



2550 M Street NW
Washington DC 20037
(202) 457-6000

Facsimile (202) 457-6315

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Paul D. Rubin
(202) 457-5646
prubin@pattonboggs.com

VIA HAND-DELIVERY AND E-MAIL

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

Re: Comments Regarding the Food and Drug Administration's Draft Guidance
on Marketed Unapproved Drugs; Compliance Policy Guide
[Docket 2003D-0478]

Dear Sir or Madam:

On behalf of Galderma Laboratories, L.P. ("Galderma"), Patton Boggs LLP is submitting these comments in response to the Food and Drug Administration's ("FDA's" or "Agency's") notice announcing the availability of a draft guidance document entitled "Marketed Unapproved Drugs; Compliance Policy Guide."¹ As a leading manufacturer and distributor of FDA-approved dermatological products, Galderma is very concerned about the illegal marketing of unapproved "new drugs" that have never been reviewed for safety or efficacy by the FDA. As the FDA noted in its compliance policy guide ("CPG") notice and related press release, as many as several thousand drug products are currently being illegally marketed in United States without required FDA approval.

As explained herein, for public safety reasons, and in order to provide appropriate incentives for companies to pursue FDA approval for unlawfully marketed drug products, Galderma believes the Agency's proposed CPG should be strengthened. Specifically, Galderma believes the Agency should require all companies to comply immediately with the law and obtain new drug application ("NDA") approval from the Agency in order to market "new drugs" in the United States. To the extent the

¹ See FDA's Notice, 68 Fed. Reg. 60702 (Oct. 23, 2003).

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FDA believes requiring immediate, full compliance is too burdensome, at a minimum the Agency should immediately require NDA approval for all unapproved “new drugs” being promoted unlawfully. In addition, the Agency should immediately act to restrict the initial introduction of new unapproved “new drugs” (and drugs that are not identical to pre-1962 drugs) into the market.

Galderma is also enclosing survey data confirming that health care professionals mistakenly believe that all prescription drug products have been approved by the FDA and found to be safe and effective. Moreover, the health care professionals surveyed overwhelmingly believe the absence of such approval should be disclosed. Accordingly, in order to correct this mistaken assumption, Galderma believes FDA enforcement discretion should be contingent upon drug companies prominently disclosing – in FDA-approved labeling – that their drug products have not been approved by the Agency. Disclosure of this material fact would prevent health care professionals from being deceived and would cure what Galderma believes would otherwise be a material, and deceptive, omission in drug labeling. Galderma believes a statement such as the following may cure this material omission: “THIS DRUG PRODUCT HAS NOT BEEN APPROVED BY THE FDA.”

In addition to public disclosure in drug labeling, Galderma also believes the FDA should maintain a public list of unapproved “new drugs” that are being marketed in the absence of FDA approval. Such a list, which should be displayed on FDA’s website, would enable health care professionals – and consumers – to easily determine which drug products have not been approved by the Agency. Furthermore, such public disclosure would provide companies with an incentive to obtain NDA approval. Based upon recent Agency statements and First Amendment case law encouraging more disclosure as opposed to less, Galderma believes such a public database would be an inexpensive method of disclosing material information to health care professionals and consumers.

I. Background

A. Absence of Safety and Efficacy Data for Unapproved “New Drugs”

The FDA has acknowledged that as many as several thousand drug products are currently being illegally marketed in United States without required FDA approval. Many of these drugs were developed and marketed before modern standards for drug approval were established – while most have never been reviewed for either safety or efficacy by the Agency.

As the FDA acknowledged in its proposed CPG, the belief by health care professionals and consumers that these drugs are safe and effective is not based on scientific evidence, but rather on anecdotal data. The Agency has indicated on numerous occasions, however, that anecdotal data are insufficient to establish drug product safety and/or efficacy. In particular, the FDA’s NDA regulations require substantial evidence consisting of adequate and well-controlled investigations

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that a drug product seeking NDA approval will have the effect it purports or is represented to have.² The regulations clearly delineate the characteristics of an adequate and well-controlled study, without making any reference to inclusion of anecdotal data as an acceptable methodology. Specifically, the regulations provide that “[i]solated case reports, random experience, and reports lacking the details which permit scientific evaluation will not be considered” in the decision to approve an NDA.³ In the absence of well-controlled investigations, it is not possible to know whether these drugs are, in fact, safe and effective, or whether they are ineffective or even dangerous.

