FDA Regulatory and Compliance Monthly Recap

JANUARY 2018

KEY FINDINGS

N.J. finalizes rule limiting physician payments, gifts from pharmaceutical industry

The rule prohibits prescribers from accepting an array of gifts from drugmakers, ranging from pens and notepads to travel and vacations. It caps allowable meals at $15. It places an annual aggregate cap on the amount of money physicians can receive from drugmakers for speaking, advisory or consulting services and requires physicians to disclose payments received when speaking at educational or promotional events.

The attorney general of New Jersey finalized a new rule placing limits on interactions between pharmaceutical companies and physicians, subjecting physicians to a $10,000 aggregate annual cap on payments from all drugmakers and placing limitations on gifts, including a $15 meal cap. The rule, effective Jan. 15, is designed to ensure relationships with drugmakers don't interfere with physician decision-making. It applies to industry payments for consulting and speaking fees, but excludes payments pertaining to research and education.

Per the rule, prescribers are not allowed to accept any financial benefit or benefit-in-kind from a pharmaceutical company, including gifts and charitable contributions. Prescribers are similarly barred from accepting entertainment or recreational items, such as tickets to sporting events or vacation trips. The rule also bars prescribers from accepting "any item of value that does not advance disease or treatment education," including pens, mugs, items of personal benefit to the prescriber, cash or cash equivalent payments, and any payment to a nonfaculty prescriber to support attendance at an educational or promotional event. The rule also prohibits prescribers from accepting a meal from a pharmaceutical company agent with limited exceptions.

Permissible gifts under the rule include items for educational purposes that have limited or no value to the prescriber outside of professional duties, such as anatomical models or material for prescriber education,

subsidized registration fees at educational events as well as modest meals, defined as food or refreshment not exceeding $15 in value. Also permissible are compensation for participation in advisory bodies; reasonable payments for travel, lodging, or personal expenses related to research activities or employment recruitment; and royalties and licensing fees paid in exchange for contractual rights to use or purchase a patent or a legally recognized discovery.

The rule also permits compensation for bona fide services, defined as those provided by a prescriber under a formalized and written agreement, as a speaker, organizer, or consultant for an educational or promotional event. However, these services are subject to a $10,000 cap, which applies to the aggregate from all drugmakers in any calendar year for services as speakers, part of advisory boards or consultants. Per the rule, written agreements should describe the services provided, the dollar value of the consideration provided to the prescriber, the legitimate need for services, and the link between the prescriber's expertise or knowledge and the identified purpose. The agreement must also include information about how the prescriber will retain records about the arrangement and a statement indicating that the decision to provide services isn't unduly influenced by a drugmaker's agent. The rule also requires that prescribers working as a speaker at an educational or promotional event disclose the acceptance of payment within the preceding five years.

OPDP issues fourth enforcement letter of 2017 to Avanthi for misleading promotional material for weight loss treatment

The letter, which marked the fourth issued by the OPDP in 2017, calls out Avanthi for making claims about a drug's benefits in a conference exhibit panel but failing to disclose information about the drug's risks and limited efficacy. It calls on Avanthi to distribute corrective messaging to address the issues with the exhibit panel.

The FDA's Office of Prescription Drug Promotion (OPDP) sent Avanthi a warning letter after inspectors determined an exhibit panel for Lomaira, an adjunctive treatment for short-term weight loss, made false or misleading claims and misbranded the drug. A review of Avanthi's exhibit panel at the Endocrine Society's 99th Annual Meeting and Expo and at the American College of Cardiology's 66th Annual Scientific Session and Expo reveals the drugmaker made false or misleading claims or representations about the drug by omitting risk information.

The OPDP noted that while the panel made representations about the treatment's benefits, including a recommendation that it be added to a patient's weight management plan, it failed to disclose any risk information. The letter takes issue with the failure to communicate material information such as the drug's indication as a short-term adjunct treatment for patients with an initial BMI greater than or equal to 30 kg/m^2, or greater than or equal to 27 kg/m^2 in the presence of other risk factors. It also raises concerns about the exhibit's failure to disclose that the limited usefulness of agents such as Lomaira should be weighed against possible risk factors with their use. These failures create a misleading impression about the approved indication for the drug and thus misbrand the drug.

