S. HRG. 103-419

LEGISLATIVE ISSUES RELATED TO THE REGULATION OF DIETARY SUPPLEMENTS

HEARING

OF THE

COMMITTEE ON LABOR AND HUMAN RESOURCES UNITED STATES SENATE

ONE HUNDRED THIRD CONGRESS

FIRST SESSION

ON

EXAMINING HOW THE FEDERAL GOVERNMENT SHOULD REGULATE THE MARKETING AND USE OF DIETARY SUPPLEMENTS, AND RELATED MEASURES, INCLUDING S. 784, TO STRENGTHEN FEDERAL STANDARDS WITH RESPECT TO DIETARY SUPPLEMENTS

OCTOBER 21, 1993

Printed for the use of the Committee on Labor and Human Resources

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THURSDAY, OCTOBER 21, 1993

U.S. SENATE,
COMMITTEE ON LABOR AND HUMAN RESOURCES,
Washington, DC.

The committee met, pursuant to notice, at 2:35 p.m., in room SD–430, Dirksen Senate Office Building, Senator Edward M. Kennedy (chairman of the committee) presiding.

Present: Senators Kennedy, Pell, Metzenbaum, Simon, Harkin, Bingaman, Wellstone, Wofford, Kassebaum, and Hatch.

The CHAIRMAN. We will come to order.

We understand the schedule of our very good friend and colleague, Congressman Richardson, requires his presence over in the House presently. We will proceed to hear from him, and then have the opportunity for the members to make some brief comments. Then we will proceed with the hearing.

Congressman, we are delighted to have you here. We know how involved you have been in this issue. I think all of us on this committee are very much aware of your strong interest, and I think all of us have benefited from the opportunity to work with you on it. We are delighted to welcome you here and look forward to your testimony.

STATEMENT OF HON. BILL RICHARDSON, A REPRESENTATIVE IN CONGRESS FROM THE STATE OF NEW MEXICO

Mr. RICHARDSON. Thank you very much, Senator, and thanks to all your colleagues, the majority and minority side, my Senator and my cosponsor in this bill, Senator Hatch.

Mr. Chairman, when I first began working on this issue, it was very clear to me that the people of my State, where a lot of alternative medicine started, care very deeply about making sure that they have full access to vitamins and dietary supplements. They continue to send that message to me frequently. And I believe by now all of the members of this committee have received the same message through thousands of letters and phone calls, and I want to thank those of you who have responded to your constituents' concerns by cosponsoring the Hatch-Richardson legislation.

Mr. Chairman, there are positive effects of supplements on health care costs. I am sure all of us have seen copies of the President's draft plan to reform our Nation's health care system. The President believes Americans are ready to take responsibility for their own health.

Clearly the President trusts the American people to practice preventive health care when the public is given adequate incentives. Why can't we also trust consumers to choose dietary supplements that will help them prevent illness and disease?

Mr. Chairman, this is what this issue is all about—freedom of choice. The safe use of dietary supplements could save this country billions of dollars in health care costs each year if adequate information could be given to the public on labels and pamphlets and the public was allowed to make choices. There is a need for a sensible regulatory process.

Mr. Chairman, I believe all of us agree that the current regulatory process for dietary supplements makes little sense. In fact, there really is not any process at all. Federal courts have found recently that the FDA's attempts to regulate supplements as food additives, in the words of the First Circuit Court's opinion, is "nonsensical and, hence, incorrect." And in the words of the Seventh District Court's opinion, it "defies logic and common sense." The Seventh District Court went as far as to say that FDA's efforts represented "an Alice in Wonderland approach to regulation."

As a legislator and a strong consumer Member of Congress with a rating of over 80 percent in my 10 years in the House, I have resented the FDA using its and our limited resources to litigate cases by reasoning that has been repeatedly rebuked by Federal courts. It is time we get busy and formulate a sensible process to balance public safety with the need for consumers to get the products that they desire.

There are adequate precautions for safety in the Hatch-Richardson legislation. We must always be concerned about potential risks of fraud and injury to consumers. I believe legislation that we pass must address these concerns. I believe that we must require that all supplement manufacturers employ good manufacturing practices, as well as to notify the FDA prior to any significant changes in their manufacture. I also believe that health claims must be truthful, nonmisleading, and based upon the totality of scientific evidence.

The FDA must continue to have strong enforcement powers to prosecute misleading and false claims. The agency currently has those enforcement powers, and if anything, those enforcement powers should only be strengthened in the future.

