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Evidence-Based Engagements and Communications in Response to an Ever-Changing External Environment


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Introduction

The life sciences and healthcare sector continues to evolve in response to an ever-changing external environment propelled by technological advances, geopolitical tensions, and socio-economic and macroeconomic conditions. Despite these changing landscapes, many breathtaking therapeutic transformations continue to be developed with a particular focus on personalising the treatment pathway for patients. Patients and healthcare professionals ("HCPs") are increasingly demanding up-to-date information on the latest therapeutic approaches. Payors are increasingly relying on health economic tools to determine adoption of a new treatment in the respective national health systems and timely access to emerging information to guide an informed assessment on relative clinical effectiveness and cost-effectiveness.

The sharing of knowledge and information and collaborating with external stakeholders is powerful in science and medical research as ideas can be translated into innovation. Depending on the audience and context, legitimate scientific communications primarily seek to convey accurate information that may be important for predictive relevance in terms of healthcare needs, building trust and stimulating debates on contentious scientific issues.

The concept of "expert patient" has evolved over the last four decades and now recognises the fact that patients are increasingly taking an active participatory role in the choice of treatment, and that they have significant knowledge in disease management. Patients are empowered to act as champions to represent the "patient voice" often with HCPs in decision-making and in medical research with the objectives of improving health outcomes and patient care. Some have argued that engaging patients in collaborative care and shared decision-making has improved health outcomes and could effectively manage healthcare costs through behavioural change that may arise in a chronic disease setting.

The movement from passive recipients of treatments to active partners in their bespoke care and treatment pathways as well as "disease educators" has significantly shifted the way health-related information and evidence is communicated to patients and HCPs. The life sciences and healthcare industry has responded positively to the need for more patient-focused product development in recognition of the fact that meaningful patient engagement is required for the authentic patient voice to inform research and regulatory decisions. To this end, various stakeholders have advocated a structured approach to patient engagement that is to be applied systematically and consistently with a view to identifying, capturing and evaluating clinical outcomes that are patient-specific and relevant to patients who live with the medical condition and/or are knowledgeable about the condition. The purpose is to provide an estimate of the effectiveness of the therapy in terms of how patients feel, function or survive, and an estimate of treatment safety.

Moreover, greater emphasis is now being placed on data generation to guide best practices and decision-making. Evidence-based decision-making – using the best available evidence from multiple sources to make informed decisions – is critical to the success of a research and development programme, but this goes against timely market access in an increasingly cost-conscious healthcare delivery system.

Historically, clinical trials have required research participants to travel to trial sites through a centralised approach based on standardised processes and procedures for the conduct of clinical research. The COVID-19 pandemic has catalysed the greater adoption of an alternative approach to conducting clinical trials based on hybrid and fully decentralised clinical trials. Incorporation of digital health technologies in decentralised clinical trials has gained traction. In contrast to a centralised clinical trial, a decentralised clinical trial refers to a clinical trial that includes decentralised elements where trial-related activities occur at locations other than traditional clinical trial sites. Technological advances have expanded the types of trial-related data that can be obtained remotely from participants continuously. The objective of adopting a decentralised approach is to reduce the burden on trial subjects and their caregivers – particularly those subjects with limited mobility or limited access to traditional clinical trials – and hence engender greater efficiency in clinical development. This may also help improve engagement, enrolment and retention of trial subjects and therefore improve the strength and generalisability of the evidence afforded by a decentralised clinical trial. A successful decentralised clinical trial inevitably involves greater participation of trial subjects and relevant information being imparted by study sponsors and medical researchers so that trials are brought closer to the patients.

These developments have raised and will continue to raise novel regulatory compliance and enforcement questions in relation to proper oversight of advertising and promotional activities. This is because regional and national laws and industry codes of practice define advertising and promotion very broadly to capture two principal elements: the business conduct undertaken by a company; and the effect of such conduct on promoting the prescription, recommendation, supply, administration or consumption of a healthcare product. Proper management of external communications and engagements with patients and HCPs has become the focus of regulatory compliance oversight.

