What Ever Happened to FDAMA Section 114? A Look back after 10 Years  
Peter J. Neumann, ScD

Center for the Evaluation of Value & Risk in Health, Tufts University School of Medicine, Boston, MA, USA

Correspondence to Peter J. Neumann, Center for the Evaluation of Value and Risk in Health, Professor, Tufts University School of Medicine, Institute for Clinical Research and Health Policy Studies, 800 Washington Street, Tufts Medical Center, No. 063, Boston, MA 02111, USA. E-mail: pneumann@tuftsmedicalcenter.org [Value in Health. 2009;12(2):189-190]

ABSTRACT

No Abstract

ARTICLE TEXT

The United States Food and Drug Modernization Act (FDAMA) took effect in 1998 with high expectations from the pharmacoeconomics community. Section 114 of the Act stipulated the conditions under which drug companies could promote health economic information to their managed care customers, and seemingly would make it easier for pharmacoeconomic modelers and outcomes researchers to communicate their work. A small survey (n = 36) of pharmaceutical and managed care representatives, conducted in the months after Section 114’s enactment, found that most respondents believed the Act would encourage companies to present more health economic data to managed care plans [1].

In fact, 10 years later, one hears little about Section 114. The Food and Drug Administration (FDA) never issued guidance. Congress never revisited the legislation. An Internet search of the topic confirms the lack of attention—symposia and articles on the topic, circa 1999, are among the leading entries. An unscientific personal survey of industry and FDA sources reinforces the notion: Drug company economists have largely moved on; agency officials say that submission levels have been low under Section 114, and that they are somewhat surprised by the trend.

What Happened?

Several theories could explain the lack of attention to Section 114.

Theory No. 1: Section 114 Was Too Restrictive

The first theory holds that rather than stimulating drug company promotion of health-care economic information, Section 114 actually dampened enthusiasm for it.

The reason is that while Section 114 illuminated the conditions under which companies could promote health economic information—and relaxed the standard for
such information from "adequate and well-controlled trials," to "competent and reliable scientific evidence"—it also codified substantial restrictions. For one thing, the Section applies only to health economic communications to "formulary committees or similar entities" (as opposed to physicians or consumers). More importantly, the Section states that health economic information provided under Section 114 must be "directly related to a labeled indication."

The "directly related" clause seems to restrict economic promotion to end points studied in Phase III randomized clinical trials (and then only to those that made it into the label). Indeed, a strict reading of Section 114 suggests that it would prohibit the use of economic models that extrapolate from surrogate end points to longer-term outcomes, if those long-term outcomes were not included (and did not demonstrate statistical significance) in trials. Models that extrapolate from surrogate end points such as lipid levels to estimates of cost per life-years gained are not permitted, unless Phase III trials of the drug under investigation demonstrated a mortality gain. Similarly, Section 114 seems to ban most cost per quality-adjusted life-year estimates, which are based on such surrogate markers, although they are widely recommended and used in the health economics community, because they imply mortality gains.

In fairness, the FDA has apparently permitted some flexibility in its interpretation of Section 114's "directly related" clause if a drug company has established evidence from clinical trials on "hard" surrogate end points such as cardiac events. That is, while a drug company could not use Section 114 to make a claim based on a modeling projection from lipid levels to cost per QALYs, it could make such claims based on projections if it possessed sufficient evidence on the drug's impact on myocardial infarction or stroke (Joe Jackson, personal communication). Section 114 would also allow cost per surrogate end point comparisons.

The fact that FDA never released guidance on Section 114 may have made drug companies even more cautious. The uncertainty surrounding what constitutes appropriate dissemination of health economic information may have had a spillover chilling effect on health economic promotion in medical journal advertisements, which fell from 16% of all print ads in 1997 to 4% in 2002, even though print ads are not covered by Section 114 [2].

**Theory No. 2: The AMCP Format Co-Opted Section 114**

The second possibility is that the development of the Academy of Managed Care Pharmacy (AMCP) Format [3] and its use by health plans have made Section 114 much less relevant. By calling on health plans to request that drug companies submit dossiers that include economic information, the AMCP has co-opted Section 114.

