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E-ALERT | Food & Drug

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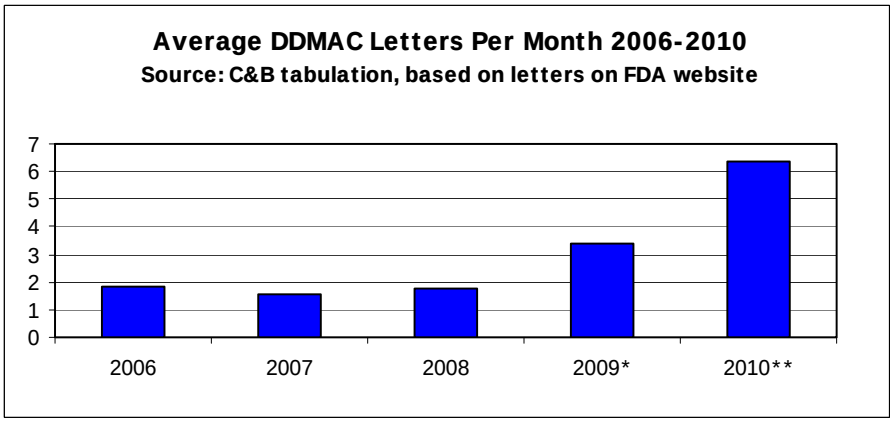
MID-YEAR UPDATE: DDMAC ENFORCEMENT ACTIVITY

This client alert discusses enforcement activity by FDA's Division of Drug Marketing, Advertising, and Communications (DDMAC) during the first six months of 2010. The frequency with which DDMAC issued enforcement letters from January through June 2010 was almost twice that of 2009 and more than three times that of any of the preceding three years. In this alert, we analyze trends in the enforcement letters from the first half of 2010 and discuss two key issues: the presentation of risk information and disease awareness communications.

I. Increased DDMAC Enforcement Activity During the First Six Months of 2010

DDMAC issued 38 enforcement letters during the first six months of 2010, at an average rate of 6.3 letters per month. This is almost as many letters as DDMAC issued in 2009 as a whole (41). The rate of issuance also reflects a marked increase compared to previous years.



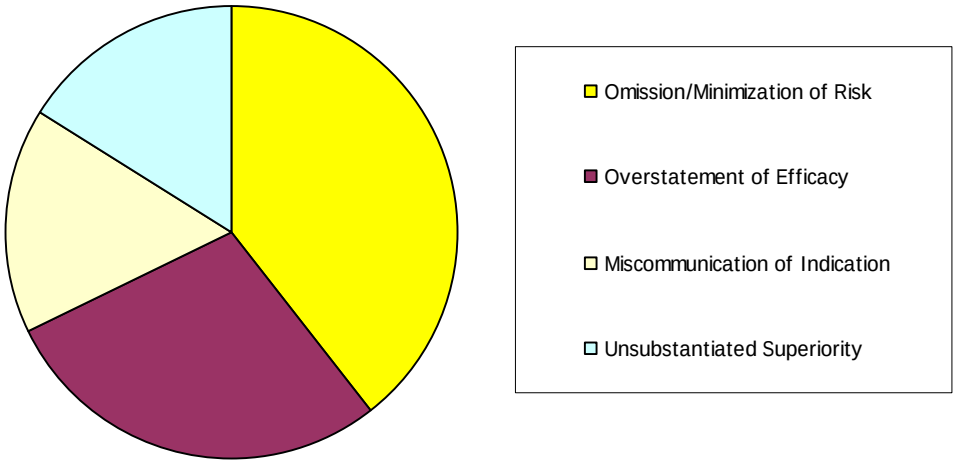
* This calculation includes 14 letters issued on a single day in March 2009.
** This calculation is based only on the first six months of 2010.

As of the end of June 2010, there does not appear to be an upward trend in the issuance of warning letters relative to untitled letters, as compared to 2009. Of all the letters issued in the first half of 2010, 21% were warning letters (compared with 32% in 2009). Additionally, 61% of the letters issued in 2010 addressed materials specifically directed at healthcare professionals, a rate comparable to that of 2009 (54%).

The 2010 enforcement letters reflect an increased focus on the validity and accuracy of the overall message communicated by the promotional piece. While many of these letters reflect concerns commonly cited by DDMAC in the past—such as omission or minimization of risk information, overstatement of efficacy, miscommunication of indication, and unsubstantiated superiority claims—

taken as a whole, the letters could be regarded as DDMAC applying a heightened standard of review for these issues.

