FDAMA Section 114 and Comparative Effectiveness Research

September 28, 2011
1:00PM—2:30PM, EDT
The Panelists

- **Peter J. Neumann, ScD.**, Director CEVR, Tufts Medical Center and Professor of Medicine, Tufts University School of Medicine
- **Paul W. Radensky, M.D.**, Partner, McDermott Will & Emery LLP.
- **Tom Hughes, Ph.D.**, Director, Market Access and Reimbursement, Optum Insight (17 years with Eli Lilly)
Neumann Overview

- What is FDAMA Section 114?

- Is there anything “new” about it?

- CER and 114

- What do we know about uses of, and opinions about, 114?
What is FDAMA Section 114?
Motivation for Section 114

- Increase the amount of health economic information that drug companies can share with managed care audience

- "Substantial evidence" (2 well-controlled trials) is not appropriate for HCEI
The FDA Modernization Act of 1997 (Section 114)

- **Health care economic information** provided to a formulary committee, or other similar entity,....with respect to the selection of drugs ...is based on **competent and reliable scientific evidence**...

- HCEI shall not be considered false or misleading ...if the information **directly relates to an indication approved**...
Key provisions

- Health care economic information
- Formulary committee or similar entity
- Competent and reliable scientific evidence
- Directly related to the approved indication
An EXAMPLE

Drug → RCT → Fracture ↓ → Database → Health costs ↓

Can the company promote the drug to health plan audiences as cost saving? Probably okay.
An EXAMPLE

Drug → RCT → BMD↑ → Model → Fracture↓ → Model → Cost/QALY

Can a cost/QALY claim be made under FDAMA 114? Probably NOT okay
How to think about 114?

- Health economists’ view
  - Information is good
  - Can lead to efficiencies
  - Payers are demanding this kind of information
  - Informed buyers and sellers

- Concerns (regulators’ view)
  - Misleading claims
  - Risks of implied safety and effectiveness claims
  - Remove incentives to do the actual studies
Why not more attention to Section 114?

a. The rules are murky
b. Section 114 is very restrictive
c. AMCP dossiers (unsolicited request process) co-opted 114
d. Section 114 promotions continue at some unknown level
e. All of the above

- Adapted from Neumann, 2009 Value in Health
What is new about Section 114?

- Nothing?
  - No new legislation
  - No FDA guidance
  - No FDA warning letters or untitled letters

- Something?
  - Intensifying interest in promoting value
  - Compliance concerns
  - CER
Survey of U.S. outcomes directors at leading drug companies

- Internet survey
- HEOR directors at all PhRMA-member companies and top 11 biotech (n=33)
- 16/33 respondents (RR=46%)
<table>
<thead>
<tr>
<th>Question</th>
<th>% Stating familiar or very familiar</th>
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<tbody>
<tr>
<td>How familiar are you with the FDAMA Section 114?</td>
<td>93.8%</td>
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<tr>
<td>Question</td>
<td>% Stating frequently or always</td>
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<td>How often do you consider using Section 114 when making promotional claims?</td>
<td>81.3%</td>
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<td>Question</td>
<td>% Saying yes</td>
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<td>Does your company have internal legal/regulatory guidance on Section 114?</td>
<td>100%</td>
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<td>Question</td>
<td>% Stating</td>
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<td>For what % of your drugs that had evidence to support their economic value, did you create a Section 114 promotional piece?</td>
<td>56.3%</td>
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<td>Question</td>
<td>% Saying 0-2 pieces</td>
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<td>For drugs that had evidence to support their economic value, how many Section 114 pieces do you create per drug year?</td>
<td>93.7%</td>
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<td>Question</td>
<td>% Agree</td>
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<td>Why did you choose not to use Section 114?</td>
<td></td>
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<td>Not feeling comfortable using Section 114</td>
<td>25.0%</td>
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<td>Economic value information may not be included in the product label</td>
<td>12.5%</td>
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<td>Not certain efforts of creating a Section 114 piece was worth the benefit</td>
<td>12.5%</td>
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<td>Question</td>
<td>% Agree</td>
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<td>Which is more valuable, Section 114 promotion or economic information in AMCP dossiers?</td>
<td>62.5%</td>
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<tr>
<td>Section 114 promotion of economic information more valuable</td>
<td>62.5%</td>
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<td>Equal in value</td>
<td>31.3%</td>
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<td>Economic content in AMCP dossiers</td>
<td>6.3%</td>
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<td>Question</td>
<td>% Saying more often</td>
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<td>Did you expect to use Section 114 more often or less often in the future?</td>
<td>75.0%</td>
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<td>Question</td>
<td>% Saying yes</td>
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<td>Should the FDA issue guidance in this area?</td>
<td>75.0%</td>
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<td>Question</td>
<td>% Agree</td>
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<td>If the FDA were to release guidance on Section 114, what area is most critical to address?</td>
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<td>Competent and reliable scientific evidence</td>
<td>48.3%</td>
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<td>Health care economic information</td>
<td>37.5%</td>
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<td>Directly related to an approved indication</td>
<td>12.5%</td>
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<td>Formulary committee or other similar entity</td>
<td>6.2%</td>
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<td>Question</td>
<td>% Agree or strongly agree</td>
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<td>Do you agree or disagree that the increased focus on comparative</td>
<td>68.8%</td>
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<td>effectiveness will increase the use Section 114 promotions?</td>
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"Tufts Medical Center"
Conclusions

