KING & SPALDING

Client Alert

FDA & Life Sciences Practice Group

January 20, 2017

FDA Issues Draft Guidance Addressing Communications with Payors

On January 18, the Food and Drug Administration (FDA or the Agency) issued a draft guidance, *Drug and Device Manufacturer Communications with Payors, Formulary Committees, and Similar Entities – Questions and Answers*. This draft guidance was issued as one of a series of actions[i] taken by the Agency in the final days of the Obama Administration. The draft guidance creates a new safe harbor, expressly permitting manufacturers to disseminate certain information about investigational products to payors prior to approval or clearance. The draft guidance also clarifies how FDA interprets the healthcare economic information (HCEI) provision of Section 502(a) of the Federal Food, Drug, and Cosmetic Act (FD&C Act) (formerly referred to as FDAMA 114, and recently amended by Section 3037 of the 21st Century Cures Act).

New Safe Harbor for Certain Pipeline Communications to Payors

The most significant aspect of the draft guidance is the new safe harbor for limited pre-approval communications with payors regarding investigational drugs and devices. Due to payor demands for pipeline information for planning purposes, many companies have engaged in a limited manner with payors prior to approval, but without clear guardrails or FDA sanction. This draft guidance is the first time that FDA has expressly granted permission for such exchanges. Now, communications disseminated in compliance with the draft guidance will not be considered violations of the prohibition on promotion of an investigational product in 21 C.F.R. §§ 312.7(a) and 812.7(a).

Importantly, this safe harbor extends only to communications about investigational products (defined by FDA as products that are not yet approved or cleared *for any use*.) The safe harbor does not expressly apply to communications about unapproved or uncleared uses of approved or cleared products.

The draft guidance lists the types of information about investigational products that may be disseminated pre-approval to payors. Examples cited in the draft guidance include: information about the indication sought, anticipated timeline for approval/clearance, pricing information, patient support programs, and the like. Results of clinical and preclinical studies are also permitted if presented without characterizations or conclusions regarding

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safety or efficacy. All information provided must be "unbiased, factual, accurate and non-misleading" and must be accompanied by a clear statement of the product's investigational status and information on the stage of product development (e.g., clinical trial phase and status within the overall development plan). FDA also suggests that companies follow-up with payors to provide updated information as necessary (e.g., if information becomes outdated, or the application's status with FDA changes).

At the FDA public meeting[ii] held on off-label issues in November 2016, a number of stakeholders proposed a safe harbor for communications with payors on investigational products. In response, the FDA panel requested comments specifically addressing timing of these communications (i.e., *how early* FDA should permit these communications with payors in advance of approval or clearance). Notably, the draft guidance is silent as to specific timing. Although acknowledging payors' need to "plan for and make coverage and reimbursement decisions far in advance of the effective date of such decisions," the draft guidance does not expressly impose any time-based restrictions on how early prior to approval or clearance companies may provide information to payors about investigational products.

Clarification of HCEI Provision

The HCEI provision resides in Section 502(a) of the FD&C Act, and it was added by Section 114 of the Food and Drug Administration Modernization Act of 1997 (FDAMA 114). A number of provisions in FDAMA 114 were ambiguous and subject to rigorous debate. In December 2016, as part of the 21st Century Cures Act (Cures), Congress amended the HCEI provision in Section 502(a) of the FD&C Act to address some of those ambiguities. FDA, in its draft guidance, interprets some of the new statutory language and addresses some of the remaining ambiguities in the HCEI provision. According to FDA, if HCEI is distributed in a manner that is consistent with the draft guidance, the Agency will not consider the information to be false or misleading or use it as evidence of a new intended use. In other words, the Agency will consider the HCEI to be lawfully distributed.

The new HCEI provision, added by Cures, permits the dissemination of HCEI to "a payor, formulary committee or other similar entity" if the HCEI "relates to an approved indication" and is "based on competent and reliable scientific evidence." The draft guidance provides the following clarifications:

- **"Payor, formulary committee or other similar entity"** – As background, FDAMA 114 limited the provision of HCEI to "a formulary committee or other similar entity," which raised uncertainty about whether the provision applied more broadly to all payors. Section 3037 of Cures changes this language to clarify that such information may 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." Thus, although the prior statutory provision was unclear about whether all payors were a covered audience, the new provision clearly establishes that they are. The new draft guidance further clarifies this point by giving additional examples of appropriate audiences, including, for example, drug information centers, technology assessment panels, and pharmacy benefit managers, among others. The draft guidance also makes clear that the target audience must be a health care decision maker (e.g., making population-based decisions on drug selection, reimbursement, formulary placement, coverage) and have the "knowledge and expertise" needed to interpret HCEI and its limitations.

