



Scientific Exchange: Grey Areas and Best Practices

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Scientific Exchange

Where things stand

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Disclaimer

The views and opinions expressed in the following slides are my own and do not necessarily represent the views of my employer, FDLI or anyone employed by, or affiliated with, either organization.

Where It All Began

21 CFR §312.7

a) *Promotion of an investigational new drug**. A sponsor or investigator, or any person acting on behalf of a sponsor or investigator, shall not represent in a promotional context that an investigational new drug is safe or effective for the purposes for which it is under investigation or otherwise promote the drug.

This provision is not intended to restrict the **full exchange** of scientific information concerning the drug, **including** dissemination of scientific findings in scientific or lay media. Rather, its intent is to restrict promotional claims of safety or effectiveness of the drug for a use for which it is under investigation and to preclude commercialization of the drug before it is approved for commercial distribution.

*Presumably applicable to unapproved uses of approved products, but what about communications related to approved uses of approved products?

Further Clarification

Preamble to Final Rule on IND Regulations; Treatment Use & Sale¹

- “FDA's understanding of commercial promotion does not place limits on the free exchange of scientific information (e.g., publishing results of scientific studies, letters to the editor in defense of public challenges, investigator conferences).
- “However, responses by sponsors or investigators to unsolicited media inquiries or statements made in the exchange of scientific information should
 - 1) Make clear that the drug is investigational;
 - 2) Make no claims that the drug has been proven to be safe or effective; and
 - 3) Be truthful and non-misleading when measured against available information on the drug – and fairly represent available information – as set forth in materials such as investigators' brochures and patients' informed consent sheets.”

¹52 FR 19466 May 22, 1987

So... What is Scientific Exchange?

- Non-promotional
 - i.e., no conclusions of efficacy, safety...
- Includes:
 - Presentation/publication of study data
 - Dissemination of reprints, medical/scientific texts & clinical practice guidelines pertaining to unapproved uses (per FDA draft guidance)
 - Investigator meeting materials
 - Responses to unsolicited requests
- Besides these limited communications, what else constitutes scientific exchange?
 - Proactive product discussions (on- or off-label)?

Revised Draft Guidance on Distributing Scientific & Medical Publications on Unapproved New Uses (Feb. 2014)

- “...while reprints [and scientific/medical reference texts & clinical practice guidelines] may be distributed at medical or scientific conferences in settings appropriate for scientific exchange, reprints should not be distributed in promotional exhibit halls or during promotional speakers’ programs.”
- “To the extent that the recipients of the [above materials] have questions, the sales representative should refer the questions to a medical/scientific officer or department... independent of the sales and/or marketing departments.”

FDA Guidance on Drug & Device Manufacturer Communications With Payors (June 2018)

Investigational Products/Uses

- Firms may communicate (no timeframe specified):
 - Product information
 - Drug Class/Device Design (disclose investigational status)
 - Target Indication/Population
 - Development Phase
 - Study design/Results (Preclinical and/or Clinical)
 - Anticipated approval timing
 - Pricing information
 - Patient utilization projections (e.g., epidemiological data projection on incidence & prevalence)
 - Product-related programs or services (e.g., patient support programs)
 - Removed in final guidance: “Targeting/marketing strategies & other programs/services”

FDA Guidance on Drug & Device Manufacturer Communications With Payors (June 2018)

Caveats

- Information must be accurate, factual, non-misleading & unbiased
- Communications must not represent that an investigational product is
 - FDA-approved
 - Safe or effective for investigational uses
- Update payers on changes/new information (e.g., conflicting/differing results from subsequent studies)

Still Waiting...

- December 28, 2011, *Federal Register* Notice
 - FDA opened docket on communications related to unapproved/uncleared uses & products
 - Docket opened in response to Citizen Petition filed on behalf of 7 pharma companies requesting FDA policy clarification
 - Comments on “scientific exchange” specifically requested, primarily around its yet-to-be-defined scope
 - To date, no guidance or policy statement on scientific exchange apart from limited payer example

Commercial or Medical – Does It Matter?

- FDA public statements & enforcement suggest the message trumps the messenger
 - Regulations draw no distinction between Commercial & Medical Functions
 - As such, Medical staff neither de facto scientific exchange agents nor exempt from promotional regulations governing sales & marketing activities
 - OPDP regulates “Oral Presentations made by representatives of the company which include Sales Reps, Hired Spokespeople, Medical Science Liaisons”⁴

⁴ Amy Toscano (former OPDP Team Leader), DIA 2013 Annual Meeting

Biogen Untitled Letter (March 25, 2010)

Tysabri[®] (natalizumab)

- 8 Promotional Webcasts (Oct. & Nov. 2009) conducted by Medical Affairs & focused on risk of progressive multifocal leukoencephalopathy (PML)
- Cited Violations
 - Minimization of Important Risk Information
 - Omission of Indication
 - Failure to Submit (Form FDA-2253)

