15th DIA Japan Annual Meeting 2018

Promoting Better Collaboration to Drive Global Health and Innovation in an Era of Medical and Scientific Transformation

November 11-13, 2018 | Tokyo Big Sight

PMDA Perspectives on Oncology Panel

REIKO YANAGIHARA, Ph.D.
Office of In Vitro Diagnostics
PMDA

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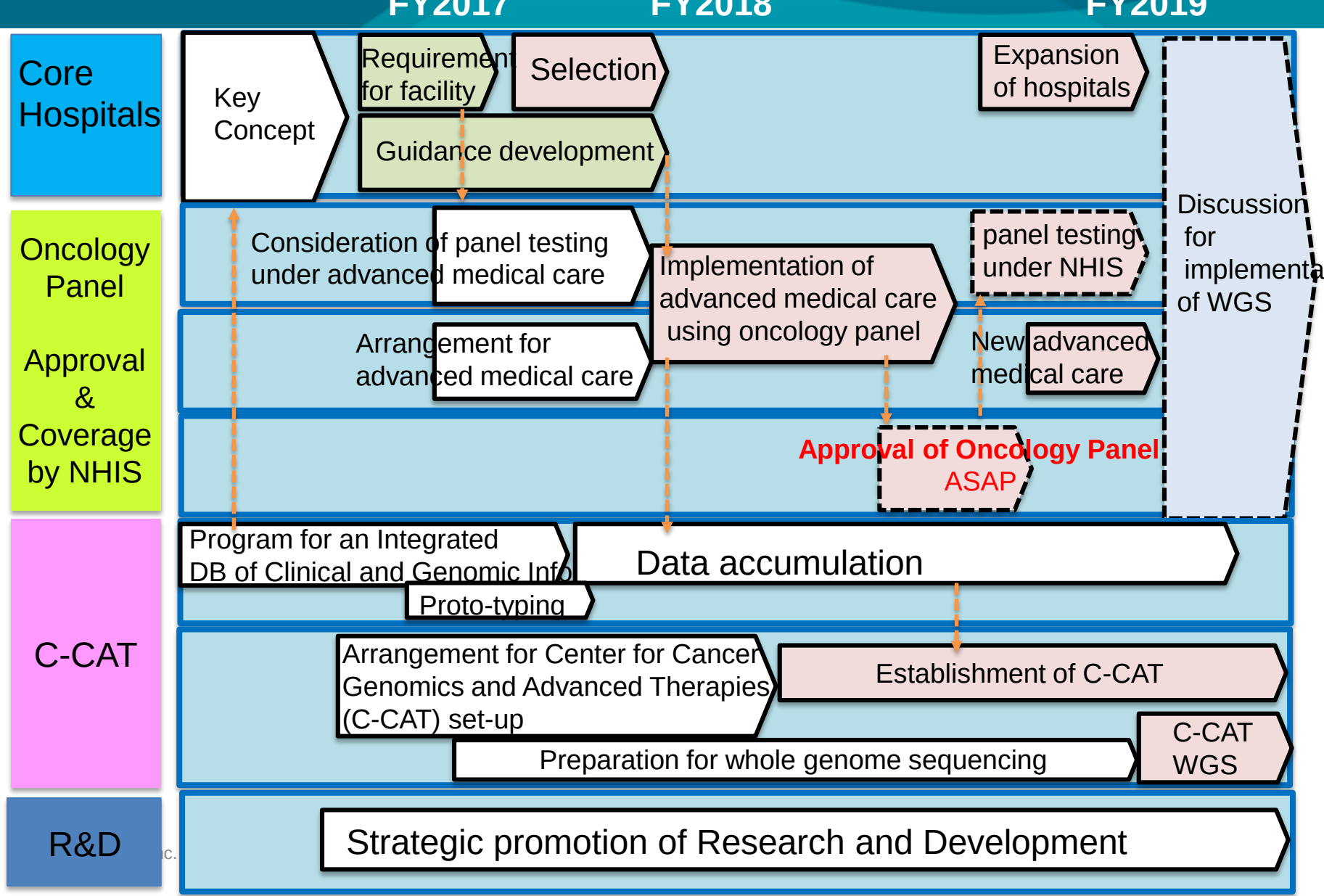
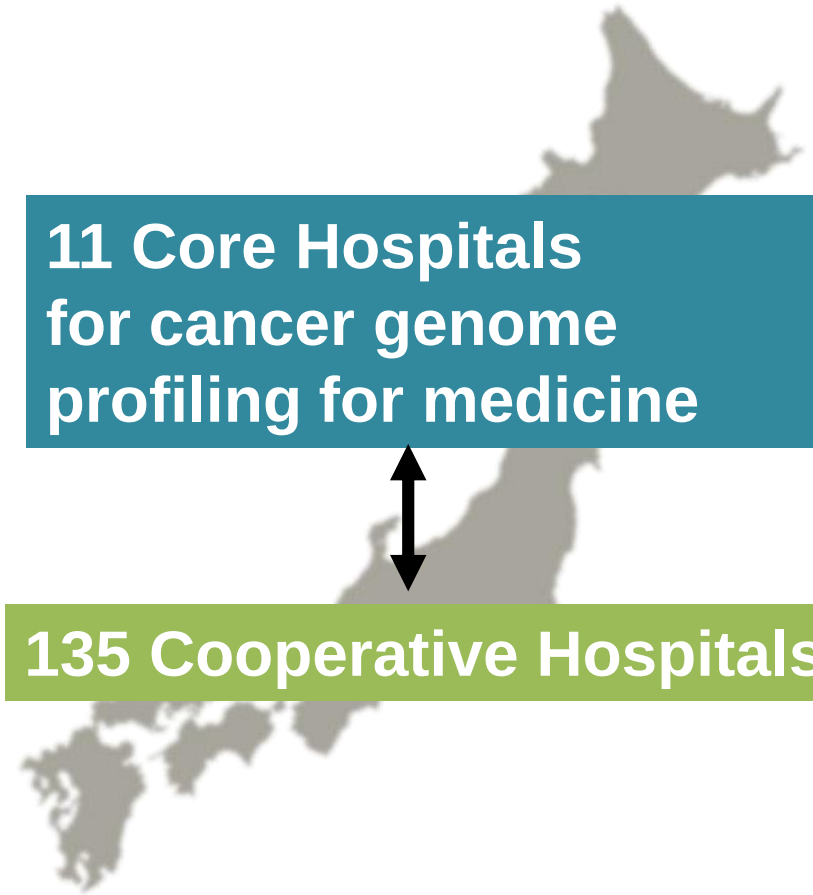
Regulatory Status of Oncology Panel in Cancer Genome Medicine in Japan

