#1125

ACCUTANE

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May 17, 1988

Dr. Frank Young
Commissioner
Food and Drug Administration
5600 Fishers' Lane
Rockville, Maryland 06520

Re: Accutane Petition

Dear Dr. Young:

Enclosed is a copy of the Accutane petition that we are filing with you and Secretary Bowen today. It is urgent that you and Secretary Bowen act immediately to stop the large number of extremely serious and avoidable birth defects and abortions that Accutane is causing. To accomplish this, we are requesting that the distribution of the drug be limited, as has already been done in Europe, where there have been a fraction of the birth defects from the drug that have occurred in this country. For many years, the agency's official position has been that it does have the authority to limit the distribution of drugs to particular medical specialties. The time to use that authority is now.

As you are well aware, your own agency has concluded that Accutane has already caused as many as 600 serious birth defects. There have also been countless unnecessary abortions. As a result, on April 26, 1988, almost a month ago, the FDA's Dermatologic Drugs Advisory Committee recommended that the distribution of Accutane be limited in some way.

FDA data demonstrates that these birth defects have been caused by physicians who have consistently prescribed Accutane for minor conditions to women of child-bearing age, and then have not helped their patients take the necessary precautions to avoid pregnancy. According to the data presented to the Advisory Committee, whereas fewer than 5,000 women may appropriately be treated with Accutane each year (because they have recalcitrant cystic acne and have not responded to other treatments), close to 100,000 women have been treated with Accutane every year since it was first approved in 1982.

Typically, the FDA would ban a drug which caused anywhere near the number of birth defects that have been caused by Accutane. But Accutane is clearly a valuable drug when appropriately used. We believe that it should be left on the

market for a limited trial period if limitations on its distribution of the type we are proposing are adopted. If the only choice were continuing to allow physicians to misprescribe the drug or to ban it, then we would favor a ban.

The purpose of this petition is to request you to find that the agency has the authority to adopt the Advisory Committee's recommendation. While the Committee did not specify the type of limitations on distribution that it was recommending, we urge the FDA to: (1) permit only dermatologists to prescribe Accutane; (2) permit Accutane to be used only for FDA-approved uses and prohibit physicians from prescribing the drug for minor types of acne, as apparently is common; (3) require physicians to obtain informed consent from their patients; and (4) and impose mandatory patient package inserts and several other requirements, many of which Hoffmann-La Roche has already agreed to. The key and most controversial recommendation is limiting the distribution of Accutane to dermatologists.

As you may know, since 1972 the agency's official position has been that it does have this authority. Attorneys at your Chief Counsel's office have informed me that that continues to be the agency's position today.

We in the United States like to brag that we have the best drug approval system in the world, the strongest laws protecting American citizens and the world's safest drug supply. Yet many European countries have imposed restrictions on the distribution of Accutane that are much more stringent than the ones that we are requesting in this petition. As a result, in Europe Accutane has caused only a small fraction of the birth defects that have occurred in this country.

We believe that it would be odd indeed for the agency to take the position that its only choices are a ban of this valuable drug or to allow widespread misprescribing by pharmacists, leading to countless birth defects and unnecessary abortions.

Where industry interests have been at stake, the FDA has been willing to be innovative in interpreting the Food, Drug and Cosmetic Act. Its de minimis policy has allowed carcinogenic color additives to remain on the market and its health claims policy has for the first time allowed food manufacturers to make drug-like claims on their products without prior FDA approval. Both policies rejected many years of past interpretation of the Food, Drug and Cosmetic Act by the FDA. The first policy has been declared illegal and we believe that the second is illegal as well. In this case, we are asking the agency to adhere to what has been its official position since 1972, and to take a position that has far more support in terms of the statute and precedent than either the de minimis policy or the health claims policy.

The FDA has been terribly indecisive on the question of whether it believes it has the authority to limit the distribution of Accutane and other drugs. It is imperative that you issue a decision immediately, and certainly within the next 30 days. If the agency does not believe that it has this authority, then we will either seek judicial review of the agency's legal ruling or ask Congress to give the agency the authority to limit the distribution of the drug. Unless you act quickly on this petition, you will be impeding both efforts.

