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# IOM – MEETING
# NOVEMBER 10, 2014

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# MolDX Program

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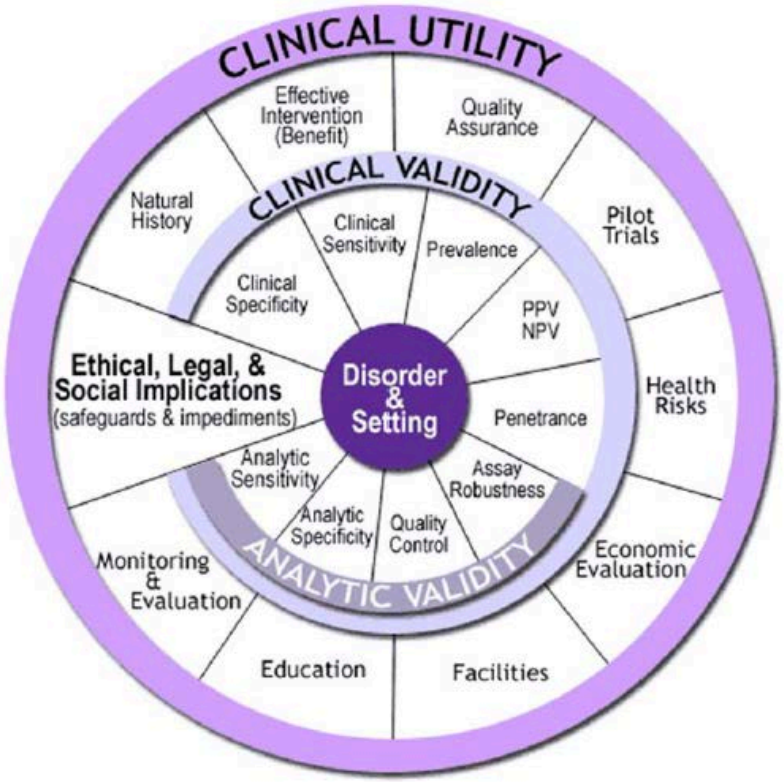
# CMS Statement of Work to MolDX

Started November 2011 as a CMS "Pilot" by Elaine Jeter MD

"The (MolDX) methodology will use an evidence framework that is consistent with the ACCE criteria developed by the CDC for the evaluation of genetic tests as articulated from 2009 onward in the application of the ACCE criteria to Medicare coverage . . ."

# CDC ACCE Criteria




Centers for Disease Control (CDC) ACCE Criteria Overview
*http://www.cdc.gov/genomics/gtesting/ACCE/*

- Starting 2000 – Office of Public Health Genomics (OPHG) at Centers for Disease Control (CDC)
- 4 Essential Areas
  - Analytical Validity (A)
  - Clinical Validity (C)
  - Clinical Utility (C)
  - Ethical, Legal and Social Implications (E)

# Impact of Program

- Helped protect patients/physicians from unproven testing
- Filled a gap that is not currently being covered by any private or public entity
- Has reduced waste of unnecessary testing
- Has also developed “new pathways” forward to nurture advancement of testing
- And . . .

# HR 4302 – Protecting Access to Medicare Act of 2014 (PAMA)

"Unique HCPCS Codes for Test. . ."

''DESIGNATION OF ONE OR MORE MEDICARE ADMINISTRATIVE CONTRACTORS FOR CLINICAL DIAGNOSTIC LABORATORY TESTS .—The Secretary may designate one or more (not to exceed 4) medicare administrative contractors to either establish coverage policies or establish coverage policies and process claims for payment for clinical diagnostic laboratory tests, as determined appropriate by the Secretary."

*HR 4302*

# Determining R&N (Clinical Validity and Clinical Utility)

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# R&N and CV/CU

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## Not Medicare Benefit?

