FDA Actions against Misleading or Unsubstantiated Economic and Quality-of-Life Promotional Claims: An Analysis of Warning Letters and Notices of Violation

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ABSTRACT

Objectives: The objective of this study was to understand the types of economic and quality-of-life promotional claims the FDA considers false or misleading.

Methods: Publicly available FDA letters (n = 569) sent to pharmaceutical companies from 1997 through 2001 for inappropriate promotional claims were reviewed. A standard data collection form was developed, including six categories for economic violations and three for QOL violations. For QOL, only letters with explicit violations for false or misleading claims using the words “quality of life” or patient “well-being” were considered. Other information collected included type of regulatory letter and media in which violations were found.

Results: Twenty-eight (4.9%) letters cited false and/or misleading economic claims. The most common economic violation was “unsupported comparative claim of effectiveness, safety, or interchangeability” (n = 14). Twenty-eight (4.9%) letters cited QOL violations, of which four contained both economic and QOL violations. The most common QOL violation was “lack of substantial evidence for QOL claims” (n = 15). None of the FDA letters used the term “patient reported outcomes.” Violations were found most frequently in brochure and Web site-based promotions.

Conclusions: The body of evidence that is emerging illustrates how the FDA is regulating promotional material containing misleading or unsubstantiated economic and QOL claims. However, knowing what constitutes an appropriate claim remains challenging because there are no formal guidelines describing what constitutes a violation, nor what level of substantiating evidence is required. More guidance may be needed to ensure appropriate use of these claims in drug promotions.

Keywords: drug advertising claims, violations, economic, quality of life, FDA.

Introduction

Actions by the Food and Drug Administration (FDA) for inappropriate safety and/or efficacy claims by drug companies have recently generated considerable public attention [1–4]. Although it has not received as much attention, the FDA also regulates promotional material containing economic and quality-of-life (QOL) claims, such as a drug’s cost-effectiveness or ability to improve quality of life [5]. These types of promotional claims are increasingly used by pharmaceutical companies to promote their products [6,7].

Accurate and appropriate advertising claims can provide valuable information about a drug to both consumers and prescribers. Pharmacoeconomic information may be particularly useful in the current cost-conscious environment. Section 114 of the Food and Drug Administration Modernization Act of 1997 provides guidelines for dissemination of health economic information to managed care formulary committees and similar entities [8,9]; however, there are no federal guidelines that specify the use of economic claims in promotions directed at individual professionals (e.g., physicians, nurses, pharmacists) and consumers. As a result, there may be some confusion about what types of economic claims are appropriate, including the level of evidence required. There may also be confusion about evidentiary requirements surrounding QOL claims. In particular, the language surrounding QOL measures is often vague and may be difficult to separate from clinical improvements (i.e., “improved functioning”) [5]. It also may be difficult to determine
whether improvements in only certain domains of QOL instruments versus improvement in all domains are truly representative of improvements in QOL.

We analyzed regulatory citations pertaining to US-based advertising and promotional activities to better understand the types of economic and QOL claims the FDA considers false or misleading. Our objectives were to determine the number and frequency of economic and QOL claim violations, the nature of the violations, and whether FDA remedial actions taken by the companies on these types of violations have increased over time.

In the United States, the Division of Drug Marketing, Advertising and Communications (DDMAC), a unit of the FDA’s Center for Drug Evaluation and Research (CDER), monitors and reviews pharmaceutical promotions and takes action against advertisements found to be “false, lacking in fair balance, or otherwise misleading” (FDA regulatory standards are set forth in the various provisions of the Federal Food Drug and Cosmetic Act and Code of Federal Regulations for Prescription Drug Advertising and Labeling) [10]. All pharmaceutical promotional pieces distributed in the United States must be submitted to DDMAC at the time of initial dissemination, required under FDA (regulation 21 C.F.R. Sect. 314.81b,3,I [April 28, 1002]) [11]. For those pieces that DDMAC considers in violation of regulatory standards, action may include either a warning letter or an untitled letter of notice of violation, both of which detail promotional pieces or practices that are in violation of the law. The difference between warning letters and untitled letters is that warning letters are more serious than untitled letters, and failure to address issues raised in warning letters may result in recalls, seizures, injunctions, administrative detention, and criminal prosecution [12–14].

Our analysis included all publicly available regulatory letters sent by the DDMAC to drug companies between January 1997 and December 2001. To our knowledge, this is the first study to formally evaluate regulatory letters issued on the basis of economic and QOL claims.

