IN THE UNITED STATES OF AMERICA
BEFORE THE
DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
FOOD AND DRUG ADMINISTRATION

In the matter of:

A Rulemaking Proceeding : Docket No. 77N-0048
Concerning Laetrile : 

MEMORANDUM OF THE AMERICAN CANCER SOCIETY

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IN THE UNITED STATES OF AMERICA
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In the matter of:
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Docket No. 77N-0048

MEMORANDUM OF THE AMERICAN CANCER SOCIETY

Pursuant to the Rules and Regulations of the Food and
Drug Administration, the American Cancer Society, a parti­
cipant in the above-captioned proceeding, hereby submits its
memorandum of facts and law applicable to the issues in the
notice of rulemaking on "Laetrile" contained in 42 Federal
Register 10066 (February 18, 1977). 1/

INTRODUCTORY STATEMENT

This rulemaking proceeding was initiated pursuant to a
referral order of Judge Luther L. Bohanon of the Federal District
Court for the Western District of Oklahoma, attached hereto
as Appendix A. That referral order in turn emanated from a
proceeding known as Rutherford v. United States, 399 F. Supp.
1208 (W.D. Okla. 1975), aff'd, 542 F.2d 1137 (10th Cir. 1976).

In Rutherford, the plaintiff sought and obtained from
the District Court Judge a temporary injunction directing

1/ Record citations within this memorandum are as follows:
Cited by "Tr." are from the transcript of the Hearing
conducted by the FDA in Kansas City, Missouri on May 2
and 3, 1977; "AF," "CO," and "TS" citations are to docu­
mentary submissions filed with the FDA.
the Secretary of Health, Education and Welfare ("HEW"),
of which the Food and Drug Administration ("FDA") is a branch,
to desist from preventing plaintiff from obtaining a supply
of laetrile for his own use in the treatment of cancer.

On appeal by HEW, the Tenth Circuit Court of Appeals
affirmed the District Court's issuance of a temporary in-
junction. The Circuit Court declined to review certain of
the lower court's factual rulings regarding laetrile, 1/
but found that it was incumbent on the FDA to build an adminis-
trative record to support its determination that laetrile is a
"new drug". 2/ In this regard, it directed the District
Court to remand the case to the FDA for proceedings adequate
to develop a record on this subject. 3/

Upon remand to the District Court, Judge Bohanon issued
the aforementioned referral order on January 4, 1977, and on
February 18, 1977, FDA published notice of a rulemaking pro-
ceeding to compile an administrative record on two basic issues:
"(1) Whether Laetrile is generally recognized by qualified
experts as a safe and effective cancer drug and (2) whether
Laetrile is exempt from the premarket approval requirements
for new drugs by virtue of the 'grandfather' provisions of the
Federal Food Drug and Cosmetic Act." 5/ The notice also

1/ 542 F.2d at 1139-40.
2/ Id. at 1143.
3/ Id.
4/ See Appendix A hereto.
established certain procedural guidelines.

Having participated in the subject rulemaking proceeding through written submissions 1/ and an oral presentation, 2/ the American Cancer Society ("ACS") now submits this memorandum brief in an effort to facilitate the decision-making process through an analysis of the pertinent record materials and of the controlling statutory and case law.

STATEMENT OF INTEREST

On June 21, 1911, in a message to Congress, President Taft urged action to protect the seriously ill against statements of curative effect on drugs that are contrary to fact and that seduce the ill away from proven medical treatments: 3/

Fraudulent misrepresentations of the curative value of nostrums not only operate to defraud purchasers but are a distinct menace to the public health. There are none so credulous as sufferers from disease. The need is urgent for legislation which will prevent the raising of false hopes of speedy cures of serious ailments by misstatements of facts as to worthless mixtures on which the sick will rely while their diseases progress unchecked.

The most pernicious of the hoaxes perpetrated upon the public and condemned by President Taft related to the drugs claimed effective in the treatment of life-threatening illnesses, particularly cancer.

1/ AF-05 (Dr. Arthur Holleb, Senior Vice President, Medical Affairs); AR-18 (Dr. Jonathan Rhodes); CO-195 (Dr. R. Lee Clark). Several ACS divisions also supplied comments.
2/ Tr. 109-116 (Jonathan Rhodes, M.D.).
3/ 48 Cong. Rec. Pt. 12, at 675 (1911). See Tr. 112 (statement of Jonathan Rhodes, M.D.); see also Belmont Laboratories v. FTC, 103 F.2d 538 (3d Cir. 1939).
Cancer is one of the oldest recognized diseases, being mentioned in the earliest recorded history of the human race. Little was known of the disease or done about it until the early 1900's. In this country the first organized public effort dates back to 1913 when the American Cancer Society, then called the American Society for the Control of Cancer, was organized in New York City, by a group of ten physicians and five laymen. At that time the public was completely uninformed about cancer. There were no organized programs of cancer research or cancer control. The medical profession's attitude was essentially one of disinterest and pessimism. In an effort to dispel this attitude, the American Society for the Control of Cancer set out to disseminate information concerning the symptoms, treatment and prevention of cancer, to investigate conditions under which cancer is found, and to compile statistics in regard thereto.

Working closely with state and local medical societies and health departments, during the ensuing years the Society organized affiliates in several states. Publications were distributed to the public and to the medical profession. Program emphasis was placed on reaching practitioners with information on the diagnosis and treatment of cancer. Gradually, the Society's state and county organizations became more numerous and generated increasing community support. Newspapers, magazines, and radio stations began accepting more and more
educational material from the Society concerning cancer. The Society thus stimulated an increasing interest and desire on the part of the public to "do something about cancer."

One result of this interest was the establishment of the National Cancer Institute in 1938. In 1945 the Cancer Control Society was reorganized as the American Cancer Society. Today it remains a voluntary organization fighting cancer through balanced programs of research, education, patient service and rehabilitation.

In the early 1900's when the Society was first organized, knowledge of cancer was such that few cancer patients had any hope of long-term survival. In the 1930's fewer than one of five patients was alive five years after diagnosis. By the 1950's this figure improved to one in four. Today, due to earlier diagnosis and the steady improvement of the surgical, x-ray, and chemical approaches to the management of cancer, the ratio of patients alive after five years of disease is one in three. With even earlier diagnosis and prompt treatment, half of those who get cancer each year could be saved. 1/

The Society's professional education program brings the latest developments in cancer to the medical community through conferences, local meetings, workshops, training sessions, films, professional journals and the like. Its clinical

1/ ACS 1977 Cancer Facts and Figures, Exhibit A to AF-05 (Dr. A. Holleb). See also on the growing successes of accepted cancer therapy Tr. 145-146, (Bayard Morrison, M.D. Asst. Dir., NCI); 206-207, 212, (Emil Freireich, M.D.); 336, 341-342 (James K.Luce, M.D.).
Contrast these statistics with the representation made by Ernest Krebs, Jr. that orthodox cancer therapies do not work (Tr. 237).
professorship program strives to improve cancer teaching in medical schools. The Society's service programs generally provide information and counseling services for cancer patients and families, equipment loans, home care, transportation, blood programs, social work assistance and assistance with employment problems. Its rehabilitation programs reach out to all cancer patients. The best known of these programs are the laryngectomee, reach-to-recovery and ostomy programs. The Society is second only to the National Cancer Institute as a source of funds for cancer research and has played a crucial role in providing qualified research scientists with an alternative to federal funding.

It is in the area of information and education that the Society has, its most visible and in many respects its most important impact. The American public and the medical profession look to the Society for the most up-to-date and accurate information about cancer. The public and the profession depend on the Society for the facts. Without the widespread dissemination of accurate information, such as provided by the Society, the goal of further reducing the ravages of cancer through early diagnosis and treatment will unquestionably be more difficult to achieve.

Inasmuch as early and proper treatment of cancer is a life-and-death matter, unjustified deviations from this desideratum is of concern to the Society. It follows from this that one of the areas in the forefront of public and pro-
fessional questioning addressed to the Society pertains to unproven methods of cancer management. In response to the public and professional need for information in this area, the Society in 1954 established a Committee to examine unproven cancer methods. In 1970 that committee was renamed the Committee on Unproven Methods of Cancer Management.

ACS's efforts to uncover the facts about unproven tests and remedies for cancer have stressed the following objectives:

1. To develop more effective means of dealing with claims for the diagnosis and treatment of cancer that are advanced without acceptable evidence of value;
2. To encourage investigation through, scientific or other qualified organizations of, unestablished claims for cancer diagnosis and treatment;
3. To encourage the development of legislative programs, both state and Federal, which will prevent the exploitation of the public in matters relating to the diagnosis and therapy of cancer, and to obtain the continued support of the medical community on behalf of these objectives;
4. To develop and encourage educational programs which will give to the public both information regarding specific methods of treatment and also a better understanding of the criteria for assessing the merits of new claims; and
5. To encourage physicians to provide adequate care of patients with advanced cancer because it is, in the main, these individuals who unwittingly fall prey to "cures" which have no merit.

Through its efforts the Society now maintains the world's largest reference center for the collection and dissemination of data concerning this subject. This information is available on request to physicians, science writers, editors and the general public, to assist them in evaluating claims made for unproven methods of cancer prevention, detection and treatment.

By 1962, the public's concern over the impact of drugs which were ineffective for treatment of disease prompted then President Kennedy to recommend to Congress a hard line on drug frauds. In a message to Congress recommending the strengthening of the existing food and drug laws by adoption of what became the Drug Amendments of 1962, President Kennedy stated:

The successful development of more than 9,000 new drugs in the last 25 years has saved countless lives and relieved millions of victims of acute and chronic illnesses. However, new drugs are being placed on the market with no requirement that there be either advance proof that they will be effective in treating the diseases and conditions for which they are recommended or the prompt reporting of adverse reactions. These new drugs present greater hazards as well as greater potential benefits than ever before—for they are widely used, they are often very potent, and they are promoted by aggressive sales campaigns that may tend to overstate their merits and fail to indicate the risks involved in their use. For example, over 20 percent of the new drugs listed since 1956 in the publication "New and Non-Official Drugs" were found, upon being tested, to
be incapable of sustaining one or more of their sponsor's claims regarding their therapeutic effect. There is no way of measuring the needless suffering, the money innocently squandered, and the protraction of illnesses resulting from the use of such ineffective drugs.

The physician and consumer should have the assurance, from an impartial scientific source, that any drug or therapeutic device on the market today is safe and effective for its intended use; that it has the strength and quality represented; and that the accompanying promotional material tells the full story--its bad effects as well as its good. They should be able to identify the drug by a simple, common name in order to avoid confusion and to enable the purchaser to buy the quality drugs he actually needs at the lowest competitive price.

Existing law gives no such assurance to the consumer--a fact highlighted by the thoroughgoing investigation led by Senator Kefauver. It is time to give American men, women, and children the same protection we have been giving hogs, sheep, and cattle since 1913, under an act forbidding the marketing of worthless serums and other drugs for the treatment of these animals.1/

\[\text{[Emphasis added.]}\]

\[1/\text{[1962]}\text{U.S. Code Cong.} \& \text{Ad. News} 4143-44. \text{ See also Pharmaceutical Manufacturers Ass'n v. Richardson, 318 F. Supp.301, 307 (D.Del 1970) in which the court cited witnesses before the hearings leading to the 1962 Drug Amendments corroborating President Kennedy's call for impartial judgment on drugs:}\]

"[A] collection of impressions will [not] furnish the truth... [T]his approach did not prevent doctors from having unbounded faith in the curative powers of leeches for hundreds of years before scientific evaluation became the preferred means of judging efficacy of therapy... [T]he magnitude of sales of a drug after vigorous promotion is no recommendation for its usefulness or efficacy...."
The reasons why Congress, following President Kennedy's message, articulated such precise, rigorous and potent scientific standards for proof of compliance with or exemption from the provisions of the 1962 New Drug Amendments is well set forth by Judge Smith in United States v. Articles of Food and Drug: 1/

Quite properly, it is simply not enough to show that some people, even experts, have a belief in safety and effectiveness. A reasonable number of Americans will sincerely attest to the worth of almost any product or even idea. To remove the aberrations in uniformity which can result from a well-staged "swearing match," the law requires more. Indeed, it has been heretofore held that the purpose of the normal inquiry is not to determine safety and effectiveness at all, but to ascertain the drug's general reputation in the scientific community for such characteristics. United States v. 41 Cases, More or Less, 420 F.2d 1126 (5th Cir. 1970); AMP, Inc. v. Gardner, 389 F.2d 825 (2nd Cir. 1968), cert. den. 393 U.S. 825, 89 S.Ct. 86, 21 L.Ed.2d 95 (1968). It is certain that a conflicting reputation is insufficient to establish general recognition. United States v. An Article of Drug--Furestrol Vaginal Suppositories, 294 F.Supp. 1307 (N.D. Ga. 1968), aff'd 415 F.2d 390 (5th Cir. 1969).

Therefore, what is required is more than belief, even by an expert; it is a general recognition based upon substantial scientific evidence as delineated in the regulatory guidelines. 21 CFR § 130.12. Weinberger v. Hynson, Westcott & Dunning, 412 U.S. 609, 619, 93 S.Ct. 2469, 37 L.Ed.2d 207 (1973). There is no reason to differentiate the holding in Hynson between human drugs, and animal drugs. United States v. 14 cases--Naremco Medimatic, 374 F.Supp. 922 (W.D.Mo., Number 2806, January 29, 1974). Public health considerations are similar. Further, logic would dictate no lesser standard after-the-fact than in securing an application. Indeed, the reasoning of the Supreme Court appears to be that "the reach of scientific inquiry" is the same whatever the forum. Weinberger v. Bentex Pharmaceuticals, Inc. 412 U.S. 645(b), 93 S.Ct. 2488, 37 L.Ed. 2d 235 (1973). [Emphasis added; footnote omitted.]

* * *

The proponents of laetrile are making what can only be described as a frontal assault on the federal regulatory scheme developed over the years to protect the public from being inundated by worthless drugs. This regulatory scheme does not unduly impede the development of new drugs; it merely requires full disclosure of relevant facts so that those qualified to judge the efficacy and safety of drugs may do so prior to marketing to the general public. The Society is of the opinion that the regulatory scheme properly balances the interests of drug manufacturers and of the consuming public. It would be a grave disservice to the public if this regulatory scheme were undermined as the laetrile proponents are attempting to do. The Society's participation in this proceeding is for the purpose of adding its voice to those of Presidents' Taft and Kennedy in calling for the protection of the public from unproven drugs. 1/

1/ It is truly anomalous that some laetrile proponents have accused ACS, among others, of trying to cover up the facts in order to keep laetrile off the market. Not only is such a conspiracy-of-silence theory totally repugnant to common sense in view of ACS's single-minded dedication to developing effective and safe cancer-cures but in addition it is belied by the record herein (discussed infra) which shows that it is the laetrile proponents who have consistently avoided the formal procedures under the FDA Act, which are designed to elicit all relevant and material data concerning a drug's effectiveness and safety. For references to the laetrile proponents' allegations of a conspiracy to suppress laetrile, see, e.g., Tr. 293-94, 320-37, 358. For the arguments against conspiracy, see, e.g., Tr. 176, 181-82, 201-03, 432-33 and AF-17 at 8-9 (Daniel Martín, M.D.).
STATEMENT OF THE CASE

The Food, Drug and Cosmetic Act of 1938, as amended, in conjunction with regulations promulgated by the FDA pursuant to its statutory obligation to administer the Act, constitutes a comprehensive body of law governing the marketing of drugs for human or animal use. The purpose of this body of law is to protect the public by assuring that drugs marketed in this country are both safe and effective.

In furtherance of this purpose, the statute and its implementing regulations require that any substance introduced for use as a drug undergo extensive testing for safety and efficacy. With respect to cancer drugs, the initial step in establishing safety and efficacy is a showing that the substance shows activity against an animal tumor system. Substances which do not show activity against animal tumors uniformly are found to be ineffective against human tumors. If a drug satisfies the initial animal test criteria for effectiveness, phased clinical studies must still be conducted to determine suitability and effectiveness in treating human cancers. Only about one of three substances found to have activity against animal tumor systems is able to pass the safety, pharmaceutical feasibility, and other requirements for clinical evaluation. Only about one of ten of those studied or evaluated clinically demonstrates useful activity.

1/ 21 U.S.C.A. § 301 et seq.
in the treatment of cancer in humans. A new drug can be
distributed commercially only after it has been approved by
the FDA as safe and effective after conclusive tests on
both animals and humans.

This pervasive regulatory scheme, in which the burden
of proving drug efficacy is placed squarely on the manufacturer,
has evolved from the earliest Federal efforts at drug regulation,
which did not include such pre-marketing criteria and were
deemed inadequate by Congress because, *inter alia*, the ad­
ministering Federal agencies were simply unable to establish
the inefficacy of the literally thousands of drugs flooding
the market. 1/ This rulemaking proceeding is a response to a
movement in which the purveyors of various alleged cancer
cures, by playing on the emotions and fears of cancer victims,
seek to create an atmosphere of public pressure which will
subtly shift the manufacturer's responsibility of demonstrat­
ing the effectiveness of purported remedies back to the
Federal government, which is then placed in the position of
trying to prove the negative, i.e., the lack of effective­
ness of the particular drug. Such an atmosphere makes it
more difficult for the government to fulfill its statutory
responsibility to protect the public from unproven substances
and permits the purveyors greater latitude in the illegal
marketing of their products until ineffectiveness is proven,
at which time the purveyors simply go underground until a
new "cure" for them to promote is "discovered." Then, the

1/ See Message to Congress by President Kennedy, *supra* at 8-9.
vicious cycle begins again.

Over the years the government has fought a long, hard and often unappreciated battle to discover the facts about unproven methods of cancer treatment and to eliminate those which are ineffective.

The longest FDA investigation relating to an alleged cancer cure was that undertaken with respect to the Hoxsey method of treatment. The Hoxsey treatment was found to be of no benefit to cancer patients. On the basis of statistical and scientific evidence, it was concluded that "cures" ascribed to this method fell into three categories: (1) patients who had never had cancer; (2) patients who had been cured of cancer before treatment by the Hoxsey method; and (3) patients who had cancer and either still had it or died while being treated. Of the two facilities in the United States using the Hoxsey method, one was closed through court action in 1958 and the other was prohibited in 1960 from selling or dispensing Hoxsey medications.