Here is the conclusion: The bottom line is that manufacturers of supplements must be allowed to make truthful and nonmisleading health claims when there is scientific evidence to back those claims. Let's allow science to be the determining factor for the validity of health claims for supplements and any questions involving safety. This should be our goal as we move forward.

Mr. Chairman, I believe that the Hatch-Richardson bill represents a sensible framework, a balance, for regulating dietary supplements. I certainly look forward to working with you and the minority and our colleagues on this subcommittee from both the House and the Senate to pass legislation this year that we all believe is the best solution to a very important issue.

Mr. Chairman, thank you again for allowing me to appear.

[The prepared statement of Congressman Richardson follows:]

PREPARED STATEMENT OF CONGRESSMAN BILL RICHARDSON

Mr. Chairman, I want to thank you for holding this hearing today on the regulation of dietary supplements. It is always a great pleasure to testify before your committee, particularly on such a critical issue.

I would also like to take a moment to commend Senator Hatch for his tremendous dedication to this issue. He has been working very hard for years to make supplements more accessible to the American public, and his leadership is much appreciated.

Congressman Gallegly has also dedicated much of his time and energy to lengthening the regulations on supplements and he deserves credit for his efforts.

Mr. Chairman, when I first began working on this issue, it was very clear to me that the constituents of my district cared very deeply about making sure they have full access to dietary supplements. They continue to send that message frequently.

I believe by now that all of the members of this committee have received the same message through thousands of letters and phone calls.

I want to thank those of you who have responded to your constituents' concerns by cosponsoring the Hatch-Richardson bill.

Mr. Chairman, I am sure all of us have seen copies of the President's draft plan to reform our health care system. The President believes Americans are ready to take responsibility for their own health. I share his belief.

Clearly, the President trusts the American people to practice preventive health care when the public is given adequate incentives.

Why can't we also trust consumers to choose dietary supplements that will help them prevent illness and disease?

The American people can make judicious choices if we only allow them the opportunity to see and read information on products. We have done this with food, drugs, and other products in our society. Why can't we also do this with dietary supplements?

Mr. Chairman, that is what this issue is all about—freedom of choice.

The safe use of dietary supplements could save this Nation billions of dollars in health care costs each year if adequate information could be given to the public on labels and pamphlets and the public was allowed to make choices.

Mr. Chairman, I believe all of us agree that the current regulatory process for dietary supplements makes little sense. In fact, there really isn't any process.

Federal courts have found recently that the FDA's attempts to regulate supplements as food additives in the words of the First Circuit Court's opinion is "nonsensical and hence—incorrect," and in the words of the Seventh District Court's opinion, "defies] logic and common sense." The Seventh District Court went as far as to say that FDA's efforts represented an "Alice in Wonderland approach" to regulation.

As a legislator, I resent FDA using its—and our—limited resources to litigate cases by reasoning that has been repeatedly rebuked by Federal courts.

It's time we get busy and formulate a sensible process to balance public safety with the need for consumers to get the products that they desire.

There is no question that we must always be concerned about potential risks of fraud and injury to consumers. I believe legislation that we pass must address those concerns.

I believe we must require that all supplement manufacturers employ good manufacturing practices, as well as to notify the FDA prior to any significant changes in their manufacturing.

I also believe that health claims must be truthful, non-misleading, and based upon the totality of scientific evidence.

The FDA must continue to have strong enforcement powers to prosecute misleading and false claims. The Food and Drug Administration currently has those powers and, if anything, those enforcement powers should only be strengthened in the future.

The bottom line is that manufacturers of supplements must be allowed to make truthful and non-misleading healthy claims when there is scientific evidence to back those claims.

Let's allow science to be the determining factor for the validity of health claims for supplements and any questions involving safety. This should be our goal as we move forward.

Mr. Chairman, I believe the Hatch-Richardson bill represents a sensible framework for regulating dietary supplements. I certainly look forward to working with you and our colleagues from the House and Senate to pass legislation this year that all believe is the best solution to this very important issue.

The CHAIRMAN. Well, thank you very much, Congressman. We are delighted to have you present here, and we know that you have given a great deal of thought and attention to this issue. We are grateful to you for being here. I do not have any questions myself. I do not know whether other members have any questions.

Senator KASSEBAUM. No. I would just say I appreciate it, too, and I do not think anyone could quarrel with anything that you said. I am sure we are all hoping that we can come together and address those very issues that you raised and that you hope to see resolved, as well as Senator Hatch.

Mr. RICHARDSON. Thank you.