DDMAC Letters by Allegation January-June 2010
Source: C&B tabulation, based on letters on FDA website



Omission/Minimization of Risk Information - By far, the most common DDMAC allegation was omission or minimization of risk information. Of the 38 letters issued by DDMAC in the first half of 2010, 32 (84%) included an allegation of failure to adequately disclose risk (whether through omission, minimization, or misleading presentation of risk information). This is comparable to 2009, when DDMAC included this allegation in 90% of its enforcement letters. Many of FDA's objections were based on disparities between promotional pieces and the standards set forth in FDA's 2009 guidance on the disclosure of risk information.[1] This will be discussed further in section II.

Overstatement of Efficacy - Of the 38 letters issued by the end of June 2010, 23 (61%) contained an allegation that the cited promotional piece overstated the efficacy of the product, an increase from 41% in 2009. Promotional pieces overstate the efficacy of a product when they make claims about a product's benefits that are not supported by substantial evidence or substantial clinical experience. For example, a January untitled letter cited patient testimonials in which patients described how treatment with the drug would greatly increase their walking time and distance. According to DDMAC, these statements, even if true for the individual patients, significantly exaggerated the results demonstrated in the clinical trials for the product.

Miscommunication of Indication - Thirteen (34%) letters issued during this time period alleged that a promotional piece broadened, omitted, or otherwise misstated the indication of the drug being promoted. For example, a March warning letter cited a promotional piece that depicted a graph of drug levels in all ocular tissues, despite the fact that the drug was indicated solely for treatment of patients after cataract extraction, a procedure causing inflammation only in the cornea or iris-ciliary body. DDMAC took the position that the depiction of drug levels in other ocular tissues suggested that the drug could be used to treat conditions inconsistent with the drug's indication.

[1] FDA, Draft Guidance: Presenting Risk Information in Prescription Drug and Medical Device Promotion (May 26, 2009), *available at* http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM155480.pdf.

Unsubstantiated Superiority Claims - Of the 38 letters issued during this time period, 13 (34%) contained allegations of unsubstantiated superiority claims. This reflects a considerable increase over 2009, when DDMAC included this allegation in 15% of its letters. DDMAC typically requires that a comparative or superiority claim be supported by at least two well-controlled, head-to-head clinical studies. In an April 2010 warning letter, DDMAC alleged that a promotional piece made unsubstantiated superiority claims where such claims were based only on *in vitro* studies, which were not sufficient to claim clinical efficacy. DDMAC stated that the inclusion of a footnote explaining that *in vitro* data do not necessarily correspond to clinical efficacy did not mitigate the misleading effect of the representations.

II. Presentation of Risk Information

As discussed above, the majority of DDMAC enforcement letters issued during this time period contained allegations of omission or minimization of risk information. In May 2009, FDA released a guidance document providing the agency's views on the effective presentation of risk information. As an overarching principle, the guidance explains that FDA will assess the net impression that the promotional piece conveys to a reasonable consumer. Even true claims may be misleading if they do not convey an accurate overall impression of the product. Recent DDMAC letters reflect particular attention to certain issues discussed in the guidance, as described below.

1. Location of Information

Risk information is most effectively presented when it is an integral part of the piece and located in the same area as the benefit claims, thus allowing the audience to quickly form an accurate overall impression of the product's benefits and risks. In 2010, DDMAC cited a number of promotional materials because the presentation of risk information was distinct from the promotional portion of the advertisement and was often relegated to the end of the promotional piece. For example, in a February warning letter, DDMAC cited a 16-page sales aid that presented numerous efficacy claims on its front and back covers, and on pages 1 to 12, but failed to convey any risk information specific to the drug until page 14.

Furthermore, when specific risk information is related to a particular benefit claim, that information should be proximate to the benefit claim itself. For example, in an April untitled letter, DDMAC cited a sales aid that suggested that treatment with the drug was appropriate for a patient who also took a statin to control his cholesterol. The back cover of the sales aid disclosed that the drug is contraindicated for use with certain statins, but because this risk information was directly material to the benefit claim, DDMAC took the position that it should have been proximate to the claim.

2. Format and Style of Information Presented

DDMAC's allegations during the first half of 2010 indicated that risk information must be presented with a prominence comparable to that of benefit information. This requirement of "comparable prominence" may not be met if both types of information are not presented in a similar format and style. The stylistic elements on which DDMAC typically focuses are: 1) font size and the use of white space; 2) the use of signals such as headers and bullet points; and 3) the consistent use of language appropriate for the target audience.