The continued presence of such products on the market creates a health and safety hazard for the public, raises serious questions regarding the presumed efficacy of such products, and creates a disincentive for companies to seek FDA approval for new products.

B. History of Current Compliance Policy Guide 440.100

1. Initial Development

The FDA has been grappling with the issue of marketed unapproved “new drugs” for more than a quarter-century. In 1976, after the United States District Court for the District of Columbia issued its decision in the Hoffman-LaRoche⁴ case, the FDA issued an “administrative guideline for a systematic enforcement policy” regarding marketed new drugs without NDAs.⁵ This guideline was intended to implement the Court’s holding that, after the FDA has determined a drug product is a “new drug,” it is not permitted to allow any identical, similar or related product to be marketed without approval of an NDA or ANDA. Since 1976, the guideline has been expanded, reissued, and revised on several occasions, and is now codified as Compliance Policy Guide (“CPG”) 440.100 (“Current CPG” or “CPG 440.100”).

2. E-Ferol Hearings

The 1983 E-Ferol tragedy prompted the Congressional Committee on Government Operations to hold a hearing⁶ examining the FDA’s regulation of unapproved “new drugs.” The Committee’s post-hearing report⁷ strongly criticized the FDA for permitting the marketing of unapproved DESI

² 21 C.F.R. §§ 314.125(a)(4), (a)(5).

³ 21 C.F.R. § 314.126(e).

⁴ Hoffman-LaRoche, Inc. v. Weinberger, 425 F. Supp. 890 (D.D.C. 1975).

⁵ 41 Fed. Reg. 41770 (Sept. 23, 1976).

⁶ FDA’s Regulation of the Marketing of Unapproved New Drugs: The Case of E-Ferol Vitamin E Aqueous Solution: Hearing Before a Subcommittee of the Committee on Government Operations, 98th Cong. (1984) (“Hearing”).

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and non-DESI drug products⁸ and noted a number of negative consequences resulting from Agency permissiveness that are still relevant today.

First, the FDA's failure to enforce the new drug approval requirements of the law "effectively signals to pharmaceutical manufacturers and distributors that they need not involve the Agency in their decision to market new drug products."⁹ Second, as the E-Ferol tragedy made clear, failure to review and approve new drugs prevents the FDA from assuring the safety of drugs on the market:

FDA's failure to review the safety of E-Ferol prior to permitting its continued marketing is contrary to the very purpose for which the Act was enacted. Until FDA has reviewed the safety of all changes in the composition or method of administration of a 'new drug,' as well as the quality of its manufacture, it has no basis for concluding that it is safe for its intended use. In allowing E-Ferol to remain on the market without new drug approval, FDA, in fact, may have denied itself the right to receive information critical to assessing its risks.¹⁰

Moreover, the FDA's failure to keep unapproved new drugs off the market places companies that comply with FDA requirements at a distinct disadvantage:

At the same time that FDA was permitting E-Ferol to be marketed, it was putting sponsors to the considerable time and expense of clinical trials and, in one case, the new drug approval process, for very similar types of products. FDA's conduct reflected a double standard which discriminated against firms that complied with the agency's investigational new drug and new drug approval requirements.¹¹

The report concluded: "FDA has no legal authority to permit the marketing of any unapproved 'new drug,' let alone an unapproved new drug seen as identical to another 'unapproved' new drug. Insofar as pre-1962, unapproved drugs and their post-1962 imitations are 'new drugs' within the meaning of the law, the committee concludes that they may not be marketed without new drug

⁷ "Deficiencies in FDA's Regulation of the Marketing of Unapproved New Drugs: The Case of E-Ferol," Sixty-Eighth Report by the Committee on Governmental Operations, H.Rep. No. 98-1168 (1984) ("Report").

⁸ See generally, Report.

⁹ Report, p. 19.

¹⁰ Report, p. 10.

¹¹ Report, p. 8.

