.

For questions regarding this document, contact MDDT@fda.hhs.gov.

https://www.fda.gov/media/87134/download

Summary

- Active research from OSEL has been
  - Identifying and addressing critical gaps in device evaluation of medical AI/ML
  - Putting methodology and tools into the hands of stakeholders

Acknowledgments

- I'd like to acknowledge Berkman Sahiner, Nicholas Petrick, Brandon Nelson, Elena Sizikova, Kenny Cha, and Elim Thompson for providing slides and information used this presentation.

Questions

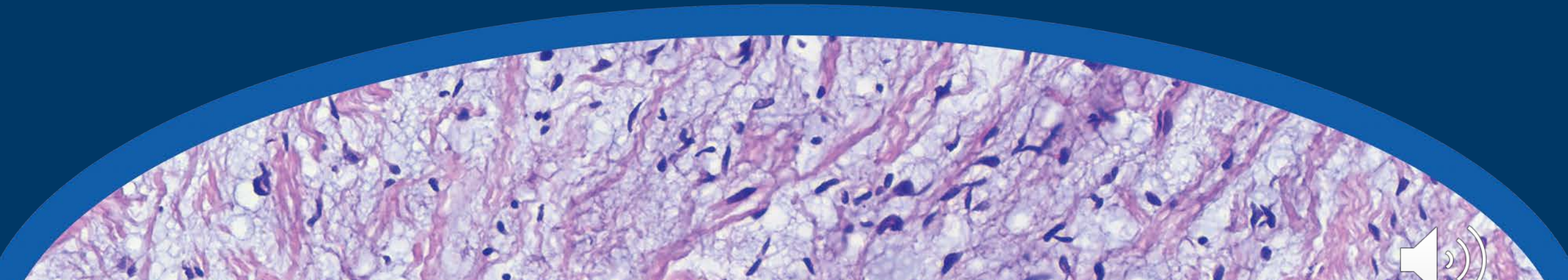

FDA
U.S. FOOD & DRUG
ADMINISTRATION

MDIC
MEDICAL DEVICE INNOVATION CONSORTIUM

Pathology Innovation Collaborative Community (PIcc)
Annual Meeting 2023

FDA Talk 4: Predetermined Change Control Plan

Ayobami Adebowale
DHCoE, CDRH, FDA



PREDETERMINED CHANGE CONTROL PLANS

Ayobami Adebowale, M.Eng
Biomedical Engineer for Digital Health Policy, CDRH Digital Health Center of Excellence
Office of Science and Technology (OST), Center for Devices & Radiological Health (CDRH), US FDA

Patients are at the Heart of What We Do

CDRH Vision

Patients in the U.S. have access to high-quality, safe, and effective medical devices of public health importance first in the world

Advancing Health Equity for All Devices is a Top Strategic Priority for CDRH

Historically, under-resourced populations lack access to quality health care.

DHTs in Clinical Trials

Transparency and Trust

Artificial Intelligence/ Machine Learning

Augmented Reality / Virtual Reality

Digital health technology (DHTs) can help bridge the divide.

Predetermined Change Control Plans for AI/ML-Enabled Devices

Predetermined Change Control Plans (PCCPs) can support ensuring that AI/ML-enabled devices better meet the needs of diverse populations.

Contains Nonbinding Recommendations

Draft – Not for Implementation

Marketing Submission Recommendations for a Predetermined Change Control Plan for Artificial Intelligence/Machine Learning (AI/ML)-Enabled Device Software Functions

Draft Guidance for Industry and Food and Drug Administration Staff

DRAFT GUIDANCE

This draft guidance document is being distributed for comment purposes only.

Document issued on April 3, 2023.

You should submit comments and suggestions regarding this draft document within 90 days of publication in the *Federal Register* of the notice announcing the availability of the draft guidance. Submit electronic comments to https://www.regulations.gov. Submit written comments to the Dockets Management Staff, Food and Drug Administration, 5630 Fishers Lane, Room 1061, (HFA-305), Rockville, MD 20852. Identify all comments with the docket number listed in the notice of availability that publishes in the *Federal Register*.

For questions about this document regarding CDRH-regulated devices, contact digitalhealth@fda.hhs.gov. For questions about this document regarding CBER-regulated devices, contact ocod@fda.hhs.gov. For questions about this document regarding CDER-regulated products, contact druginfo@fda.hhs.gov. For questions about this document regarding combination products, contact the Office of Combination Products at combination@fda.gov.