- Section 114 remains an important option
- The rules are not well defined
- CER heightens the debate
Some further reading


- The Tufts CEA Registry, [www.cearegistry.org](http://www.cearegistry.org)
FDAMA §114 in an Era of Comparative Effectiveness Research: Legal Framework

Center for Evaluation of Value and Risk in Health

Webinar September 28, 2011

Paul Radensky, MD, JD
McDermott Will & Emery LLP
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A drug or device shall be deemed to be misbranded--

(a) If its labeling is false or misleading in any particular.

Health care economic information provided to a formulary committee, or other similar entity...shall not be considered to be false or misleading...if the health care economic information directly relates to an indication approved...and is based on competent and reliable scientific evidence....
FDAMA § 114: Key Areas

- Health care economic information
- Formulary committee or similar entity
- Managed care organization or similar entity
- Directly related to an approved claim
- Competent and reliable scientific information
Directly Related to an Approved Indication

- Extrapolation from intermediate outcomes to health outcomes
  - e.g., cholesterol lowering to CV events
- Duration of use beyond label but from actual usage database
- Dosage beyond label but from actual usage database
- “Real world” settings
FDA’s Regulation of Economic Information in Promotion:

- No legal mandate for guidance on FDAMA § 114
- 1995 “guidelines” were issued for discussion purposes only
- Economic information is not a major component of promotional materials that are submitted to FDA.
- Economic information is often included in company responses to “unsolicited requests” (AMCP Dossier)
FDA surveillance of HEOR claims in promotion

- FDA staff reviews submissions
  - FDA asks for evidence to support claims if not supported directly by the approved labeling
  - If evidence is not available, a violation is cited
  - If evidence is inadequate, a violation is cited

- FDA attends professional conferences and exhibit halls
- FDA professionals work in clinical settings
- FDA depends on complaints from competitors, health professionals, and others
- FDA surfs the web
FDA Scrutiny Over HCEI

- Agency has never applied the “competent and reliable scientific evidence” standard in a regulatory letter
- Nevertheless, the agency undertakes detailed analysis of pharmacoeconomic claims
Comparison of “costs” or “price”

- Misleading comparative claims: implication that one statin is similar in effectiveness to other statins and the only difference between theses agents is cost ("based on retail pricing of the most commonly prescribed doses.")
Outcomes Study of Inpatient vs Outpatient Care

- Brochure disseminated at the meeting of the National Managed Health Care Congress

- Misleading comparative claim; “shortened mean hospital stay” not supported by study design
Compliance Audit Studies

- Journal ad and “slim jim” based on retrospective prescription audits tracking patient compliance

- Misleading because prescription audits do not provide accurate description of actual compliance due to pharmacy “switching”
Cover page and introductory letter of ongoing monitoring patient questionnaire survey involving an asthma drug and containing graphic of child and adult running side-by-side

False or misleading representation outside product labeling because product not approved for exercise-induced bronchospasm
FDA challenged formulary kit presenting burden of illness information covering quality of life, productivity and costs by inferring unsubstantiated claim for new product.

