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PRECONFERENCE I: ADVANCED MEDICAL AFFAIRS COMPLIANCE ISSUES

Medical Affairs Personnel — When is it Scientific Exchange and When is it Promotion?

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November 6, 2017

FDA REGULATIONS

- No statutory requirement to maintain a Medical Affairs department
- No statute, regulation or other guidance provides an "appropriate" organizational structure for the Medical Affairs department or defines its roles and responsibilities
- Generally, FDA regulates the promotional activities of manufacturers and their employees
  - Regulation is not based on employee title
  - FDA regulations prohibit a manufacturer "or any person acting on behalf of" a manufacturer from representing "in a promotional context" that a drug is "safe or effective" for purposes other than those for which it has been approved
    - "Promotional" is not defined by the FDA
      - The FDA "views **independence** as an indication of whether an activity is non-promotional" (emphasis added)
    - Communications by the Medical Affairs department should be "scientific exchanges" to avoid regulation as a promotional activity

OIG GUIDANCE

- OIG Voluntary Compliance Program Guidance for Pharmaceutical Manufacturers (2003)
  - Recommends separation between sales/marketing functions and activities that should involve an organization's medical personnel
    - Research contracts
      - "Research contracts that originate through the sales or marketing functions . . . are particularly suspect."
    - Medical education grants
      - ". . . manufacturers should separate their grant making functions from their sales and marketing functions. Effective separation of those functions will help insure that grant funding is not inappropriately influenced by sales or marketing motivations and that the educational purposes of the grant are legitimate."

Source: https://www.gpo.gov/fdsys/pkg/FR-2003-05-05/pdf/03-10949.pdf

SCIENTIFIC EXCHANGE VS. PROMOTION

SCIENTIFIC EXCHANGE

- Communications and/or dissemination of a scientific or medical nature, without making promotional claims related to the safety or efficacy of a product
- Activities vary by company may include some/all of the following:
  - ❑ Field MSLs
  - ❑ Scientific exchange with HCPs
  - ❑ KOL relationship development/management
  - ❑ Present educational/scientific/clinical info
  - ❑ Respond to unsolicited off-label questions
  - ❑ Assist in the publication of clinical trial data
  - ❑ IIR, CME, other third-party grants/donations
  - ❑ Pharmacovigilance
  - ❑ Health economics and outcomes research (HEOR) discussions

PROMOTION

- Express or implied promotional claims and statements (whether written or oral) made or disseminated to HCPs, patients or caregivers by a manufacturer or its agents regarding the use, safety, and effectiveness of a product
- Activities vary by company may include some/all of the following:
  - ❑ Field and/or call center sales employees
  - ❑ Brochures, sales aids, handouts, emails, etc.
  - ❑ DTC advertising
  - ❑ Social media
  - ❑ Grants, donations, sponsorships, etc.
  - ❑ Conference/meeting booths and events
  - ❑ Meals, gifts, entertainment

KEY COMPLIANCE CONTROLS

- Medical affairs reporting structure
- Medical affairs budgets
- Medical affairs compensation and bonus structure
- Medical affairs bonuses not based on individual/territory sales performance
- Medical affairs performance evaluations
- Limited interactions with sales/marketing with compliance controls
  - Separate training sessions and internal meetings
  - Separate meetings with HCPs/KOLs
- Policies, procedures and training for key activities

INDUSTRY SETTLEMENT EXAMPLES

- Cephalon (2008)
  - $425 million civil and criminal settlement
  - DOJ Press Release: “Cephalon employed sales representatives and retained medical professionals to speak to doctors about off-label uses of the three drugs.”
  - CIA: IRO review of “Cephalon's policies and procedures applicable to the manner and circumstances under which **its Medical Services department personnel (including any medical science liaisons (MSLs))** participate in meetings or events with HCPs or HCIs (either alone or with sales representatives) and the role of the medical personnel at such meetings or events . . .” (emphasis added)

Sources: https://www.justice.gov/archive/opa/pr/2008/September/08-civ-860.html; https://assets.documentcloud.org/documents/10661/cephalon.pdf

INDUSTRY SETTLEMENT EXAMPLES

- Eli Lilly (2009)
  - $1.415 billion civil and criminal settlement
  - DOJ Press Release: “Eli Lilly retained medical professionals to speak to doctors during peer-to-peer sessions about off-label uses of Zyprexa.”
  - CIA: Lilly required to implement “systems, processes, policies and procedures relating to the manner and circumstances under which ***Medical Liaisons and Outcomes Liaisons*** participate in meetings or events with HCPs or HCIs (either alone or with sales representatives or account executives) and the role of the Medical Liaisons and Outcomes Liaisons at such meetings or events, as well as how they handle responses to unsolicited requests about off-label indications of Lilly’s Government Reimbursed Products” (emphasis added)
    - IRO review of these systems, processes, policies and procedures

Sources: https://www.justice.gov/archive/opa/pr/2009/January/09-civ-038.html; http://psychrights.org/Articles/090115lillycorpintegagreement.pdf

INDUSTRY SETTLEMENT EXAMPLES

- Allergan (2010)
  - $600 million civil and criminal settlement
  - DOJ Press Release: “Allergan doubled the size of its reimbursement team to assist doctors in obtaining payment for off-label Botox injections. Allergan held workshops to teach doctors and their office staffs how to bill for off-label uses, conducted detailed audits of doctors’ billing records to demonstrate how they could make money by injecting Botox, and operated the Botox Reimbursement Hotline, which provided a wide array of free on-demand services to doctors for off-label uses. Allergan also lobbied government health care programs to expand coverage for off-label uses, directed physician workshops and dinners focused on off-label uses, paid doctors to attend ‘advisory boards’ promoting off-label uses, and created a purportedly independent online neurotoxin education organization to stimulate increased use of Botox for off-label indications.”