FDA U.S. FOOD & DRUG ADMINISTRATION

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Devices and Radiological Health
Center for Biologics Evaluation and Research
Center for Drug Evaluation and Research
Office of Combination Products in the Office of the Commissioner

The FDA's proposed approach to PCCPs would:

- Put safe and effective advancements in the hands of health care providers and users faster.

https://www.fda.gov/regulatory-information/search-fda-guidance-documents/marketing-submission-recommendations-predetermined-change-control-plan-artificial

Supporting FDA's Strategic Priority to Promote Health Equity

- PCCPs can further FDA's strategic priority by:
  - Facilitating more rapid and continuous improvement of AI/ML-enabled device performance across diverse populations
  - Ensuring important performance considerations – including with respect to race, ethnicity, disease severity, gender, age, and geographical considerations – are addressed throughout the total product lifecycle
- Draft guidance proposes to place a significant and increased emphasis on importance of clearly communicating valuable information about these considerations to device users

Continuing our Collaborative Approach

2019	2020	2021	2022	2023
• Published AI/ML-SaMD Discussion Paper • First joined Collaborative Community related to AI/ML	• Public Workshop on AI/ML in Radiological Imaging • PEAC Meeting on Patient Trust in AI/ML Devices	• Published AI/ML Medical Device Software Action Plan • Posted List of Currently Marketed AI/ML Devices • Public Workshop on Transparency of AI/ML Devices • Published Good Machine Learning Practice Principles	• Contributed to IMDRF's Key Terms & Definitions: Machine Learning Enabled Medical Devices • Published Clinical Decision Support (CDS) Final Guidance • Updated List of Currently Marketed AI/ML Devices • Recognized new Consensus Standard on AI/ML	• Published Predetermined Change Control Plan for AI/ML Devices Draft Guidance

We recognize that by working collaboratively with stakeholders we can lay out a clear path toward building a proactive patient-centered approach to the development and use of AI/ML-enabled devices.

FDA's Collaborative Patient-Centered Approach to AI/ML-Enabled Devices

2019

Discussion Paper

Proposed regulatory framework for modifications to AI/ML-enabled medical device software to assure their safety and effectiveness, including **pre-specification of software changes to enable rapid improvement of software products**

2021

Action Plan

Holistic, patient-centered strategic approach to AI/ML-enabled devices that promotes health equity, including aims to **update the proposed regulatory framework** and **foster a patient-centered approach, including transparency to users**

2023

Draft Guidance

Proposed, least burdensome approach to support safe, iterative improvement through modifications to an AI/ML-enabled device

www.fda.gov/digitalhealth

Purpose and Scope

Scope of Draft Guidance

- Applicable to machine learning-enabled device software functions (ML-DSFs) that a manufacturer intends to modify over time
- Describes proposed recommendations on information to be included in a Predetermined Change Control Plan (PCCP) provided as part of a marketing submission
- Generally, recommendations apply to device constituent part of a combination product, when the device constituent part is (or includes) an ML-DSF
- PCCP is an optional mechanism within a marketing submission for premarket authorization for modifications to an ML-DSF

Proposed Approach for Modifications for Machine-Learning Device Software Functions (ML-DSF)

Draft Policy for PCCPs

An authorized PCCP specifies planned modifications that, if not included in a PCCP, could otherwise require a new marketing submission*

The modifications can be implemented to the ML-DSF without triggering the need for a new marketing submission

Modifications made to an ML-DSF that are not specified in the authorized PCCP could require a new marketing submission*

*Note: pursuant to 21 CFR 807.81(a)(3) and 21 CFR 814.39(a), and in accordance with the "Modifications" guidances. For a list of the "Modifications" guidances, please see the Resources slide.

Proposed Components of PCCPs

Description of Modifications

"What" a manufacturer intends the algorithm to become as it learns

- Identifies specific, planned modifications to ML-DSF that the manufacturer intends to implement
- Draws a "range of FDA-authorized specifications" around initial device characteristics and performance

Modification Protocol

"How" the algorithm will learn/change while remaining safe and effective

- Describes methods that will be followed when developing, validating, and implementing the modifications to ensure the device remains safe and effective
- Methods described in Modification Protocol should be consistent with and support the modifications outlined in Description of Modifications

Impact Assessment

Describes modifications' benefits and risks, and how risks are mitigated

- Assesses benefits and risks of each individual modification, as well as collective impact of modifications, included in the Description of Modifications
- Discusses how activities proposed within Modification Protocol mitigate identified risks to continue to reasonably ensure the safety and effectiveness of the device