Moreover, in an increasingly patient-centric and cost-sensitive clinical delivery environment, national health systems, HCPs

and patients, as well as patient advocates, are demanding up-to-date information be communicated to support more equitable, inclusive and evidence-based decisions. The concept of "unmet medical need" pervading various regulatory systems worldwide seeks to incentivise the development of new therapeutic methods and to identify a particular medical need as unmet to encourage innovation. There exists an enduring unmet medical need across multiple diseases affecting various demographic strata of the population, and such diseases may disproportionately affect the most vulnerable patient populations, such as the very old and the very young. Patients have unmet medical needs when treatment options are not or no longer adequate to manage the underlying conditions. When the end of a standard treatment trajectory comes into view, a discussion on non-standard treatment options between the treating physician and the patient will become inevitable. This discussion is guided by scientific data and clinical assessment of the patient's individual circumstances to inform a decision on expanded access to unapproved treatment options, which are often experimental or investigational.

Clinical decision support systems, principally based upon digital tools, are designed to ensure that the right information is provided to the right person, in the right format, through the right channel at the right time to optimise healthcare delivery, health outcomes and allocation of resources. In response to such a changing external environment, the industry is understandably required to gain greater insights into the treatment pathways, developing roadmaps, including those concerning therapy decision-making, to optimise the value of their products for market access.

As technology has evolved, the types of media that medical product companies may use to engage in promotional and scientific communications with healthcare providers, patients and other relevant stakeholders has expanded considerably. It is noticeable that dissemination of medical practice and scientific information through social media by medical and scientific communities is increasing. The scientific community justifies such broad exposure of information to promote connectivity, overcome barriers to access to sources, stimulate debate, and solicit layperson perspectives and preferences. On the other hand, misinformation may also be disseminated to promote practices lacking scientific evidence that may erode scientific integrity.

To keep up with this changing landscape, the regulatory rules and expectations governing promotional activities and communications in certain key jurisdictions are evolving in response. At a fundamental level, regulators are focused on making certain that information provided to the marketplace is truthful, non-misleading and reliable to such an extent that it will not cause harm to treatment decision-making. In many instances, this requires the information underlying such communications to be scientifically sound, accurately characterised, and appropriately contextualised and disclaimed, as well as requiring that the risks and benefits of medical products are presented in a way that is understandable. In this way, HCPs can reliably use the information to support informed healthcare decisions.

While these general principles of truthfulness and reliability underpin the regulatory approaches of each of these key jurisdictions, there is some variation in how regulators seek to attain these ends. Within the United States alone, the change in the presidential administration that took effect in January 2025 may lead to a shift in how regulators engage with, address and enforce in this space at a practical level. As described below, key decision-makers in the new administration have publicly promoted policies and positions that would mark a significant departure from the existing regulatory framework. Though no concrete policy changes have been enacted to date, these strong public statements have injected some uncertainty as to what stakeholders should expect of the administration in terms of enforcement priorities and departures from current regulatory standards. Recent European Court decisions have clarified the meaning of "advertising medicinal products" and the EU Member States' power to restrict drug advertising activities, in view of the effect of such external communications on prescribing behaviours and purchase of medicines.

This chapter seeks to explore recent regulatory developments involving scientific and medical communications, including for unapproved uses, historically deemed non-promotional, including scientific communications, as well as how regulators view such communications as impacting promotional issues. We will also address recent developments in three key geographical regions related to the regulation of advertising and promotion, particularly as it relates to the disclosure of product risks and limitations of promotional claims.

Dissemination of Non-Promotional, Scientific Communications – Evidentiary Standard

In January 2025, the United States Food and Drug Administration ("FDA") finalised a non-binding guidance document related to firms' communications regarding scientific information on unapproved uses ("SIUU") of approved or cleared medical products ("SIUU Guidance"). The SIUU Guidance is focused on communications that are non-promotional in nature, providing recommendations for dissemination and discussion of off-label reprints, clinical practice guidelines and reference texts, among other sources. The scope of the SIUU Guidance is limited to addressing communications directed to HCPs "engaged in making clinical practice decisions for the care of an individual patient". Therefore, communications to HCPs acting in a payor or researcher capacity, as well as communications to non-HCP audiences, such as patients or caregivers, are out of scope. Though the scope of the SIUU Guidance is cabined to non-promotional, scientific communications, FDA has made clear that it may still look to these communications as evidence of part of a broader inquiry into whether a company is promoting its product for a new or unapproved intended use.

