

# Summary of themes Quality Assurance Pilot for Cancer CDx

SUSTAINABLE PREDICTIVE ONCOLOGY THERAPEUTICS AND DIAGNOSTICS (SPOT/Dx)



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## Committed stakeholders move to make the Quality Pilot a reality

On February 25, 2015, a diverse group of stakeholders convened in Washington DC for the initial meeting of the Quality Assurance Pilot for Cancer Companion Diagnostics (CDx), or “Quality Pilot” for short.

Please see Appendix A for a list of meeting participants. The Quality Pilot’s mission is to bring greater system-wide assurance that the correct patients are selected for targeted cancer therapies regardless of the particular lab or diagnostic test employed in their care. The group hopes to accomplish this goal through the creation and adoption of consensus performance standards that will enable labs to demonstrate desired levels of CDx test performance in a transparent manner. Participants aligned on the need for CDx performance standards, explored the intricacies of the proposed approach, and considered high-level operational questions. The meeting was infused with a strong collaborative spirit and the common understanding that, as a payer put it, “it’s time for the rubber to hit the road.”

### Summary of themes

- **Performance standards in molecular pathology are needed to ensure accurate patient identification and test equivalence.** Participants agreed that CDx performance standards and transparency would provide greater assurance that the correct patients are being selected for targeted cancer therapies. The link between increasingly specific biomarkers and clinical value of new medicines suggests that current proficiency testing models are no longer suitable guarantees of test performance. A molecular lab director noted “*the old CAP model of just using real world samples isn’t viable.*” Consequently pathologists welcome “*affordable, performance-standard-tools to provide greater assurance in their interpretations*” regardless of the particular platforms used in their laboratories. A payer explained: “*Most Americans, including payers, assume not only analytical validity, but also that labs understand how the measurement ties back to what’s clinically relevant vis a vis the FDA-approved drug.*” A drug developer explained that the industry’s primary concern is to ensure that labs possess the ability to discriminate between patients on opposite sides of the clinically relevant cut points. “*We want to build a set of reference materials that (1) are linked to the clinical trial findings, (2) will survive over time as diagnostic platforms change, and (3) will minimize confusion when multiple drugs are developed that rely on the same biomarker.*”

The benefits from performance standards are clear, but practical constraints of time and money may limit a lab’s ability to demonstrate quality. Because of this, all participants agreed that transparency was critical for high-performing labs to achieve sufficient and sustainable returns.

- **While reference materials may be used for a host of purposes, the Quality Pilot will focus on those that serve as CDx performance calibrators.** The group acknowledges that the term “reference materials” has different meaning to different stakeholders. Arriving at a common understanding of the purpose of the Quality Pilot’s “reference materials” was critical for the subsequent discussion to be meaningful.

# Summary of themes

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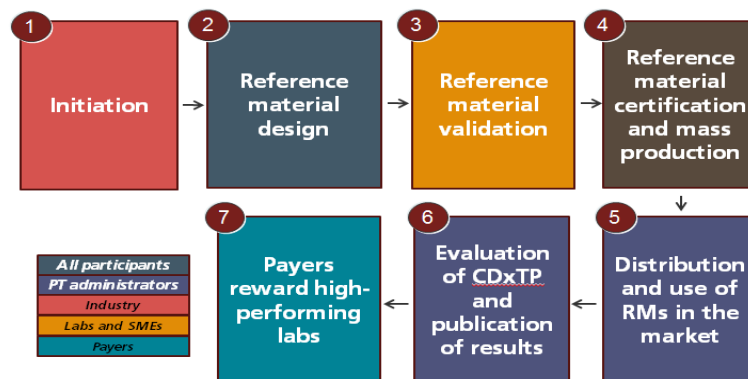
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- “Reference materials,” as traditionally understood, are high-order standards used in test validation and do not relate to test performance; whereas “proficiency testing” involves the distribution of tissue/material in order to challenge a test’s analytical performance. The Quality Pilot is more aligned with proficiency testing. Its purpose is to design tools that test a lab’s ability to appreciate the relationship between biomarker status and drug effectiveness (since the tools will be designed to reflect the evidence from clinical trials). However, the challenge materials envisioned for the Quality Pilot go beyond analytical performance to assess the subjective component of the test. For example, a lab director explained that laboratorians need to understand *“what percentage of tumor cells they need to see before their testing approach can yield a clinically useful result.”* A drug developer agreed and explained that high resolution images could be combined with contrived physical samples to effectively determine whether a lab can discern the meaningful clinical cut points (that originated from the FDA reviewed clinical trials) regardless of the platform that lab is using. This set of platform-agnostic materials would in effect serve as CDx performance calibrators.
- The group commented on what these “calibrator materials” could achieve and their practical constraints. A regulator explained how they could help FDA understand how follow-on CDx compared to previously approved tests, but also suggested that more meaningful benefits would flow from going further to link individual tests to clinical outcomes (rather than merely test results). However, a subject matter expert noted the difficulty of designing materials to evaluate all methods, i.e. to be truly platform-agnostic. The group acknowledged that there may be constraints or limitations to the calibrator materials, e.g. limited to a certain type of biomarker or structural variant. Regardless, there was strong agreement that there was value to developing and using these materials and that, in a patient advocate’s words, *“we shouldn’t let perfect be the enemy of progress.”*