Predetermined Change Control Plan

Proposed PCCP Recommendations for Marketing Submissions

Establishing a PCCP

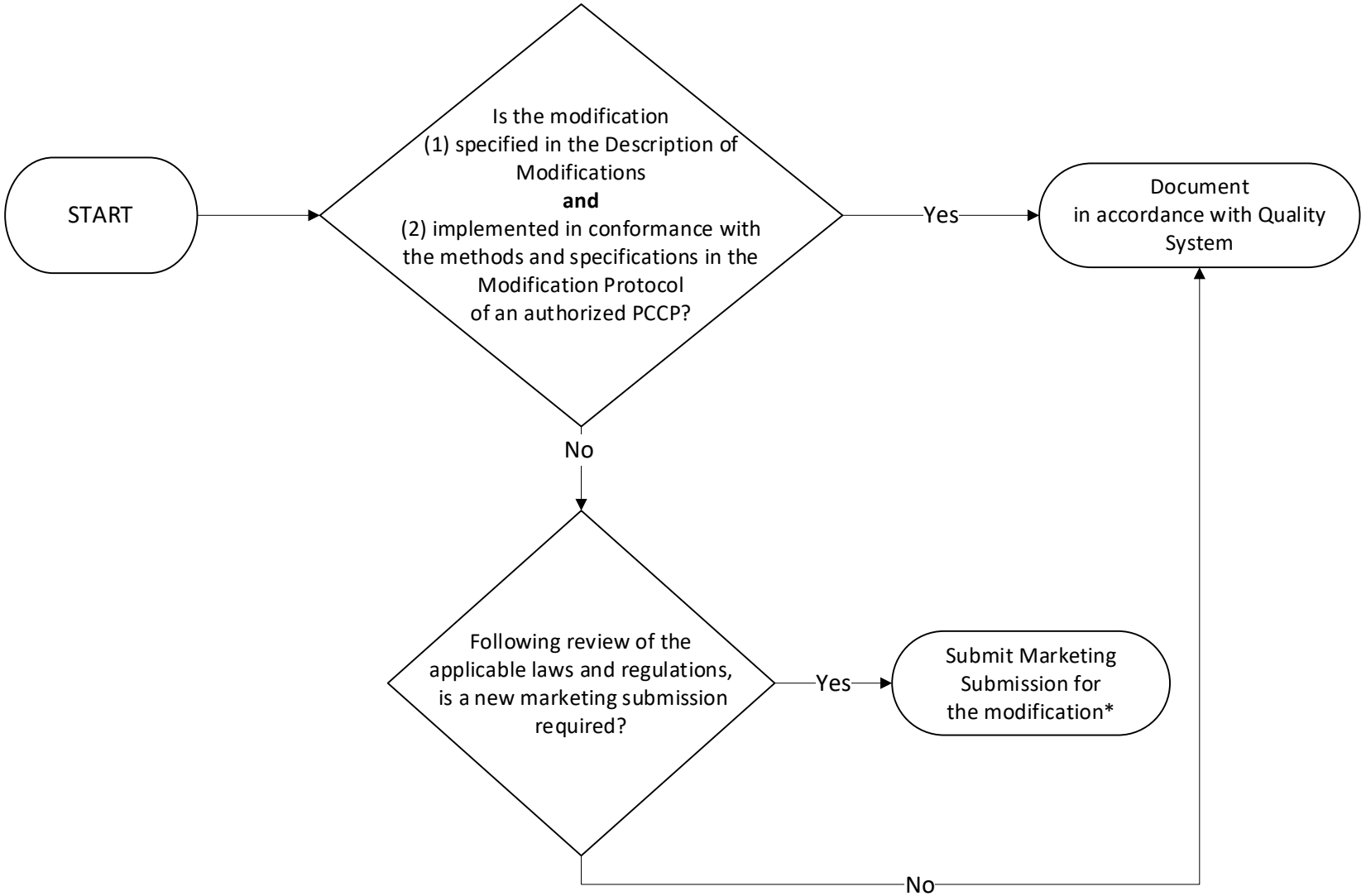
- A PCCP is **included in a marketing submission for a device and established as part of that authorization***
- An "authorized PCCP" is one that has been reviewed and established through the device marketing authorization
- To establish a new PCCP for a previously authorized device, the marketing submission must include appropriate marketing submission requirements and the proposed PCCP for the device

*Note: The term "authorization" is used to include clearance of a 510(k), granting of a De Novo, or approval of PMA

Identifying a PCCP in a Marketing Submission

- In the marketing submission, the PCCP:
  - should be a standalone section, noted in the cover letter, and listed in the table of contents as "Predetermined Change Control Plan"
  - should be discussed as part of the device description, labeling, and other relevant sections
- The PCCP should be described in the:
  - 510(k) summary,
  - De Novo decision summary, or
  - PMA summary of safety and effectiveness document (SSED) and approval order
- Details of the PCCP should be included in sufficient detail to **support transparency to users** regarding the safety and effectiveness of the device
- Labeling should include an adequate description to **ensure appropriate use of the device**

Using an Authorized PCCP to Implement Modifications



*For the modified device to have a PCCP, a PCCP should be submitted with the marketing submission so that the device and PCCP can be authorized together.

