

Duke-Margolis and FDA Convening: Informing and Refining the Prescription Drug Promotion Research Agenda

Virtual Public Meeting
November 19, 2021

Meeting Report

Executive Summary

The Office of Prescription Drug Promotion (OPDP) at the U.S. Food and Drug Administration (FDA) is tasked with helping to ensure prescription drug promotion is truthful, balanced, and accurately communicated. OPDP helps guard against false or misleading promotion through comprehensive surveillance, compliance, and educational programs. Additionally, OPDP has a research program that is integral to its public health mission.

The landscape for both direct-to-consumer (DTC) and health care provider (HCP) targeted prescription drug promotion is changing, with OPDP seeing more internet-based and algorithm-driven communications over recent years. The Robert J. Margolis, MD, Center for Health Policy at Duke University and the FDA convened an array of external experts to present their research findings in fields related to prescription drug promotion and digital marketing. The discussion was designed to help inform the FDA and other stakeholders of important emerging trends, effective study designs, and other complementary learnings that may have bearing on the Agency's research agenda and on studies carried out by researchers outside the Agency.

Meeting participants shared insights on existing study topics in prescription drug promotion including the effects of social media and influencer promotion, native advertising, and impacts on vulnerable consumers like adolescents and those with existing health conditions. Participants also identified future trends and research areas that could benefit from further study such as changes in promotion to HCPs including the rise of e-detailing, and new forms of online promotion to consumers through patient engagement portals and virtual waiting rooms, online DTC telemedicine clinics, and "advergames."

Priority questions for potential future study on prescription drug promotion were identified and discussed during the meeting. Of note, participants highlighted how evidence gaps may impact pursuit of answers to some research questions, especially those that require the use of prescription drug promotion spending data that may not be accessible to researchers. Solutions and new approaches to data analysis, including artificial intelligence (AI) capabilities like natural language processing (NLP) and machine learning, may help researchers in addressing gaps in the literature. In addition to a need for more research on topics in prescription drug promotion, meeting participants articulated that regulatory science needs to be adaptive to the changing digital ecosystem to ensure consumer protection both now and in the future.

Background

Office of Prescription Drug Promotion (OPDP)

The mission of the FDA's OPDP is to protect public health by helping to ensure that prescription drug promotion is truthful, balanced, and accurately communicated. OPDP carries out this mission through comprehensive surveillance, compliance, and educational programs to help guard against false or misleading prescription drug promotion. OPDP's activities include fostering better communication of information to help consumers and HCPs make informed decisions about their treatment options.

OPDP has a research program that is integral to its public health mission. This research program supports FDA's goal of implementing science-based policy and also informs FDA's other efforts to facilitate the communication of truthful and non-misleading drug information to consumers and HCPs. OPDP's research is focused on promotional communications for prescription drugs and includes investigating issues impacting HCP and consumer usage of information, enhancing understanding of the audience's perception and comprehension of information presented, and assessing the accuracy and effectiveness of information and how it is conveyed. OPDP researchers also measure the impact of prescription drug promotion on consumer and HCP behaviors and work to measure how audience variables like health literacy level and age influence research findings. This helps to illuminate what populations may be most vulnerable to false or misleading promotion.

It is important to note that federal regulations do not require drug sponsors to submit promotional communications to OPDP for review prior to use except in [certain limited circumstances](#). [Federal regulation](#) requires all promotional communications disseminated by or on behalf of a drug sponsor to be submitted to FDA at the time of initial publication or dissemination to the public, meaning that most promotional communications in the public domain have not been reviewed by OPDP. Of note, this also means that promotional communications that are *not* disseminated by or on behalf of a drug sponsor are not subject to FDA regulatory requirements for prescription drug promotion.

While it is the drug sponsor's responsibility to ensure that their promotional communications comply with existing laws and regulations, OPDP is responsible for protecting public health by, for example, monitoring drug sponsors' promotion. For this reason, research on current and future trends in prescription drug promotion and how these trends may impact public health are key to OPDP's work and mission fulfillment.