Senator HATCH. If I could just comment, I want to than you, Bill, for the leadership that you have provided here. I am very proud of what you have been able to do over in the House. I know you are approaching 200 cosponsors of our bill, and it has not been easy to do that. But you deserve a lot of credit, and I just want to personally thank you and publicly thank you.

Mr. RICHARDSON. Thank you.

Senator BINGAMAN. Mr. Chairman, let me just compliment Congressman Richardson also. This is a very important issue in our State. The Congressman very ably represents part of the country which I also represent where there is a tradition of use of herbs and other medicines. That tradition has caused great concern among many of Congressman Richardson's constituents and my constituents. And for that reason, I think he has done exactly what he should in bringing this issue forward and trying to get it resolved legislatively.

Thank you.

The CHAIRMAN. Thank you very much, Senator Bingaman.

Thank you, Bill.

OPENING STATEMENT OF SENATOR KENNEDY

The CHAIRMAN. Today's hearing deals with important issues relating to dietary supplements. As citizens have become increasingly health-conscious, dietary supplements have become highly popular. They are also a significant part of the economy. Vitamins, minerals, herb products, amino acid products, and other nutritional substances now comprise a $4 billion industry.

Millions of Americans use supplements, and recent Federal legislation has raised widespread concern about the degree to which access to these products will be affected. All of us in Congress have received a large number of calls and letters from constituents afraid that the supplements they rely on may no longer be available. Our hearing today addresses these concerns.

Last year, Senator Hatch and I sponsored legislation which established a 1-year moratorium on the enforcement of certain FDA regulations affecting supplements. The moratorium was intended to provide an opportunity to learn more about supplements and to ensure that regulations are appropriate.

There is broad agreement that consumers should have access to all safe dietary supplements and that the burden should be on FDA to remove products identified as unsafe, not on supplements to prove they are safe. The current statutory provision requires what

is called "significant scientific agreement" before a health claim can be made for any food.

The standard is appropriate. It means that consumers can trust what is on the boxes and labels of the food they buy. Supplements should be held to the same standard. A consumer in the supermarket should be able to compare a health claim on food and the same health claim on a supplement and know they are just as accurate.

It is essential that decisions on the validity of health claims for supplements be based on a fair assessment of the available evidence. Senator Hatch has introduced the Dietary Supplement Health Education Act which proposes a set of reforms, and there are several bills in the House. The House has also held hearings on this issue, and our goal is to meet the moratorium deadline and pass consensus legislation this year.

We have heard from Congressman Richardson, who is the sponsor of legislation in the House, and we will hear from Commissioner David Kessler of the FDA to describe the FDA's approach. They will be followed by two panels of witnesses who will testify on issues relating to access to dietary supplements and issues relating to health claims.

So we welcome our witnesses. I am confident that their testimony will be informative and helpful to the Congress in reaching a satisfactory resolution of the current controversy.

Senator Kassebaum.

Senator KASSEBAUM. Mr. Chairman, I do have a statement, but first I would like to yield to Senator Hatch who has, for a long time, been a real leader on this issue and has provided, of course, the clarion call to some of the concerns that exist surrounding this issue.

The CHAIRMAN. Senator Hatch.

OPENING STATEMENT OF SENATOR HATCH

Senator HATCH. Well, thank you. I appreciate my ranking leader and, of course, the chairman. I would be happy to wait.

The CHAIRMAN. Go ahead.

Senator HATCH. Well, thank you, Mr. Chairman, and thank you, Senator Kassebaum, and thanks to Congressman Richardson and Congressman Gallegly, our leaders in the House on this issue.

We stand at a crossroads today. Either we can choose to move forward: we can resolve the issue of dietary supplements. We can move S. 784 to the House. And we can allow consumers what they demand—free access to safe dietary supplements.

Or we can double back: We can choose to do nothing. We can allow the FDA to continue its life and death grip on products which have been proven to enhance public health. We can watch the moratorium on health claims expire and wait for up to 100 million angry American citizens to descend.

Frankly, I would not want to be in Washington if we allow the latter to happen. [Laughter.]

It is no secret to anyone in this room how I feel about dietary supplements. I really believe in them. I use them daily. They make me feel better, as they make millions of Americans feel better. And I hope they give me that little added edge as we work around here.

And if anyone in the room doubts that, just check with your mailroom. I think they will tell you the real story.

It is no secret that the dietary supplement industry is large in Utah, some $700 million to $1 billion a year.