- Screening without symptoms and not specified by law
- Confirmatory
- Determining prognosis only
- Measuring the quality of a process
- Non-specified testing
- Investigational or experimental by available literature

**Medicare Benefit**

## Meets R and N?

**Clinical Validity**

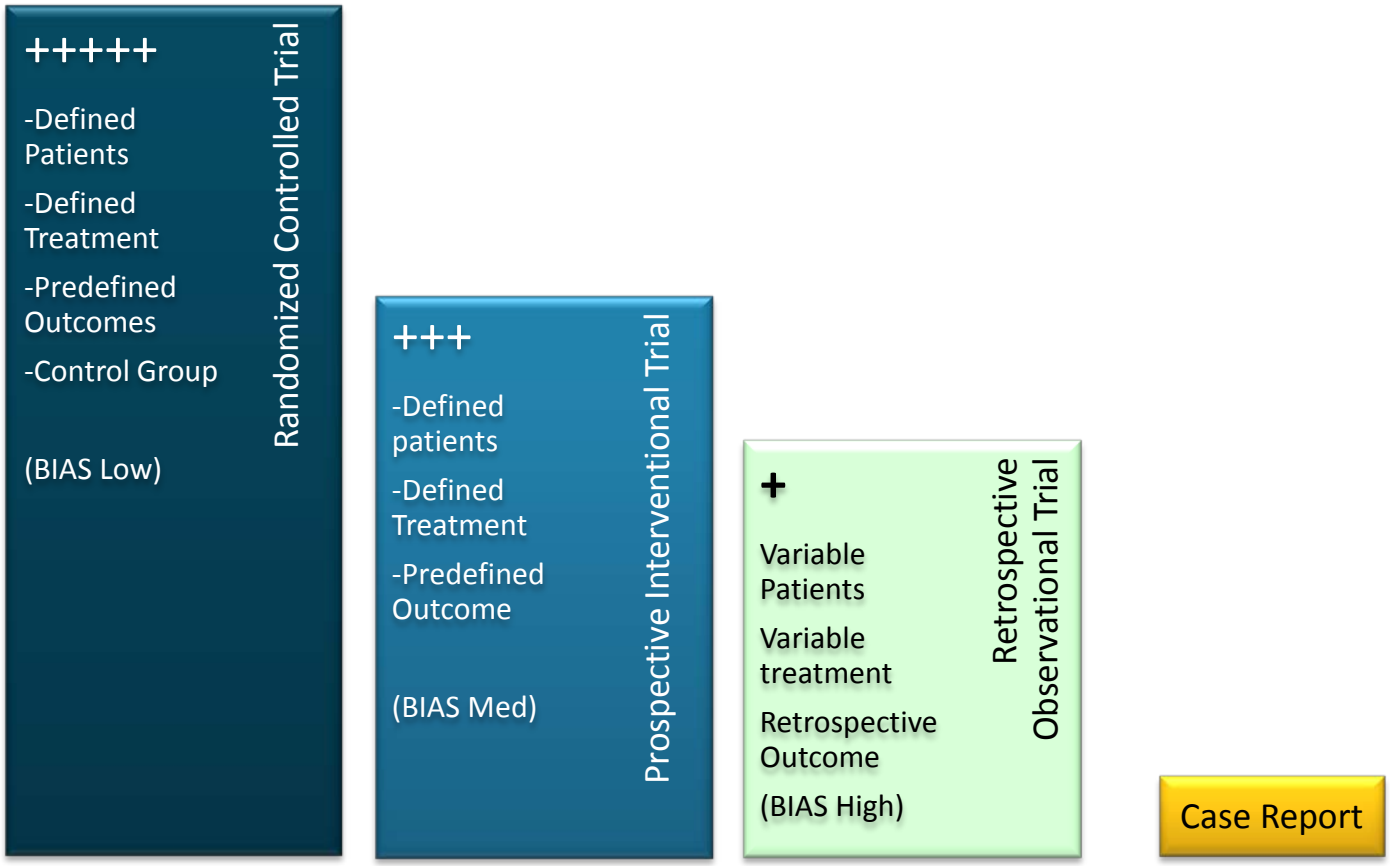
- Who should be tested and under what conditions?
- What does the test tell us that we do not know?

- Can we act on the information provided by the test?
- Will we act on the information provided by the test?
- Does it/will it change the outcome?