Meeting Objective

The broader landscape for prescription drug promotion continues to evolve as consumers and HCPs increasingly use digital tools to inform and manage aspects of care and drug sponsors look to these tools to reach target audiences. While some of these tools and communication channels are being used by individuals or entities that may be outside of FDA's statutory jurisdiction, understanding the broader digital marketing landscape is an important prerequisite to informing and refining both FDA's research agenda as well as the research agenda of others engaged in fields such as health communication, marketing, and public health. Identifying potential touchpoints where collective research could improve and safeguard the information that makes its way to consumers and HCPs can lead to more strategic, impactful, and collaborative work in this space.

The Duke-Margolis Center for Health Policy and the FDA convened an array of experts to present and discuss research findings in prescription drug promotion and digital marketing to help inform the FDA and other stakeholders of important emerging trends, effective study designs, and other learnings that may complement the Agency's research agenda as well as studies carried out by researchers outside the Agency. Participants explored a wide range of topics related to current and anticipated future trends in prescription drug promotion, how prescription drug promotion can affect patient and HCP thinking and decision making, and how to best support research at the FDA and elsewhere that is both impactful and actionable.

Current Research Topics on Prescription Drug Promotion in the Digital Space

Meeting participants discussed current research topics related to prescription drug promotion in the digital space. Key areas of ongoing research include prescription drug promotion that occurs via social media and the use of social media influencers.

Prescription Drug Promotion via Social Media Platforms

Drug sponsors are increasingly turning to internet-based promotion in addition to traditional forms of advertising, namely TV and print ads, to reach consumers. While social media is still a comparatively new avenue, prescription drug promotion can be found on a range of social media platforms such as YouTube, Instagram, Twitter, TikTok, Facebook, and Twitch. Meeting participants stressed that social media is not a monolith; each platform has different audiences with various ways of engaging and interacting with users. It was also pointed out that social media is not restricted by geographic boundaries. This creates unique challenges for regulators, each with different rules and regulations, tasked with protecting the public health of discrete populations.

One meeting participant noted that in her review of FDA compliance letters, one of the key concerns evident to her was that drug sponsors have been using social media platforms like YouTube to promote products that are not approved, framing the products as "breakthrough" drugs, despite a lack of scientific evidence. The researcher further noted that this violative practice could have a disproportionate impact on vulnerable individuals with chronic or hard-to-treat conditions.

That participant also noted that FDA compliance letters shine a light on issues of risk imbalance in social media prescription drug promotion. Some prescription drug promotion that occurs on social media may be imbalanced due to how the information is presented to consumers. Risk information may not be immediately visible to consumers due to the use of creative techniques, such as making risk information available when the viewer's cursor moves over a photo or other graphic. As a result, consumers may not fully view risk information when coming across this type of digital prescription drug promotion. In addition, promotional communications within and across social media platforms are less standardized compared to print ads or television ads and may take many shapes and forms. Consumers, as a result, may have varied experiences interacting with promotional communications even when presented with the same promotional content. These differences in format and user experience may impact audience perceptions and comprehension of the information presented.

In addition, social media posts on a variety of social media platforms may contain native advertising. Native advertising is advertising that is seamlessly integrated with entertainment or editorial content. Native advertising may reduce skepticism by consumers, especially those with low media literacy and a lower ability to distinguish between the promotional and non-promotional components of the content. Researchers are studying how consumers evaluate these posts, and native advertising generally, to better understand how this unique format may impact consumer comprehension of the core drug information.

Lastly, the use of high-powered algorithms that present personalized and targeted promotional communications to users on platforms, such as TikTok, were explored. Marketers can use metadata – data that is descriptive of other data rather than including the direct content – generated through social media activity to target drug promotion to consumers with a high degree of precision, including for “off-label” uses for some drugs. Vulnerable populations, including adolescents and individuals with chronic or hard-to-treat conditions or those with depression, may be particularly impacted by targeted promotional communications on social media platforms. Of note, there is limited transparency surrounding the use of metadata for digital targeting. Meeting participants stated that there is a need for more research on how these targeted prescription drug promotions may impact all users, especially vulnerable audiences that use social media platforms.