Another well-known alleged cancer cure -- Krebiozen -- was tested extensively by the Federal government in 1963. The test process involved animal tumor systems which showed no effect. Review by the FDA of records of over 500 patients who allegedly benefited from its use disclosed no evidence of therapeutic effect. The FDA review committee concluded that Krebiozen could not be accepted for clinical trials.
The laetrile controversy closely follows the outline of its predecessors. A cancer remedy is introduced based on a novel idea. The promoters, while giving the appearance of welcoming scientific testing of their product, actually try to elude it by providing incomplete data, making samples of the compound for testing difficult to come by, and alleging at every rebuff by the scientific community that there is a conspiracy to suppress their ideas. 1/ The promoters seek reinforcement from the public by presenting themselves as champions of the underdog against the establishment. Public pressure is exerted to force the government to create an exception to its rule that the purveyors of a new drug must demonstrate its worth. Tests are undertaken by the qualified scientific community, and the result is confirmation of the worthlessness of the substance involved.

Laetrile is the name given to a purified version of an amygdalin compound in 1949 by Ernest Krebs, Jr. The amygdalin approach to cancer treatment was begun by Dr. Ernest Krebs, Sr. in the 1920's, but abandoned by him as too toxic in the form he used. His son, Ernest Krebs, Jr., refined the chemical and developed what he considered a purified version safe for use on humans in 1952. The purified compound, which was used only for investigational purposes prior to 1962, has undergone many changes as to formulation since that time so that it is dif-

1/ See, e.g., Rutherford v. American Medical Ass'n., 379 F.2d 641 (7th Cir. 1967) (Krebiozen); Tutoki v. Celebrezze, 375 F.2d 105 (7th Cir. 1967) (Krebiozen); United States v. 10 Cartons, 152 F. Supp. 360 (W.D. Pa. 1957) (Hoxsey).
ficult to know with any certainty what the composition of laetrile was at any given time.

Many theories have been advanced as to how laetrile might work and how it might ameliorate or prevent cancer. It was originally hypothesized by its proponents that laetrile is hydrolyzed by beta-glucoside enzymes, thus releasing glucose, benzaldehyde and hydrogen cyanide, which allegedly is lethal to cancer cells. Supposedly, cancer cells contain more beta-glucoside enzymes than do normal cells and consequently receive a larger dose of cyanide. Also, normal cells are said to contain another enzyme, rhodanese, which detoxifies the cyanide and therefore prevents unwanted destruction of healthy tissue.

A second theory that has been advanced by the supporters of laetrile is that cancer is a manifestation of a vitamin deficiency and that laetrile or Vitamin B-17, is this magic vitamin which prevents and cures cancer.

A third theory which has been advanced recently is that laetrile has a positive synergistic effect when used with other chemotherapeutic drugs.

None of these theories has yet been supported by scientific evidence. Indeed, the evidence is to the contrary.

The proponents of laetrile at one time or another have claimed that the product prevents, controls, cures, mitigates, and/or palliates cancer. They sometimes claim
that it should only be used in conjunction with conventional cancer therapy, but more often claim that it should be used as the sole treatment. It is also claimed to have a pain relief effect.

In 1962 and 1970 the purveyors of laetrile made application to the FDA for approval to use the drug for investigational purposes. The application was reviewed and rejected by an independent outside review committee of cancer experts. The rejection was based upon insufficient scientific evidence that the product was safe and effective in the treatment of cancer.

In response to public pressure, a number of government-financed animal studies of the drug were conducted in 1972 and 1973 by the National Cancer Institute, Sloan-Kettering, and the Catholic Medical Center. No antitumor activity was found in any of the systems tested. The studies at Sloan-Kettering Institute were carried out by a Dr. Kanematsu Sugiura. In a preliminary unpublished report, Dr. Sugiura stated that 78% of the mice in control groups had lung metastases, while metastases developed in only 17% of those treated with laetrile. This preliminary report was obtained by laetrile proponents who gave it wide publicity. However, a corroborative experiment carried out by Dr. Sugiura and Dr. Daniel Martin of the Catholic Medical Center had negative results. In these tests, there were no differences between tumors in the mice treated with laetrile and the control mice. Two
similar studies at the Sloan-Kettering Institute, as well as similar studies conducted at Arthur D. Little and Southern Research Institute, also were negative. 1/

The proponents of laetrile are undaunted by the scientific evidence arrayed against them on the efficacy of laetrile as a cancer treatment. In their defense of laetrile at the Kansas City oral arguments, they focused on laetrile as a pain agent and as a control or preventative of cancer. Additionally, in an effort to promote legalization of laetrile on a state-by-state basis, they now direct their energies to the proposition that laetrile is not a drug, but rather a food, food additive, or vitamin. The laetrile advocates advance as a further ground for the legalization of laetrile the charge that conventional therapy, which they characterize as the cut, burn, poison cancer treatments, does not work. Finally, they claim that cancer patients should be free to choose their method of treatment and that governmental prohibitions on the marketing of laetrile constitute an abridgement of individual freedom.

Similar arguments have been presented to Congress and the courts by both the purveyors of fraudulent cures for disease and their unwitting victims since the commencement of deliberations on the need for a pure food and drug act in 1906. Congress, and the courts, repeatedly have rejected such arguments as spurious and deceptive. Congress and the courts have considered it essential to the public health, safety and welfare to keep off the United States drug market any food

1/ See discussion of the research studies, infra at 51-55.
preparation that is not effective, and particularly those intended to be offered to patients with life-threatening illness.

The 1962 Drug Amendments require the manufacturers of a drug to demonstrate the efficacy of their product. When that showing has been made, the drug may be marketed. The consumer may then make a truly free and intelligent choice among drugs, on the market, all of which have been shown to be safe and effective.

Dr. Daniel Martin of the Catholic Medical Center pointed out in the record the fallacies of a principal argument of the laetrile proponents that since patients have the right to choose their physicians, they should also have the right to choose their drugs and treatment. Dr. Martin noted that since the physicians that we choose from are subjected to a rigid licensing procedure to assure their fitness, one's choice is confined to qualified doctors -- and the same choice is available as to qualified drugs:

I would like to discuss freedom of choice, ... one of the bits of testimony that is given on freedom of choice, is that patients have the right to have the freedom of choice to choose their own
physician. And that is true. And then the statement goes on, why not have the freedom of choice to choose drugs and your own treatment? Well, it is just like choosing your own doctor. You have consumer protection laws in this society. Nobody in this audience is allowed to call himself a doctor. He must get a license. In order to get that license, he has to prove not that he went to medical school but that he went to an accredited medical school, and that he satisfactorily passed that accredited medical school's program.

And further, he then has to take an examination to prove that he is qualified. And then he gets a license. And then you have the freedom of choice to pick out anybody with a license. So that in your own protection, you just can't have somebody coming to you and saying, well, I'm a doctor and I'll take care of you, when he really isn't.

Well, now the same thing goes for the drugs that you get. You can choose one cancer drug over another. Those cancer drugs, however, all have package inserts. A package insert is that little piece of paper that is in everyone of these—and FDA approved cancer drugs. And what that says, as has been brought out here, is some of the dangers of these drugs. And their dangers have also been brought out here by almost every single drug, not just in cancer, but in anything. And you take them all the time.

But also that package insert gives the clear proof of the fact there is beneficial effects to these drugs. They say that they are relevant to this disease or that disease, where they have produced this good effect and that good effect. No package insert can say this about laetrile whatsoever. There is no evidence for that. 1/

1/ Tr. 433-35 (Testimony of Daniel Martin, M.D.) (emphasis added).
The framework within which the public exercises its freedom of choice as to physicians and medical treatments described by Dr. Martin brings into perspective the real freedom of choice issue presented in this proceeding -- the role of the Federal government. This issue is well stated by Dr. David Carr of the Mayo Clinic:

The real issue is what kind of a government do we want in the United States of America. Do we want a government that has responsibilities for protecting the consumers from vendors with worthless goods and services? Do we want a government that permits the strong to take advantage of the weak, or do we want a society that protects the consumer.

A society that sets standards and requires that all live up to those standards. Our democratic process has decided that we want that kind of a government, a government that protects the consumer and requires that vendors establish the value of their material and that they follow orderly processes distributing and selling their material.

It seems to me that we should retain that kind of a government and that to legalize laetrile without requiring that it follow the orderly process of proving its safety and efficacy, would be a step backward into the olden days, the bad old days, if you will when the shopper could not trust the vendor. The shopper realized that unless he was very, very sharp he would be taken.

And I don't think that most Americans want to go back to that kind of a society. ¹/

¹/ Tr. 185 (Testimony of David Carr, M.D.)
Cancer victims constitute a minority group in our society, but like any other group, they have a right not to be exploited. A century ago, the victimization of those afflicted with cancer by useless drugs was blatant. The quack medicines of that time, that prompted the evolvement of the 1906 Food and Drug Act, would be quickly rejected by the sophisticated consumer of today. But quackery has likewise become more sophisticated during the last generation. The patient who is approached by the purveyors with claims that laetrile cures cancer and who, not knowing that the expert medical community considers it to be a worthless substance, succumbs to the pressures of the purveyor and well-meaning, but equally ignorant friends and relatives, is being denied his freedom of choice:

For the patient ignorant of Laetrile as an anti-cancer drug there is an overriding concern that he not be denied his individual freedom of untimely death from cancer from having relied on Laetrile to help. This is a cruel deprivation of individual freedom, since the patient does not get a second chance. 1/

The propaganda campaign for laetrile, which capitalizes on the patient and his family's fears of cancer, has taken two approaches. One approach, discussed above, relies on the freedom-of-choice rubric. The other approach is well stated by Orville Kelly, a cancer patient, who is the founder 1/ TS-20 at 2 (Statement of James F. Holland, M.D.)
of "Make Today Count", an organization for seriously ill patients, their family members and interested health care persons. Mr. Kelly, an advocate of conventional therapy, 1/speaks of the hard sell used by laetrile proponents. He refers to the false rumors that he had taken laetrile started by the purveyors because of his prominence. Finally, he notes the vulnerability of the cancer patient and his family with particular reference to his own circumstances. 2/

He recounted in his statement the pressures brought to bear on him to abandon conventional therapy and take laetrile:

The pressure upon me as a cancer patient and upon my wife, as a family member, to begin laetrile therapy commenced when publicity about myself and the Make Today Count organization grew nationwide. The pressure has never stopped.

Typical conversations centered around the contention from the proponents of laetrile that the "chemotherapy drugs were poison and were killing me." Then, the caller, or writer, would urge me to try the harmless but effective substance, laetrile or Vitamin B-17, which the AMA, ACS and NCI were suppressing because "cancer drugs are a big business commodity."

One man from Canada called my wife to convince her I should quit receiving medical treatment and try laetrile. When she resisted his arguments for laetrile, he exclaimed, "You're letting them kill your husband!" This, to me, represents nothing but pressure. My wife soon learned to hang up the telephone receiver when she received this type of call.

1/ AF-34 (Testimony of Orville Eugene Kelly).
2/ Id.
3/ Id.
The proponents of laetrile are not advocating freedom of choice. Freedom of choice is based on verifiable medical knowledge, i.e. on facts. The laetrile proponents are asking for freedom to pressure the cancer patient on emotional grounds, to provide him with false proofs of efficacy, to overbear his judgment with fallacious arguments rather than those based on scientifically proven grounds, to deprive him of free choice and to substitute choice by peer pressure.

Under the guise of "freedom of choice", advocates of laetrile are seeking to repeal our modern protection of this group's civil rights, and return us to the dark ages of medical quackery and fraud. Cancer victims would once again be exposed to the mercies of those who, either innocently or by design, play on their emotions, their fears, and their special vulnerabilities in order to sell them products that are worthless and to persuade them to abandon the therapies that science has shown to be their only hope for survival.

The alleged "choice" offered is very attractive. It holds out a treatment which is totally painless and offers the promise of cure. In contrast, conventional cancer treatments can be uncomfortable and at times include debilitating side effects. The cancer patient is in effect coerced into utilizing the painless cure first. This choice delays recourse to proven cancer treatments and leads to an increase in suffering and the hastening of death.
The claim is made that laetrile could be used only in advanced, incurable cancer. Even if this were true, yesterday's incurable cancer is today's therapeutic advance. Patients with previously fatal disease are now surviving because of concerted, step-by-step research with treatments that have been tested on animal cancers and found to be effective before being studied in man. If the patient removes himself from the conventional treatment process, he is removing himself from the possibility that his case could be one in which a breakthrough is made which would rescue him from death or prolong his life. 1/

Laetrile is not proposed merely as a placebo which medical experts find ineffective, but which patients in extremis might find psychologically helpful. The proponents of laetrile do not ask for use of the substance as a placebo; they hold it forth as a cure, a palliative agent or prevention agent, a controller of cancer. This was the approach used on Mr. Kelly, and it is the approach employed with other cancer patients and their families.

There is no effective way by statute or general court order to approve laetrile, which is put forth as a treatment for cancer, for use by patients whose only benefit if any, 1/ See, TS-20 (Statement of James F. Holland, M.D.). Nor should it be imagined that regulatory attempts to isolate a class of "incurable" cancer patients would be anything short of disastrous. The practical ease with which a laetrile seller could find some authority to certify that a patient was "incurable" demonstrates the susceptibility to virtual emasculation of the protective provisions of the Food and Drug Act. The Act itself, of course, contains no such exception.
will be a placebo benefit as differentiated from those who can possibly benefit from standard treatment. Further, the only way to achieve the placebo effect itself is for some authority to indicate that the drug could be effective. But as this record demonstrates, laetrile is not effective. Therefore, there exists no legal or ethical way to justify creating an exception for a class of cancer patients who theoretically are beyond hope.

The practical and ethical impropriety of carving out such an exception to the applicability of the Food and Drug laws was pointedly addressed by Dr. Samuel Klagsbrun:

Use of the term "terminally ill" is inappropriate when dealing with an individual cancer patient. Although specific forms of cancer may have a statistically expectable mortality rate, that rate is meaningless when applied to an individual patient. Oncologists are all familiar with experiences where severe cancers, which were statistically considered to be hopeless, have, in some small percentages of cases, undergone a sudden remission. It would be tragic to condemn any individual cancer patient to death because, as a statistical matter, that patient's particular form of cancer may not be curable.

A decision to allow patients who are diagnosed as having a cancer which, as a statistical matter is expected to lead to their death, would move all such patients away from orthodox therapy and condemn even the individual patient whose cancer may unexpectedly move into remission to Laetrile, a worthless and ineffective drug. In addition, such a decision would thereafter remove the patients from the possibility of receiving continuing chemotherapy or radiation therapy which could enhance the effects of any remission. Most physicians have undergone the experience of predicting the moment of death and have been unexpectedly and repeatedly proven wrong to a considerable degree.
The prolongation of life, therefore, becomes a goal, not simply for the sake of prolongation, but also to render patients available to either a recent advance in chemotherapy or simply to enhance the quality of the time left available to the patients. 1/

Any gloss of legality, even as a mere placebo, will lead more and more of the unwary and unknowing to seek laetrile out as a first resort in the treatment of their cancers. The "exclusive" reliance on laetrile from the inception of disease is the approach urged by the proponents who tried to convince Mr. Kelly to use the drug, and it is the approach frequently used in direct contacts with other cancer patients and their families. Clearly, if laetrile is legalized, the pressures to rely on it as a first resort will increase; the result, -- cancer which is successfully manageable by conventional, proven therapies will spread unchecked and lead to certain death for many who could be saved.

The dangers of this so-called freedom of choice and the importance of adherence to the sound standards of the drug laws are succinctly expressed in the affidavit of Vincent T. DeVita, Jr., Director of the Division of Cancer Treatment at the National Cancer Institute:

The argument has been made that patients with cancer should be allowed to freely select their treatment. This idea is a snare and a delusion. In dealing with cancer, the patient should have the information necessary to select a well-qualified physician who can assure the patient that the best of available diagnostic and therapeutic methods will be applied in the best available facilities. It is essential that there be assurance that the properties of the drugs and of the methods used to treat cancer

1/ AF-49 at 6 (affidavit of Samuel C. Klagsbrun, M.D.).
have been defined and documented. These are complex matters that can be assured only through the effective functioning of complex societal processes which include medical training and licensure, medical research, and careful formal evaluation and regulation of materials, methods, and facilities. Without these processes there would be little assurance of any quality and effectiveness in medical care. The patient would be fair game for the callous or well-intended advocate of methods that might be ineffective if not harmful. Free access to amygdalin or any other drug of unproved merit would represent a backward step that could nullify the advantages of research and development efforts which, by making increasingly effective treatment available to cancer patients, are making important therapeutic inroads on a major disease problem. 1/[Emphasis added.]

The Federal government, through the Food and Drug Act, has made it clear that the manufacturers of all drugs must prove their products safe and efficacious before they can be offered to the consuming public. This valid Congressional mandate cannot be fulfilled on a discriminatory basis, where some remedies are banned as ineffective and others which have failed to meet identical scientific standards of efficacy are allowed to be marketed. Discriminatory enforcement raises questions of the most serious kind relating to equal protection of the laws, and exposes the entire regulatory apparatus to ethical and legal assault.

The developers and manufacturers of laetrile have touted its palliative, curative, preventative merits for nearly 25 years. This is clearly adequate time for a drug to establish its worth; adequate time for the proponents to have met

1/ AF-03 at 5 (affidavit of Vincent T. DeVita, Jr., M.D.).
the standards which are equally applied to all drugs seeking recognition from the government and scientific community; and adequate time to have run the prescribed animal tests, collected the data and the verified case histories. But to date this has not been done. The proponents of laetrile have been given numerous opportunities to prove their case -- they have not. The government has specifically funded studies to explore the nature of proponents' claims -- the studies have in the final analysis proved laetrile worthless. Once again, in this proceeding, the proponents have been presented with the opportunity to fill the record with hard data in support of their claims. The record is devoid of such evidence; rather, it convincingly demonstrates the contrary.
THE STATUTORY AND JUDICIAL GUIDELINES APPLICABLE TO THIS RULEMAKING PROCEEDING

As observed in the Introductory Statement to this Memorandum, this rulemaking proceeding is being conducted for the purpose of compiling an evidentiary record adequate to support a decision by the FDA on (1) whether laetrile is a "new drug" for purposes of the Food, Drug and Cosmetic Act and (2) if so, whether it is nevertheless exempted by either of two statutory grandfather provisions from the requirements of pre-market testing for safety and efficacy imposed on new drugs by Section 505 of the Act. 1/

Prior to discussing the specific details of the record established herein on laetrile with respect to these issues, and the actions required of the FDA by that record, ACS believes it will be of value to undertake first a general examination of the statutory provisions of the Food, Drug and Cosmetic Act of 1938 which are involved, and the respective burdens these provisions place on the FDA and the proponents of new drugs generally. Following this general statutory review, this portion of the memorandum will address briefly the special conditions imposed on the FDA by the Rutherford decision of the Tenth Circuit Court of Appeals.

2/ The statutes relevant to this proceeding are set forth as Appendix B to this memorandum.
A. The Provisions Of The Food, Drug, And Cosmetic Act Pertinent To These Proceedings.