Sincerely yours,

William B. Schultz

Enclosures

BEFORE THE
COMMISSIONER OF THE FOOD AND DRUG ADMINISTRATION AND THE
SECRETARY OF THE DEPARTMENT OF HEALTH AND HUMAN SERVICES

Petition of Public Citizen to Declare Accutane an Imminent Hazard and to Immediately Approve Limitations on its Distribution	)	Docket No. _____

Public Citizen hereby petitions the Commissioner of the Food and Drug Administration ("FDA") and the Secretary of the Department of Health and Human Services ("HHS") to invoke the imminent hazard provisions of the Federal Food, Drug and Cosmetic Act ("FDC Act"), in order to immediately limit the prescribing of Accutane to dermatologists who have agreed in advance to follow the approved indications for the drug. We also petition the agency to impose certain other limitations on prescribing the drug.

As we discuss in more detail below, 62 Accutane-induced birth defects have been reported in this country and the FDA estimates that the actual number is about ten times that amount, in excess of 600 serious birth defects. These figures are a stark contrast to the three birth defects that have been reported in all of Europe, where regulatory authorities have placed much more stringent restrictions on the distribution of the drug. In light of obvious seriousness and the enormous proportions of this crisis, we urge FDA and HHS to act immediately to limit the distribution of Accutane, consistent with the April 26, 1988 recommendation of the agency's Dermatologic Drugs Advisory

Committee.

In support of this petition, we hereby incorporate the Public Citizen Health Research Group's April 26, 1988 testimony to the Dermatologic Drugs Advisory Committee and its September 13, 1984 petition of the FDA requesting a change in Accutane's label.[1]

A. FACTUAL BACKGROUND

The material facts that support this petition are that, despite a change in the drug's labeling in 1985, physicians have continued to over-prescribe Accutane, leading to at least several hundred avoidable birth defects.[2]

1. Birth Defects Caused by Accutane.

As mentioned above, 62 severe birth defects caused by Accutane have been reported to the FDA. At the April 26, 1988 Dermatologic Drugs Advisory Committee Meeting, FDA officials estimated that between 3,876 and 21,100 American women have

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[1]Public Citizen is a public interest organization with about 60,000 members, some of whom are women of child-bearing age. Unless the Food and Drug Administration ("FDA") takes prompt action, there is a substantial likelihood that in the future some of these women will use Accutane, even though it is not indicated for them. Therefore, they would unnecessarily be placed at risk of giving birth to a deformed child or of having a spontaneous abortion. We also are filing this petition on behalf of our members who have an interest in clarifying the FDA's authority to limit the distribution of drugs which pose a serious health hazard because of the substantial likelihood that in the future the exercise of such authority will be needed for drugs that those members will be using.

[2]Unless otherwise noted, all references to FDA data in this petition are to data presented at the April 26, 1988 Advisory Committee Hearing.

become pregnant while on the drug. It has also been estimated these woman have had spontaneous abortions at close to three times the rate of spontaneous abortions in the general population,[3] and the agency estimates that roughly 60% of pregnant women who have used Accutane have chosen to obtain abortions. Thus, according to the FDA's estimates, approximately 600-5,400 women who have taken the drug have given birth to a child and 25% of these children, or roughly 600, have severe birth defects caused by Accutane. We recognize that these numbers are only estimates, but it seems very likely that there have been several hundred birth defects caused by Accutane.

As many witnesses testified at the Advisory Committee Hearing, regardless of how many birth defects have occurred since the change in Accutane's labeling, the number is significant and unacceptable. Therefore, the FDA should immediately take steps that will ensure, to the greatest extent possible, that the birth defects cause by Accutane be reduced to the lowest possible number.

There is one other general point that needs emphasis. It is sometimes argued that the FDA's principal role should be limited to informing doctors and consumers about the risks of drugs and that the agency should let doctors and consumers make their own decisions. In the case of Accutane, however, that argument has

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[3]Dr. Lammer presented Accutane data in his testimony at the April 26, 1988 hearing; for information on the abortion rate in the general population, see Ventura, S, et. al., "Estimates of Pregnancies and Pregnancy Rates for U.S. 1976-85," American J. of Public Health, Vol. 78, No. 5, pp. 506.

absolutely no relevance because the ultimate victim will be an unborn fetus who cannot give consent. This factor provides additional support for our position that the FDA employ all of its regulatory authority to ensure that injuries from the drug are minimized.

Usually, this will mean that the product should be removed from the market. However, we recognize that Accutane is valuable for the treatment of severe and non-responsive recalcitrant cystic acne, a condition that can be disfiguring. Therefore, we are supporting a one-year trial period during which distribution of the drug would be limited in accordance with the conditions outlined below. If prescribing of the drug to women of childbearing age is not reduced significantly and if the number of birth defects is not reduced to a rate comparable to those found in those European countries that restrict the distribution of Accutane, then we believe that the drug should be removed from the market. However, we believe that limiting the distribution and prescribing of the product will reduce the number of birth defects to at or near zero as has apparently been accomplished in European countries.

