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November 22, 2002

Dockets Management Branch (HFA-305)
Food and Drug Administration
Room 1061
5630 Fishers Lane
Rockville, MD 20852

Re: Citizen Petition on Unapproved Extended Release Single
Ingredient Guaifenesin Drug Products
FDA Docket No. 02P-0483

In accordance with 21 C.F.R. 10.30(d), Adams Laboratories, Inc. hereby submits the following comments with respect to the Citizen Petition submitted by four law firms on behalf of their clients requesting FDA to withdraw the seventy warning letters sent with respect to unapproved extended release single ingredient guaifenesin drug products and to refrain from regulatory action regarding these products. The Citizen Petition concedes that there is no form of FDA approval under the Federal Food, Drug, and Cosmetic Act (FD&C Act) for any of the drug products subject to these warning letters.

As these comments document, all of the manufacturers involved were given prior written warning more than twenty years ago, through a Compliance Policy Guide and FDA regulations, that (1) there is no legal basis for marketing these unapproved drug products, (2) continued marketing without conducting the required studies, submission of an NDA or ANDA, and FDA approval, placed the products at risk of regulatory action, and (3) such regulatory action could be undertaken at any time. Adams Laboratories is the only manufacturer who has

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heeded this FDA admonition and has undertaken the investment necessary to obtain NDA approval. Accordingly, Adams Laboratories urges FDA to complete the regulatory action initiated with the seventy warning letters and promptly to remove each unapproved extended release single ingredient guaifenesin drug product from the market until it has been tested, an NDA or ANDA has been submitted, and the application has been approved by FDA.

I. The Citizen Petition

The Citizen Petition requests that FDA establish a complex formal process for each separate unapproved non-DESI drug product.¹

First, the Citizen Petition requests that a separate Federal Register notice be published with respect to each such drug product.

Second, the Citizen Petition requests the establishment of new procedural requirements with respect to these drug products.

Third, the Citizen Petition requests that a guidance document be prepared for each individual drug product that will set forth the specific scientific data required by FDA for the approval of an NDA or ANDA.

Fourth, the Citizen Petition requests that FDA establish a separate schedule for each of these drug products with respect to the submission and approval of an NDA or an ANDA.

This process would take decades, imposing major new burdens on FDA without any prospect of user fees to support the agency's work. Thus, the Citizen Petition is a transparent attempt to thwart FDA implementation of the Drug Amendments of 1962. After forty years of relative inaction by FDA to apply the requirements of the 1962 Amendments to unapproved non-DESI

¹ Citizen Petition at pages 2 and 16.

drug products, it is ironic that the Petitioners request a process that could well take another forty years before it could be implemented, if ever. And in the interim, this process would allow the illegal drug products subject to the seventy warning letters to remain on the market.

II. The Heart of the Matter

The fundamental issue presented by the Citizen Petition is whether FDA is serious about implementing the statutory requirement of proof of effectiveness under the Drug Amendments of 1962.² The Citizen Petition presents no evidence that any, much less all, of the drug products subject to the seventy warning letters were marketed prior to 1962 and otherwise fall within the very narrow scope of the grandfather clause under the 1962 Amendments.³ It offers no credible response to FDA's decades-old enforcement policy requiring an NDA for every extended release drug product,⁴ and provides no data to show that any of the drug products subject to these warning letters has been tested to assure compliance with the rigorous requirements applicable to extended release products.⁵ It fails to recognize that for more than two decades FDA has warned the industry that all competing unapproved drug products that are not subject to the FDA Drug Efficacy Study Implementation (DESI) program ("non-DESI" drug products) will be removed from the market once a post-1962 NDA is approved for any member

² 76 Stat. 780 (1962).

³ Section 107(c) of the Drug Amendments of 1962, 76 Stat. 780, 788 (1962).

⁴ 24 Fed. Reg. 3756 (May 9, 1959), 21 C.F.R. 3.512; 61 Fed. Reg. 29502 (June 11, 1996), 62 Fed. Reg. 12083 (March 14, 1997), 21 C.F.R. 310.502(a)(14).

