Promotional Review Best Practices: Mitigating Risks, Maximizing Success

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Agenda

Promotional Review Best Practices

- Promotional Review Committee (PRC) SOP and Escalation Policy
- Legal/Regulatory Framework and New Developments
- Who are the Typical Players in PRC? What are their roles/perspectives?
- PRC Best Practices
- Examples of Recent Warning Letters and Settlements
- Overview of FTC Law
- Interaction with FTC, FDA and State Attorneys General
- Review of Pertinent Cases

Promotional Review SOP

Clearly Define Roles and Responsibilities, Escalation Process

- Important to have an SOP which:
  - Identifies Standing and Adjunct Members of Promotional Review Committee
  - Defines Roles and Responsibilities of Each Member/Function
  - Explains Escalation Process when PRC fails to reach agreement
  - Identifies who “owns” PRC from an administrative standpoint
  - Set timelines for submission of documents in advance of next PRC
  - Contemplates what is stored in electronic/paper review system
  - Describes the Process for submission of documents by Regulatory to the Office of Prescription Drug Policy (OPDP)

Legal/Regulatory Framework for Promotional Review

Legal/Regulations Consideration for PRC

- PRC plays a crucial role in review of materials to ensure legal/regulatory/medical compliance prior to external or internal use!

Food Drug and Cosmetic Act (FDCA) and Title 21 of Code of Federal Regulations (Title 21)

- FDCA and Title 21 primarily govern prescription drug advertising and promotions
- The FDA approves drugs for specific indications and prohibits manufacturers from commercially promoting a drug "off-label" (i.e., for any unapproved use)
- The FDCA also requires that advertising and promotional materials:
  - Be consistent with approved prescribing information;
  - Be truthful and not misleading; include material information; and
  - Present a fair balance about a drug's effectiveness and risks.
- Failure to adhere to the provision of the FDCA and Title 21 may deem a drug "misbranded"
- Violations of the FDCA and Title 21 are punishable by civil/criminal penalties

Additional Legal/Regulatory Considerations for PRC

- **The Anti-Kickback Statute**
  - The Anti-Kickback Statute makes it a violation of the law to offer or pay, directly or indirectly, "remuneration" – that is, anything of value – to a HCP or customer, to induce that person to prescribe, order, or recommend products or to reward past purchases or use of products reimbursed, in whole or in part, by a federal healthcare program
- New Regulatory Developments
  - First Amendment Cases asserting ability to discuss topics outside the label due to free speech and scientific exchange considerations
  - June 2018 FDA Guidance Documents
    - *Medical Product Communications that are Consistent with the FDA-Required Labeling – Questions and Answers* (referred to as the "CFL Guidance"); and
    - *Drug and Device Manufacturer Communications With Payors, Formulary Committees, and Similar Entities – Questions and Answers*
- **Failure to appropriately review materials leads to Untitled or Warning Letters, fines, Corporate Integrity Agreements and impact a company's reputation and financial success**

Typical Players in PRC, Roles and Responsibilities

Question for Audience #1

What role do you serve in your company?

(a) Marketing

(b) Medical Affairs

(c) Regulatory

(d) Legal/Compliance

(e) Other

Different Roles and Responsibilities Can Create Conflict

- Differing roles and responsibilities may (and often does) lead to conflict
- Sometimes parties won't budge in their positions

- Other times it can be all out war

Typical Players in PRC #1 (Marketing/Medical)

Primary Responsibilities and General Characteristics

- **Marketing** – want to maximize sales and prescriptions – create optimal messaging to potential prescribers, staff, patients and other relevant parties
  - Responsibilities: Creating marketing and sales materials
  - Role characteristics: creative, assertive, think outside the box
- **Medical** – review materials from a medical/clinical perspective to make sure materials accurately reflect efficacy and safety
- Responsibilities: Review of materials and references to ensure data and claims accurately reflect label and source materials from medical/clinical perspective
  - Role characteristics: scientific, clinical, conservative, focus on data

Typical Players in PRC #2 (Regulatory/Legal)

