Diagnostic Quality Assurance Pilot

Frequently Asked Questions

About the Diagnostic Quality Assurance Pilot

What is this initiative?

The Diagnostic Quality Assurance Pilot addresses a standardization gap in personalized medicine by creating a process to compare diagnostics for targeted therapies in cancer treatment. The pilot helps to ensure that diagnostics provide clinicians with consistent and correct answers, regardless of which laboratory conducts the test and which diagnostic platform the laboratory uses. To achieve this goal, the pilot will design and equip molecular pathology laboratories with traceable reference samples to assess whether participating laboratories' appropriately validated tests can achieve diagnostic performance comparable to a companion diagnostic (CDx) for targeted cancer therapy. These reference samples are intended to complement internal quality controls that should already be used by laboratories to gauge the accuracy of each assay run, or lot, as is routinely done in clinical chemistry.

Why is this pilot needed?

New molecular techniques for biomarkers are increasing the scope and value of molecular diagnostics, creating a need for greater system-wide assurance that clinicians select the correct patients for targeted cancer therapies. The US Food and Drug Administration (FDA) and legislators continue to consider novel ways to optimize regulatory oversight of laboratory-developed tests (LDTs), including Next Generation Sequencing (NGS) assays, in order to provide a "flexible, adaptive regulatory approach that ensures that patients receive accurate and meaningful results, while accommodating innovation in test development."[1] The development of consensus reference samples for laboratories can help ensure that LDTs used as diagnostics for targeted therapies will meet certain analytical performance standards (defined below) and will identify appropriate patient populations.

How will the pilot address the need?

This initial proof of concept pilot is oncology-focused with a candidate CDx comprised of a two-gene, multiple-variant NGS panel voluntarily proposed by biopharmaceutical developer Amgen and Amgen's CDx partner, Illumina. Performance standards will be set by the specifications of the Illumina CDx for a targeted colorectal cancer therapy undergoing FDA review for a new indication *(note: subsequent to the pilot's commencement, the FDA approved the relevant treatment and corresponding CDx).*[2]

Through participation in the pilot process, laboratories can demonstrate their ability to accurately discriminate a subset of the clinical decision points for the targeted therapy regardless of whether they are using the FDA-approved CDx developed by Illumina or an LDT. Specifically, laboratories

will analyze samples using a variety of NGS platforms and informatics tools to report specific sequence variants traceable to the volunteer CDx. The long-term goal is to help ensure that by utilizing the reference samples, a laboratory could reliably and accurately identify the appropriate patient population that would benefit from the associated targeted therapy, regardless of the type of test used.

Who is participating in the pilot?

The pilot's technical components are implemented by the College of American Pathologists (CAP) and guided by a scientific technical working group (STWG) comprising leading experts in the field of molecular pathology and NGS. Amgen and Illumina have contributed relevant technical specifications of the candidate CDx as design inputs for the reference materials, and Amgen underwrites associated costs.

An independent, multistakeholder Steering Committee (SC) provides governance for the pilot, advises CAP and the STWG, offers feedback from member organizations' perspectives, and informs constituent organizations about the pilot. The SC includes representatives from the patient advocacy community, payers, clinical oncologists, and industry. Liaisons from the FDA, the US National Cancer Institute, and others participate as observers. Tapestry Networks advises and supports the SC and its Chair.

A complete list of individuals and organizations involved in the STWG and SC can be found in the Annex to this document. For additional details on the pilot's genesis within the Sustainable Predictive Oncology Therapeutics and Diagnostics Working Group convened by Tapestry Networks, please read more here.

When will the pilot be completed?

The pilot launched in Q2 2016. Results were shared with the SC in mid-2019, and manuscripts for publication are planned for 2021.

Where can I find more information?

The goal of the pilot is to be transparent and share outcomes with the public to facilitate continuous learning across key stakeholder groups, especially those working in complementary areas. Additional updates and communications will be shared as the pilot progresses and results are learned. In the meantime, for further details please contact:

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John Pfeifer, Scientific Technical Working Group Chair (former): pfeifer@wustl.edu

About the Diagnostic Quality Assurance Pilot and this document

The views expressed in this document represent consolidated views of those participating in the Diagnostic Quality Assurance Pilot Steering Committee as members and liaisons. Participation in the Steering Committee and written materials reflecting the Steering Committee's activities are not intended to represent the particular policies or positions of the individual participants or their affiliated organizations.