- **"HCEI *related* to an approved indication" –** FDAMA 114 required that HCEI be "directly related" to the approved indication. The recent Cures provision broadens the range of permissible HCEI by amending "directly relates" to "relates." Nevertheless, post-Cures, the ambiguity remained around what "related to" the approved indication meant in practice. The draft guidance helps provide some clarity, defining "related to an [approved] indication" as related to "the disease or condition, manifestation of the disease or condition, or symptoms associated with the disease or condition in the patient population for which the drug is [approved]." The draft

guidance also provides examples of HCEI that would be "related" to the approved indication and HCEI that would not be "related." Examples of HCEI "related" to the approved indication include: duration of treatment, disease burden (e.g., economic consequences of lost work days), dosing, patient subgroups, length of hospital stay, and patient-reported outcomes (e.g., adherence, work productivity). Examples of HCEI that would not be considered "related" to an approved indication include HCEI on patient populations outside of the indicated population and HCEI on use of a drug for prevention of a disease, if the drug is only approved to treat symptoms.

- **Based on "competent and reliable scientific evidence" (CARSE) –** The draft guidance also provides much needed clarity on the meaning of the "competent and reliable scientific evidence" standard for HCEI. When discussing the requisite evidentiary support, FDA's draft guidance focuses both on how HCEI should be developed (i.e., it must be based on CARSE) and what information should accompany it. Both elements must be met to ensure that the HCEI will not be viewed as false or misleading. FDA's draft guidance provides a broad definition of CARSE – "generally-accepted scientific standards, appropriate for the information being conveyed, that yield accurate and reliable results." The Agency also points to standards and good research practices developed by other authoritative bodies, such as the International Society for Pharmacoeconomic Research and Outcomes Research. The draft guidance states that the CARSE standard applies to all components of the HCEI, including all inputs and assumptions. Additional contextual information that must accompany HCEI includes information on study design, methodology, generalizability, limitations, and sensitivity analyses, as well as other material information relevant to providing a balanced and complete presentation (e.g., FDA approved labeling, risk information, disclosure of the existence of omitted studies or data sources (if any) and reasons and implications of the omissions, potential financial / affiliation biases).

In addition to addressing and clarifying some of the ambiguity in the HCEI provision, the draft guidance expressly states that proactive dissemination of HCEI will be considered promotion. Therefore, HCEI information for drugs and biologics provided under this draft guidance must be submitted at the time of initial dissemination to the Agency under Form FDA 2253. Although past enforcement letters suggest that proactive presentations to formulary committees may have long been considered promotional activities by the Agency, this statement eliminates any doubt on that point. It will be interesting to see to what extent FDA will review HCEI submitted under 2253 for compliance with the CARSE standard and if we see an uptick in enforcement based on payor-related communications.

Takeaways from the New FDA Draft Guidance on Communications with Payors

FDA first mentioned its intention to publish guidance on HCEI in 2014, and the HCEI guidance was on the Agency's guidance agenda in 2015 and 2016. Given FDA's failure to issue the guidance in 2015 and 2016, FDA's issuance of the draft guidance on January 18, 2017, in the very last days of the Obama Administration, strikes us as politically motivated. Indeed, in the last several weeks, FDA has issued a series of documents[iii] regarding medical product manufacturer communications to healthcare practitioners and payors. Despite the long waiting period, there is nothing in this draft guidance that is particularly unexpected, especially given the revisions to the HCEI provision in the statute by Cures. That said, this draft guidance provides industry with much needed clarity and guardrails around dissemination of HCEI to payors. Moreover, for the first time, FDA also expressly assents to the dissemination of certain information to payors in advance of approval.

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King & Spalding's FDA & Life Sciences Practice Group was selected by Law360 as "Life Sciences Practice Group of the Year" for 2016, and it is comprised of nearly 40 attorneys and consultants who are based in the U.S. and Europe. Our team provides practical legal counseling and technical consulting on a full array of issues involving all FDA-regulated products. In addition, our team calls upon the expertise of lawyers in several related areas within the firm,

including the civil and criminal litigation group, the appellate litigation group, and the government advocacy and public policy group, which have effectively represented clients who are the targets of government initiated lawsuits and investigations. Please let us know if you have any questions.

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[i] In addition to the draft guidance on payor communications that is the subject of this client alert, FDA also took a series of other actions this year with implications for manufacturer communications with health care practitioners and payors. (For an overview and background on the substance and history of two of these actions, see the King & Spalding Client Alert, "FDA Takes Action in the Last Days of the Obama Administration to Clarify Some of Its Views on Off-Label Communications" (January 18, 2017), available here. A separate client alert will be issued shortly on the FDA memorandum referenced below.) These actions include: (1) On January 9, FDA issued a final rule to clarify, among other things, the meaning of the term "intended use" in connection with FDA's authority to regulate medical products. (See 82 Fed. Reg. 2193 (Jan. 9, 2017)); (2) On January 17, FDA issued a draft guidance, entitled, "Medical Product Communications That Are Consistent With the FDA-Required Labeling – Questions and Answers." This draft guidance addresses how the Agency will treat information that is "consistent" with, but not contained in, FDA-required labeling; and (3) On January 18, FDA posted a memorandum to the docket associated with the public meeting that the Agency held on off-label issues in November 2016. The memorandum is entitled, "Memorandum: Public Health Interests and First Amendment Considerations Related to Manufacturer Communications Regarding Unapproved Uses of Approved or Cleared Medical Products."

[ii] See FDA Notification of Public Hearing on Manufacturer Communications Regarding Unapproved Uses of Approved or Cleared Medical Products, 81 Fed. Reg. 60,299 (Sept. 1, 2016).

[iii] *Id.*