Primary Responsibilities and Personality Types

- **Regulatory** – review materials to ensure accuracy with label, fair balance and submit materials to FDA/OPDP
  - Responsibilities: Make sure that materials are fairly balanced, ensure materials tie to language in label, focus on prominence of references to ISI and PI, responsible to submit materials to FDA/OPDP
  - Role characteristics: Detail oriented, apply the rules, risk averse
- **Legal**
  - Responsibilities: Review materials to ensure on-label, spot issues that raise legal concerns (e.g., false claims, kickbacks, lack of fair balance)
  - Role characteristics: Assertive, detail-oriented, may be conservative or risk averse (depending on background and experience in-house)

Question #2

Whose role is the most important on the Promotional Review Committee?

(a) Marketing

(b) Medical Affairs

(c) Regulatory

(d) Legal

(e) All of the Above

CLE Announcement #1

PRC Legal Reviewer Responsibilities

Legal Reviewer must ensure the following:

- Confirmation that material (s) are in compliance with all relevant US national, state and local laws, rules, regulations and company policies in consultation with other legal subject-matter experts
- Must spot issues and ensure:
  - The presence of a balance between risk and benefit information (fair balance);
  - Information is not false or misleading;
  - The appropriateness of any comparative claims, statements or presentations under the applicable regulations and legal principles; and
  - Images or graphics convey appropriate target population.

PRC Legal Reviewer Responsibilities (continued)

Legal Reviewer must also ensure:

- The presentation of information must be in the appropriate context (e.g. based on the audience, content, and the medium used for dissemination);
- Appropriate use of trademarks, copyrights and other intellectual property (of the company or third party); and
- Consideration of non-FDA legal issues (e.g., fraud & abuse, kickbacks and/or inappropriate reimbursement, patient assistance programs/HUB services).
- Limit company's exposure to liability

PRC Medical Reviewer Responsibilities

Medical Reviewer must ensure that:

- Information, claims and comparisons are **medically and scientifically accurate**, clinically and statistically relevant, and presented in appropriate context and level of detail;
- Information is not false or misleading;
- **References** used to support claims are appropriate (i.e., reflect adequate and well- controlled studies) and applicable (i.e., based on clinical studies and not extrapolations from non-clinical data);
- Statements around clinical trial data match the results;
- Carve outs of sub-data are label consistent and reflect study results; and
- Images or graphics convey appropriate target population, are on label and as necessary, are medically accurate.

PRC Regulatory Reviewer Responsibilities

Regulatory reviewer must ensure that:

- The material(s) comply with FDA laws, regulations and published guidance;
- Information presents a balance between risk and benefit (fair balance);
- Presentations of risk information/fair balance is distributed properly throughout the materials;
- Appropriate “prominence” of safety v. efficacy information;
- Current approved Prescribing Information (PI) is used to support claims;
- Information is not false or misleading; and
- Images or graphics convey appropriate target populations and are on label for dosing, treatments, outcomes, etc.

PRC Regulatory Reviewer Responsibilities (continued)

Regulatory reviewer must also ensure that:

- Any comparative claims are supported by substantial evidence as that term has been interpreted by relevant regulatory guidance; and
- Other PRC members are aware of PI and label changes and relevant regulatory actions, e.g., Untitled or Warning Letters.
- Approved materials to be forwarded for submission package to the Office of Prescription Drug Promotion (OPDP) of the FDA

Note: Certain materials may be submitted for pre-approval and/or comments to OPDP – PRC needs to make strategic decision whether to pre-submit materials or submit in conjunction with use in the field

PRC “Best Practices”

PRC Best Practices – How Can Everyone Get Along?

Members of PRC Share the Same Goal!

- It is important to level set and remind members of the PRC that they share the same goal – to create materials that effectively promote the product in a manner that is compliant with applicable regulations and company policy
- When PRC teams work together – it is more like this!

- The marketing team works hard to create materials that resonate with healthcare professionals and patients.
- It is often difficult for Marketing to have Legal/Medical/Regulatory put the brakes on and/or revise or limit the concepts/materials they've worked on
- So what do we advise?

Commercial Interest v. Medical, Legal and Regulatory

How to Accomplish Business Goals and Still Keep the Company Safe!