And it is no secret that Bill Richardson, Elton Gallegly, and I are leading the army of citizen protestors for whom we drafted the Dietary Supplement Health and Education Act, S 784 and H.R. 1709. Congressmen Richardson and Gallegly have done a great job on this, and I, of course, appreciated Congressman Richardson's testimony this afternoon.

But you, Mr. Chairman, and you, Senator Kassebaum, are not getting the credit you deserve.

You are the generals in this army. Your efforts behind the scenes are leading us toward passage of a bill, toward a victory for free choice.

And I want to recognize publicly today the commitment to resolving the issue that you both have demonstrated. It is the only way we are going to end the "Vitamin Wars," as I believe we will.

This is a tremendously complicated legal issue which can be expressed very simply: Are we in Congress going to allow one tiny agency to restrict the access of millions of Americans to safe products they wish to use to improve their health? Are we in Congress going to elevate to red-button priority our national dialogue on health care reform, then turn around and allow one misguided cadre of bureaucrats to restrict the information consumers need to be more healthy?

Clearly, 59 Members of the Senate, 59 bipartisan Members of the Senate, and over half of this committee have responded with a resounding "No."

And three times as many House members have joined with Bill Richardson and Elton Gallegly to halt this nonsense.

"Nonsense" is the polite term for what I see happening at the FDA.

Let me say for the record what I have told many of you privately. I have the greatest admiration for Commissioner Kessler. He is an honorable man. He has worked with many of us, and he is first-rate. And I think you would search long and hard to find any Member of Congress who is a bigger fan of the FDA than I.

But on this issue, the FDA is simply wrong. I want it to be clear. Congress is on the record as saying so.

There are two primary issues that have prompted this great consumer outcry over FDA's treatment of dietary supplement. One is access; the other is claims.

On access, the FDA has used tortured legal authorities to try to remove dietary supplements from the marketplace. Some of these products were never alleged to be unsafe, much less proven to be unsafe. As you will hear later, and as Congressman Richardson said, the court has termed FDA's actions "Alice in Wonderland." And I, for one, am tired of the tea party.

On claims, the FDA has used a jumbled-up process and a strict interpretation of a good law, one that Senator Metzenbaum and I and many others worked to put through, to block most consumers from receiving truthful and scientifically accurate information about dietary supplements.

The FDA has come to Congress decrying "snake oil." The Commissioner has testified before the House that "we are back at the turn of the century, when snake oil salesmen could hawk their potions with promises that couldn't be kept."

The Commissioner's deputies have hit the air waves, holding up products you are sure to see later, showing claims they believe to be false and misleading.

And I have a simple question. If the FDA feels there is a problem, why doesn't it remove them from the marketplace and protect the public rather than condemn the product of the house on TV?

One month, the FDA sends a report to Congress stating, "The vast majority of dietary supplements consumed today do not raise serious health or regulatory concerns."

The next month, the Commissioner testified before the House that "for every dietary supplement in the marketplace that may have some value, there are 100 or 1,000 that are worthless."

The FDA says that 80 percent of the market is safe and of no concern. By FDA's own estimate, there are only about 40,000 products. If 1 per 100 or 1 per 1,000 is bad, how can 80 percent be safe? I sure would not want the FDA keeping my checkbook. [Laughter.]

The FDA has presented the Congress with a report, "Unsubstantiated Claims and Documented Health Hazards in the Dietary Supplement Marketplace."

This false and misleading document is so riddled with inaccuracies that it lacks any evidentiary value and raises serious questions about the motives of those who are responsible for its preparation.

There can be little doubt that the report was hastily thrown together for a dramatic unveiling at a House hearing.

The FDA completely ignored the rigorous preapproval requirements for surveys in the Paperwork Revolution Act—or Reduction Act. Excuse me. It should be Revolution Act. [Laughter.]

According to the agency's own internal documents, barely 3 weeks before the July 29th hearing, 63 agency officials were sent out in a nationwide "undercover survey" to find examples of health food store employees making unsubstantiated claims.

Their operating instructions were laid out in a "not for public distribution" memorandum, which instructed these employees on how to dress and act, what leading questions should be asked, and they were cautioned not to discuss the assignment outside of the office.

The results of their investigation were to be conveyed secretly on a specially prepared reporting form. It is hard to imagine a clearer case of Government entrapment and misuse of taxpayer dollars.

I will just read a short excerpt from one of these cloak-and-dagger field reports:

"The CSO [Consumer Safety Officer] entered the store as a person off the street. She walked through the aisles to the east wall, where various nutritional supplements were displayed on shelves."

