

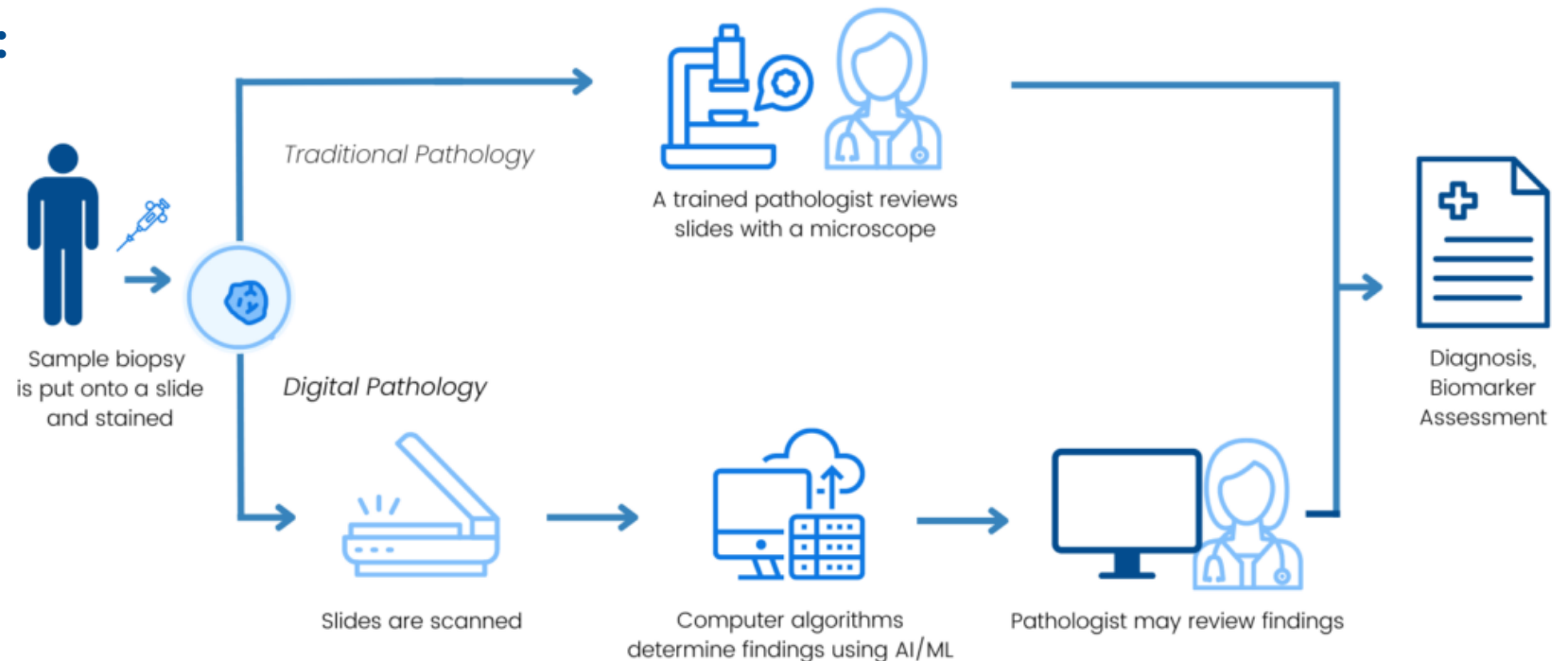
The Digital and Computational Pathology Tool Harmonization Project

The Digital PATH Project

Digital and Computational Pathology

Challenges in Computational Pathology:

- Lack of standardization in image acquisition, analysis, and interpretation can lead to variability in biomarker results and difficulty comparing data across different studies
- Limited guidelines and need for a framework to guide evidentiary needs



Digital PATH Project

Landscape Assessment

Demonstration Project

Objectives

- Characterize uses of computational pathology in oncology
 - Provide proposals to facilitate robust development of computational pathology platforms
- Assess concordance of biomarker measurements across different algorithms and compared to pathologists
 - Identify opportunities for alignment and propose best practices

Approach

- Assemble a multi-stakeholder working group to develop a white paper to provide a landscape assessment of challenges and opportunities
- Develop a demonstration project to identify variability among algorithms in HER2 scoring in breast cancer and support opportunities for harmonization

Project Timeline

Public Virtual Meeting
Released Landscape White Paper

Public Hybrid Meeting
Launched Demonstration Project

| 2023 | | | | 2024 | | | |
|------|----|----|----|------|----|----|----|
| Q1 | Q2 | Q3 | Q4 | Q1 | Q2 | Q3 | Q4 |

Working Group Conducted Landscape Analysis

Prepare for Demonstration Project including Identify Use Case

Demonstration Project (*anticipate data readout in Q4 2024-Q1 2025*)

Digital PATH Project

The Research Question: What factors contribute to variability in biomarker assessment across computational pathology platforms and what performance metrics support improved evaluation and alignment?

The Use Case: HER2 assessment in breast cancer

Distribute Whole Slide Images

- **Obtain and distribute WSIs** → Distribute whole slide images from >1,000 breast cancer samples to computational pathology model developers to analyze HER2

Run Digital Pathology Models

- **Computational pathology developers run models** → Analyze whole slide images
- **Return data to *Friends*** → Template to return HER2 status calls and scores

Compare Models

- **NCI performs analysis** → Use statistical analysis plan (SAP) to compare models to determine concordance
- **Report findings** → Align on key findings

Analysis Strategy Overview

Primary Analysis

Descriptive analysis describing concordance

HER2 categorical scores: 0, 1+, 2+, 3+

Secondary/ Exploratory Analysis

Factor Associations

Association of patient, specimen, and model attributes with HER2 categorical scores

Pathologist Concordance

Concordance between models and pathologists

Quantitative Measurements

Concordance between models providing quantitative biomarker measurements

Additional Categorical Scores

Concordance between models that provide ultra-low, low, and other categories