The SIUU Guidance, which finalises a prior draft version published in 2023, adheres to FDA's longstanding position that firms can disseminate certain forms of truthful, non-misleading, factual, unbiased scientific information that relates to unapproved uses of medical products. The SIUU Guidance expands on the 2023 draft version, which had represented a significant departure from FDA's prior position on dissemination of off-label scientific information in a number of ways. Perhaps most notably, the draft guidance had expressly acknowledged that firms can develop their own presentations about off-label reprints to share with HCPs; in response to comments submitted by industry and other actors, FDA takes this a step further in the final SIUU Guidance, clarifying that a firm-generated presentation may be based on any type of source/publication described in the SIUU Guidance (i.e., clinical practice guidelines, scientific or medical reference texts, and digital clinical practice resources) in addition to off-label reprints. The SIUU Guidance does, however, draw lines on what would constitute an appropriate means of communication in a firm-generated presentation. Specifically, the SIUU Guidance identifies two "communication techniques" that would be inappropriate for the communication of SIUU communications: (i) presentations that "encourage the unapproved use of

the medical product based on elements other than the communication's scientific content", such as through the use of celebrity endorsements, emotional appeals unrelated to the scientific content, gifts, promotional tag lines, jingles and premium offers; and (ii) presentations that include any "calls to value that pre-judge the benefit(s) of the medical product for patients", which the SIUU Guidance defines as a "communication technique that includes both a call to action and a value proposition that tells the audience what this action will translate into for them" (e.g., while it may be acceptable to state "Click here to access the full article for free", it would not be acceptable to state "Click here to start improving your patients' lives today"). Additionally, the SIUU Guidance recognises that social media and in-person visits with HCPs can both be appropriate in some circumstances for the dissemination of SIUU of approved/cleared medical products.

The SIUU Guidance also recommends that SIUU communications only describe studies that are "scientifically sound". While FDA does provide some general concepts to inform the definition of these terms, it does not provide clear definitions, and the language of the SIUU Guidance seems to reserve significant discretion for FDA to assess whether the standard is met on a case-by-case basis. For example, the SIUU Guidance states that studies other than randomised, double-blind, concurrently controlled superiority trials "*may…be* scientifically sound when adequately designed and conducted", that "a scientifically sound study *could* include an early-phase randomized, double-blind, parallel assignment clinical study with a prespecified statistical analysis plan comparing the pharmacokinetics, pharmacodynamics, safety, and immunogenicity of two…products", and that "other examples of studies that *could* be consistent with this recommendation include meta-analyses, cohort or case-control studies, open-label studies, single-arm studies, externally controlled trials, and non-interventional (observational) studies" (emphasis added). Additionally, the SIUU Guidance does not address how this new standard should be understood to interact with existing substantiation standards in other contexts, such as the "scientifically appropriate and statistically sound" standard that FDA has established for promotional communications that are consistent with FDA-required labelling ("CFL communications"). This proliferation of varying standards for scientific communications may be difficult for firms to distinguish and manage.

Finally, the SIUU Guidance provides numerous recommendations regarding presentation of communications materials and disclosures that should accompany SIUU communications. Though the SIUU Guidance attempts to provide detailed recommendations, the extensive disclosure expectations that the SIUU Guidance enumerates may be onerous in practice. For example, the SIUU Guidance recommends including both a copy of the FDA-approved labelling as well as separate statements reiterating certain statements from the labelling, as well as a list of standard disclaimer-type statements providing extensive contextual information. Perhaps most onerous, however, is the SIUU Guidance's recommendation that SIUU communications also include a description of any conclusions from other relevant studies that "evaluated the same or similar hypothesis or research questions" that are "in conflict with the conclusions from the studies or analyses described", a phrase that is not then further clarified or defined.