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approval.”¹² The Committee recommended that the FDA take action “to secure the voluntary removal from the market of any unapproved ‘new drug,’ pending a determination of the drug’s safety and effectiveness pursuant to the submission of an appropriate new drug application.”¹³

3. The Current Compliance Policy Guide

Following the E-Ferol report, the FDA revised its Compliance Policy Guide regarding the marketing of unapproved “new drugs” and articulated an enforcement policy that has been maintained throughout the past 20 years. Under the current CPG (440.100), as under previous versions, the likelihood that the FDA will take enforcement action against a marketed unapproved prescription drug depends upon how that drug is categorized.¹⁴ In particular, the current CPG distinguishes between drugs that fall under the rubric of the DESI review and those that do not:

- Part A of the CPG covers DESI prescription drugs for which the FDA has made a final determination of effectiveness and “new drug” status, and for which a Federal Register notice has been published requiring ANDA or NDA approval prior to marketing. Under Part A, drugs are placed into one of seven categories in order of enforcement priority.
- Part B covers DESI and other pre-1962 prescription drugs for which a final determination of regulatory or legal status has not been made. This category includes certain drug products containing ingredients marketed before 1962 that are not covered by an NDA, and are marketed based on their manufacturer’s belief that such products are not subject to the “new drug” provisions of the Federal Food, Drug, and Cosmetic Act. Part B drugs may be reviewed under the regulatory scheme “under Part A as final determinations are made regarding their effectiveness, new drug status, or grandfather status.”
- Finally, regardless of the above, the current CPG preserves the FDA’s right to take enforcement action against drugs that fall within the following categories:
 - 1) where a drug subject to the policy violates another provision of the FFDCA;
 - 2) when the Agency receives significant new information that questions the safety or effectiveness of the drug;

¹² Report, p. 21.

¹³ Report, p. 22.

¹⁴ See Compliance Policy Guide 440.100.

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- 3) where a drug is on the market without an approved NDA and is identical or related to a post-1962 drug approved for safety and effectiveness or contains a new chemical entity not previously marketed;
- 4) where a drug was introduced to the market after Nov. 13, 1984 and that drug differs from a product covered by Part B in: (a) formulation; (b) dosage or strength; (c) dosage form; (d) route of administration; (e) indications for use; or (f) intended patient population; or
- 5) where an unapproved drug covered in Part B, described above, makes a change after Nov. 13, 1984, in: (a) formulation; (b) dosage or strength; (c) dosage form; (d) route of administration; (e) indications for use; or (f) intended patient population.

II. The FDA Should Establish a More Stringent Policy to Enforce Against Unapproved “New Drugs”

A. The Proposed CPG Must Recognize That All Unapproved Drug Products Pose Potential Risks to Health and Safety – and Such Risks Exceed the Risks the FDA has Identified for Drug Products Reimported into the United States

Under the proposed CPG, the FDA would prioritize enforcement against drugs that pose potential safety risks. Clearly, to the extent that the FDA is aware that a particular unapproved “new drug” does in fact pose a safety risk, it should enforce against that drug immediately. The current CPG (440.100) provides for just such a scenario, by stating that regardless of whether a drug falls outside of the Agency’s established enforcement priorities, the FDA reserves the right to initiate action against any drug should the Agency receive significant new information which questions the drug’s safety or effectiveness.¹⁵ At a minimum, this provision should be incorporated into any new CPG to ensure that manufacturers are on notice that any safety concerns will lead to immediate enforcement.

To the extent that the FDA is truly concerned with safety, it should be concerned with the safety of all unapproved “new drugs.” Any unapproved “new drug” poses a potential, unknown safety risk and should be removed from the market as quickly as possible.

¹⁵ See Compliance Policy Guide, § 400.100.

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As Commissioner McClellan's recent comments¹⁶ on the safety risks inherent in unregulated *reimported* drugs make clear, the FDA is already aware of the significant threat to public health posed by drugs over which the Agency has had no oversight:

When it comes to buying drugs internationally, outside of our regulatory protections, beyond the authorities of the Federal and state watchdogs for drug safety, FDA has consistently said for many years that we can't in good faith endorse "buyer beware" approaches to the problem of affordable drugs. . . .

