January 18, 2008

Recent Trends in DDMAC Enforcement Activity

This client alert reviews the warning and untitled letters issued by FDA's Division of Drug Marketing, Advertising, and Communications (DDMAC) during 2007 and within the larger context of all such letters issued by DDMAC between 2004 and 2007.

We examined the 93 warning and untitled letters issued by DDMAC between 2004 and 2007. We tabulated the most frequent allegations in these years, leaving out allegations included in only a few letters. In addition, we reviewed the summary information for all warning and untitled letters issued between 1997 and 2003, which is posted on the website of the Center for Drug Evaluation and Research (CDER), but we did not review the actual letters for this period.

Overall, DDMAC issued fewer letters in 2007 than it has in any other year since 1997. Just over half of those letters were warning letters, which is lower than last year but consistent with prior years. Although the allegations in the letters issued in 2007 were generally similar to those issued in previous years, the number of letters in which DDMAC alleged misleading or unsubstantiated comparative or superiority claims spiked in 2007.

Our discussion of the warning and untitled letters focuses only on DDMAC's allegations and not on the promotional materials in question or the recipient's response to DDMAC.

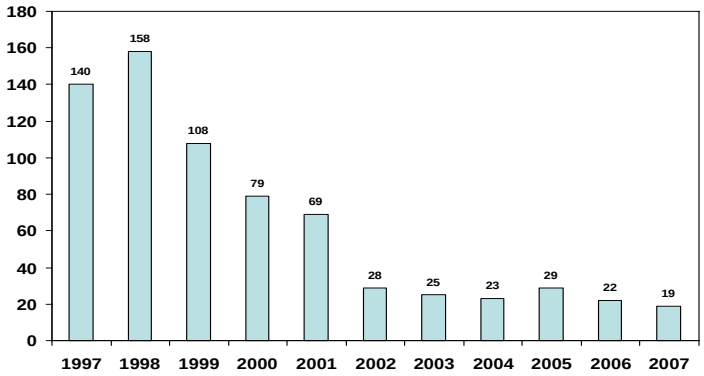
I. Number of Letters

A. Warning and Untitled Letters, Combined

In recent years, there has been a decline in the total number of letters issued by DDMAC, with the number of letters reaching a low of 19 in 2007—down from a high of 158 letters in 1998.

Total DDMAC Letters 1997-2007

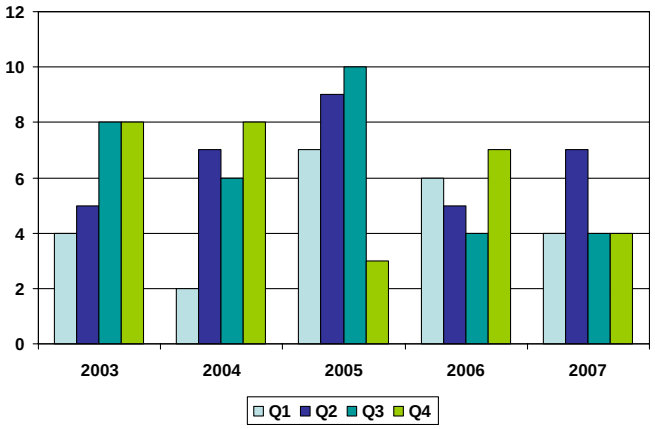
Source: C&B tabulation, based on letters on FDA website



The overall decrease in the number of letters is likely attributable to at least two factors. First, in 2005, most drug companies adopted a policy of submitting all DTC television advertisements to DDMAC for review prior to initial broadcast.[1] Second, a Health and Human Services policy, implemented in January of 2002, requires all warning and untitled letters to be reviewed by the Office of the Chief Counsel before they are issued.

Prior to 2006, DDMAC's enforcement activity was greater during the latter half of the year. But in 2006 and 2007, DDMAC reversed this pattern, issuing more letters in the first half of the year than in the second half. In 2007, DDMAC issued four letters in the first quarter, seven letters in the second quarter, four letters in the third quarter, and four letters in the fourth quarter.