EU pharmaceutical law expressly requires the advertising and promotional materials to be compatible with the approved particulars of the Summary of Product Characteristics ("SmPC"), which reflects the agreed conditions of use of an approved medicinal product. Consistent with the Council of Ministers' position during the initial legislative procedure, the European jurisprudence requires the term "advertising of medicinal products" to be broadly interpreted with the focus on the promotional purpose of the message at issue. Advertising and promotion of an unapproved medicinal product and unapproved therapeutic use is expressly prohibited. The European jurisprudence distinguishes between promotional and non-promotional communications – including information communicated through digital and electronic means – by focusing on the effect of such communications on promoting the prescription, supply, sale or consumption of medicinal products. However, a material or communication that is purely informative, without promotional intent, is not covered by the provisions of the EU advertising and promotional rules for medicinal products. The European Federation of Pharmaceutical Industries and Associations states in its Code of Practice that the Code is not intended to restrain or regulate the provision of non-promotional medical, scientific and factual information. Nor is the Code intended to restrain or regulate activities directed towards the general public that relate solely to non-prescription medicinal products. Similarly, EU medical devices law prohibits: text, names, trademarks, pictures and figurative or other signs that may mislead the user or the patient with regard to the intended purpose, safety and performance characteristics of the medical device by ascribing functions and properties that the device does not have; creating a false impression regarding treatment or diagnosis, functions or properties that the device does not have; failing to inform the user or the patient of a likely risk associated with the use of the device according to its intended purpose; and suggesting uses for the device other than those covered by its approved intended purpose that has been the subject of the conformity assessment.

In addition, the EU heads of agencies representing all national competent authorities in the EU and the EEA, as well as the European Medicines Agency ("EMA"), have considered the need for regulatory authorities and industry to embrace an effective communication strategy to present information that is accurate, meaningful and actionable to a varied audience, such as patient groups, the general public and HCPs, to build trust in scientific developments and the regulatory systems. From a historical perspective, since 2010, the confidentiality paradigm began to shift towards transparency for either proactive or reactive disclosure of clinical trial data. The EMA's policies were adopted with the primary objective of allowing developers, the scientific community and other third parties access to detailed clinical trial data in order to learn from past successes and failures, develop new knowledge in the interest of public health, verify the original analyses and conclusions, and to conduct further analysis.

Decision-makers have traditionally been sceptical about alternative methodological approaches to randomised control trials ("RCT") to support a therapeutic claim because of the risk of research bias that arises from a lack of a parallel control group. Research bias is generally considered a systematic error that can occur during the design, conduct or interpretation of a study that could impact the reliability and validity of the scientific findings, and hence lead to an inaccurate or false conclusion being drawn. For this reason, clinical evidence is placed in hierarchies and RCT evidence has traditionally been considered the gold standard for reliably assessing treatment effects because of its perceived scientific rigour. However, RCTs are generally performed in patient populations pre-selected according to the criteria set out in the study protocol for a finite, usually relatively brief, period of time. In a real-world clinical setting, a therapeutic intervention is likely to be used in more diverse

populations often with co-morbid illnesses and for longer periods. Therefore, RCT evidence cannot be extrapolated or generalised to wider patient population. In view of this, there has been a call for a stronger and more sustainable approach to clinical evidence generation and for decision-makers to consider a variety of data sources, including those generated from observational studies, to guide decision-making. The EMA has set out the vision for "Clinical Evidence 2030" – to look at clinical evidence generation more holistically, and decision-making should be based on the full spectrum of data and valid methodological alternatives. This published policy is in recognition of the fact that the healthcare landscape in Europe is evolving and the convergence of several factors, including increasing focus on patients' needs and methodological advances.