Methods

Letters of Notice of Violation and Warning Letters

The CDER Web site (http://www.fda.gov/cder/warn/) contains all notices of violation and warning letters sent by either DDMAC or FDA headquarters from January 1997 through December 2001 (under the Freedom of Information Act (FOIA), the FDA is required to post all notices of violation and warning letters sent to pharmaceutical companies) [15]. All letters on the Web site (n = 642) were downloaded and printed, and all warning letters and notices of violation that pertained to US-based advertising and promotional activities of pharmaceutical companies (n = 569) were included for further analysis. Both warning letters and notices of violation were included, as both types of communication result from the same review process [16]. Letters pertaining to manufacturing site inspections or good laboratory practice (n = 49), investigator- or sponsor-related problems (n = 16), IRB issues (n = 4), and sales of illegal drugs by foreign companies in the United States (n = 4) were not included for further analysis.

Data Abstraction Form

A data abstraction form (available from the authors upon request) was developed by reading a sample of letters to understand their basic content and then by pilot-testing the form on a sample of letters. Background information collected on the form includes reviewer information (i.e., reviewer initials and date of review), company and drug information (e.g., name of company, NDA of drug(s) cited, product name), and type of letter (e.g., warning letter or untitled letter). The form also includes categories of media cited for violations and the target audience (e.g., print advertisements directed to professionals, print advertisements directed to consumers, brochures directed to professionals, brochures directed to consumers, letters to professionals, sales aids, presentations/sales pitches, Web sites, press releases, and television commercials). If a letter cited brochures and/or print advertisements but did not specify whether professionals or consumers were the target audience, we assumed that the materials were directed to professionals.

Information collected about economic violations included the media cited for economic violations, target audience for advertisement, subtitle of paragraph describing the economic violation, type of violation, key phrases in the letter, and supporting evidence (e.g., AWP, published sources, data on file). We considered six types of false or misleading claims based on public remarks from FDA officials (categories 1–5) [5] and our pilot-testing experience (category 6):

1. Unsupported comparative claim of effectiveness, safety or interchangeability;
2. Implied claims of cost-savings to a broader audience than applicable;
3. Claims of cost savings when there are obvious additional costs that may affect cost savings;
4. Cost comparisons of dosages that are not comparable;
5. Claims that encouraged switching based on lower price when there may be risks associated with the switch;
6. Other misleading price comparisons.

Because no published descriptions of types of QOL violations were found, we did not include any predetermined categories of QOL violations on the data collection form. Rather, four open fields, in which to transcribe key sentences describing the violations, were included. QOL violations were subsequently categorized into the following three categories:

1. Lack of substantial evidence for QOL claims;
2. Promoting QOL claims for an investigational or unapproved drug;

None of the FDA letters we reviewed used the term “patient-reported outcomes” (PROs) to describe QOL violations [17]. To be consistent with language in the letters, only “QOL” was used to describe these types of violations.

Data Abstraction and Analysis

One author (KAS) reviewed each letter and entered all data onto an electronic form developed in Microsoft Access 2000. The other author (PJN) reviewed a sample of letters, including all letters citing economic and QOL violations. Identification of economic and QOL violations was based on either subtitles or key words within letters that described economic or QOL violations. Examples of subtitles identifying economic violations include “cost claims” [18], “misleading economic claims” [19], and “misleading pharmacoeconomic claims” [20]. Key words used to identify economic violations in letters without subtitles include “cost-effectiveness,” “cost,” “pricing,” and “expenditure.” Examples of subtitles describing QOL violations include “unsubstantiated quality-of-life claims” [21], “misleading health-related quality-of-life claims” [22], and “quality-of-life claims” [23]. For those letters without identifying subtitles, keywords used to identify QOL violations in letters were “quality-of-life” and “well-being.” We purposefully used a narrow definition of QOL keywords to avoid confusion with clinical outcomes related to functioning and to exclude claims related to satisfaction.

We report frequency of economic and QOL violations, as well as Fisher’s exact test to determine whether the proportion of violations differed over the study time frame. Statistical analyses were conducted using Microsoft Excel (Microsoft Corporation, Seattle, WA) and Stata (v. 7, 2000; Stata Statistical Software, College Station, TX, USA).

