

LAW OFFICES

KLEINFELD, KAPLAN AND BECKER, LLP

1140 NINETEENTH STREET, N.W.

WASHINGTON, D. C. 20036-6606

TELEPHONE (202) 223-5120

FACSIMILE (202) 223-5619

www.kkblaw.com

THOMAS O. HENTELEFF
RICHARD S. MOREY
KINSEY S. REAGAN
PETER R. MATHERS
ANTHONY L. YOUNG
BONNIE A. BEAVERS
DANIEL R. DWYER
GLENN E. DAVIS
STACY L. EHRLICH
JENNIFER A. DAVIDSON
STACEY L. VALERIO
ROBERT O. WINTERS

WEST COAST OFFICE:
ONE MARKET STREET
STEUART TOWER, SUITE 1450
SAN FRANCISCO, CA 94105-1313
TELEPHONE (415) 538-0014
FACSIMILE (415) 538-0016

VINCENT A. KLEINFELD
1907-1993

ALAN H. KAPLAN
1930-2001

OF COUNSEL:
HARVEY A. SUSSMAN

December 22, 2003

Division of Dockets Management (HFA-305)
Food and Drug Administration
5630 Fishers Lane, rm. 1061
Rockville, MD 20852.

RE: Docket No. 2003D-0478; Draft Guidance, "Marketed Unapproved Drugs: Compliance Policy Guide," 68 Fed. Reg. 60702, October 23, 2003.

Dear Madam/Sir:

The undersigned submits these comments on the above-referenced Federal Register notice and Guidance document, on behalf of several clients of this firm who are potentially affected by the agency policies described in the Guidance. As elaborated below, our comments are:

1. As a document designed to set forth administrative and procedural considerations relating to the Agency's regulation of the marketing of drug products without NDA or ANDA approvals, comments about the substantive legality or illegality of such unapproved drugs are not germane to this Guidance, and all such statements by the Agency should be excised from the final Guidance document; and
2. The particular statements inserted in the draft Guidance about the illegality, or likely illegality, of unapproved marketed drug products, are unwarranted, misleading and harmful overgeneralizations which are not based on an appropriate administrative record.

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Statements about the legality of unapproved marketed drug products are not appropriate to include in the Guidance

The stated purpose of the Guidance is to document how the Agency intends to exercise its authority to regulate the marketing of drug products that do not have “required” NDA or ANDA approval or that are not marketed in accordance with an OTC monograph. In so doing, the Guidance properly sets forth considerations relating to the prioritization of drug products for potential administrative or judicial enforcement efforts. These include consideration of alleged safety risks, lack of efficacy, or fraudulent marketing claims. They also include consideration of the interests of patients, physicians and the healthcare system generally in the availability and use of unapproved drug products as a cost-effective means to meet important medical needs. In so doing, the Guidance states that the Agency will apply certain priorities in choosing drug products against which regulatory action may be initiated, in choosing the means by which to initiate such action, and in setting timetables and procedures by which the status of affected drug products would be desired or expected by the Agency to be resolved.

In setting these compliance policies, there is clearly neither need nor basis for the Agency to establish substantive grounds on which particular unapproved products may be subject to regulatory action – and the Agency does not do so. In each case that may be initiated, the substantive grounds for alleging a violation of applicable legal standards will necessarily turn on specific evidence (or lack thereof) of the safety and efficacy of the affected products, the marketing history of the products, and any applicable statutes and legal precedents that may bear on the products’ status. *See Weinberg v. Hynson, Westcott & Dunning, Inc.*, 412 U.S. 609, 93 S.Ct. 2469, 37 L. Ed.2d 207 (1973). Recognizing that specific determinations will need separately to be made as to whether particular drug products are potentially subject to regulatory action under these policies, the Guidance speaks consistently in terms of its application to products that lack “required” NDA or ANDA approval. Whether such approval is or is not required for a particular product is thus clearly outside of the scope, and the intended scope, of the Guidance.

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Despite this, however, the draft Guidance is riddled with unnecessary and gratuitous statements improperly suggesting that many, or even all, general categories of drug products marketed without NDA or ANDA approval are illegal.

“FDA considers all products described in this paragraph [i.e., products subject to completed DESI proceedings] to be marketed illegally.” (Draft Guidance, page 8.)

“Drugs that were subject to the Prescription Drug Wrap-Up are all marketed illegally, except in the very unlikely circumstance that a manufacturer of such a drug can establish that its drug is grandfathered or otherwise not a *new drug*.” (Draft Guidance, page 9.)

“As mentioned above, the Agency believes it is very unlikely that any currently marketed product is grandfathered or is otherwise not a *new drug*. However, the Agency recognizes that it is at least theoretically possible that such a product exists.” (Draft Guidance, page 10.)

“Some unapproved drugs were first marketed (or changed) after 1962. These drugs are on the market illegally. Some also may have already been the subject of a formal Agency finding that they are new drugs. See, e.g., 21 CFR 310.502 (discussing, among other things, controlled/timed release dosage forms).” (Draft Guidance, page 10.)

Even when these statements reflect the Agency’s recognition that unapproved products may legally be marketed if they are subject to one or more “grandfather” provisions or otherwise are not covered by the definition of “new drug,” the Guidance gratuitously describes this legal status as “theoretical” or “unlikely”. All of these statements are outside of the necessary and appropriate, and apparently intended, scope of the draft Guidance and should be excised from the final Guidance.