Asia, by comparison, has largely prohibited or limited off-label promotions. China, for example, has remained relatively stringent in its prohibition of off-label advertisement and promotion, and such regulations have remained unchanged. Companies may not promote products off-label. Similarly, Singapore's Medicines Act holds that "unauthorised recommendations" (i.e., recommendations for off-label uses or purposes) are punishable offences. Japanese regulatory authorities have not provided regulations detailing exactly what information should be included in pharmaceutical advertising aimed at the general public, but the Ministry of Health, Labour and Welfare Standards states that if the advertising contains certain information such as names of the products, dosage, administration or safety, then the advertising must follow certain rules, including a prohibition on using language that constitutes off-label promotion.

Direct-to-Consumer ("DTC") Advertisements

Unlike many other jurisdictions, the United States currently permits manufacturers of prescription drug products to market such products directly to consumers. However, leadership under the new presidential administration that took office in January 2025 – including the Secretary of the Department of Health and Human Services ("HHS") under which FDA operates, Robert F. Kennedy, Jr. – has been vocally critical of DTC pharmaceutical advertising and has advocated for bans on pharmaceutical firms' abilities to engage in DTC advertising activities. Critics of DTC advertising have raised concerns that it serves to, among other things, promote unnecessary medication use, contribute to escalating healthcare costs and raise conflicts of interest. To date, there has been no official action to ban or meaningfully restrict DTC advertising. Importantly, a ban on DTC advertising would require legislative action and would face significant opposition from industry stakeholders on First Amendment grounds, among other objections. That said, it is possible that Congress could pass more tailored amendments to DTC advertising laws (e.g., based on current proposals to prohibit DTC advertisements for new drugs during the first year post-approval, or that give FDA more authority to regulate social media influencers), and FDA could also engage in various administrative steps that could impact the ability of firms to engage in DTC advertising (e.g., expanding its existing DTC Television Ad Pre-Dissemination Review Program to require all TV advertisements be submitted at least 45 days before dissemination; slowing review of such advertisements; proposing new regulations or guidance to require more risk disclosures).

Even before the new administration took office, there had been a renewed focus on DTC advertising in both Congress and at FDA. Throughout 2024, United States senators had engaged in continuous communication with FDA regarding concerns about pharmaceutical product promotion on social media, including perceived gaps in FDA's oversight of product communications by telehealth companies, social media influencers and other third parties. Additionally, FDA had issued various enforcement actions directed toward pharmaceutical companies' DTC advertising practices in late 2024. For example, in August 2024, the Office of Prescription Drug Promotion ("OPDP") issued an "untitled" letter to AbbVie related to a DTC TV advertisement for UBRELVY that featured tennis star Serena Williams. In its letter, OPDP stated that "the use of a celebrity athlete in this TV advertisement amplifies the misleading representations and suggestions made and increases the potential for audiences to find the misleading promotional communication more believable due to the perceived credibility of the source". OPDP subsequently issued similar letters to other pharmaceutical manufacturers citing concerns about, among other things, the use of celebrities in DTC advertising (e.g., an October 2024 "untitled" letter to Merz Pharmaceuticals raised concerns about an Instagram advertisement for XEOMIN posted by TV personality and designer Nate Berkus).

FDA's approach to regulating DTC advertising is in line with the unique considerations that underpin the specific requirements and regulations governing DTC advertising under the Federal Food, Drug, and Cosmetic Act. This unique approach is due, in large part, to the fact that the broader population may be less capable of assessing the risks and benefits of such products. Among these regulations is the requirement that DTC human prescription drug advertisements in TV or radio format that state the name of the drug and its conditions of use also present the major statement relating to side effects and contraindications ("Major Statement") in a clear, conspicuous and neutral manner. In November 2023, FDA published a long-awaited final rule amending its prescription drug regulations to reflect this requirement and to establish standards to help ensure that manufacturers understand how to comply with this requirement ("Major Statement Rule").

The Major Statement Rule establishes five standards for conveying the Major Statement in a clear, conspicuous and neutral manner. These standards include:

1. the Major Statement should be presented in consumer-friendly language and terminology that is readily understandable;
2. the audio presentation of the Major Statement is at least as understandable as the audio in the rest of the advertisement;
3. for advertisements in TV format, the Major Statement is presented concurrently in both audio and text and for long enough for the text to be read easily;
4. for advertisements in TV format, text information is presented in easy-to-read format; and
5. during the Major Statement, the advertisement does not include audio or visual elements, alone or in combination, that are likely to interfere with comprehension.

