



**GLOBAL LIFE SCIENCES: US-FDA UPDATE**

**Review of DDMAC / OPDP Warning and Untitled Letters By Therapeutic Category**

Since the beginning of 2009, the Division of Drug Marketing, Advertising, and Communications (DDMAC) (newly renamed the Office of Prescription Drug Promotion (OPDP)) of the U.S. Food and Drug Administration (FDA) has issued 115 warning and untitled letters. Of the products cited in these letters, nearly 17 percent were antineoplastic agents. Other frequently cited therapeutic categories include analgesics, genitourinary agents, and central nervous system agents, which were each cited ten times in letters.

The letters alleged violations arising out of the promotion of products in 40 therapeutic categories according to the United States Pharmacopeial Convention’s Model Guidelines v. 5.0 (Mar. 2011).<sup>1</sup> The table below sets forth the number of allegations for each therapeutic category.<sup>2</sup>

Therapeutic Category	Citations	Percentage of Products Cited
Antineoplastic	29	16.6%
Analgesic	10	5.7%
Genitourinary Agent	10	5.7%
Central Nervous System Agent	10	5.7%
Cardiovascular Agent	9	5.1%
Ophthalmic Agent	8	4.6%
Respiratory Tract Agent	8	4.6%
Dermatological Agent	7	4.0%
Antidepressant	6	3.4%
Antiviral	6	3.4%
Anti-Inflammatory Agent	5	2.9%
Blood Glucose Regulator	5	2.9%
Radiological Agent	5	2.9%
Therapeutic Nutrients/ Minerals/ Electrolytes	5	2.9%
Anti-Addiction / Substance Abuse Agent	4	2.3%

<sup>1</sup> The guidelines are available at <http://www.usp.org/hqi/mmg/revisions.html>. Certain products, such as radiological products, did not fall squarely into a therapeutic category established by the Model Guidelines, and were assigned to a therapeutic category not named by the Model Guidelines based on the product’s FDA review division and other publicly available information. A product was assigned to more than one therapeutic category if it had more than one therapeutic use.

<sup>2</sup> Because some products were assigned more than one therapeutic category, a product is counted once for each therapeutic category to which it was assigned.

Therapeutic Category	Citations	Percentage of Products Cited
Antibacterial	4	2.3%
Anxiolytic	4	2.3%
Birth Control Agent	3	1.7%
Hormonal Agent, Stimulant/Replacement/Modifying (Sex Hormones/Modifiers)	3	1.7%
Inflammatory Bowel Disease Agent	3	1.7%
Metabolic Bone Disease Agent	3	1.7%
Anticonvulsant	2	1.1%
Antidementia Agent	2	1.1%
Antiemetic	2	1.1%
Antimigraine Agent	2	1.1%
Antiparasitic	2	1.1%
Bipolar Agent	2	1.1%
Dental and Oral Agent	2	1.1%
Gastrointestinal Agent	2	1.1%
Immunological Agent	2	1.1%
Sleep Disorder Agent	2	1.1%
Antimycobacterial	1	0.6%
Antiparkinson Agent	1	0.6%
Antipsychotic	1	0.6%
Blood Products/Modifiers/Volume Expanders	1	0.6%
Erectile Dysfunction Agent	1	0.6%
Hormonal Agent, Stimulant/Replacement/ Modifying (Pituitary)	1	0.6%
Hormonal Agent, Suppressant (Sex Hormones/ Modifiers)	1	0.6%
Mucolytic Agent	1	0.6%

The most frequently cited violations included: (1) omission of risk information and/or minimization of risk; (2) overstatement of efficacy/unsubstantiated efficacy claim; (3) broadening of indication; (4) unsubstantiated or misleading superiority or comparative claim; and (5) omission of material fact. The table below sets forth the frequency of cited violations.

Type of Violation	Citations	Percentage of Letters
Omission of Risk Information and/or Minimization of Risk	96	83.5%
Overstatement of Efficacy/Unsubstantiated Efficacy Claim	62	53.9%
Broadening of Indication	46	40.0%
Unsubstantiated or Misleading Superiority or Comparative Claim	35	30.4%
Omission of Material Fact	20	17.4%
Failure to Submit Under Form FDA-2253	15	13.0%
Failure to Use or Inadequate Presentation of Established Name	15	13.0%
Promotion of Unapproved Use or Unapproved Drug	9	7.8%
Failure to State Indication	9	7.8%
False or Misleading Statement	8	7.0%
Unsubstantiated Compliance or Convenience Claim	8	7.0%
Misleading Dosing Claim/Promotion of Unapproved Dosing Regimen	5	4.3%
Use of Unapproved or Outdated Product Labeling	5	4.3%
Promotion of an Investigational New Drug	4	3.5%
Failure to Provide Adequate Directions for Use	4	3.5%
Unsubstantiated Mechanism of Action Claim	3	2.6%
Failure to Submit During Preapproval Review Period	3	2.6%
Misleading Presentation	2	1.7%

Though copy review processes are designed to manage the full range of risks presented by manufacturer promotional activities, this review points up the disproportionate risk mitigation benefit of focusing those processes on the appropriate presentation of risk information, the careful calibration of efficacy-related statements, and the full and accurate description of a product's labeled indication. Measures to assure compliance with the relatively straightforward regulatory requirements for the submission of specimens of promotional pieces to FDA with a Form FDA-2253 (21 C.F.R. § 314.81(b)(3)(i)) and the presentation of the established name would also mitigate risk to a disproportionate degree given the number of alleged violations of those requirements. Though off-label promotion remains a focus of Department of Justice enforcement, a mere nine percent of warning and untitled letter allegations concerned those violations.

If you have any questions regarding this update, please contact Maura Martin Norden (+1.202.736.8458, [mnorden@sidley.com](mailto:mnorden@sidley.com)) or the Sidley lawyer with whom you usually work.

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For further information on the FDA Practice, please contact:

Raymond A. Bonner	Coleen Klasmeier
+1.202.736.8679	+1.202.736.8132
<a href="mailto:rbonner@sidley.com">rbonner@sidley.com</a>	<a href="mailto:cklasmeier@sidley.com">cklasmeier@sidley.com</a>

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For further information on the Global Life Sciences Practice, please contact:

Scott Bass	James C. Stansel
+1.202.736.8684	+1.202.736.8092
+1.212.839.5613	
<a href="mailto:sbass@sidley.com">sbass@sidley.com</a>	<a href="mailto:jstansel@sidley.com">jstansel@sidley.com</a>

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