

Marketed Unapproved Drugs—Past, Present and Future?

By Kurt R. Karst

In June 2006, the Food and Drug Administration (FDA) announced the publication of the agency's final Compliance Policy Guide (CPG) concerning its risk-based enforcement policy for marketed unapproved drugs. Since then, FDA has enforced those policies aggressively, and has signaled its intent to increase such enforcement actions in 2007. This change, compared to past enforcement initiatives, might be due to new leadership in FDA's Office of Compliance and increasing Congressional interest in marketed unapproved drugs. This article describes the different "categories" of drugs currently marketed in the US, FDA's enforcement policies and recent actions concerning different "categories" of marketed unapproved drugs, and discusses the future regulatory environment for such products.

Overview

Whether a product is a "drug" generally depends upon its "intended use."¹ A product that is a "new drug" within the meaning of § 201(p) of the *Federal Food, Drug and Cosmetic Act (FD&C Act)* may not be introduced into interstate commerce unless there is an approved marketing application (e.g., a New Drug Application (NDA)) or an exemption has been granted permitting the introduction of the drug into interstate commerce (e.g., an effective Investigational New Drug Application).² However, not all drugs are considered new drugs for which premarket approval is required. A drug is not a "new drug" if: it has been used "to a material extent or for a material time under those conditions;" and it is Generally Recognized As Safe and Effective (GRASE) by qualified experts under the conditions of use for which it is labeled.³

Legally marketed drugs are those marketed in accordance with an approved NDA, generic copies of such drugs marketed under an approved Abbreviated NDA ["ANDA"], and drugs that are exempt from the NDA requirement. This latter category includes pre-1938 and pre-1962 "grandfathered" drugs, drugs subject to an ongoing Drug Efficacy Study Implementation (DESI) proceeding, GRASE prescription drugs, and drugs marketed in accordance with a final or tentative Over-the-Counter (OTC) drug monograph.

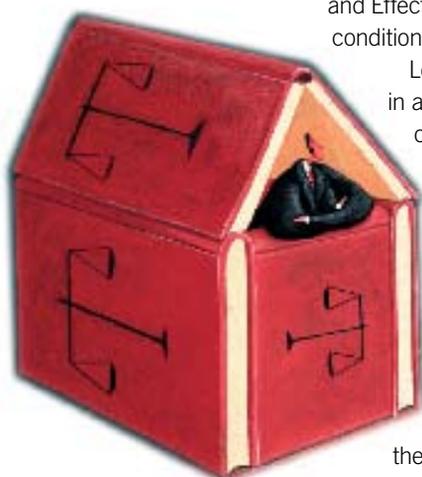
Illegally marketed drugs subject to FDA enforcement action include drugs marketed outside an OTC drug final or tentative final monograph, drugs found to be effective under DESI but for which an NDA or ANDA has not been submitted, drugs subject to a completed DESI proceeding that found them to be ineffective, drugs subject to the Prescription Drug Wrap-Up, new unapproved drugs, and drugs that do not meet the GRASE requirements or that differ in some respect from pre-1938 or pre-1962 "grandfathered" drugs. Although FDA estimates that there are several thousand such drugs that are being marketed illegally, it has exercised its discretion not to take enforcement action against many of them. To that end, the agency has articulated a risk-based enforcement approach that has been and will continue to be the basis for enforcement action.

Past: Historical Development of the FD&C Act

The 1938 Amendments

The *Pure Food and Drugs Act* of 1906⁴ first brought drug regulation under federal law by prohibiting the sale of adulterated or misbranded drugs. However, the statute did not require that drugs be approved by FDA in order to be marketed. In 1938, Congress passed the *FD&C Act*, which added the requirement that new drugs—that is, drugs not Generally Recognized As Safe (GRAS)—be approved for safety in an NDA. The active ingredients in many currently marketed drugs were first introduced, at least in some form, before 25 June 1938 (the date on which the *FD&C Act* was enacted). Drugs on the market prior to that date are exempt from new drug status under a grandfather clause and, therefore, are exempt from the requirement of submitting an NDA, provided the drug contains the same chemical composition, indications and other conditions for use as the grandfathered drug.