"She was approached by a store employee (white female, blond hair, approximately five feet five inches) who asked if she could help the CSO."

Maybe we should do a bill to merge the FDA with the FBI.

The FDA has participated in—notice I did not say conducted—at least one armed raid of a medical doctor who was dispensing supplements.

The FDA has gone on television assuaging the public that it does not want to remove supplements from the marketplace, yet has issued Federal Register proposals revealing an intent to restrict amino acids, herbal products, and high potency vitamins.

Today, I am releasing a report prepared by my staff entitled, "False and Misleading: FDA's Report: Unsubstantiated Claims and Documented Health Hazards in the Dietary Marketplace." Based on this analysis, it is clear that the FDA report is so riddled with inaccuracies that it lacks any evidentiary value and raises serious questions about the motives of those who are responsible.

I am asking the Clinton administration today to withdraw the report and to take the necessary steps to make sure in the future information provided to Congress and the American people is both accurate and unbiased and is gathered pursuant to Federal law.

The FDA has taken a solid law, the Nutrition Labeling and Education Act, and turned it on its head. The pint of the NLEA was to educate the consumer about good nutrition, not to block information.

I was cosponsor of the NLEA, but my work on the legislation pales in comparison to your legendary efforts, Mr. Chairman, and those of Senator Metzenbaum.

I remember when the bill was on the floor and Senator Metzenbaum and I worked so diligently to make sure certain dietary supplements were treated properly. I remember when we talked about wanting to provide the public with better nutrition information and wanting to enable consumers to select foods to protect and improve their health.

I remember when Senator Metzenbaum said that whatever approach the Secretary of HHS chose to take on supplement labeling, the "system must be based on the same considerations that guide other agency decisions: public health, sound scientific principles, and consumer fraud."

Who could disagree with that?

The FDA could, that is who.

Is FDA protecting the public health by refusing to allow pregnant women to be informed that 0.4 mg of folic acid taken daily could dramatically reduce their change of having a baby with birth defects?

Is FDA protecting the public health when 100 babies are born a month whose birth defects could have been prevented?

Is FDA protecting the public health by holding up the shield of "significant scientific agreement" to block all supplements but calcium from bearing health claims?

Is FDA protecting the public health when it turns down a health claim for antioxidants, even though surveys show 8 out of 10 doctors regularly use Vitamin E?

Before I close, Mr. Chairman, I would like to recognize several outstanding people who have worked closely with us. Our schedule did not allow them to testify, but I want to make sure that their statements are included in the record, along with a number of others I will submit.

Finally, Mr. Chairman, I want to thank you for scheduling this hearing. I know it was not easy. Your plate is extremely full, and

especially at this time of the year, and your capable staff has been most helpful to us.

I want to thank you, too, Senator Kassebaum, for your generous offer to work with us to effect a solution. I believe your influence on this process clearly has been felt.

I say to all here, in all sincerity, that I want to resolve this issue. I believe we will do so.

I recognize the concerns many, even cosponsors, have expressed that S. 784 does not adequately address the safety issue.

I recognize concerns that the language is not drawn tightly enough to prevent false and misleading claims.

I recognize concerns over setting up a dual standard under the NLEA for foods and for supplements.

I want to resolve all these concerns. I do not intend that we allow "snake oil" to be marketed or that we allow unsafe products on the market or that foods be treated unfairly.

What I do intend, Mr. Chairman, is to allow consumers access to safe products and to information about those products.

What I do intend is to stop FDA's regulatory over-reach and allow the agency to focus on real problems, such as medical devices.

And, finally, what I do intend, Mr. Chairman, is to get a bill to the President as quickly as possible. I hope that we can count on you for your support.

There are a number of groups and individuals who have worked closely with us during our consideration of this issue. I would like to recognize those groups and individuals and submit their statements for the record: Citizens for Health, a grass-roots consumer organization; and the Alternative Treatment Committee of the AIDS Coalition to Unleash Power, ACT-UP, if you will, in San Francisco, both of which have provided me with tremendous amounts of assistance and help. Their representatives were not able to be here with us today but would like to submit their statements for the record.

Another individual who has been a great help to me is Dr. Julian Whitaker, a noted physician, author of the monthly newsletter "Health and Healing," and president of the American Preventive Medical Association. He has provided a statement entitled "Regulation of Dietary Supplements."

In the audience today is Claire Farr, president of Claire Industries in San Marcus, CA, who will submit information for the record on amino acids. And I would also like to recognize Dr. John C. Godfrey and Dr. Robert Pollock who are with us today. They are two of the pre-eminent researchers on amino acids in the scientific community today. I am submitting their statement for the record.