1. The definition of "Drug".

A threshold requirement for application of the Act to any product is that the substance involved be a "drug" for purposes of the Act. Section 201(g)(1) of the Act defines the term "drug" as encompassing "articles intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease in man or animals..." 1/ (Emphasis added.) This broad statutory definition of drug is intended to allow broader coverage of the Act than any strict medical definition might allow. 2/ Thus, under the Act, it is the intended use of a product that determines whether it falls within the statutory category of a "drug" and hence the regulatory requirements of the Act. 3/ The intended use of a product may be ascertained from its label, any accompanying promotional material, advertising or any other relevant source, 4/

including oral and written representations about the product. 1/ Additionally, the protection of the public health dictates that the statutory definition of drug as an article intended for use in diagnosis, cure, mitigation, treatment, or prevention of disease "be construed liberally." 2/

Once a substance is found to be a "drug", it is subject to the other provisions of the Act unless specifically exempted.

2. The statutory definition of a "New Drug".

If a substance is determined to be a "new drug", it is subject to the stringent requirements of Section 505 of the Act with respect to pre-market approval by the FDA. 3/

Section 201(p) of the Food, Drug and Cosmetic Act of 1938, as amended in 1962, 4/ defines a "new drug" as:

(1) Any drug ... the composition of which is not generally recognized, among experts qualified by scientific training and experience to evaluate the safety and effectiveness of drugs, as safe and effective for use under the conditions prescribed, recommended, or suggested in the labeling thereof ... or

(2) Any drug ... the composition of which is such that such drug, as a result of investigations to determine its safety and effectiveness for use under such conditions, has become so recognized, but which has not, otherwise than in such investigations, been used to a material extent or for a material time under such conditions.

Under the statutory definition set forth in Section 201(p)(1) (Appendix B hereto) a drug escapes "new drug" status only if it has (1) attained general recognition among qualified experts (2) as being safe and effective for its intended use. Additionally, Section 201(p)(2) requires that once general recognition of safety and effectiveness has been attained among experts, the drug still must be used to a "material extent" and for a "material time" before losing its "new drug" status.

The legal import of the "new drug" definition set forth in Section 201(p) of the Act has been the subject of a great deal of controversy and litigation. However, a series of four decisions handed down by the Supreme Court in 1973 1/ exhaustively addressed Section 201(p) and clarified substantially the effect of that section on drugs generally.

First, in Weinberger v. Hynson, Westcott & Dunning, Inc., 412 U.S. 609 (1973) the Supreme Court confirmed that the FDA is vested with the power to determine whether a particular drug is a "new drug" within the meaning of Section 201(p) of the Act. 2/ According to the Court:

2/ Hynson, 412 U.S. at 624.
FDA is indeed the agency selected by Congress to administer the Act, and it cannot administer the Act intelligently and rationally unless it has authority to determine what drugs are "new drugs" under Section 201(p) .... 1/

The Hynson Court conceded, however, that while Section 201(p) of the Act was both "quantitative and qualitative," on its face it failed to offer definitive guidance to the FDA with respect to its enforcement because a definition of what constitutes "general recognition" among experts was not to be found in the Act. Consequently, the Court looked to the overall statutory scheme of the Act and the overriding purpose of the 1962 Amendments before concluding that

a drug can be "generally recognized" by experts as effective for intended use within the meaning of the Act only when that expert consensus is founded upon "substantial evidence" as defined in § 505(d). 2/

Section 505(d) defines "substantial evidence" as evidence consisting of adequate and well-controlled investigations, including clinical investigations, by experts qualified by scientific training and experience to evaluate the effectiveness of the drug involved, on the basis of which it could fairly and responsibly be concluded by such experts that the drug will have the effect it purports or is represented to have under the conditions of use prescribed, recommended, or suggested in the labeling or proposed labeling thereof. 3/

1/ Id. The Court also found that the FDA was empowered to determine whether a new drug was exempt by virtue of the grandfather clause of § 107 (c)(4) of the Act from the efficacy requirements of the 1962 amendments. Id. The grandfather clause of § 107(c)(4) will be discussed at 71-88, infra.

2/ Hynson, 412 U.S. at 632.

3/ Section 505(d); 21 U.S.C.A. § 355(d).
The Court further expanded on the necessity of establishing "general recognition" for purposes of Section 201(p) by reliance on clinical testing and reference to scientific literature in *Weinberger v. Bentex Pharmaceuticals, Inc.*, 412 U.S. 645, 652 (1973), where it observed as follows:

> Whether a drug is a "new drug", depends in part on the expert knowledge and experience of scientists based on controlled clinical experimentation and backed by substantial support in scientific literature .... It may, of course, be true that in some cases general recognition that a drug is efficacious might be made without the scientific support necessary to obtain the approval of an NDA. But, as we indicated in *Hynson*, supra, at 631, 37 L.Ed 2d at 224, the reach of scientific inquiry under both § 505(d) and under § 201 (p) is precisely the same. (Emphasis added.)

Thus *Hynson* and *Bentex* conclusively establish that the FDA must find that a drug is a "new drug" under Section 201(p) as defined in Section 505(d) of the Act, at least until it is demonstrated by "substantial evidence," that the drug has attained general recognition among qualified experts for safety and effectiveness in use. Finally, even after a "new drug" has attained this general recognition for safety and effectiveness, it nevertheless retains its new drug status until it has been used to a material extent for a material time.

In sum, Section 201(p) is designed so that drugs on the market, unless exempt, will have mustered the requisite scientifically reliable evidence of effectiveness long before
they are in a position to drop out of active regulation by ceasing to be a new drug. 1/

3. The pre-market testing requirements of the Food, Drug and Cosmetic Act.

Section 505 of the Food, Drug and Cosmetic Act 1/ establishes the conditions under which new drugs may be marketed to the consuming public. Essentially, this section of the Act prohibits the marketing of any new drug unless it is first demonstrated to be both safe for use and effective in use.

The procedure adopted by Section 505 for assuring that unsafe and ineffective drugs are kept off the market is set out in subsection 505(b) of the Act. This subsection addresses the contents of applications which must be filed by the proponents of new drugs with the FDA. A new drug may not be marketed until such an application has been approved by the FDA. Section 505(b) requires that new drug applications contain the following information:

(1) Full reports of investigations which have been made to show whether or not such drug is safe for use and whether such drug is effective in use;
(2) a full list of the articles used as components of such drug; (3) a full statement of the composition of such drug; (4) a full description of the methods used in, and the facilities and controls used for manufacture, process, and packaging, of such drug; (5) such samples of such drug and of the articles used as components thereof as the Secretary may require; and (6) specimens of the labeling proposed to be used for such drug.

1/ Hynson, 412 U.S. at 609.
Thus, Section 505(b) imposes upon proponents of new drugs the obligation to come forward with detailed information pertaining to the composition, labeling, manufacture, and safety for use and effectiveness in use of such drugs.

Section 505(d) of the Act sets forth the standards to be adhered to by the Secretary when acting to approve or deny such new drug applications. Section 505(d) provides in pertinent part as follows:

If the Secretary finds ... that (1) the investigations, reports of which are required to be submitted to the Secretary pursuant to subsection (b) of this section, do not include adequate tests by all methods reasonably applicable to show whether or not such drug is safe for use under the conditions prescribed, recommended, or suggested in the proposed labeling thereof; (2) the results of such tests show that such drug is unsafe for use under such conditions or do not show that such drug is safe for use under such conditions; (3) the methods used in, and the facilities and controls used for, the manufacture, processing, and packaging of such drug, are inadequate to preserve its identity, strength, quality, and purity; (4) 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 sufficient information to determine whether such drug is safe for use under such condition; or (5) evaluated on the basis of the information submitted to him as part of the application and any other information before him with respect to such drug, there is a lack of substantial evidence that a drug will have the effect it purports or is represented to have under the conditions of use prescribed, recommended, or suggested in the proposed labeling thereof; (6) based on a fair evaluation of all material facts, such labeling is false or misleading.
in any particular; he shall issue an order refusing to approve the application. If, after such notice and opportunity for hearing, the Secretary finds that clauses (1) through (6), do not apply, he shall issue an order approving the application.

Even a cursory analysis of these prerequisites for approval set forth in Section 505(d) reveals the determination of Congress to protect the public from dangerous or ineffective drugs and underscores the fact that it is the responsibility of the proponents of new drugs to demonstrate clearly and convincingly to the FDA, prior to marketing, that the new drug is both safe and effective. For example, with respect to the safety of a drug, it is incumbent upon the proponent of a new drug to conduct "adequate tests by all methods reasonably applicable" to show whether the drug is safe for use as prescribed. \[1\] Failure to conduct the required tests for safety will lead to rejection of an application. Similarly, if the tests conducted show that the drug is unsafe for use as prescribed, rejection by the Secretary will follow. An additional safety-related condition is the requirement that the application provide evidence to assure that the identity, strength, quality, and purity of the drug will be maintained. Finally, Section 505(d)(4) leaves substantial discretion to the Secretary to determine when the available evidence is insufficient to establish that the drug is safe under the

\[1\] Section 505(d)(1), 21 U.S.C.A. § 355(d)(1); emphasis added.
conditions prescribed. Unless the Secretary is convinced that the evidence is sufficient, he must reject the application.

The Secretary also is directed to refuse to approve a new drug application unless there exists substantial evidence establishing that the drug will have the effect it is represented to have. 1/

Taken together, Sections 505(a), (b), and (d) establish a comprehensive Federal regulatory scheme intended to keep drugs that have not been affirmatively demonstrated to be both safe and effective, off the market. Additionally, the statute leaves very little discretion to either the proponent of a drug or the FDA. Unless substantial evidence that is both clear and convincing is presented by the proponents of a new drug, the Secretary may not approve a new drug application and consequently the drug itself may not be marketed to the general public.

4. The grandfather provisions.

Two "grandfather" provisions are applicable to the Food, Drug and Cosmetic Act and affect the need for a drug which otherwise qualifies as a "new drug" under Section 201(p) of the Act to comply with the pre-marketing requirements of Section 505. The first of these grandfather provisions is set forth in Section 201(p) itself and provides 1/ The requisites of substantial evidence are discussed supra at pp 34-35.
that notwithstanding the lack of general recognition of safety and effectiveness, a drug shall not be declared to be a "new drug"

if at any time prior to the enactment of this chapter [June 25, 1938] it was subject to the Food and Drugs Act of June 30, 1906, as amended, and if at such time its labeling contained the same representations concerning the conditions of its use .... 1/

The second grandfather exemption consists of the transitional provisions enacted as Section 107(c)(4) of the 1962 amendments of the Act, 2/ which states:

In the case of any drug which, on the day immediately preceding the enactment date [October 10, 1962], (A) was commercially used or sold in the United States, (B) was not a new drug as defined by Section 201(p) of the basic Act as then in force and (C) was not covered by an effective application under Section 505 of the Act, the amendments of Section 201(p) made by this Act shall not apply to such drug when intended solely for use under conditions prescribed, recommended or suggested in labeling with respect to such drug on that day.

The effect of the two grandfather provisions is to eliminate the requirement of obtaining an NDA for any drug subject to the 1906 Act marketed in the United States from June 30, 1906, to June 25, 1938, or for any drug commercially used or sold in the United States which had attained general recognition among qualified experts as safe for its intended purpose, as the term "safe" was then properly

2/ Pub.L. 87-781, reprinted in Appendix B hereto.
Whether or not a drug is exempted from the pre-marketing requirements of Section 505 by virtue of either of the above grandfather provisions is to be determined initially by the FDA. Additionally, it is incumbent upon the party seeking to grandfather a drug to establish that the drug is in fact entitled to such status.

B. Guidelines Designated By The Rutherford Court.

The Tenth Circuit Court of Appeals in Rutherford v. United States, 542 F.2d 1137, 1141-43 (10th Cir. 1976), charged the FDA to respond to questions involving the status of laetrile with respect to the requirement of obtaining an NDA pursuant to Section 505 of the Act. The threshold question is whether laetrile is a "new drug" under the 1962 Drug amendments. If so, the issue remains whether the drug is grandfathered by reason of the transitional provisions of the 1962 or 1938 Acts.

The rulemaking procedure followed by the FDA on referral tracks procedures generally recognized by the courts as meeting due process requirements for the purpose of airing the issues, evidence, and relevant factors to be considered by

1/ Durovic v. Richardson, 479 F.2d 242 (7th Cir. 1973), cert. denied, 414 U.S. 944.
an agency in determining the status of a drug. 1/

All parties concerned as to the status of laetrile were given notice of the proposed action via notice of rulemaking published on February 18, 1977 in the Federal Register. 2/
The notice invited those interested to submit documents, data and affidavits. Opportunity was afforded to examine the initial submissions and to submit reply statements. Hearings were held, at which oral arguments were permitted. At the oral arguments, Mr. Coe indicated that he would be briefing the issues in the proceeding at a later time. 3/ The ACS agrees that briefs analyzing the large evidentiary record established in this rulemaking proceeding in the light of relevant statutory criteria and judicial precedent are clearly called for. Indeed, such submissions appear to be anticipated by reason of the citation in the "Notice" to § 314.200 of the FDA's Administrative Rules. This memorandum is submitted in response to that section of the FDA's rules. 4/


Contrary to the statement made by Mr. Coe, counsel to Mr. Rutherford at the hearing in Missouri (Tr. 443), Judge Bohanon's referral order of January 10, 1977 did not set forth the type of hearing process to be followed on remand, thus, leaving the selection to the process set forth at 21 C.F.R. § 2.14.


3/ Tr. 443. Mr. Coe is the attorney for Glen Rutherford, the petitioner in Rutherford v. United States. See Introductory Statement at 1-3, supra.

4/ 21 C.F.R. § 10.60(c)(8); § 16.95(a); § 314.206(b) also support the right of the Society to submit a legal memorandum in this rulemaking proceeding. These regulations are discussed in the memorandum of law accompanying the Society's motion to file its brief to June 17, 1977.
However, this "rulemaking by reference" proceeding arguably differs from the usual rulemaking proceeding with respect to the standard of proof. In setting the legal parameters of this reference proceeding, the Court in Rutherford seemed to conclude that the FDA must present substantial evidence to support the proposition that laetrile is not generally recognized among qualified experts as "safe and effective" and that laetrile is not grandfathered by either of the exemptions mentioned above. 1/ In the usual proceeding, the burden of substantial evidence lies with the proponents of the drug, 2/ not with the Federal agency. The usual course is for the district court to dismiss the petition for a declaratory judgment and to request that the FDA conduct a formal administrative rulemaking proceeding. Following the administrative proceeding, the proponents, if aggrieved, may then seek judicial review in a court of appeals. 3/ However, the Society submits

1/ 542 F.2d at 1143 and see Judge Bohanon's order of Jan. 4, 1977 (appendix A hereto).
2/ Weinberger v. Hynson, Westcott and Dunning, Inc., 412 U.S. 609, 617 (1973); Upjohn Co. v. Finch, 422 F.2d 944, 955 (6th Cir. 1970); North American Pharmacal, Inc. v. HEW, 491 F.2d 546, 550-51 (8th Cir. 1973). In rejecting a request for a declaratory judgment which sought relief closely paralleling the relief requested by the laetrile proponents before Judge Bohanon, Judge Kiley in Tutoki v. Celebrezze, 375 F.2d 105 (7th Cir. 1967), suggested that the plaintiff cancer patients could sponsor a new drug application for Krebiozen before the FDA. Id.
that even judges against the improper and unprecedented burden-of-proof standard arguably established by the Rutherford court, the record before the FDA shows by substantial evidence that laetrile is a "new drug" and that it is not exempted by either of the grandfather clauses. ¹/

¹/ The credentials of the witnesses relied upon by the Society in support of the denial of laetrile's recognition as safe and effective are summarized on Appendix C hereto.
ARGUMENT

I. LAETRILE IS A NEW DRUG AS DEFINED IN SECTION 201(p) OF THE ACT AND THEREFORE IS SUBJECT TO THE PREMARKETING REQUIREMENTS FOR SAFETY AND EFFICACY SET FORTH IN SECTION 505 OF THE ACT.

As discussed supra at 32-36, whether laetrile is a "new drug" for purposes of Section 201(p) of the Act 1/ depends upon its being a drug that is not generally recognized as safe and effective for its intended use by experts qualified by scientific training and experience to evaluate the safety and effectiveness of drugs. 2/ Furthermore, general recognition for safety and effectiveness is premised upon complex chemical and pharmacological considerations. 3/ In addition to attaining such "general recognition" among qualified experts, it is necessary for laetrile to have been used to a material extent and for material time to avoid new drug status. 4/ Laetrile does not meet these requirements and therefore is a "new drug."

A. Laetrile Is A Drug.

Laetrile unquestionably is a "drug" as that term is defined by Section 201(g)(1) of the Act, 5/ which identifies the intended use of a substance as controlling its drug status. The record established in this proceeding is replete with evidence confirming that laetrile

is claimed and intended to be used and useful in the cure, mitigation, palliation, control, prevention, treatment or management of cancer. 1/

The evidence adduced in this proceeding -- including sworn affidavits from experts in the cancer field, written claims by laetrile manufacturers, actual labeling obtained from laetrile containers, and much more -- clearly meets the judicially recognized standards for establishing "intended use" of a substance. 2/ In fact, laetrile's status as a drug already has been judicially confirmed. 3/ Indeed, the Rutherford court itself observed:

[Rutherford] argues that [laetrile] is in the nature of a diet supplement or a vitamin, but the cases recognize that even if a substance is also a food, it may be subjected to the requirements of the Act if it is used in the diagnosis, cure, mitigation, treatment or prevention of disease in man or animals. 2/ Intended use is an important aspect in the determination of

1/ AF-15 (A. Sherwood Lawrence, M.D.) at 4, 7 (cure), 5 (palliate), 5-17 (prevent, control, ameliorate, cure); Attech. 2 at 325 (therapy); Attech. 3 at 32-40 (palliative), Attech. 6 (treatment), Attech. 7 at 31 (treatment, cure), Attech. 8 (cure not palliate, treatment of cancer); AF-16 (Carl M. Leventhal, M.D.) at 3-8 (prevent, cure, mitigate, arrest, reduce pain, placebo); AF-17 (Daniel S. Martin, M.D.) at 7-9 (placebo); AF-22 (Philip S. Schein, M.D.) at 5-6 (placebo); AF-27 (Robert J. Temple, M.D.) at 2, 14 (prevent, cure, control, palliate); AF-30 (Robert S. K. Young, M.D., Ph.D.) at 3-6 (palliate, not cure); AF-33 (Jack R. Cooper, M.D.) at 3-6 (palliate) and Exhibit 5 at 2-5 (palliate not cure); AF-37 (David M. Greenberg, Ph.D.) at 7-8 (placebo only).


Unquestionably, Laetrile is intended at least as a treatment for cancer....