Modification Protocol

"How" the algorithm will learn/change while remaining safe and effective

Modification Protocol

- Methods described in Modification Protocol should be **consistent with and support** modifications outlined in Description of Modifications
- Four primary components of a Modification Protocol:
  - (1) data management practices,
  - (2) re-training practices,
  - (3) performance evaluation protocols, and
  - (4) update procedures, including communication and transparency to users and real-world monitoring plans
- Include description of how proposed methods are similar to, or are different from, methods used elsewhere in marketing submission

Traceability between Modification Protocol and Description of Modifications

PCCP should clearly delineate which parts of Modification Protocol are applicable to each modification within Description of Modifications

	Modification Protocol Component			
Modification	Data management practices	Re-training practices	Performance evaluation	Update procedures
Modification #1	Method A (see Section X.A)	Method D (see Section X.D)	Method G (see Section X.G)	Method J (see Section X.J)
Modification #2	Method A (see Section X.A)	Method E (see Section X.E)	Method H (see Section X.H)	Method J (see Section X.J)
Modification #3	Method B (see Section X.B)	Method F (see Section X.F)	Method I (see Section X.I)	Method J (see Section X.J)

Table 1. Example of Description of Modifications to Modification Protocol Traceability Table

Impact Assessment

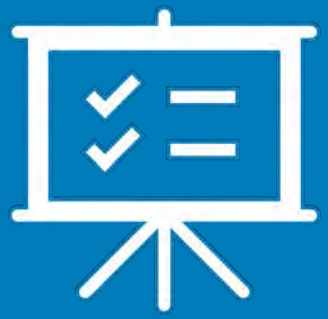
Describes modifications' benefits and risks, and how risks are mitigated

Impact Assessment

Documentation for an Impact Assessment provided to the Agency in a marketing submission containing a PCCP should:

1. Compare version of device with each modification implemented to version of device without any modifications implemented
2. Discuss benefits and risks of each individual modification
3. Discuss how activities proposed within Modification Protocol continue to reasonably ensure safety and effectiveness of device
4. Discuss how implementation of one modification impacts implementation of another
5. Discuss collective impact of implementing all modifications

KEY POINTS



- ✓ The PCCP draft guidance describes FDA's proposed approach to ML-DSFs to support their iterative development and improvement over time
- ✓ The introduction of PCCPs build on the Agency's longstanding commitment to developing innovative approaches to ensuring safe and effective digital health technologies are available to patients
- ✓ The PCCP Draft guidance introduces proposed recommendations on information to be included in a PCCP provided as part of a marketing submission for an ML-DSF
- ✓ The draft guidance also specifies that modifications made to an ML-DSF in accordance with an authorized PCCP can be implemented to the ML-DSF without a new marketing submission

Further Questions or Feedback

www.fda.gov/digitalhealth

DigitalHealth@fda.hhs.gov

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Center for Devices and Radiological Health, U.S. Food and Drug Administration

Email: Ayobami.Adebowale@fda.hhs.gov

The Food and Drug Omnibus Reform Act ("FDORA") Included a Provision for PCCPs

FDA

FDORA grants authority for PCCPs*

- *Changes to a device consistent with an approved predetermined change control plan do not require a supplemental application. It may also require that change control plans include labeling required for safe and effective use of the device.*

The PCCP provision applies to more than just AI/ML-enabled devices

- *This provision applies to all devices—it is not specific to AI/ML-enabled devices or software devices. It applies to both premarket approval (PMA) applications and 510(k) applications.*

2023 Draft Guidance on PCCPs for AI/ML-Enabled Devices


Marketing Submission Recommendations for a Predetermined Change Control Plan for Artificial Intelligence/Machine Learning (AI/ML)-Enabled Device Software Functions