Also in the audience, Dr. Alvin B. Siegelman from my home State of Utah, vice president of corporate health sciences at Nature's Sunshine Products. Dr. Dennis Jones, an internationally recognized researcher on herbal products, has provided me with information that I also ask to be made part of the record.

I want to thank all of these individuals and the many, many others who have worked with us so closely in development of S. 784 and its House counterpart, and I want to thank you again, Mr.

Chairman, and you, Senator Kassebaum, for allowing me the time to express my viewpoints on this issue.

The CHAIRMAN. Thank you very much.

As you can tell, Senator Hatch has not got a strong feeling about this issue. [Laughter.]

We are delighted to hear from him. I think all of us have heard from him a good deal on this issue. We are always glad to. I appreciate your kind remarks.

Senator HATCH. Thank you, Mr. Chairman.

The CHAIRMAN. Senator Metzenbaum.

OPENING STATEMENT OF SENATOR METZENBAUM

Senator METZENBAUM. Senator Hatch is, indeed, an extremely able advocate. He is persuasive. He is knowledgeable. He is intelligent. And when he supports a project or person, you have to take heed.

So several years ago, when he came to me and said, "I do not think we ought to wait the regular time. There is a man up for confirmation to be the Food and Drug Administrator, and I think he is absolutely superb. He is qualified. He has a tremendous background. He is intelligent. He understands the issues as far as safety for the American people are concern. There could not be a better choice for the position, and instead of going through the normal procedures, Howard, I would appreciate it if you would just sign off and we could confirm him promptly." Having been implored and entreated by such a persuasive and respected Member of the Senate, I went along. And today we are here——

Senator HATCH. I wish all things were that easy with Senator Metzenbaum. [Laughter.]

Senator METZENBAUM. Today we are here knowing full well that Dr. Kessler and the Food and Drug Administration and Senator Hatch are not in total agreement on this issue.

But I think it is important that we convene the hearing in order to focus on that legislative proposal. It is an important issue and one that has generated thousands of postcards, letters, and phone calls from consumers of dietary supplements.

In fact, the New York Times noted that this issue has generated more mail than the President's health care reform package. It has been truly a remarkable grass-roots movement to pass this legislation.

I have actually heard reports that some nutritional supplement stores even hand-write letters for their customers to sign. No stamp is needed. The store sends the letter.

However, we have seen virtual panic from the propaganda that has been distributed to drum up support for this legislation. One manufacturer has instructed consumers that they should "write to Congress today or kiss your supplements good-bye." That is more than a little bit of an overstatement.

I have gotten phone calls from constituents who are convinced that the Food and Drug Administration is going to ban Vitamin C. That is just not true in any respect. Consumers of dietary supplements have been told that they will need a prescription from their doctor to purchase supplements in the future.

Of course, these events have not escaped the attention of the press. In a New York Times editorial, to quote it, "Using scare tactics and misinformation, the dietary supplement industry has managed to rally thousands of health-minded Americans to support legislation that would actually deprive consumers of reliable health information."

Now, I think it is time to set the record straight. No one in the Congress nor the administration is proposing to ban the sale of dietary supplements. I want to repeat that. No one in the Congress nor the administration is proposing to ban the sale of dietary supplements. Nor is anyone proposing that a dietary supplement be regulated as a prescription drug. Those claims are totally false.

Under current law, the Food and Drug Administration is authorized to prohibit the sale of dietary supplements if, as with all food products, they are contaminated in some way and, therefore, unfit for human consumption. Furthermore, manufacturers or retailers of any dietary supplement may not make a claim that the supplement will prevent, treat, or cure a disease unless there is sound scientific evidence to support that claim.

I have to agree with that point of view. That is sound regulatory policy for the health and safety of the American people. And yet the industry that has waged this campaign of misinformation wants to be able to make health claims without the approval of the Food and Drug Administration. Frankly, I am not sure that all of those manufacturers can be trusted. Some certainly cannot.

If we are going to allow a manufacturer to make a health claim, then we need some independent review of the basis for that claim. In my opinion, well-designed studies conducted in a manner consistent with generally recognized scientific principles yield the necessary information for health claims. Moreover, there needs to be substantial agreement among qualified experts in the scientific community that the claim is true. To allow health claims to be made outside the accepted practice poses an unacceptable threat to the American public.

For example, I have here a bottle of Happy Camper. On the bottle, it claims that if you consume this product, you can relive your childhood.