Thus, the remaining question centers on whether laetrile is a "new drug" for purposes of the Food Drug and Cosmetic Act.

B. Laetrile Is A New Drug.

1. Laetrile does not enjoy general recognition among qualified experts as being safe and effective for the treatment or cure of cancer.

Laetrile's status as a new drug is dependent in part upon the current opinion of qualified experts on its safety and efficacy for its intended use. 2/ The record in this rulemaking proceeding establishes by overwhelming evidence

1/ 542 F.2d at 1140
2/ 21 U.S.C.A. § 321(p). As discussed supra, at 32-33, 45. In addition to achieving the general recognition of qualified experts as being a safe and effective drug for its intended purpose, it is necessary also that laetrile be used in the United States to a material extent and for a material time in order to avoid new drug status. 21 U.S.C.A. § 321(p)(2).
that laetrile is not generally recognized by experts qualified to pass judgment as safe or effective for the treatment or cure of cancer. To the contrary, there exists a clear consensus of opinion among such experts that laetrile is useless as a cancer drug and is both a fraud on the public and a danger to cancer victims.

An indication that a drug is not generally recognized as safe and effective for its intended usage is that those experts who are in a position to be aware of drugs within their field testify that the drug is not generally recognized. 1/ Dr. Carl M. Leventhal, Deputy Director of The Bureau of Drugs of the Food and Drug Administration and a physician with wide experience in the scientific study of drug therapy of cancer, testified on the status of laetrile as a "new drug." Dr. Leventhal stated that he was familiar with laetrile and the results of tests conducted to evaluate its efficacy. 2/ Based upon his knowledge, Dr. Leventhal concluded:

Laetrile is not now, nor was it on October 9, 1962 generally recognized among experts qualified by scientific training and experience to evaluate safety and efficacy of drugs intended for use in cancer therapy, as either safe or effective for the prevention, cure, mitigation, or treatment of any form of cancer or pain associated with cancer. 3/

2/ The scientific testing of laetrile is discussed infra at 51-55.
3/ AP-16 at 6. (Affidavit of Carl M. Leventhal, M.D.)
Dr. Leventhal's expert opinion regarding laetrile is shared by the overwhelming majority of experts who rendered testimony in this proceeding. 1/ Typical of the testimony submitted is that of Dr. Alfred Soffer, Professor of Medicine at the University of Chicago School of Medicine. 2/

In addition to his duties as a Professor of Medicine, Dr. Soffer is the editor of three major medical journals, with the responsibility of reviewing and evaluating scientific papers and reports on various forms of therapy worldwide. Dr. Soffer also stated in his affidavit that through review of scientific papers as an editor and by reading medical and scientific literature he keeps informed of drugs that currently are recognized as safe and effective for their intended uses. 3/ With respect to laetrile, Dr. Soffer states:

I am informed and understand that amygdalin is a cyanogenic glycoside. Cyanogenic glycosides are chemicals which contain in their molecular structure a sugar, a non-sugar, and the cyanide group, (C≡N). I know of no cyanogenic glycoside that is generally recognized as safe and effective for the treatment, prevention, or cure of cancer, for the relief of pain associated with cancer, or for any medical purpose.

The composition of the cyanogenic glycosides, in general, and of amygdalin, in particular, is such that I do not recognize them, and they are not generally recognized among experts qualified through scientific training and experience to evaluate drugs, as safe and effective for the treatment of cancer.

1/ The testimony of Dr. Dean Burk was submitted in support of laetrile. Although Dr. Burk has had wide experience as a research chemist, his analysis of laetrile and his testimony are subject to serious challenge. A virtual line by line rebuttal of Dr. Burke's testimony and conclusions was submitted by Dr. Jukes, AF-42. Such testimony as that offered by Dr. Burk does not begin to meet the "substantial evidence test on this critical issue.

2/ AF-31 (Affidavit of Alfred Soffer, M.D.).

3/ Id. at 2.
for prophylaxis against cancer, for relief of pain associated with cancer, or for any medical use. Neither amygdalin nor any other cyanogenic glycoside was generally recognized as safe for any such uses on October 10, 1962. None of these substances have ever been so recognized in cancer management. The scientific literature contains no reports of adequate, well-controlled scientific studies, or other evidence upon which such recognition may be predicated. I know of no recognized medical text in which use of amygdalin or any cyanogenic glycoside is recommended for the treatment of cancer. I know of no medical school where use of these substances for such purposes is taught. I know of no expert in cancer chemotherapy who is of the view that there is evidence these substances have any useful effect in treating cancer. I know of no report in the scientific literature describing an adequate, well-controlled study which demonstrates that amygdalin or any cyanogenic glycoside is safe and effective in the cure, mitigation, treatment or prevention of cancer. 1/ (Emphasis added.)

For purposes of ascertaining whether "general recognition" exists among qualified experts as defined in Section 201(p) of the Act, Dr. Soffer's testimony that the scientific literature contains no reports of adequate, well-controlled studies or other evidence on which general recognition may be predicated is of particular significance. In United States v. An Article of Drug Labeled "Entrol-C-Medicated," 2/ a case involving the condemnation of an animal drug, the

1/ Id. See also affidavits of: Dr. Robert C. Eyerly, M.D. (AF-1 at 3); Dr. George J. Hill, II, M.D. (AF-04 at 2-4); Dr. David T. Carr., M.D. (AF-08 at 4-5); John T. P. Cudmore, M.D. (AF-10 at 2); Bernard T. Korbitz, M.D. (AF-13 at 4); W. Sherwood Lawrence, M.D. (AF-15 at 9-10); Carl M. Leventhal M.D. (AF-16 at 6); Daniel S. Martin, M.D. (AF-17 at 4-5, 7-9, 10); Joseph f. Ross, M.D. (AF-21 at 6-8); Philip S. Schein, M.D. (AF-22 at 5); Michael B. Shimkin, M.D. (AF-23 at 2-3); Jesse L. Steinfeld, M.D. (AF-24 at 5-6); C. Chester Stock, Ph.D. (AF-25 at 7-8); Susan J. Mellette, M.D. (AF-44 at 1).

2/ 362 F. Supp. 424 (D. Cal. 1973), aff'd, 513 F.2d 1127. See also, United States v. 41 Cases, More or Less, 420 F.2d 1126, 1130 (5th Cir. 1970).
District Court found that one indication that a drug is not generally recognized as safe and effective for its intended use is the absence of any published medical or scientific literature relating to the usage of the drug.

The record in this proceeding demonstrates both by the affirmatively expressed opinions of experts such as Dr. Leventhal and Dr. Soffer, and by the fact that there exists no scientific or medical literature, based upon adequate, well-controlled studies, supporting laetrile, that general recognition for safety and efficacy for purposes of Section 201(p) of the Act does not and cannot exist at this time. 1/

2. The controlled scientific studies that have been conducted confirm that laetrile is ineffective as a cancer drug.

Laetrile's lack of efficacy as a cancer remedy has been confirmed in scientifically controlled preclinical tests conducted by a number of leading research centers and institutions at great public and private expense. 2/ For example, between 1957 and 1975 the Cancer Institute conducted

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1/ As is addressed in detail at 73-81 infra, the term "laetrile" actually applies to a series of drug formulations with varying labeling claims. Under the provisions of the Act, each of these drug variations and each substantive labeling change gives rise to a separate "new drug" for purposes of the Act. United States v. Articles of Drug Labelled "Quick-O-Ves", 274 F. Supp. 443 (D. Md. 1967). It is evident from the testimony of record, however, that the qualified experts universally condemn all known variations of laetrile.

2/ See e.g., AF-03 (Vincent T. DeVita, Jr., M.D.); AF-33 (Jack R. Cooper, M.D.); AF-37 (David M. Greenberg, M.D.).
five separate tests of laetrile. In each of these tests the compound failed to demonstrate a reproducible anti-tumor effect. The results of these tests were summarized at the Kansas City hearings by Dr. Bayard Morrison, Associate Director of the Cancer Institute:

I'd like to define just a little bit more what has gone on in terms of the preclinical testing of laetrile. Since 1957 up to the present time, the Cancer Institute has sponsored-other organizations have conducted-tests of laetrile at various dosage levels in a variety of animal tumor systems, probably exceeding 15 or more, probably closer to 20.

This indeed really is about the most extensive that NCI and other laboratories in the aggregate have tested of essentially a nonactive substance. For in all of these tests which include tumors ranging from carcinomas, sarcomas, lymphomas, any kind of tumor which parallels to a a large degree the human type of tumor. The results have been essentially negative. There have been occasional, marginal evidences of activity which have not been reproducible.

So, in balance, laetrile has failed the test of demonstrating activity in the preclinical animal tumor systems that we know now predict for activity in human cancer.

And I should add that the 30 or 40 drugs that are now regularly available and known to have effect in certain kinds of human cancer all these drugs have demonstrated activity, significant activity, in one or more of these animal tumor systems. 1/

During the period 1973-1977, the Sloan-Kettering Institute for Cancer Research of the Memorial Sloan-Kettering Cancer

1/ Tr. 146A-47; to the same effect, see AF-25 (Chester Stock, Ph.D.); AF-37 (David M. Greenberg, M.D.); AF-15 (W. Sherwood Lawrence, M.D.); AF-16 (Carl M. Leventhal); AF-17 (Daniel S. Martin, M.D.).
Center carried out the most extensive animal tests ever conducted on laetrile. 1/ The first Sloan-Kettering test was conducted by Dr. Kanematsu Sugiura and indicated that laetrile had an inhibitory effect on the development of lung metastases in a breeding colony of laboratory mice. 2/ However, subsequent efforts at Sloan-Kettering to reproduce the results of Dr. Sugiura's first test were unsuccessful. 3/

The Sugiura tests were rerun at New York's Catholic Medical Center by a two-man team consisting of Dr. Sugiura and Dr. Daniel S. Martin, who maintained the special breeding colony of mice used by Dr. Sugiura in his first experiment. The conditions of the experiment were identical with the conditions of Dr. Sugiura's first test, with the exception of two changes introduced to decrease the possibility of subjectivity in the results:

1/ See generally AF-25 (Chester Stock, Ph.D.).
2/ The raw data from Dr. Sugiura's first test was obtained by the Committee for Freedom of Choice in Cancer Therapy and has been cited as authority for establishing the effectiveness of laetrile. See submission of Dean Burke. However, as was pointed out in the affidavit of Dr. Jukes AF-42, this initial test, the results of which could not be reproduced, fails to qualify as the type of scientific evidence of efficacy required by cancer experts. Consequently, it fails to meet the requirements of Section 505 of the Act.
3/ In what may well be the most preposterous allegation of laetrile proponents, Sloan-Kettering's refusal to recognize Dr. Sugiura's initial laetrile test as scientifically valid has been characterized as a cover up which is part of a larger conspiracy to prevent laetrile's value from being known. See Dean Burk's submission, and Tr. 312, 358, 370-71.
(1) In the original test, Dr. Sugiura knew which animals were receiving laetrile and which were not. The second test with Dr. Martin was done "blind" -- that is, neither Dr. Sugiura nor Dr. Martin knew which animals were receiving laetrile and which were receiving a placebo.

(2) In determining the presence of cancerous tissue, personal observation of the researcher, and histologic evaluation by the pathologist, both of which were used in the first test and both of which introduce subjective elements, were supplemented by bioassay. This consists of transplanting a whole lung of an experimental mouse to a fresh host. In the recipient animal healthy transplanted tissue disappears but malignant cells proliferate. The animal itself therefore determines whether or not cancer cells are present and human impressions are eliminated. 1/

It proved impossible in the subsequent tests to reproduce Dr. Sugiura's initial results. 2/

Four additional animal studies were undertaken by Southern Research Institute under NCI auspices. Laetrile

1/ Dr. Martin indicates that the animal tests of laetrile have been done both in transplanted and spontaneous mouse tumors and the results of both types were the same, -- no efficacy. Tr. 427-28.
2/ See AF-25 and Tr. 427-29 (Daniel S. Martin, M.D.).
was tested against Ridgeway Osteogenic sarcoma, Lewis Lung carcinoma, and leukemia P 388. Of these types of cancer, Ridgeway osteogenic sarcoma has been shown to be particularly sensitive to anti-tumor chemical agents. But neither it nor any of the other forms of cancer were in any way affected by the laetrile.

Similar experiments were documented by Arthur D. Little, with leukemia L1210 and P 388, melanoma B16 and Walker 256 carcinosarcoma. No results were achieved, either through the use of amygdalin alone or in combination with beta-glucosidase. 1/

Although not included in the record of this proceeding, in the week of June 13, 1977, Memorial Sloan-Kettering reported the results of a four-year laetrile study on laboratory animals which shows no beneficial results from laetrile as a curative or preventative agent against cancer. This information is not a part of the hearing record but clearly should be obtained and considered by the Commissioner in arriving at his decision in this rulemaking proceeding. This new information provides additional confirmation to the expressed consensus of expert medical opinion that laetrile is ineffective as a cancer drug.

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1/ See submission by Dean Burke, Exh. E and F attached thereto, and AF-15 (Carl Leventhal, M.D.), Exh. 3C and 3D.
3. Testimonial and anecdotal evidence supporting the efficacy of laetrile fails to meet the statutory requirements of Section 201(p) of the Act.

Standing against the testimony of recognized experts in the cancer field to the effect that laetrile is neither safe nor effective for use as a cancer drug and against the known results of controlled preclinical tests which confirm the drug's total lack of efficacy, are testimonial submissions from users of laetrile as well as anecdotal reports, and "case histories" 1/ which purport to prove that laetrile is safe and effective.

However sincere and well intended such testimonial and anecdotal submissions are, the simple fact remains that they do not meet the Congressionally dictated standards of "substantial evidence" set forth in Section 505(d) of the Act which must be met if a showing of "general recognition" of safety and efficacy is to be made.

1/ In medical terminology, testimonials are statements made by an individual to the effect that they used a product or treatment personally and, in their opinion, it helped them. Anecdotal reports are descriptions of single cases by an individual other than the person who was treated but which are lacking in scientific methodology, full data, full medical records, or controls. Neither type of evidence is accepted by the scientific or research community as evidence that any substance or treatment is medically effective. Long experience has shown that this type of "evidence" can be, and has been, collected in large amounts to support the alleged "effectiveness" of innumerable worthless and fraudulent cures and remedies.
According to Section 505(d)

"substantial evidence" means evidence consisting of adequate and well-controlled investigations, including clinical investigations, by experts qualified by scientific training and experience to evaluate the effectiveness of the drug involved.

The FDA has interpreted this language as precluding consideration of anecdotal submissions and has been upheld on this point by the Supreme Court. In Weinberger v. Hynson, Westcott & Dunning, supra, the Court noted with respect to the FDA regulations regarding the nature of evidence required to establish efficacy that

[The FDA's] strict and demanding standards, barring anecdotal evidence indicating that doctors "believe" in the efficacy of a drug, are amply justified by the legislative history. The hearings underlying the 1962 Act show a marked concern that impressions or beliefs of physicians, no matter how fervently held, are treacherous. (Emphasis added.)

The Court also noted that the Act requires that the FDA disapprove an NDA when there is a lack of "substantial evidence" that a drug is effective and, further, that evidence of efficacy may be accepted only if it consists of adequate and well-controlled investigations, including clinical investigations, by experts qualified by scientific training and experience to evaluate the effectiveness of a

1/ See 21 CFR § 130.12 regarding the determination of whether there is substantial evidence to support claims of effectiveness for new drugs.

2/ 412 U.S. at 619. The Congressional hearings referred to by the Court were: Hearings on S.1552 before the Subcommittee on Antitrust and Monopoly of the Senate Committee on the Judiciary, 87th Cong., 1st Sess., pt. 1, pp. 195, 282, 411-12.
new drug. 1/ As for the status of a drug as a "new drug", the Court concluded:

In the absence of any evidence of well-controlled investigation supporting the efficacy of [the drug], a fortiori [the drug] would be a "new drug" subject to the provisions of the Act. 2/

The record established in this proceeding is such that even absent the sworn testimony of qualified experts and the results of well-controlled tests to the effect that laetrile is in fact ineffective as a cancer cure, the total absence from the record of any adequate and well-controlled investigations supporting the efficacy of laetrile is such that, as a matter of law, laetrile is a "new drug" for purposes of the Food Drug and Cosmetic Act of 1938, as amended.

Although the statutory requirements of the Act make reference to the testimonial and anecdotal submissions of laetrile's proponents unnecessary, nevertheless an examination of this "evidence" is worthwhile in that it serves to underscores the wisdom of Congress in defining "substantial evidence" as it did.

The credibility problems posed by such evidence is well demonstrated by the testimony of Mr. Glen L. Rurterford. 3/ Mr. Rutherford claims that he was diagnosed as having cancer, but refused conventional treatment in the United States and instead went to Mexico for treatment with laetrile. According to Mr. Rutherford, his cancer is now cured and he attributes

1/ 412 U.S. at 630.
2/ Id. at 629-30.
3/ Tr. 306. Mr. Rutherford is a party to the judicial proceeding in Oklahoma which led to this administrative rulemaking proceeding.
this to laetrile. While there does not seem to be much doubt that Mr. Rutherford in fact had cancer and refused conventional treatment in the United States, his cure cannot be attributed to laetrile. In addition to laetrile, while in Mexico Mr. Rutherford had his cancerous polyp cauterized. Cauterization is a conventional form of cancer treatment and probably caused the satisfactory results experienced by Mr. Rutherford. 1/

Case histories of other patients treated with laetrile are equally inconclusive. In many cases there is no documented evidence that the patients had cancer in the first place. In other cases, where cancer was diagnosed by biopsy and there was evidence of remission, conventional treatment was used in addition to laetrile. 2/ Under such circumstances it is impossible to attribute curative effect to laetrile.

1/ Tr. 431-432 (Daniel Martin, M.D.).
2/ See e.g., AF-15 (W. Sherwood Lawrence, M.D.) AF-16 (Carl M. Leventhal, M.D.); AF-30 (Robert S. K. Young, M.D.) AF-47 (Bryant L. Jones, M.D.).
Frequent reference has been made by laetrile proponents to the success experienced by a Mexican doctor named Contreras in his Mexican laetrile clinic. Dr. Contreras was invited by the FDA to provide clinical evidence of laetrile's effectiveness.