- Appreciate that the Marketing team is paid to be creative and come up with ideas that optimize the attributes of the product
- Marketing has a difficult job to differentiate the company's products from existing competitor products in the marketplace
- BUT - Marketing needs to respect the role of Legal/Medical/Regulatory to keep the company safe by making sure materials and claims are:
  - On-label ("label consistent" data may be appropriate)
  - Consistently and fairly represent the studies and data within the label
  - Fairly balanced
  - Medically/scientifically accurate based on the label and references cited

PRC Best Practices

Mitigating Conflicts and Learning to Play and Fight Fair in PRC

- Identify the overarching goal of marketing campaign and particular piece
- Appreciate the role that each person plays – get value from each participant
- See things from other's perspective – shared understanding of goals/issues
- Rather than saying "no" – come up with alternative/creative suggestions to get to "yes"
- Always maintain a professional tone and be respectful
- Avoid taking things personally
- Try to find common ground… "we agree on this, but this one aspect may need to be changed."
- Ask questions that engage your peers – try to understand the "why"

Additional PRC Best Practices

Establish efficient ways to work together from differing perspectives

- Core Claims Review
  - Working together up front on a core claims review will limit discussion and/or conflict as the same set of issues come up in different pieces
- Reach agreement on alternative language when certain topics arise
  - Similar issues tend to present themselves, and it is helpful to be able to say “been there, done that” and have an agreed upon approach
- When possible, provide comments and revisions in advance of live PRC meeting so that reviewers are aware of each other’s feedback
  - Also allow marketing to prioritize issues and make live meeting more focused, productive and efficient

Additional PRC Best Practices

Additional suggestions to optimize PRC

- Try to connect on a personal level – it often helps to set up some sort of social event or otherwise allow PRC members to engage outside of the PRC context and/or discuss topics other than PRC
  - If you establish a trust and/or friendship, this helps when conflicts arise
- Meet early and often – as you approach approval and launch the stress level ramps up considerably
- Best way to manage stress is to be prepared, having vetted issues and materials in advance of deadlines
- When you reach an impasse, elevate to decision-makers to make the call
  - This helps to limit conflict and allow a more neutral party to decide
  - When escalating an issue, don't present the questions as "pick a side" – present issues objectively, identifying inherent opportunities & associated risks

How to Overcome Challenges from a Co-Promote

Lessons Learned and Suggested Best Practices

- Get to know your counterpart in a co-promote and have off-line discussions when possible to align in advance of PRC
- Understand the differences between your organization and theirs
- Address ground rules early on (set expectations)
- Meet in person in advance of heavy activity to develop relationships
- When necessary, escalate issues of disagreements to senior level business executives and have them facilitate decision making
- Try to create a level of trust and shared goal of appropriately promoting the product – find the common ground!
- Respect your counterpart and try to understand their viewpoint
- Pick your battles and align internally

Examples of Recent Warning and Untitled Letters

- DTC print ads and banners make misleading claims and/or representations about the risks associated with brand as well as the efficacy
  - Print ad provides evidence that brand is intended for new use for which it lacks approval (i.e., "off label")
  - Leads to Warning Letter and claim of misbranding
- Webpage focusing only on efficacy of products without "fair balance" including risk information leads to Warning Letter
- Facebook post sponsored by manufacturer of boxed warning drug includes only efficacy information and not any representations of safety/risks
  - Suggestion of no safety risks leads to Warning Letter/misbranding
- Direct to consumer video of an interview by company spokesman aired on television, product and company website also fails to include information regarding serious risks associated with product
  - Untitled Letter deems video "false and misleading" and misbranding

Overview of Laws and Interactions with FDA, FTC and State Attorneys General

Products Liability?

- "For state officials, a key appeal of these cases is that they generally don't have to prove that a drug maker's marketing caused any specific injuries or harm. They need only convince a judge or jury that a drug's promotion was deceptive in some way."
- "The industry and its defense lawyers say the state allegations of deceptive marketing amount to overreach because there has been little evidence that patients have been harmed by the alleged conduct."
- Wall Street Journal, *States Take Drug Makers to Court over Marketing*, April 22, 2013

Product Liability?