Results

Of the 569 letters reviewed, 522 (92%) were notices of violation and 47 (8%) were warning letters. From 1997 through 2001, 28 (4.9%) letters including 24 notices of violation and 4 warning cited false and/or misleading economic claims (Table 1). During the same period, 28 (4.9%) letters including 27 notices of violation and one warning cited false and/or misleading QOL claims (see Table 1). Four of the letters contained citations for both violative economic and QOL claims. There was no significant difference in the proportion of violations for economic claims over time (Fisher’s exact test, \( P = .45 \)), but there was a significant difference in QOL violations (Fisher’s exact test, \( P = .028 \)).

The most common economic violation involved an “unsupported comparative claim of effectiveness, safety, or interchangeability” (\( n = 14 \)), followed by “claims of cost savings when there are obvious additional costs that may affect cost savings” (\( n = 9 \)), and misleading price comparisons (\( n = 5 \)) (Table 2). Appendix A contains direct quotes from selected FDA letters describing the nature of the violations.

Table 3 reports the most common reasons cited for QOL violations including “lack of substantial evidence for QOL claims” (\( n = 15 \)), “promoting

| Table 1 Warning letters and notices of violation for economic and quality of life (QOL) claims (1997–2001) |
|---|---|---|---|---|---|---|
| Total No. of letters by year (n) | 1997 (145) | 1998 (164) | 1999 (109) | 2000 (82) | 2001 (69) | Total (569) |
| No. (%) with economic violations | 8 (5.5) | 5 (3.1) | 5 (4.6) | 7 (8.5) | 3 (4.3) | 28 (4.9) |
| No. (%) with QOL violations | 5 (3.5) | 5 (3.1) | 3 (2.8) | 7 (8.5) | 8 (11.6) | 28 (4.9) |

Note: Fisher’s exact test for economic violations, \( P = 0.4480 \); Fisher’s exact test for QOL violations, \( P = 0.0279 \).
Together, violations for economic and QOL claims were found most frequently in brochures (17.9% of all letters with economic and/or QOL violations), on Web sites (12.5%), and in letters which did not specify the media of the promotion (i.e., “nonspecified” materials) (12.5%) as indicated in Table 4.

### Discussion

Our results demonstrate that the FDA has sought to regulate promotional material containing unsubstantiated economic and QOL claims in recent years.

Although reasons for economic violations varied, almost 50% resulted from economic messages with unsupported comparative claims of effectiveness, safety, or interchangeability. These advertisements could be problematic if they induce physicians and patients to switch from a safer or more efficacious drug to a less safe or efficacious drug based purely on alleged cost savings or cost-effectiveness. For example, in a warning letter sent to one company, the FDA cited a television advertisement that “misleadingly suggests that [a drug] is similar in effectiveness to other cholesterol-lowering agents [. . .] and that the only difference between these agents is cost.”[24] The letter further states that “[the company] has not demonstrated that [drug . . .] is comparable in effectiveness to these other agents for its indicated uses”[24]. Other letters to

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**Table 2 Economic violations cited by DDMAC in warning letters and notices of violation (N = 28 letters)**

<table>
<thead>
<tr>
<th>Violation</th>
<th>n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Unsupported comparative claim of effectiveness, safety, or interchangeability</td>
<td>14 (50.0)</td>
</tr>
<tr>
<td>Claims of cost savings when there are obvious additional costs that may affect cost savings</td>
<td>9 (32.1)</td>
</tr>
<tr>
<td>Implied claims of cost savings to a broader audience than applicable</td>
<td>3 (10.7)</td>
</tr>
<tr>
<td>Cost comparisons of dosages that are not comparable</td>
<td>2 (7.1)</td>
</tr>
<tr>
<td>Encouraged switch based on lower price when there may be risks associated with the switch</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td>Misleading price comparisons</td>
<td>5 (17.9)</td>
</tr>
</tbody>
</table>

*DDMAC, Division of Drug Marketing, Advertising, and Communications. †Percentages add to more than 100% because 4 letters were categorized as having more than one type of violation.

**Table 3 QOL violations cited by DDMAC in warning letters and notices of violation (N = 28 letters)**

<table>
<thead>
<tr>
<th>Violation</th>
<th>n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lack of substantial evidence for QOL claims</td>
<td>15 (53.6)</td>
</tr>
<tr>
<td>Promoting QOL claims in investigational or unapproved drug</td>
<td>10 (35.7)</td>
</tr>
<tr>
<td>Selective presentation of QOL information</td>
<td>3 (10.7)</td>
</tr>
</tbody>
</table>

QOL claims in investigational or unapproved drug” (n = 10), and “selective presentation of QOL information” (n = 3). Appendix B provides direct citations from several letters detailing the nature of these violations.

