Hypothetical Off-Label Cases

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Overview

- Three Hypotheticals
  - Common scenarios
  - Drug and device industries

- Informal discussion
  - Feel free to ask questions along the way

Hypothetical #1

- FDA approved a new drug with an indication for the management of severe hypertension.
- During the approval process, the manufacturer proposed including a specific indication for the reduction of serious cardiovascular outcomes associated with severe hypertension, but FDA did not agree to include the language in the indication.
- FDA told the manufacturer that the studies submitted with the NDA were not sufficient to support the claim.

Hypothetical #1, cont.

- Two new studies published in well-regarded journals reinforce the link between severe hypertension and serious cardiovascular outcomes.
- The manufacturer's VP of Sales would like to have sales reps proactively distribute the studies during their sales calls.
- VP of Sales is not interested in distributing the studies in accordance with FDA's guidances on "unsolicited requests" or reprint distribution.
- The reimbursement team would also like to utilize the studies in discussions with payors.
- CEO has an upcoming appearance scheduled on CNBC's "Squawk Box" and would like to discuss the studies.

Hypothetical #2

- ABC MedTech has received a 510(k) clearance for its new ablation catheter. The catheter is cleared for soft tissue ablation, except for cardiac ablation.
- The company expects that the device will be used for a broad range of procedures, including tumor ablation, treatment of uterine fibroids, urological procedures, and treatment of Barret's esophagus.
- Several physicians have successfully used the catheter with robotic navigation systems, including procedures to treat atrial fibrillation.

Hypothetical #2, cont.

- ABC's marketing VP has come up with a number of proposed initiatives to help increase physician and public awareness of the device.

- Peer-to-Peer Education – The company intends to organize dinner meetings, typically in connection with major society meetings, to permit physicians interested in the device to meet physicians who are experienced with the device. The company will pay the experienced physicians a fee to attend the meeting and present cases, and will provide dinner to all participants.

- Social Media Presence –ABC posts case studies, patient and physician interviews on its website and links to these materials from its Facebook and LinkedIn pages. ABC encourages physicians to post videos and patient interviews, and encourages its employees to share links to these materials from their own social media accounts.

Hypothetical #2, cont.

- Publication strategy – the company intends to fund investigator-initiated studies using the device. The company will invite potential investigators to submit proposals. For approved proposals, the company will assist in protocol development and will provide a grant to fund research. Grant payments will be milestone-based, with the last payment made upon submission of study results for publication to a peer-reviewed journal.

- Podium strategy – the company plans to fund travel to society meetings for physicians who will be presenting study results.

- Training – the company requires its personnel to stay "on label." Physicians frequently ask personnel about the different applications for the new catheter. Reps are advised that they may discuss all uses of the device for soft tissue ablation, but may not discuss cardiac ablation. When physicians ask about cardiac ablation they are directed to medical affairs.

Hypothetical #3

- FDA approved an antibiotic for use as third-line therapy:
  - in adults for the treatment of certain serious or severe infections caused by certain strains of *staphylococcus aureus,*
  - in pediatric patients ages 5 to 17 (for one strain of *staphylococcus aureus* only).
- Manufacturer of the drug seeks to have a medical science liaison provide payors with health care economic information (HCEI) on length of hospital stay compared to antibiotic approved as first-line therapy.
- Data includes both adult and pediatric populations.
- Data would be presented to individual healthcare provider who serves in the capacity of a formulary decisionmaker.

Key Considerations for Assessing Risk

- Legal and regulatory underpinnings, including 21 C.F.R. 312.7, and Sections 502(a) and (f) of the FDCA.
- FDA guidances, including draft payor guidance (Jan 2017), draft consistent communications guidance (Jan 2017), revised draft reprints guidance (Feb 2014), and draft unsolicited requests guidance (Dec 2011).
- FDA-approved labeling (e.g., FDA-approved prescribing information, cleared 510(k)).
- Benefit-risk profile (e.g., REMS, abuse or misuse).

Key Considerations for Assessing Risk

- Previous FDA communications with the company (e.g., advisory comments, correspondence, labeling negotiations).
- Recent First Amendment cases, recent enforcement and advisory actions (e.g., warning and untitled letters).
- FDA and DOJ activity and statements under the current administration.
- Related company promotional and non-promotional activities, including pipeline, and company policies.