2. Physicians Have Over-Prescribed Accutane, Leading to Unnecessary Birth Defects.

Since 1982, the only indication for which Accutane has been approved is "severe recalcitrant cystic acne." While the drug has been contraindicated for pregnant women since it was first approved, in 1985 the labeling was significantly strengthened to

include a bold, prominent boxed warning stating that "Accutane must not be used by females who are pregnant or intend to become pregnant while undergoing treatment" because of the risk of "major fetal abnormalities," and that women put on the drug should first be given a pregnancy test. In addition, since 1985, Hoffmann-La Roche ("Roche"), the manufacturer of the product, has distributed patient package inserts ("PPIs") to pharmacies. While we believe that the labeling and the PPIs should be strengthened even further, experience to date indicates that such requirements are not likely to provide a sufficient incentive to physicians to abide by the indications of the drug, which is essential to reducing birth defects and pregnancy exposures to the lowest possible level.

The FDA's own research provides strong support for our claim. In the United States there are currently about 400,000-500,000 cases cystic acne, but only about 70,000 females have this condition. Since the disease is spread out over a several year period and since only a fraction of the women who have the disease are not responsive to other therapies, less than 5,000 females a year may appropriately be medicated with this drug, according to the FDA. Yet, according to Roche's own estimates, about 560,000 women have been treated with Accutane since 1982, and approximately 287,000 since the drug's labeling was changed in 1985. This is approximately 100,000 cases per year or twenty times the number of women who actually should be using the drug.

The data suggests that there are two distinct problems with

respect to the prescribing of Accutane. The first is that physicians are not taking sufficient precautions to ensure that women treated with Accutane do not become pregnant. Second, the impact of this failure on the part of physicians is magnified by the general tendency of doctors to prescribe Accutane for minor acne and other conditions which have not been approved by the FDA and which are not justified in light of the extraordinary risks of this drug. Any plan to adequately regulate Accutane must address both these problems.

Therefore, we believe that Roche's proposals for patient package inserts, stronger warnings and written informed consent will be inadequate to eliminate all the avoidable birth defects. In addition to making these requirements mandatory, it is also essential that the FDA limit the distribution of the drug to dermatologists who would be required to prescribe the drug in accordance with the indications and conditions approved by the FDA.

B. Action Requested.

We request the Commissioner of the FDA and the Secretary of HHS to employ the imminent hazard provision of section 505(e) of the Food, Drug and Cosmetic Act, 21 U.S.C. § 355(e), to revoke the agency's current approval of the new drug application (NDA) for Accutane and to simultaneously approve a NDA for Accutane with the conditions described below.

We also request that the Commissioner issue regulations to accompany the modified NDA to ensure that pharmacists and

physicians comply with the new limitations that we are requesting be placed on Accutane. Violation of these regulations should be made subject to the criminal penalties contained in section 303 of the FDC Act, 21 U.S.C. § 333.

1. Only Dermatologists Should be Permitted to Prescribe Accutane. If Roche is to be permitted to market Accutane, then the FDA must limit the drug's distribution, as recommended by the Dermatologic Drugs Advisory Committee. We favor permitting only dermatologists who have registered with the FDA to prescribe the drug.

There are approximately 7,000 dermatologists in the United States so that a regulation that limited the prescribing of Accutane to this specialty would make it feasible for the FDA to protect patients adequately. In addition, dermatologists are better able to ensure that other therapies have been attempted before prescribing Accutane, which should be used only if it has been determined that no other treatment is effective.

We request the FDA to modify the NDA for Accutane so that Roche is prohibited from promoting Accutane to physicians who are not board certified or board eligible dermatologists. Since the modified NDA would only apply to Roche, however, we also request FDA to use its general rulemaking authority, 21 U.S.C. § 371(a), to issue regulations prohibiting physicians other than dermatologists from prescribing Accutane and prohibiting pharmacists from knowingly filling prescriptions from physicians who are not

dermatologists.[4]

2. Dermatologists Should Be Prohibited From Prescribing Accutane for Unapproved Indications. The regulations should also prohibit dermatologists from prescribing Accutane outside its approved indications and require them to take the precautions outlined in our testimony. Specifically, the regulation should state that dermatologists may prescribe the drug only for severe recalcitrant cystic acne and only where other specified therapies have not been successful.