The letter calls on Avanthi to immediately stop misbranding the drug and requests that the drugmaker provide a list of all promotional materials that contain statements such as those in the exhibit panel. The OPDP also requests that the drugmaker provide a plan for discontinuing the use of such materials or that it stop distributing the misbranded drug. It also requests that Avanthi provide a plan to disseminate truthful, nonmisleading and complete corrective materials to those exposed to the violative material to address the issues cited. The letter recommends that the corrective messages include a description of the violative material and messages, with information correcting them. These corrective

messages shouldn't include promotional claims and should be distributed using the same media as for the violative material.

FDA publishes draft guidance on formal meetings with drug, biologics developers

The guidance describes how sponsors may submit a formal request for Type A, B and C meetings; sets timelines for FDA response; and outlines the information that should be included in meeting packages to ensure efficient, consistent, timely and effective meetings.

The FDA published draft guidance to provide sponsors with recommendations for formal meetings with the Center for Drug Evaluation and Research (CDER) and the Center for Biologics Evaluation and Research (CBER). The guidance applies to sponsors of drug or biological drug products, but not to generics makers, biosimilars developers or medical device companies.

It outlines the principles of good meeting management practices (GMMPs) and applies to four types of formal meetings under the Prescription Drug User Fee Act (PDUFA):

1. **Type A:** Meetings needed for an otherwise delayed product development program, such as dispute resolution meetings, meetings to address clinical holds or meetings following a refuse-to-file letter.

2. **Type B:** Meetings held prior to submitting an IND, emergency use authorization, NDA or BLA, as well as meetings pertaining to risk evaluation and mitigation strategies or to postmarketing requirements that take place outside the context of a marketing application review, or meetings to discuss the overall development program for breakthrough therapies.

3. **Type B (EOP):** Certain end-of-phase 1, end-of-phase-2 or pre-phase 3 meetings.

4. **Type C:** Any meeting that doesn't fall under the above categories pertaining to the development and review of a product, including meetings to facilitate early discussion on the use of a biomarker as a surrogate endpoint never previously used to support product approval.

In cases in which a meeting is needed, sponsors are directed to submit a written request to the CBER or CDER, which should include the application number, product name, chemical and established name, proposed regulatory pathway, proposed indication of development, and type of meeting requested, as well as suggested dates and times for the meeting and a list of proposed questions. The request should also include information on the proposed meeting format (face-to-face, video/teleconference, written response only) as well as a brief statement of the purpose of the meeting and the issues to be addressed. It may also include a summary of completed or planned studies and clinical trials or data to be discussed. Sponsors should provide a list of anticipated outcomes, a proposed agenda and a list of requested FDA attendees.

While requesters can ask for any meeting format for any of the meeting types, the guidance cautions that the FDA may determine a written response only (WRO) is most appropriate for offering feedback in pre-IND and Type C meetings, except those discussing new biomarkers as endpoints. No more than one of each of the Type B meetings will generally be granted for each potential application or combination of related products developed by the same company. Per the guidance, the FDA may deny meetings based on a "substantive reason" and will provide an explanation for the denial to the requester. The guidance establishes timelines for responding to meeting requests, ranging from 14 days for Type A and Type B (EOP) to 21 days for Type B and Type C. Timelines for scheduling meetings or issuing a WRO are set at 30 days for Type A, 60 days for Type B, 70 days for Type B (EOP) and 75 days for Type C.

If a meeting is granted, the FDA asks that a meeting package be provided in a timely manner that includes a summary of information pertinent to the product as well as any supplementary information needed to respond

to issues raised by the requester. Although the meeting package contents will vary depending on the product, indication, phase of development and issues to be addressed, the guidance recommends that sponsors identify any area in which a product development plan deviates from ICH or FDA guidance. It also recommends that known difficult design and evidence issues, such as use of adaptive designs or noninferiority studies, be raised for discussion. The meeting package should include a background section that provides a brief history of the development program and any substantive changes in development plans. It should also include data to support the meeting discussion, organized based on FDA discipline and question.

