CMTP OVERVIEW

April 21, 2015
Sean R. Tunis, MD, MSc.
Focusing on work that aims to:

• Promote the development of better evidence of effectiveness, safety and value…
• While sustaining investment in life sciences and promoting high value innovation…
• In light of the need to reduce health care spending
HIGH PRIORITY PROGRAMS

- Green Park Collaborative
- Scientific Advice for Market Access
- EXCITE – Maryland
- A reimbursement policy framework for “precision medicine”
THE UNIFYING FRAMEWORK: “REIMBURSEMENT SCIENCE”
“Regulatory Science is the science of developing new tools, standards, and approaches to assess the safety, efficacy, quality, and performance of all FDA-regulated products.”

“FDA will advance regulatory science to speed innovation, improve regulatory decision-making, and get products to people in need…. (and) to protect and promote the health of our nation and the global community.”
WHY REGULATORY SCIENCE IS IMPORTANT

• Several legitimate social objectives related to medical products:
  – Ensure that marketed products are safe and effective
  – Promote rapid patient access to promising new products
  – Promote life sciences innovation
  – Minimize burdens on product developers
• These objective create tension with respect to evidence standards
• Regulatory science provides an opportunity to develop a scientific framework that reflects multiple legitimate competing views
• Requires all stakeholders, transparency, iterative
• FDA provides the natural platform to support this process
“Reimbursement Science is the science of developing new tools, standards, and approaches to assess the comparative effectiveness, value of products covered by public and private health plans.

(GPC) will advance reimbursement science to (speed innovation), improve reimbursement decision-making, and get products to people in need…. (and) to improve population health outcomes and efficient use of resources.”
A multi-stakeholder forum to clarify the evidence expectations of public and private payers
  – Informed by input from patients, clinicians, and regulators,
  – Focus on comparative effectiveness and value

Other Key Stakeholders
  – CMS, numerous private payers engaged
  – FDA, NIH, PCORI, AHRQ, VA, etc.
  – Ongoing involvement of life sciences

Output / Activities
  – Develop “effectiveness guidance documents”
  – Condition and technology specific workshops
GPC – USA ADVISORY COMMITTEE

Advisory Committee Structure

Gary Palmer  Alexandra Clyde  James Murray  Alan Rosenberg  Murray Ross  Lew Sandy

Sean Tunis Chair

Donna Cryer

Ex Officio

<table>
<thead>
<tr>
<th>FDA</th>
<th>CMS</th>
<th>PCORI</th>
<th>NIH</th>
<th>AHRQ</th>
<th>VA</th>
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<tr>
<td>Bob Temple</td>
<td>Patrick Conway</td>
<td>Rachael Fleurence</td>
<td>Michael Lauer</td>
<td>Jean Slutsky</td>
<td>David Atkins</td>
<td>Tanisha Carino</td>
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<td>Murray Sheldon</td>
<td>Louis Jacques</td>
<td>Jason Gerson</td>
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<td>Peter Marks</td>
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Board Composition Key

Other

Payers

Life Sciences
Payers Involved in GPC - USA

- America’s Health Insurance Plan
- BCBSA
- CMS central office
- MACs (Palmetto, Novitas, others)
- Humana
- Aetna
- United
- Kaiser
- Wellpoint
- Many regional payers (e.g. Johns Hopkins Health Plan)
Specific recommendations on design of clinical utility studies
Multi-stakeholder process
Aim to balance validity, feasibility, time, cost
Targeted to researchers working in industry or academic settings
Analogous to FDA guidance
<table>
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<tr>
<th>TWG Member Name</th>
<th>Stakeholder Category</th>
<th>Affiliation</th>
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<tbody>
<tr>
<td>Linda Bradley</td>
<td>Geneticist/Lab Director</td>
<td>Women &amp; Children's Hospital of Rhode Island</td>
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<td>Louis Jacques</td>
<td>Payer</td>
<td>Centers for Medicare &amp; Medicaid Services</td>
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<tr>
<td>Gary Lyman</td>
<td>Clinician</td>
<td>Duke University</td>
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<tr>
<td>Howard McLeod</td>
<td>Researcher</td>
<td>UNC Institute PGx &amp; Individualized Therapy</td>
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<tr>
<td>David Nelson</td>
<td>Industry</td>
<td>Epic Sciences, Inc.</td>
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<tr>
<td>Robert McCormack</td>
<td>Industry</td>
<td>Veridex LLC, a Johnson &amp; Johnson company</td>
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<tr>
<td>David Parkinson</td>
<td>Venture Capital</td>
<td>New Enterprise Associates</td>
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<tr>
<td>Margaret Piper</td>
<td>Payer</td>
<td>Kaiser Permanente (formerly BCBSA TEC)</td>
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<tr>
<td>Richard Simon</td>
<td>Methodologist</td>
<td>National Cancer Institute</td>
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<tr>
<td>Mary Lou Smith</td>
<td>Patients &amp; Consumers</td>
<td>Research Advocacy Network</td>
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MOLECULAR DIAGNOSTICS ADVISORY GROUP