Social Media Influencers and Prescription Drug Promotion

In addition to the presence of prescription drug promotion on social media described above, meeting participants articulated that there are different risks associated with different types of influencers engaging in promotion on these platforms. Social media influencers engaging in prescription drug promotion come in different varieties, including patient influencers, physician influencers, celebrity influencers, and micro-influencers. Micro-influencers are influencers with a larger following than a normal social media user, but with fewer followers than a celebrity and typically with expertise in a certain niche.¹ Given their smaller audience, micro-influencers may be more likely to engage with followers directly and participate in dialogue about prescription drugs or other products. Additionally, micro-influencers and their followers may bond over shared health conditions. These factors may impact how promotion is perceived by the targeted audience. On the other hand, celebrity influencers may have substantially larger followings as well as more followers that engage in parasocial relationships with the celebrity. A parasocial relationship is a one-sided relationship experienced by an audience that may lead to an overinflated sense of trust in celebrities and their recommendations. In addition, parasocial relationships mediated via social media platforms can lead to health information disclosures by audience members, which may become a privacy issue for consumers engaging in this behavior.²

One meeting participant noted that some promotional strategies may encourage influencers to build empathy online, especially for promotional campaigns that focus on user-generated content. Drug sponsors may have influencers make an illness disclosure and openly talk about their condition as a part of the promotional strategy, which can immerse consumers in the storyline and make them feel as if the promotional material is organic. This empathy-building tactic may reduce advertising skepticism in consumers, which may increase patient inquiries about the product to their HCPs and reduce their ability to accurately assess the benefit and risk information provided for the product.

In the same vein, one participant noted ethical issues that arise from some influencer marketing practices. Some social media posts by influencers appear to include personal, unbranded content about a disease state or health condition that the influencer is experiencing. The posts do not appear to include any prescription drug promotional messaging. However, the influencer uses the post to direct followers to links that then bring those followers directly to branded prescription drug promotional websites. The participant highlighted that there are ethical concerns with the lack of transparency around these marketing techniques.

In addition, TV ads with testimonials from influencers, where the influencer speaks to their experience with the prescription drug product, may also encourage consumers to inquire about certain prescription drugs. A meeting participant noted that testimonials for prescription drugs are potentially problematic given that prescription drug effectiveness varies from patient to patient. Meeting participants noted that more research could help elucidate how influencer marketing can affect consumer health behaviors.

Physician influencers on social media may also engage in promotion of prescription drug products. A meeting participant spoke on the value of investigating the association between high volumes of consulting payments and physicians' online profiles to understand any associations between promotional content posted online by these physicians and consulting payments. Of note, the relationship between the volume of payments physicians receive as indicated in the CMS [Open Payments database](#) and their social media posts is a new area that could benefit from additional research.

Emerging Trends in Prescription Drug Promotion and Additional Research Gaps

The rise of prescription drug promotion in the digital space and the changing health landscape have contributed to several emerging trends in prescription drug promotion to consumers and HCPs that warrant further research. Meeting participants identified emerging trends in prescription drug promotion as well as broader digital promotion trends to watch and discussed key research gaps with these emerging drug promotion methods.

Trends in Prescription Drug Promotion to Consumers

Patient engagement portals are an emerging platform for prescription drug promotion. These portals allow individuals to receive lifestyle “coaching” for certain conditions. Meeting participants stressed that this can lead to direct advertising to consumers that is not as visible as traditional promotion from drug sponsors or third parties, which can make it difficult for researchers to assess the impacts of these types of promotion on consumers.

