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*Health Policy Analysis*

# FDA Actions Against Health Economic Promotions, 2002–2011

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ABSTRACT

**Objective:** To investigate Food and Drug Administration (FDA) regulatory actions against drug companies' health economic promotions from 2002 through 2011 to understand how frequently and in what circumstances the agency has considered such promotions false or misleading. **Methods:** We reviewed all warning letters and notices of violation ("untitled letters") issued by the FDA's Division of Drug Marketing, Advertising and Communications (DDMAC) to pharmaceutical companies from January 2002 through December 2011. We analyzed letters containing a violation related to "health economic promotion," defined according to one of several categories (e.g., implied claims of cost savings due to work productivity or economic claims containing unsupported statements about effectiveness or safety). We also collected information on factors such as the indication and type of media involved and whether the letter referenced Section 114 of the Food and Drug Administration Modernization Act. **Results:** Of 291 DDMAC letters sent to pharmaceutical companies during the study period, 35 (12%) cited a health economic violation. The most common type of violation cited was an implied claim of cost savings due to work productivity or functioning (found in 20 letters) and economic claims containing unsubstantiated comparative claims of effectiveness, safety, or interchangeability (7 letters). The violations covered various indications, mostly commonly psychiatric disorders (6 letters) and pain (6 letters). No DDMAC letter pertained to Food and Drug Administration Modernization Act Section 114. **Conclusion:** The FDA has cited inappropriate health economic promotions in roughly 12% of the letters issued by the DDMAC. The letters highlight drug companies' interest in promoting the value of their products and the FDA's concerns in certain cases about the lack of supporting evidence.

***Keywords:*** FDAMA Section 114, Food and Drug Administration, health economics, promotional claims.



The U.S. Food and Drug Administration (FDA) regulates pharmaceutical labeling and advertising to ensure that claims made by drug companies about their products are not false or misleading. The agency has interpreted its mandate broadly to include "virtually all information dissemination activities by or on behalf of a prescription drug manufacturer" [1]. Thus, FDA oversight includes promotional materials containing *health economic* claims, such as statements that a drug "saves money" or "lowers costs."

The FDA's Division of Drug Marketing, Advertising and Communications (DDMAC) monitors and reviews pharmaceutical promotions and takes action against advertisements found to be "false, lacking in fair balance, or otherwise misleading" [2]. (DDMAC was renamed the Office of Prescription Drug Promotions in September 2011, but we retain the name DDMAC in this article because it prevailed during all but 4 months of the study period.) All pharmaceutical promotional pieces distributed in the United States must be submitted to the DDMAC at the time of initial dissemination [3]. For promotions that the DDMAC considers in violation of regulatory standards, actions may include an "untitled" letter of notice of violation or a formal warning letter [4]. Warning letters are more serious than untitled letters, and failure to address issues raised in them may result in recalls, seizures, injunctions, administrative detention, and criminal prosecution [4].

Drug company promotion of health economic information targeted toward individual physicians or consumers must adhere to FDA's conventional "substantial evidence" provision, which typically means that statements must be supported by two adequate and well-controlled clinical trials [5,6]. U.S. law makes an exception for health economic information targeted to formulary committees or similar entities. Such communication is governed by Section 114 of the Food and Drug Modernization Act (FDAMA), which stipulates that health economic information provided under these circumstances shall not be considered false or misleading if it directly relates to an indication approved and is based on "competent and reliable scientific evidence" (rather than substantial evidence) [7].

Little is known about how the FDA has regulated health economic promotions, including how vigilantly it has overseen the area, and the types of economic promotions it has found lacking. Previously, we analyzed FDA regulatory actions on health economic promotions from 1997 through 2001 [8]. We found that roughly 5% of the letters issued during that period cited a false or misleading health economic claim—most commonly an economic promotion containing an "unsupported comparative claim of effectiveness, safety, or interchangeability." Since 2001, the health care landscape has changed with ever more intense focus on the

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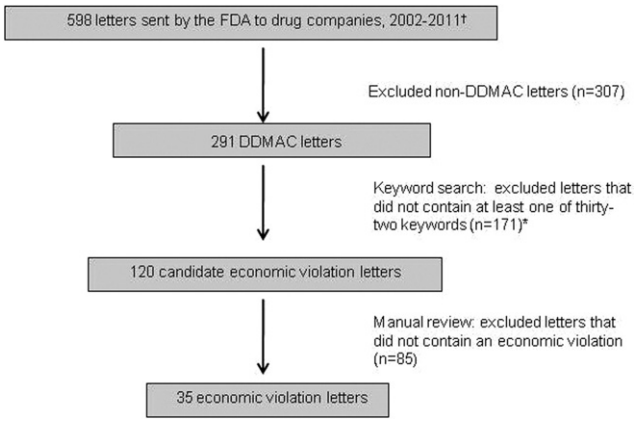