Source: https://www.justice.gov/opa/pr/allergan-agrees-plead-guilty-and-pay-600-million-resolve-allegations-label-promotion-botox

INDUSTRY SETTLEMENT EXAMPLES

- Allergan (2010) (cont.)
  - Complaint: “The use of Regional Scientific Specialists (RSS), known in the industry as ‘medical liaisons,’ typically PhD's, pharmacists, or physicians by training, who worked closely with the sales force to target physicians for off-label use, enticing them with kickbacks (which have included clinical trials, studies, or grants). ***These RSS's worked with and under the direction of the sales and marketing department***.”
  - Complaint: “These false statements were made through concerted and coordinated efforts of Allergan management and employees in different divisions of the company to aggressively promote Botox for unapproved indications . . .”, including Allergan’s medical liaisons
  - Complaint: “[Relator] Rushin has observed attempts by Allergan’s . . . Regional Scientific Services Managers (Allergan's medical liaisons) to coach doctors into changing patient diagnoses . . . in order to justify the use of, and reimbursement for, Botox”

INDUSTRY SETTLEMENT EXAMPLES

- Allergan (2010) (cont.)
  - CIA: Includes Medical Affairs personnel within its definition of "Covered Persons"
    - Requires, among other things, the following related to Medical Affairs:
      - "Documentation of such review, approval, and funding activities [for research-related activities and journals] shall be maintained by Allergan Medical Affairs."
    - IRO review of "Allergan's systems, processes, policies and procedures applicable to the manner and circumstances under which ***personnel from Medical Affairs (e.g., Regional Scientific Services, or RSS)*** interact with or participate in meetings or events with HCPs or HCIs (either alone or with sales representatives) . . . ***This includes any Medical Affairs Monitoring Plan designed to monitor the activities of the RSMs***." (emphasis added)

Source: https://assets.documentcloud.org/documents/10985/allergan-executed-cia-with-appendices.pdf

INDUSTRY SETTLEMENT EXAMPLES

- Novo Nordisk (2011)
  - $25 million civil settlement
  - One of the two whistleblowers was a former MSL for the company
  - Complaint: “Novo Nordisk specifically directed its employees, including sales representatives and medical science liaisons, to promote Factor VIIa for uses not contemplated by the FDA-approved label.” Allegations included the following:
    - Training of sales representatives and MSLs at national sales meetings on promoting the product for unapproved uses
    - Paid HCPs to “evaluate” sales representatives and MSLs on their product presentations
    - Set goals for MSLs related to off-label medical education, encouraging off-label publications, and developing KOLs who would support and promote off-label use of product

Source: https://www.justice.gov/opa/pr/danish-pharmaceutical-novo-nordisk-pay-25-million-resolve-allegations-label-promotion

INDUSTRY SETTLEMENT EXAMPLES

- Novo Nordisk (2011) (cont.)
  - CIA: Novo Nordisk implemented policies and procedures related to "the manner and circumstances under which ***medical personnel from Medical Affairs*** interact with or participate in meetings or events with HCPs or HCIs (either alone or with sales representatives or account executives) . . ."
  - IRO must review of Novo Nordisk's "systems, processes, policies and procedures applicable to the manner and circumstances under which ***personnel from Medical Affairs (e.g., medical science liaisons or other medical or scientific personnel)*** interact with or participate in meetings or events with HCPs or HCIs (either alone or with sales representatives) and the role of the Medical Affairs personnel at such meetings or events, including the manner in which the Medical Affairs personnel handle responses to unsolicited requests about off-label indications of Government Reimbursed Products . . ."

Source: http://amlawdaily.typepad.com/Novologagreement.pdf

INDUSTRY SETTLEMENT EXAMPLES

- Wyeth (2013)
  - $490.9 million civil and criminal settlement
  - Criminal Information: “Wyeth used Transplant Science Liaisons ["TSLs”] as part of marketing and sales efforts. TSLs typically were employees with medical experience, such as pharmacists or nurses. Although drug companies were prohibited from introducing drugs into interstate commerce for intended uses that had not been approved, the use of medically-trained employees to provide scientific information about unapproved uses to doctors in response to unsolicited requests, was protected under FDA regulations for most of the relevant time period. However, the activities of Wyeth TSLs during the relevant time period were not limited to responding to unsolicited requests for information. **By strongly encouraging collaboration between TAMs and TSLs, Wyeth's use of TSLs reflected the intended use of Rapamune in that TSLs were integral members of the company's coordinated off-label sales and marketing efforts. As a result, TSLs accompanied TAMs on sales calls, TAMs attended off-label presentations that TSLs gave to health care providers, TSLs trained TAMs on off-label uses, and TSLs regularly coordinated with the sales force at sales meetings**.” (emphasis added)

Sources: https://www.justice.gov/opa/pr/wyeth-pharmaceuticals-agrees-pay-4909-million-marketing-prescription-drug-rapamune-unapproved; https://thebeatatcooleyhealth.files.wordpress.com/2013/07/wyeth-criminal-information.pdf

KEY TAKEAWAYS

- Increased Governmental scrutiny of, and CIA requirements related to, the role of Medical Affairs personnel/MSLs
- Implementation of a firewall between Sales/Marketing and Medical Affairs to ensure that Medical Affairs' activities are:
  - Scientific exchanges
  - Independent of Sales/Marketing influence
  - Are not "promotional" in nature
- Clear delineation of Medical Affairs' responsibility for specific activities without Sales/Marketing involvement or influence

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QUESTIONS?

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