# Let's Get Real: Meredith Manning Urges FDA to Allow Greater Communication of Real World Data Within Its Current Regulatory Framework

Blog **Focus on Regulation**

## Hogan Lovells

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On October 26, 2016, Hogan Lovells partner Meredith Manning submitted a comment to the U.S. Food and Drug Administration (FDA) urging the agency to allow the use of observational data in manufacturers' advertising and promotion of drugs and medical devices. The FDA is holding a public meeting on "Manufacturer Communications Regarding Unapproved Uses of Approved or Cleared Medical Products," on November 9 and 10, 2016. Meredith argues that FDA can and should update its policies on the kinds of data manufacturers may rely on in marketing products to better serve public needs, and it can do so without upending its existing regulatory scheme.

**Background**

Observational studies or "real world data" refer to clinical data about a drug product that is derived from sources other than randomized controlled trials ("RCTs"). RCTs, considered the gold standard in showing substantial evidence of a product's safety and efficacy, aim to isolate treatment effects on an efficacy measure—typically a surrogate or intermediate endpoint—by eliminating noise from other confounding factors. In contrast, real world data focuses on how actual use of a drug in clinical practice affects a variety of outcomes for a broader population of patients.

FDA increasingly expects companies to conduct observational studies for post-marketing safety and monitoring, but requires RCT data to support a drug sponsor's promotional statements. FDA regulations mandate that any therapeutic claims in promotions be supported by "substantial evidence or substantial clinical experience." 21 CFR § 202.1(e)(6)(i). The agency interprets "substantial evidence" as RCT data based on the statutory definition of the term—i.e., data gathered from "adequate and well-controlled" clinical investigations. 21 U.S.C. § 355(d). Without providing guidance for "substantial clinical experience," FDA has over time conflated "substantial clinical experience" with "substantial evidence," and consequently, with RCT data.

With respect to health care economic information ("HCEI"), the Food and Drug Administration Modernization Act of 1997 (FDAMA) allows HCEI claims to be based on "competent and reliable" scientific evidence. 21 U.S.C. §352(a). FDA has not explicitly invoked or defined this standard, but in enforcement letters has applied it under the label of

"adequate evidence" to mean RCT-based data. Yet the Federal Trade Commission (FTC), which also deals with false or misleading advertising claims, has interpreted "competent and reliable" more flexibly to cover objectively-evaluated evidence based on relevant professional expertise yielded by generally-accepted procedures in the profession. FTC's approach shows that nothing in the statute requires FDA to limit FDAMA's "competent and reliable" standard to RCT data.

**Why Real World Data?**

In the United States and elsewhere, government agencies and private payors alike recognize the value of real world data about pharmaceutical and biological products. Various agencies now call for real world data in their approval and post-approval monitoring processes, including the Center for Devices and Radiological Health (CDRH), the Centers for Medicare and Medicaid Services (CMS), the Agency for Healthcare Research and Quality (AHRQ), the United Kingdom's National Institute for Health and Clinical Excellence (NICE), and the European Medicines Agency (EMA). So too do private payors like the Academy of Managed Care Pharmacy (AMCP), which calls for real world data in formulary applications. FDA is behind on this growing trend.

FDA should heed the call to accept high-quality real world data as valid bases for therapeutic and HCEI promotional statements. Meta-analyses have shown that real world data can closely track RCT data in determining efficacy and incidence of side effects. But real world data also provides information that RCT data simply cannot reveal. It can shed light on other outcomes that may be more valuable to patients and payors: cost, utilization, cost-effectiveness, and impact on quality of life. It can also provide comparative information across different treatments and show how confounding factors typically designed out of an RCT affect patients using the product. Observational data thus provides unique and valuable information to FDA, as well as to physicians, patients, and the parties it regulates.

Most importantly, Meredith illustrates in her comment that FDA can incorporate observational data without undermining the statute's approval standards. First, FDA can more clearly define "substantial clinical experience" in its regulations to include such data, as distinct from the clearly RCT-based "substantial evidence" standard. It can do so by issuing a guidance document or by amending the language in the regulations. Second, FDA can articulate a definition of "competent and reliable" evidence for HCEI claims that tracks FTC's practices. By taking these steps, FDA can bring the unique advantages of real world data into the pharmaceutical space in a way that helps the agency and the constituencies it serves.

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