Virtual waiting rooms are another relatively new venue for prescription drug promotion and are becoming more utilized with the increasing prevalence of telehealth visits. Participants noted how these virtual waiting rooms assure marketers of a captive audience that may be uniquely motivated to listen to health-related messaging. Research is needed to evaluate issues like whether patients in these rooms are more vulnerable to priming effects, and how the promotional messaging they experience shapes the

interaction with their HCP that immediately follows. Virtual waiting rooms are typically hosted on the same platform in which patients disclose sensitive health information, meaning that drug sponsors may use tailored advertising to target these patients as they wait for their telehealth appointments. One meeting participant noted that virtual waiting rooms raise questions about data privacy given the sensitivity of the information that patients share with their HCPs during telehealth visits.

Meeting participants also noted that digital applications (“apps”) that are represented as health support tools for consumers are another emerging venue for prescription drug promotion. These apps may be linked to wearable technology and may prompt consumers to enter information about their health. This information can then be used to push in-app ads that are targeted at that specific consumer based on their behaviors and health information. This trend again highlights issues of data privacy and, one participant noted, could lead to ads being directed at individuals who are not appropriate candidates for the promoted drug (off-label marketing).

Another important emerging trend that may impact understanding of what balanced and accurately communicated third-party promotion to consumers looks like online is the rise of direct-to-consumer (DTC) telemedicine clinics. Visits to these telemedicine clinics are distinct from traditional telemedicine visits with an HCP. DTC telemedicine clinics connect consumers to medical advice and treatment options and do not require patient referral to the clinic by a clinician. Of note, these clinics may be highly specialized in providing only a limited number of therapeutic options, with some focused on providing access to only a single product. Questions remain about how DTC telemedicine clinics’ advertisements may impact consumer assessment and utilization of promoted treatment options, including advertisements for products that may be prescribed through such services for off-label use. One meeting participant noted that online DTC telemedicine clinics can increase privacy and patient accessibility to HCPs. However, clinics may also have financial incentives to overprescribe or to prescribe products for off-label use. Meeting participants articulated that information being communicated to consumers about DTC telemedicine clinics may be considered promotional, and these clinics should present balanced, truthful, and accurate information about their products and services to patients. Interestingly, however, the promotional messaging from these clinics may not be subject to FDA regulations as the promotion of the prescription drug may not be conducted by or on behalf of the drug sponsor.

Broadcast advertising is still a prominent form of prescription drug promotion; however, broadcast ads are appearing in new contexts to target new demographics. Meeting participants discussed streaming services as a new frontier for broadcast advertising, potentially reaching younger or different demographics compared to traditional TV ads. Researchers also mentioned that longer-form broadcast-style ads may begin appearing in more digital spaces where consumers seek entertainment or when searching for information about health conditions. Drug sponsors are also using new promotional techniques to connect with consumers. The use of narrative transportation and consumer engagement, through concepts such as “advergames,” may facilitate consumer education about prescription drug products.³ Narrative transportation is an advertising technique that immerses readers into a storyline. One meeting participant noted that narrative transportation may be especially prevalent in more traditional forms of drug promotion, including TV advertising. Narrative transportation is an important concept in current prescription drug promotion research, as the strategy is often used only to present

prescription drug benefit information in the TV ads, while the risk information is kept distinct from the narrative storyline. This may affect the attention paid to the presentation of the risk information and consumers' ability to properly understand risk information.

One additional trend that may have bearing on how consumers assess prescription drug promotion information is law firm ads on drug harms. While not a new trend, law firm ads about drug harms, which focus on communicating safety risks about a given product or products, may affect medication adherence and subsequently may cause negative patient outcomes. Meeting participants emphasized that media and health literacy are important for consumer empowerment and that consumers may face risks as these promotional strategies may make benefit-risk information more difficult to understand. Of note, law firm ads are almost completely unregulated, and more research is needed to understand how messaging in these ads impacts consumer comprehension of the risks and benefits of prescription drugs, as well as the ads' impacts on consumer health behaviors.

