DMH BioPharm Advisors, LLC.

# Late Breaking News:

## 21st Century Cures Act Draft Bill Update: Off-Label Information Dissemination & FDAMA 114

### DMH BioPharm Advisors, LLC

On May 14, 2015, The U.S. House Energy & Commerce Subcommittee on Health approved the 21st Century Cures draft bill. This legislation aims to accelerate the discovery, development, and delivery of promising new treatments and cures to patients. The draft bill is scheduled for markup by the full Energy and Commerce Committee on May 21, 2015.

Three provisions in the 21st Century Cures legislation are 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. A provision in an earlier draft enabling "one click away" access to contraindication information in Internet drug ads will be reintroduced soon by Rep. Billy Long (R-Mo.) as a stand-alone bill according to the Coalition for Healthcare Communication. [1]

While the draft bill covers many proposals, this article will focus on the portions of the bill that relate to off-label information dissemination and FDAMA 114.

### Off-Label Information Dissemination:

The latest draft version of the 21st Century Cures bill contains a deadline for the FDA to update its policy on off-label information dissemination, according to Michael McCaughan reporting for the Pharma & MedTech Business Intelligence. McCaughan reports, "The new legislative text is a straightforward directive for FDA to publish a guidance on the subject within 18 months.

***Not later than 18 months after the date of enactment of this Act, the Secretary of Health and Human Services shall issue draft guidance on facilitating the dissemination of responsible, truthful, and non-misleading scientific and medical information not included on the label of drugs***

Assuming the language is ultimately enacted later this year or early next year, that would set a deadline for FDA of mid-to-late-2017 to issue a guidance."[2]

### Food and Drug Modernization Act of 1997 - FDAMA 114:

The 21st Century Cures Bill contains a section entitled: "Facilitating Dissemination of Healthcare Economic Information" (HCEI). This section proposes changes to FDAMA 114 to provide more clarity and flexibility on information exchange between manufacturers and payers concerning real-world outcomes and economic impacts of their products. In particular, the draft (1) clarifies that payers are included within the audience permitted to receive health care economic information; (2) permits sharing HCEI that is "related to" the approved indication, as opposed to "directly related"; and (3) indicates that all components of the economic analysis, including the data, inputs, clinical or other assumptions, methods, results, and other components comprising the analysis, are included with the definition of HCEI (and thereby subject to the competent and reliable scientific evidence standard).[3] This is a result of a 17-year request for more clarity from the FDA, which has, up to this point, been unanswered.

## Past Challenges Related To FDAMA 114

### The Lack Of Definitional Clarity

The Food and Drug Administration Modernization Act of 1997 (FDAMA) included section 114, which was intended to provide guidance on dissemination of HCEI. Section 114 states that HCEI provided to a formulary committee 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."

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.

The only indication of FDA enforcement regarding HCEI utilization appeared in 2010 when an untitled letter was sent to Cumberland Pharmaceuticals accusing the company of making unsubstantiated superiority claims based on economic data. The confusion continued due to the fact that unsubstantiated superiority claims is a standard that is applied to promotional issues. HCEI, according to FDAMA 114, had to be supported by "competent and reliable scientific evidence."

### Citizen Petition 1:

In July 2011, The Medical Information Working Group (MIWG), a coalition of more than a dozen pharmaceutical and device manufacturers, interested in seeking clarity in government policies governing promotional practices, filed a citizen petition tasking the FDA to clarify its policies on four types of manufacturer communications about off-label uses: (1) responses to unsolicited requests; (2) scientific exchange; (3) communications with formulary committees and payers; and (4) the dissemination of third-party CPGs.

On December 2011, the FDA in response to the request issued draft guidance on the responding to unsolicited requests and opened a public docket on scientific exchange. Thus guidance was given on only one of the four topics.

In 2012 Robert Temple, Deputy Director of Clinical Science of the Center for Drug Evaluation and Research, spoke at the National Pharmaceutical Council Meeting. His talk included an interpretation of FDMA 114 in which he stated, "Any comparative claims must be supported by substantial evidence that directly compares the treatments in question (i.e. head-to-head clinical trials that provide a valid comparison of two drugs)." This statement only added to the confusion and complexity of the issue and raised more questions than answers.

### Changes In The Regulatory Landscape

In 2011 & 2012 the regulatory landscape saw two important first amendment cases that gave rise to constitutional vulnerability of regulations concerning communications between a manufacturer and a healthcare provider.[4]

## Citizen Petition 2:

As a result, the Medical Information Working Group filed a second citizen petition in 2013[5] asking the FDA to respond to all four requests in the 2011 citizens petition and asking the FDA to do a comprehensive review of its regulatory approach on communications between biopharmaceutical manufacturers and healthcare providers given the recent cases.

In response, the FDA in February of 2014 issued draft guidance on "Distributing Scientific and Medical Publications on Unapproved New Uses-Recommended Practices." The draft guidance created a narrow safe harbor concerning distribution of new (post approval) risk information in peer-reviewed publications that rebuts or mitigates risk information in the approved labeling. The definition of "new risk information" excludes new risks that more serious than risks identified in approved labeling.

PhRMA authored a white paper to reinforce their position that the FDA needs to "clarify the guidance under which a biopharmaceutical company can disseminate health care economic data pursuant to FDAMA section 114 without facing enforcement or regulatory action from the agency." Without such guidance pharmaceutical companies are hesitant to conduct trials, which has a negative impact on payers and formulary committees who are trying to make informed public health decisions.

## FDA Response And Current Direction

In March 2014, A Federal Register Notice said that the FDA is seeking input from the public on issues related to section 114 of the Food and Drug Administration Modernization Act (FDAMA). It stated that agency is considering writing draft guidance to clarify how biopharmaceutical companies discuss their products with payers and other audiences.

In June 2014, the FDA said the agency, "plans to issue, by the end of the calendar year, additional guidance that addresses manufacturer responses to unsolicited requests distributing scientific and medical information on unapproved new uses, manufacture discussions regarding scientific information more generally, and distribution of health care economic information to formulary committees and similar entities." In addition, FDA Chief Counsel, Elizabeth Dickinson, stated that the agency planned to hold a public meeting in the near future to hear the industry's concerns regarding off-label communication. The date of that meeting has not been released.

## SUMMARY

The partially unanswered citizen petitions to the FDA, the changes in the regulatory landscape regarding truthful, non-misleading communication between companies and health care providers, and the 21st Century Cures Act legislation is causing renewed interest in clarifying issues surrounding scientific exchange and the utilization of Health Care Economic Information.

### Foot Notes:

[1]Parisi G. May 18, 2015. "21st Century Cures Legislation Poised for Full House Committee Vote This Week." Retrieved from http://www.cohealthcom.org/2015/05

[2]McCaughan, Michael. May 15, 2015. "FDA's Deadline To Update "Off-Label" Policy." Retrieved from https://www.pharmamedtechbi.com/publications/rpm-report/first-take/2015/2/off-label

[3] Ropes & Gray. May 7,2015. "Progressing Toward a Cure: House Committee Unveils Revised, Streamlined 21st Century Cures Discussion Draft." Retrieved from Ropes & Gray News & Insights

[4]See *Sorrell v. IMS Health, Inc.,* 131 S. Ct. 2653 (2011); *United States v. Caronia*, 703 F.3d 149 (2d Cir. 2012).

[5]Medical Information Working Group. September 3, 2013. "Citizens Petition" Retrieved from http://www.cohealthcom.org/wp-content/uploads/2013/09/citizen-petition.pdf

## About DMH BioPharm Advisors, LLC

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