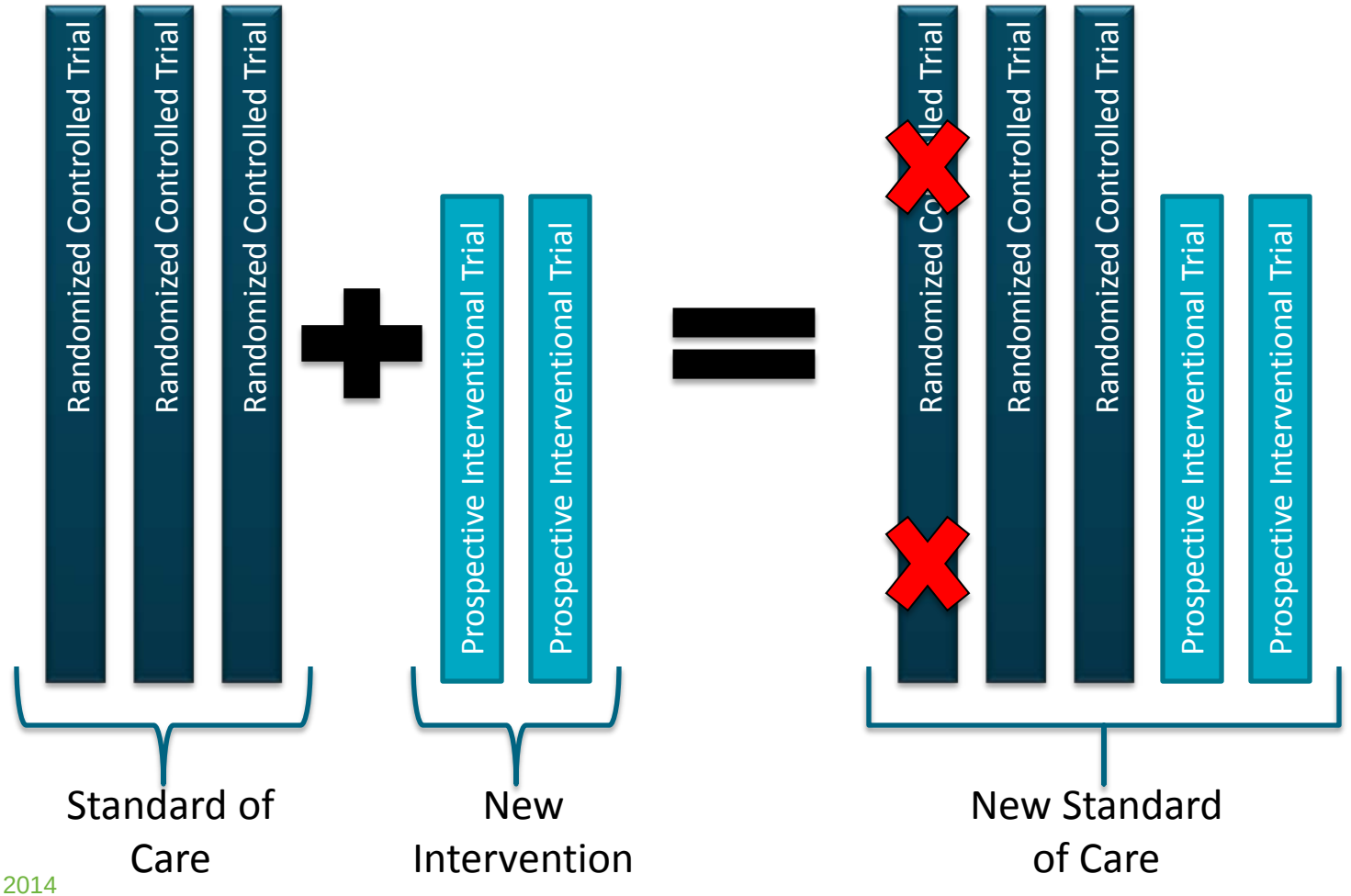
**Clinical Utility**

*(Question adapted from Freuh/Quinn)*

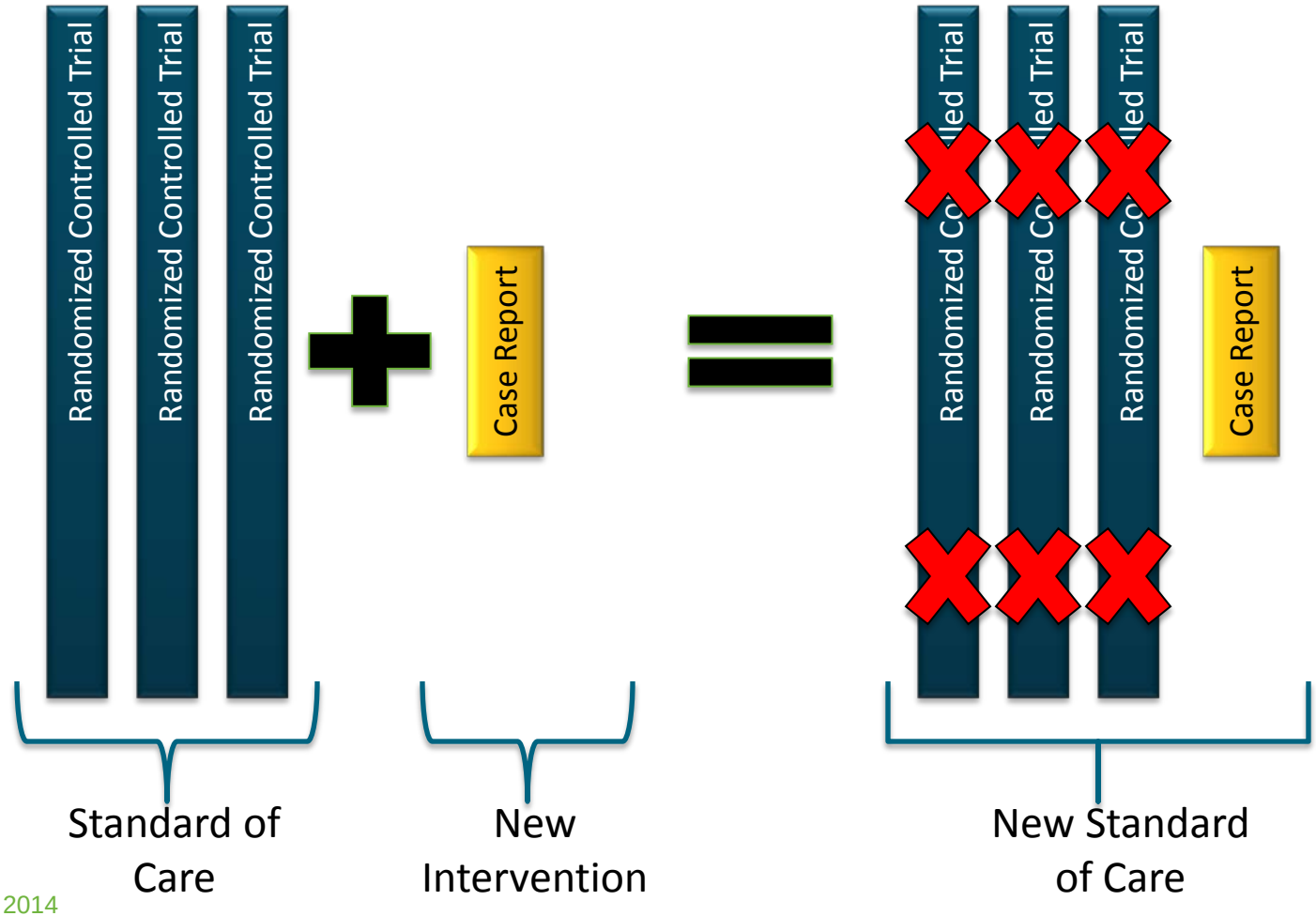
# Levels of Evidence



# Standard of Care Migration



# A Concerning Push in LOE



# Clinical Test Evaluation Process (CTEP)

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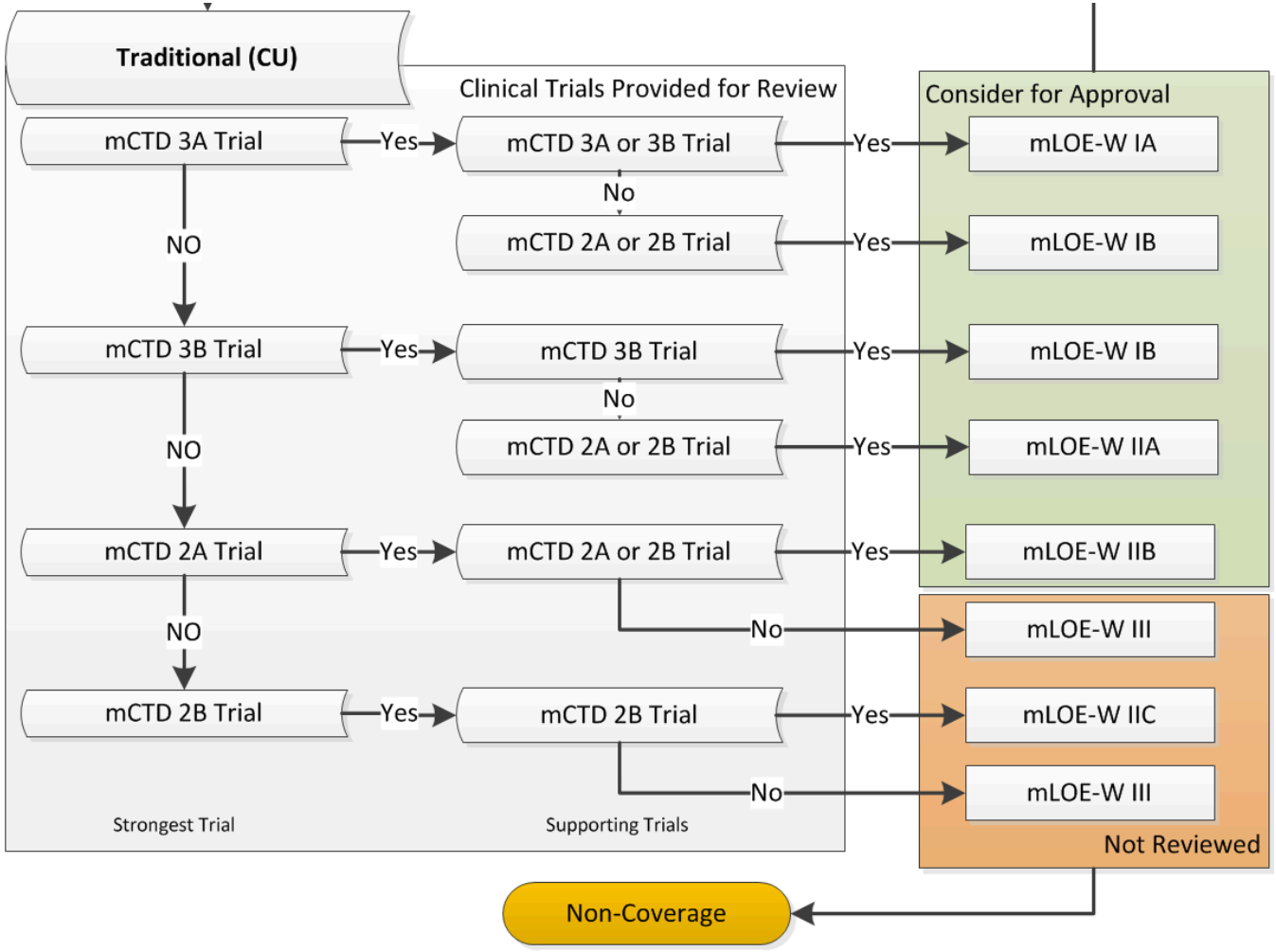
# MolDX Trial Types

- **MolDX Clinical Trial Determination (mCTD)**
  - Follow generally the same classification as FDA Trial Phases
- **mCTD 3A - Prospective Controlled Trial (PCT)** directly addressing the molecular test as the actionable item leading to significant improvement compared to a current accepted standard of care. End points of the trial must be something widely considered as being significant by the respected medical community (e.g. overall survival). The trial must be adequately powered to address the outcome of the intervention based on the test.
- **mCTD 3B - Prospective-Retrospective Trial (PRT).** Previously reported prospective trial using archived sample, looking at how a given molecular test can be shown to improve outcomes in a very specific patient population based on the results from the original trial. Often only samplings of patients from the original trial are evaluated. The samples must be well defined as to associated patient characteristics and treatments so as to adequately determine exactly what type of patients benefit from the given test.

# MolDX Trial Types

- **mCTD 2A - Prospective Observational Study (Prospective Interventional Trial) (POS or PIT)** where patients are prospectively enrolled in a registry, and then treated according to a defined pathway using the molecular test as an integral part of the care plan.
- **mCTD 2B – Retrospective Data Modeling (RDM)** complex data modeling to determine risk-benefit of a given test using large data sets to estimate impact of a given molecular test on the standard of care approach.
- **mCTD 1 - Retrospective Observational Study (ROS)** where there is no stipulation of treatment or follow-up based on the molecular study.
- **mCTD 0 - Preclinical Studies (PS)** Preclinical data or related studies or trials.