If a drug obtained approval between 1938 and 1962, FDA generally permitted Identical, Related, or Similar (IRS) drugs to the approved drug to be marketed without independent approval. Many manufacturers also introduced drugs onto the market between 1938 and 1962 based upon their own conclusion that the products were GRAS, and thus exempt from the statutory new drug definition, or based upon a formal



opinion from FDA that the products were not new drugs.

The 1962 Drug Amendments and the Drug Efficacy Study Implementation Program

In 1962, Congress amended the FD&C Act to require that a new drug be demonstrated to be effective, as well as safe, to obtain FDA approval.⁵ However, under a “grandfather clause” included in the 1962 Drug Amendments, a drug is exempt from the effectiveness requirement if its composition and labeling has not changed since 10 October 1962 (the date on which the 1962 Drug Amendments were enacted), and if, on the day before the 1962 Drug Amendments became effective, the drug was: used or sold commercially in the United States; not a new drug as defined by the FD&C Act at that time; and not covered by an effective application.⁶

The 1962 Drug Amendments also required FDA to evaluate the effectiveness of drug products approved as safe between 25 June 1938 and 10 October 1962. FDA engaged the National Academy of Science/National Research Council (NAS/NRC) to evaluate the effectiveness of the more than 3,400 products approved based upon safety. The NAS/NRC review was broken down into specific drug categories. Review results were submitted to FDA, which then reviewed and reevaluated the NAS/NRC findings and published its own findings in the *Federal Register*.

FDA's administrative implementation of the NAS/NRC reports was called the DESI program. DESI covered the products specifically reviewed by the NAS/NRC, as well as the even larger number of IRS products that had entered the market without FDA approval. If FDA's final determination classified a drug as effective for its labeled indications, the agency frequently required sponsors of approved NDAs (referred to as “deemed approved” NDAs) to supplement their applications for continued marketing of the drug, and sponsors of IRS drugs to submit ANDAs seeking approval.⁷ If FDA's final determination classified a drug as ineffective, then, because DESI products were covered by “deemed approved” NDAs, the agency was required to follow administrative hearing procedures in the FD&C Act and regulations to withdraw the NDA.

Some currently marketed products are subject to completed DESI proceedings but, nevertheless, lack approved marketing applications. This includes a number of products IRS to DESI products for which approval was withdrawn because they lacked substantial evidence of effectiveness. It also includes a number of products IRS to those DESI products for which FDA made a final determination that the product is effective, but that lack approved ANDAs as

required under the statute and FDA's long-standing enforcement policy.⁸ FDA considers all of these products to be unapproved and marketed illegally, but generally uses its enforcement discretion to take action against firms marketing products the agency believes present a potential safety risk, lack evidence of effectiveness, or are deceptively promoted.⁹

Some currently marketed products are unapproved but are still undergoing DESI reviews without a final efficacy determination to date. This includes unapproved products IRS to those products specifically reviewed.¹⁰ In many of these proceedings, FDA has made an initial determination that the products lack substantial evidence of effectiveness, and the manufacturers have requested a hearing on that finding. Under a long-standing FDA policy, products subject to an ongoing DESI proceeding, including IRS drugs, may remain on the market during the pendency of the proceeding.¹¹

Prescription Drug Wrap-Up

As noted previously, numerous drugs came onto the market before 1962 without FDA approvals. Many of these products claimed to be marketed prior to 25 June 1938 or IRS to such a drug and, therefore, may have a colorable claim to “grandfather” status.¹² Drugs that did not have pre-1962 approvals or were not IRS to drugs with pre-1962 approvals were not subject to DESI. For a period of time, FDA allowed these drugs to remain on the market and allowed new unapproved drugs that were IRS to these pre-1962 drugs to enter the market without approval.