In October 1971, Dr. Contreras responded by forwarding twelve case histories which, in his opinion, possessed outstanding value for documenting the effectiveness of laetrile therapy. Of the patients these cases histories involved, one could not be traced and two refused to cooperate in the study. Of the remaining nine, six are dead of cancer, one has progressive cancer, one died of another cause following cancer surgery and the ninth, still alive, had radiation and established chemotherapy treatment as well as laetrile. 1/

While some of the claims made by laetrile proponents are inconclusive, others are simply false. For example, the proponents of laetrile seek to bolster their case with the claim that Israel has recognized laetrile as safe and effective and is conducting clinical trials with it. 2/

Appended to this memorandum is a copy of a message received from Israel which indicates that laetrile trials are not being conducted in Israel. 3/

1/ AF-16 (Carl M. Leventhal, M.D.); Exh. 1 and 2.  
2/ See Tr. 43-47, 100-01, 238, 355-56.  
3/ Appendix D.
It also is significant to note that in Mexico, the locus of Dr. Contreras' clinic and possibly the country with the most comprehensive clinical experience with laetrile, the Mexican Department of Health banned laetrile in October of 1976. The effect of this action will be to close down the manufacture of laetrile by Cytopharma and Kem Laboratories. The manufacturers have made an administrative appeal of the Department of Health's ruling and at this writing a decision has not been forthcoming. However, on May 3, 1977, Dr. Francisco Durazo Quiroz, Director of the Food, Beverages and Drug Division, Secretariat of Health and Welfare, reinforced the likelihood that this ruling will be upheld. 1/ According to a telegram from the U.S. Embassy in Mexico to the U.S. State Department (appended hereto as Appendix E), Dr. Quiroz, was quoted in a newspaper article as stating that "permission to manufacture (after temporary 90-120 day permits for experimentation) has not been granted because there is no evidence to sustain claims that [laetrile] cures cancer." He further stated that "sale of these products as 'cancer cures' in Mexico - U.S. Border Towns is illegal and health department agencies in states where sales are being made had been alerted to prosecute manufacturers, distributors, and other outlets." It is indeed ironic that while Mexico seeks

1/ See TS-38 and Appendix E to this memorandum.
to remove laetrile from their markets because their experience
with it (which ostensibly includes extensive clinical trials
through Dr. Contreras' facilities) shows it to be ineffective
as a cancer drug, proponents in the United States seek through
both political pressure and attacks on the Federal regulatory
scheme to permit the unfettered and widespread manufacture,
distribution and sale of laetrile in this country.

4. The developers, manufacturers and proponents
of laetrile have been accorded every opportunity
to establish the safety and efficacy of the
drug.

This rulemaking proceeding is not the first time that
proponents of laetrile have had an opportunity to demonstrate
the safety and efficacy of their products. Indeed, the
purveyors of laetrile and its predecessor formulations have
championed the drug as a palliative, useful in pain relief,
a control, a preventative, a cure, or a treatment for cancer
for over twenty-five years, during which time they have been
afforded ample opportunity to establish laetrile's value.

The procedures set out in Section 505 of the Act for
obtaining an approved new drug application have always been
available to laetrile. In fact, an application for an NDA
was initially filed with the FDA by the John Beard Memorial
Foundation on October 3, 1962. However, this application
failed to provide data sufficient to demonstrate either the
safety or efficacy of laetrile and was declared incomplete
by the FDA on February 25, 1963. 1/ There is no indication that the John Beard Memorial Foundation came forth at that time with supplemental data adequate to cure the deficiencies in its application.

Again, in 1970 another attempt was made to obtain FDA sanction for the sale of laetrile. This application was made by the McNaughton Foundation and sought an Investigational New Drug Exemption (IND) pursuant to Section 505(i) of the Act. The purpose of an IND is to allow a drug that has demonstrated its safety and efficacy in pre-clinical tests (i.e. animal tests), to proceed to "investigational" testing on human subjects. 2/

The FDA initially awarded the IND (No. 6734), but shortly thereafter, in the course of a routine review of the IND application, found serious problems with the applicant's clinical data. The FDA immediately requested that the applicant respond to two questions on manufacturing controls, seven questions on pre-clinical tests and four medical questions on data mentioned in the application but not submitted. When the missing data was not provided by McNaughton

1/ The Beard Foundation's 1962 application and the circumstances surrounding its rejection are recounted in a letter from the FDA files which is in the record as Attachment 12 to AF-15 (Affidavit of W. Sherwood Lawrence, M.D.).

2/ An IND does not allow the indiscriminate marketing of a drug. Drugs on the market pursuant to an approved IND are subject to stringent regulatory controls. Certain minimum standards are set forth in the statute itself, which is set forth in Appendix B hereto.
within the usual ten-day period allowed by the FDA for the elimination of deficiencies, the IND was terminated. 1/

It was not until some four months later that the McNaughton Foundation responded to the FDA data request. 2/

The FDA's action in terminating the laetrile IND generated some Congressional interest. In response to this interest, the FDA appointed a special committee of non-government experts to review the entire laetrile data file. 3/ The committee found that independent laboratory assays provided no in vitro or in vivo evidence in animal models to warrant trial of the substance in humans and thereby affirmed the propriety of the FDA's action.

Critics of the FDA's laetrile decision, specifically, Dean Burk, who at that time was on the National Cancer Institute staff, and Andrew L. McNaughton, who was a party to the application, had the opportunity to participate in the

1/ To a layperson, the FDA's action in terminating the laetrile IND when supplemental data was not immediately forthcoming may seem precipitous. However, the Act is clear with respect to the FDA's obligation to protect the consuming public from unsafe and ineffective drugs. That the FDA takes its statutory responsibilities seriously is something all should be thankful for. E.g., were it not for the persistence of the FDA in insisting that a new drug called thalidomide affirmatively demonstrate that it was safe for use in pregnant women, the United States might have been afflicted with a wave of birth deformities comparable to that experienced several years ago in Europe, where drug premarketing requirements apparently are more lenient or less stringently enforced.

2/ See AF-16 (Carl M. Leventhal, M.D.), Exh. 2 and 3.

3/ Id.
committee's assessment but failed to do so. Rather than attempt to remedy the deficiencies in the application pointed out by the special committee, the laetrile proponents instead chose to withdraw the application. 1/

The history of laetrile with the FDA clearly demonstrates that its proponents have had opportunities to demonstrate the safety and effectiveness of the drug. Rather than using these opportunities to come forward with proof of safety and efficacy, as is uniformly required of all new drugs, laetrile's proponents have elected instead to withdraw the drug from expert scrutiny.

C. Laetrile Is Neither A Food Nor A Vitamin.

Numerous proponents of laetrile have urged that the drug is in fact a vitamin. 2/ Inasmuch as the status of laetrile as a food or a vitamin is irrelevant to its status as a "drug" for purposes of the Food Drug and Cosmetic Act, 3/ technically these claims need not be addressed here. The "vitamin issue" was addressed at some length on the record, however, and therefore will be commented on here. Not surprisingly, once again the evidence reveals that a claim made for laetrile (in this case that it has nutritive value)

1/ See e.g., Tr. 51, 55, 81, 234, 405-08, 416, 485. It is interesting to note, however, that before laetrile was promoted, no one had suggested that its alleged principal ingredient -- amygdalin -- was a vitamin. Indeed, the name Vitamin B-17 was first applied to laetrile following the rejection of an application to the Food and Drug Administration for the use of laetrile as a drug. Tr. 215-16 (Thomas H. Jukes, Ph.D.).

2/ Id.

3/ As discussed supra at 31-32, the intended use of a substance determines whether it is a drug for purposes of the Act.
withers in the spotlight of expert scrutiny.

The term "vitamin" applies to a certain group of substances with the following characteristics:

1. They are externally-supplied organic substances that are required in small amounts for the health and well-being of the organism;

2. They function to promote a physiological process or processes vital to the continued existence of the organism;

3. Their absence causes certain clearly defined diseases to afflict the organism. These diseases arise only because of the absence of the vitamin and are entirely cured by supplying the vitamin. 1/

Dr. Richardson, a proponent of laetrile, made the claim at the Kansas City hearings that laetrile, or Vitamin B-17, is a vitamin because it contains the following characteristics:

1/ See e.g., AF-02 (David H. Greenberg, Ph.D.); AF-16 (Carl M. Leventhal, M.D.); AF-37 (David M. Greenberg, Ph.D.). Tr. at 216-17 (Thomas H. Jukes, Ph.D.).
One, vitamin B-17 is organic and water soluble, (2) Vitamin B-17 as a nitiloside (sic) is present ubiquitously in seeds of fruits and grains and grain-fed animals, (3) Vitamin B-17 will increase appetite, cause weight gain, reduce pain and produce a feeling of well-being. (4) Absence of vitamin B-17 may produce headaches, anorexia, bizarre muscular pains, skin changes, anemia, sense of impending doom, loss of weight, bowel changes, nitritenitrate imbalance, high blood pressure, sickle cell anemia and finally, tumefaction. (5) The degradation products of vitamin B-17 are excreted as thiocyante and benzoic acid. Vitamin B-17 does not produce energy by itself. All forms of vitamin B-17 are of low molecular weight or small molecules, and (7) Vitamin B-17 is water soluble.1

Significantly, Dr. Richardson's claims for laetrile are unsupported by any studies, tests or scientific recognition, criteria that must be met if it is to be established that a substance has properties as a vitamin.

The criteria employed to establish the existence of a vitamin are well stated in the record by Dr. Jukes:

To establish a vitamin as actually existing, several steps are necessary. The first step is publication in a recognized scientific journal of the experimental work, including a complete and repeatable description of the procedures used in the research.

This is followed by confirmation by other scientists, or lack of confirmation. Such journals require that manuscripts be reviewed by other scientists before publication.

The burden of proof in establishing the existence of a vitamin is upon the scientist who claims that it exists. Sometimes the work cannot be repeated even after a number of tries. In such cases, the existence of the vitamin is not recognized and claims for its are not accepted.

This has occurred in the case of some of the B vitamins, including the so-called Vitamins B-13 and B-14. If the vitamin has crossed the preceding hurdles, there will be an extensive research, including analysis of foods for its presence. Also, isolation of the vitamin in pure form, determination of its exact chemical, molecular structure and demonstration of the effectiveness as the pure, usually crystalline, preparation of the vitamin.

1 Tr. 465-466 (testimony of John A. Richardson, M.D.)
Each time that a new vitamin has reached this stage, many scientists have moved into the field of research and publication to participate in the new discovery and to get a piece of the action.

This has not happened with laetrile because laetrile is not a vitamin.

Finally, chemical synthesis of the vitamin is carried out by organic chemists and the results are not accepted until it is shown that by exhaustive chemical and biological tests that the synthetic and natural vitamins are identical.

Such synthesis and acceptance has—synthesis and testing has been carried out for all the accepted vitamins. 1/

Not only has laetrile failed to affirmatively demonstrate that it is a vitamin, the consensus of qualified opinion, as expressed on the record, conclusively demonstrates that laetrile in fact is not a vitamin or a nutrient. 2/ For example, according to the testimony of Dr. Carl Leventhal, "Laetrile is not a vitamin because its absence from the diet (i.e. the absence of a cyanogenetic glycoside) does not produce a specific deficiency disease in vertebrate animals such as man." 3/

Further, no evidence has ever been found that laetrile is an essential nutrient. Laboratory animals have been kept alive and healthy for generations without having any of it in their diets. 4/ "Experiments with laboratory animals on purified diets show no indication whatever of a nutritional

1/ Tr. at 218-19 (Testimony of Thomas H. Jukes, Ph.D., D.Sc.).
2/ See e.g., study referred to at TS-19, and AF-02, Exh. 2 (David M. Greenberg, Ph.D.); AF-03 at 4 (Vincent Devita, M.D.); AF-10 at 2 (John Cudmore, M.D.); AF-16 (Carl M. Leventhal, M.D.); AF-17 at 6 (Daniel S. Martin, M.D.); AF-27 at 4-9 (Robert J. Temple, M.D.); AF-32 at 3 (R. L. Hingle, R.Ph.); AF-33 at 5 (Jack R. Cooper, M.D.); AF-37 at 16 (David Greenberg Ph.D.); AF-42 at 3-7, 10-11, 13, 14, 20, 24, 31 (Thomas Jukes, M.D.); AF-50 at 7 (Carl Leventhal, M.D.) and TS-190.
3/ AF-16 at 3 affidavit of Carl M. Leventhal, M.D.).
4/ Tr. 221 (Thomas H. Jukes, Ph.D.); Tr. 355 (James K. Luce, M.D.); AF-02 and AF-37 (David M. Greenberg, Ph.D.); AF-16 at 3 (Carl M. Leventhal, M.D.).
need for amygdalin, laetrile. These substances have none of the characteristics of vitamins." 1/ Nor has laetrile ever been shown to promote any physiological process vital to the existence of any organism. 2/

No specific disease state has been linked to the lack of laetrile in any animal, including man. 3/ With specific regard to cancer, there is no evidence that it results from lack of laetrile, or is cured by supplying laetrile. 4/ If laetrile were a vitamin, and if, as asserted, cancer is the result of a laetrile deficiency, laetrile should prevent all cancer and cure all cancer that has not spread far enough to damage vital organs. Animal studies and an evaluation of human case reports prove that laetrile does not achieve this result. 5/

Moreover, contrary to the claims of its proponents in this proceeding, 6/ laetrile is neither a food nor a nutrient. Its primary ingredient -- amygdalin -- belongs to the class of "toxicants occurring naturally in foods" and is not used as

1/ Tr. 220, Statement of Dr. Jukes.
2/ Tr. 335. See, e.g., AF-02 (David M. Greenberg, Ph.D.); AF-03 at 4 (Vincent DeVita, M.D.); AF-10 at 2 (John T. P. Cudmore, M.D.); AF-16 (Carl M. Leventhal, M.D.); AF-17 at 6 (Daniel S. Martin, M.D.); AF-27 at 4-9 (Robert L. Temple, M.D.); AF-32 at 3 (R. L. Hingle, Rp.H.); AF-33 at 5 (Jack R. Cooper, M.D.); AF-37 at 16 (David M. Greenberg, Ph.D.); AF-42 at 3-7, 10-11, 13-14, 20, 24, 31 (Thomas H. Jukes, Ph.D.); AF-50 at 7 (Carl M. Leventhal, M.D.); TS-19 (University of Wisconsin).
3/ Id.
4/ Id.
5/ AF-27 at 9 (Robert J. Temple, M.D.).
6/ See, e.g., Tr. 81, 234, 303, 420.
a food. 1/ In fact, one of its proponents expressly warned that preparations containing amygdalin should not be used as foods. 2/

A recent statement of the National Nutrition Consortium summarized the consensus of expert opinion when it said, "The Committee on Nomenclature of the American Institute of Nutrition finds 'no scientific evidence for the existence of a nutrient identified as B-17.' This terminology is neither recognized nor used by qualified nutritionists. The Committee finds no scientific evidence that laetrile has nutrient properties or is in any way of nutritional value for either animals or humans."3/ Member societies of the National Nutrition Consortium include the American Dietetic Association, the American Institute of Nutrition, the American Society for Clinical Nutrition, the Institute of Food Technologists, the Society for Nutrition Education, the American Academy of Pediatrics, and the Food and Nutrition Board of the National Academy of Sciences -- National Research Council.

The resounding rejection by qualified experts of the claims that laetrile has value as a vitamin or a nutrient serves to underscore the total worthlessness of the substance and the magnitude of the fraud perpetrated on the consuming public by those who knowingly or otherwise advocate reliance on it as a cancer drug.

1/ AF-42 at 12, 13, 31 (Thomas Jukes, Ph.D.); TS-19; AF-15 at 16. (Sherwood Laurence, M.D.).
2/ AF-42 at 22 (Thomas Jukes, Ph.D.).
3/ Tr. 216-217 (Thomas Jukes, Ph.D.).
II. LAETRILE IS NOT ENTITLED TO EXEMPTION FROM THE "NEW DRUG" REQUIREMENTS OF THE FOOD AND DRUG ACT BY VIRTUE OF THE GRANDFATHER PROVISIONS OF THE 1962 AMENDMENTS.

A. General Criteria.

Entitlement to the grandfather exemption of the 1962 amendments, i.e. Section 107(c)(4) of the Food and Drug Act, 1/ is limited to drugs which:

1. feature today the identical chemical composition, recommended dosages, and claims made in labeling as existed on October 9, 1962, and

2. were used or sold commercially in the United States on October 9, 1962, and

3. were generally recognized by the experts as safe; and

4. were not covered by an effective new drug application. 2/

The failure of a drug to meet just one of these criteria extinguishes altogether its entitlement to grandfather status. The record in this proceeding clearly demonstrates that laetrile fails to meet each and every one of the four criteria.

1/ Pub. L. 87-781, found as a note to 21 U.S.C. § 321. Section 107(c)(4) is quoted in full in Appendix B hereto.

2/ United States v. Allan Drug Corp., 357 F.2d 713, 718-19 (10th Cir. 1966), cert. denied, 385 U.S. 899; United States v. 1,048,000 Capsules, More or Less, 347 F. Supp. 768 (S.D. Tex. 1972); see also Rutherford v. United States, 542 F.2d 1137, 1141 (10th Cir. 1976). The Commissioner concedes issue No. 4 in the Notice of Rulemaking and it need not be addressed here.
As a further prefatory note, it must be observed that the grandfather exemption of the 1962 amendments is to be strictly construed against the one who invokes it. 1/ In United States v. Allan Drug Corp., 2/ the Tenth Circuit clearly recognized the soundness of placing on those seeking a grandfather exemption the burden of proving its applicability. Inexplicably, in Rutherford the Tenth Circuit has inverted the respective responsibilities of the proponents of a drug and the FDA in this regard and has directed that the FDA must bear the burden of proving by substantial evidence that laetrile is not grandfathered. 3/ Thus, the FDA is charged with the extremely difficult task of attempting to ascertain and present "substantial evidence" pertaining to laetrile's pre-1962 status, when the agency's decision that laetrile is a new drug might otherwise rest substantially on the fact that such information simply does not exist.

However improper or unreasonable the evidentiary standard imposed by the Court on the FDA in this regard, the record now compiled on laetrile does affirmatively demonstrate, and by substantial evidence, that laetrile is not entitled to the grandfather exemption of the 1962 amendments.

2/ 357 F.2d 713, 718 (10th Cir. 1966), cert. denied, 385 U.S. 899.
3/ 542 F.2d at 1143. See discussion of the meeting at 41-44 supra.
B. **Laetrile Is Not Entitled To Grandfather Status**
Because Its Chemical Composition And Labeling
As To Use Are Not The Same Today As They Were
On October 9, 1962.