Coming to the next product, there is the product for men: Manhood Plus. Supposedly, if a man consumes this combination of vitamins and amino acids derived from bull prostate, he will be more virile.

Will the consumption of raw brain and amino acids give you mental wisdom? The manufacturers of this supplement would lead you to believe that.

However, these claims are fairly mild. What about the products that are being sold to fight AIDS? If I have AIDS, will Immune Action help me? Will it keep me from catching AIDS? I have not heard of any who have been cured by it. I do not think so. But that is the implicit claim in this product.

I know that some will respond that if the supplement does not injure a person, then there is really no harm in making the claim. But that is not the issue. It is not an issue of no harm. It is a matter of deceptive advertising. It is a matter of being honest and truthful with consumers. And I know that I am not alone on this.

The American College of Physicians, the American Nurses Association, and the American College of Preventative Medicine oppose this bill. Although the opposition of these groups alone might make me suspicious by reason of their self-interest, I also understand and have been informed that the American Heart Association, the American Cancer Society, the American Institute for Cancer Research, the Consumers Union, the American Association of Retired Persons, and a number of other groups all oppose the legislation proposed by the Senator from Utah.

I am concerned also that allowing health claims without independent review provides an inherent conflict of interest for the industry. How can an industry objectively evaluate a health claim that will ultimately facilitate the marketing of its own product?

As more and more Americans begin to live much healthier lifestyles, unscrupulous supplement manufacturers are licking their collective chops at the prospect of making health claims on their products that are unsubstantiated or barely supported by scientific evidence.

However, this is not to suggest that all dietary supplement manufacturers are unscrupulous. Of course, they are not. I understand that there are some very, very responsible manufacturers. But I have heard reports that the president of one supplement manufacturing company stated at a trade show that sales could triple if the Hatch-Richardson bill passes. Unfortunately for these manufacturers, too often the truth takes a back seat to marketing.

I can only wonder what the claims will be on products like the ones I have here, the products I have previously mentioned. Will we see the claim that an herb will cure a brain tumor or that an amino acid can cure leprosy? One can only wonder.

I am not opposed to the marketing of dietary supplements. I believe it should be done in a responsible manner that does not put the consumer at risk.

In closing, let me State that I believe consumers should have access to safe dietary supplements that are sold without fraudulent or misleading claims. And I hope to be able to work with the Senator in connection with this subject, as we have on so many others, to see that we can work together to protect the consumer and not be unfair to any of the supplement manufacturers.

Thank you, Mr. Chairman.

The CHAIRMAN. Senator Kassebaum.

OPENING STATEMENT OF SENATOR KASSEBAUM

Senator KASSEBAUM. Well, thank you, Mr. Chairman. We have already gotten some very thoughtful statements from all sides.

I would just like to make one comment, though, about information that I understand was on some of the radio talk shows this morning that you, Mr. Chairman, and myself were blocking access to C-SPAN's coverage of this hearing. I would just like to say for the record, if anyone knows any politicians, they would hardly ever block C-SPAN coverage. [Laughter.]

And C-SPAN, furthermore, makes its own decisions about what to cover, and there were a number of hearings going on here today. But I just did not want you or me to get in trouble in assuming we had blocked coverage because I think everybody obviously is

tremendously interested in this issue. The mail has been tremendous, and I think there is a great deal of concern, some of it stemming, I think, from the fact that the moratorium passed last year will end on December 15. It had been hoped that the moratorium provided an opportunity for all the interested parties to work out a reasonable resolution of the issues. But that opportunity was lost, and that is why I believe this hearing is so important.

For example, some of the concerns have been raised because the FDA, the Food and Drug Administration, proposed a very broad interpretation of what would be considered unapproved labeling. As some of us would read the regulations, for instance, a retailer who made available to customers studies or news accounts of studies on dietary supplements published in respected scientific journals such as the New England Journal of Medicine would be guilty in the FDA's eyes of making unapproved health claims.

Instead of rethinking what has certainly been interpreted as a heavy-handed approach to protecting consumers against misleading claims and other controversial issues, the agency simply reissued the original regulations. At the same time, further fueling public alarm, the agency published the recommendations of the Dykstra report and a notice of proposed rulemaking that, taken together, give very strong indications that the agency is bent on requiring prescriptions for some supplements and removing others from the market entirely.

As Senator Metzenbaum has stated, that is not the case. There were some recommendations in that report that clearly moved it much further than the agency itself had even suggested, but coming together as it did with the notice of proposed rulemaking created a lot of fear and alarm that has become ever exaggerated in the telling.