# mLOE by Trial Type



# Addressing New Paradigms

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# New Paradigms

- Archived Tissues Samples
- Trials that will never be duplicated
- Less than perfect science in areas were there is substantial unmet need
- Smaller patient numbers due to rare mutations
- Often low (or negative) ROI on research in advanced molecular testing

# New Paradigms Standard of Care?

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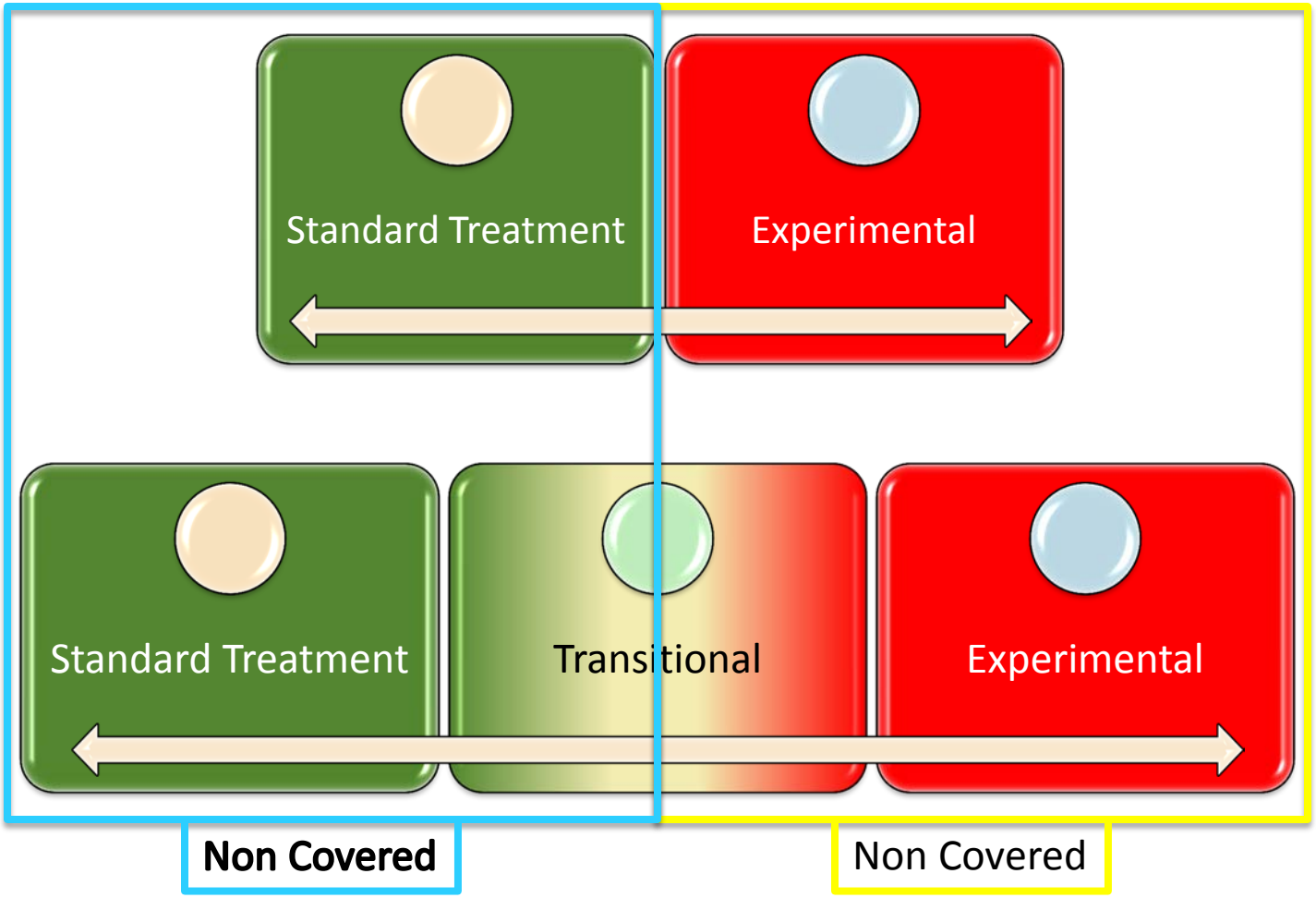
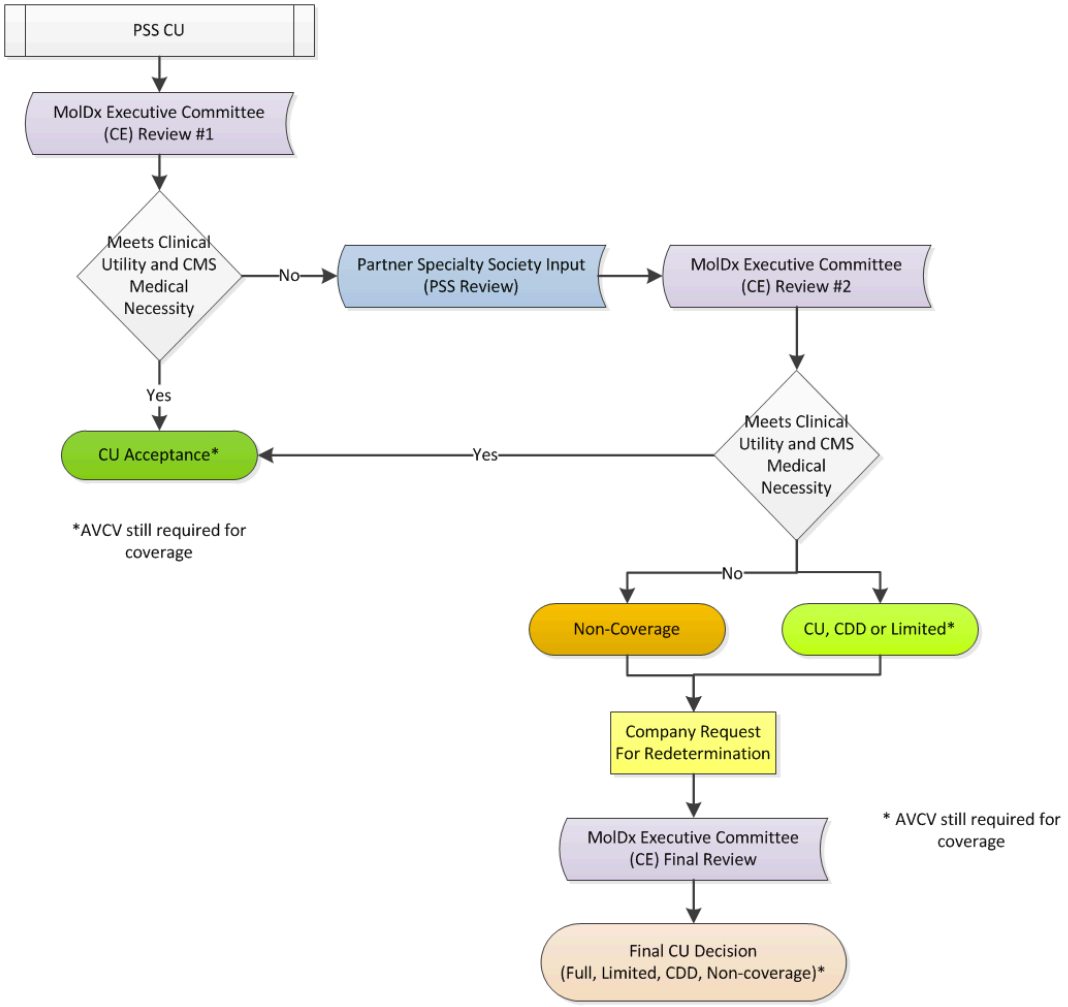
OLD