Trends in Prescription Drug Promotion to Health Care Providers

It is important to note that the majority of industry funds for prescription drug promotion are directed towards HCPs rather than DTC promotion. Promotion to HCPs has historically included written and print communications along with other forms of promotion such as speaker programs, conferences, and in-person detailing via visits from sales representatives.⁴

Promotion to HCPs is also taking new forms. Due to the ongoing COVID-19 pandemic, drug sponsors have shifted from in-person detailing to e-detailing. E-detailing, which has become a major form of promotion to HCPs, may be less expensive for sponsors given the reduction in expenses related to travel and meals. Compared with more traditional in-person detailing, e-detailing may also reach more HCPs, especially providers in rural or hard-to-reach areas. Promotion via electronic health records (EHRs) is also a relatively new venue for prescription drug promotion to HCPs; however, this strategy is not currently widespread. Prescription drug promotional communications have been embedded in clinical decision-making software that HCPs routinely use, raising concerns about how these communications may alter prescribing behavior. Little research exists surrounding the effect of promotional communications embedded into EHRs, but researchers are keen to study the topic further given the historical impact of other forms of promotion to HCPs on prescribing and patient outcomes.

One meeting participant also noted that promotion to HCPs may be shifting towards targeting payors and other higher-level authorities who have power over formularies and other key decisions. This type of promotion is more tailored than past techniques, which have targeted many individual physicians to encourage them to prescribe certain prescription drugs. Many academic medical centers, hospitals, and private practices no longer allow sales representatives to speak directly to physicians, which raises questions surrounding how the volume of promotion to HCPs will change going forward.

Future Research Needs

Meeting participants proposed research areas for further study and provided insights on strategies to overcome gaps in available research and evidence. Among other topics, participants raised questions about the future of promotion to HCPs, the use of new social media platforms and strategies, and the difficulties associated with obtaining and analyzing data related to digital promotion.

Key Research Topics for Further Study

More research, regardless of who conducts it, is needed to understand how changes in promotion to HCPs impacts understanding of the risks and benefits of a given product as well as prescribing behaviors. E-detailing in particular warrants further research given the dramatic rise in this form of promotion during the COVID-19 pandemic. In addition, promotion to HCPs via EHRs is an area that meeting participants identified as warranting further exploration.

Researchers may consider exploring questions such as:

- 1) How might the shift from in-person to e-detailing affect the volume of promotion to HCPs?
- 2) How might the growth of e-detailing and marketing through EHRs impact HCP information seeking and prescribing behaviors?
- 3) Is there data to suggest that marketing of controlled substances to HCPs should be subject to different statutory requirements than other types of prescription drug products?
- 4) How have changes enacted by the Physician Payments Sunshine Act of 2010 (PL 111-148) impacted consumers and the patient-HCP relationship?
- 5) How do prescribing rates differ between e-detailing and in-person detailing?
- 6) How might e-detailing influence appropriate versus inappropriate drug selection and use?

Meeting participants identified prescription drug promotion on social media and influencers as important areas for further research. A better understanding of how prescription drug promotion over different social media platforms may shape patient-HCP interactions, as well as health outcomes, may inform understanding of how different promotion formats and venues impact consumer assessment and comprehension of product information. While meeting participants acknowledged that determining causality in the current data landscape is difficult, valuable insights into the impacts of digital prescription drug promotion could be gained by looking at topics like the relationship between digital promotion and medication adherence, and how this type of promotion influences open communication between patients and HCPs.

Research questions on promotion via social media, by influencers, and through other digital media tools suggested by meeting participants include:

- 1) How might drug promotion via social media shape patient-HCP interactions?
- 2) How might drug promotion via social or digital media channels prime patients to discuss certain questions or ideas with their HCPs?
- 3) How might social media and other emerging digital media channels for promotion positively impact health behaviors such as medication adherence?
- 4) How do health literacy and media literacy influence consumer skepticism and behavior in response to social media promotion?
- 5) How do hidden DTC prescription drug promotion messages in native advertising and implicit claims in vehicles like advergames impact consumer beliefs, skepticism, and behavior?
- 6) How can disclosures be used to effectively signal to consumers that the messaging they are seeing is marketing?
- 7) How do the different media consumption practices of different age cohorts impact belief formation, decision making, and persuasion outcomes in those cohorts?

