Value Propositions in Contractual Relationships:

Real World Evidence, Outcomes Research, and Comparative Effectiveness

October 22, 2015

Presented by:

BJ D'Avella
Senior Director, Huron Life Sciences, New York, NY (Moderator)

Kathleen Peterson
Special Counsel, Cooley LLP, Washington, DC

Joseph Zimmerman
Former Senior Vice President and Chief Compliance Officer, Actavis plc;

Agenda

1. The Evolving Healthcare Marketplace and HEOR
2. FDAMA 114: Overview
3. Other Key Considerations in Contractual Value Propositions
4. Compliance Program Elements in the HEOR Context
5. Case Study: Emerging HEOR Practices and Risks

The Evolving Healthcare Market Place and HEOR

Market Access

Demonstrating Economic Value

In an industry where much of the product entry hurdles have been defined in terms of demonstrating safety and efficacy:

- What additional hurdles does the need to demonstrate economic value present for new product candidates and their commercializing enterprises?
- What can a manufacturer communicate about the components of economic value and to whom may they direct that communication?
- How much of a manufacturer's market access success depends on its Health Economics and Outcomes Research (HEOR)?
  - Reimbursement status and level
  - Product utilization
  - Patient eligibility through guidelines and protocol development
  - Treatment duration
  - Cost sharing approaches

Impact of Cost & Value on Decision Making

The Commercial Landscape

- On May 28, 2014, a major payer announced launch of program with tools and reimbursement incentives ($350 per patient) for oncologists' adherence to recommended cancer treatment regimens[1]
  - Recommended treatment options were to be based on clinical benefit (i.e., efficacy, side effects, strength of national guideline recommendations and cost.
  - In 2013, a large PBM preferred formulary designated 40+ drugs as "not covered," including specialty drugs, signifying an ongoing reluctance among payers to reimburse treatments that are high cost and not considered to be more clinically effective[2]
  - In the summer of 2015 a major retailer/PBM announced a list of medications it was adding to its "excluded list" for 2016[3]
  - Media coverage quoted a company statement: "For those drugs excluded, equally effective products with lower overall costs remain available"
  - One article went on to say: "Since 2012, the list of excluded drugs has ballooned from 34 to 124 in 2016."[2]

Sources:
1.WellPoint. Cancer Care Quality Program. 2014
2.Staton T. Express Scripts stops covering key Big Pharma drugs on clinical, cost-effectiveness grounds. October 10, 2013.
3.http://money.cnn.com/2015/08/06/news/companies/cvs-viagra/

Impact of Cost & Value on Decision Making

Costs May Contribute to Opening of National Coverage Analysis (NCA)

While CMS does not explicitly consider cost in coverage decisions, cost is often an impetus for why Medicare will open a national coverage analysis*

"In June 2010, CMS opened an NCA on Provenge, a treatment for advanced prostate cancer, only two months following its FDA approval. CMS' reference to informal inquiries received for an NCD on Provenge left experts speculating on the subject of those informal inquiries, chief among them, Provenge's $93,000 price tag."

- Avalere Health[1]

*CMS National Coverage Decisions (NCDs) are only for physician administered products. For oral products like recent hepatitis C drug, Sovaldi, CMS makes decisions through Medicare Part D Formulary Creation and Review Process. Part D drug plans develop and maintain formularies through Pharmacy & Therapeutics committees, which make coverage and formulary management recommendations on multiple factors, including costs.