Draft Guidance for Industry and Food and Drug Administration Staff

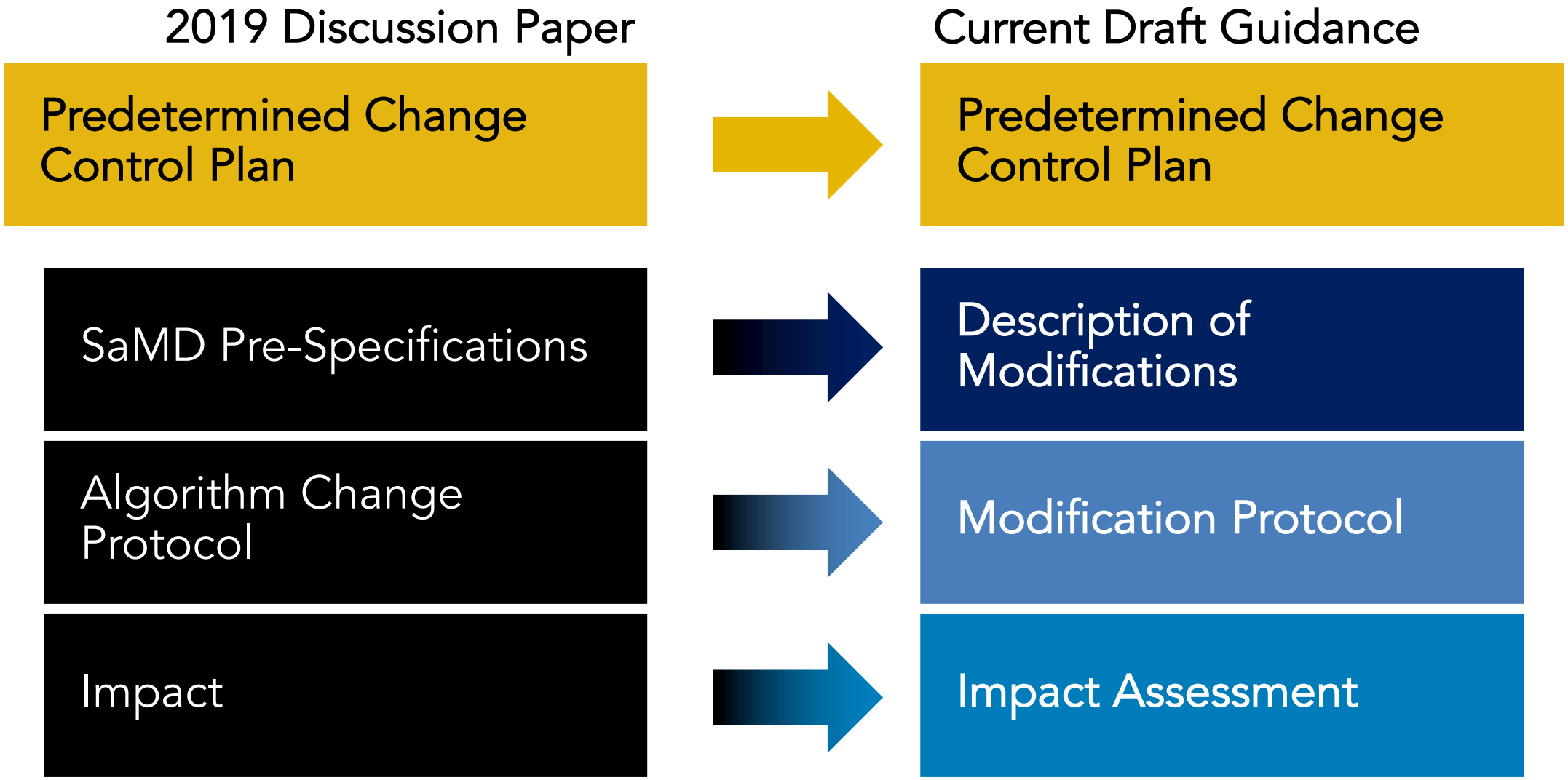
DRAFT GUIDANCE

U.S. FOOD & DRUG ADMINISTRATION

- *This Draft Guidance provides proposed recommendations specifically for ML-DSFs that a manufacturer intends to modify over time. Consistent with the addition of section 515C, this draft guidance discusses the submission of PCCPs in marketing submissions for ML-DSFs.*

*Per section 3308 of FDORA, Title III of Division FF of the Consolidated Appropriations Act, 2023, enacted on December 29, 2022, which added section 515C to the Federal Food, Drug, and Cosmetic Act (FD&C Act).

Term Mapping



SaMD = Software as a Medical Device

Resources/ Modification guidances

Cited Resource	URL
Deciding When to Submit a 510(k) for a Software Change to an Existing Device	www.fda.gov/regulatory-information/search-fda-guidance-documents/deciding-when-submit-510k-software-change-existing-device
Deciding When to Submit a 510(k) for a Change to an Existing Device	www.fda.gov/regulatory-information/search-fda-guidance-documents/deciding-when-submit-510k-change-existing-device
Modifications to Devices Subject to Premarket Approval (PMA)	www.fda.gov/regulatory-information/search-fda-guidance-documents/modifications-devices-subject-premarket-approval-pma-pma-supplement-decision-making-process
21 CFR 807.81(a)(3)	www.ecfr.gov/current/title-21/chapter-I/subchapter-H/part-807/subpart-E/section-807.81#p-807.81(a)(3)
21 CFR 814.39(a)	www.ecfr.gov/current/title-21/chapter-I/subchapter-H/part-814/subpart-B/section-814.39#p-814.39(a)