Consequently, when Americans import drugs that are not regulated and approved in the United States, it presents real safety risks, risks that are becoming more common.¹⁷ (Emphasis added.)

As the Commissioner correctly noted, it is simply not enough to forgo the comprehensive Federal and state systems for assuring drug safety and to assume, instead, that seemingly legitimate companies outside the United States will produce safe drugs: "In spite of what some say, none of these drugs will have gone through the approval, monitoring, and prescribing process required in the United States."¹⁸

Rather, Commissioner McClellan emphasized that until new technologies and mechanisms are in place to assure drug safety:

FDA needs all of the authorities it has now to assure the safety of legal prescription drugs. This includes the ability to require or conduct tests of product authenticity and potency; the ability to identify and when necessary inspect those involved in the distribution of pharmaceuticals; and the authority to issue regulations and when necessary take decisive action to block the distribution of potentially unsafe drugs. It's certainly not the time to weaken these authorities, or to allow products into this country that are not subject to these consumer protections . . .¹⁹ (Emphasis added).

¹⁶ Remarks by Mark B. McClellan, MD, Ph.D., Commissioner, Food and Drug Administration, Speech before the Fifth Annual David A. Winston Lecture, National Press Club, Washington D.C., Oct. 20, 2003. Available at <http://www.fda.gov/oc/speeches/2003/winston1020.html> (last visited Nov. 19, 2003).

¹⁷ Id.

¹⁸ Id.

¹⁹ Id.

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The FDA should harbor at least the same concern for unapproved domestic drugs as it does for reimported drugs. In fact, Galderma believes the Agency should be even more concerned about the potential safety risks posed by unapproved domestic drugs, which may be even greater than that of reimported drugs. Many drugs coming into the United States from other countries are being reimported into the United States after receiving FDA approval and being exported to other countries. While the safety and efficacy of such drugs upon reentry cannot be guaranteed, it is at least the case that these drugs were subject to evaluation, safety checks, and approval prior to exportation. In contrast, unapproved domestic drug products that have not been evaluated and approved by the FDA have never been subject to the safety checks noted by Commissioner McClellan, and should not be presumed to be safe. Rather, they should be presumed to pose potential risks to health and safety, in the same manner that reimported drugs are presumed to be unsafe.

In light of the FDA's clear concerns about drug safety, it is utterly illogical to allow domestically manufactured drugs to avoid the very protections the Agency is arguing must be applied to reimported drugs and to allow unapproved "new drugs" to remain on the market at all, let alone indefinitely. The FDA should make clear in any new CPG that it intends to make every effort to remove these products from the market immediately.

B. The Proposed CPG Must Recognize That Allowing Unapproved Drug Products To Remain on the Market Seriously Undermines the Agency's Goal of Providing Incentives for Companies to Obtain NDA Approval and Otherwise Comply with the Law

In its proposed CPG, the FDA expressly states that one of its primary goals is to encourage companies to voluntarily comply with "new drug" requirements because "it benefits the public health by increasing the assurance that marketed drug products are safe and effective" and "reduces the resources FDA must expend on enforcement."²⁰ To the extent that the Agency exercises broad discretion in enforcing against marketed unapproved drugs and permits such products to remain on the market, however, the FDA undermines this goal and in fact creates a disincentive for companies to seek approval.

First, the FDA's failure to require all companies to obtain NDA approval prior to marketing new drugs creates an enormous financial disincentive for companies to seek such approval. Obtaining NDA approval requires the expenditure of significant time and financial resources. It is entirely unfair and inappropriate to require companies that are willing to comply with the law to spend millions of dollars on clinical research and user fees, while companies that ignore the law are permitted to avoid these costs and to market their products without approval. Furthermore,

²⁰ See Draft Guidance, "Marketed Unapproved Drugs; Compliance Policy Guide," pp. 4-5 (Oct. 23, 2003), *available at* <http://www.fda.gov/cder/guidance/5704dft.pdf> (last visited Dec. 10, 2003).

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companies have no incentive to expend the considerable resources necessary to seek and obtain NDA approval if they know they can simply place their products on the market and avoid FDA enforcement.