⁵ E.g., FDA, Guidance for Industry: Extended Release Oral Dosage Forms: Development, Evaluation, and Application of In Vitro/In Vivo Correlations (September 1997).

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of the class.⁶ It does not deal with the fact that the Durham-Humphrey Amendments⁷ were enacted in 1951 explicitly to prohibit the marketing of a drug with a prescription legend once FDA has switched that drug to nonprescription status. Finally, it fails to address the policy and case law precedent in prior FDA actions.

Instead, the Petitioners request that FDA adopt, by rulemaking, a lengthy, detailed, and highly complex procedure not contemplated either by the Compliance Policy Guide or the FD&C Act and that could not possibly be implemented for unapproved non-DESI drug products for decades. Thus, the real issue presented by the Citizen Petition is whether FDA will remain serious about enforcing the policy established in the Compliance Policy Guide in order to implement the Drug Amendments of 1962.

All of the companies represented by the Petitioners have had the same opportunity as Adams Laboratories to obtain approval of an NDA for their products. They chose to ignore the prior FDA warnings and have not submitted the required applications for approval. They now propose an endless process that they know is not remotely practical or feasible for FDA in the foreseeable future. In short, they propose to continue to market unapproved drug products for years to come.

FDA should use this proceeding to establish, once and for all, that it will in fact enforce the Drug Amendments of 1962 by taking action under its Compliance Policy Guide once an NDA is approved for any previously unapproved non-DESI drug product. This will provide

⁶ FDA, Compliance Policy Guides Section 440.100 (attached as Appendix A to these comments).

⁷ 65 Stat. 648 (1951).

an incentive for the regulated industry to take the Compliance Policy Guide seriously. FDA identified 2,399 unapproved non-DESI drug products on the market at the time of the E-Ferol hearings in May 1984.⁸ That number has undoubtedly increased, as “me-too” copies have proliferated in the interim eighteen years.⁹ If FDA does not take strong, decisive, and prompt action in this instance, no one will take the agency seriously on this matter, there will be no further NDAs submitted for unapproved non-DESI drug products, and after forty years the Drug Amendments of 1962 will remain unenforced with respect to these products.

III. Background

Under the Drug Amendments of 1962, FDA was required (1) to review all NDAs that became effective during 1938-1962 to assure that they demonstrate adequate evidence of effectiveness as well as safety and (2) beginning in 1962, to require substantial evidence of safety and effectiveness for any new drug first marketed on or after the date of enactment of the 1962 Amendments. Following the review of the 1938-1962 NDAs by the National Academy of Sciences, FDA undertook to implement the resulting reports through the DESI program. After a series of policy vacillations, the United States District Court for the District of Columbia intervened in 1975 to lay down the rule in the Hoffman-LaRoche case that, after FDA has determined that a drug product is a new drug, the agency has no statutory authority to authorize

⁸ “Deficiencies in FDA’s Regulation of the Marketing of Unapproved New Drugs: The Case of E-Ferol,” Sixty-Eighth Report by the Committee on Government Operations, H. Rep. No. 98-1168, 98th Cong. 2d Sess. 17 (1984) (“Congressional Report”).

⁹ *Id.* at 21.

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the marketing of that product prior to approval of an NDA or ANDA.¹⁰ After FDA embraced this rule, it was upheld by the Supreme Court in the Generix case.¹¹

As early as October 1976, FDA established Compliance Policy Guide No. 7132c.08 in order to implement the Hoffman-LaRoche decision.¹² That Compliance Policy Guide was expanded and reissued as No. 7132c.02 in April 1981,¹³ revised in September 1984,¹⁴ May 1987, and March 1995, and now codified as Section 440.100 of the FDA Compliance Policy Guides (copy attached as Appendix A). Beginning with the April 1981 version of the Compliance Policy Guide and continuing through the current version, FDA made clear its enforcement position with respect to unapproved drug products:

First, all drug products first marketed after the Drug Amendments of 1962 require an approved NDA or ANDA prior to marketing. This policy was established in the Hoffman-LaRoche decision and confirmed by the Supreme Court in the Generix decision.