Process Sheet for Cancer Genome Medicine

Roundtable Consortium on the Promotion of Cancer Genomic Medicine



Framework of Cancer Genome Medicine in Japan



11 Core Hospitals for cancer genome profiling for medicine

135 Cooperative Hospitals

CGP by Oncology Panel

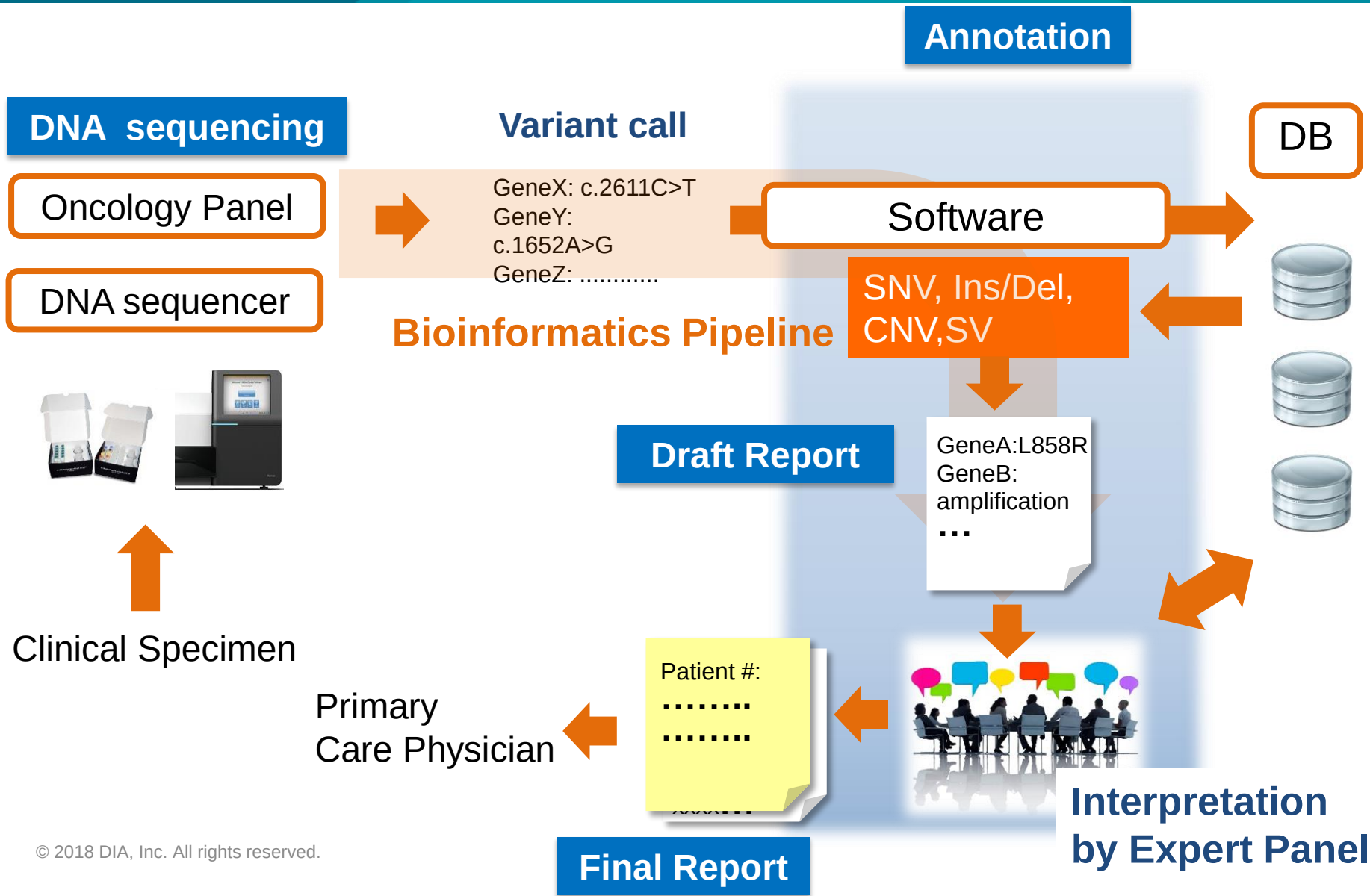
↓ Draft Report

Evaluation by Expert Panel
-clinical evidence of variants
-available therapies

↓ Final Report

Primary Care Physician

Implementation of Oncology Panel in Japanese Medical Setting



Oncology Panel as a IVD Medical Device

IVD Medical Device

DNA sequencing

Oncology Panel

Variant call

GeneX: c.2611C>T
GeneY: c.1652A>G
GeneZ: .....

Annotation

Software

DB

SNV, Ins/Del, CNV,SV

Bioinformatics Pipeline

DNA sequencer

Draft Report

GeneA:L858R
GeneB: amplification
...