Due to a tragedy involving an unapproved Vitamin E intravenous injection (E-FEROL), and in response to Congressional concern about the thousands of unapproved drugs marketed, in 1984, FDA assessed the pre-1962 non-DESI marketed drug products. The program for addressing these marketed but unapproved drugs and certain others like them became known as the “Prescription Drug Wrap-Up.”¹³ FDA believes that most Prescription Drug Wrap-Up drugs first entered the market before 1938, at least in some form. For the most part, FDA has evaluated neither the safety nor effectiveness of these drugs. However, according to FDA's interpretation, drugs subject to the Prescription Drug Wrap-Up are all marketed illegally, unless such a drug's manufacturer can establish that the drug is grandfathered or otherwise not a new drug.

New Unapproved Drugs

Some unapproved drugs were first marketed, or were changed, after the 1962 Drug Amendments were enacted (i.e., drugs that were not covered in the Prescription Drug Wrap-Up). Still other drugs are the

subject of a formal “new drug” finding (e.g., timed-release drugs, and parenteral drugs in plastic containers).¹⁴ FDA has taken the position that drugs in this category are all marketed illegally and subject to enforcement action, unless covered by an approved marketing application.¹⁵

Scope of the Grandfather Clauses and the GRASE Exemption

The 1938 and 1962 grandfather clauses in the FD&C Act have been construed very narrowly by FDA and the courts. FDA believes that there are few, if any, marketed drugs that are actually entitled to grandfather status, because the drugs currently on the market likely differ from the previous versions in some respect, such as formulation, dosage form, strength, method of manufacture, route of administration, indications or intended patient population. If a company claims that its product is grandfathered, FDA considers it the firm’s burden to prove that assertion.¹⁶ FDA has stated that it believes “it is not likely that any currently marketed prescription drug product is grandfathered or is otherwise not a new drug,” but recognizes that “it is at least theoretically possible” that such a product exists.¹⁷

As discussed previously, a product determined to be GRASE and to have been used “to a material extent or for a material time” for its labeled conditions is not a new drug and, thus, may be marketed legally without an approved NDA.¹⁸ As with the pre-1938 and pre-1962 grandfather clauses, this exemption has been construed very narrowly by FDA and the courts.¹⁹

Over-the-Counter Drugs

OTC drugs originally were included in DESI, but FDA eventually concluded that this was an inefficient use of resources. In 1972, the agency initiated a process (i.e., the OTC Drug Review) of reviewing OTC drugs by therapeutic classes (e.g., antacids, antiperspirants, cold remedies) through rulemaking. The OTC Drug Review is intended to result in the publication of a final monograph for each therapeutic class. The monographs delineate permissible claims, labeling and active ingredients for OTC drugs in each class.²⁰ Drugs marketed in accordance with a final monograph are considered to be GRASE. They do not require FDA approval of a marketing application because GRASE substances are exempt from the statutory definition of a new drug.

Final monographs have been published for the majority of OTC drugs. Proposed monographs (designated as “tentative final monographs”) have been issued for virtually all remaining OTC drug categories. FDA also has finalized a number of “negative mono-

graphs” that list therapeutic categories in which no OTC drugs can be marketed without approval through an NDA.²¹ In addition, the agency has promulgated a list of active ingredients that cannot be used in certain unapproved OTC drugs because inadequate data exist to establish that they are GRASE.

FDA has taken the position that OTC drugs covered by ongoing OTC monograph proceedings may remain on the market, subject to current enforcement policies.²² This position has been extended to cover products sold as prescription drugs with ingredients under the OTC Drug Review, deferring action until the monograph is final.²³ OTC drugs that require approval because their ingredients or claims are not within the scope of the OTC Drug Review, or are not allowed under a final monograph or another final rule, are illegally marketed unless they are the subject of an approved marketing application.