Second, to the extent the FDA wishes to exercise enforcement discretion and carve out specific areas of enforcement priority, the Agency should not exercise this discretion in a manner that creates a disincentive to comply with the law. For example, even if FDA should decide that certain drugs will not be subject to NDA requirements, it should not permit companies to market those exempt drugs in violation of other regulatory requirements such as drug listing, labeling requirements, advertising and promotion requirements, etc. To the extent that the FDA allows companies to market unapproved drugs freely and without regulatory scrutiny, companies would have no incentive to comply with any regulatory requirements.

Where approval is required but the Agency exercises enforcement discretion, companies that comply are penalized in that they become subject to considerable FDA scrutiny of labeling, claims, promotional materials, etc., while companies that choose to ignore the law are allowed to market freely. Certainly this creates a significant disincentive for companies to seek NDA approval. Alternatively, where approval is not required, allowing drugs to use their exempt approval status as a means to avoid other regulatory requirements is both unfair and illogical. Therefore, the proposed CPG should make explicit that: 1) FDA will enforce against any illegal marketing of drug products, regardless of approval status, and 2) enforcement discretion for drugs marketed in the absence of NDA approval will be immediately terminated in the event an unapproved “new drug” is labeled or marketed unlawfully or other FDA-regulatory requirements are violated. The proposed CPG should indicate that any enforcement discretion is contingent upon otherwise lawful behavior – and an immediate “new drug” charge will be brought by the Agency against an unapproved “new drug” in the event other FDA-regulatory requirements are violated.

C. The FDA Should Vigorously Enforce Against Products Containing Active Ingredients Not Proven to be Effective

We strongly support the FDA’s intent to remove from the market products that lack evidence of effectiveness. As the FDA states, these products prevent the public from seeking effective treatment, and may pose safety risks as well. To the extent there is any question about a drug product’s efficacy, the FDA should seek to remove it from the market immediately. This is particularly true where efficacy claims are made for ingredients that have never been evaluated by the FDA for their intended use.

Currently, numerous products are being marketed with false and misleading claims that promote “inactive ingredients” as active ingredients. These claims clearly violate Agency regulations regarding false and misleading advertising of prescription drug products, in that they feature “inert inactive ingredients in a manner that creates an impression of value greater than their true functional

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role in the formulation.”²¹ Such misleading promotional practices induce consumers to buy products that may not provide their claimed benefit, perhaps forgoing other effective treatments. Clearly this leads to the type of “health fraud” the FDA has identified in the proposed CPG. Moreover, as noted above, to the extent that competitors are able to make fraudulent claims of efficacy without undergoing FDA scrutiny, companies are provided with yet another disincentive to pursue NDA approval.

D. The FDA Should Take Immediate Enforcement Action against any Unapproved “New Drugs” that are not Identical to Pre-1962 Drugs

The proposed CPG would eliminate the DESI/non-DESI distinction as a primary basis for enforcement. Instead, the proposed CPG would make the DESI/non-DESI distinction a mere factor to be considered as the FDA exercises its enforcement discretion. We believe the DESI/non-DESI distinction should not be eliminated, but rather should be strengthened.

Under the proposed CPG, the FDA would prioritize and enforce against drugs according to: 1) potential safety risk; 2) lack of evidence of efficacy, and 3) health fraud. As written, these categories are exceedingly narrow and fail to account for the wide number of unapproved “new drugs” that are being marketed illegally and/or fraudulently, and which need to be removed from the market as quickly as possible. The FDA should make explicit that it will immediately remove from the market any product – single ingredient or combination - that is not identical, similar or related to a pre-1962 approved drug.

Specifically, current CPG (440.100) explicitly reserves the FDA’s right to enforce against an unapproved prescription drug first marketed after November 13, 1984, if the product is not identical to a pre-1962 drug and differs in formulation, dosage or strength, dosage form, route of administration, indications for use, or intended patient population. A formulation is considered different if the active ingredient is different in substance or quantity; if it is a non-oral, non-topical product that contains inactive ingredients that differ in substance, amount or proportion so as to require disclosure on the labeling; or if it is an oral or topical preparation containing one or more inactive ingredients not customarily used in such a product.²² These provisions, which are in the current CPG, are not included in the proposed CPG.