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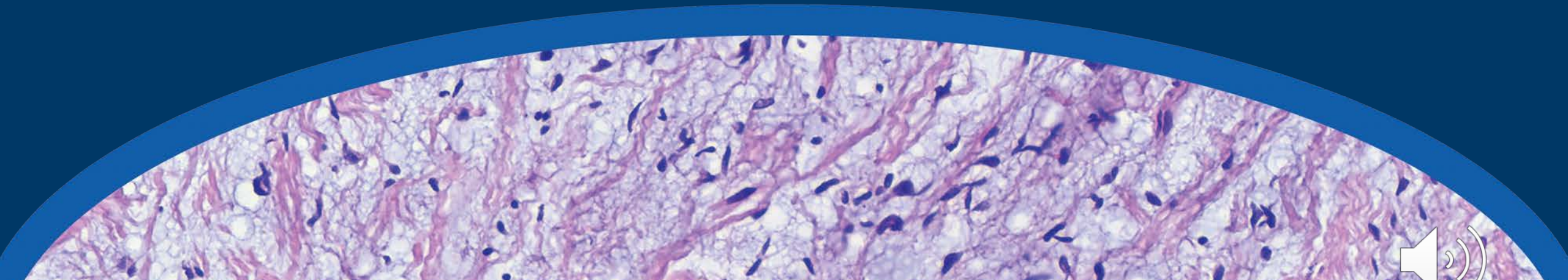
Pathology Innovation Collaborative Community (PIcc)
Annual Meeting 2023

Panel Discussion/Q&A

Moderated by
Ed Margerrison



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Pathology Innovation Collaborative Community (PIcc)
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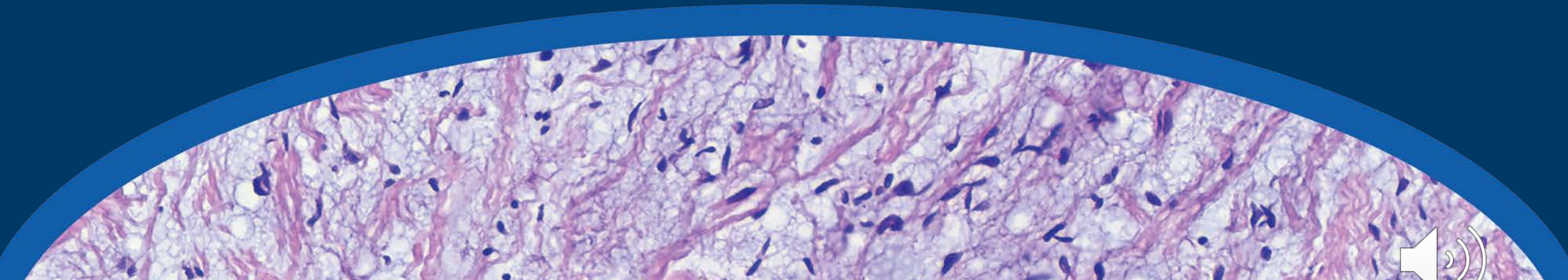
Coffee Break



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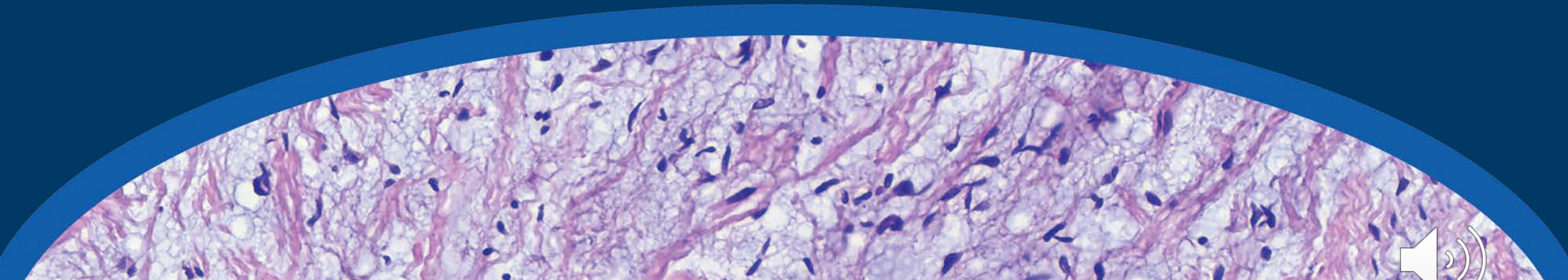
Pathology Innovation Collaborative Community (PIcc)
Annual Meeting 2023