Robert A. Beckman, MD
Executive Director, Clinical Development Oncology
Daiichi Sankyo Pharmaceutical Development

Donald A. Bergstrom, MD, PhD
Associate VP and Global Head, Translational and Experimental Medicine
Sanofi, Oncology

Jeff Bush, CT(ASCP), MBA
Director, Worldwide Reimbursement & Reimbursement Policy
Becton, Dickinson and Company

Lorrie Carr, MBA
Senior Director, US Market Access
Millennium: A Takeda Oncology Company

Nicholas Ferenc, MS, MBA
Director
Sanofi Oncology

Sheikh Usman Iqbal, MD, MPH, MBA
Head of Oncology, Global Evidence & Value Development
Sanofi

Theresa LaVallee, PhD
Senior Director, Translational Medicine
MedImmune

Ash Malik, MS, MBA
Director
PricewaterhouseCoopers (PwC)

Rajiv Mallick, PhD
Director HEOR
Daiichi Sankyo Inc

Gerald McDougall
Partner,
PricewaterhouseCoopers (PwC)

Matthew Monberg, MS
Manager, US Health Outcomes
GlaxoSmithKline

William E. Murray
Vice President, Intellectual Property – Oncology
Cepheid

Scott D. Patterson, PhD
Executive Director, Medical Sciences
Amgen Inc.

Alissa Pereira, MPH
Senior Manager, Public Policy and Reimbursement, Government Affairs
Genentech Inc.

Steven L. Richardson, MD, MSc
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Genomic Health Inc.

Greg Rossi, PhD
VP Payer Evidence
Astrazeneca

Rupa Roychowdhury, PhD
US Medical Affairs Pathfinder, Immunotherapeutics BU
GSK

Michele Schoonmaker, PhD
Vice President of Government Affairs
Cepheid

Art Small, MD
Director Oncology Outcomes Research US Medical Affairs
Genentech Inc.

William Trepicchio, PhD
Senior Director, Translational Medicine, Millennium Pharmaceuticals: A Takeda Oncology Company

Richard J. Wenstrup, MD
Chief Medical Officer
Myriad Genetic Laboratories, Inc.
Measuring outcomes for CU studies

CU studies of MDx tests should include outcome measures that assess patient benefits and harms

- Should include patient-reported outcome measures appropriate and validated for the clinical context
- May also include endpoints such as survival and downstream health care resource utilization
- Process measures are insufficient
- Studies designed to report intended care plans following an MDx test are insufficient to demonstrate CU
Clinical Utility — RCTs

When assessing CU of an MDx biomarker with RCTs:

• RCT should evaluate the effectiveness of the clinical decision relative to control for both marker-positive and marker-negative patients

• Enrichment designs excluding patients with a particular marker status should be avoided

• Marker-based strategies randomizing patients to genomics-guided treatment vs. usual care are not optimal
In some circumstances, longitudinal observational study designs are acceptable options for assessing CU

- Must have compelling rationale for not doing RCT
- Steps to minimize confounding must be documented
- Good research practices followed
- Retrospective studies not adequate for CU of MDx tests
- Secondary databases may be one source for data collection, but prospective data collection is needed
RECOMMENDATION 2: DON’T EXCLUDE PATIENTS WITH OTHER CONDITIONS

Diabetes patients with other medical conditions are often excluded from studies, which makes it difficult to know how treatments will affect these patients.