3. Patients Should be Given Written Informed Consent. It is also critical that physicians prescribing Accutane be required to obtain informed consent from female patients and a written agreement from the patient that she will use contraception or other measures to avoid pregnancy. At a minimum, the consent form should identify the estimated risk of severe birth defects to children born to women who become pregnant while on Accutane (which we understand to be 20-25%) and should contain a photograph of an affected infant. If the FDA adopts this approach, which should be made mandatory through regulations, we will provide other suggestions as to the content of the informed consent form.

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[4]To facilitate enforcement, we urge the FDA to assign prescribing numbers to dermatologists who would be required to register with the agency, and to certify by affidavit that he or she has read and will follow the regulations and is aware that a dermatologist who violates the regulations is subject to criminal penalties. The regulations should prohibit pharmacists from selling Accutane unless the prescription contains the FDA prescribing number.

4. Other Restrictions. We also urge the agency to modify the NDA and adopt regulations imposing the additional restrictions discussed in the comments that we submitted to the Dermatologic Drugs Advisory Committee. While Roche has agreed to undertake many of these changes voluntarily, it is critical that they be made mandatory so that the public receives the maximum possible protection against exposure to Accutane by women during pregnancy. The additional restrictions include (1) important changes in the drug's labeling, (2) mandatory PPIs, (3) lowering the initial dose for the drug, and (4) photographs of affected infants on any promotions materials which contain photographs of a patient with acne.

C. Statement of Grounds.

The HHS and the FDA have authority to adopt the measures urged in this petition under the provisions of the FDC Act that give the agencies the authority to limit the conditions under which a new drug may be marketed and to adopt regulations in furtherance of the purposes of the FDC Act. 21 U.S.C. §§ 355, 701(a). The Secretary may suspend approval of the NDA prior to a hearing where there is an "imminent hazard to public health," as we believe is plainly the case here. 21 U.S.C. § 355(e).

Under section 505 of the FDC Act, 21 U.S.C. § 355, the Commissioner must reject the NDA or withdraw it if

> upon the basis of the information submitted to him as part of the application, or upon the basis of any other information before him with respect to such drug, he has insufficient information to determine whether such drug is safe for use under such conditions.

21 U.S.C. § 355(d)(4). The "conditions" referred to are "the conditions prescribed, recommended, or suggested in the proposed labeling" for the drug. 21 U.S.C. § 355(d)(1). Thus, the statute gives the agency the authority both to revoke the current NDA for Accutane, on the ground that without limitations on the drugs' distribution, Roche cannot carry its burden of proving the drug safe, and to grant an NDA imposing labeling conditions under which the drug may be used. If those conditions are not adequate to ensure the drug's safety, then under section 701(a), the FDA has authority "to promulgate regulations for the efficient enforcement of [the] Act." 21 U.S.C. § 371(a). Here, the regulations that we are requesting will clearly promote "the efficient enforcement" of the central provisions of the Act that are designed to protect public health, and therefore section 701(a) gives the agency authority to limit the distribution of Accutane if it chooses to do so.

We understand that some officials at the FDA do not believe that it has authority to adopt the measures we are requesting, particularly the provision limiting prescribing of the drug to dermatologists. It would be both unfortunate and peculiar for the agency to adopt such an "all or nothing" interpretation of the FDC Act which would limit its choices to permitting unrestricted marketing of Accutane or banning its sale.

In fact, for many years, the FDA has asserted that the agency has the authority that we are requesting it to exercise here. This position was officially set out in 1972 in a Federal

Register notice, where the FDA stated as follows:

> Where the unapproved use of an approved new drug becomes widespread or endangers the public health, the Food and Drug Administration is obligated to investigate it thoroughly and to take whatever action is warranted to protect the public. Several alterative courses of action are available to the Food and Drug Administration under these circumstances, depending upon the specific facts of each case. These actions include: Requiring a change in the labeling to warn against . . . the unapproved use, . . . restricting the channel of distribution, or even withdrawing approval of the drug or removing it from the market in extreme cases. When necessary, the Food and Drug Administration will not hesitate to take whatever action of this nature may be required to bring possible harmful use of an approved drug under control.

Legal Status of Approved Labeling for Prescription Drugs; Prescribing for Uses Unapproved by the Food and Drug Administration: Notice of Proposed Rule Making, 37 Fed. Reg. 16503 (August 15, 1972) (emphasis supplied). The agency has never modified this policy statement, and we have been informed by the office of Chief Counsel that it currently represents official FDA policy.