The Format obviates the need for Section 114 because the FDA considers health plan appeals for information—for economic models, for retrospective database analyses, for off-label data, and for unpublished studies—"unsolicited requests," which sidestep regulatory rules governing substantiating evidence (including those contained in Section 114). If health plans request AMCP Format-type dossiers, drug companies are
permitted great flexibility—well beyond that allowed under Section 114—to disseminate pharmacoeconomic information [4]. Evidence indicates that many health plans in the USA now use the AMCP Format or related processes [5–7] and virtually all major manufacturers prepare and submit these dossiers for their important drugs. The Format is, in effect, a "safe harbor" for manufacturers for their entire economic toolbox. As a result, Section 114 has become something of a sideshow.

**Theory No. 3: Companies Do Use Section 114 but Quietly**
A third possibility is that drug companies are, to some unknown degree, using Section 114 to communicate health economic information to managed care audiences. It is difficult to know the extent to which this occurs, because FDA does not require companies to designate promotional materials submitted to the agency as Section 114 submissions. Moreover, FDA only scrutinizes a small percentage of the promotional materials it receives.

Privately, drug firm and agency officials acknowledge that some promotional activities under Section 114 do occur. More formal research (e.g., a survey of manufacturers about their practices) would be useful. In theory, one could also issue a request under the Freedom of Information Act (FOIA) for all promotional materials submitted to FDA and sift through them to find examples of Section 114 cases, but it would be impractical. FDA receives over 50,000 promotional submissions per year, and only a tiny fraction is related to Section 114. Moreover, a telephone call to the FOIA office at FDA reveals that there is a several year backlog for FOIA inquiries and that bulk, unspecific requests to their office would not be given high priority.

**What Next?**
It is likely that all of the theories noted above hold some truth: Section 114 provided a relatively minor boost to the dissemination of pharmacoeconomic data; over time, requests for economic information via AMCP dossiers began to overshadow Section 114; and some level of Section 114 promotion continues. Yet another reality is that other events—from safety to comparative effectiveness—have assumed greater importance since FDAMA was enacted, and that industry and FDA have more pressing concerns.

While Section 114 has garnered little attention, however, it remains the law of the land. There are still instances in which companies desire to promote health economic information proactively to P&T committee members and others at health plans. While the AMCP Format may have relegated Section 114 to a back burner, it did not remove it entirely. Yet, 10 years after the legislation's enactment, what is permissible under Section 114 remains murky.

The FDA could still issue guidance on Section 114, although the agency does not seem predisposed to do so, given its other priorities, and the fact that there is little external pressure on the matter. Given the increasing importance of unsolicited requests for economic information, FDA could also issue guidance on unsolicited
requests. The agency had once promised to issue guidance on unsolicited requests, but this too now seems unlikely, given thorny regulatory and legal issues it raises regarding free speech.

The absence of guidance leaves open questions: Where is the "line" for Section 114 promotions? What constitutes appropriate communication surrounding requests for AMCP-Format-type submissions? When are requests for dossiers genuinely unsolicited? and When is health economic information—even if provided in response to an unsolicited request—false or misleading? A legitimate question is whether FDA guidance would help or hinder the field. On the one hand, guidance could clarify the regulatory terrain. On the other, by setting down rules, it might simply serve to further restrict useful communication.

Without formal guidance, the field will carry on. Preferably, FDA will interpret Section 114 as flexibly as possible if challenges arise. Ideally, the spirit behind Section 114—that business-to-business communications about health economic data should be permitted more latitude—will prevail. The outcomes research community can help by continuing to monitor the field and by setting standards for modeling and for "real world" data [8].

Section 114 was an attempted solution to a peculiarly American problem. In other countries, the regulatory authorities do not worry as much about health economic promotions to managed care, because the "customers" in these countries are government health officials, who can decide for themselves what information they would like to review. In the USA, because of the private nature of the health system, regulations of these business communications were deemed required.

A decade after its enactment, Section 114 endures but has not fulfilled its promise. Even so, the field of pharmacoconomics has continued to develop and even thrive. The state of the art for modeling has advanced. Health plans are adopting the AMCP Format (which in fact provides a better vehicle for communication than Section 114 because it empowers plans to become active participants in debates about evidence and value). The measurement of value is at the forefront of the US health-care agenda. This progress has occurred despite Section 114, not because of it.

References


3 Academy of Managed Care Pharmacy. The AMCP Format for Formulary