**Table 4 Economic and QOL violations in various media**

<table>
<thead>
<tr>
<th>Medium</th>
<th>Economic (N = 28 letters) n (%)</th>
<th>QOL (N = 28 letters) n (%)</th>
<th>Total (N = 56 letters) n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Brochures</td>
<td>6 (21.4)</td>
<td>4 (14.3)</td>
<td>10 (17.9)</td>
</tr>
<tr>
<td>Web sites</td>
<td>2 (7.1)</td>
<td>5 (17.9)</td>
<td>7 (12.5)</td>
</tr>
<tr>
<td>Nonspecified materials</td>
<td>5 (17.9)</td>
<td>2 (7.1)</td>
<td>7 (12.5)</td>
</tr>
<tr>
<td>Press releases</td>
<td>1 (3.6)</td>
<td>4 (14.3)</td>
<td>5 (8.9)</td>
</tr>
<tr>
<td>Homemade materials, nonspecified</td>
<td>3 (10.7)</td>
<td>1 (3.6)</td>
<td>4 (7.1)</td>
</tr>
<tr>
<td>Print ads, professionals</td>
<td>2 (7.1)</td>
<td>2 (7.1)</td>
<td>4 (7.1)</td>
</tr>
<tr>
<td>Sales aid</td>
<td>1 (3.6)</td>
<td>2 (7.1)</td>
<td>3 (5.4)</td>
</tr>
<tr>
<td>Presentations/sales pitches</td>
<td>0 (0.0)</td>
<td>3 (10.7)</td>
<td>3 (5.4)</td>
</tr>
<tr>
<td>Letter to professional</td>
<td>3 (10.7)</td>
<td>1 (3.6)</td>
<td>4 (7.1)</td>
</tr>
<tr>
<td>Formulary kit</td>
<td>2 (7.1)</td>
<td>1 (3.6)</td>
<td>3 (5.4)</td>
</tr>
<tr>
<td>Exhibit booth panels</td>
<td>0 (0.0)</td>
<td>2 (7.1)</td>
<td>2 (3.6)</td>
</tr>
<tr>
<td>Promotional card</td>
<td>2 (7.1)</td>
<td>0 (0.0)</td>
<td>2 (3.6)</td>
</tr>
<tr>
<td>Reprint articles or reprint carrier</td>
<td>1 (3.6)</td>
<td>1 (3.6)</td>
<td>2 (3.6)</td>
</tr>
<tr>
<td>Posters</td>
<td>0 (0.0)</td>
<td>1 (3.6)</td>
<td>1 (1.8)</td>
</tr>
<tr>
<td>Box</td>
<td>1 (3.6)</td>
<td>0 (0.0)</td>
<td>1 (1.8)</td>
</tr>
<tr>
<td>Teleconference</td>
<td>0 (0.0)</td>
<td>1 (3.6)</td>
<td>1 (1.8)</td>
</tr>
<tr>
<td>Slim jim</td>
<td>0 (0.0)</td>
<td>1 (3.6)</td>
<td>1 (1.8)</td>
</tr>
<tr>
<td>Patient starter kit</td>
<td>0 (0.0)</td>
<td>1 (3.6)</td>
<td>1 (1.8)</td>
</tr>
<tr>
<td>TV ads</td>
<td>1 (3.6)</td>
<td>0 (0.0)</td>
<td>1 (1.8)</td>
</tr>
</tbody>
</table>

*In is the number of times cited at least once in a letter. †Percentages add to more than 100% because some letters were cited for more than one type of violation.
pharmaceutical companies also cite pharmacoeconomic claims where the efficacy and/or outcomes of different therapies are assumed incorrectly to be the same [19,25,26] as well as cost comparisons based on drugs with differing indications [27,28] and lack of adequate evidence for economic claims [29,30].

Economic promotions based on drug price comparisons and overall costs of treatment are being scrutinized by the FDA. For example, the FDA cited several companies for misleading comparative pricing analyses [31,32]. The FDA found these promotions inappropriate because most purchasers (i.e., consumers and managed care organizations) face different drug prices and comparative price claims in advertisements may not accurately reflect actual cost to consumers [31,32]. In addition, the FDA cited several companies for claiming that overall cost savings would result from the use of their drug when they failed to evaluate all pertinent costs of therapy beyond drug acquisition costs [20,33].