Second, some categories of drug products require FDA approval of an NDA or ANDA regardless of the time (pre- or post-1962) when the drug product is marketed. An example of this is all extended release drug products, which FDA has unequivocally stated since

¹⁰ Hoffman-LaRoche, Inc. v. Weinberger, 425 F. Supp 890 (D.D.C. 1975).

¹¹ United States v. Generix Drug Corp., 460 U.S. 453 (1983).

¹² 41 Fed. Reg. 41770 (September 23, 1976).

¹³ "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, House of Representatives, 98th Cong., 2d Sess. 365 (1984) ("Congressional Hearing").

¹⁴ 49 Fed. Reg. 38191 (September 27, 1984).

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May 1959 cannot be marketed prior to FDA approval of an NDA or ANDA.¹⁵

Third, an unapproved non-DESI drug product that was first marketed prior to the Drug Amendments of 1962 (including any copy of such a drug) may remain on the market until (1) FDA makes a final determination that it is a new drug, or (2) it violates another provision of the statute, or (3) there is new information on safety or effectiveness, or (4) an NDA is approved for the drug after 1962.

This enforcement position has remained unchanged since April 1981. FDA did not establish or promise any additional procedure or notification with respect to the determinations described above, and the FD&C Act contains no such requirement.

Following the E-Ferol tragedy in 1984, Congress held a hearing¹⁶ and subsequently issued a report¹⁷ criticizing FDA's failure to take regulatory action against unapproved DESI and non-DESI drug products. FDA responded by revising the April 1981 version of the Compliance Policy Guide and issuing a new version in September 1984.¹⁸ For all unapproved non-DESI drug products, FDA reiterated the policy described above that it had established in the April 1981 version.

¹⁵ Note 4 supra.

¹⁶ Note 13 supra.

¹⁷ Note 8 supra.

¹⁸ 49 Fed. Reg. 38191 (September 27, 1984).

IV. Application of the Compliance Policy Guide

It is therefore essential to analyze how the specific provisions of the Compliance Policy Guide, which establish the conditions under which FDA will take enforcement action, apply to unapproved non-DESI extended release single ingredient guaifenesin drug products.

A. Post-1962 Unapproved Non-DESI Drug Products

Under the Compliance Policy Guide, FDA will take immediate regulatory action if the drug product involved is not a copy of a pre-1962 non-DESI drug product. As discussed below, the Citizen Petition fails to provide adequate evidence that there are pre-1962 versions of all of the extended release single ingredient guaifenesin drug products subject to the seventy warning letters. It is virtually certain that many of these marketed drug products have no pre-1962 counterpart and thus are inherently illegal.

B. New Drug Determination

The Compliance Policy Guide promises regulatory action once the agency determines that an unapproved drug product is a new drug, and indeed the Hoffman-LaRoche and Generix decisions require such action. Adams Laboratories met with FDA in March 1998 and was told that extended release single ingredient guaifenesin drug products are new drugs that require an approved NDA. Adams Laboratories submitted an IND in June 1998 and an NDA in June 2000, and FDA approved the NDA in July 2002. All of these actions constitute a definitive FDA determination that all extended release single ingredient guaifenesin drug products are new drugs that require FDA approval of an NDA or ANDA to justify continued marketing.

C. Violation of Other Provisions

The Compliance Policy Guide states that a pre-1962 non-DESI drug product will be removed from the market by FDA if it violates other provisions of the FD&C Act.

Unapproved non-DESI single ingredient guaifenesin drug products in fact currently violate two other requirements of the FD&C Act.

First, the guaifenesin drug products subject to the seventy warning letters violate the FDA enforcement policy first established in a statement of policy in May 1959 and codified as a formal regulation following notice-and-comment rulemaking in March 1997,¹⁹ requiring all extended release drug products to be the subject of an approved NDA or ANDA. There is no exception to this rule. Whether it is regarded as a statement of policy (which it once was) or as a regulation (which it now is), it has unequivocally set forth FDA's enforcement position for more than forty years.