Present: FDA’s Enforcement Priorities

FDA has estimated that, “in the United States today, perhaps as many as several thousand drug products are marketed illegally without required FDA approval.”²⁴ Despite that observation, the agency has stated that it will follow a risk-based approach with regard to enforcement against such unapproved products. Under this approach, FDA gives higher priority to enforcement action against unapproved drugs in the following categories:

- drugs with potential safety risks
- drugs that lack evidence of effectiveness
- drugs that present a “health fraud”²⁵
- drugs that present direct challenges to the new drug approval and OTC drug monograph systems
- unapproved new drugs that are also violative of the FD&C Act in other ways (e.g., Current Good Manufacturing Practice [CGMP] regulation violations)
- drugs that are reformulated to evade an FDA enforcement action (e.g., when a firm, in anticipation of FDA enforcement action, changes its unapproved drug product by, for example, adding an active ingredient, in an attempt to evade such enforcement action)²⁶

FDA evaluates whether to initiate enforcement action on a case-by-case basis. The agency generally does not give special or advance notice that an unapproved drug may be subject to enforcement action, unless such notice is necessary given specific circumstances or because notice would be appropriate to protect the public health. However, marketed unapproved products that are subject to a completed DESI proceeding or that do not comply with a final OTC

drug monograph proceeding are often given a grace period to be brought into compliance with the law.²⁷

There are several recent examples of FDA enforcement action against firms marketing unapproved drugs that fall into some of the above categories.²⁸

- In May 2006, FDA issued a Warning Letter to Neil Laboratories that included, among other things, unapproved new drug charges.²⁹ These charges were added after FDA found other FD&C Act violations, including CGMP violations. FDA relies on the decision in *United States v. Sage Pharma., Inc.*, 210 F.3d 475 (5th Cir. 2000), to permit the addition of unapproved new drug charges after finding other FD&C Act violations. In *Sage*, the United States Court of Appeals for the Fifth Circuit agreed that FDA was permitted “to address the unapproved status of a particular drug outside the established priorities in the same enforcement proceeding as other violations of the [FD&C Act].”³⁰
- In June 2006, FDA announced that it plans to take enforcement action against companies marketing unapproved drug products containing carbinoxamine (either single-entity or combination products), because: “(1) Carbinoxamine is a drug with potential safety risks . . . ; and (2) the agency has approved an application to market a carbinoxamine-containing product, and thus the continued marketing of unapproved carbinoxamine products is a direct challenge to the drug approval process.”³¹ FDA’s planned enforcement action was timed to coincide with the announcement of the availability of the agency’s Unapproved Drugs CPG, and after the agency had approved two ANDAs in March and April 2003, submitted by Mikart, with an anticipated supplement to these applications concerning the products’ use in children under two years (due to safety concerns).
- In July 2006, Warning Letters issued to Concord Laboratories and Sheffield Laboratories added unapproved new drug charges to CGMP violations.³²
- In August 2006, FDA issued a Warning Letter to Activis Totowa that added unapproved new drug charges to FD&C Act and regulatory violations concerning the firm’s failure to submit postmarketing adverse drug experience reports.³³ FDA also negotiated in August 2006 a consent decree of permanent injunction with Syntho Pharmaceuticals and Intermax Pharmaceuticals that, among other things, enjoins the firms from manufacturing and distributing

various unapproved drugs and requires them to recall their unapproved drugs from distribution.³⁴

- In September 2006, FDA negotiated a consent decree of permanent injunction barring C.R. Canfield Co. from manufacturing and distributing unapproved drugs and drugs that do not satisfy CGMP requirements.³⁵
- In December 2006, FDA announced that it is ordering firms to stop marketing unapproved drug products containing quinine. FDA took this action for safety reasons and to preserve the integrity of the drug approval process after the agency approved Mutual Pharmaceutical Co.’s QUALAQUIN (quinine sulfate) Tablets in August 2005, and once the company began commercially distributing its drug in 2006.³⁶ FDA’s action in this case is similar to its previous action on single-entity, extended-release guaifenesin products. In October 2002, FDA sent Warning Letters to 66 firms marketing unapproved single-ingredient, extended-release guaifenesin products claiming that the products are illegally marketed new drugs.³⁷ The agency’s action was initiated after it approved an NDA for MUCINEX (extended-release guaifenesin) Tablets in July 2002. The MUCINEX approval provided FDA with the impetus to immediately enforce the FD&C Act.

And Future?

