

Frequently Asked Questions

DIAGNOSTIC QUALITY ASSURANCE PILOT



About the Diagnostic Quality Assurance Pilot – updated June 2018

1. 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 lab conducts the test and which diagnostic platform the lab uses. To achieve this goal, the pilot will design and equip molecular pathology labs with traceable reference samples to assess whether participating labs' 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 labs to gauge the accuracy of each assay run, or lot, as is routinely done in clinical chemistry.

2. 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 regardless of the particular lab or diagnostic test utilized. This need has become more acute with the advent of the President's Precision Medicine Initiative (PMI).¹

Additionally, the U.S. 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."² The development of consensus reference samples for labs 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.

3. 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 treatment and corresponding CDx were approved by the FDA in June 2017*).³ Through participation in the pilot process, labs can demonstrate their ability to accurately discriminate a

¹ "The Precision Medicine Initiative." White House, accessed July 13, 2016.

² U.S. FDA, *Developing Analytical Standards for NGS Testing*, (Washington DC: U.S. 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 U.S. 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: U.S. FDA, 2018).

³ For more information, see U.S. 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.

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

4. 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, Centers for Medicare and Medicaid Services, and the U.S. National Cancer Institute 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](#).

5. When will the pilot be completed?

The pilot launched in Q2 2016 and final results are expected by early 2019.

6. 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 communications will be published as the pilot progresses and results are learned. In the meantime, for further details please contact:

Barbara Zehnbaauer, Steering Committee Chair: bzahnba@emory.edu

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

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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. This material is prepared and copyrighted by Tapestry Networks with all rights reserved. It may be reproduced and redistributed, but only in its entirety, including all copyright and trademark legends. Tapestry Networks and the associated logo are trademarks of Tapestry Networks, Inc.

Annex: Pilot Participants

Scientific Technical Working Group (STWG)

- Julia A. Bridge, MD, Professor, College of Medicine, Department of Pathology and Microbiology, University of Nebraska Medical Center
- Suzanne Kamel-Reid, PhD, University of Toronto, Laboratory Medicine and Pathology and Toronto General Hospital and Research Institute
- Robert D. Loberg, PhD, Executive Director, Head of Clinical Biomarkers & Diagnostics, Medical Sciences, Amgen, Inc.
- Jason Merker, MD, PhD, Assistant Professor of Pathology, Stanford University Medical Center
- Marina N Nikiforova, MD, University of Pittsburgh Medical Center, Professor of Pathology, Division of Molecular and Genomic Pathology and Director, Molecular Genomic Pathology Laboratory
- John D. Pfeifer, MD, PhD, Vice Chair for Clinical Affairs, Department of Pathology, Washington University School of Medicine (*Chair*)
- Patricia Vasalos, Technical Manager, Proficiency Testing, College of American Pathologists (*STWG Project Manager*)
- Barbara Zehnbauer, PhD, Adjunct Professor of Pathology, Emory University School of Medicine and Journal of Molecular Diagnostics, Editor in Chief (*Liaison to the Steering Committee*)

Steering Committee

- Jeff Allen, PhD, Executive Director, [Friends of Cancer Research](#)
- Jim Almas, MD, MolDX Medical Director, Palmetto GBA
- Naomi Aronson, PhD, Executive Director, Clinical Evaluation, Innovation and Policy, Blue Cross and Blue Shield Association
- Karen Gutekunst, PhD, Vice President of Diagnostic Development, Illumina
- Daniel F. Hayes, MD, FASCO, Stuart B. Padnos Professor of Breast Cancer Research, University of Michigan Comprehensive Cancer Center; Past-President, American Society of Clinical Oncology (ASCO) 2016-2017

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- Robert D. Loberg, PhD, Executive Director, Head of Clinical Biomarkers & Diagnostics, Medical Sciences, Amgen, Inc.
- John Pfeifer, MD, PhD, Vice Chair for Clinical Affairs, Pathology and Immunology, Washington University School of Medicine (*Liaison to the STWG*)
- Girish Putcha, MD, PhD, Director of Laboratory Science, MolDX, Palmetto GBA
- Richard L. Schilsky, MD, FACP, FASCO, Senior Vice President and Chief Medical Officer, ASCO
- Patricia Vasalos, Technical Manager, Proficiency Testing, College of American Pathologists (*Liaison to the STWG*)
- Barbara Zehnbaauer, PhD, Adjunct Professor of Pathology, Emory University School of Medicine and Journal of Molecular Diagnostics, Editor in Chief (*Chair*)

Advisors to the Steering Committee and Chair

- Lindee Goh, PhD, Partner, Tapestry Networks
- Elizabeth Shaughnessy, Senior Associate, Tapestry Networks

Liaisons

- Julia A. Beaver, Associate Director, Division of Oncology Products 1, Office of Hematology Oncology Products, Center for Drug Evaluation and Research (CDER), U.S. Food and Drug Administration (FDA)
- Gideon Blumenthal, Associate Director, Precision Therapeutics, Office of Hematology Oncology Products, CDER, FDA
- Yun-Fu Hu, Deputy Director of the Division of Molecular Genetics and Pathology, Office of In Vitro Diagnostics and Radiological Health Center for Devices and Radiological Health, CDRH
- Eunice Lee, PhD, Office of In Vitro Diagnostics and Radiological Health, Center for Devices and Radiological Health (CDRH), FDA
- Lisa Meier McShane, PhD, Chief, Biostatistics Branch, Biometric Research Program, Division of Cancer Treatment and Diagnosis, U.S. National Cancer Institute
- Michael Pacanowski, PharmD, MPH, Associate Director, Genomics and Targeted Therapy, Office of Clinical Pharmacology, Office of Translational Sciences, CDER, FDA
- Julie A. Schneider, Regulatory Scientist, Office of Hematology and Oncology Products, CDER, FDA
- Katherine Szarama, Evidence Development Division, Coverage and Analysis Group, U.S. Centers for Medicare and Medicaid Services
- Zivana Tezak, PhD, Associate Director for Science and Technology, Office of In Vitro Diagnostics and Radiological Health, CDRH, FDA