Breakout Session Topics



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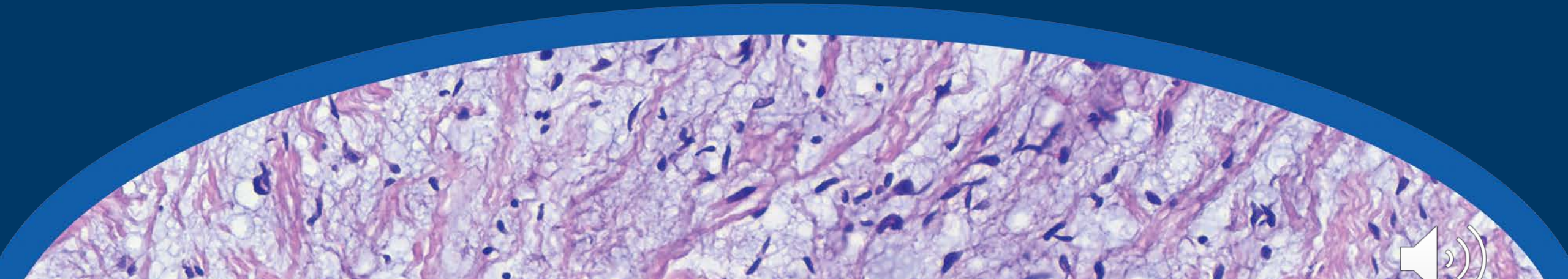
Pathology Innovation Collaborative Community (PIcc)
Annual Meeting 2023

Breakout Session Topics

Remote Work

Mike Isaacs, Matthew Leavitt, Doc de Baca



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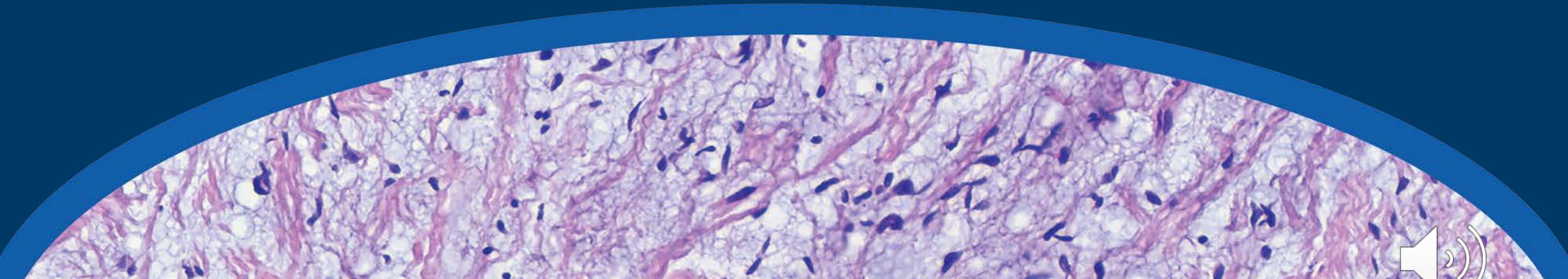
Breakout Session Topics

PCCP

Emre Gulturk, Kevin Schap, Alexej Gossmann



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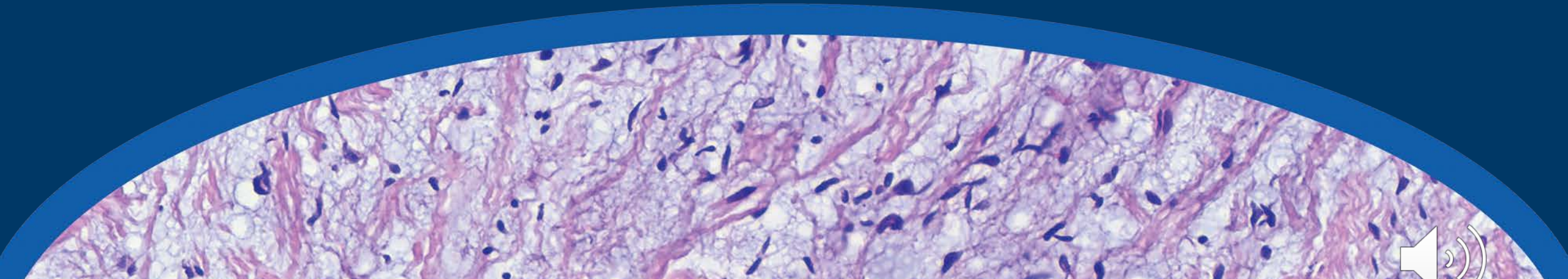
Breakout Session Topics