FDA states that each of the enforcement actions listed above is “part of the agency’s broader initiative, launched [in 2005], to ensure that consumers and the health care community are provided with established and emerging drug safety information so that they can make the best possible medical decisions about the safe and effective use of drugs.”³⁸ However, aside from this broad drug safety initiative, there are other factors catalyzing FDA enforcement action that portend future enforcement action and perhaps more broad-based changes affecting marketed unapproved drugs.

The FDA office primarily charged with enforcing the agency’s Unapproved Drugs CPG and with “assuring that safe and effective drugs are available to the American people by protecting Americans from unsafe or ineffective drugs” is the Office of Compliance (“OC”) in the Center for Drug Evaluation and Research.³⁹ In September 2006, Deborah Autor was named as OC Director. Under Autor’s leadership, the OC plans to continue and increase enforcement actions concerning marketed unapproved drugs. Indeed, Ms. Autor recently stated that in 2007 her office “will work even more quickly to address the

problem of unapproved drugs.⁴⁰ This stated agenda is consistent with other FDA communications in which the agency has stated that it “expects to further accelerate its enforcement efforts against marketed unapproved drugs in 2007.”⁴¹

The possibility of increased Congressional involvement might be another reason for FDA’s current and anticipated aggressive enforcement action initiative against firms marketing and distributing unapproved drugs. In 2007, Congress must reauthorize the Prescription Drug User Fee Act of 1992 (PDUFA).⁴² Some members of Congress might view PDUFA as a vehicle to tighten FDA oversight of marketed unapproved drugs. In fact, earlier this year, US Representative Ed Markey (D-MA) and US Senator Charles Grassley (R-IA) each sent letters to FDA expressing concern about marketed unapproved drugs and requested information from the agency on such products, patient safety and enforcement actions.⁴³ In addition, Rep. Markey recently indicated that he “would push to add to [PDUFA reauthorization legislation] language tightening FDA oversight of unapproved [drugs].”⁴⁴ Details about this language are not yet available, but legislative action could include increased FDA funding (perhaps through new PDUFA user fee revenue) for unapproved drug enforcement actions, or a broad-based fix, such as the establishment of a monograph system similar to the OTC drug monograph system.

FDA would welcome increased revenue to pursue enforcement action against firms marketing unapproved drugs. Indeed, the general lack of enforcement action over the past few decades has been due, in large part, to scarce enforcement resources. FDA likely would not welcome the establishment of a monograph system similar to that for OTC drugs. Although FDA has previously suggested the possibility of creating a monograph system for old prescription drugs (as far back as 1968 and as recently as 2003), and Congress has considered legislation (in 1978) to establish such a monograph system, the agency reported to Congress in 2004 that “it would not be feasible to establish safety, efficacy, quality, and appropriate labeling for prescription drugs by class FDA believes that prescription drug products have characteristics that, when taken together, do not lend themselves to marketing under monographs developed for classes of drugs without an application-specific review”⁴⁵

Although increased enforcement action against firms marketing unapproved drug products might lead to greater, industry-wide compliance with the FD&C Act and FDA’s regulations and policies, the agency and Congress should also consider other ways to encourage compliance. For example, PDUFA user fee relief, less onerous clinical testing requirements

and strengthened marketing incentives. By offering such incentives to firms marketing unapproved drugs (which typically are off-patent), as opposed to wielding only the threat of enforcement action, it is possible that the agency would see greater compliance with the law. In addition, such a “carrot and stick” approach could decrease the need for additional funding for FDA compliance enforcement actions.

In November 2006, FDA announced a public workshop to be held in January 2007 to discuss issues related to the application process for seeking approval for marketed unapproved drugs.⁴⁶ According to the draft agenda, the agency will discuss, among other things, application content, user fees and marketing exclusivity.⁴⁷ This article was submitted for publication prior to the January FDA workshop. Although it is possible that FDA will use the workshop as an opportunity to announce new policies concerning marketed unapproved drugs, it seems more likely that it will take the opportunity to reinforce the agency’s intent to enforce the Unapproved Drugs CPG. Specific policies to incentivize firms to seek FDA approval for their marketed unapproved drugs are more likely to occur with Congress during PDUFA reauthorization.