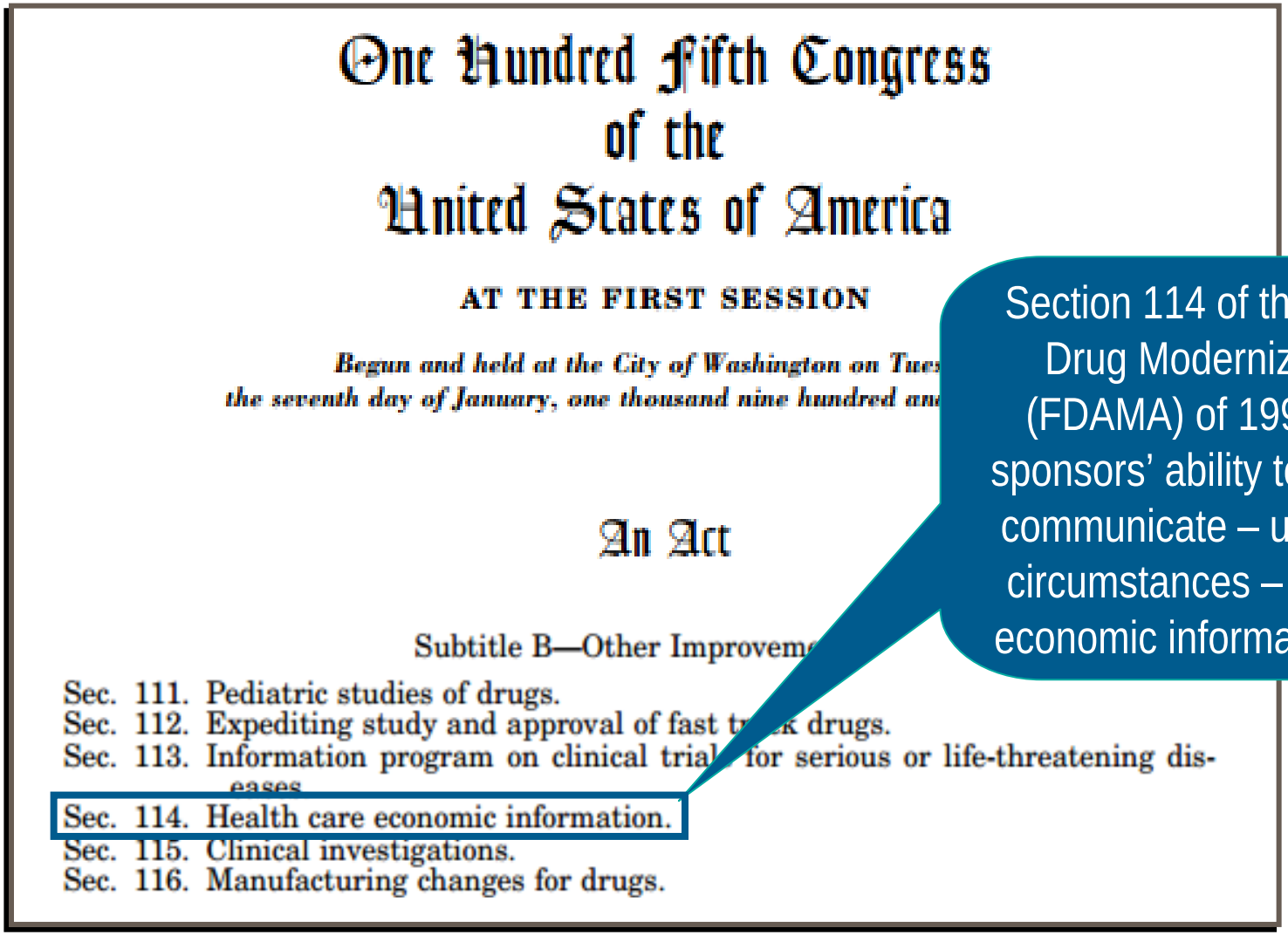
Note: In its proposed decision memo issued on March 30, 2011, CMS proposed to cover the drug for its FDA-approved indication: asymptomatic or minimally symptomatic metastatic castration-resistant prostate cancer.

Source: 1. Avalere Health. Choe SH, Carino T, Mendelson D. Is Provenge a Harbinger for Future CMS Decision Making? 2011.

FDAMA 114: Overview

FDAMA Section 114

Provides a Pathway for Industry to Communicate Economic Data Proactively



One Hundred Fifth Congress
of the
United States of America

AT THE FIRST SESSION

Begun and held at the City of Washington on Tues
the seventh day of January, one thousand nine hundred and

An Act

Subtitle B—Other Improveme

Sec. 111. Pediatric studies of drugs.
Sec. 112. Expediting study and approval of fast t[illegible]k drugs.
Sec. 113. Information program on clinical trial[illegible] for serious or life-threatening diseases.
Sec. 114. Health care economic information.
Sec. 115. Clinical investigations.
Sec. 116. Manufacturing changes for drugs.