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Statements in the draft Guidance about the legality of unapproved drug products are unwarranted, misleading, and harmful overgeneralizations

Since the purpose of the Guidance is limited to an explanation of the procedural and policy aspects of how the agency intends to prioritize and pursue regulatory action against products that lack required NDA or ANDA approval, there is no reason for any statements to be included about the substantive standards for determining whether such approval may or may not be required. However, even if such statements were germane to the Guidance, or were otherwise believed to be helpful to an understanding of the procedures and policies being set forth, the particular statements made in the draft Guidance are inappropriate on a number of grounds.

The FDCA does not empower FDA to make legally binding determinations of new drug or grandfathered status.

Nowhere in the FDCA is FDA entrusted with the authority to make a binding legal determination of the legality of an unapproved marketed drug product. The FDCA prohibits the interstate marketing of a drug product in violation of the “new drug” approval requirements of the Act. The Act also provides the FDA with various enforcement tools which it may use in the event that it seeks to halt or prevent the marketing of a particular drug product. Each of those enforcement tools, however, requires that FDA initiate an action in an appropriate Court. Moreover, in order to obtain relief in such an action, FDA is required to make a particularized showing that the product in question meets the applicable statutory definition of a “new drug” and to refute evidence that the product is exempt from new drug approval requirements based on any of several “grandfather” provisions that have been adopted over the years. Only if a Court concurs with FDA and so orders, can a drug product be declared to be a “new drug” that must be the subject of FDA approval before it can legally be marketed.

In this context, FDA statements about the legality or illegality of any particular drug product or category of drug product, are merely assertions of Agency opinion and do not carry the force and effect of law. It is therefore inappropriate for FDA to make any definitive statement, such as those made

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in the draft Guidance, to the effect that a particular drug product or category of drug product being marketed without NDA or ANDA approval is being marketed illegally.

With limited exceptions, FDA does not follow formal procedures to make administrative determinations of “new drug” status.

Except for OTC drugs subject to the OTC Review Program, and certain drugs for which FDA is willing to offer an opportunity for an administrative hearing concerning “new drug” status, there are no formal administrative proceedings in which the agency makes “new drug” determinations. Even when formal administrative procedures are followed, there remains the possibility that agency determinations, or their applicability to particular drug products, may be challenged on appeal or collaterally in an enforcement action.

Similarly, the Agency’s codified general statements of policy and interpretation with respect to new drugs are of limited legal effect. Specifically, the codified Agency statements regarding time-release drug products and combination drug products were not adopted pursuant to notice and comment rulemaking and, even when their applicability to a particular product may appear clear, do not have any determinative effect on the legal status of any product apart from the ability of FDA to demonstrate the validity and applicability to that product of the policies stated therein.

With respect to a number of additional categories of marketed drug products, FDA does not have any regulation or review program that purports to make or enable FDA to make a definitive judgment whether those products are subject to new drug approval requirements, apart from FDA’s ability to persuade a Court to so rule.

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Generalized statements in the draft Guidance about whether marketed drug products require NDA or ANDA approval are unwarranted and misleading.

In the absence of a systematic review of long-marketed unapproved drug products and the scientific evidence and marketing history that underlay their legal status, it is unwarranted and misleading for FDA to state, as it does in the draft Guidance, an off-hand opinion that some, or some categories, of those products are illegal or “likely” to be illegal. Even more so, a general statement that all such products are illegal or “likely” to be illegal is entirely inappropriate.

In the absence of a specific call for information about the basis on which the products are marketed, and a detailed review of that information, FDA is simply in no position to make categorical statements about the legal status of these products. Moreover, in making such statements, the Agency misleadingly suggests to the reader that it has made such an inquiry and assessment when no such effort has actually been made.

While it might reasonably be pointed out that the standards for establishing not-new-drug or grandfathered status for drugs are generally very high, the agency has no basis to state categorically that an adequate showing cannot or would not be made by the manufacturer of any such product if and when the manufacturer finds itself in a procedural posture in which it is necessary and/or appropriate for such a showing to be made.

Generalized statements in the draft Guidance about whether marketed drug products require NDA or ANDA approval are gratuitously and inappropriately harmful.

The new draft Guidance is intended to update and supercede long-standing FDA Compliance Policy Guides. Under those Compliance Policy Guides, FDA established and continues to maintain policies and safe harbors under which firms interested in competing in the market for unapproved prescription drug products can be reasonably assured that their products will not be singled out for regulatory action while other, similar products are not.

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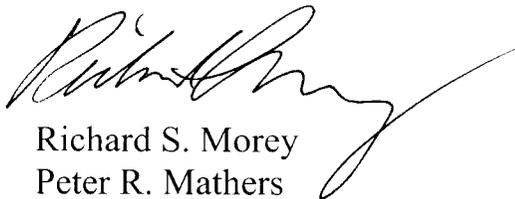
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The vigorous market for high-quality unapproved prescription drug products described by FDA in the draft guidance has developed in no small part due to the explicit encouragement of the FDA, as embodied in these Compliance Policy Guides. Nothing in the draft Guidance suggests that the Agency intends the new Guidance to contradict these long-standing policies.

However, by overstating the degree to which the Agency can reasonably conclude, based on the current state of its review procedures, that the unapproved products covered by the Guidance are illegally marketed, the Agency indirectly contradicts these policies. These gratuitous Agency statements also create ammunition, readily taken out of context, for third parties to use inappropriately against the regulated industry and the Agency itself.

As those statements are both unnecessary to the purpose of the Guidance and, more importantly, overstated, they should be omitted from the final Guidance. Rather, the Guidance should simply reflect that the marketed products addressed therein are subject to legal action, in accordance with the policies stated therein, when and if the agency makes a determination that such action is warranted and that it appears the marketing of such products without approval is contrary to the requirements of the FFDCA.

Sincerely,



Richard S. Morey
Peter R. Mathers