Galderma believes it is critically important that the proposed CPG be revised to include these enforcement provisions. The number of unapproved “new drugs” available in the United States should not continually expand but rather should be limited to the greatest extent possible. In the event the Agency opts not to take immediate enforcement action against all unapproved “new

²¹ 21 C.F.R. § 201.10(c)(4).

²² See Compliance Policy Guide, §400.100.

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drugs,” at a minimum the Agency should take action to prevent the marketing of new unapproved “new drugs” by limiting such products to those identical to pre-1962 drugs

E. The FDA Should Broaden the “Health Fraud” Category to Encompass All “New Drugs” that are Illegally or Fraudulently Marketed or that Fail to Comply with FDA Regulatory Requirements

As written, the proposed CPG would give enforcement priority to “health fraud drugs.” The FDA defines “health fraud” based upon Compliance Policy 120.500, “Health Fraud – Factors in Considering Regulatory Action.” According to CPG 120.500, health fraud encompasses the “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.”²³ The health fraud CPG focuses specifically on drugs that pose a direct or indirect risk to health - that is, on drugs that are likely to cause injury, death, or other serious adverse effect when used as directed or that are likely to cause a consumer to delay or discontinue appropriate medical treatment in reliance on the product.²⁴

Such a narrow definition ignores a variety of improper promotional practices that should prompt immediate FDA enforcement. Many of the unapproved “new drugs” on the market are being marketed with false or misleading claims that may not necessarily result in injury, death, or delayed treatment. Thus, in order to encourage lawful promotional practices this third category of enforcement priority should be expanded to require enforcement against unapproved “new drugs” that are promoted unlawfully. As discussed above, failure to enforce against such products provides a disincentive for companies marketing such products – and their competitors – to pursue NDA approval based upon the fear that the Agency would scrutinize the drug and prohibit such promotional practices once approval was obtained.

Specifically, the new CPG should make clear that the FDA will no longer exercise enforcement discretion when a company: 1) unfairly promotes a product by touting an inactive ingredient as an active ingredient; 2) impermissibly broadens the indications for use; 3) makes unsubstantiated claims of efficacy; or 4) makes any other fraudulent, misleading, or unsubstantiated claim. Even where a product is arguably identical, similar or related to a pre-1962 drug product, it should not be promoted in a manner that exceeds the scope of the pre-1962 intended use. Rather, the new CPG should articulate that the FDA will take immediate enforcement action against any company that makes a claim that differs from a pre-1962 product claim with regard to content, efficacy or safety. The law regarding the marketing of unapproved “new drugs” is clear, and companies should be expected to comply with that law or face certain enforcement.

²³ See Compliance Policy Guide § 120.500.

²⁴ *Id.*

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Finally, Galderma believes swift enforcement should result from violations unrelated to promotional practices such as the failure to report adverse events to the Agency, failure to properly register drug establishments, and failure to properly list drug products with the FDA. As a matter of both fairness and incentive, companies that fail to comply with these regulations should expect and receive immediate enforcement. Consistent enforcement will provide companies with added incentive to comply with the law, and eliminate any disincentive to avoid an NDA submission based upon FDA regulatory scrutiny resulting from such a submission.

III. The FDA Should Mandate Public Disclosure of Unapproved “New Drug” Status

In addition to strengthening the proposed CPG by incorporating certain elements from the current CPG and by making a commitment to enforce against any unapproved “new drug” improperly on the market, Galderma strongly believes the Agency should take additional steps to ensure that health care professionals and consumers are clearly informed that certain drug products have never been approved by the FDA.

The FDA has acknowledged, in response to First Amendment case law on issues of product labeling, that the public has a significant interest in access to “useful and truthful information about medical products”²⁵ The FDA has indicated that truthful claims concerning drugs, among other products, may improve public health by leading to better informed consumers and by encouraging more consumers to visit their physicians.²⁶

At the same time, the FDA has cautioned that false or misleading claims concerning these products may harm individuals who rely on those claims and may have a negative effect on public health, particularly “where advertising of prescription drugs results in the inappropriate prescription of pharmaceuticals.”²⁷ Based upon the mistaken assumption by physicians that all prescription drug products have been FDA-approved for safety and efficacy, it is quite likely that the marketing of such products – in the absence of an appropriate disclosure – has led to inappropriate prescribing. In order to cure this material omission, consumers and health care professionals should be made aware that specified drug products have never been approved by the Agency. As explained below, the absence of FDA approval should be disclosed in drug labeling, and a publicly accessible database of unapproved “new drugs” should be maintained on FDA’s website.