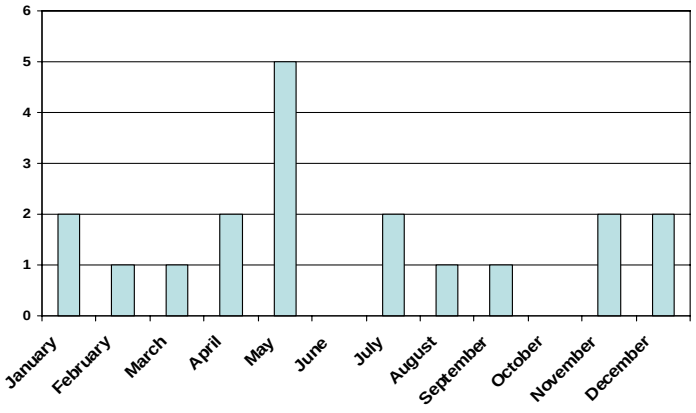
Total DDMAC Letters By Quarter 2003-2007
Source: C&B tabulation, based on letters on FDA website



[1] *See* Pharmaceutical Research and Manufacturers of America, *Guiding Principles on Direct to Consumer Advertisements About Prescription Medicines* (2005), *available at* http://www.phrma.org/files/DTCGuidingprinciples.pdf.

Moreover, throughout the course of 2007, DDMAC's enforcement activity was somewhat erratic. In May, DDMAC issued five letters (26.3 percent of the total), whereas in June and October, DDMAC did not issue any letters. On average, DDMAC issued 1.6 letters per month.

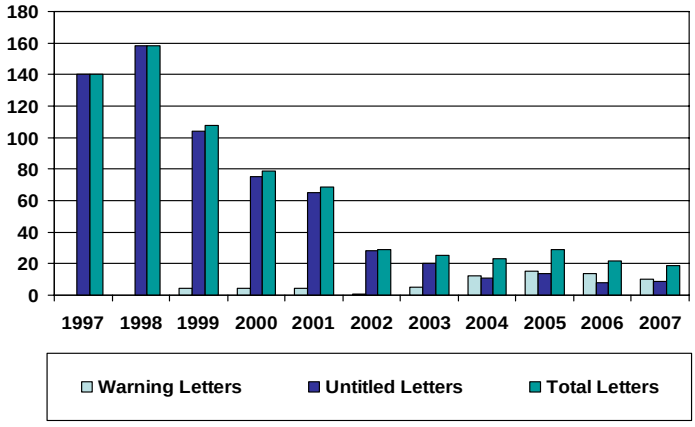
2007 DDMAC Enforcement Activity By Month
Source: C&B tabulation, based on letters on FDA website



B. Warning Letters

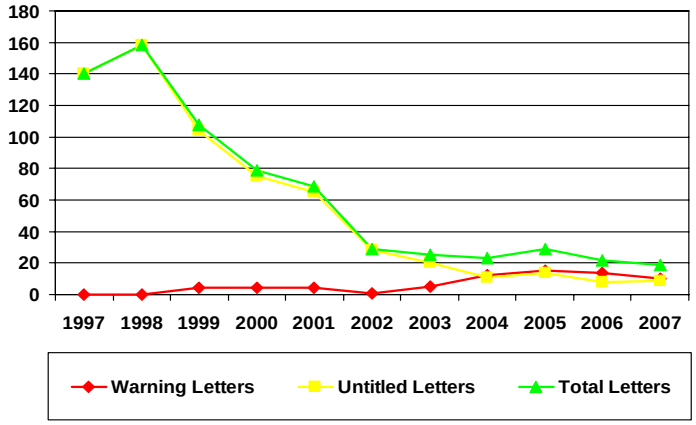
In 2007, DDMAC issued ten warning letters and nine untitled letters, continuing its recent trend (beginning in 2004) of issuing slightly more warning letters than untitled letters.

DDMAC Warning and Untitled Letters 1997-2007
Source: C&B tabulation, based on letters on FDA website



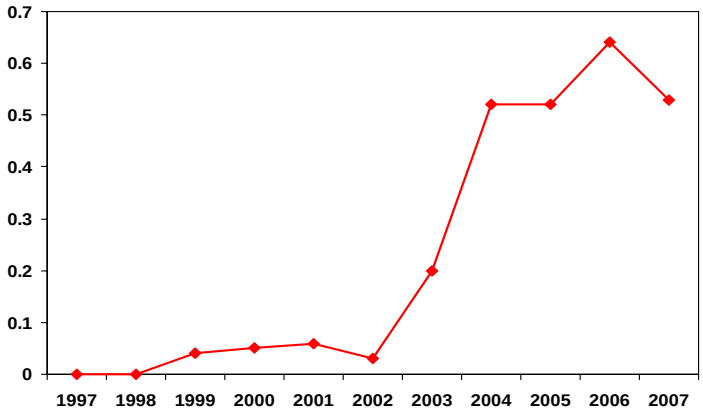
DDMAC's enforcement activity did not, however, fall to pre-2004 levels, when it issued more warning letters than untitled letters.