The agency's regulation of clinical investigators of new drugs supports our argument that it has the authority to regulate the circumstances under which physicians can prescribe a drug, where such regulation is necessary to protect patients. Although the statutory provision applicable to investigational new drugs, 21 U.S.C. § 355(i), does not mention regulating clinical investigators, we believe, as apparently does the agency, that the FDA plainly has authority to impose record-keeping and other requirements on clinical investigators and to disqualify investigators who do not comply with the regulatory requirements.

See 21 C.F.R. § 312.70 (1987). Similarly, the agency has implicit authority to impose direct limitations on doctors and pharmacists where such limitations are a necessary prerequisite to finding that a new drug meets the safety requirements in section 505, 21 U.S.C. § 355. Failure to abide by the regulations on the part of the manufacturer, physicians or pharmacists should be made subject to criminal penalties, pursuant to 21 U.S.C. § 331.[5]

Section 301(d) of the FDC Act, 21 U.S.C. § 331(d), prohibits the "introduction or delivery for introduction into interstate commerce of any article in violation of . . . section 505," the provision applicable to new drugs. We are suggesting that manufacturers, pharmacists and physicians all be required to abide by the FDA regulations that we are proposing for Accutane. There can be little doubt that such regulations could be made applicable to manufacturers, since they are already barred from promoting drugs in any way that is inconsistent with the product's indications. Similarly, the agency already regulates

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[5] The FDA has occasionally used its authority to regulate investigational new drugs, 21 U.S.C. § 355(i), as a means of limiting the distribution of new drugs, even when there are no ongoing investigations of the drugs. For example, although the FDA never approved Thalidomide, for many years it has allowed the drug to be used for treating leprosy under an approved IND application. Similarly, when the agency invoked the imminent hazard provision of the FDC Act to revoke the NDA for phenformin, the oral diabetes drug, it allowed the drug to be made available to a limited number of patients under an approve IND application. We believe that this use of the IND provisions to make drugs which are not being investigated available for treatment is probably illegal and that the better course would be to approve a limited NDA as requested in this petition.

pharmacists by requiring that they distribute patient package inserts ("PPIs") for certain drugs, and it could use that authority to prohibit pharmacists from filling prescriptions written by physicians who had not been "certified" by the FDA. The PPI regulations were issued pursuant to the section 505 and the agency's general rulemaking authority, 21 U.S.C. § 355, 371(a), and they were upheld in Pharmaceutical Manufacturers Association v. Food and Drug Administration, 484 F. Supp. 1179 (D.Del. 1980).

The record before the FDA supports a finding that, without restrictions on physicians of the type that we are requesting, Accutane cannot meet the safety requirements of section 505. Therefore, we believe, section 701(a) gives the FDA the authority to prohibit misprescribing of the drug "for efficient enforcement of the Act." This may be accomplished by regulations permitting only dermatologists to prescribe Accutane and restricting prescriptions to patients with the FDA-approved indications.

We also believe that the agency could enforce such regulations under the criminal penalties in section 303(d), 21 U.S.C. § 331(d). If the FDA required Roche to state in Accutane's labeling that the drug may be prescribed by a dermatologist, then Roche would be violating section 303(d) if it promoted the drug for use by physicians other than dermatologists. Similarly, a physician who is not a dermatologist who prescribes the drug is aiding and abetting Roche in the "introduction or delivery for introduction into

interstate commerce" of a drug "in violation of section 505," which itself is a violation of section 301(d).

We recognize that the FDA usually relies on the state laws to regulate prescribing of approved drugs by physicians, although it has adopted regulations regarding the use in investigational new drugs by physicians in their medical practice. We do not envision a change in this allocation of responsibilities in the usual case. However, we are advocating that in the unusual case where the facts require that restrictions be placed on the prescribing of drugs, as we believe is clearly the case with respect to Accutane, then the agency should exercise its authority to impose such conditions.[6]

The closest analogy to the action that we are requesting in this petition is the agency's regulation of methadone. Under its regulations, the FDA has specifically prohibited physicians from using that drug for treatment of narcotic addicts without prior FDA approval. 21 C.F.R. § 291.505(b)(4) (1987). The regulations also prescribe the indications that methadone may be used for, the doses that may be used and, finally, that informed consent be obtained from patients. 21 C.F.R. §§ 291.505 (b)(4), (c)(8), (d)(3)(i), (d)(3)(ii) (1987). While it is true that the agency

