Talk This Way, Pt. 2: FDA Issues Final Guidances on Medical Product Communications

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Once again channeling Aerosmith's 1975 single, "Walk This Way," and the song lyric, "Talk This Way," the Food and Drug Administration has issued two final guidance documents on medical product communications. These final guidances, issued in June 2018, address medical product communications that are consistent with the approved labeling, as well as communications with payors and formulary committees.[1] These guidances are largely consistent with the January 2017 draft guidances on the same topics, which we have written about previously.[2] Rather than summarize these documents anew, we will provide our analysis of the significant changes from the draft to the final versions.

It is important to recognize that the final guidance is not legally binding and, in light of past litigation, it is not clear in what direction we might see FDA proceed with enforcement in the off-label promotion area. However, the guidance reflect FDA's current thinking and indicate a shift, to some extent, to a more permissive approach.

Communications that are Consistent with the FDA-Required Labeling

This guidance document addresses communication of information that is consistent with, but may not be expressly included in, the FDA-required labeling for medical products.[3] Though the draft guidance stated that this type of communication would not "alone" be considered evidence of a new intended use, the final guidance says that, "FDA does not intend to rely on that communication to establish a new intended use." Thus, the final guidance takes the position that the agency will exercise enforcement discretion when communication follows these guidelines.

- The final guidance clarifies how the recommendations apply to 510(k)-cleared devices, noting that manufacturers should consult FDA's "Deciding When to Submit a 510(k) for a Change to an Existing Device" guidance. If a communication triggers the need for a new 510(k), FDA views that communication to be inconsistent with the FDA-required labeling.
- FDA expands its explanation of the "increased risk" factor of analyzing a communication. According to the guidance, if a particular communication makes representations or suggestions about the use of the product that "would reasonably be expected to introduce new risks that are not included in the FDA-required labeling or to materially increase the rate of occurrence or severity of existing risks included in the FDA-required labeling, the communication would not be consistent with the FDA-required labeling." The agency already weighs the risks and benefits of a product when evaluating an application for marketing. If

1 Medical Product Communications That Are Consistent With the FDA-Required Labeling – Questions and Answers, available at https://www.fda.gov/downloads/drugs/guidancecomplianceregulatoryinformation/guidances/ucm537130.pdf; Drug and Device Manufacturer Communications with Payors, Formulary Committees, and Similar Entities – Questions and Answers, available at https://www.fda.gov/downloads/drugs/guidancecomplianceregulatoryinformation/guidances/ucm537347.pdf.

2 Our previous Bulletins are available at https://www.agg.com/files/Publication/b6ac81b0-8bf0-4c5b-abd4-230663b000c0/Presentation/PublicationAttachment/85a0e439-fa47-4272-b133-29cc98141a0c/Minsk-Mulkey-Talk-This-Way-FDA-Provides-Guidelines-on-Medical-Product-Communication.pdf and https://www.agg.com/files/Publication/31bcbf7f-b2e7-446a-8f35-2a334d6f63ef/Presentation/PublicationAttachment/a1ea2883-9d89-4194-86f4-35480ef367b8/Minsk-Richardson-FDA-Says-Sharing-Medical-Product-Information-is-Caring-to-an-Exten.pdf.

3 As defined in the guidance, "The term medical product(s) refers to drugs and medical devices for humans, including those that are licensed as biological products, and animal drugs."

a communication about the product shifts the balance by increasing the potential harm to a patient, the communication is inconsistent with the FDA-required labeling.

- The final guidance expands the description of the types of product communications that could be consistent with the labeling, adding specific examples of communications regarding adherence, convenience, mechanism of action, and tolerability.
- There is greater detail on how a manufacturer can, and should, substantiate a particular communication. The guidance points out that the amount and type of evidence needed to support a communication depends on the claim. For example, "different evidence would be needed to support a long-term efficacy presentation than would be needed to support a presentation about a product's mechanism of action."

