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AMCP Seeks an End to 20 Years of Confusion Over FDAMA Section 114

The law was supposed to give drugmakers freedom to share health care economic information about their products. Efforts to get clarity from the FDA are stepping up.

Michael D. Dalzell
Senior Contributing Editor

Value-based purchasing in health care has reached the point of no return, no matter who wins the White House or if the ACA were to get scrapped. The health care reform law has enabled or inspired so many changes in the infrastructure of American health care — ACOs and integrated delivery systems, federal and commercial quality-incentive programs, and CMS's alternative payment models — that it's hard to imagine that we'll go back to a time when dollars and outcomes traveled in different orbits.

The pharmaceutical industry may be the next frontier. As specialty drug costs began to challenge payer budgets and providers took on risk, demand for evidence of pharmacoeconomic value was inevitable. But even when manufacturers conduct health economics research, they frequently hesitate to promote it because of legal ambiguities about what they can say and to whom.

During President Clinton's second term, Congress passed the Food and Drug Administration Modernization Act (FDAMA). The act's much-talked-about Section 114 gave the pharmaceutical industry a safe harbor from the threat of penalties for off-label promotion when sharing economic information with decision makers. But the FDA issued no guidance on how to interpret the law, neutering it from the outset. A year after the law was passed, Nancy Cahill, a prominent health care attorney, told

a International Society for Pharmacoeconomics and Outcomes Research briefing that "the totally positive spin being put on the new legislation is alarming" and warned pharma to educate the FDA about health economics research or risk facing "regulations that run 180 degrees counter" to the intent of Section 114.

The Academy of Managed Care Pharmacy hopes to meet with the FDA soon to discuss clarifying Section 114, says Susan Cantrell, the organization's CEO.

In fact, the FDA never issued regulations to clarify the boundaries of promotion of pharmacoeconomic data. In turn, pharma companies, fearful of being penalized for off-label promotion, have erred on the side of caution, hesitating to take advantage of Section 114. "From our perspective, the issue is being able to have access to health care economic information that in some cases companies have but aren't free to give to managed care pharmacy professionals," says Susan Cantrell, CEO of the Academy of Managed Care Pharmacy (AMCP).

Why no guidance has been issued after almost 20 years is a matter of speculation, says Peter Neumann, director of the Center for the Evaluation of Value and Risk in Health at Tufts Medical Center in Boston. The FDA could have more pressing priorities, he says, or may recognize the difficulty of drawing fine lines. "It's hard, and in a way you could argue that the FDA shouldn't even worry about it, as long as these are companies talking with formulary committees. 'Let them figure it out' — which is kind of what FDA has said in not saying anything."

The FDA's inaction regarding clarifications to Section 114 could stem from a difficulty in drawing fine lines, says

Or, he says, the agency's inaction could stem from "a feeling in certain places that we shouldn't allow drug companies to promote health economic information outside the clinical trials because they will mislead customers, including managed care. You'll take away the incentives to do the trials they should be doing if they can promote based only on database studies and models."

Another reason for the FDA's silence may relate to the AMCP's release of its Format for Formulary Submissions in 2000. Manufacturers often include pharmacoeconomic data or modeling in an AMCP dossier. When a health plan makes an unsolicited request for an AMCP-style dossier, the

Peter Neumann of Tufts Medical Center.

prevailing opinion is that pharma needn't worry about running afoul of the law; Section 114 refers only to direct promotion of pharmacoeconomic information. Payers often question the validity of pharma-generated economic data in the dossiers, but their inclusion has, at least, eased some of the angst over lack of clarity on Section 114 and given pharma an opening for making an economic case for their products to formulary committees, even if on a limited basis.

In recent years, however, with payers scrutinizing the value of high-cost specialty drugs and with provider groups taking on financial risk tied to outcomes, there is renewed interest in clarifying Section 114.

Four troublesome phrases

At an AMCP-sponsored forum last March, pharmaceutical companies, managed care organizations, academics, providers, and patient advocates developed recommendations for clarifying Section 114. AMCP touts the recommendations, published in July in the *Journal of Managed Care & Specialty Pharmacy*, as representing informed consensus for the development of FDA guidance.

Four clauses in Section 114 give drugmakers pause. In summary, Section 114 says (ambiguous phrases *italicized*) that FDA will not consider *health care economic information* that is provided to a *formulary committee or other similar entity* to be misleading if it *directly relates to an indication* and is based on *competent and reliable science*. At just 217 words, Section 114 is too lean to parse out the meaning of these four phrases, carving a wide path for interpretation.

Start with the difficulty of determining what health care economic information actually is. For instance, what if an insulin maker calculates and promotes lower downstream costs from avoidance of renal disease, based on known adherence rates for its product? That information won't be in the drug's labeling. But is it "health care economic information" under Section 114 — thus protecting the company from fines for off-label promotion? "There's a lot of nuance to health economic information," says Neumann. "All health economic information contains clinical assumptions, and you're potentially letting drug companies make clinical claims about their products through economic analysis."

In the end, the AMCP group defined health care economic information as "any analysis that identifies, measures, or compares the economic, clinical, or quality of

life consequences for any treatment."