Second, they are marketed as prescription drugs, in violation of the FDA determination that they may be marketed only as nonprescription drugs. Congress enacted the Durham-Humphrey Amendments of 1951²⁰ explicitly to preclude the marketing of the same pharmaceutical active ingredient, for the same indication, and with the same dosage, as both a prescription and a nonprescription drug at the same time. Thus, following FDA's determination, through the approval of the Adams Laboratories NDA, that extended release single ingredient

¹⁹ Note 4 supra.

²⁰ Note 7 supra.

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guaifenesin drug products are nonprescription rather than prescription products, all of the existing prescription products on the market became per se unlawful.

D. Significant New Information

The Compliance Policy Guide states that FDA will institute enforcement action on the basis of significant new information which "questions" the safety or effectiveness of the drug. Adams Laboratories has previously provided to FDA in vitro dissolution analyses of leading extended release single ingredient guaifenesin drug products, demonstrating a wide variation in the release profiles of currently marketed drug products -- all the way from dose dumping at six hours to failing to provide an adequate dose throughout twelve hours. These data (attached as Appendix B to these comments) document the need for an FDA determination regarding the safety and effectiveness of each extended release single ingredient guaifenesin drug product, through approval of an NDA or ANDA, before marketing may be permitted.

E. FDA Approval of a Post-1962 NDA

Perhaps most important, since April 1981 the Compliance Policy Guide has stated that FDA will initiate regulatory action against any drug on the market without an approved NDA or ANDA if it is identical or related to a post-1962 NDA approved for safety and effectiveness. This is itself dispositive of this matter. Once the Adams Laboratories NDA was approved, this provision in the Compliance Policy Guide obligates FDA to take all identical or related drug products off the market immediately. That is exactly what the agency is doing through the seventy warning letters -- taking enforcement action explicitly required by the Compliance Policy Guide.

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V. The Failure of the Citizen Petition to Provide Critical Information

In several respects, the Citizen Petition is silent on important information. The following present a few examples.

A. No Evidence of Pre-1962 Marketing

As described above, immediate FDA regulatory action is required with respect to an unapproved non-DESI drug product unless it is a copy of a pre-1962 non-DESI drug product. Nonetheless, the Citizen Petition presents no evidence that even one extended release single ingredient guaifenesin drug product was marketed prior to 1962.

The Citizen Petition states that single ingredient guaifenesin drug products have been marketed in the United States for over sixty-five years.²¹ This is, of course, irrelevant. The issue is whether an extended release version of these drug products was marketed prior to 1962.

The Citizen Petition also states that the list of unapproved non-DESI drug products provided by FDA to Congress in September 1984²² included one 600 mg extended release guaifenesin drug product.²³ This is also irrelevant. The fact that one 600 mg extended release drug product was marketed in September 1984 does not mean that the product was also marketed more than twenty years earlier, prior to 1962. And it certainly provides no basis for marketing other dosage levels of the drug, in direct violation of the Compliance Policy Guide.

²¹ Citizen Petition at page 3.

²² Congressional Hearing at page 221.

²³ Citizen Petition at page 3.

Far from establishing that these drug products are pre-1962, the Citizen Petition provides strong evidence that there were no pre-1962 versions of an extended release single ingredient guaifenesin drug product prior to enactment of the Drug Amendments of 1962. Under the Hoffman-LaRoche and Generix decisions, this is itself dispositive of the matter and fully justifies the seventy warning letters.

B. Insufficient Information on Effectiveness

The Citizen Petition presents no information on the effectiveness of any of the extended release single ingredient guaifenesin drug products subject to the seventy warning letters. The data and information attached in Appendix B to these comments, which were previously provided to FDA by Adams Laboratories, raise serious issues about the effectiveness of the extended release mechanism of these marketed products. Ultimately, the only way that it can be determined whether the manufacturers of these marketed products have in fact conducted testing that meets the rigorous FDA standards for extended release approval is through NDAs and ANDAs.