REFERENCES

1. See FD&C Act § 201(g)(1) (defining the term “drug”); 21 CFR § 201.128 (defining the meaning of “intended use”).
2. FD&C Act § 505(a).
3. *Id.* at § 201(p).
4. Pub. L. No. 59-384, 34 Stat. 768 (1906).
5. See The Drug Amendments of 1962, Pub. L. No. 87-781, 76 Stat. 780 (1962) (“1962 Drug Amendments”).
6. See *id.* at § 107(c)(4); see also *USV Pharm. Corp. v. Weinberger*, 412 U.S. 655, 662-66 (1973).
7. The ANDA procedures developed by FDA were created in 1970 to apply to pre-1962 IRS drugs. See 35 Fed. Reg. 6574 (Apr. 24, 1970). Conventional ANDAs were created in 1984, when Congress, through the Hatch-Waxman Act, created FD&C Act § 505(j).
8. See 21 CFR § 310.6.
9. See FDA, Guidance for FDA Staff and Industry, Marketed Unapproved Drugs – Compliance Policy Guide, at 3 (June 2006) (Unapproved Drugs CPG), available at www.fda.gov/cder/guidance/6911fnl.pdf.
10. See 21 CFR § 310.6.
11. See Unapproved Drugs CPG at 8.
12. FDA’s regulation specifying the content of a hearing request for a drug claimed to qualify for the pre-1938 “grandfather” clause suggests that FDA regards small changes in composition and labeling as relevant to such status. See 21 CFR § 314.200(e)(2).
13. The Prescription Drug Wrap-Up is also sometimes referred to as “DESI-2.” FDA’s Prescription Drug Wrap-Up list is over 1,500 pages long, and identifies approximately 5,150 unapproved, marketed products. FDA claims that most of the drugs included in the list are pre-1938 and unapproved pre-1962 drugs (or drugs that are IRS to such a product), but has acknowledged that the list is incomplete and may also include post-1962 unapproved drugs.
14. See 21 CFR § 310.502.
15. See Unapproved Drugs CPG at 11.
16. See 21 CFR § 314.200(e)(5).

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17. Unapproved Drugs CPG at 11 (*italics in original*).
18. FD&C Act § 201(p).
19. See e.g., *Weinberger v. Hynson, Westcott & Dunning Inc.*, 412 U.S. 609 (1973); see also FDA Response, Docket No. 97N-0314 (26 April 2001), available at www.fda.gov/ohrms/dockets/dockets/97n0314/pdn0002.pdf (finding that SYNTHROID—a levothyroxine sodium product—was not GRASE).
20. See e.g., 21 CFR Part 333.
21. See e.g., *id.* at § 310.530 (topically applied hormones).
22. See CPG Manual, Sec. 450.200—General Provisions and Administrative Procedures for Recognition as Safe and Effective (CPG 7132b.15), available at www.fda.gov/ora/compliance_ref/cpg/cpgdrg/cpg450-200.html; CPG Manual “Sec. 450.300—General Provisions and Administrative Procedures for Recognition for Marketing Combination Products (CPG 7132b.16),” available at www.fda.gov/ora/compliance_ref/cpg/cpgdrg/cpg450-300.html.
23. See 21 CFR § 330.13.
24. Unapproved Drugs CPG at 2.
25. *Id.* at 3. FDA defines health fraud to mean “[t]he deceptive promotion, advertisement, distribution or sale of articles . . . that are represented as being effective to diagnose, prevent, cure, treat, or mitigate disease (or other conditions), or provide a beneficial effect on health, but which have not been scientifically proven safe and effective for such purposes. Such practices may be deliberate, or done without adequate knowledge or understanding of the article.” *Id.* at 3 (quoting FDA Compliance Policy Guide § 120.500).
26. *Id.* at 3-4.
27. See Unapproved Drugs CPG at 4-5.
28. Examples of FDA enforcement action on unapproved drug, in addition to those discussed below, are described on FDA’s

website at www.fda.gov/cder/drug/unapproved_drugs/enforcement.htm.