As for who can receive health care economic information, the group proposed broadening the definition of "formulary committee or other similar entity" to include payer-like organizations that didn't exist when Section 114 became law, along with their employees "who make health care decisions for patient populations," such as clinical executives in a risk-bearing ACO. The group also included "organizations that develop value frameworks," such as the American Society of Clinical Oncology and the Institute for Clinical and Economic Review.

One of the issues concerning companies that develop drug compendia is determining the sources for their information, says Mary Jo Carden of AMCP.

The definition also includes organizations that develop drug compendia, such as Truven Health Analytics' MicroMedex DrugDEX and the National Comprehensive Cancer Network's Drugs and Biologics Compendium. "One of the issues with the compendia is: Where are they getting their information and what kind of information are they getting?" says Mary Jo Carden, AMCP's vice president for government and pharmacy affairs. Including compendia among entities eligible for receipt of health care economic information, she says, would improve the transparency and robustness of compendia information. The compendia form a key basis for Medicare payment — especially in the murky area of oncology, where compendia listings support determinations of medically accepted off-label use of cancer therapies.

All of this assumes the information meets Section 114's standard for "competent and reliable science," but what is that exactly? Section 114 does not provide standards. "In a way, that's the big one," says Neumann. "It's not always easy to figure out if something is competent and reliable, but we kind of know what it means: A study should be clear in their methods and transparent. They should do statistical controls in certain ways, they should do sensitivity analysis, they should control for bias as best they can. That's a competent and reliable study."

The AMCP group decided that competent and reliable should mean "truthful and non-misleading," but did not designate a body that would develop standards or serve as referee. One option, Carden suggests, is to use the principles of the CER Collaborative tool, a joint venture of AMCP, the International Society for

Pharmacoeconomics and Outcomes Research, and the National Pharmaceutical Council, as a rubric for judging the credibility of pharma-generated health care economic information.

Section 114's term "directly related to an indication," says Neumann, has always caused a lot of debate. "It seems to imply you can't make off-label claims in an economic analysis, but it leaves open the question of extrapolations across time and populations. Those lines can be fuzzy." The AMCP group viewed "directly related to an indication" to mean "information about a product that may vary from the parameters utilized in a randomized control trial, such as dosage forms, settings, or populations studied," as long as the information relates to the approved indication. That could, for instance, give pharma leeway to model savings to the health care system beyond the length of the clinical trial or for subpopulations, to name two examples. The AMCP group's final recommendation for FDA guidance called for changing "directly related to an indication" to "related to an indication."

That could work for products on the market, but what about products in the pipeline? Cantrell says payers at the AMCP forum made it loud and clear that waiting for product approval is too late to allow for actuarial adjustments. Carden recalls what happened when the new hepatitis C drugs hit the market: Plans were legally constrained from adjusting premiums or formulary tier cost sharing during the plan year, resulting in pharmacy costs running out of whack, and it was too late to file rate changes for the following year. "Had there been more ability to share information 12 to 18 months prior to approval, that planning could have occurred," she says. A future AMCP gathering will explore solutions to this issue in depth.

Walking the talk

Two years ago, the FDA published a notice that it would, at last, issue a clarification of Section 114. But the world is still waiting. Now, AMCP is moving to force the issue.

"We've been speaking to individuals who can help with this on Capitol Hill. We also are hoping to meet with FDA soon to share our recommendations and our members' perspectives on the issues, as well as the findings that came out of the forum," says Cantrell.

And AMCP is backing its talk with action, she adds: "We are working on language that could form the basis of guidance on FDAMA 114."

Congress has kicked the tires of Section 114 reform, inserting clarifying language in the 21st Century Cures Act. But with the bill stuck in an election-year meat grinder in the Senate, the next opportunity for legislative action may come next September, when Congress must reauthorize the Prescription Drug User Fee Act.

"We think there will be something on communication in that package," says Carden. "What specifically it is obviously will depend on what Congress does, but we think that the clarification of FDAMA Section 114, at a minimum, might be included in there."

Are pharma's fears justified?

The degree to which pharmaceutical companies invoke Section 114 of the Food and Drug Administration Modernization Act (FDAMA) when promoting product-related economic information is unclear, but the use of Section 114 is estimated to be low. Vague rules are thought to be the main reason, leaving manufacturers fearful of hidden tripwires when promoting a drug's potential for, say, cost savings or reduced resource utilization.

Research by Peter Neumann, director of the Center for the Evaluation of Value and Risk in Health at Tufts Medical Center, may offer some insight into pharma's tepid reception to Section 114. In a 2012 study published in the journal *Value in Health*, Neumann found that between 2002 and 2011, the FDA's Division of Drug Marketing, Advertising, and Communications (since renamed the Office of Prescription Drug Promotions) issued 291 warning letters for misleading promotions — 12% of which contained what the division considered to be inappropriate economic claims. More than half of these violations related to claims of cost savings stemming from improved functioning or work productivity.

Interestingly, however, none of those letters mentioned a violation of Section 114, "nor have there been any, to my knowledge, since then," Neumann tells Managed Care. "That tells you something about the difficulty in interpreting [Section 114] and the FDA's reluctance to write [warning] letters about this."