C. No Evidence That Existing Products Are Grandfathered

The Drug Amendments of 1962 contain a very narrow grandfather clause.²⁴ As interpreted by FDA and the United States Court of Appeals for the Tenth Circuit as early as 1966,²⁵ the grandfather clause requires that the formulation and labeling of a specific drug product must be unchanged since prior to 1962. Any change in the formulation (such as the

²⁴ Note 3 supra.

²⁵ United States v. Allan Drug Corp., 357 F.2d 713 (10th Cir. 1966).

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dosage level) or in the indications, directions, or other labeling after 1962 would break the grandfather status. By failing to submit the formulation and labels of pre-1962 versions of unapproved extended release single ingredient guaifenesin drug products, the Petitioners have failed to carry their burden of demonstrating the applicability of the grandfather clause.

D. The Lack of Adequate Supporting Documentation

By presenting broad conceptual arguments without supporting facts, the Citizen Petition attempts to obscure the real issues involved in this matter. Contrary to assertions in the Citizen Petition, each manufacturer has the right to address these determinative factual matters in response to the seventy warning letters. If they are unable to produce adequate documentation -- and failed to read or understand the Compliance Policy Guide and related FDA precedent -- there is no justification for the continued marketing of the drug products involved.

VI. Response to Legal and Policy Arguments

The Citizen Petition raises numerous policy arguments and some that are referred to as legal arguments. None is persuasive.

A. Lack of Notice

The Petitioners argue that they have not received adequate notice. This is patently untrue. The Compliance Policy Guide clearly states, beginning in April 1981, the grounds under which FDA would remove from the market unapproved non-DESI pre-1962 drug products, and unapproved non-DESI post-1962 drug products. Since May 1959, FDA has had an unambiguous published enforcement policy that all extended release products require FDA approval of an NDA or ANDA.

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By referring to two instances in which FDA concluded, in its discretion, to establish specific requirements for medically necessary pre-1962 drug products (digoxin and levothyroxine), the Petitioners attempt to construct a legal requirement that FDA must in all instances follow this approach. This argument fails for three related reasons. First, there is no requirement for a public procedure under the FD&C Act prior to enforcement action against illegal marketed drug products. Second, there is no such requirement under the Compliance Policy Guide or any other related FDA document. And third, FDA has in fact previously undertaken the kind of action that it is taking in the current situation without any form of public notice or procedure.

In August 1990, FDA promulgated a final monograph for nonprescription wart remover drug products.²⁶ FDA determined, on the basis of this action, that all unapproved non-DESI prescription wart remover drug products must be removed from the market at the same time, and issued fourteen warning letters to achieve this result. Attached as Appendix C is a letter from the Deputy Director of the FDA Center for Drug Evaluation and Research, dated December 15, 1992, describing this policy and the resulting FDA compliance action. All of the prescription drug products involved were in fact taken off the market by FDA. There was no notice or complex procedure used then, and none is needed or justified now.

²⁶ 55 Fed. Reg. 33246 (August 14, 1990).

B. The Lack of an Established Scientific Guidance Document

It is the responsibility of a drug manufacturer to meet with FDA and obtain information with regard to the scientific data needed to obtain FDA approval of an NDA or ANDA for a pre-1962 unapproved non-DESI drug product. Nothing in the FD&C Act or in FDA regulations requires FDA to establish written guidance of this type for the use of the regulated industry.

In this instance, Adams Laboratories approached FDA to obtain sufficient information to undertake the testing needed to obtain an approved NDA. All of the manufacturers who currently market unapproved drug products could have done the same, but chose not to do so. If they had approached FDA and asked for oral guidance, they would have received it. But FDA had no obligation to seek out the manufacturers in order to provide such oral guidance or to prepare its guidance in written form.