²⁵ 67 Fed. Reg. 34943 (May 16, 2002) (seeking public comment on First Amendment issues related to FDA’s regulation of commercial speech).

²⁶ *Id.*

²⁷ *Id.*

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Importantly, the mandatory disclosure of the unapproved status of such products would provide added incentive for companies to seek NDA approval. At present, many companies correctly assume that health care professionals are unaware that certain drugs have never been approved by the Agency. If required to disclose a product's unapproved status, companies may reconsider their decision to market such a product and may instead opt to submit an NDA to the Agency.

In order to expedite such disclosures, the FDA should indicate in its proposed CPG that any enforcement discretion for unapproved "new drugs" will be contingent upon disclosure of unapproved status in drug labeling and in the FDA's public database.

A. A Health Care Professional Survey Confirms that Physicians Mistakenly Assume All Prescription Drug Products Have Been FDA-approved – and Physicians Believe the Absence of FDA-approval Should be Disclosed in Drug Labeling

A recent survey confirms that health care professionals mistakenly assume that all prescription drug products are FDA-approved.²⁸ In this survey, 85% of the 165 physicians polled believed that the FDA has approved all marketed prescription drug products.²⁹ Clearly, most health care professionals incorrectly assume that the drug products they are prescribing to their patients are FDA-approved simply because the products are being marketed in the United States.

Health care professionals, if they are to properly serve their individual patients' needs, should be armed with as much information as possible about the prescription drugs available to them. This includes the knowledge that a particular drug is, or is not, FDA-approved. And in fact, 85% of the physicians surveyed indicated that doctors should be able to determine whether the FDA has approved a prescription drug product.³⁰ Moreover, the vast majority of physicians surveyed (87%) agreed that it would be helpful for drug labeling (for example, labeling contained in the Physician's Desk Reference®) to disclose that a prescription drug has not been FDA approved.³¹

B. The FDA Should Mandate Disclosure on Drug Labeling

Currently, there is no mechanism to easily discern whether a drug product has been FDA-approved. Based upon the above-mentioned concerns, the FDA should require drug products on the market that have not been FDA-approved to clearly state on their labeling: "THIS DRUG PRODUCT

²⁸ This survey of 165 dermatologists was conducted online between November 6, 2003 and November 11, 2003.

²⁹ See Attachment, Question 1.

³⁰ See Attachment, Question 2.

³¹ See Attachment, Question 3.

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HAS NOT BEEN APPROVED BY THE FDA.” This will ensure that health care professionals are properly informed regarding the drugs at their disposal, so that they may choose, on the basis of full, truthful information, which products to prescribe for their patients.

Moreover, such a requirement would be entirely consistent with FDA’s new final rule requiring electronic submission of labeling with NDAs. FDA has stated that the rule is intended to help “[get] important, up-to-date information on medications to doctors and patients more quickly,” to “promote higher-quality care for patients,” and “to communicate information that doctors and patients need in order to use a product.”³² These are precisely the goals such a disclosure requirement would meet – mandatory disclosure labeling would help ensure that doctors and patients have ready access to up-to-date information about products, in order to ensure high quality care.

C. The FDA Should Establish a Database of Unapproved “New Drugs”

In addition to the mandatory disclosure on drug labeling, the FDA should also create a public database of unapproved “new drugs” being marketed in the United States. As with labeling indicating approval status, such a database would provide physicians and consumers with valuable information in determining how best to treat their patients. Such public disclosure would also provide companies with an added incentive to pursue NDA approval. Moreover, such a database would enable FDA to better track the approval status of products on the market for the purpose of facilitating enforcement.