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[6]In F.T.C. v. Simeon Management Corp., 391 F. Supp. 697 (N.D. Calif.1975), a district court judge ruled that the FDA does not have the authority under section 505 of the FDC Act, 21 U.S.C. § 355, to regulate the administration of a drug by a physician. However, the court did not consider the issue of whether under section 701(a), 21 U.S.C. § 371(a), the agency would have the authority to issue substantive, binding regulations applicable to physicians, as we are requesting in this petition.

relies in part on the Public Health Service Act and the Controlled Substances Act as authorities for its regulation of Methadone, these regulations provide a good model for the regulation of Accutane.[7]

D. Environmental Impact.

The requested action will have an insignificant impact on

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[7]In American Pharmaceutical Ass'n v. Weinberger, 377 F. Supp. 824 (D.C. Cir. 1974), affirmed, 530 F.2d 1054 (D.C. Cir. 1976) (per curiam), the Court held that the FDA could not limit the distribution of methadone to certain hospital and drug treatment centers, an approach that petitioners are not advocating. While it might be argued that the methadone case would bar the FDA from limiting the distribution of Accutane to specific physicians, excluding distribution to pharmacies, nothing in that case limits the agency's ability to mandate that physicians follow the indications for the drug or to require that a physician meet the requirements of a specialty in order to prescribe the drug. In addition, the agency's attorneys have consistently taken the position that the holding of American Pharmaceutical Association is limited to methadone and that thus the court's decision does not impair the agency's ability to limit the distribution of other drugs, such as Accutane.

In addition, cases decided by the Supreme Court since American Pharmaceutical Association case make it clear that agencies such as the FDA are to be given great deference in interpreting their own regulatory statutes, casting considerable doubt on whether American Pharmaceutical Association is still good law, even as limited to methadone. See, e.g., Young v. Community Nutrition Institute, 476 U.S. 974 (1986), where the Court reversed the D.C. Circuit, which had overturned the FDA's interpretation of section 406 of the FDC Act and held that the agency's interpretation of a statute will be upheld if it is "sufficiently rational to preclude a court from substituting its judgment for that of the FDA." 476 U.S. at 981; see also Chevron U.S.A., Inc. v. Natural Resources Defense Council, Inc., 467 U.S. 837 (1984).

We recognize that the methadone regulation refers to both an investigational and a treatment use. 21 C.F.R. § 291.505. However, the limitations on the drug's distribution plainly apply to the treatment use, and thus the regulations stand as a precedent for limiting the distribution of a drug such as Accutane.

the environment.

E. Economic Impact.

The requested action may have a short-term adverse impact on the financial condition of Hoffmann-La Roche. However, in the long-term it will benefit both the manufacturer of Accutane and the physicians who are negligently prescribing it by reducing the incidence of malpractice and product liability lawsuits. Although the economic impact on consumers is trivial in comparison to the avoidable physical injuries and unnecessary abortions caused by Accutane, granting the petition will also have a beneficial economic impact by eliminating the unnecessary medical and other costs associated with children born with severe birth defects and both spontaneous and voluntary abortions.

F. Certification.

The undersigned certifies, that, to the best knowledge and belief of the undersigned, this petition includes all information and views on which the petition relies, and that it includes representative data and information known to the petitioner which are unfavorable to the petition.

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We recognize that the FDA has never approved an NDA on the condition that its use be limited to a particular specialty. Similarly, the FDA has invoked the imminent hazard provision of the FDC Act on only one occasion since it was enacted in 1962. We also cannot imagine a stronger case for invoking either

authority, given the seriousness and number of adverse reactions caused by Accutane and fact that there is a definable population (males and woman who do not become pregnant) for whom the drug is valuable. Therefore, we believe that it is imperative that both agencies use their full authority to limit the distribution of Accutane.

We also recognize that certain officials within the FDA have raised questions as to whether the FDA has the authority to limit the prescribing of a drug to a specialty and whether it may require informed consent for an approved drug. However, legal officials at the agency have informed us that the FDA has taken the position that it does have the authority to limit the distribution of drugs. If the FDA rules that it does not have such authority, then we will consider seeking review of that determination in federal court as well as seeking legislation in Congress. In either event, it is imperative that this issue be decided as expeditiously as possible.

Given the nature of the issue before the FDA, we request action on this petition within 30 days, including a final ruling on the agency's authority to adopt the measures that we have requested. We believe that failure to act on the petition within that period of time would constitute "unreasonable delay" in violation of the Administrative Procedure Act.

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