29. See FDA, Warning Letter to Neil Laboratories Inc., (31 May 2006) available at www.fda.gov/foi/warning_letters/g5878d.pdf.
30. 210 F.3d at 479-80; see also *United States v. Pharmakon Laboratory Inc.*, Case No. 8:03-CV-1663-T-26MSS (M.D. Fl. 25 July 2005), available at www.fda.gov/cder/drug/unapproved_drugs/PharmakonJuly_25_order.pdf.
31. FDA, Notice; Carbinoxamine Products; Enforcement Action Dates, 71 Fed. Reg. 33,462, 33,464 (9 June 2006).
32. See FDA, Warning Letter to Concord Laboratories Inc., (11 July 2006) available at www.fda.gov/foi/warning_letters/g5973d.pdf; FDA, Warning Letter to Sheffield Laboratories, Div. of Faria Ltd. LLC, (24 July 2006) available at www.fda.gov/foi/warning_letters/g5960d.pdf.
33. See FDA, Warning Letter to Actavis Totowa, L.L.C., (15 Aug. 2006) available at www.fda.gov/foi/warning_letters/g6007d.pdf.
34. See Consent Decree of Permanent Injunction, (10 Aug. 2006) available at www.fda.gov/cder/drug/unapproved_drugs/syntho_CD_entered.pdf.
35. See Consent Decree of Permanent Injunction, (18 Sept. 2006) available at www.fda.gov/cder/drug/unapproved_drugs/CanfieldConsentDecree.pdf.
36. See FDA, Notice, Drug Products Containing Quinine; Enforcement Action Dates, 71 Fed. Reg. 75,557 (15 Dec. 2006).
37. See e.g., FDA, Warning Letter to Allscripts Healthcare Solutions, (11 Oct. 2002), available at www.fda.gov/cder/warn/2002/GuaifenesinLetters2.pdf.
38. FDA, News, FDA Advances Effort Against Marketed Unapproved Drugs, (11 Dec. 2006) available at www.fda.gov/bbs/topics/NEWS/2006/NEW01521.html.
39. FDA, CDER, Office of Compliance Website, available at www.fda.gov/cder/Offices/Compliance/default.htm.
40. Inside Health Policy, “Lawmaker Hopes Action On Quinine Signals Tougher FDA Crackdown on Unapproved Drugs,” 12 Dec. 2006.
41. FDA, News, FDA Advances Effort Against Marketed Unapproved Drugs, (11 Dec. 2006).
42. Pub. L. No. 102-571, 106 Stat. 4491 (1992), as amended by the FDA Modernization Act, Pub. L. No. 105-115, 111 Stat. 2296 (1997), as amended by the Medicare Prescription Drug, Improvement, and Modernization Act, Pub. L. No. 108-173, 117 Stat. 2066 (2003).
43. See Inside Health Policy, “Lawmakers Press FDA to Address Unapproved Drugs; Markey Eyes Bill,” 30 Oct. 2006.
44. Inside Health Policy, “Lawmaker Hopes Action On Quinine Signals Tougher FDA Crackdown on Unapproved Drugs,” 12 Dec. 2006; see also Inside Health Policy, “Lawmakers Press FDA to Address Unapproved Drugs; Markey Eyes Bill,” 30 Oct. 2006.
45. FDA, Congressional Report, “Feasibility and Cost of a New Monograph System for Marketed Unapproved Drugs,” House Rep. No. 108-193 & Sen. Rep. No. 108-107, at 3 (July 2004) available at www.fda.gov/cder/drug/unapproved_drugs/Congressional%20Report.pdf.
46. See FDA, Notice of Public Workshop, Marketed Unapproved Drugs, 71 Fed. Reg. 64,284 (1 Nov. 2006).
47. See FDA, Unapproved Drugs Workshop, Draft Agenda, available at www.fda.gov/cder/drug/unapproved_drugs/unapproved-Drugs_agenda.pdf.

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