While the number of letters containing QOL violations is relatively low, we found a significant increase in the proportion of letters with QOL violations over time. This suggests that pharmaceutical companies may increasingly consider QOL a key attribute on which to promote a product, and/or that the FDA is becoming more vigilant in its oversight of QOL violations. The most frequent violation associated with QOL promotions was “lack of substantial evidence for QOL claims.” For example, an FDA letter to one company stated that “Materials that claim that [a drug] can ‘enhance daily living’ or that it offers ‘quality control of symptoms for daily living’ are considered to be false or misleading in the absence of adequate and well-controlled studies using validated instruments to determine benefit to health-related quality of life” [23].

More than one-third of the letters with QOL violations cited pharmaceutical companies for promoting improved QOL in unapproved or investigational drugs. The use of both off-label promotions and promotions of unapproved or investigational drugs have been the subject of much general debate and controversy [34,35]. These data suggest that QOL promotional claims need to be part of the discussion.

The third QOL violation apparent in the letters was “selective presentation of QOL information.” For example, the FDA cited one company for “present[ing] only the significant findings for two of six health related domains but fail[ing] to include the results for the four domains with nonsignificant findings” [36]. Although the least frequent QOL violation, it is potentially the most troubling as it underscores the difficulty in measuring and defining QOL in a meaningful way. In particular, there may be some confusion about which levels of health status measures are required to substantiate QOL claims. Ongoing discussions between FDA and industry to better define and understand QOL outcomes may help to clarify these issues in the future [34].

In general, more direction regarding the appropriate role and use of economic and QOL claims in drug promotions may be helpful. Currently, regulators and pharmaceutical companies face some uncertainty about what constitutes a nonviolative economic or QOL claim because there are no formal guidelines detailing what constitutes a violation, nor what level of substantiating evidence is required. The FDA continues to review issues related to economic and QOL claims on a case-by-case basis [5]. Development of guidelines for economic and QOL promotions along with examples of appropriate and inappropriate claims may help minimize the confusion and controversy about requirements for substantiating evidence and potentially reduce the number of violations.

There are several limitations to this study. First, we have no data on the total number of submissions of promotional materials to DDMAC, nor the number of these submissions that are actually reviewed by the FDA. We also have no data on regular correspondence between DDMAC and pharmaceutical companies that did not result in either a notice of violation or a warning letter, as this type of information is not collected by the FDA (L. Burke and L. Palmer, personal communication, DDMAC, August 6, 2001). It was sometimes difficult to determine, based on details provided in the letters, whether the target audience for advertisements consisted of physicians, decision makers in managed care organizations, pharmacists, other professionals, or consumers. Further research on the audience targeted by the claims would be useful.

Also, we took a conservative approach in defining QOL violations and did not include citations for false and misleading claims pertaining to attributes such as patient satisfaction and/or functioning. As noted, we also did not find any reference to “patient-reported outcomes,” a relatively new term being used to describe information collected from patients (e.g., QOL, functional status, treatment satisfaction) during clinical trials [17]. We also cannot draw any conclusions about overall trends in economic and QOL advertising and promotion, based solely on an analysis of regulatory letters. In
particular, promotions cited for violations may be different from promotions not cited for violations.

In the future, it would be helpful to explore other issues, such as whether a relationship exists between competition within a class of drugs and/or time since launch and use of misleading economic and QOL claims as when a drug company launches a new drug belonging to an established class of drugs and may promote its drug aggressively, thereby increasing the likelihood of using unsubstantiated or misleading economic and/or QOL claims. Furthermore, a better understanding of the precise evidence used to substantiate economic and QOL claims may also provide insights into problematic claims. It also would be useful to understand whether economic and QOL claims are developed by marketing departments, by outcomes research departments, or jointly. Ongoing analysis of these and other issues pertaining to promotion of economic and QOL attributes of drugs would help both industry and regulators to set mutually understandable guidelines for promoting drugs based on such end points.

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References
2 Carroll J. FDA orders Pfizer to pull drug ads that may mislead. The Wall Street Journal. 2001 Aug 1; Sect. B (col. 4).
17 Leidy NK. ISPOR participates in efforts to harmonize regulatory requirements for patient reported outcomes. ISPOR Newslett 2001 Aug 7;15(7):11.
Appendix A

Selected Examples of Economic Violations Cited by DDMAC in Warning Letters and Notices of Violation

1. Unsupported comparative claim of effectiveness, safety or interchangeability

“In the absence of substantial evidence that demonstrates that the treatment effects are comparable, the product cost comparisons are misleading.”

“... misleading because it implies that [a drug] is equally safe, effective and interchangeable with [competitor] for the doses compared.”