**Fig. 1 – Search methodology. *Includes letters sent by FDA's Division of Drug Marketing, Advertising and Communication (DDMAC), Division of Compliance Risk Management and Surveillance, Division of Manufacturing and Product Quality, Division of New Drugs and Labeling Compliance, or the Division of Scientific Investigations between January 22 and December 2011. DDMAC was renamed the Office of Prescription Drug Promotions in September 2011, but we retain the name DDMAC in this article because it prevailed during the study period. †Keywords included cost, savings, expenditure, expensive, expense, spending, price, pricing, economic, affordable, value, cost-effectiveness, cost effectiveness, cost-benefit, cost benefit, pharmacoeconomic, hospitalization, utilization, doctor visit, physician visit, office visit, registry, observable data, copay, co-pay, budget, productivity, Section 114, fired, job, and work (defined as place of employment [n.] or to be employed [v.]).**

economic value of therapies. In this article, we expand on our previous analysis and update it through 2011. Our objectives were to understand the frequency and nature of FDA regulatory actions against inappropriate health economic promotions since 2001. We also investigated whether the FDA has ever issued a regulatory action pertaining to a violation of FDAMA Section 114.

## Methods

### *FDA notice of violation and warning letters*

The FDA's Web site provides the full text of all warning letters and notices of violation ("untitled letters") issued to pharmaceutical companies for various kinds of infractions [9,10]. Between January 2002 and December 2011, the FDA issued 598 such letters. We restricted our review to the subset of letters issued by FDA's DDMAC during this time period (n = 291). Thus, we excluded letters pertaining to manufacturer site inspections or good laboratory practices, investigator- or sponsor-related conduct, approval and labeling requirements and drug security, and other uncategorized compliance issues (Fig. 1).

### *Data abstraction and analysis*

We searched the DDMAC letters for health economic violations in several stages. First, we entered all 291 DDMAC letters into a single pdf file and searched it electronically by using 32 key words, such as "cost," "savings," "expenditure," "spending," "price," "economic," "affordable," "pharmacoeconomics," and "productivity" (see Notes to Fig. 1 for the full list).

The key words were selected on the basis of our earlier work and expanded upon to include economic terms found in health economic print advertisements [8,11]. Note that we included "productivity" claims, because work productivity is an important component of health economic analysis, though we had neglected to include it in our previous work. This search yielded 120 candidate letters. We randomly selected a sample of 30 of the 291 DDMAC letters for manual reading to examine whether any contained health economic claims not captured in the electronic search. We identified no such letters.

One of us (SKB) then read the entire text of each of the 120 candidate letters to determine whether it contained a genuine health economic violation. We considered a letter to contain a health economic violation if it included an infraction cited by the FDA pertaining to drug price or co-payment, cost per dosage, failure to consider or advertise certain costs, misleading or inappropriate claims about work productivity, or avoided hospitalization or surgery, or any mention of other economic or financial issues. Finally, we reviewed each of the resulting economic violation letters with the aid of a data abstraction form. On the basis of public remarks by a DDMAC official about the type of action that may constitute a health economic violation [12] and an expansion of our earlier work [8], we categorized each letter into one of several possible categories:

- Implied claims of cost savings due to work productivity/functioning;
- Unsupported claim of effectiveness, safety, or interchangeability;
- Implied claims of cost savings to broader audience than applicable;
- Claims of cost savings when there are obvious additional costs that may affect cost savings;
- Cost comparisons of dosages that are not comparable;
- Claims that encouraged switching on the basis of a lower price when there may be risks associated with the switch; and
- Other misleading price comparisons.

We also collected information from each correspondence on the type of letter (warning or untitled), the company, product, indication, type of media involved (e.g., print, video), target audience (consumers, professionals), and whether the letter made any mention of FDAMA Section 114. FDA requires pharmaceutical companies to submit all pieces of promotional labeling or advertising for a drug product at the time of its initial release, and each must be accompanied by Form 2253, "Transmittal of Advertisements and Promotional Labeling for Drugs and Biologics for Human Use" [3]. We based our media category on the scheme used on Form 2253.

We pilot-tested the form on a sample of 25 letters and revised it for clarity and completeness. Most warning or untitled letters on the FDA's Web site are accompanied by the actual promotional materials containing economic violations, either as separate documents or at the end of letters themselves. In the majority of the cases (32 out of the 35 letters with health economic violations), we were able to download the promotional materials containing the economic violation. For the three cases in which we could not download the promotional materials, one was an oral statement made at a conference, one was a DVD that was not posted, and one provided a link to a file that was not working.

## Results

Of the 291 DDMAC letters issued to pharmaceutical companies (196 untitled letters and 95 warning letters), 35 (12%) cited an economic violation (including 14 warning letters and 21 untitled letters). The number of economic violation letters has remained