- The group supports the general pilot process depicted below, but also feels that expertise-based workstreams should be used moving forward to articulate the technical details.** In the

afternoon breakout session, the group divided into stakeholder-specific subgroups to consider the process steps most relevant to their individual expertise. Each of the three subgroups, or workstreams, briefly considered whether the “joint standards body” required additional stakeholders, and the “who” and “how” questions associated with each of their assigned



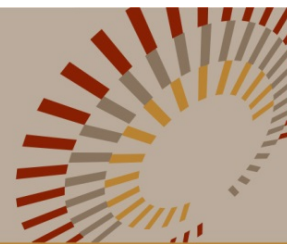
process steps. Please see Appendix B for a more detailed description of the joint standards body and the pilot process.

The groups shared important insights and potential improvements to the pilot process including: (1) the

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addition of guideline-setting bodies such as the National Comprehensive Cancer Network to the joint standards body, (2) considerations for when it would be appropriate to initiate this process (for example, it may not be needed if the new drug also benefits biomarker negative patients), and (3) the integration of a provider-education feature. Additionally, payer comments on the feasibility of introducing performance measures into distinct reimbursement environments triggered a broader discussion amongst the group on the merits of “*carrot versus stick approaches*” and whether all phases would need to be established before pilot commencement. Additional refinements articulated at the meeting, as well as initial responses to some of the questions raised, will be shared with the entire group in a forthcoming protocol document.

- **The “pilot” is a collaborative proof of concept in need of a few champions (as opposed to a formalized, stand-alone consortium).** Participants agreed with a diagnostic developer’s suggestion that, within the context of any organizational or description documents, the pilot “*should focus on one development program to demonstrate if we can establish a performance standard and a process in which labs would publish their data.*” With respect to governance, rather than a formal consortium, most participants preferred to conduct the pilot project through a less formal memorandum of understanding that would lay out contemplated roles and responsibilities. In terms of who would house the pilot, or at least host the joint standards body, some participants felt that it should be a governmental body such as the CDC, NIST, or Reagan-Udall Foundation. Others felt that a mission-driven non-profit organization, such as the Association for Molecular Pathology or the National Biomarker Development Alliance, could also provide a suitable venue. A subject matter summarized: “*We seem to agree on the need for these consensus standards. The question is, are real champions for this project going to self-select themselves?*”

### Next steps

The meeting closed with participants’ reflections on the tremendous amount of motivation in the room to get this started, from a patient advocate opining that “*we shouldn’t wait*” to a payer noting that “*5 year plans are often the demise of innovation.*” In the coming days, Tapestry will debrief committed participants who were unable to attend the launch, engage the identified additional stakeholders who may be helpful for the project, and schedule small group calls to further flush out operational details by workstream. We will integrate the full feedback from the group and the broader landscape into a more detailed pilot protocol. We look forward to continuing to work with you to advance this important project.

### About this document

*The views expressed in this document represent those of the Quality Assurance Pilot for Cancer CDx, a group of leading stakeholders from the public and private sectors committed to improving patient outcomes by equipping US healthcare leaders with the tools needed to optimize the diagnosis and treatment of cancer. This document is not intended to represent the particular policies or positions of the Quality Pilot’s 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.*

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### Appendix A:

#### Participants

##### Patient/policy advocates

- Jeff Allen, Executive Director, Friends of Cancer Research\*
- Calaneet Balas, Chief Executive Officer, Ovarian Cancer National Alliance
- Andrea Ferris, President and Chairman, LUNGeivity Foundation
- Marina Kozak, Science Policy Analyst, Friends of Cancer Research
- Nancy Roach, Founder and Chairman, Fight Colorectal Cancer \*

##### Payers

- Naomi Aronson, Executive Director, Clinical Evaluation, Innovation and Policy, Blue Cross and Blue Shield Association \*
- Michael Kolodziej, National Medical Director, Oncology Solutions, Aetna
- Girish Putcha, Director of Laboratory Science, Palmetto GBA
- Jeff Roche, Lead Medical Officer, Coverage and Analysis Group, Center for Clinical, Centers for Medicare and Medicaid Services \*
- James Rollins, Director, Coverage and Analysis Group, Division of Items and Devices, Standards and Quality, Centers for Medicare and Medicaid Services
- Alan Rosenberg, MD-VP Medical & Clinical Pharmacy Policy, Anthem, Inc

