DMH BioPharm Advisors, LLC.

Late Breaking News Update:

The FDA issues Draft Guidance on, "Drug and Device Manufacturer Communications with Payors, Formulary Committees, and Similar Entities".

DMH BioPharm Advisors, LLC - Dee Mahoney and Mary Holloway

In May of 2015, we reported the approval of the 21st Century Cures draft bill. The intent of the bill was to accelerate the discovery, development, and delivery of promising new treatments and cures to patients. There were three provisions in the legislation that were especially important to device and biopharmaceutical manufactures: (1) exemption of reprints and reference texts from reporting under the Sunshine Act; (2) expanded authority for biopharmaceutical companies to provide economic information to payers; and (3) direction to the FDA to provide further guidance on off-label marketing to professionals.

The second provision concerning the expanded authority for biopharmaceutical companies to provide economic information to payors, left manufacturers asking for additional guidance. The understanding of how treatments work in the real world is an important task for health plans, providers and the biopharmaceutical industry. Payors are interested in knowing about real-world patients and comparative effectiveness research and manufacturers are interested in providing comparative economic claims to payors and formulary managers.

The Food and Drug Administration Modernization Act of 1997 (FDAMA) included Section 114, which was intended to provide guidance on dissemination of healthcare economic data (HCEI). Section 114 states that HCEI provided to formulary committees will not be considered false or misleading if the HCEI directly relates to an approved indication and is supported by **"competent and reliable scientific evidence."** Those *highlighted terms* -"competent and reliable scientific evidence"- have been the subject of ongoing debate.[1]

The biopharmaceutical industry, wanting to comply with the statute, requested the FDA to clarify what was considered "competent and reliable scientific evidence." Was this a more flexible standard than the "substantial evidence" standard that is required when making efficacy and safety claims in promotion? With no further guidance biopharmaceutical companies were hesitant to distribute HCEI information and were left trying to interpret the guidelines through ad hoc reviews of enforcement letters and comments made by the FDA.[2]

FDA - Draft Guidance Released:

In response to industry's request for further guidance on communicating health care economic data, on January 18, 2017 the FDA released new draft guidance "Drug and Device Manufacturer Communications with Payors, Formulary Committees, and Similar Entities." It explains the FDA's current thinking and recommendations on firms' communication of health care economic information (HCEI) about approved drugs under section 502(a) of the FD&C Act, which was recently amended by the 21st Century Cures Act.

This guidance will each help provide clarity for drug and device companies, as well as other interested parties, on FDA's current thinking and recommendations regarding communication of health care economic data (HCEI). It also answers common questions and provides the FDA's recommendations regarding firms' communications to payors about investigational drugs and devices that are not yet approved or cleared for any use.[3]

Answers to Common Questions:

The draft guidance provides answers to the issues that the industry has pondered for the past 15 years. Click this link to review the draft document and the entire list of questions and answers. Listed below are answers to a few of the questions answered in the draft guidance.[3]

1. **What is the appropriate scope of the audience for the communication of HCEI about approved drugs?**
   - Section 502(a) specifies that HCEI can be provided to "a payor, formulary committee, or other similar entity with knowledge and expertise in the area of health care economic analysis, carrying out its responsibilities for the selection of drugs for coverage or reimbursement."
   - This audience includes payors, formulary committees (e.g., pharmacy and therapeutics committees), drug information centers, technology assessment panels, pharmacy benefit managers, and other multidisciplinary entities that review scientific and technology assessments to make drug selection, formulary management, and/or coverage and reimbursement decisions on a population basis for health care organizations.
   - Such entities are constituted to consider HCEI (and other types of information) through a "deliberative process" and should have the appropriate range of "knowledge and expertise in the area of health care economic analysis" needed to interpret HCEI presented to them to inform their population-based decision-making process. Expertise in this area is essential to understand and evaluate health care economic analyses and their limitations.
   - This guidance doesn't apply to dissemination of HCEI to other audiences, such as health care providers who are making individual patient prescribing decisions or consumers.

2. **What evidentiary support should firms have for their HCEI under section 502(a) so it will not be considered false or misleading?**
   - HCEI shall not be considered false or misleading if, among other things, it is "based on competent and reliable scientific evidence."
   - FDA considers HCEI to be based on competent and reliable scientific evidence (CARSE) if the HCEI has been developed using generally-accepted scientific standards, appropriate for the information being conveyed, that yield accurate and reliable results. In evaluating whether the amount and type of evidence that forms the basis for a particular communication of HCEI meets the generally-accepted scientific standards for such information, FDA will consider the merits of existing current good research practices for substantiation developed by authoritative bodies (e.g., International Society for Pharmacoeconomic and Outcomes Research (ISPOR), Patient-Centered Outcomes Research Institute).