Section 114 of the Food and Drug Modernization Act (FDAMA) of 1997 codifies sponsors' ability to proactively communicate – under limited circumstances – healthcare economic information (HCEI).

The Demand for Guidance Has Increased

PhRMA, Media and Now FDA Looking Ahead to Updated Guidance for Industry

1980 ← 17 Years → **1997** → 17 Years → **2014**

- The Miracle on Ice
- The Empire Strikes Back
- Pac-Man

- FDAMA 114

One Hundred Fifth Congress
of the
United States of America

AT THE FIRST SESSION

Begun and held at the City of Washington on Tuesday, the seventh day of January, one thousand nine hundred and ninety-seven

An Act

Subtitle B—Other Improvements

Sec. 111. Pediatric studies of drugs.
Sec. 112. Expediting study and approval of fast track drugs.
Sec. 113. Information program on clinical trials for serious or life-threatening diseases.
Sec. 114. Health care economic information.
Sec. 115. Clinical investigations.
Sec. 116. Manufacturing changes for drugs.

- Increased volume & frequency of calls for detailed guidance
- FDA indicates plans to provide it

FEDERAL REGISTER
The Daily Journal of the United States Government

Revised Draft Guidance for Industry on Distributing Scientific and Medical Publications on Unapproved New Uses–Recommended Practices

Healthcare Economic Information (HCEI)

Definition from FDAMA 114

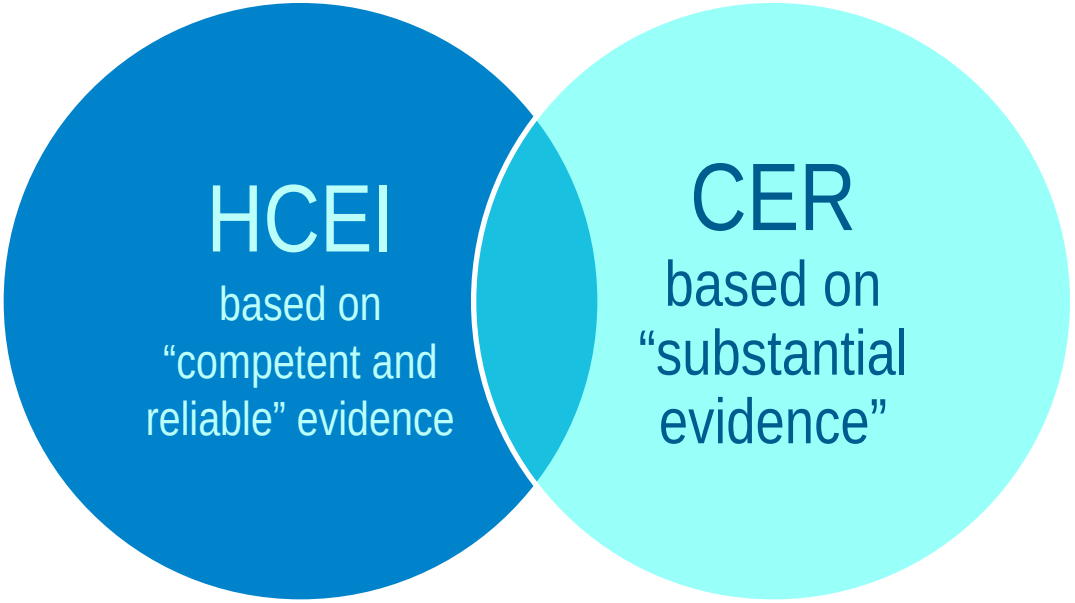
"Any analysis that identifies, measures, or compares the economic consequences, including the costs of the represented health outcomes, of the use of a drug to the use of another drug, to another health care intervention, or to no intervention."

"This provision is not intended to provide a path for promoting new off-label indications or claiming clinical advantages of one drug over another when these claims do not satisfy FDA's evidentiary standards for the claims being made."