“. . . the misleading impression that [drug’s] costs to the customer or pharmacy will be lower than competitor’s at every dose or that its indications are the same as comparator drugs”

“. . . it implies economic superiority based on the assumption that the outcomes of the different therapies are the same.”

“The relative costs of [drug] to other cholesterol lowering agents is the focus . . . this focus, coupled with the misleading suggestions that these products provide comparable clinical benefit, suggests that that [drug] is the preferred cholesterol lowering treatment.”

2. Claims of cost-savings when there are obvious additional costs that may affect cost savings

“These claims imply that all costs associated with therapy have been evaluated, not simply the acquisition price of the drug.”

“These claims are misleading because they suggest, without adequate evidence, that [drug] reduces the overall cost of care in treating patients with BPH.”

“. . . there may be additional costs incurred for laboratory tests and office visits because of the need to titrate the dose of [drug].”

“. . . misleadingly suggest that [drug] positively impacts medical costs and productivity loss, when such has not been demonstrated by adequate evidence.”


3. Implied claims of cost savings to a broader audience than applicable
   “... misleading because retail pricing varies from community to community and may affect cost savings to patients.”
   “... misleading without the addition of context to clarify that the prices presented may not reflect actual prices paid by consumers or pharmacies.”
4. Cost comparisons of dosages that are not comparable
   “... patients... are not likely to understand that they may need a different dose of [drug] in order to obtain the same effect, and that this difference may reduce any potential savings.”
5. Misleading price comparisons
   “... comparative pricing claims are misleading because they lack adequate context... The cost-effectiveness claim is misleading because the claim is not supported by reference to AWP.”
   “The comparative price/cost conclusion of a ‘47% difference’ is misleading because the above price/cost comparison is based on an undefined time frame and therefore the conclusion of a 47% difference suggests a greater savings than what is supported by AWP data.”
   “DDMAC considers the headline regarding generic prices that references a table with only one generic drug to be misleading.”

Appendix B

Selected Examples of QOL Violations Cited by DDMAC in Warning Letters and Notices of Violation

1. Lack of substantial evidence for HRQL claims
   “[Company’s] broad claim of ‘patient well-being’ is not supported by substantial evidence and is therefore misleading.”
   “... false or misleading in the absence of adequate and well-controlled studies using validated instruments to determine benefit to health-related quality of life... The tagline ‘quality control’ is false or misleading because it is used out of context and can be interpreted to mean, without adequate substantiation, that [drug] can control health-related quality of life.”
   “... suggests, without adequate evidence, that [drug] improves quality of life.”
   “... not supported by substantial evidence. There have been no adequate and well-controlled studies examining the potential of [drug] to improve quality of life for patients or their families.”

   “... [Company] claimed that patients using [drug] demonstrated ‘improvement in well-being’... DDMAC objected to this claim... because the questionnaire did not meet the substantiation requirements for health-related quality of life claims.”
   “The [drug] formulary kit... suggests that treatment with [drug] has a positive effect on the HQRL of IBS patients. These representations are misleading because they are not based on substantial evidence, and overstate the efficacy of [drug] on the HRQL of IBS patients.”
   “Health-related quality of life claims such as these require substantial supporting evidence in the form of adequate and well-controlled studies designed to specifically assess these outcomes.”
2. Promoting QOL claims in investigational or unapproved drug
   “... [Company] is promoting [drug] as a safe and effective drug prior to its approval... [e.g., ] ‘[drug] provides statistical improvement in physical performance, mental skills, etc., and in the constellation of activities we call medically, the quality of life.’”
   “... you make several superiority claims... these claims include... ‘significantly greater increase in mean overall global improvement score at weeks 8 and 12’... These superiority claims for [drug] are false or misleading because the safety and efficacy of [drug], an unapproved new drug, has not been established.”
   “[Company] has engaged in promotional activities that state or suggest that [drug] is safe and effective for use in treating multiple myeloma [unapproved indication]. [Company] has also represented to physicians that [drug] can... promote a feeling of ‘general well-being’ in these same patients.”
3. Selective presentation of QOL information
   “[Company] has selectively presented only those quality of life parameters that suggest that [drug] is more effective than [competitor] in the treatment of osteoarthritis, omitting those parameters where the results for the 2 drugs were similar.”
   “... misleading selective presentation or “cherry-picking” of quality of life (QoL) data, and unsubstantiated asthma-specific quality of life claims for [drug]...”
   “[Company] presents only the significant findings for 2 of 6 health related domains but fails to include the results for the 4 domains with non-significant findings.”