Multi-stakeholder approaches for addressing barriers to precision medicine: Diagnostic Quality Assurance pilot

CDDF workshop, Brussels, BE

25 September 2018

Quality Pilot context

- Quality Pilot emerged out of the multistakeholder Sustainable Predictive Oncology Therapeutics and Diagnostics (SPOT/Dx) working group.
- Launched in 2013, SPOT/Dx focused on precision medicine for improving patient outcomes by equipping healthcare leaders with tools to advance clinical decision-making for the diagnosis and treatment of cancer and the regulatory and reimbursement infrastructure.
- SPOT/Dx included representatives from patient advocacy, providers/clinicians, drug developers, diagnostic/ medtech companies, regulators and public/ private payers.
- In service to the SPOT/Dx mission, participants proposed a Diagnostic Quality Assurance Pilot to address a key barrier to precision medicine access to diagnostics: assurance on molecular diagnostic quality. Pilot launched in 2015.

US background

- Current environment for precision medicine in the US:
  - Advent of Precision Medicine Initiative
  - Ongoing FDA consideration of hospital –developed/ lab-developed tests (LDTs) / NGS oversight
  - Existing standardization gap in precision medicine diagnostics
    - No process to compare CDx and LDTs for targeted therapies in cancer treatment
    - Patient access challenges to diagnostics due to reimbursement challenges - quality assurance of diagnostics being a key issue to reimbursement. “Is NGS = NGS”

Problem statement

- What are we solving for?
  - ***Vision:*** Help ensure that diagnostics will provide clinicians with consistent and correct answers, regardless of which lab conducts the test and which diagnostic platform the lab uses
  - ***Quality Pilot objective:*** 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. Accuracy of genotyping will be determined regardless of whether labs use the FDA-approved CDx or an LDT

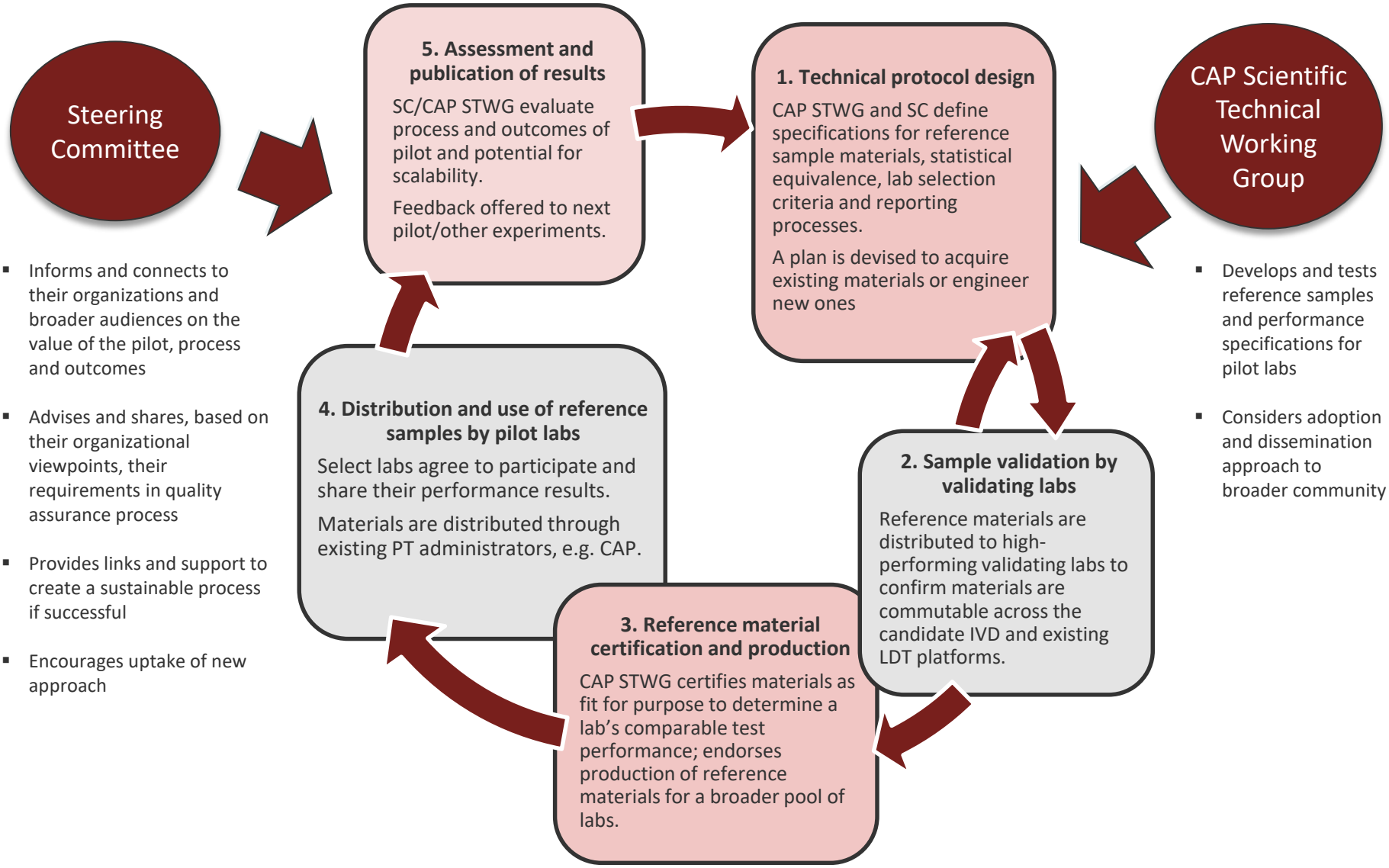
Core principles and differentiators associated with the Quality Pilot