- No Harm?
- No Defect?
- No Problem!

FTC Act

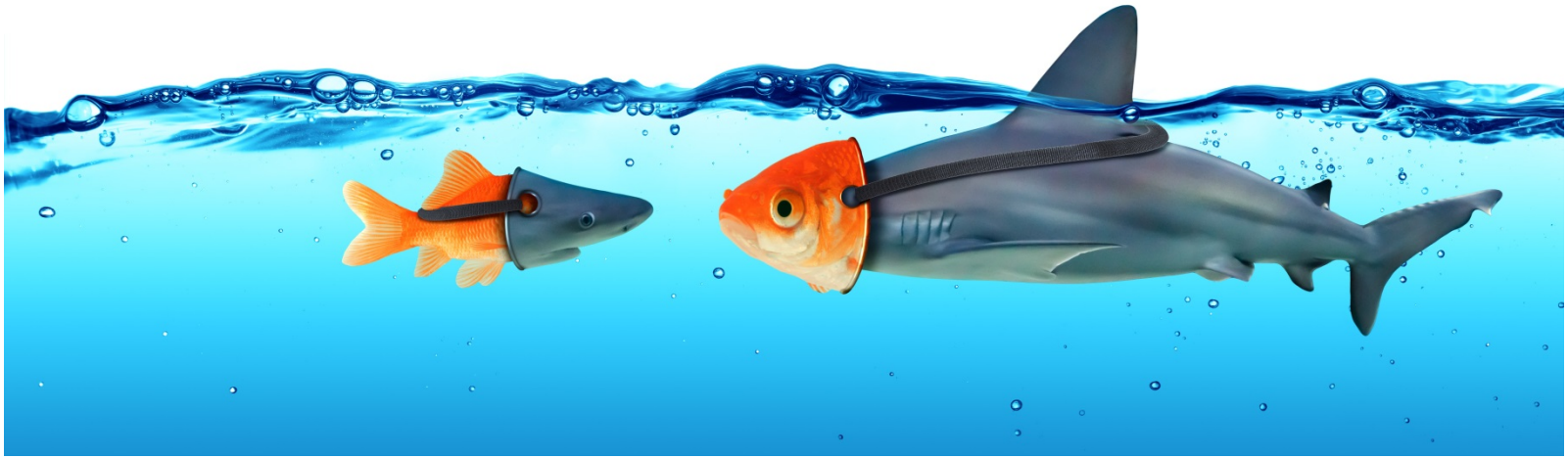
- FTC Act
- Enacted 1914
- Prohibits Deceptive and Unfair Acts

FTC Statement on Deception (in pertinent part)

- First, there must be a representation, omission or practice that is likely to mislead the consumer . . .
- Second, we examine the practice from the perspective of a consumer acting reasonably in the circumstances. If the representation or practice affects or is directed primarily to a particular group, the Commission examines reasonableness from the perspective of that group.
- Third, the representation, omission, or practice must be a "material" one. The basic question is whether the act or practice is likely to affect the consumer's conduct or decision with regard to a product or service. If so, the practice is material, and consumer injury is likely, because consumers are likely to have chosen differently but for the deception.

Deception

- No need for literal falsity; overall net impression
- No scienter
- No harm



CLE Announcement #2

Little FTC Acts

- Same elements
- Follow FTC precedent
- Responsive to consumers
- Bipartisan efforts

FTC / FDA

- **MOU 225-71-8003 - Memorandum of Understanding Between The Federal Trade Commission and The Food and Drug Administration**

(Pertinent Provisions)

- Section III A - With exception of prescription drugs, the Federal Trade Commission has primary responsibility with respect to the regulation of the truth or falsity of all advertising (other than labeling) of foods, drugs, devices, and cosmetics.
- Section III B - The Food and Drug Administration has primary responsibility with respect to the regulation of the truth or falsity of prescription drug advertising.
- Section III C - The initiation of proceedings involving the same parties by both agencies shall be restricted to those highly unusual situations where it is clear that the public interest requires two separate proceedings.