C. Ceding Enforcement Discretion to a Private Party

The Petitioners argue that, because Adams Laboratories followed the dictates of the Drug Amendments of 1962 and the Compliance Policy Guide -- and obtained an approved NDA while others ignored the statute -- compliance action to enforce the statute cedes enforcement discretion to a private party. Nothing could be further from the truth. As already noted, all of the manufacturers who have received a warning letter relating to this matter have had full notice of what would happen if one company obtained an approved NDA. They chose to ignore their responsibilities and cannot now be heard to complain.

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This is not the first time that FDA has taken action that inures to the benefit of one company that followed the law, at the expense of another company that failed to follow the law. In the North American Pharmacal case, only one company responded to a notice of opportunity for hearing and FDA proceeded to take all of the other related drug products off the market. The FDA action in that instance was upheld in the courts.²⁷ Similarly, in this instance the failure of the companies that have received warning letters to exercise their right and obligation to pursue an approved NDA or ANDA does not justify allowing them to remain on the market once another company has proceeded to obtain such approval -- as the Compliance Policy Guide warned everyone more than twenty years ago.

D. Monopoly Prices

The Petitioners argue that, if only one company has an extended release single ingredient guaifenesin drug product on the market, it will be able to charge monopoly prices. First, this is not an FDA issue. FDA does not approve or disapprove drug products based upon its view of the reasonableness of prices charged in the marketplace. Second, it is far from certain what price Adams Laboratories will be able to charge, when competing against other products in the nonprescription cough-cold field. Third, Adams Laboratories is fully justified in charging a premium in order to recoup the investment it made in obtaining an approved NDA. And finally, the Petitioners are hardly in a position to criticize Adams Laboratories, when Adams

²⁷ North American Pharmacal, Inc. v. The Department of Health, Education, and Welfare, 491 F.2d 546 (8th Cir. 1973).

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Laboratories is the only company that in fact has complied with the clear requirements of the FD&C Act and the Compliance Policy Guide.

E. Violation of FDA Policy

The Petitioners argue that FDA violates consistent agency policy. The basis for this argument is simply inexplicable. As documented above, FDA has followed its regulations, policy, and Compliance Policy Guide, as well as judicial decisions applicable to this situation. There is no requirement for the complex and unworkable procedure that the Petitioners request. As already documented in subsection (A) above, FDA is following the same procedure here that it has followed before with respect to wart remover drug products.

F. A Rash of Other Compliance Actions

The Citizen Petition argues that FDA will trigger a rash of other compliance actions if the agency fails to implement the complex procedures requested by the Petitioners. On this point, Adams Laboratories agrees with the Petitioners. This would be a welcome development. It would provide a major incentive for companies to develop, submit, and obtain approval of NDAs for other unapproved non-DESI drug products, with the result that unlawful drug products will be taken off the market. This is the policy that FDA adopted in the Compliance Policy Guide more than twenty years ago, and it is the policy that FDA should vigorously enforce now and in the future. It is only in this way that the 2,000-plus non-DESI drug products remaining on the market will ever be brought under regulatory control.

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G. Market Disruption

The Petitioners argue that, if all unapproved extended release single ingredient guaifenesin drug products are removed from the market, there will be market disruption. Once again, the Petitioners are wrong. Adams Laboratories has informed FDA that it has the capacity to source the entire United States market for this drug, and it stands by that statement. There will be no shortage of this drug product, and Petitioners offer no evidence that such a shortage will occur.

H. The Extended Release Regulation

The Petitioners contend that FDA's position that extended release drug products require approval through an NDA or ANDA relies only on a statement of policy and therefore does not have the force of law. This is simply not true. It originated as a "statement of interpretation" in May 1959 but, as explained above, it was converted to a regulation through notice-and-comment rulemaking in compliance with the Administrative Procedure Act in March 1997.²⁸ But even if it were only regarded as a statement of policy -- similar, perhaps, to the statements of policy contained in the Compliance Policy Guide -- it clearly states the FDA enforcement position. FDA should adhere to that enforcement position regardless of the precise legal status of the current regulation.