Guidance finalized on communication between FDA staff, IND sponsors

The finalized guidance outlines what sponsors can anticipate during milestone meetings, such as end-of-phase meetings and pre-NDA/BLA meetings, and describes the FDA's thinking regarding timely communications, the scope of appropriate interactions and what forms of advice sponsors may request.

The FDA finalized guidance outlining best practices for communication between IND sponsors and agency staff during the IND phase of drug development and biosimilar biological product development. The guidance addresses a commitment by the FDA, under PDUFA V, that the CDER and CBER would publish joint guidance on drug development communication. It recognizes that providing advice to sponsors on matters related to an IND, such as the adequacy of technical data or the design of a clinical trial, may improve the efficiency of the drug development process.

The guidance notes that the review division regulatory project manager (RPM) is the primary point of contact between a sponsor and the FDA, but outlines limited instances in which it is appropriate for sponsors to directly contact FDA RPMs other than the review division RPMs. For example, the CDER's formal dispute resolution project manager may be contacted for resolution of scientific or medical disputes that can't be resolved at the divisional level. The guidance discourages contact between sponsors and reviewers assigned to their INDs. However, it points out that there may be rare instances in which it may be appropriate for reviewers to communicate directly with sponsors, with supervisory approval, about specific issues related to their drug development programs. In these cases, the review team members will document the conversation in a memorandum attached to the IND, and a copy of the record will be provided to the FDA RPM.

To ensure efficient communications, the guidance recommends a communication strategy be developed early in the development program. This may include the preferred method and frequency of communication as well as approaches for managing information requests and responses. It should also address mutual expectations for the timing of responses to inquiries. Formal communication plans should be agreed to during pre-submission meetings or at the initial comprehensive multidisciplinary meeting for breakthrough therapies.

Per the guidance, sponsors may ask for advice during development programs for regulatory issues such as waivers of specific studies and submission of proprietary name requests, as well as for scientific issues such as planned trials to support effectiveness, safety issues in nonclinical or early trials, REMS, dose selection and population, analytical similarity assessments, or proposed pediatric development plans. However, the guidance recommends that sponsors first try to answer their questions using available resources or via independent consultants.

The guidance points out that sponsors may sometimes raise questions that they believe to be simple or clarifying in nature, requiring only minimal time for response, but that are actually more complex and require significant review. It notes that the FDA "needs to take a thoughtful approach" to answering

such questions, and that complex questions may be best addressed in requests for formal meetings or in formal submissions. Generally, the agency takes a collaborative approach to responding to questions in meeting packages or submissions, based on prespecified timelines. For inquiries not included in meeting requests or submissions, the FDA RPM will work to acknowledge the communication within three days, with either the response itself or an estimated timeline for response.

Given that the FDA and sponsors use various communication methods, the guidance offers best practices that enhance each method. These include, but are not limited to:

- **Submissions from sponsors:** Regulatory submissions should be submitted per required timelines, adhere to FDA regulations and principles for content and format, be complete and well-organized, and address any issues or areas of concern by fully describing them and soliciting feedback on specific issues.
- **Email exchanges:** Sponsors may establish secure email with the FDA to allow for communications that include confidential information, by contacting the Office of Information Management and Technology.
- **Telephone calls:** Although general or administrative questions may be suited to telephone discussion, if complex issues are discussed, the caller should follow up with a written communication.

For more information on any of these FDA regulatory and compliance updates, please contact Scott S. Liebman at sliebman@loeb.com.

Loeb & Loeb LLP's FDA Regulatory and Compliance Practice

Loeb & Loeb's FDA Regulatory and Compliance Practice comprises an interdisciplinary team of regulatory, corporate, capital markets, patent and litigation attorneys who advise clients on the full spectrum of legal and business issues related to the distribution and commercialization, including marketing and promotion, of FDA-regulated products. Focusing on the health and life sciences industries, including pharmaceuticals, biologics, medical devices, wellness products, dietary supplements and organics, the practice counsels clients on regulatory issues, compliance-related matters and risk management strategies; advises on laws and regulations related to product advertising and labeling; counsels on FDA exclusivity policies and related Hatch-Waxman issues; and provides representation in licensing transactions and regulatory enforcement actions.