The five standards are aimed at addressing a longstanding concern by FDA and Congress that DTC advertisements may inadequately convey risk information to consumers. FDA has attempted to address this concern in the past by issuing numerous "untitled" letters to pharmaceutical companies for TV advertisements that contain attention-grabbing, distracting visual and audio elements (e.g., a person dancing to an upbeat song) and superimposed text slogans during the presentation of risk information that competed for the viewer's attention and allegedly made it difficult to adequately process risk information.

While the Major Statement Rule represents a step toward clarity by FDA, some of the standards in the rule include

broad and potentially subjective language, and FDA has yet to clarify how it will apply such standards in practice. In December 2023, FDA published a guidance document aimed at providing context and additional clarity for the implementation of these standards ("Major Statement Guidance"), but certain areas of ambiguity remain. For example, the terms "consumer-friendly" and "readily understandable" language are imprecise and have the potential to cause confusion. While the Major Statement Guidance provides some added clarity, stating that "medical or technical jargon or terms usually more familiar to health care providers" would generally not be considered "consumer-friendly" or "readily understandable", it does not provide sufficient clarity for implementation, particularly in contexts where risk considerations are complex, and some "jargon" may be necessary to avoid oversimplifying such risk information. Similarly, the rule does not provide additional context for how FDA interprets the phrase "at least as understandable" with regard to, for example, volume, articulation or pacing of audio. Additionally, the rule explicitly applies to prescription drug advertisements in "television and radio format" but does not provide clarity as to how broad the scope of that term is. The preamble to the rule acknowledges that "evolving technologies have allowed for DTC TV/radio advertisements to be presented on a broader range of devices and disseminated via a broader range of platforms" such as streaming platforms, podcasts, social media platforms or other digital communications channels, but FDA has not provided an explicit view on whether these media are within or outside the scope of this rule.

Whether and how FDA under the new presidential administration will increase regulatory scrutiny or adjust regulatory expectations in this space remains to be seen. However, HHS under Secretary Robert F. Kennedy, Jr. has advertised a philosophy of "radical transparency", stating that "FDA and HHS are committed to developing new guidelines for the industry on how they market drug risks and side effects, so the American people can make informed choices about their health". Though no such guidelines or policy initiatives have been formalised to date, such a position could lead to a significant evolution in the scope and type of disclosures that are expected or required to be made in advertising and promotional materials. It may also signal a re-focusing of enforcement priorities, with FDA turning a more discerning eye toward advertising and promotional materials that it views as insufficiently balanced as it relates to risk, use limitation and contextual disclaimers, among other things.

The proposed legislative revisions to the EU pharmaceutical law were positively adopted by the European Parliament on 10 April 2024. On 4 June 2025, the European Council adopted its position on the legislative proposal with more amendments being introduced. The Council will be ready to start negotiations with the European Parliament for the legislative texts to be finalised. The EU legislative process requires the European Parliament and the European Council to reach an agreement before a new piece of EU legislation can be passed by the so-called "co-decision procedure". The legislative proposal continues to restrict advertising of prescription medicinal products as well as medicinal products containing substances classified as psychotropic or narcotic to the general public. In addition, the proposed legislation imposes additional restrictions on advertising to the general public by requiring the advertising not to contain, among others, any material that: gives the impression that a medical consultation or surgical operation is unnecessary, by offering a diagnosis or by suggesting treatment by mail; refers to a purported recommendation by scientists, HCPs or persons who are celebrities with the effect of encouraging the consumption of medicinal products; suggests the safety or efficacy of a medicinal product because it is "natural"; or refers to claims of recovery in improper, alarming or misleading terms.