FTC / FDA Joint Warning Letters / Areas of Interest

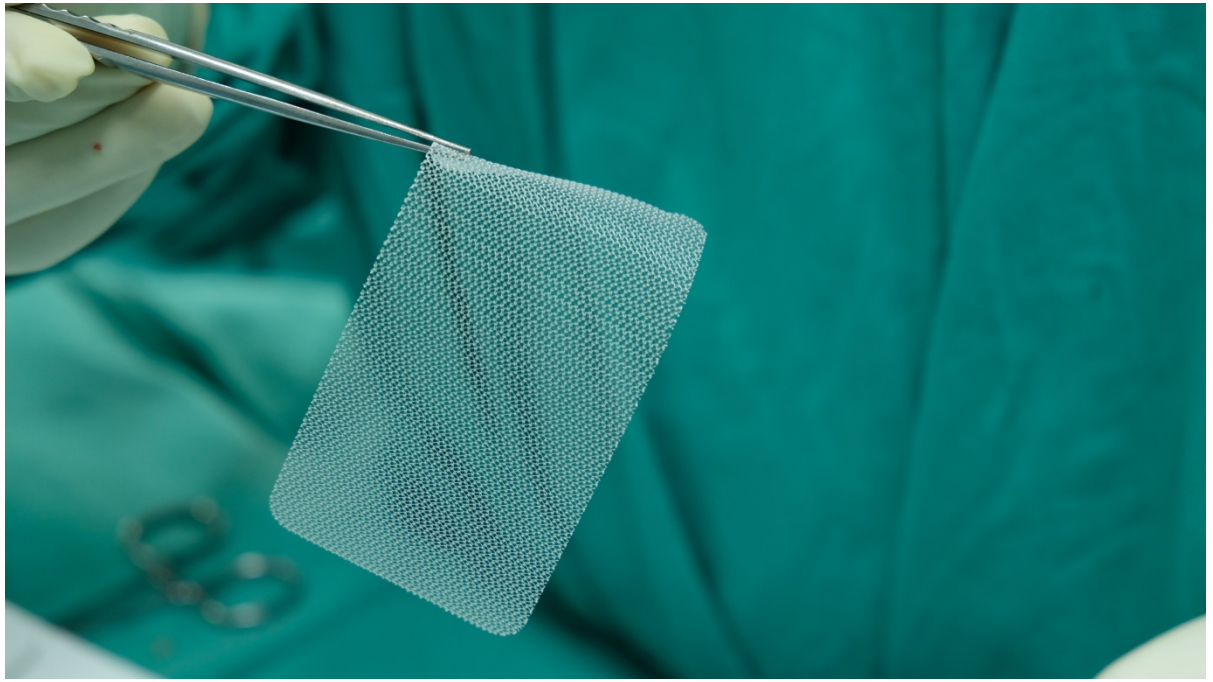
- Opioids, January, 2018
- Stem Cells, October, 2018

Simeon Management Corp. v. FTC, 579 F.2d 1137 (9th Cir. 1978)

- The Commission found that (1) some consumers will reasonably believe that the government exercises control over the promotion and use of prescription drugs; (2) this belief is intensified by the advertisements' representations that the weight loss treatments are safe, effective and medically approved; and (3) the representations may therefore reasonably lead consumers into the mistaken belief that the claims of safety and effectiveness are based, not on the advertiser's own opinion, but on a determination by the FDA. It further found that, in view of the public's belief that the government strictly regulates drugs, the fact that the treatments involve administration of a drug lacking FDA approval for such use may materially affect a consumer's decision to undergo the treatment. Accordingly, the Commission declared that the failure to disclose that the weight reduction treatments involve injection of a drug lacking FDA10 approval for such use renders the advertisements deceptive and thus in violation of s 5 of the FTCA.

STATE AGs – Washington Attorney General

- Surgical Mesh
- $9.9M settlement
- Knowledge of issues, lack of communication with doctors



State AGs – Multistate

- Hip Implants
- $120M settlement
- Extensive details regarding future marketing controls

State AGs – Multistate

- HIPAA
- State AGs in federal court on federal cause of action
- $900K settlement
- 3rd party monitor

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Wrap-Up

Thank you!

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