Communications with Payors, Formulary Committees, and Similar Entities

This guidance addresses how companies can communicate information on the effectiveness, safety, and cost-effectiveness of their approved or cleared medical products with entities making product selection, formulary management, and coverage and reimbursement decisions. FDA recognizes that these entities may request information that differs from, or is in addition to, the information the agency reviews. Because these payor decisions affect a large patient population, FDA "believes it is critical that HCEI [healthcare economic information] provided by firms to payors about their approved drugs and approved/cleared devices be truthful and non-misleading."[4] After evaluating comments from industry, the agency incorporated several updates to the draft guidance.

- The final guidance expands the background and explanation of FDA's rationale, noting that payors are a "sophisticated audience with a range of expertise in multiple disciplines." Thus, unlike patients (or, potentially, even individual healthcare providers), payors are able to closely scrutinize the clinical and economic information provided by manufacturers when making their decisions.
- Although the language addressing HCEI in Section 502(a) of the Federal Food, Drug, and Cosmetic Act (FD&C Act) applies only to drugs, FDA explicitly states in this guidance that the agency considers its recommendations regarding HCEI to apply to medical devices as well.
- The guidance adds slide presentations and payor brochures as examples to the list of types of communications through which a company may present HCEI.
- The guidance also notes that payors include both public and private sector entities, as well as third-party administrators.
- There are examples of what constitutes a "material difference" from the FDA-approved labeling, requiring a conspicuous and prominent statement describing these differences
    - new or increased risks
    - different endpoints
    - more limited or targeted patient populations.
    - different dosing or use regimens
        - e.g., "If a particular HCEI presentation is based on real-world data where actual patient use of the drug falls outside of the recommended dosing/use regimen in the FDA-approved labeling, the firm could include a statement such as, 'The dosing regimen used in the study varies from the dosing regimen in the FDA-approved labeling,' in conjunction with the HCEI presentation and in a font size comparable to that used for the other information in the presentation."
- FDA confirms that HCEI is considered promotion and, thus, is subject to the requirements for submission of promotional materials (e.g., submitting such materials to FDA at the time of initial publication or dissemination on a Form FDA 2253).
- While the guidance covers communication of HCEI in the course of discussions between firms and payors related to risk-sharing and other value-based contracts, FDA does not regulate the terms of these contracts, and they are not subject to FDA's postmarketing reporting requirements.
- The draft guidance contained recommendations regarding communications on unapproved products, but many comments requested guidance on communication of unapproved uses of approved products. Thus, the final

4 See Federal Register Notice of Availability, https://s3.amazonaws.com/public-inspection.federalregister.gov/2018-12632.pdf.

guidance discusses FDA's current thinking on this topic.

- When providing information on unapproved uses, manufacturers should provide the context to support any claims made, rather than making characterizations or conclusory statements. For example, it may be appropriate to provide information on whether an investigational drug met the endpoint of a clinical trial, but it would not be appropriate to say that the product "shows superior efficacy to [active control]" or "We expect the product to be the drug of choice for [new indication.]"
- Similar to the draft guidance's recommendations for unapproved products, manufacturers communicating on unapproved uses of approved products should make clear that the particular use has not been approved by FDA. In addition, manufacturers should include a prominent statement disclosing the indication for which FDA has approved, cleared, or licensed the product, along with a copy of the most current FDA-required labeling.

AGG Observations

- FDA appears to have considered and incorporated many comments from industry in making these revisions. The updated guidance documents contain additional examples and detail on how FDA approaches each analysis, which will be helpful for industry in applying these principles.
- The agency further emphasized that the target audience of a particular communication matters. By further explaining the unique resources and experiences of payors, FDA provides a justification for the somewhat more flexible approach manufacturers may take in these communications (and further differentiates these communications from conversations with individual healthcare providers and patients).
- Manufacturers must still consider promotional activities as a whole. Once a company makes a decision that a particular study or data point is consistent with a product's labeling, each piece utilizing this information should still be evaluated to determine whether it tells the whole story. For example, space constraints in a one-page document may not allow the company to add the appropriate context and disclaimers; if that is the case, a one-page document may not be the appropriate forum for the company to present the information. We recommend that the company's internal promotional review committee review all pieces, not only the underlying concepts that will be used to develop a piece. In addition, the internal committee should review each promotional item because, even if the committee approved the message in one setting, the venue or message might have changed, and the whole story, in totality, could change.

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