NEW



# Partner Specialty Society Expedited Review



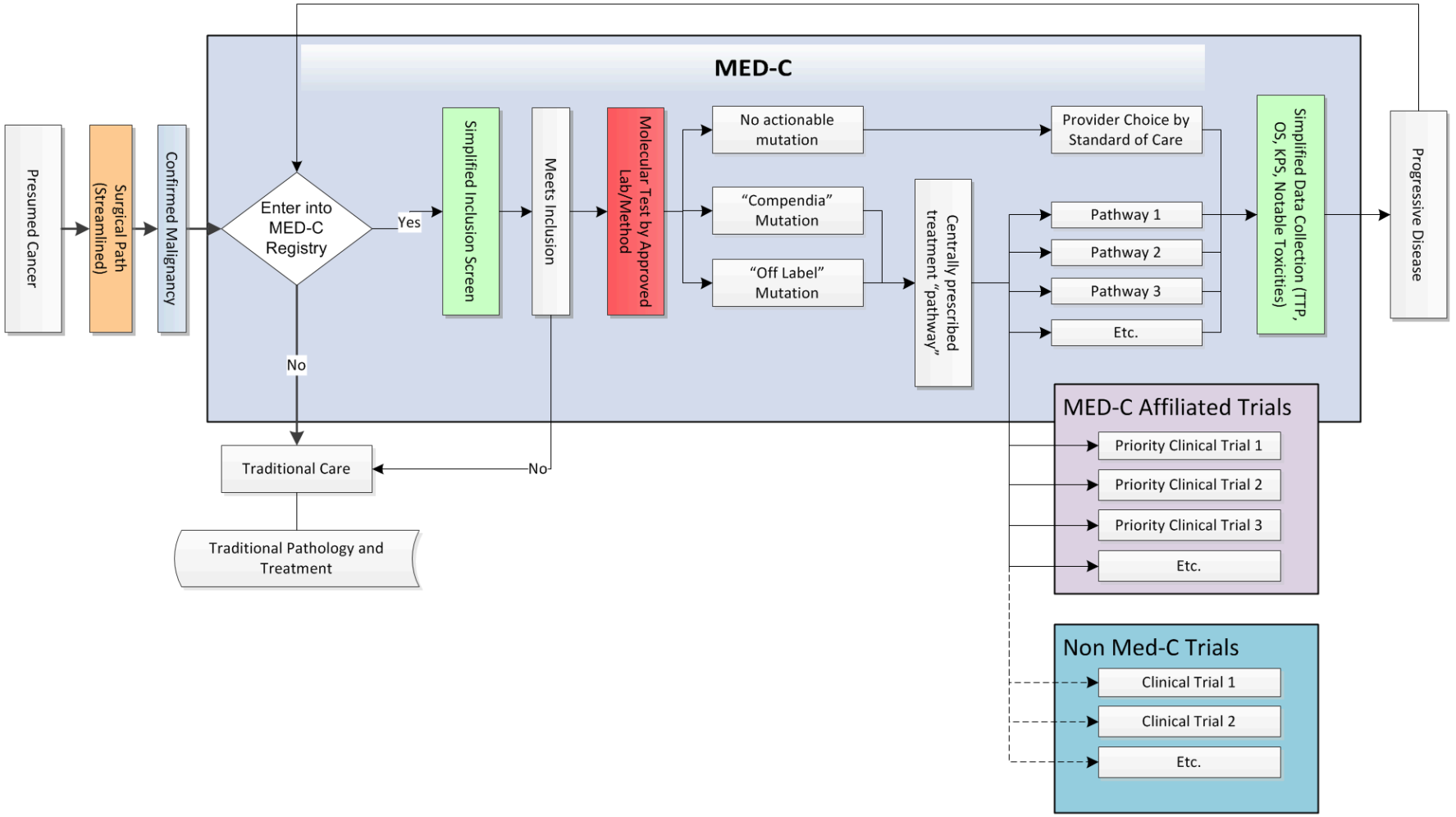
# Addressing New Paradigms

- Expedited Review for Promising Science (Partner Specialty Society Review)
  - Developing an MolDX advisory committee (MolDAC) of mainly molecular pathologists
  - Frequent communication with labs, academicians, societies, KOLs, SME, etc.
- The MolDX Executive Committee reviews every dossier to identify these rare cases that meet R&N and high impact on patients BUT may not strictly fit inside of other criteria

# Coverage with Data Development

- Method of covering testing with promise
- Molecular Approach similar to FDA Accelerated Approval
- Areas of:
  - Significant un-met clinical need
  - Potential for dramatic improvement in patient care
  - Widespread acceptance by medical community without robust CU data being available

# MED-C Project



# Dealing with Multiplex Testing and Panels

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# Multiplex Panels

- Standardization amongst platforms?
  - Until an accepted standard need to look at each panel and each laboratory separately
  - Each test (or group) must show AV/CV and CU
- Disease Specific
- Hierarchical Reporting
  - Standard
  - Transitional
  - Experimental
- Asymptotic costs