The Court of Justice of the EU ("CJEU") has clarified in recent rulings that the term "advertising of medicinal products" should be applied broadly to take account of the effect of the dissemination of information – including those related to financial incentives – on the purchase of medicinal products (both over-the-counter medicines and prescription-only medicines). The test resides on whether the disseminated information distracts from an objective evaluation of the need to consume a medicinal product. The Court further clarified that EU rules on advertising do not preclude a prohibition being introduced by EU Member States in their respective national domestic law.

Substantiation of Claims

Though enforcement by OPDP had briefly waned – with OPDP issuing no warning or "untitled" letters in over a year from June 2022 to June 2023 – a flurry of OPDP enforcement activity since mid-2023 has provided some insight into FDA's enforcement priorities. Since June 2023, OPDP has issued 12 enforcement letters, including its first warning letter since February 2022, and a significant portion of OPDP's relatively rare enforcement letters in recent years has focused on key issues raised by FDA's guidance on CFL communications, which addresses communications regarding information and data that do not appear within a product's approved labelling but are nonetheless consistent with such labelling. OPDP's recent enforcement letters indicate that, in addition to FDA's continued focus on the presentation of risk information in promotional materials, FDA is taking a particularly close look at CFL communications.

In an August 2023 warning letter issued to AstraZeneca related to its promotion of BREZTRI AEROSPHERE – OPDP's first warning and only warning letter since early 2022 – OPDP focused on promotional claims based on clinical trial data that did not appear in the labelling. In the letter, FDA stated that, among other things, the failure of the study to show significant results on endpoints higher in the analysis hierarchy, as well as potential compounding factors, made it such that "no conclusions…can be drawn from the…trial". Similarly, FDA issued an "untitled" letter in January to Novartis related to its promotion of KISQALI in TV advertisements. Among the issues raised by FDA was Novartis's inclusion of quality-of-life claims based on patient-reported outcome ("PRO") data obtained during the course of a clinical trial because, among other things, the PRO data was considered an exploratory secondary endpoint. Given this, and due to other limitations associated with the PRO analysis, FDA took the position that the data did not support the quality-of-life claims. Notably, FDA also took issue with the way in which necessary contextual disclaimers were presented in the TV advertisement, noting that the presentation of material information about the product's efficacy is "undermined by multiple, competing presentation aspects that distract the viewer".

More recently, OPDP appears to have taken an even more aggressive stance in various warning letters. For example, in August 2024, OPDP issued an "untitled" letter to Mirati Therapeutics related to clinical data provided on an HCP-branded website related to KRAZATI, which had been approved under FDA's accelerated approval pathway. Though there was little to no characterisation of the data, the letter takes issue with the fact that all of the data was presented in the context of a website layout that connected the data with the concept of

"efficacy" when, from FDA's perspective, some of the underlying data were not capable of supporting, or of conclusively supporting, efficacy claims. Notably, the webpage included numerous disclaimers and disclosures explaining the limitations of the data, but OPDP stated that these were "not sufficient to mitigate the overall misleading impression created by the inclusion of [the] presentation" of the data. OPDP issued a similar letter to Taiho Oncology in March 2025 related to clinical data provided on an HCP-branded website related to its oncology drug, LYTGOBI, which had also been approved under the accelerated approval pathway. As in the KRAZATI letter, the LYTGOBI letter objected to the inclusion on the "Efficacy Results" page of graphs/data on certain endpoints – despite the fact that the data were not accompanied by characterising statements – due to concerns that the underlying data were insufficient to support efficacy claims. Also, as in the KRAZATI letter, the LYTGOBI letter acknowledged the existence of disclaimers and disclosures contextualising the limitations of the studies, but ultimately dismissed them as insufficient to "correct or mitigate the misleading representations or suggestions of the presentation" of the data.