##### Regulators

- Jonathan Jarow, Acting Deputy Office Director, Office of Hematology and Oncology Products, FDA – CDER \*
- Penny Keller, Division of Laboratory Services, Center for Clinical Standards and Quality, Centers for Medicare and Medicaid Services
- Christopher Leptak, Office of New Drugs (OND), Biomarker Lead, FDA – CDER
- David Litwack, Personalized Medicine Staff, Office of In Vitro Diagnostics and Radiological Health, FDA – CDRH
- Michael Pacanowski, Associate Director, Genomics and Targeted Therapy, Office of Clinical Pharmacology, Office of Translational Sciences, FDA – CDER \*
- Erasmus Schneider, Associate Director for Research and Technology, New York Department of Health \*
- Stephanie Shulman, Director, Clinical Laboratory Evaluation Program, New York Department of Health \*

*(\*) Indicates participant or sponsor representative was unable to attend the February meeting*

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### Participants

*continued*

### Subject matter experts/technology specialists

- Steve Anderson, Global Head, Clinical Trials. Chief Scientific Officer, Oncology and Genetics, LabCorp Clinical Trials \*
- Steven Choquette, Group Leader, Bioassay Methods Group, NIST
- Kenneth D. Cole, Team Leader, Bioassay Methods Group, NIST
- Carolyn Compton, Chief Medical Officer, National Biomarker Development Alliance \*
- Sandi Deans, Scheme Director, UK NEQAS for Molecular Genetics, Department of Laboratory Medicine, Royal Infirmary of Edinburgh \*
- Karen Gutekunst, Vice President of Diagnostic Development, Illumina
- Karen Kaul, Chair, Department of Pathology and Laboratory Medicine, NorthShore University Health System
- Maryellen de Mars, Senior Director, Standards Resource Center (SRC), ATCC
- Doug Moeller, Medical Director, McKesson Health Solutions
- Richard Schilsky, Chief Medical Officer, American Society of Clinical Oncology
- Robyn Temple-Smolkin, Director, Clinical & Scientific Affairs at the Association for Molecular Pathology
- Mary Williams, Executive Director, Association for Molecular Pathology
- Mickey Williams PhD, Director, Molecular Characterization Laboratory, Frederick National Laboratory for Cancer Research \*
- Barbara Zehnbaauer, Branch Chief - Senior Service Fellow, Centers for Disease Control and Prevention

### Sponsor representatives

- Ken Bloom, Chief Medical Officer, GE Healthcare – Clariant Diagnostic Services
- Cindy Collins, Chief Executive Officer, Clariant, GE Healthcare
- Chris Jowett, Global Commercial Head, Companion Diagnostics, Abbott Molecular
- Cathy Lofton-Day, Principal Scientist, Medical Sciences, Amgen
- Meghan C. Moore, Marketing Director, GlaxoSmithKline
- Jonathan Pan, Director, Oncology Companion Diagnostic and Disease Strategy, GlaxoSmithKline\*
- Scott Patterson, Executive Director, Medical Sciences, Amgen
- Pamela Swatkowski, Director, Regulatory Affairs, Abbott Molecular

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### Appendix B:

<b>STRAW MAN PROCESS FOR THE QUALITY PILOT</b>	
<p>Drug and diagnostic developers will actively partner with a joint standards body to design, evaluate, and distribute CDx performance calibrator materials. The joint standards body should have representation from pathologists, oncologists, standards subject matter experts, the FDA, payers, lab accrediting groups, and a trusted voice to publish lab performance data.</p>	
<b>1. Initiation</b>	<p>Approx. 18 months prior to product launch, drug developer approaches the joint standards body to explain the need for robust performance calibrators (PCs). Industry may have pre-existing controls or materials that could be used to highlight the most important, or troublesome, clinical cutoffs/decision points.</p>
<b>2. Performance calibrator design</b>	<p>Developer works with the joint standards body to agree on desired level of test performance to guide the design of a set of PCs. Together they will also devise a plan to either acquire existing materials or engineer new ones.</p>
<b>3. Performance calibrator validation</b>	<p>PCs are distributed to an early set of validating labs to make sure they are commutable across the candidate IVD and existing LDTs. A third party subject matter expert on standards could coordinate and analyze the statistical data from these early interlab comparisons.</p>
<b>4. Performance calibrator certification and mass production</b>	<p>Joint standards body certifies the PCs as fit for purpose to determine a lab's companion diagnostic test performance (CDxTP). Industry could choose to fund the creation of a larger amount of PCs for a broader distribution to the lab community</p>
<b>5. Distribution and use of performance calibrators in the market</b>	<p>PCs are distributed to labs that agree to publicly share their CDxTP results. The PCs could be distributed through either existing PT administrators or by the industry/third-party manufacturer in tandem with the candidate IVD. All agree that PCs must be offered to labs that are legally running LDTs (or planning to).</p>
<b>6. Evaluation of CDx test performance and publication of results</b>	<p>The entity responsible for grading an individual lab's CDxTP will make its determination based on criteria developed by the joint standards body. CDxTP results will be made publicly available via a centralized website/database.</p>
<b>7. Payers reward high-performing labs</b>	<p>As a carrot, payers will reward high-performing labs through some combination of enhanced reimbursement and increased test volume (via preferred laboratory status). As a stick, payers may require labs to participate in the CDxTP process when negotiating lab contracts.</p>