Patients should not be excluded just because they have cardiovascular disease, depression, a history of cancer, mild cognitive impairment, or diabetes complications.
RECOMMENDATION 4: REPORT QUALITY OF LIFE MEASURES

Quality of life is an important factor for patients evaluating treatments

Studies should include quality of life measures, specifically the Audit of Diabetes-Dependent Quality of Life (ADDQoL-19) and the Diabetes Treatment Satisfaction Questionnaire before treatment and after 1 year of treatment.
**GPC PROGRESS REPORT – 2014/2015**

- **Next Generating Sequencing**
  - July 2014, workshop to discuss methods and standards for evaluation of clinical utility of NGS-based testing
  - April 2015, workshop to discuss a “straw man” framework for covering next generation sequencing in clinical oncology

- **Oncology Consortium**
  - Place in Therapy EGD to be released in April 2015

- **Endo-Met Consortium**
  - Diabetes EGD released in July 2014
  - Manuscript based on EGD submitted to Diabetes Care in February 2015

- **Weight Loss and Obesity**
  - January 2015, workshop held in collaboration with FDA and AHIP to explore the steps needed to improve research on the comparative effectiveness and value of interventions for treating obesity.
TOPICS UNDER DEVELOPMENT

- Assessing quality of “real world evidence”
- Core Outcomes Sets – Advancing the field
- NGS – clinical utility and reimbursement policy
- Creating a workable version of “CED” (CMS and commercial payers)
SCIENTIFIC ADVICE FOR MARKET ACCESS
SCIENTIFIC ADVICE - OVERVIEW

• Technical input on medical device clinical development plans from US private payers and HTA organizations.
  – Informed by clinical and research experts
  – Specific study design recommendations
  – Aligned with regulatory expectations

• Service provided by CMTP, in cooperation with FDA/CDRH, AHIP and BCBSA
  – Service costs covered by device company
RATIONALE FOR SCIENTIFIC ADVICE

- Device companies and life sciences investors identify reimbursement as major challenge
- Significant uncertainty about evidence required
- Input on clinical development plans from payers and HTA organizations is not readily available
- Current mechanisms have some limitations
  - Payer advisory boards
  - Arranging one-off mtgs. with health plans
• FDA/CDRH approached AHIP re payers at IDE pre-submission mtgs (spring 2014)
• AHIP requests support from CMTP (GPC)
• AHIP, FDA/CDRH, CMTP develop principles of collaboration and process (summer 2014)
• Initial outreach to device companies, investors, health plans (fall 2014/ongoing)
• Pilot scientific advice projects (early 2015)
BASIC PROCESS

- Initial request for PRSA service from device company
- Informal discussion with CMTP
- Briefing book created
- Background work conducted
- In-person meeting with payers, HTA and research experts, CMTP, FDA (if desired).
- Recommendations drafted and shared with company
- Final report drafted
EXCITE PROGRAM
ONTARIO → MARYLAND → USA?

CENTER FOR MEDICAL TECHNOLOGY POLICY
MaRS Excellence in Clinical Innovation and Technology Evaluation program

MaRS is a member of

Ontario Network of Entrepreneurs
Our Future Matters

March 2015

MaRS EXCITE Concept

U

Pre-Market

Systematic review

Cost Effectiveness

- Efficacy
- Safety
- Value (CE)
- Affordability
- Ethical & societal
- Post-market conditions

Post-Market

Systematic review

Cost Effectiveness (CE)

- Efficacy
- Safety
- Value (CE)
- Affordability
- Ethical & societal
- Post-market conditions

Regulation

Reimbursement

Diffusion

Obsolescence

Yes

Unconditional No

TIME
The EXCITE Collaboration Model

Management Board

MaRS EXCITE Secretariat

Scientific Collaborative

OHTAC (Reimbursement)

Safety Advisory Committee

Health Canada (Regulatory)