In the first half of this year, DDMAC took enforcement actions where, according to DDMAC, the stylistic presentation of risk information was de-emphasized through a smaller font size, block text without white space, or the use of technical medical terms when the promotional material was directed to consumers. For example, in a January untitled letter, DDMAC cited a waiting room sign that presented benefit information in a large, colorful font with graphics, but presented risk

information at the bottom of the sign in extremely small font size and a single-spaced format that made the information very difficult to read. Furthermore, DDMAC stated that benefit claims were presented in consumer-friendly language, but some of the risk information was presented in medical terminology that was unlikely to be understood by consumers.

3. Omission of Material Risk Information

Several enforcement letters issued in 2010 targeted promotional pieces that allegedly omitted material risk information. The 2009 FDA guidance defines "material information" as those facts "that would influence reasonable consumers (or healthcare professionals . . .) about a product."[2] DDMAC typically cites promotional materials for omitting material risk information in three situations: 1) where the piece omits a serious risk that would be material to *any* presentation of benefits; 2) where the piece fails to apprise the reader of less serious, but very common risks; or 3) where the piece omits an entire class of risk information, such as the drug's contraindications. For example, a March warning letter cited a promotional piece that included the drug's most common adverse events but, according to DDMAC, omitted the most serious warning—the possibility of a life-threatening allergic reaction.

Finally, the 2010 enforcement letters reflect DDMAC's position that the inclusion of references or redirects to the product's full prescribing information fails to mitigate the omission of risk information or the misleading presentation of such information in the promotional piece itself.

III. Disease Awareness Materials

In the first six months of 2010, DDMAC issued enforcement letters to two companies for purported disease awareness communications. A disease awareness communication discusses a health condition but does not mention a particular drug. But "where a supposed disease awareness communication is determined to, by implication, identify a particular drug," the communication can be considered advertising and can be regulated by the FDA.[3] According to FDA, depending on the context of the piece, the inclusion of the company's name along with the disease state reference could potentially constitute drug product promotion. To distinguish whether a piece educates healthcare professionals and patients about a disease or promotes a specific treatment, DDMAC assesses whether the audience would know that the piece refers to a specific product. This may be the case when a drug product is the only drug of its type, the only drug of its type marketed by the company whose name appears on the piece, or the only drug of its type indicated for the class of patients that the communication addresses.

DDMAC's first letter this year related to a disease awareness communication came in an April untitled letter. In the letter, DDMAC alleged that a journal ad for a drug was actually promotional messaging for the unnamed product. The ad contained the company's logo and claimed that a new treatment for a specific disease had recently been approved. Because only one particular product manufactured by that company had recently been approved to treat the condition, DDMAC concluded that the communication advertised the drug. Because the advertisement was styled as a disease awareness communication, it did not have any risk information or limitations on the product's indication.

In an April warning letter, DDMAC alleged that two disease awareness websites were actually advertisements for a drug product. The websites were registered to a drug company, included the

[2] *See id.* at 12.

[3] *See* FDA, Draft Guidance: "Help-Seeking" and Other Disease Awareness Communications by or on Behalf of Drug and Device Firms 3-4 (Jan. 26, 2004), *available at* http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/ucm070068.pdf [hereinafter *Disease Awareness Guidance*].

company logo, and discussed the use of a particular type of drug for a particular condition. Only one drug product manufactured by that company fit those specifications. The websites also referenced third-party communications that referred to the underlying product by name. Furthermore, according to DDMAC, the websites were stylistically similar to the branded product website and presented data and references to studies using the product. This combination of factors led DDMAC to conclude that the websites did not qualify as disease awareness communications.

By classifying these disease awareness communications as deficient promotional pieces, DDMAC has indicated that it may scrutinize purported disease awareness pieces closely to determine whether they fit within FDA's 2004 Disease Awareness Guidance and the agency's evolving standards.

IV. Conclusion

DDMAC enforcement in the first half of 2010 is markedly higher than it was in 2009. At the current rate, DDMAC could potentially issue double the number of letters by the end of 2010 than it did in 2009. This uptick in activity could be attributed to Commissioner Hamburg's call for increased enforcement, as well as changes in the process for review and issuance of enforcement letters. In addition, it is possible that the rate of enforcement letters could accelerate as implementation of FDA's "Bad Ad" program continues. Launched in May 2010, the "Bad Ad" program is aimed at training healthcare professionals to detect and report misleading promotional pieces to FDA.[4] For these reasons, pharmaceutical companies must continue to be vigilant and should seek to incorporate FDA's evolving standards into the creation, review, and approval of promotional materials.

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[4] *See* Truthful Prescription Drug Advertising and Promotion (Bad Ad Program), *available at* http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Surveillance/DrugMarketingAdvertisingandCommunications/ucm209384.htm.