The record established in this proceeding clearly demonstrates that laetrile is not a compound which has enjoyed any continuity of composition or recommended conditions of use. Rather, it is a product which traces its genesis to the work of Dr. E. T. Krebs, Sr. with amygdalin in the 1920's, 1/ but its evolution since that time has changed its chemical composition materially. Dr. Krebs himself admits that the name was not coined until 1949, and that the name has been used since that time for the final form of the amygdalin produced by Krebs, regardless of its actual chemical composition. 2/

The degree of change in the composition of Krebs' amygdalin, or laetrile, over the years and the precise dates on which changes were effected, are difficult to pinpoint due to the general lack of knowledge and information on the product. However, Dr. Krebs admits that between 1936 and 1960 the "purity" of the amygdalin rose from 60% in 1936 to 99.8% in 1960. Correspondence from Spicer-Gerhart Co., a manufacturer of laetrile, also addresses the evolving nature of the drug's composition. In a 1953 letter to Dr. Jack R. Cooper, the Company wrote that the preparation was evolving in the sense that "the volume of HCN released from a given quantity of laetrile in the presence of a fixed amount of beta-glucuronidase is now approximately three times greater than it was six months ago." 3/

1/ AF-16 (Affidavit of Carl M. Leventhal, M.D.) Exh. 6.
2/ Id.
3/ AF-33 (Affidavit of Jack R. Cooper, M.D.) Exh. 3.
Just as the chemical composition of laetrile has been in a state of evolution over the years, so too has its labeling with respect to the dosage to be administered and the purpose of the drug. For example, the shipment of laetrile to Dr. Cooper in 1952, which clearly was for investigational purposes, 1/ was accompanied by a letter which addressed dosage as follows:

In these early days it is difficult to be too specific about a good many things, but the consensus of opinion at the moment is that the following dosage schedule is best:

- For the rapid or high-grade malignancies 50 mg. every other day;
- For the slow or low-grade malignancies 50 to 100 mg. every five or seven days;
- For the usual or intermediate case 50 mg. every three to five days. 2/

[Emphasis added.]

In fact, in the early 1950's uncertainty about the use of laetrile was such that in some respects Spicer-Gerhart refrained from advising on the method of use:

The injection usually is given intramuscularly although when it is possible to give it directly into the malignant lesion, this may be done with advantage. However, perhaps one had better leave directions of that sort for a little later, after you have had some personal experience with the substance. 3/

On one point, Spicer-Gerhart was quite firm: laetrile was not to be taken orally. According to a mimeograph prepared by the Company for guidance to doctors on the use of laetrile, the substance was described as "extremely toxic by [oral] route of administration" 4/

1/ Id., Exh. 2.
2/ Id.
3/ Id., Exh. 4 (emphasis added).
4/ Id., Exh. 5.
In 1952 Spicer-Gerhart described the theory behind laetrile as follows:

In order that there shall be no misunderstanding, may I remind you that, according to the theory outlined, Laetrile has a destructive effect only. Certainly, this destructive effect is very definite and sometimes very quick, but it does have to be borne in mind that Laetrile makes no contribution whatever toward the remainder of the patient's problem—reconstruction and repair. From the very nature of the action of Laetrile, it will be obvious that under certain circumstances, hemorrhage might take place and mechanical problems involving the disposal of necrotic breakdown products might arise. 1/

Later, in a pre-1963 pamphlet by Dr. Krebs, Sr., the following statements were made with respect to laetrile:

Laetrile does not palliate, it acts chemically to kill the cancer cell selectively without injury to the normal tissues of the body.

The usual daily dose of Laetrile is 10 mg. of the glucoside amygdalin for every pound of the patient's weight. Some patients may need 15 or even 20 mgs. but rarely more except in cases of pancreatitis enzymes insufficiency due to inhibition...

Laetrile is dissolved in sterile distilled water using 4 to 5 cc for every 1000 mgs. of Laetrile.

The injections should be given intravenously every day until...

They are not only important food for nutrition they also act as a vitamin to supply the body with the CN group for the biosynthesis of another vitamin cyanocobalamine. 2/

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1/ Id., Exh. 2.
2/ AF-15 (Affidavit of W. Sherwood Lawrence), Attach. 8.
The record abounds with other examples of labeling changes with respect to laetrile. For instance, the affidavit and supporting exhibits submitted by Robert S.K. Young, Ph.D., compared the labeling and other information contained in the New Drug Application for laetrile (NDA 14-032) received by the FDA on October 3, 1962 with labeling for the drug obtained by the FDA during an establishment inspection of Krebs Laboratories on April 23, 1965. Dr. Young identified some of the significant labeling differences as follows:

(a) The formulation of the drug had been changed. In 1962, the formulation contained N, N diisopropylammonium iodide and saccharides in addition to amygdalin and these materials were to be reconstituted with an isotonic solution. In 1965, the formulation contained only amygdalin and this material was to be reconstituted with water, which is not isotonic.

(b) The class of patients for whom the drug is recommended had been changed. In 1962, the label characterizes the drug as a palliative agent for use in "cancers beyond aid by standard agents," and warns that "It is not to be employed to the exclusion of surgery, radiation or similar standard modalities so long as they are indicated." The 1965 labeling states that "Laetrile does not palliate, it acts chemically to kill the cancer cell selectively without injury to the normal tissues of the body." It goes on to warn that "The physician who is using laetrile to palliate his patients is not doing justice to his patient."

(c) The interaction of Laetrile with other forms of cancer treatment had been changed. In 1962, the label states Laetrile "has no known therapeutic incompatibilities." It goes on to warn that "the general enhancement of the clinical condition of the patient is not to be considered as justification for the exclusion of standard modalities so long as they are applicable." In the 1965 material, the directions state that "The less drugs and medicines given, during the Laetrile treatment, the better. What should be especially avoided is... other cancer therapies, strong drugs...etc."
(d) The recommended route of administration had changed. In the 1962 labeling, "intravenous administration is preferred." The 1965 labeling advises that "Whenever it's possible to administer Laetrile by injection into the artery supplying the involved area this administration should be used." Specifically, injection into the external carotid or its branches, abdominal aorta, or internal iliac arteries is recommended. The 1965 labeling also recommends injection into the vault of the vagina and scrotal sac, and rectal enemas. I am generally familiar with the literature and reports relating to Laetrile and am aware that since 1965, there has been commercial distribution of dosage forms of Laetrile including tablets containing Amygdalin, capsules of ground defatted apricot kernels, and a milkshake mix containing Amygdalin all intended for oral use.

(e) The claimed mechanism of action of the drug had changed. In the 1962 material, the "Beardian thesis" was discussed as a theory. The 1962 labeling made no claim that Laetrile is a vitamin or provitamin, or that cancer is a deficiency disease. The 1965 labeling states that "Cancer is a deficiency disease" and there is a presentation of what role amygdalin plays in the therapy of cancer in light of cancer as deficiency disease.

11. All of the above changes are medically important or have medically important implications that must be reviewed scientifically. In the same order as I have reviewed them in 10, they are:

   a. Formulation changes may reflect changes in the drug substance, and always reflect changes in the material to be administered.

       Whenever the material to be administered is changed, it is important that the new material be essentially identical to the old material in strength, quality and purity.

   b. The 1962 labeling restricts the use of Laetrile to those patients who all have had conventional therapy, and prescribes use for the purpose of palliation of their disease. The 1965 labeling states that this drug should be used to mitigate the effects of the disease and implies that the drug is of curative value. Since Laetrile has no demonstrable effect on cancer, to use Laetrile in lieu of conventional therapy is to condemn to certain death those patients with curable forms of cancer, and to prolong the pain and suffering of those patients with treatable forms of cancer.
c. The 1962 labeling warns that the conventional therapy not be withheld during Laetrile administration. The 1965 labeling suggests a harmful interaction between Laetrile and conventional therapy. Again, since Laetrile has no demonstrable effect on cancer, to use Laetrile in lieu of conventional therapy is to condemn to certain death those patients with curable forms of cancer and to prolong the pain and suffering of those patients with treatable forms of cancer.

d. Changes in the route of administration of a drug must always be scientifically validated. A drug may not be effective or may be more toxic when given by different routes of administration. The recommendation in 1965 that the drug be given by intra-arterial injection is particularly hazardous. These high pressure blood vessels are difficult to enter successfully and are prone to continued bleeding after entry with a needle.

e. The claimed mechanism of action strongly suggest that Laetrile has a rational basis as a cancer therapy. Since it has no demonstrable value as a cancer therapy, to suggest that it has may influence some to use it who might not otherwise use it. 1/

Dr. Young's conclusion regarding "the numerous changes which have occurred in the composition, labeling, routes of administration, dosage form, intended uses and identity" of laetrile between 1962 and 1965 2/ in and of itself precludes laetrile from entitlement to the grandfather exemption contained in Section 107(c)(4). 3/

Ernest Krebs, Jr. at the hearings in Missouri stated that the dosage recommended for amygdalin has grown from 50 milligrams in 1932 to 17,000 milligrams today. 4/ The book "World Without Cancer" discredits the 1953 California report of the analysis of patients treated with laetrile on the basis that the dosage

1/ AF-30 (Affidavit of Robert S. K. Young, Ph.D.) at 2.
2/ supra at 2.
4/ Tr. 238 (Testimony of Ernest Krebs, Jr.).
given them was too low, only one fifteenth of the dose used now. 1/

It is abundantly clear that both the composition of laetrile and the manufacturer's claims with respect to its use have changed dramatically over the years. Accordingly, laetrile does not meet the continuity-of-labeling requirements of the 1962 grandfather exemption and thus is not excused from the "new drug" requirement of the Food and Drug Act.

C. Laetrile Is Not Entitled To Grandfather Status

Because It Was Not Used Or Sold Commercially Within the United States Prior To October 9, 1962.

Although the record contains evidence of use by physicians and others of a substance called laetrile prior to October 10, 1962, this limited use fails to constitute commercial use or sale as required by the grandfather provisions of the 1962 amendments. The requirements of commercial use or sale within the United States set forth in qualification (A) of the 1962 grandfather clause 2/ means that the item must have been openly and readily available in the ordinary course of business as well as free of restrictions for investigational use. 3/ Laetrile fails to meet either of these criteria.

1/ Tr. 333.
First, laetrile certainly has not been openly and readily available in the ordinary course of business. The only evidence of record with respect to its marketing concerns limited and isolated manufacturing and distribution in the United States and some use outside of the United States. Use outside of the United States is not relevant to the grandfather exemptions in that the law specifically limits applicability to substances sold in the United States. The sales of laetrile that did take place within the United States were neither widespread nor unqualified.

According to the developer of laetrile, the use of the drug in the U.S. clearly was for investigational purposes only. In an affidavit executed by Dr. Krebs, Sr. in 1965, he claimed:

7. As early as 1926 and up through 1962, I first began to ship and have done so continuously thereafter the Sarcarcinase extract (cf.2), first the amygdalin (cf 3), then the purified amygdalin (cf 4), then the purified and lyophilized amygdalin (5), and then since 1949 (cf 6) the latter under the name Laetrile to persons in other States outside of the State of California and in many other countries. The above shipments were for investigational use only. 1/

In fact, the record demonstrates that the manufacturers of laetrile held it forth for investigational use only as late as 1970. In 1962, an application for an NDA was submitted to the FDA for its consideration and in 1970 an application for an IND

1/ AF-15 (Affidavit of W. Sherwood Lawrence, M.D.), Attach. 6, at 2 (emphasis added).
also was submitted. 1/ These actions are significant because it has been judicially recognized that the presentation of an IND or NDA to the FDA implies that on those dates the drug involved was a "new drug"; otherwise the NDA or IND would not be required. 2/

Thus, the proponents of laetrile by their own actions have characterized laetrile as "new" and "investigational," and hence not "commercial" within the meaning of the 1962 transitional provisions. Consequently, laetrile is not entitled to a grandfather exemption.

1/ See Id., AF-16; AF-30; and AF-47 (Affidavits of W. Sherwood Lawrence, M.D., Carl M. Leventhal, M.D., Robert S. K. Young, M.D., Bryant L. Jones).

2/ Durovic v. Richardson, 479 F.2d 247 (7th Cir. 1973), cert. denied, 414 U.S. 944.
D. Laetrile Is Not Entitled To Grandfather Status Under The 1962 Amendments Because It Never Has Been Generally Recognized As Safe For The Treatment Of Cancer.

Laetrile's entitlement to a grandfather exemption from the new drug requirements of the Food and Drug Act depend both on it being safe for its intended use, i.e. control and cure of cancer, on October 9, 1962, and on its having attained "general recognition" among the experts as being safe for its intended use by that date. Laetrile fails to meet either of these requirements.

Additionally, with respect to the "safety" requirement, it is necessary that laetrile be both non-toxic and effective in the treatment of cancer on October 9, 1962. The effectiveness requirement exists because cancer is a life-threatening disease. It is recognized that treatment of a life-threatening disease such as cancer with an ineffective drug is not sound medical practice because any delay in the institution of effective therapy, whether radiation, surgery or chemotherapy, allows the disease to progress unchecked until it is beyond control. 1/

Consequently, the FDA has properly considered the "effectiveness" of drugs as a factor relating to safety. 2/

In 1961, in testimony before the Senate, the Secretary of HEW explained the FDA's attitude as follows:

If the drug is offered for the treatment of progressive or life threatening diseases, such as cancer, or if the drug is seriously toxic or has alarming side effects, we now consider its effectiveness. 3/

1/ Durovic v. Richardson, 479 F.2d 247, 250 (7th Cir. 1973).
2/ Id.
Congress, when it was considering whether to add an
effectiveness criterion to the Act, was well aware that
evaluations by the FDA of the safety of therapeutic agents used
in treating diseases like cancer necessarily already included
an evaluation of effectiveness. The Senate, in its Report
No. 1744 on the Drug Amendments of 1962, recognized that

The Food and Drug Administration now requires, in
determining whether a "new drug" is safe, a showing
as to the drug's effectiveness where the drug is
offered for use in the treatment of a life-threatening disease, or where it appears that the "new
drug" will occasionally produce serious toxic or
even lethal effects so that only its usefulness
would justify the risks involved in its use. 1/

Indeed, the initial Senate Report on the legislation which
proposed to confer on the FDA the power to suspend outstanding
new drug applications for lack of effectiveness, made clear
that the proposal was "in no way intended to affect any existing
authority of the [FDA] to consider and evaluate the effectiveness
of a new drug in the context of passing upon its safety." 2/

The requirement that drugs used in the treatment of life-
threatening diseases be effective in order to meet the "safety"
standards of the 1962 grandfather exemption was squarely
addressed in the Durovic decision. After recounting the
administrative interpretation accorded by the FDA to the safety
requirement and after reviewing pertinent legislative history,
the Court of Appeals in Durovic concluded:

1/ S. Rep. No. 1744, 87th Cong., 2d Sess., reprinted in
S. Rep. No. 1744, supra, at Pt. II. (Emphasis added.)
Bearing in mind the weight properly accorded to administrative construction, and Congressional awareness of the administrative view that the concept of safety in the law before the 1962 amendments included the concept of effectiveness for its indicated use where the drug is offered for use in the treatment of life-threatening disease, we think the definition of new drug before the amendments should be construed accordingly. It would follow that a drug offered for use in the treatment of cancer is now, and was before the amendments, a new drug unless it has achieved general recognition among the experts as safe and effective for such use.

Under that analysis, the status of a drug offered for such use would be subjected to the same test before and after the amendments, and the grandfather clause would have no effect on it. 1/

The record established in this proceeding clearly demonstrates that there exists an overwhelming consensus among qualified experts that laetrile was not generally recognized as safe for the treatment of cancer on October 9, 1962. Typical of the views of qualified experts toward laetrile is that of David T. Carr, M.D., a Professor of Medicine at the Mayo Medical School with wide experience in the cancer field. According to Dr. Carr:

I am informed and understand that amygdalin is a cyanogenic glycoside. Cyanogenic glycosides are chemicals which contain in their molecular structure a sugar, a non-sugar, and the cyanide group, (-C=\text{EN}). I know of no cyanogenic glycoside that is generally recognized as safe and effective for the prevention, treatment or cure of cancer, for the relief of pain associated with cancer, or for any medical purpose. The composition of the cyanogenic glycosides, in general, and of amygdalin, in particular, is such that I do not recognize them, and they are not generally recognized among experts qualified through scientific training and experience to evaluate drugs, as safe and effective for the treatment of cancer, for prophylaxis against cancer, for relief of pain associated with cancer, or for any medical use. Neither amygdalin nor any other cyanogenic glycoside was generally recognized as safe for any such uses on October 19, 1962. None of these substances has ever been so recognized. The scientific literature contains no reports of

1/ 479 F.2d at 250 (footnote omitted).
adequate, well-controlled, scientific studies, or other evidence upon which such recognition may be predicated. I know of no recognized medical text in which use of amygdalin or any cyanogenic glycoside is recommended. I know of no medical school where use of these substances is taught. I know of no expert in cancer chemotherapy who is of the view that there is evidence these substances have any useful effect in treating cancer. I know of no report in the scientific literature describing an adequate, well-controlled study which demonstrates that amygdalin or any cyanogenic glycoside is safe and effective. Furthermore, I know of no cancer expert who would want a member of his family or himself to be treated with amygdalin if cancer should develop. 1/

It is considered particularly significant by the courts in determining the presence or absence of general recognition by experts as to safety whether adequate and well-controlled investigations of the drug have been accomplished and whether there is present a body of credible literature affirming safety. 2/. The record in this case is devoid of evidence establishing that such investigations have been accomplished. To the contrary, the record abounds with sworn testimony by specialists well acquainted with the relevant literature...

1/ AF-08 at 4. See also affidavits of:
Robert C. Eyerly, M.D. (AF at 3); George J. Hill, II., M.D. (AF-04 at 2-4); David T. Carr, M.D. (AF-08 at 4-5.); John T.P. Cudmore, M.D. (AF-10 at 2 ); Bernard T. Korbitz, M.D. (AF-13 at 4); W. Sherwood Lawrence, M.D. (AF-15 at 9-10); Carl M. Leventhal, M.D. (AF-16 at 6); Daniel S. Martin, M.D. (AF-17 at 4-5, 7-9, 10); Joseph F. Ross, M.D. (AF-21 at 6-8); Philip S. Schein, M.D. (AF-22 at 5); Michael B. Shimkin, M.D. (AF-23 at 2-3); Jesse L. Steinfeld, M.D. (AF-24 at 5-6); C. Chester Stock, Ph.D. (AF-25 at 7-8); Alfred Suffer, M.D. (AF-31 at 2-3); Susan J. Mellette, M.D. (AF-44 at 1).

and the state of expert opinion concerning cancer research, who declare without exception that no recognized expert in the field of cancer believes now or has ever believed that laetrile is safe or effective for the treatment of that disease. Consequently, laetrile is not entitled to the grandfather exemption of the 1962 amendments. 1/

1/ Assuming, arguendo, that the safety standard applicable to drugs used in the treatment of life-threatening diseases were limited to lack of toxicity, laetrile still fails to meet the requirements of the 1962 grandfather clause because on October 9, 1962, it had not attained general recognition among qualified experts as being safe even in that limited sense. In the opinion of many experts, laetrile is highly toxic when taken orally (see, e.g., affidavits of Joseph F. Ross, M.D., AF-18 at 11; Chester Stock, Ph. D., AF-25 at 9; Donald C. S. Tan, M.D., AF-26 at Exh. 5, p. 1.). Other experts note that there is a lack of evidence establishing that laetrile is non-toxic when taken parenterally. According to the affidavit of Thomas H. Jukes, Ph.D.:

Most items used as foods are not safe for injection, and amygdalin under the name, "laetrile", is frequently injected into cancer patients, apparently, without immediate toxic effects. The toxic effects of injecting foreign substances may not show up for months or years. To be safe for injectable purposes, a compound must be shown by means of long-term toxicity tests not to produce pathological changes. No such data are available for amygdalin. (AF-42 at 8.)