Methodology Centres

• Advice on science, methodology
• Allocation of projects
• Heads of 5 methodology centres
  • Dr. Les Levin, CSO

• Review protocols for safety
  • Chair Tony Easty

• Advice, oversight, direction
• Approve technologies, protocol, budget
• Senior reps: health, economic development, HTA, AHSCs, industry

• Dr. Les Levin, CSO
• Dr. Zayna Khayat, Director
• Adel Aziziye, Project Manager
• Lily Lo, Coordinator

• Advise prioritization of technologies
• Advice on clinical study design
• Support in conditions of adoption
• Comprised of implementation sub-committee of OHTAC

Methodology Centres

• Excellence in complex clinical trial design and execution in collaboration with 24 Research Hospitals
  • Contracted in by EXCITE
  • Design study with industry;
  • Execute and publish the study

AHRC
APPLIED HEALTH RESEARCH CE! Collaborative
theta Collaborative
PATH
THE OTTAWA HOSPITAL UNIVERSITY D'OTTAN
Healthcare Human Factors
The EXCITE Process: 3 points of value-added

1. Prioritization
2. Study Design
3. Conditions Of Adoption

Med Tech Innovators
- Multinational
- Small and Medium enterprises

Good Fit?
Robust Study Design?
Strong Evidence?

Application
Consultation
Evaluation / Conditions of Adoption

Regulatory Licensing
Reimbursement
Patient and Clinician Use

EXCITE Involvement
Evaluations range from 12-36 months

- **Trial Initiation**
  - Company obtains regulatory approval for trial
  - MC contracts / activates participating sites

- **First Patient Enrolment**

- **Completion of Clinical Trial**
  - MC prepares an evaluation report
  - The report is then submitted to OHTAC

- **Evaluation Report**

- **EXCITE Secretariat conducts**
  - quarterly Check-In meetings with company and MC
  - MC submits quarterly report on trial progress to EXCITE

The evaluation phase takes 12-36 months depending on the technology and study design
HIGH VALUE INNOVATION GRANTS

• Feb 2015 Press Release:
  – BioMaryland Center Awards $865,000 to Accelerate Life Sciences Commercialization

• For this year's awards, the BioMaryland Center launched a new partnership with Maryland's Department of Health and Mental Hygiene (DHMH) and the Center for Medical Technology Policy (CMTP) to incorporate improved health care quality and cost reduction criteria into the selection process.
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<tr>
<th><strong>ASSEMBLING EXCITE-MD</strong></th>
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<tr>
<td><strong>• Build on GPC, SAMA, CED, Collaboratory experience</strong></td>
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<tr>
<td><strong>• Working relationships with payers, employers, FDA, CMS, patient groups, professional societies</strong></td>
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<td><strong>• BioMaryland DBED grants (with DHMH)</strong></td>
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<td><strong>• BioHealthInnovation, ProductSavvy</strong></td>
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<td><strong>• Maryland Medicare waiver links</strong></td>
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<td>- Strong pressure to reduce costs, improve outcomes, pop health</td>
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<td>- HSCRC, DHMH, Carefirst, Maryland Hospital Association</td>
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<td><strong>• Relevant programs and people at JHU / UMD</strong></td>
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<td><strong>• Initial funding through DBED/local foundations; later funding through companies (like MaRS)</strong></td>
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A REIMBURSEMENT FRAMEWORK FOR PRECISION MEDICINE
OVERVIEW OF STRAW MAN PROPOSAL

Disease specific or other "established" variant panels (Covered)

- Uses variants already covered for clinical use when analyzed by older methods
- Only admits FDA-approved therapies
- Relatively low uncertainty*

General onco-panels (Covered with preauthorization under certain conditions)

- Established and "emerging" variants
- High medical need
- Opportunity to promote systematic data-gathering
- Requires preauthorization; stds, data collection
- Higher uncertainty*

Whole exome sequencing (Generally not covered)

- Investigational
- Not generally covered
- *High uncertainty

* = cumulative knowledge of utility + likelihood panel will produce VUS + likelihood panel will lead to off-label prescribing
CONTACT INFO

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- 410-963-8876 (M)