Biogen Untitled Letter

- Webcasts Misleadingly Implied:
 - Patients who developed PML & received treatment experienced lessened effects of PML
 - Patient outcomes improve if treatment is stopped at first sign of PML
 - Significant portion of patients who develop PML survive & and may only experience non-severe disabilities
 - PML risk can be predicted based on established treatment time range
- Despite clinical tone, absence of branding elements & delivery by Medical staff, webcasts held to promotional standard
 - Statements lacking support (substantial clinical evidence)
 - Omission of full indication
 - Failure to submit at time of first use

Biogen's Defense

- Biogen asserted that webcasts “were medical communications from our medical team to treating neurologists in response to the interest and need expressed by the medical community for reliable timely and accurate information on Tysabri.”⁵
- “The aim of those webcasts was to help doctors and patients make informed treatment decisions, and we believed that the content and the means for communicating the safety information was appropriate, timely, factual and not promotional.”⁵
- Promotion or Scientific Exchange?

⁵Haley, S. “Tysabri Webcast Citation May Signal That FDA Could Treat All Social Media Interactions As Promotional; Biogen's PML Strategy Also Takes A Hit”. *The Pink Sheet*, April 12, 2010.

Manufacturer – Payer Communications

Susan A. Cantrell, RPh, CAE

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FDLI: Advertising and Promotion for Medical Products Conference

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Washington, D.C.



AMCP

- 8,000 members, including pharmacists and other health care professionals
- Provides education, networking, advocacy, and other member-focused services
- AMCP members manage pharmacy benefits for over 270 million Americans



Helping ensure patients have access to the medications they need at a cost they can afford.



Mission

To improve patient health by ensuring access to high-quality, cost-effective medications and other therapies.

Payers' Need for Information from Manufacturers

- Patient access to new therapeis
- Budgeting/cost reporting
- HCEI
- Preapproval information
- Unapproved uses
- Reduce regulatory uncertainty

<https://www.amcp.org/sites/default/files/2019-03/AMCP-Format-V4.pdf>

The AMCP *Format* for Formulary Submissions

Version 4.0

A Format for Submission of Clinical and Economic Evidence
in Support of Formulary Consideration

April 2016

AMCP

Academy of
Managed Care

Milestones

March 2016: AMCP Partnership Forum, “FDAMA 114: Improving the Exchange of Pharmacoeconomic Data”

July 2016: AMCP releases consensus recommendations

September 2016: AMCP Partnership Forum on “Enabling the Exchange of Clinical and Economic Data Pre-FDA Approval”



Milestones

January 2017: FDA draft guidance, “Drug and device manufacturer communications with payors, formulary committees, and similar entities – questions and answers”

April 2017: Rep. Brett Guthrie (R-Ky.) introduces “Pharmaceutical Information Exchange (PIE) Act of 2017” (H.R. 2026)

January 2018: House Energy and Commerce Committee Subcommittee on Health approves H.R. 2026

June 2018: FDA issues final guidance

June 2019: Burr Amendment

AMCP Opportunities

- Science and Innovation Theaters
- www.formularydecisions.com
- PIE webinars
- Stakeholder group



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October 18, 2019

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Ropes & Gray LLP



Key Scientific Exchange Considerations

- Regulation applies on its face only to investigational drugs but has in practice been applied to investigational uses of approved products
- No audience limitation – scientific exchange can be with HCPs, payors, patients, etc., though considerations will vary depending on the audience
- No speaker limitation – as a legal matter, scientific exchange could technically be communicated by any manufacturer representative
 - In practice many companies limit scientific exchange to medical affairs, MSAs, and related personnel to reduce execution and perception risks related to off-label promotion
- Communications can be proactive or reactive
 - As with choice of speaker, there are perception and execution risks to consider

Scientific Exchange vs. Promotion

Factors to Consider in Assessing Scientific Exchange vs. Promotion

Note that none of these are dispositive

- **#1 Importance of the information shared**

The more critical the information, the stronger the argument for dissemination via scientific exchange

- **#2 Novelty of the information shared**

Generally speaking, the more frequently the same information is shared with the same audience, the more likely it is to feel like promotional messaging rather than scientific exchange

- **#3 Reach of the communication**

Stronger rationale for sharing information with health care professionals, payors, patients, and others who have a need for it and can appropriately evaluate its merit

Scientific Exchange vs. Promotion (cont'd)

- **#4 Venue**

Scientific forums such as medical congresses are more likely to be viewed as conducive to scientific exchange, as opposed to locations or events where promotional activities are conducted

- **#5 Commercial involvement**

Absence or limitation of commercial involvement can help mitigate perception of promotional intent

Best Practices for Scientific Exchange

- Provide information necessary for contextualization (e.g., disease state overview, description of study design)
- Avoid conclusions or characterizations with express or implied safety or effectiveness claims
- Retain scientific language where possible
- Emphasize that FDA approval – and the timeline for potential approval – is uncertain
- Summarize important safety information
- Disclose expected limitations to indication and patient population
- Exercise particular care when providing information on the current treatment landscape, other therapies, etc.



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