In this respect, it must be kept in mind that the grandfather exemption requires a positive showing that a drug had been generally recognized by qualified experts as non-toxic. There is no "presumption" of such general recognition; it is not necessary to affirmatively demonstrate toxicity. Rather, the burden of proof remains on those who seek to invoke the grandfather exemption. Such an affirmative showing is absent from this record. Additionally, where there has been little testing of a drug or where there is a dearth of medical literature on the question of its toxicity, the drug cannot possibly meet the grandfather requirements of general recognition among qualified experts. United States v. 41 Cases, More or Less, 420 F.2d 1126 (5th Cir. 1970). See discussion at 32-35, supra.
E. The 1962 Exemption From The New Drug Requirements Was Intended By Congress To Apply Only To Established Drugs For Use In Other Than Life-Threatening Illnesses Where Safety Was Universally Recognized.

Finally, it is clear that the exemption provision of the 1962 Act only applies to established drugs for use in other than life-threatening illnesses where safety is unquestioned and that therefore the 1962 exemption provision does not apply to laetrile.

Senator Eastland explained this exemption provision as applicable to "[e]stablished drugs which have never been required to go through new drug procedures...." 1/

The Supreme Court in Weinberger v. Hynson, Westcott and Dunning, Inc., 412 U.S. 609, 634 n26 (1973) in its description of the drugs that Congress intended to be exempted under Section 107 (c)(4) of the Drug Amendments of 1962, incorporates the rationale of Senator Eastland as follows:

The provision, however, does exempt drugs that, as a generic class, were never subject to new drug regulation. These consist primarily of over-the-counter drugs which, although they were not "grandfathered" under the 1938 Act, were not subject to new drug regulation because of universal recognition of the safety of their old, established ingredients at the time they came on the market. [Emphasis added.]

Judge Fairfield in Durovic v. Richardson, 470 F.2d 242, 251 (7th Cir. 1973), cert. denied, 414 U.S. 944 in refusing

1/ 108 Cong. Rec. 17366
"grandfather coverage" to another alleged cancer drug — Krebiozen — applied the same narrow rationale to the grandfather exemption espoused by the Supreme Court in *Hynson*:

Realizing, however, that there were already on the market or might come to be, drugs offered to the public which already were, or would be, so clearly recognized as safe (before the 1962 amendments) or as safe and effective (thereafter) that subjecting them to the administrative process would be unnecessary and wasteful, Congress allowed them to bypass the NDA procedure. We think the standard of general recognition by qualified experts was intended to be strictly construed so that unless a drug is clearly entitled to proceed through the direct channel, it must proceed through the NDA channel.

The Supreme Court in *Weinberger v. Hynson, Westcott and Dunning, Inc.*, 412 U.S. 609 (1973), *U.S. v. Pharmaceutical Corp. v. Weinberger*, 412 U.S. 655 (1973), and *Weinberger v. Bentex Pharmaceuticals*, 412 U.S. 645 (1973), and Judge Fairfield in *Durovic, supra*, make it clear that with the exception of the types of drugs described in the quote set forth above, all drugs, whether prescription or proprietary, or subject to an existing NDA, were ripe for review for efficacy under the Drug Amendments of 1962.

In short, laetrile falls outside both the letter and the spirit of the exemption provision of the 1962 grandfather clause since not only does it fail to meet any of the specific standards of Section 107(C)(4) but in addition it is not even among the class of drugs intended to fall within Section 107(C)(4).
III. LAETRILE IS NOT ENTITLED TO AN EXEMPTION UNDER THE GRANDFATHER CLAUSE OF THE 1938 FOOD AND DRUG ACT.


Shall not be deemed to be a "new drug" if at any time prior to enactment of this Chapter [i.e., June 25, 1938] it was subject to the Food and Drugs Act of June 30, 1906, as amended, and if at such time its labeling contained the same representations concerning the conditions of its use....

The 10th Circuit Court in Rutherford 1/ paraphrased this provision as follows:

...if Laetrile was marketed or officially recognized as a cancer drug [before June 25, 1938, but after June 30, 1906] it would not have to be subjected to the instrumentalities which exist for new drugs under the 1962 Amendments even though it is not generally recognized as safe or effective.

The key to grandfather status is whether the drug put forth today as a treatment for cancer is essentially identical in composition and labeling to the drug put forth prior to June 25, 1938. Also, as the Tenth Circuit recognized, it had to have been marketed or officially recognized as a cancer drug during that time. Laetrile meets neither of these criteria.

Developments in pharmacology in the last 40 years have resulted in vast changes in products, chemical compositions

1/ Rutherford v. United States, 542 F.2d 1137, 1141-42 (10th Cir. 1976).
and claims so as to render this exemption of diminishing importance. These changes in product composition and recommended dosage and usage are particularly striking as applied to laetrile.

As a threshold matter it is acknowledged that the word laetrile was not used until 1949. 1/

The difference in product composition and dosage was acknowledged by Dr. Krebs, Sr. in an affidavit which is part of this record. 2/ In that affidavit, he identified the amygdalin compound which he arrived at as sarcarsinase. This compound is identified in an Irish patent at TS-26, Exhibit 1 as a therapeutic agent for treating malignant growths by dissolving them. It was held out as containing amygdalase, prunase, oxynitrilase catalase, peroxydese and a proteolytic enzyme. 3/ A biochemical analysis of the compound described in the patent showed that it contained less than 5% amygdalin. 4/

Not only is the administration described differently but the dosages prescribed have undergone a clear change. The meager dosage information available prior to 1938 shows a dosage of 0.1 gram every two or three days. Today's laetrile proponents recommend a dosage of up to 3 grams daily. 5/

1/ AF-16 (Affidavit of Carl M. Leventhal, M.D.) Exh. 6.
2/ Id.
3/ See AF-50 (Affidavit of Carl M. Leventhal, M.D.) at 6 (Krebs Sr.'s sacarcinase substance may not even have contained amygdalin due to the effect of the hydrolze process).
4/ TS-26 (Statement of Eric E. Conn).
5/ AF-50, supra, at 6.
Since the name, composition and labeling of the drug today are different from what they were in 1938, the drug is clearly not grandfathered under the 1938 transitional clause. Therefore, as a matter of law, there is no need to examine the remaining grounds for exemption put forth by the proponents under the 1938 exemption. However, those other claims will be dealt with below to demonstrate how devoid the record is of any information which would support a 1938 Act exemption.

The record shows that before 1938 and probably as late as 1962, the proponents of the amygdalin-based cancer drug compounds admitted that their compounds were being used purely for investigational purposes. The record shows that Harry Pincus Jacobson was the first M.D. to use laetrile on humans. That event occurred in June of 1952.

Further, the labeling on the drug samples showed to Federal agents in 1952 restricted laetrile's use to investigational use only.

An affidavit of Dr. Krebs, Sr. indicates that from 1926 through 1962 any amygdalin compound shipped was for purely investigational purposes.

Dr. Krebs' affidavit further indicates that he changed his drug's composition in 1936 so the only active principle remaining was amygdalin and that he changed the composition between 1936 (amygdalin purity 66%) and 1960 (amygdalin purity 26%).

AF-15 (Affidavit of W. Sherwood Lawrence, M.D.), Attach. 6 at 2.
AF-16 (Affidavit of Carl M. Leventhal, M.D.) Exh. 5 at 2.
Id. at 3.
AF-15, supra, Exh. 13; AF-16, supra, Exh. 6.
purity 99.8%). Since, as noted above, sacarcinase at best contained less than 5% amygdalin, and laetrile as constituted in 1960 contained almost 100% amygdalin, it is clear that the composition of the compound changed from the 1920's and is certainly not today the compound it was prior to 1938.

Further, the usage was different. Dr. Krebs Sr., prior to 1938, talks of a single injection process for his sacarcinase. However, Dr. Krebs, when talking of laetrile, talks of a double injection process -- an injection of cyanogenetic glucoside followed by an injection of beta-glucosidase. Also, the admission of Dr. Krebs that usage prior to 1962 was confined to investigational purposes clearly shows that it was not marketed.

1/ See AF-50 at 6.
2/ Id., AF-16 at 9.
3/ The affidavits of Leake and Gurchot appended to Dean Burk's testimony contain no data supportive of 1938 grandfather rights. They all speak of amygdalin but do not give the name of the finished preparation used, nor do they give the form, dosage, strength, purity, or any of the other criteria of labeling and recommended usage required by the 1938 act. (See AF-42 at 22-23, AF-50 at 2-6.) Since the Krebs' on this record identify their compounds as crystalline and Dr. Gurchot identifies the compound he is referring to as a liquid oil, it is clear that they are not talking about the same compound. (Compare AF-50, supra, at 5 with TS-26, Exh. 1)
4/ AF-16, Exh. 6 at 2.
5/ AF-16 at 9.
during the time that the 1938 grandfather clause applies. 1/

The proponents of laetrile receive no assistance in their grandfather claim from the fact that there were substances commercially available on the market before 1938 which contained natural or extracted amygdalin. That these substances, which include apricot kernels and oils derived from fruit kernels, contained natural amygdalin does not give protection to a "finished dosage form" labeled and offered for drug use which was manufactured from that commercially available product. For example, as explained by Dr. Leventhal:

In this regard amygdalin is no different from many other chemicals and botanical substances from which newer preparations are derived. For instance, raувольфия серпента, a climbing shrub, contains in its root, reserpine, and has been used for centuries for medicinal purposes. However, when reserpine was extracted from raувольфия ресерпина, processed into a finished dosage form, and labeled for particular therapeutic uses, it was and is considered to be a new entity. The same is true of Laetrile or Vitamin B-17 for these drugs are different in not only their composition and dosage form, but bear labeling claims which were not associated with the ancient botanical sources. 2/

The ingredients used to manufacture the alleged cancer drug may have been available commercially but the commercially available substances were not sold as a treatment for cancer. 3/

Rather it is the product produced from the various

2/ AF-50 at 2-3; see AF-42 at 22-23.
3/ Id.
chemically available compounds that the FDA is called upon to evaluate, and the scant information produced by the proponents of laetrile for the record prior to 1938 shows, as discussed previously, that the amygdalin derivative cancer agent recommended after 1938 was not the same compound recommended prior to 1938. 1/

The rationale of proponents' argument that amygdalin is present in natural foods commercially available was made by the operators of an alleged cancer clinic in Pennsylvania about the natural penicillin found in their alleged cancer drug -- mucorhicin -- and it was found wanting by the Court:

Certain evidence was presented by the plaintiff that the defendants here claimed for Mucorhicin antibiotic qualities by reason of a relationship with penicillin. The defendants countered this by their claim that Mucorhicin contained a strain of penicillium and that the many strains of penicillium in themselves are actually a part of many foods, as for instance in the case of such food as roquefort and camembert cheese. While in fact it may be true that mold growth exists naturally in certain foods and that such foods are sold regularly there is essentially this difference, that such foods are sold only as foods and not for treatment, mitigation and prevention of disease. If cheese were to be sold by any processor for the cure, treatment, mitigation and prevention of disease under the classification of food within the provisions of the Food and Drug Act, it would be necessarily a drug. The fact that salt normally forms a part of the average person's dietary intake would not justify the marketing of a salt solution for gargling and mouth rinses to prevent disease as a food. Where mineral water in its original state is served as a beverage, after processing and separation of the constituent elements, it is no longer usable as a beverage but as a commercial water in small quantities.

1/ See AF-50 and AF-42, supra.
there is justification for classifying it as a drug. Goodwin v. United States (C.A. 6, 1924), 2 F.2d 200. 1/

This same logic applies to laetrile and its amygdalin content.

Further, the commercially available chemical compounds referred to by Dr. Burk, the bitter almond listed on the "GRAS" list (Generally Regarded As Safe) of the FDA, is an oil used for flavoring and contains no amygdalin. It is not, as suggested by proponent Burk, 2/ laetrile.

The oil of bitter almond compound referred to in the Merck Index is not the compound suggested for cancer treatment by Dr. Krebs. And the references to its use in Egypt or Russia for malignancies is pure and unsubstantiated hearsay. 3/

Indeed, the use in Russia was of a sweet almond mixture thought to be narcotic. 4/

The claims made by proponents of laetrile that the drug is grandfathered under the 1938 clause because it was contained in the Merck index or used by the ancient Egyptians were in substantial part presented for Court judgment in Hanson v. United States, 417 F. Supp. 30, 36 (D. Minn. 1976) and found wanting by the Court:

2/ Exhs. I and J.
4/ AF-50 at 2a.
The only evidence presented by the plaintiffs to try to establish that their tablets and vials of laetrile are exempt under the "grandfather" clause of § 321(p)(1) consists of the 1896 edition of Merck's Index and hearsay concerning the use of amygdalin during historical times dating back to the ancient Egyptians. This evidence is patently insufficient to demonstrate that the exemption applies. Merck's Index contains no information about the intended use of amygdalin, providing only certain facts as to its physical appearance, melting point, and source. The only reference to the conditions of its use is the phrase "Keep well stoppered." There is no indication therein that amygdalin in tablet form or in liquid form was in use for any purpose whatsoever; there is certainly no indication that amygdalin liquid was being injected intravenously into human beings or that amygdalin tablets were being ingested by human beings. In short, there has been no showing by the plaintiffs that laetrile tablets or liquid were "subject to" the Act prior to the enactment of § 321(p)(1), and no showing that "at such time its labeling contained the same representations concerning the conditions of its use."

Thus, it is clear from the record that laetrile is not entitled to an exemption from the "new drug" laws by reason of the 1938 grandfather clause. The record evidence set forth above makes it clear

(1) that laetrile was not in existence prior to 1938;
(2) that the chemical composition of the drug laetrile differs from the alleged amygdalin-derived drug which existed for investigational purposes only prior to 1938;
(3) that amygdalin was not marketed or officially recognized as a cancer drug before 1938;
(4) that the labeling claims for the alleged amygdalin-based cancer drug used for investigational purposes only prior to 1938 differed from the claims made for laetrile; and
(5) that experts in the field of cancer treatment did not recognize it as a cancer treatment between 1906 and 1938. 1/

CONCLUSION

WHEREFORE, for the foregoing reasons, the American Cancer Society respectfully requests that the Commissioner make the following affirmative findings:

(1) laetrile is a "new drug" subject to the premarketing requirements of proof of safety and efficacy set forth in the Food, Drug and Cosmetic Act, as amended; (2) laetrile is not exempted from the premarketing requirements of the Act by reason of the grandfather clause in the 1938 Act in that on or before June 25, 1938 it was neither marketed nor officially recognized as a cancer drug and its labeling during that time contains different representations as to its formulation and conditions of usage those made today; (3) laetrile is not exempted from the premarketing requirements

1/ See, e.g., AF-16, supra, (Carl M. Leventhal, M.D.) at 9-10; AF-42, supra (T. H. Lukes, Ph.d); AF-50 supra (Carl M. Leventhal, M.D.); TS-15, supra, (Ellis Hospital, R.H. Lange, M.D.) at 2. Following the rationale set forth in United States v. El-O-Pathic Pharmacy, 192 F.2d 62, 74 (9th Cir. 1951) the evidence of the witnesses appearing in support of "new drug" status for laetrile in this proceeding is of greater credibility and therefore entitled to greater weight in this proceeding than that of the proponents of laetrile.
of the Act by reason of the 1962 grandfather clause in that on or before October 9, 1962 it was (a) not commercially used or sold in the United States and (b) it was not generally recognized among experts qualified by scientific training and experience to evaluate cancer drugs as safe for use in the cure, mitigation, treatment or prevention of cancer; and (4) if laetrile is exempt from the Act by reason of either of the grandfather clauses, it is hereby ordered withdrawn from interstate commerce for violations of Section 301 of the Act, 21 U.S.C. § 331.

Respectfully submitted,

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June 17, 1977
On December 30, 1976, this matter came on for pretrial conference, the plaintiffs appearing by their attorneys Kenneth Coe and Burton J. Johnson, Oklahoma City, Oklahoma; and the defendants appearing by William S. Price, Assistant United States Attorney, Oklahoma City, Oklahoma, and Jay H. Geller, Associate Chief Counsel, Food and Drug Division, Department of Health, Education and Welfare, Los Angeles, California.

The United States Court of Appeals for the Tenth Circuit in its Opinion filed October 12, 1976, in this case stated in part:

"We are unable . . . to see how the FDA can escape the obligation of producing an administrative record to support its determination of the first and more fundamental issue that Laetrile is a new drug, for it is not a new drug merely because they say it is. . . . It seems doubtful that the FDA has in fact developed an administrative record adequate under 5 U.S.C. Section 554(c) and hence there is probably nothing which is presently available for a court to review. Nothing in the record suggests that the FDA has dealt with Laetrile in a rule-making proceeding under Section 701 of the Act, 21 U.S.C. Section 371. . . . Hence, if this is true the appropriate procedure for the district court is to remand the case back to the FDA for proceedings adequate to develop a record supportive of the agency's determination; the procedure should give Laetrile proponents an opportunity to express their views. This is a result which is also supported by the Supreme Court decision in Weinberger v. Benton Pharmaceuticals, 412 U.S. 645 (1973). There the district court faced with a similar problem referred the matter to the FDA for initial determination. See 412 U.S. at 652-54. The question whether the drug is to be recognized as 'safe and effective' or was 'excepted' merely because it is 'peculiarly the kinds of issues suited to initial determination by the FDA.' id. at '53."

MEMORANDUM OPINION AND ORDER

REX B. HAWKS
CLERK U.S. DISTRICT COURT
BY
DEPUTY
JAN 4 1977
Subsequent to the Circuit Court's remand to this Court, counsel for the defendants admitted in open court that the FDA, in determining Laetrile* to be a new drug, had failed to create an administrative record consonant with the procedures outlined in the Administrative Procedure Act or in accordance with the rule-making procedure outlined in the Food, Drug and Cosmetic Act at 21 U.S.C. §371. In so doing the FDA has left little to be reviewed beyond its bare determination. Under such circumstances there would be much injustice in sustaining the FDA's unsupported conclusion while, on remand, it sought ex post facto to muster evidence in support of such conclusion.