IV. Conclusion

Galderma is encouraged by the FDA’s increased focus on the marketing of unapproved “new drugs.” The FDA’s recent actions regarding guaifenesin and levothyroxine sodium indicate the Agency’s renewed commitment to take enforcement action against illegally marketed “new drugs.” Galderma supports the FDA in its efforts to clarify and strengthen its enforcement policies and to remove unapproved prescription drugs from the market. To that end, we applaud the goals of the proposed CPG.

As explained above, however, we have a number of concerns with the proposal. In particular, we are concerned that the FDA is still not taking immediate enforcement action against companies marketing unapproved “new drugs.” We are also concerned with the proposed CPG’s apparent omission of several key elements that are included in the current CPG (440.100). The absence of key provisions makes the proposed CPG less stringent in a number of respects than the current

³² See “FDA Publishes New Requirements for E-Labeling of Drug and Biologics Applications”, FDA White Paper (Dec. 9, 2003), available at <http://www.fda.gov/bbs/topics/NEWS/2003/NEW00991.html> (last visited Dec. 10, 2003); see also Requirements for Submission of Labeling of Human Prescription Drugs and Biologics in Electronic Format, 68 Fed. Reg. 69009, 69010 (Dec. 11, 2003).

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version. At a minimum, any new CPG implemented by the FDA must be more stringent than the current version, not less so. Galderma strongly believes all manufacturers should be subject to the same regulatory requirements and the same level of regulatory scrutiny.

Under the proposed CPG, the FDA has correctly emphasized the importance of providing companies an incentive to seek NDA approval for their drug products or to remove those products from the market. We believe, however, that the Agency needs to be more stringent in exercising its enforcement discretion. In the absence of strict, consistent enforcement, the Agency will in fact be creating a disincentive for companies to seek NDA approval. This is particularly true where companies are marketing products unlawfully. When companies are aware that competitor products are on the market without FDA approval, they have no incentive to pursue FDA approval and the considerable regulatory scrutiny involved in the approval process.

It is critical that the FDA take a firm stance against the marketing of unapproved “new drugs” and that the Agency make clear its intent to take immediate and consistent enforcement action against such marketing. Permitting these products to remain on the market, even temporarily, poses a potential health and safety risk to the public; furthermore, it will create a disincentive to pursue FDA approval and undergo the added scrutiny of promotional practices that accompanies such approval.

Accordingly, we request that the Agency strengthen its enforcement policy by modifying the proposed CPG to:

- Require companies to obtain NDA approval in order to market “new drugs” in the U.S. – subject to immediate enforcement.
- In the event the Agency decides not to take immediate enforcement action against all unapproved “new drugs,” at a minimum the Agency should:
 - Require NDA approval for all unapproved “new drugs” being promoted unlawfully. One method of accomplishing this would be to broaden the “health fraud” category to encompass all “new drugs” that are illegally or fraudulently marketed or that fail to comply with FDA regulatory requirements.
 - Take immediate action to restrict the initial introduction of unapproved “new drugs” (and drugs that are not identical to pre-1962 drugs with regard to content or claims) into the market.
 - Explicitly reserve FDA’s right to enforce against an unapproved prescription drug first marketed after November 13, 1984 if the product is not identical to a pre-1962 drug and differs in formulation, dosage or strength, dosage form, route of administration, indications for use or intended patient population.

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- Require public disclosure of unapproved "new drug" status through mandatory product labeling and creation of an FDA database of unapproved "new drugs". Agency enforcement discretion should be contingent upon providing such disclosures.

By taking these steps, the FDA would provide appropriate incentives for companies to pursue FDA approval for unlawfully marketed products, ensure that "new drugs" are not marketed fraudulently, be in a position to assess the safety and efficacy of "new drugs" on the market, and provide consumers and physicians with complete, truthful information associated with marketed prescription drugs.

Thank you for the opportunity to provide these comments. If you have any questions, please feel free to contact me at (202) 457-5646.

Very truly yours,



Paul D. Rubin
Patton Boggs LLP
Counsel to Galderma Laboratories, L.P.

cc: Mr. Steven D. Silverman
Acting Director, Division of New Drug Labeling and Compliance
Food and Drug Administration

Mr. Quintin Cassady
General Counsel
Galderma Laboratories, L.P.

Ms. Anne D. Spiggle
Patton Boggs LLP