²⁸ Note 4 supra.

I. The OTC Drug Monograph for Guaifenesin

The OTC cough-cold drug monograph determines the conditions under which non-extended-release guaifenesin is safe, effective, and properly labeled for nonprescription marketing and use.²⁹ Because of the FDA policy that all extended release drug products require an NDA or ANDA, however, the OTC drug monograph does not apply to extended release products. Nor is the requirement of good manufacturing practices (GMP) sufficient to assure that all extended release drug products are safe and effective. If that were true, the FDA regulation requiring NDAs and ANDAs for extended release drug products should be withdrawn. In short, the OTC drug monograph is relevant to the current matter only in that it underscores that the unapproved prescription drug products that are the subject of the seventy warning letters are completely illegal.

J. FDA's Burdens

The Petitioners contend that substituting the lengthy, detailed, and complex procedure described in the Citizen Petition will, in some way, reduce the burdens placed on scarce agency resources. This is obviously untrue. The procedure described by the Petitioners would place enormous additional burdens on FDA resources for the foreseeable future. In contrast, enforcement of the seventy warning letters will be a far less burdensome -- and more expeditious -- approach to achieve compliance with the FD&C Act.

²⁹ 21 C.F.R. part 341.

K. No Reasonable Opportunity for Challenge

Finally, the Petitioners argue that they should be given a reasonable opportunity to challenge the position taken by FDA in the seventy warning letters. The easy answer to this is that each recipient of a warning letter has the right to challenge it in two ways. First, there is the opportunity to provide specific and detailed factual information to FDA, in response to a warning letter, to justify whatever position the recipient believes constitutes a satisfactory response under the FD&C Act, the FDA regulations, and the Compliance Policy Guide. For example, the manufacturer could document the existence of a pre-1962 non-DESI version of its drug product and demonstrate that neither the formulation nor the labeling has changed. Second, if its response to the warning letter is unavailing and the company wishes to continue its challenge to the FDA position, the recipient can continue to market its products, await a seizure, and contest the FDA position in the courts. Thus, each manufacturer has adequate opportunity to challenge the FDA enforcement policy on whatever factual and legal grounds it believes are applicable.

VII. Federal Agency Contract Purchases

The final sentence of the Compliance Policy Guide states that, in addition to direct compliance action to enforce the policy set forth in that document, FDA:

“...will deny FDA approval for contract purchase by other Federal government agencies (DOD, VA, PHS) of any drug subject to this policy which does not have an approved NDA or ANDA.”

Adams Laboratories hereby requests that FDA immediately implement this policy by informing the relevant federal agencies that the drug products subject to the seventy warning letters are no longer approved for federal government purchase.

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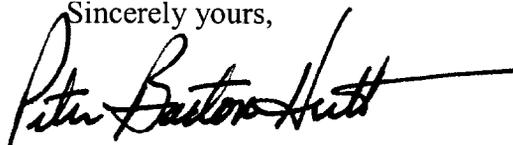
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VIII. Conclusion

For the reasons set forth in these comments, Adams Laboratories urges FDA promptly (1) to deny the Citizen Petition submitted by the four law firms, (2) to affirm that the Compliance Policy Guide, the regulation on extended release drug products, and the decision on the nonprescription status of extended release guaifenesin drug products requires that the existing unapproved prescription versions be removed from the market immediately, (3) to pursue compliance with the seventy warning letters vigorously, and (4) to inform other federal government agencies immediately that none of the companies who received a warning letter has FDA approval for contract purchase of an extended release single ingredient guaifenesin drug product. Unless FDA takes this action, it is unlikely that the requirements of the Drug Amendments of 1962 will be applied to unapproved non-DESI drug products in the foreseeable future.

Sincerely yours,

A handwritten signature in black ink that reads "Peter Barton Hutt". The signature is written in a cursive style with a long horizontal line extending to the right.

Peter Barton Hutt

Counsel for Adams Laboratories, Inc.