DDMAC Warning and Untitled Letters 1997-2007
Source: C&B tabulation, based on letters on FDA website



Moreover, although the percentage of warning letters issued in 2007 was lower than in 2006, it was generally consistent with previous years.

Warning Letters as a Percent of Total Letters
1997-2007
Source: C&B tabulation, based on letters on FDA website

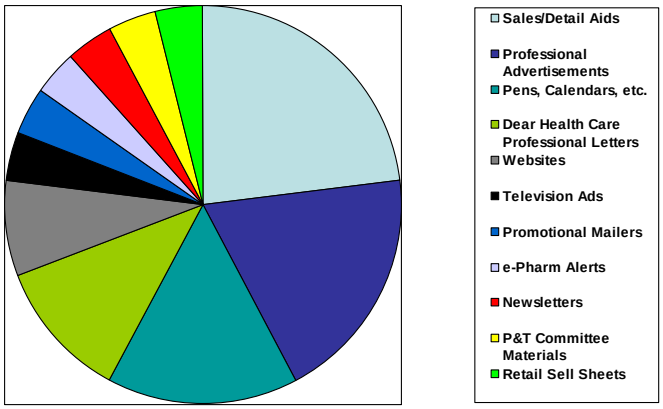


II. Content of Warning and Untitled Letters

A. Promotional Pieces at Issue

The promotional pieces at issue in 2007 included journal advertisements, sales aids, exhibit booth panels, Dear Health Care Professional letters, websites, and promotional mailers.

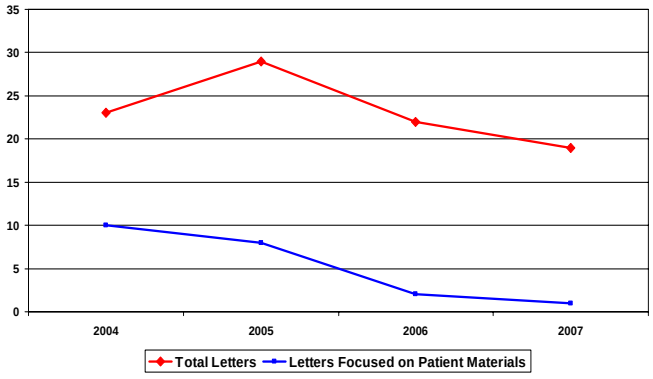
Types of Promotional Pieces 2007
Source: C&B tabulation, based on letters on FDA website



As in previous years, promotional materials intended for healthcare professionals have been a significant focus of DDMAC enforcement activity. From 2004 to 2007, DDMAC sent 93 letters. Of these, 21 (22.6 percent) addressed DTC advertising or other patient-directed materials, such as a product brochure. (This calculation does not include product websites.) But in 2007, only one of the 19 letters issued by DDMAC involved materials directed to patients. The piece at issue in that letter was a DTC television advertisement. The decrease in the number of letters regarding DTC advertisements is likely a result of the 2004 decision by drug companies to pre-submit all DTC advertisements for DDMAC review.

DDMAC Letters 2004-2007

Source: C&B tabulation, based on letters on FDA website

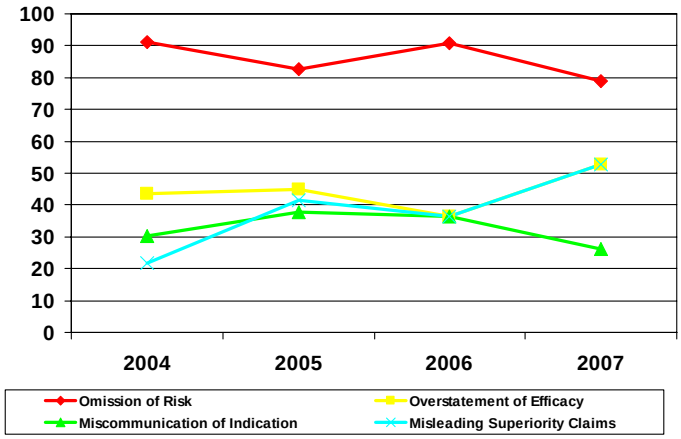


B. DDMAC's Allegations

In recent years, DDMAC has focused most on (1) omission or minimization of risk information, (2) overstatement of efficacy or unsubstantiated effectiveness claims, (3) broadening, omission, or misleading communication of indication, and (4) misleading or unsubstantiated comparative or superiority claims.