What nexus between burden of illness information and product claims is acceptable?
FDAMA § 114: Implications

- If a promotional piece comprising economic information is challenged, the appropriate review standard would be competent and reliable scientific evidence to support the claim—not substantial evidence based upon adequate and well-controlled trials.

- Increased flow of promotional information due to lowered standard, but with substantial restrictions on audience.
FDAMA Section114 in an Era of Comparative Effectiveness Research: Case Studies

Center for Evaluation of Value and Risk in Health Webinar September 28, 2011

Tom Hughes Ph.D., Director, Market Access and Reimbursement, Optum Insight
Tom.Hughes@innovus.com
Question #1 – Will the claim only be used with formulary committees or similar entities?

Question #2 – Is the claim based on health care economic evidence?

Question #3 – Is the evidence related to an approved indication?

Question #4 – Is the evidence competent and reliable?
Case Studies
FDAMA 114: Case Study #1

- Diabetes
  - Research: retrospective database study
  - Claim: patients taking Drug A demonstrate significantly superior adherence and lower healthcare costs compared to patients taking drug B. Both drugs are being used on-label.
  - Poster at professional meeting
  - Audience – Payers

- Can this be used as a FDAMA 114 piece?
  - Payer use only?
  - Health care economic evidence claim?
  - Directly related to an approved indication?
  - Competent and reliable?
Lesson Learned

• Eligible for FDAMA 114 consideration
FDAMA 114: Case Study #2

- Oncology
  - Research: Randomized clinical trial
  - Claim: drug A is cost-effective compared to drug B, based on greater survival and lower cost. Both drugs are being used on-label.
  - Peer reviewed publication
  - Audience – Payers

- Can this be used as a FDAMA 114 piece?
  - Payer use only?
  - Health care economic evidence claim?
  - Directly related to an approved indication?
  - Competent and reliable?
Lessons Learned

• It may be eligible for FDAMA 114 consideration, you are making 2 claims
  – Clinical – survival
  – Economic – cost

• Do you have:
  – Substantial evidence for the clinical claim?
  – Competent and reliable evidence for the economic claim?
FDAMA 114: Case Study #3

- Asthma
  - Research: retrospective burden of illness study
  - Claim: Asthma costs $10 billion per year in the US
  - Peer reviewed publication
  - Audience – Payers

- Can this be used as a FDAMA 114 piece?
  - Payer use only?
  - Health care economic evidence claim?
  - Directly related to an approved indication?
  - Competent and reliable?
Lessons Learned

• Not eligible for FDAMA 114 consideration

• What is the claim?
FDAMA 114: Case Study #4

- Hypertension
  - Research: randomized clinical trial
  - Claim: Patients taking Drug A demonstrate significantly lower blood pressure compared to patients taking drug B. Both drugs are being used on-label.
  - Poster
  - Audience – Payers

- Can this be used as a FDAMA 114 piece?
  - Payer use only?
  - Health care economic evidence claim?
  - Directly related to an approved indication?
  - Competent and reliable?
Lessons Learned

• Not eligible for FDAMA 114 consideration

• What is the claim?
FDAMA 114 Opportunities and Challenges

• Opportunities
  – A promotional channel to communicate value with US payers
  – Great information if the pharma / payer relationship is strong
  – Great opportunity to demonstrate the commercial relevance of the Health Outcomes function

• Challenges
  – You need evidence to make a claim
  – Tepid information if the pharma / payer relationship is weak
  – Internal colleagues (legal, regulatory) may not be familiar with FDAMA 114
FDAMA Section 114 and Comparative Effectiveness Research

Questions and Discussion