Clinical Specimen

Physician

Patient #:
.....
.....

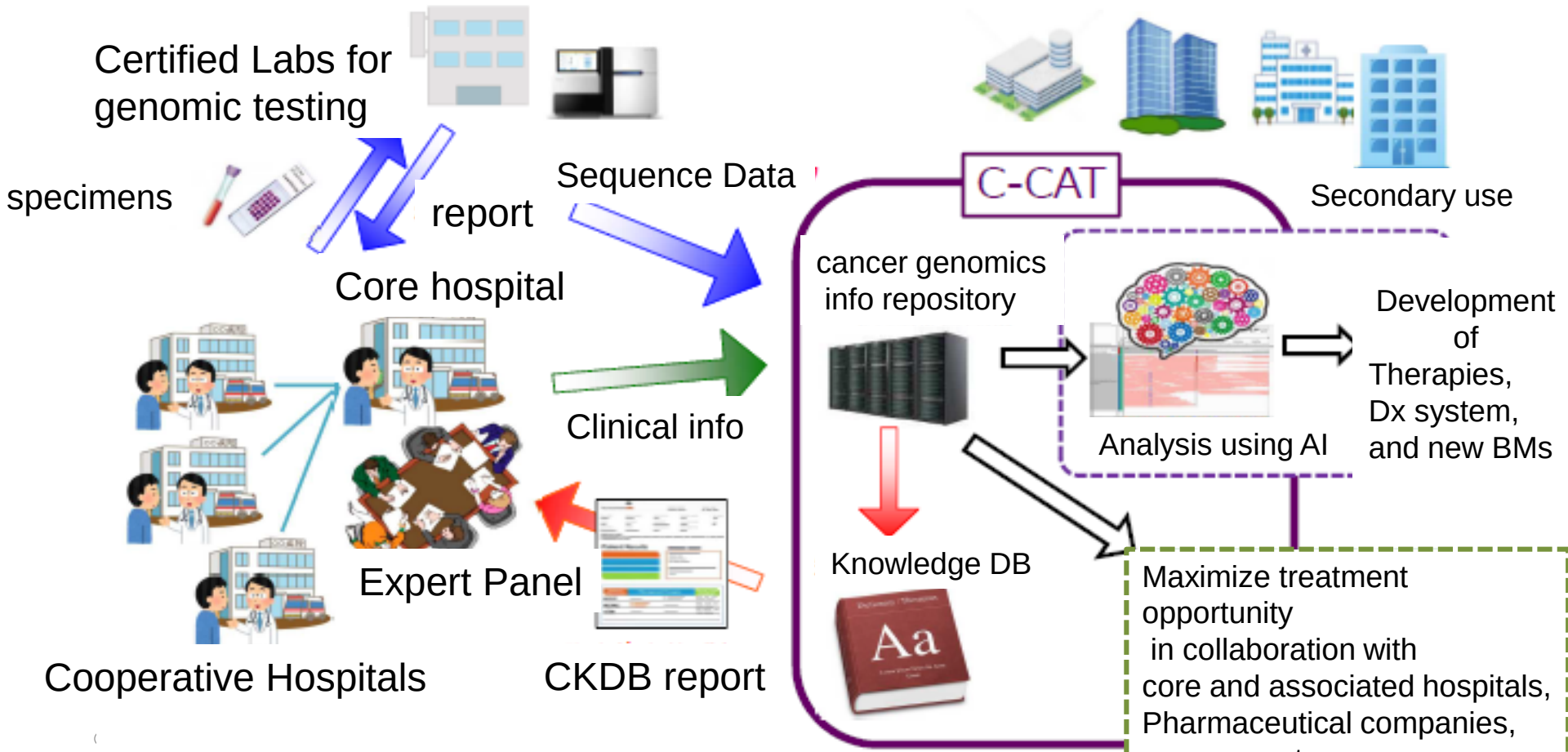
Interpretation by Expert Panel

Final Report

Promotion of Cancer Genome Medicine using Approved Oncology Panel

Center for Cancer Genomics and Advanced Therapeutics: C-CAT

Modified from https://www.ncc.go.jp/en/information/2018/0601/index.html



Regulatory Perspectives on Oncology Panel

Review Policies on conventional *in vitro* diagnostic MD

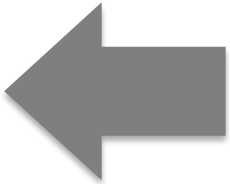
Proposed IVD Medical Device is reviewed on the following aspects:

- Analytical Performance
- Clinical Performance
- Clinical Utility

Review Policies on NGS-based Oncology Panel

Clinical Performance

Expert Panel



- **Design of Panel Content**
- **Analytical Performance**
- **Identification of possible driver genes**

Reference Database:

- Public DB: specified
- Proprietary DB: specified, DB procedures and operations are reviewed.
- Critical procedures to identify the clinically significant variants are subjected to the approved matter.

Clinical Utility is expected to be established through implementation of the approved or advanced medical care-covered oncology panel and accumulation of genomic and clinical data in CKDB.

Analytical Performance

- Validation characteristics to be evaluated:
  - Accuracy, Precision(repeatability, intermediate precision), specificity, Detection Limit
  - Potentially interfering materials
- Representative validation approach:
  - Validation sample set should cover the variant categories (SNVs, indels, and others) that NGS panel intended to detect.
  - Scientific justification of representative set of variants are required.

Analytical Performance: Points to consider and Challenges

- Accuracy
  - By comparison to an orthogonal method
- Test performance across tumor tissue types

- Challenges:

  Availability of the validated orthogonal method other than approved CDx in Japan

	BRACAnalysis CDx	Comprehensive Genomic Profiling Test
Ref DB	Proprietary DB	Public DB and proprietary DB