- 8) How do the research findings related to more traditional forms of DTC advertising compare to research findings on DTC promotion through social media?
- 9) How might drug promotion via social media impact inappropriate prescription drug use?

Evidence Needed to Support Further Research

To address the key research topics above, new and different types of data will be needed. As one meeting participant noted, it is hard to determine the impact of promotion on health outcomes without access to data on advertisement spending, as well as data on how the promotional communications are being used and targeted. Participants noted that there is less data granularity from digital advertising than from TV and other more traditional forms of advertising, which impacts the level of data available for conducting research. In addition, individual drug sponsors and technology companies have access to their spending data and information about marketing to certain demographics, but this information is largely unavailable to researchers or the public. Some social media platforms are more open than others; for example, Twitter made some ad spending data available to researchers. However, even in these cases, data made available by social media platforms may be lacking in important ways. Of note, influencers may be paid via third parties rather than directly by drug sponsors, which makes obtaining spending data more difficult.

Meeting participants noted difficulties in obtaining and analyzing data on promotion in the digital space for academic research. Obtaining access to data for research is expensive, and various datasets may have a political valence that researchers may wish to avoid. One participant added that it can be hard to scrape data from platforms such as Instagram, as images can have powerful influences in addition to text content, which can be more easily scraped. Additionally, a significant gap in understanding of prescription drug promotion in the digital space is how data brokers facilitate promotion, which poses health privacy information problems for patients.

Despite difficulties with obtaining and analyzing data on digital promotion, researchers have identified strategies for analyzing promotional communications and their effect on consumers. Content analysis, for instance, is one method that has been used to analyze the landscape of promotion on social media, and this method may be especially relevant for analyzing images, user profiles, and online conversations surrounding promotional communications. Natural language processing (NLP) and machine learning may allow for analysis of larger groups of social media posts, especially when looking at social media platforms that allow larger bodies of text, such as Twitter and Reddit. One meeting participant added that research methodology may need to differ between social media platforms due to the way information is presented to users. Participants further noted that the user reactions to promotional communications are important to study in addition to the promotional communications themselves.

Conclusion

Prescription drug promotion is evolving and taking new forms with internet-based promotion becoming increasingly popular. In the meeting, participants discussed important new developments in the prescription drug promotion research landscape, including the rise of social media promotion, use of influencers, and increases in e-detailing, among other topics. The impact of these new promotional strategies on consumers and HCPs is largely unknown, and more research into these topics is warranted

to help ensure patient safety, especially as prescription drug promotion continues to rapidly change in the digital age.

Priority questions for future study on prescription drug promotion were identified and discussed during the meeting. Of note, participants highlighted how evidence gaps may impact pursuit of answers to some research questions, especially those that require the use of prescription drug promotion spending data, which may not be accessible to researchers. Solutions and new approaches to data analysis, including artificial intelligence (AI) solutions, may help researchers in addressing gaps in the literature.

Meeting participants articulated that regulatory science needs to be adaptive to the changing digital ecosystem to protect consumers both now and in the future. Beyond research into the promotional material itself, understanding the way consumers are targeted in the digital space will be important for effective oversight of prescription drug promotion. As one meeting participant noted, understanding and addressing misleading messaging is one challenge, but understanding misleading marketing practices and how to protect consumers from those practices is another challenge entirely. Meeting participants also noted that guidance related to the “fair balance” regulatory provision may need to be modernized given evolving digital formats and previous research demonstrating that consumers have a lesser understanding of prescription drug risks compared with drug benefits. Meeting participants questioned whether drug sponsors may benefit from more concrete guidelines about how drug benefit-risk information should be conveyed in promotional communications, especially given the rise of new forms and formats for promotion in the digital space.

Overall, as new forms of prescription drug promotion emerge, regulators and the broader research community must work together to better understand how promotional communications in the digital space impact consumers and HCPs and how to best protect public health.

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