– Robert Temple, MD, Deputy Center Director for Clinical Science, FDA CDER
February 9, 2012

Comparative Effectiveness Research (CER)

May be Covered by FDAMA 114



The Evidence Standard

Claims Must Be Supported by “Competent and Reliable” Scientific Evidence

FDA has relied on FTC’s definition for “competent and reliable”

To date, neither federal legislation nor FDA guidance has formally defined what constitutes “competent and reliable” scientific evidence

FTC defines “competent and reliable” scientific evidence as: “tests, studies or other research based on the expertise of professionals in the field which have been objectively conducted and evaluated by qualified people using procedures that give accurate and reliable results”

Proactive HCEI Communication Safe Harbor

A Provision of FDAMA 114

FDAMA section 114 provides a statutory exemption (i.e. “safe harbor”) from the “substantial evidence” standard.

The FDAMA 114 Safe Harbor: Summary

HCEI Definition	“Any analysis that identifies, measures, or compares the economic consequences, including the costs of the represented health outcomes, of the use of a drug to the use of another drug, to another health care intervention, or to no intervention”
Evidence Standard	“Competent and reliable”
Type of Information	Directly related to an FDA-approved indication
Audience	“Formulary committee, or other similar entity”

Other Key Considerations in Contractual Value Propositions

Federal Health Care Program Anti-Kickback Statute

- Legal analysis of value-based contract proposal is critical:
  - Safe harbors may not be a snug fit for value-based contract
  - Facts and circumstances?
    - Potential to interfere with, or skew, clinical decision-making?
    - Potential to increase costs to the FHCPs or beneficiaries?
      - FHCP "carve-outs" may not be determinative (OIG concerned with "seeding")
      - The closer costs are to product competitors, the lower the risk of harm to a federal health care program payor
      - Mitigate risk of billing for "free" product?
    - Potential to be a disguised discount to circumvent GP calculations?
    - Potential to increase the risk of overutilization or inappropriate utilization?
      - *The lower the barriers to clinical "switching" to competitive therapy, the lower the risk of harm to a federal health care program payor*
    - Patient safety or quality of care concerns?
    - Can payments be properly accounted for by *recipient?* (e.g., Medicare Part D TrOOP, DIR reporting)

Government Price Program Considerations

- GP should analyze proposed contract terms sooner rather than later:
  - Can discounts be adequately accounted for in government price calculations?
    - Are there multiple products and/or services and/or reporting periods involved in offer?
    - Restatements/smoothing
  - Will arrangement result in a $0 or “nominal” Medicaid Best Price?
    - Certain entities (e.g., 340B) can get nominal prices w/o BP/ASP impact
  - Will arrangement result in an unduly low base date AMP?
  - If applicable, will discount unduly lower Medicare Average Sales Price (generally used for Part B drug reimbursement to providers)?
  - Will arrangement increase 340B discounts/refunds?
  - Impact of arrangement on FSS Pricing?

Other Key Legal Considerations

- “Adverse event” reporting/pharmacovigilence
- Antitrust laws (e.g., Robinson Patman)
- State “consumer protection” laws
- State and federal privacy laws (e.g., HIPAA)
- False Claims Act(s) – federal and state
- Federal Criminal Health Care Fraud Statute
- CMP Prohibitions on Beneficiary Inducements
- Medicare Part D reporting obligations
  - Will plan(s) be able to appropriately account for discount on PDE and/or DIR as applicable?

Compliance Program Elements in the HEOR Context

Risk Drivers

- Competitive pressures: Some industry and media commentary suggests that the lack of guidance related to FDAMA 114 fosters an asymmetry of information in the marketplace, which may work to the detriment of both the industry and patient health

- Lack of both wide and deep understanding of the standard for HEOR claims, due to the fact that guidance is forthcoming (but has not yet been provided…)

- Scalability: the provisions of FDAMA may prove inadequate in a world where patients and providers are becoming more active, value-conscious participants in the health economics discussion?