Annex: Pilot Participants

Scientific Technical Working Group

- Julia A. Bridge, Professor, Director, Division of Molecular Pathology, The Translational Genomics Research Institute (TGen), Professor, Department of Pathology and Microbiology, University of Nebraska Medical Center
- Suzanne Kamel-Reid, University of Toronto, Laboratory Medicine and Pathology and Toronto General Hospital and Research Institute
- Jason D. Merker, Associate Professor of Pathology and Laboratory Medicine & Genetics, The University of North Carolina at Chapel Hill School of Medicine, Lineberger Comprehensive Cancer Center
- John D. Pfeifer, Vice Chair for Clinical Affairs, Department of Pathology, Washington University School of Medicine *(Chair - former)*
- David Stanforth, Director, Clinical Biomarkers and Diagnostics Head of Diagnostics Strategy and Development Translational Medicine, Amgen
- Patricia Vasalos, Technical Manager, Proficiency Testing, College of American Pathologists (CAP) *(STWG Project Manager)*
- Barbara Zehnbauer, Adjunct Professor of Pathology, Emory University School of Medicine *(Liaison to the Steering Committee)*

Steering Committee

Members

- Jeff Allen, President and CEO, Friends of Cancer Research

Steering Committee Members *(contd.)*

- Naomi Aronson, Executive Director, Clinical Evaluation, Innovation and Policy, Blue Cross and Blue Shield Association
- Gabriel Bien-Willner, Medical Director, MolDx, Palmetto GBA
- Karen Gutekunst, Vice President of Diagnostic Development, Illumina
- Daniel F. Hayes, Stuart B. Padnos Professor of Breast Cancer Research, University of Michigan Comprehensive Cancer Center; Past-President, American Society of Clinical Oncology (ASCO) 2016-2017
- Tom Oliver, Director, Clinical Practice Guidelines Division, ASCO
- John Pfeifer, Vice Chair for Clinical Affairs, Pathology and Immunology, Washington University School of Medicine *(Liaison to the STWG)*
- Blase Polite, Associate Professor of Medicine, Deputy Section Chief for Clinical Operations, and Executive Medical Director for Cancer Accountable Care, University of Chicago Medicine, and ASCO board member
- Girish Putcha, Chief Medical Officer, Freenome
- Richard L. Schilsky, Senior Vice President and Chief Medical Officer, ASCO
- David Stanforth, Director, Clinical Biomarkers and Diagnostics Head of Diagnostics Strategy and Development Translational Medicine, Amgen
- Patricia Vasalos, Technical Manager, Proficiency Testing, CAP *(Liaison to the STWG)*
- Barbara Zehnbauer, Adjunct Professor of Pathology, Emory University School of Medicine *(Chair)*

Advisors to the Steering Committee and Chair

- Lindee Goh, Partner, Tapestry Networks
- Elizabeth Shaughnessy, Principal, Tapestry Networks

Liaisons

- Lisa McShane, Associate Director, Division of Cancer Treatment & Diagnosis, Chief, Biometric Research Program, National Cancer Institute
- Michael Pacanowski, Director, Division of Translational and Precision Medicine, CDER, FDA
- Julie Schneider, Associate Director for Research Strategy and Partnerships, OCE, FDA

- Zivana Tezak, Associate Director for Science and Technology, Personalized Medicine Policy, Office of In Vitro Diagnostic Device Evaluation and Safety, CDRH, FDA

Endnotes

[1] US FDA, *Developing Analytical Standards for NGS Testing*, (Washington DC: US FDA, 2015), 1. The FDA has also issued more recent guidance on standards for NGS diagnostics, but these are applicable only to germline diseases. See US FDA, *Considerations for Design, Development, and Analytical Validation of Next Generation Sequencing (NGS) – Based In Vitro Diagnostics (IVDs) Intended to Aid in the Diagnosis of Suspected Germline Diseases.* (Washington DC: US FDA, 2018).

[2] For more information, see US FDA, "FDA granted marketing approval to the Praxis Extended RAS Panel," accessed August 8, 2017, and Amgen, "FDA Approves Vectibix® (Panitumumab) For Use In Wild-Type RAS Metastatic Colorectal Cancer," news release, June 29, 2017.