Viewing the agency's description of Laetrile as a "new drug," from the standpoint of the judicial review standards outlined at 5 U.S.C. §706, the Court would be compelled to find such determination to be "unsupported by substantial evidence," and to conclude that the agency had failed to comply with its burden of proof in this matter.

In the above-quoted Opinion, the Circuit Court emphasizes that Laetrile is not to be considered a "new drug" under the law merely because the FDA has said so, but rather that said determination must be supported by substantial evidence. The statutory presumption in favor of administrative determinations is based on the premise that such determinations are presumed to be supported by substantial evidence until a reviewing court has determined otherwise. Such presumption was overcome when FDA counsel admitted that no competent administrative record had ever been developed in support of the agency's determination. As a matter of law then, such determination is not supported by substantial evidence and cannot be sustained. Nickol v. United States, 501 F.2d 1389 (10th Cir. 1974); Heber Valley Milk Co. v. Butz, 503 F.2d 96 (10th Cir. 1974); Bailey v. Weinberger, 380 F.Supp. 863 (D.C. Ka. 1974).

*The Court finds from the record that Laetrile, Amygdalin and Vitamin B-17 are all one in the same, and the term Laetrile will be used to represent all three.
Having ascertained, during the December 30, 1976, hearing, that a competent administrative record did not exist, the Court then requested that the FDA make available to the Court the written basis for the agency's determination with regard to Laetrile, no matter how casual or unstructured its form or content might be; whereupon the Court was advised that no such rationale existed in any form. Clearly, federal agencies may not rule by fiat invoking only some unexplained application of their own expertise in defense of policy decisions they have made. Chemical Leasman Tank Lines, Inc. v. United States, 368 F.Supp. 925 (D.C. Del. 1973). Based on the complete absence of any evidence tending to establish a rational basis for the agency's determination, the Court would also be compelled to find, in applying the standards of 5 U.S.C. §706, that the agency's determination was "arbitrary, capricious," and represented "an abuse of discretion," and that it should also be overturned for these additional reasons.

In consideration of the fact, however, that the lack of an administrative record precludes judicial review at this time in any meaningful sense, and in order to grant both sides an opportunity to fully prepare and present their respective points of view, and consistent with the Circuit Court Opinion in this matter, the Court has determined that this case should be remanded to the FDA so that an administrative record can be constructed and a meaningful judicial review subsequently held. In view, however, of the complete absence of any good-faith agency record in support of its position in this case, as the record here is not merely incomplete, but virtually nonexistent; and in appreciation of the fact that depriving a terminally ill cancer patient of a substance he finds therapeutic, whether such benefit is physical or psychological, creates the very real risk that irreparable injury might be sustained,

IT IS HEREBY ORDERED, pursuant to 5 U.S.C. §705, that while this case is on remand to the FDA, and until such time as the FDA proffers to the Court an administrative record containing substantial
evidence in support of its determination that Laetrile is a "new drug" under the terms of the relevant statute, such determination is held to be without force or effect as to the plaintiff class in this case, and defendant FDA is hereby enjoined and restrained from preventing plaintiffs' transportation of interstate transportation of Laetrile for purposes of their own consumption under the terms of the Food and Drug Act, including §505(a) of the Act, 21 U.S.C. §355(a).

IT IS FURTHER ORDERED that on remand an administrative record shall be developed within 30 days from the date hereof, and a copy of such record and administrative determinations resulting therefrom shall be filed with the Clerk of this Court and the plaintiffs within 30 days thereafter.

Such administrative hearing should be concerned with the issue of whether Laetrile is exempt from the "new drug" application requirements of the Food and Drug Act, §505(b), 21 U.S.C. §355(b), by virtue of the "grandfather" clauses, and also with the issue of whether Laetrile is "safe and effective," as set out in the Circuit Court Opinion.

The plaintiffs herein have moved this Court for an Order directing the FDA to hear testimony and evidence of Dr. Dean Burk, Washington, D.C., and Dr. Ernest Krebs, Jr., San Francisco, California, as experts in their field, and also evidence and testimony of Mike Culbert, Edward Griffin and Mike Spencer, as research historians. This Court is without authority to enter such an Order; however, the Court believes that the FDA might desire to invite these persons to participate in the administrative proceedings and to receive into evidence their views with reference to the history and safety and effectiveness of Laetrile.

Pursuant to the request of the plaintiffs and based upon the pleadings and evidence in this case, it is hereby determined that this suit meets the class action requirements of Rule 23, Federal Rules of Civil Procedure, and therefore,
IT IS FURTHER ORDERED that this suit shall be certified and hereafter treated as a class action.

Dated this 14th day of January, 1977.

[Signature]
UNITED STATES DISTRICT JUDGE
STATUTORY APPENDIX

FOOD, DRUG, AND COSMETIC ACT

Section 107(c)(4), Public Law 87-781

(4) In the case of any drug which, on the day immediately preceding the enactment date, (A) was commercially used or sold in the United States, (B) was not a new drug as defined by section 201(p) of the basic Act as then in force, and (C) was not covered by an effective application under section 505 of that Act, the amendments to section 201(p) made by this Act shall not apply to such drug when intended solely for use under conditions prescribed, recommended, or suggested in labeling with respect to such drug on that day.

Section 201(g)(1), 21 U.S.C. § 321(g)(1)

(g)(1) The term “drug” means (A) articles recognized in the official United States Pharmacopoeia, official Homoeopathic Pharmacopoeia of the United States, or official National Formulary, or any supplement to any of them; and (B) articles intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease in man or other animals; and (C) articles (other than food) intended to affect the structure or any function of the body of man or other animals; and (D) articles intended for use as a component of any article specified in clauses (A), (B), or (C) of this paragraph; but does not include devices or their components, parts, or accessories.

Section 201(p), 21 U.S.C. § 321(p)

(p) The term “new drug”: means—

(1) Any drug (except a new animal drug or an animal feed bearing or containing a new animal drug) the composition of which is such that such drug is not generally recognized, among experts qualified by scientific training and experience to evaluate the safety and effectiveness of drugs, as safe and effective for use under the conditions prescribed, recommended, or suggested in the labeling thereof, except that such a drug not so recognized shall not be deemed to be a “new drug” if at any time prior to the enactment of this chapter it was subject to the Food and Drugs Act of June 30, 1906, as amended, and if at such time its labeling contained the same representations concerning the conditions of its use; or

(2) Any drug (except a new animal drug or an animal feed bearing or containing a new animal drug) the composition of which is such that such drug, as a result of investigations to determine its safety and effectiveness for use under such conditions, has become so recognized, but which has not, otherwise than in such investigations, been used to a material extent or for a material time under such conditions.
Section 505, 21 U.S.C. § 355

§ 355. New drugs—Necessity of effective approval of application

(a) No person shall introduce or deliver for introduction into interstate commerce any new drug, unless an approval of an application filed pursuant to subsection (b) of this section is effective with respect to such drug.

Filing application; contents

(b) Any person may file with the Secretary an application with respect to any drug subject to the provisions of subsection (a) of this section. Such person shall submit to the Secretary as a part of the application (1) full reports of investigations which have been made to show whether or not such drug is safe for use and whether such drug is effective in use; (2) a full list of the articles used as components of such drug; (3) a full statement of the composition of such drug; (4) a full description of the methods used in, and the facilities and controls used for, the manufacture, processing, and packing of such drug; (5) such samples of such drug and of the articles used as components thereof as the Secretary may require; and (6) specimens of the labeling proposed to be used for such drug.

Period for approval of application; period for notice, and expedition

of hearing; period for issuance of order

(c) Within one hundred and eighty days after the filing of an application under this subsection, or such additional period as may be agreed upon by the Secretary and the applicant, the Secretary shall either—

1. approve the application if he then finds that none of the grounds for denying approval specified in subsection (d) of this section applies, or
(2) give the applicant notice of an opportunity for a hearing before the Secretary under subsection (d) of this section on the question whether such application is approvable. If the applicant elects to accept the opportunity for hearing by written request within thirty days after such notice, such hearing shall commence not more than ninety days after the expiration of such thirty days unless the Secretary and the applicant otherwise agree. Any such hearing shall thereafter be conducted on an expedited basis and the Secretary's order thereon shall be issued within ninety days after the date fixed by the Secretary for filing final briefs.

Grounds for refusing application; approval of application; “substantial evidence” defined

(d) If the Secretary finds, after due notice to the applicant in accordance with subsection (c) of this section and giving him an opportunity for a hearing, in accordance with said subsection, that (1) the investigations, reports of which are required to be submitted to the Secretary pursuant to subsection (b) of this section, do not include adequate tests by all methods reasonably applicable to show whether or not such drug is safe for use under the conditions prescribed, recommended, or suggested in the proposed labeling thereof; (2) the results of such tests show that such drug is unsafe for use under such conditions or do not show that such drug is safe for use under such conditions; (3) the methods used in, and the facilities and controls used for, the manufacture, processing, and packing of such drug are inadequate to preserve its identity, strength, quality, and purity; (4) 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; or (5) evaluated on the basis of the information submitted to him as part of the application and any other information before him with respect to such drug, there is a lack of substantial evidence that the drug will have the effect it purports or is represented to have under the conditions of use prescribed, recommended, or suggested in the proposed labeling thereof; or (6) based on a fair evaluation of all material facts, such labeling is false or misleading in any particular; he shall issue an order refusing to approve the application. If, after such notice and opportunity for hearing, the Secretary finds that clauses (1) through (6) do not apply, he shall issue an order approving the application. As used in this subsection and subsection (e) of this section, the term “substantial evidence” means evidence consisting of adequate and well-controlled investigations, including clinical investigations, by experts qualified by scientific training and experience to evaluate the effectiveness of the drug involved, on the basis of which it could fairly and responsibly be concluded by such experts that the drug will have the
effect it purports or is represented to have under the conditions of use prescribed, recommended, or suggested in the labeling or proposed labeling thereof.

Withdrawal of approval; grounds; immediate suspension upon finding imminent hazard to public health

(e) The Secretary shall, after due notice and opportunity for hearing to the applicant, withdraw approval of an application with respect to any drug under this section if the Secretary finds (1) that clinical or other experience, tests, or other scientific data show that such drug is unsafe for use under the conditions of use upon the basis of which the application was approved; (2) that new evidence of clinical experience, not contained in such application or not available to the Secretary until after such application was approved, or tests by new methods, or tests by methods not deemed reasonably applicable when such application was approved, evaluated together with the evidence available to the Secretary when the application was approved, shows that such drug is not shown to be safe for use under the conditions of use upon the basis of which the application was approved; or (3) on the basis of new information before him with respect to such drug, evaluated together with the evidence available to him when the application was approved, that there is a lack of substantial evidence that the drug will have the effect it purports or is represented to have under the conditions of use prescribed, recommended, or suggested in the labeling thereof; or (4) that the application contains any untrue statement of a material fact: Provided, That if the Secretary (or in his absence the officer acting as Secretary) finds that there is an imminent hazard to the public health, he may suspend the approval of such application immediately, and give the applicant prompt notice of his action and afford the applicant the opportunity for an expedited hearing under this subsection; but the authority conferred by this provision to suspend the approval of an application shall not be delegated. The Secretary may also, after due notice and opportunity for hearing to the applicant, withdraw the approval of an application with respect to any drug under this section if the Secretary finds (1) that the applicant has failed to establish a system for maintaining required records, or has repeatedly or deliberately failed to maintain such records or to make required reports, in accordance with a regulation or order under subsection (j) of this section, or the applicant has refused to permit access to, or copying or verification of, such records as required by paragraph (2) of such subsection; or (2) that on the basis of new information before him, evaluated together with the evidence before him when the application was approved, the methods used in, or the facilities and controls used for, the manufacture, processing, and packing of such drug are inadequate to assure and preserve its identity, strength, quality, and purity and were not made adequate within a reasonable
food and drugs

21 § 355

Time after receipt of written notice from the Secretary specifying the matter complained of: or (3) that on the basis of new information before him, evaluated together with the evidence before him when the application was approved, the labeling of such drug, based on a fair evaluation of all material facts, is false or misleading in any particular and was not corrected within a reasonable time after receipt of written notice from the Secretary specifying the matter complained of. Any order under this subsection shall state the findings upon which it is based.

Revocation of order refusing, withdrawing or suspending approval of application

(f) Whenever the Secretary finds that the facts so require, he shall revoke any previous order under subsection (d) or (e) of this section refusing, withdrawing, or suspending approval of an application and shall approve such application or reinstate such approval, as may be appropriate.

Service of orders

(g) Orders of the Secretary issued under this section shall be served (1) in person by any officer or employee of the Department designated by the Secretary or (2) by mailing the order by registered mail or by certified mail addressed to the applicant or respondent at his last-known address in the records of the Secretary.

Appeal from order

(h) An appeal may be taken by the applicant from an order of the Secretary refusing or withdrawing approval of an application under this section. Such appeal shall be taken by filing in the United States court of appeals for the circuit wherein such applicant resides or has his principal place of business, or in the United States Court of Appeals for the District of Columbia Circuit, within sixty days after the entry of such order, a written petition praying that the order of the Secretary be set aside. A copy of such petition shall be forthwith transmitted by the clerk of the court to the Secretary, or any officer designated by him for that purpose, and thereupon the Secretary shall certify and file in the court the record upon which the order complained of was entered, as provided in section 2112 of Title 28. Upon the filing of such petition such court shall have exclusive jurisdiction to affirm or set aside such order, except that until the filing of the record the Secretary may modify or set aside his order. No objection to the order of the Secretary shall be considered by the court unless such objection shall have been urged before the Secretary or unless there were reasonable grounds for failure so to do. The finding of the Secretary as to the facts, if supported by substantial evidence, shall be conclusive. If any person shall apply to the court for leave to
adduce additional evidence, and shall show to the satisfaction of the court that such additional evidence is material and that there were reasonable grounds for failure to adduce such evidence in the proceeding before the Secretary, the court may order such additional evidence to be taken before the Secretary and to be adduced upon the hearing in such manner and upon such terms and conditions as to the court may seem proper. The Secretary may modify his findings as to the facts by reason of the additional evidence so taken, and he shall file with the court such modified findings which, if supported by substantial evidence, shall be conclusive, and his recommendation, if any, for the setting aside of the original order. The judgment of the court affirming or setting aside any such order of the Secretary shall be final, subject to review by the Supreme Court of the United States upon certiorari or certification as provided in section 1254 of Title 28. The commencement of proceedings under this subsection shall not, unless specifically ordered by the court to the contrary, operate as a stay of the Secretary's order.

Exemptions of drugs for research: discretionary and mandatory conditions; direct reports to Secretary

(i) The Secretary shall promulgate regulations for exempting from the operation of the foregoing subsections of this section drugs intended solely for investigational use by experts qualified by scientific training and experience to investigate the safety and effectiveness of drugs. Such regulations may, within the discretion of the Secretary, among other conditions relating to the protection of the public health, provide for conditioning such exemption upon—

(1) the submission to the Secretary, before any clinical testing of a new drug is undertaken, of reports, by the manufacturer or the sponsor of the investigation of such drug, of preclinical tests (including tests on animals) of such drug adequate to justify the proposed clinical testing;

(2) the manufacturer or the sponsor of the investigation of a new drug proposed to be distributed to investigators for clinical testing obtaining a signed agreement from each of such investigators that patients to whom the drug is administered will be under his personal supervision, or under the supervision of investigators responsible to him, and that he will not supply such drug to any other investigator, or to clinics, for administration to human beings; and

(3) the establishment and maintenance of such records, and the making of such reports to the Secretary, by the manufacturer or the sponsor of the investigation of such drug, of data (including but not limited to analytical reports by investigators) obtained as the result of such investigational use of such drug, as the Secre-
tary finds will enable him to evaluate the safety and effectiveness of such drug in the event of the filing of an application pursuant to subsection (b) of this section.

Such regulations shall provide that such exemption shall be conditioned upon the manufacturer, or the sponsor of the investigation, requiring that expert using such drugs for investigational purposes certify to such manufacturer or sponsor that they will inform any human beings to whom such drugs, or any controls used in connection therewith, are being administered, or their representatives, that such drugs are being used for investigational purposes and will obtain the consent of such human beings or their representatives, except where they deem it not feasible or, in their professional judgment, contrary to the best interests of such human beings. Nothing in this subsection shall be construed to require any clinical investigator to submit directly to the Secretary reports on the investigational use of drugs.

Records and reports; required information; regulations and orders; access to records:

(j) (1) In the case of any drug for which an approval of an application filed pursuant to this section is in effect, the applicant shall establish and maintain such records, and make such reports to the Secretary of data relating to clinical experience and other data or information, received or otherwise obtained by such applicant with respect to such drug, as the Secretary may by general regulation, or by order with respect to such application, prescribe on the basis of a finding that such records and reports are necessary in order to enable the Secretary to determine, or facilitate a determination, whether there is or may be ground for invoking subsection (e) of this section: Provided, however, That regulations and orders issued under this subsection and under subsection (i) of this section shall have due regard for the professional ethics of the medical profession and the interests of patients and shall provide, where the Secretary deems it to be appropriate, for the examination, upon request, by the persons to whom such regulations or orders are applicable, of similar information received or otherwise obtained by the Secretary.

(2) Every person required under this section to maintain records, and every person in charge or custody thereof, shall, upon request of an officer or employee designated by the Secretary, permit such officer or employee at all reasonable times to have access to and copy and verify such records.

APPENDIX C

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MRS DE HARVEN AMERICAN CANCER SOCIETY 777 THIRD AVE
NEW YORK

YOUR LETTER APRIL 1ST CLINICAL TRIALS LAETRILE
PROVED NOT EFFICIENT LETTER FOLLOWS
ISRAEL CANCER ASSOCIATION

COL LT 777 1ST

cce Dr. Wood
Dear Gerry,

I would like to apologise for the delay in answering your letters of 1. and 18. April owing to the necessity to make clear some points regarding clinical trials with Laetrile in Israel. (this following our cable of 24.4).

We are authorized by the hospitals mentioned in your letters: Beilinson; Shiba Medical Center and Hadassah University Hospital, Jerusalem, to inform you categorically that no clinical trials with Laetrile have been or are being performed in these hospitals and Laetrile is not being used for treatment of cancer patients in Israel.

Both physicians - Dr. Rubin and Dr. Issahary, are no experts in oncology treatment and up to our best of knowledge are not giving treatment to cancer patients.

Dr. Rubin approached some time ago, Prof. Z. Fuks, Head of Oncology Department, Hadassah University Hospital, Jerusalem and Prof. N. Goldblum, Head of Virology Department, University Medical School, Jerusalem, and asked them to perform trials with the above medicine. His request was totally rejected.

We also contacted the unit for clinical trials at the Israeli Ministry of Health who confirmed as well, that no such clinical trials have been performed in Israel.

Tel-Aviv, April 27, 1977

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