- Complexity/novelty of legal issues and GP calculations

Organization and Management Structure

Key Questions For Your Organization

- What are the reporting lines for personnel charged with producing and discussing HEOR studies?
  - Does the management framework promote proper oversight?
- Is the broader commercial organization and product messaging personnel aware who is tasked with HEOR communication?
- Are the contracting personnel familiar with HEOR communication parameters?
  - What is the process for reviewing value-based contract terms?
    - Potential for implied claims
    - Regulatory/PRC coordination with Pricing Committee or contracting group?

Policy Framework

Key Questions For Your Organization

- Do relevant, standalone policy and procedure documents exist to address the duties, opportunities and limitations presented by HEOR?
  - Who can present HEOR information?
  - When?
  - To whom? (e.g., what is a “similar committee”)
  - What information may be presented?
    - Distinction between HCEI and CER?
    - Who approves? PRC?
    - Any discretion, or are specific “claims” approved?

- If not, do existing policies sufficiently cover HEOR activities, or is it left to inference?

Training and Education

Key Questions For Your Organization

- How broadly are the relevant provisions of FDAMA 114 understood?
- Are HEOR policies and procedures and/or FDAMA 114 requirements part of standard enterprise-wide training?
- If not, who receives the training?
  - Just HEOR personnel?
  - Just Legal or Compliance?
  - Just the “payer facing” functions?
  - Sales?
- Who *provides* the training?

Auditing and Monitoring

Key Questions For Your Organization

- Are HEOR studies subject to the same approval processes as scientific and/or promotional materials?
  - What about “value-based” contracts?
- Are reviewers properly skilled to review the publications/work product?
- Are HCP consultants engaged to conduct HEOR studies?
  - Are they appropriately classified as HCPs to enable compliance with broader HCP compliance programs?
  - Are presentations monitored by Compliance?

Auditing and Monitoring

Key Questions For Your Organization

- Does the company sponsor HEOR studies through grants?
  - Are the HEOR grants managed similarly to other research grants (e.g. IIS)?
  - Has the risk of “ghost writing” allegations been assessed & addressed?

- Are pharmacoviligence policies complied with consistently with respect to value-based discussion/contracts?

Case Study: Emerging HEOR Practices & Risks

Real World Evidence Clinical Trials: Overview

A Hybrid HEOR/RCT Model That Is Growing in Frequency

- A clinical study (usually Phase IV) launched at or soon after new product launch, combining elements of HEOR with Randomized Controlled Trials (RCTs)
- Involves a contractual relationship with a payer, usually the research arm of the payer
- Requires continual and close collaboration between staff at sponsor, payer partner, vendor, and clinical trial sites – as well as across functional areas and territories
- Trials can be designed to study factors including: differences in patient and provider reported/perceived outcomes, healthcare resource utilization, treatment persistence over time, and comparative efficacy versus standard of care treatments
- Very few of these types of studies have been conducted to date, meaning there are few benchmarks and predicate practices upon which companies can rely as they break new ground.

Real World Evidence Clinical Trials: Overview

Case Study: The Role of Compliance and Legal

Situation	• The Company had never run a study of this type before, and found that neither its clinical policies and SOPs nor its HEOR policies and SOPs provided a sufficient governance model • The study had to be “real world” in nature – for example, the sponsor could not pay the sites for the study drug and have it provided to the patient, as in an RCT – because it would impair the “real world” conditions. The company had to develop new, compliant ways to finance the study drug.
Lessons Learned	• Bring in Legal and Compliance early and often – especially if this is your company’s first trial of this type, it takes time to break new ground and do so in a compliant manner • Build in enough time up front for Quality, Legal, and Compliance reviews (e.g. vendor qualification, fair market value, contract terms, scientific materials, etc.) – it’s critical that there be enough time to identify the issues, develop solutions, and get comfortable with the level of risk being managed. • Communicate the need for full cross-functional collaboration – it’s not just a clinical study, it’s not just a HEOR study - it's a new model and requires agility
Outcome	While this company stumbled a bit at first – because it was learning these better practices (and a slew of others) the hard way – it is now several months into enrollment and things are moving along on schedule, as planned.

THANK YOU