Statistics

Brandon Gallas, Kim Blenman, Gina Giannini



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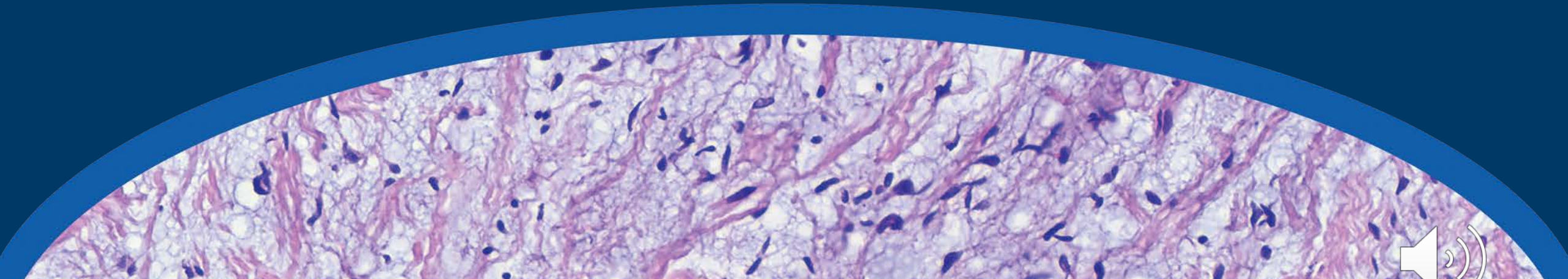
Annual Meeting 2023

Breakout Session Topics

"Open Topic"

Jeni Caldera, Joe Lennerz



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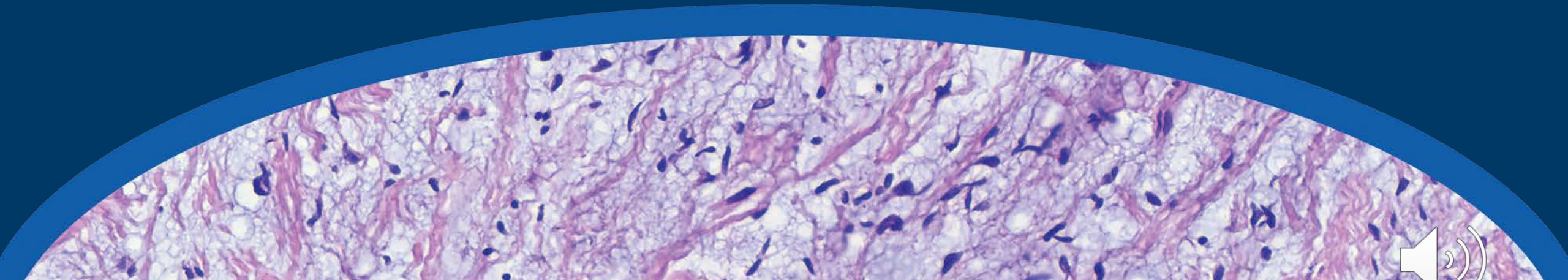
Dinner Reception



PIcc23 Day 2

June 28

Welcome

PIcc23

Breakout Session Overview

Introduction of all Participants (each table)

- Name, title, organization – two minutes total

We have identified Breakout Topic Leads

- Deliver 1-slide summary in plenary session (feel free to change if ok)

Rules of Engagement

- Every member in the group should contribute
- Share your experience and perspective
- Respect the opinions of others
- Maintain confidentiality and respect antitrust requirements
- Focus on the topic at hand and try not to move on to tangential issues
- Use parking lot for important topics for subsequent discussion

Last Five Minutes

- Confirm champion is prepared
- Check 1-slide summary for consolidation and projection in plenary session

Breakout Session Format

Overview – "Name of the group"

- What is missing to move "XXX" forward
- 3 key elements that the group considered most meaningful next steps including timelines
- What is the goal of this project and timeline?
- "How will these elements be valuable from a clinical, regulatory, and R&D perspective?"
- What is the clinical impact and/or relevance to the patient?
- What are possible concerns/risks to the patient?
- Explain the regulatory implications and advantages of pursuing this project in relation to digital pathology.

BREAKOUT SUMMARY SLIDE: _____ SESSION: _____

Key Elements, Next Steps, Timeline

Pros for Patient, Clinical, R&D, and Regulatory

Deliverables and Timeline

Concerns for Patients, Clinical, R&D, and Regulatory

Implications and efforts

Breakout Session 1

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Remote Work

Mike Isaacs, Matthew Leavit, Doc de Baca, Joe Sirintrapun

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Emre Gulturk, Kevin Schap, Alexej Gossmann

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Statistics

Brandon Gallas, Kim Blenman, Gina Giannini

Open Topic

Jeni Caldera, Joe Lennerz

Create Summary Slide

Coffee Break + Rotate

Breakout Group Presentations

Vote

PIcc23

Keynote II: MedPerf Open and Standardized Benchmarking of Medical Artificial Intelligence

Alex Karargyris

Breakout Session 2

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Remote Work

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Open Topic

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Create Summary Slide

Coffee Break + Rotate

Breakout Group Presentations

Vote

Lunch

Sponsored by DDX Foundation

Final Breakout Session

Create Summary Slide

Coffee Break + Rotate

Breakout Group Presentations

Vote

Next Steps