- **Sustainability:** quality control materials that are commercially maintainable
- **Transparency of results:** visibility of outcomes
- **Accelerated reference material creation/availability:** in phase 3 of CDx/drug development, prior to market launch
- **Collaborative dialogue:** diversity and balance of perspectives
- **Quick action:** test proof of concept as rapidly as possible, evolve process as needed
- **Efficiency:** work within existing mandates, use existing pathways and infrastructure as much as possible

Pilot overview

- Will use a candidate CDx comprised of a:
  - Two-gene, multiple variant NGS panel volunteered by Amgen and CDx partner, Illumina
- Performance specifications set by:
  - Illumina CDx for a targeted colorectal cancer therapy
  - CDx currently in FDA review for a new indication (pre-market) *–note: subsequent to the pilot's commencement, the CDx was approved in June 2017*
- College of American Pathologists (CAP) will:
  - Select vendor for production of reference samples
  - Manage the distribution of samples to labs
  - Coordinate data collection and analysis
- Labs will demonstrate their ability to accurately:
  - Analyze reference samples for a variety of DNA variants
  - Report findings of clinical decision points for the targeted therapy

Original pilot design



- Informs and connects to their organizations and broader audiences on the value of the pilot, process and outcomes
- Advises and shares, based on their organizational viewpoints, their requirements in quality assurance process
- Provides links and support to create a sustainable process if successful
- Encourages uptake of new approach

- Develops and tests reference samples and performance specifications for pilot labs
- Considers adoption and dissemination approach to broader community

Reference samples

Will include a so-called “wet challenge” and a “dry challenge”

Wet Challenge: Blended genomic DNA samples with pre-defined variant profiles

- soup to nuts
- limited in number of genes, variants, variant allele frequencies
- expensive to develop

Dry Challenge (In Silico Files): Pre-defined variant profiles will be introduced by a computerized process into the participating lab’s own BAM and/or FASTQ files (from either amplification-based or capture-based assay designs, run on either Torrent-based or Illumina-based platforms)

- limited to bioinformatics component of the test
- virtually unlimited flexibility
- inexpensive to create

*Following an RFP, CAP retained Horizon and P&V Licensing as vendors for the wet and dry lab challenges, respectively

Steering Committee: Members and affiliations

- Jeff Allen, PhD, President & CEO, Friends of Cancer Research
- Naomi Aronson, PhD, Executive Director, Clinical Evaluation, Innovation and Policy, Blue Cross and Blue Shield Association
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Key lessons from the process

- **Multistakeholder approach comprises many perspectives**
  - Each sector's concerns constructively informed the work of other groups, providing greater transparency about priorities and processes

The way forward

- Pilot expected to be completed by early-mid 2019. All information is public at: https://www.tapestrynetworks.com/our-work/healthcare/diagnostic-quality-assurance-pilot
- Approach, if proven successful, could be scaled-up to include patient samples, more labs, and/or focus on a different CDx for a different disease
- Early thoughts scalability and implications for precision medicine community:
  - Process could be institutionalized via a "gold seal of approval" for labs that demonstrate equivalent performance of their LDTs to the CDx
  - Standards generated could be used by labs globally
  - Pilot approach could be integrated into pre-clinical development programs and/or adapted for areas beyond molecular diagnostic panels
- Pilot has helped inform recently launched effort by FDA and medical device community that are also looking into the gaps for somatic reference samples (see MDIC Clinical Diagnostics workstreams: http://mdic.org/clinicaldx/somatic-reference-samples/