Although the number of allegations of omission or minimization of risk information and miscommunication of indication has remained relatively constant since 2004, the number of allegations of misleading or unsubstantiated comparative or superiority claims and those of overstatement of efficacy or unsubstantiated effectiveness claims increased in 2007.

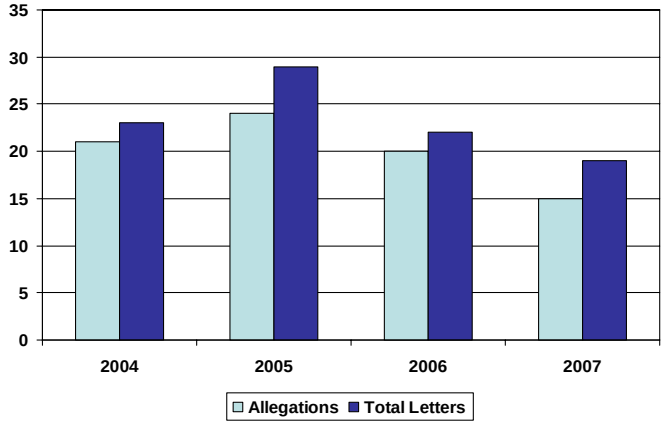
DDMAC Allegations as a Percent of Total Letters
Source: C&B tabulation, based on letters on FDA website



1. Omission or Minimization of Risk Information

The most common DDMAC allegation is omission or minimization of risk information. Of the 93 letters issued by DDMAC from 2004 through 2007, 80 letters (86.0 percent) included an allegation of failure to adequately disclose risk (whether through omission, minimization, or misleading presentation of risk information).

DDMAC Allegations of Failure to Disclose Risks
Source: C&B tabulation, based on letters on FDA website



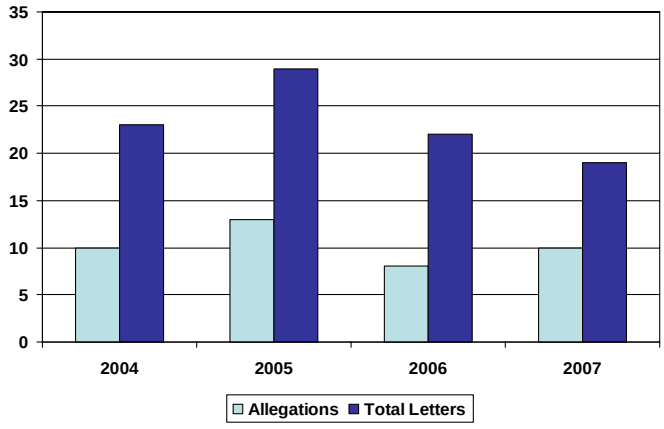
Further, 15 of the 19 letters (78.9 percent) issued in 2007 included an allegation of inadequate presentation of risk. For example, in a February warning letter, DDMAC alleged that a handout provided during a presentation failed to include any risk information, including a critical caveat from the product's labeling that patients were advised to avoid driving while taking the drug.

Similarly, in a May warning letter, DDMAC alleged that a professional journal advertisement contained information from the product's package insert (PI) regarding the product's contraindications, precautions, and less common adverse events, but it failed to communicate several important risks associated with use of the product, including the potential for cross-sensitivity reactions and potential for increased bleeding times.

2. Overstatement of Efficacy or Unsubstantiated Effectiveness Claims

DDMAC also focused on overstatement of efficacy and unsubstantiated claims of effectiveness. Between 2004 and 2007, 41 of 93 letters (44.1 percent) included this allegation.

DDMAC Allegations of Overstatement of Efficacy
Source: C&B tabulation, based on letters on FDA website



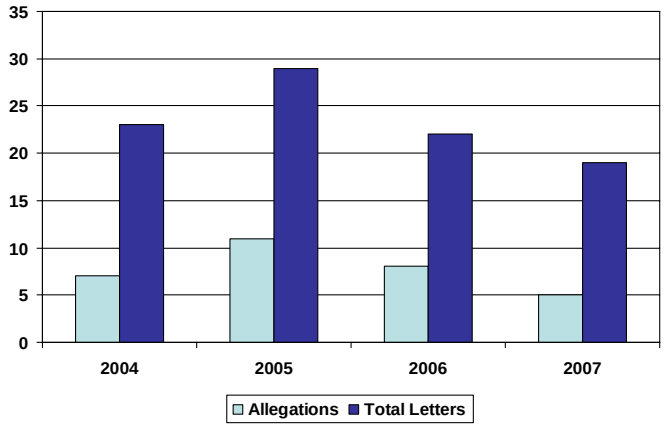
In 2007, DDMAC sent ten letters alleging unsubstantiated effectiveness claims, out of a total of 19 letters (52.6 percent). In May, DDMAC sent untitled letters to the manufacturers of two competing products alleging that detail aids for both products suggested that the products were effective in the treatment of congestion, an indication for which neither product is approved. Likewise, DDMAC alleged in a September untitled letter that a professional mailer suggested that patients treated with the drug experience significantly less pain interference with overall functioning, a claim that has not been demonstrated by substantial evidence or substantial clinical experience.