3. **What information should firms include when disseminating HCEI?**
   - To enable payors to make informed coverage and reimbursement decisions and to help ensure that the information is not false or misleading under section 502(a), firms should include appropriate background and contextual information necessary to allow payors to fully understand the HCEI. This information listed below, if applicable, should be presented clearly and prominently.
     - **Study Design and Methodology**
     - **Generalizability** – Refers to the applicability of HCEI obtained in one health care setting or patient population to another.
     - **Limitations –** Factors that may affect the interpretability and reliability of an economic analysis.
     - **Sensitivity Analysis**
     - **Additional Material Information for a Balanced and Complete Presentation**
     - **FDA-approved indication(s), disclosure of omitted studies or data sources, risk information, and financial/affiliation biases.**

Communications by Firms to Payors Regarding Investigation Products or Devices:

Medical product firms may wish to provide certain types of information to payors regarding their investigational products. Such information may help payors plan and budget for future coverage and/or reimbursement decisions prior to FDA approval or clearance of investigational products. Listed below are answers to a few of the frequently asked questions on this topic.[3]

1. **What is the FDA's approach with respect to firms that wish to provide HCEI information prior to FDA approval or clearance of an investigational product?**
    - The FDA does not intend to object, under 21 CFR 312.7(a) or 21 CFR 812.7(a) or otherwise, to the following types of information about investigational products (as defined in this guidance) provided by firms to payors prior to FDA approval or clearance, that is unbiased, factual, accurate, and non-misleading **and** when presented with information discussed in this guidance. (Product information, information from the clinical study protocol(s), factual presentations of results from clinical or preclinical studies (i.e., no characterizations or conclusions should be made regarding the safety or effectiveness of the product), anticipated timeline for possible FDA approval/clearance, product pricing, targeting/marketing strategies, and patient support programs)
    - A clear statement that the product is under investigation and that the safety or effectiveness of the product has not been established.
    - Information related to the stage of product development (e.g., the phase of clinical trial in which a product is being studied and how it relates to the overall product development plan).

2. **What other information should firms provide to payors when communicating information about their investigational products?**
    - The FDA also suggests that firms provide follow-up information to payors previously communicated information becomes outdated as a result of significant changes or as a result of new information regarding the product (e.g., failure to meet primary effectiveness endpoint in the phase 3 trial) or its review status (e.g., an application is determined to not be ready for approval upon completion of the review cycle, a study is placed on a clinical hold).

Important Note:

The draft guidance includes this important statement, "If a firm disseminates HCEI about an approved drug in accordance with this draft guidance, when finalized, FDA does not intend to consider such information false or misleading. In addition, FDA does not intend to use HCEI about approved drugs disseminated consistent with this draft guidance, when finalized, as providing evidence of a new intended use."[3]

FDA Seeking Comments

The FDA is seeking comments on this draft guidance before it begins work on the final version of the guidance. For your comments to be considered in the final draft, they must be submitted electronically or in writing by April 19, 2017.[3]

Foot Notes:

[1] Ropes & Gray - May 7, 2015 "Progressing Toward a Cure: House Committee Unveils Revised, Streamlined 21st Century Cures Discussion Draft." Retrieved from https://www.ropesgray.com/newsroom/alerts/2015/May/Progressing-Toward-a-Cure-House-Committee-Unveils-Revised-Streamlined-21

[2] DMH BioPharm Advisors - May 21, 2015 "21st Century Cures Act Draft Bill Update: "Off-Label Information Dissemination and FDAMA 114," Retrieved from http://www.dmhbiopharm.com/wp-content/uploads/2015/05/DMH-Article-21st-Century-Cures-Act-FDAMA1.pdf

[3] Federal Register / Vol. 82, No. 12 / Thursday, January 19, 2017 – DHHS – "Drug and Device Manufacturer Communications With Payors, Formulary Committees, and Similar Entities – Questions and Answers; Draft Guidance for Industry and Review Staff." Retrieved from https://www.federalregister.gov/documents/2017/01/19/2017-01011/drug-and-device-manufacturer-communications-with-payors-formulary-committees-and-similar

About DMH BioPharm Advisors, LLC

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