What is reviewed?	• DB procedures and operations • Variant interpretation • Requirement and training for personnel involved in interpretation process.. etc.	• Procedures of variant interpretation using public and proprietary DB • Procedures and operations of proprietary DB • Requirement and training for personnel involved in interpretation process .. etc.
Approved Matters	• DB procedures and operations ✓ Criteria of variant classification ✓ Variant classification procedure ✓ Variant re-classification criteria and procedure	• Procedures of variant interpretation using public and proprietary DB • Procedures and operations of proprietary DB
Approval conditions	QMS inspection • Variant classification operations following the approved SOP • Annual report on: ✓ Newly identified variant ✓ Reclassification of variant	Should be decided taking into consideration of: • Transparency and public accessibility of public DB • Clinical performance of panel is dependent on Expert Panel

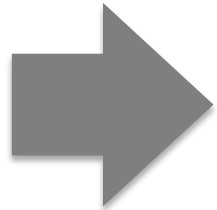
CDx vs CGP Test

	CDx	Comprehensive Genomic Profiling Test
Analytical performance	• In principle, evaluation for each specific BM • Representative validation approach is possible in some cases.	Representative validation approach is possible, if justified.
Clinical performance	Evaluated by -clinical study of the corresponding TP or -concordance study with the approved CDx	• Established by expert panel • Evaluated on whether it can appropriately provide necessary variant info for the expert panel to consider the best possible treatment for a patient.
Clinical Utility	Established in the major efficacy trials of TP	Expected to be established through the implementation of oncology panel into clinical setting

Summary

CGP test is reviewed on whether analytical report produced by the proposed MD could serve necessary information for expert panels to consider treatment possibilities for patients.

- **Design of Panel Content**
- **Analytical Performance**
- **Detectability for possible driver genes**



Clinical Performance

Expert Panel

Reference Database:

- Specified
- DB procedures and operations are reviewed for proprietary DB.
- Critical procedures to identify the clinically significant variants are subjected to the approved matter.

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