3. Broadening, Omission, or Misleading Communication of Indication

In the past four years, DDMAC has also focused on claims that allegedly broaden, omit, or otherwise miscommunicate the indication of approved drugs. Of the 93 letters sent between 2004 and 2007, 31 letters (33.3 percent) included this allegation.

DDMAC Allegations of Misleading Communication of Indication

Source: C&B tabulation, based on letters on FDA website



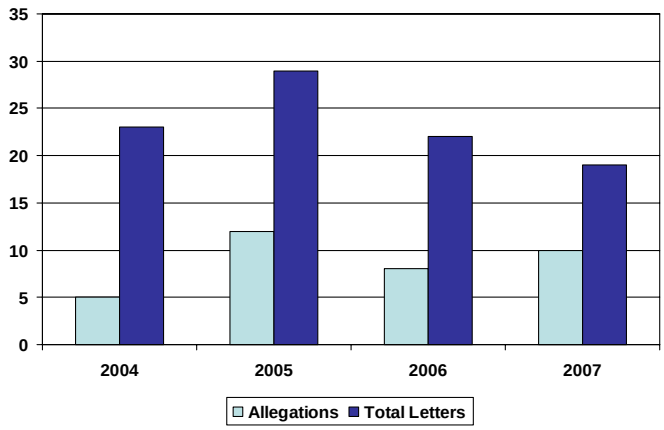
In 2007, five of 19 letters (26.3 percent) included allegations of broadening, omission, or misleading communication of the product's indication. In a July untitled letter, DDMAC alleged that a detail aid and journal ad were misleading because they suggested that the product was approved for use in combination with cryotherapy, despite the fact that the PI specifically stated that safety and efficacy of the product together with other dermal products have not been studied. Similarly, in an April warning letter, DDMAC criticized an advertisement for promoting use of the product to treat the broad population of patients with actinic keratoses, when the PI stated that the product is indicated only for treatment of minimally to moderately thick actinic keratoses of the face or scalp.

4. Misleading or Unsubstantiated Comparative or Superiority Claims

DDMAC has historically made fewer allegations of misleading or unsubstantiated comparative or superiority claims. Between 2004 and 2006, 25 of 74 letters (33.8 percent) contained this allegation, but in 2007, 10 of 19 letters (52.6 percent) alleged misleading or unsubstantiated comparative or superiority claims. In nine of these ten letters, DDMAC criticized the clinical studies and scientific evidence on which the comparative or superiority claims were based, citing, for example, inadequacies in open-label studies and failure to use pre-specified endpoints.

DDMAC Allegations of Unsubstantiated Superiority Claims

Source: C&B tabulation, based on letters on FDA website



In a January untitled letter, DDMAC criticized claims in a journal advertisement that suggested that the advantage of the advertised product over another therapy was the avoidance of treatment delay. DDMAC acknowledged that the product confers a survival benefit but noted that there was no evidence that the efficacy of the product is linked to the ability to use the product earlier. DDMAC criticized the underlying study for providing patients with the same dose of the comparison drug rather than dosing according to the patients' individual needs.

In an April warning letter, DDMAC alleged that a sales aid presented false or misleading claims and presentations regarding the superiority of the product over a competitor with regard to (1) efficacy, (2) pain relief, (3) reduction of inflammation, (4) treatment failure rate, and (5) risk profile. DDMAC cited five reasons why the references cited to support the claims were inadequate.

Conclusion

The number of letters issued by DDMAC in 2007 was lower than in previous years, and the percentage of warning letters was lower than last year. In 2007, DDMAC continued to focus on promotional materials directed to physicians and on omission of risk information, but it also showed an increased emphasis on comparative and superiority claims.

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This information is not intended as legal advice, which may often turn on specific facts. Readers should seek specific legal advice before acting with regard to the subjects mentioned herein.

If you have any questions concerning the material discussed in this client alert, please contact the following members of our food & drug practice group:

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