Given FDA's recent focus on efficacy claims that do not appear in product labelling, manufacturers engaging in such communications should be particularly conscious to avoid claims or characterisations regarding CFL data, particularly where there are study design or statistical limitations, as in the case of *post hoc* analyses, failed material endpoints and analyses not controlled for multiplicity. Additionally, manufacturers should take care when drafting disclaimers, ensuring that they are robust, prominent and complete as it relates to disclosing limitations, and clear where conclusions cannot appropriately be drawn. However, FDA's recent "untitled" letters indicate that even adhering to these limitations may be insufficient to avoid regulatory enforcement in certain contexts where FDA may view the underlying data as categorically insufficient or misleading perhaps including, for example, as it relates to drugs approved under the accelerated approval pathway. To date, there is no indication that FDA's approach to claims substantiation will change as a result of the new administration; indeed, the two letters issued in 2025 reflect similar themes to letters issued in the past. Whether the change in administration will ultimately impact FDA enforcement activity – whether as a result of shifting priorities or resource constraints due to workforce reductions at FDA – remains uncertain. Pending any demonstrable shift, it will be important to continue closely scrutinising product efficacy claims to ensure, *inter alia*, that the underlying data is sufficiently robust to support the claim, that appropriate context and disclaimers are conveyed and cover any material limitations, and that the presentation is appropriate for the intended audience.

While advertising and promotion in the EU is governed by a harmonised regulatory framework, enforcement of the requirements is undertaken nationally by the national regulatory authorities or the national self-regulatory bodies. Consistent with the prevailing EU legislative framework, the enforcement regimes implemented at a national level must be proportionate, dissuasive and effective. Enforcement actions can be judicially reviewed by the national courts, which can make a referral to the CJEU for a preliminary ruling on a question of interpretation that is new and of general interest for the uniform application of EU law. The case law of the CJEU is instructive in guiding how the harmonised advertising and promotional rules ought to be interpreted and applied. The CJEU has held in various rulings that advertising of medicinal products is liable to harm public health in the sense that it may give rise to improper use or ill-conceived or irrational use of medicinal products. The CJEU has ruled that irrational and excessive use of medicinal products may also arise as a result of advertising material. In common with the regulatory standards adopted in other countries, the EU and UK require objective claims to be supported by valid and verifiable evidence to promote rational use of a medicinal product.

Conclusion

Conversion of scientific ideas and evidence-based medical practices can improve health outcomes to benefit patients. Building a culture of trust, transparency, accountability and inclusion is increasingly essential to a vibrant life sciences ecosystem to propel the innovation agenda. Collaborations between the external stakeholders and industry are essential for advancing medical knowledge and improving patient care. Moreover, there is also an overall alignment among the international regulatory authorities as well as the industry trade associations to promote transparency in the clinical trial research process through improved and expanded disclosure of clinical trial data through publicly accessible portals.

In the world of greater transparency to gain trust in the scientific endeavours undertaken by medical researchers and industry, there is a greater demand by the scientific and medical community as well as patient advocacy groups for objective, unbiased research to be made available to inform individual clinical decisions, systematic reviews, meta-analyses and development of clinical guidelines. Some have strongly argued that HCPs and the public deserve to be in a position to make informed choices about the benefit-risk of new medical interventions.

It is now widely recognised that patients are active partners in their personal healthcare and their views are increasingly sought in the planning for research and development for innovative medical interventions and effective allocation of healthcare resources to ensure that patients are put in the centre of clinical care pathways to improve health outcomes. Providing healthcare services that respect and meet patients' and caregivers' needs are essential in promoting positive care outcomes and perceptions of quality of care, thereby fulfilling a significant aspect of patient-centric care requirements. Effective communication between patients and healthcare providers is crucial for the provision of patient care and recovery. Hence, patient-centred communication is fundamental to ensuring optimal health outcomes, reflecting long-held healthcare values that care must be individualised and responsive to patient health concerns, beliefs and contextual variables.

Compliance with the globally diverse regulatory regimes for controlling advertising and promotion for healthcare products should evolve and adapt to ensure that good practices apply to external engagements and communications with the external stakeholders.

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The authors would like to thank Michael Purcell for his invaluable assistance in preparing this chapter. Michael is an associate based in the Washington, D.C. office. He provides regulatory counsel for pharmaceutical, biotechnology, medical device, cosmetic and food companies, as well as healthcare providers and academic institutions, on a broad range of issues.

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