Because we have heard, on all sides some very similar phrases: safe use of dietary supplements, access to safe products, and truthful information regarding those products, I think that it really clearly shows that we can come together. I think today's hearing gives all sides the opportunity to come to the table and develop a framework for safeguarding consumer health, protecting consumer choice, and ensuring that consumers have the information they need to take greater responsibility for their health and make informed dietary choices.

I am confident that we can work out these issues in ways that will restore the public's confidence in the Food and Drug Administration and in its ability to fairly and reasonably regulate dietary supplements and lay to rest long-held suspicions and biases on all sides.

I think it is important, as Senator Metzenbaum stated, that this confidence in the FDA be restored and the FDA at the same time be fully cognizant of its responsibility in restoring consumer confidence.

Thank you, Mr. Chairman.

Prepared Statement of Senator Kassebaum

Mr. Chairman, I am very pleased that we are holding this hearing to examine the issues surrounding the regulation of dietary supplements. As I am sure you are well aware, many Americans

who use dietary supplements and are convinced of their efficacy are deeply concerned that the Food and Drug Administration will regulate these products in ways that limit consumers' choice of and ready access to these products and information about their potential health benefits.

The Food and Drug Administration's regulation of dietary supplements has long been controversial, but recent FDA actions have greatly heightened the public's alarm over the agency's intentions and its ability to reasonably and fairly regulate these products. In addition to conducting heavy-handed and seemingly capricious raids on some distributors, the FDA has not appeared to be responsive to a dialogue on the issues surrounding the appropriate regulation of supplements. The moratorium on the FDA's highly controversial regulations for implementing the Nutrition Labeling and Education Act provided the opportunity for all interested parties to work out a reasonable resolution of the issues, but that opportunity was lost.

For example, the agency proposed a very broad interpretation of what would be considered unapproved labeling. As my constituents and I read the rule, a retailer who made available to customers studies or news accounts of studies on dietary supplements published in respected scientific journals such as the New England Journal of Medicine would be guilty in the FDA's eyes of making unapproved health claims.

Instead of rethinking this heavy-handed approach to protecting consumers against misleading claims and other controversial issues, the agency simply reissued the original regulations. At the same time, further fueling public alarm, the agency published the recommendations of the Dykstra report and a notice of proposed rulemaking that, taken together, give very strong indications that the agency is bent on requiring prescriptions for some supplements and removing others from the market entirely.

Further heightening the public's concern that the FDA is biased against dietary supplements and incapable of fairly evaluating their potential or real contributions to health promotion and disease prevention is the agency's slowness to approve well-documented, legitimate claims. A case in point is the claim that folic acid helps to prevent birth defects. Over 2 years ago, the Centers for Disease Control recommended that folic acid was effective in preventing birth defects and that women in their childbearing years should supplement their diets. A year ago, the Public Health Service—the FDA's parent agency—made the same recommendation. Only within the past several weeks, however, has the FDA acted to approve this claim for folic acid as a dietary supplement.

The current atmosphere of increasing alarm, mistrust, and suspicion on the part of the public toward the FDA must change. Today's hearing gives all sides the opportunity to come to the table and develop a framework for safeguarding consumer health, protecting consumer choice, and ensuring that consumers have the information they need to take greater responsibility for their health and make informed dietary choices.

I am confident that we can work out these issues in ways that will restore the public's confidence in the FDA's ability to fairly and

reasonably regulate dietary supplements and lay to rest long-held suspicions and biases on all sides.

Let's set aside the rhetoric, the charges and counter-charges, the hope on both sides, roll up our sleeves, and get to work.

The CHAIRMAN. Thank you very much. I want to join Senator Kassebaum and my other colleagues to say that we are very hopeful that we can take action, and we intend to try to do so before we recess.

I want to remind our colleagues again that we have a very important group of witnesses. Just in fairness, as Senator Kassebaum will remember, we have been having hearings where Senator Kassebaum and I have been the only two committee members left. Many of these witnesses have come a long way, and we are notified by the floor that we are going to have a number of votes later in the afternoon. I would hope that we would permit an opportunity for our colleagues to make comments, but I want to indicate to our witnesses who have made a very considerable effort to be here that we will do the best we can. I hope that whatever comments will reflect the members' positions as concisely as possible.

I think Senator Simon is next.

Senator SIMON. They were ahead of me here.

The CHAIRMAN. We go by seniority in this committee.

Senator SIMON. I think the seniority rule is great right now.

The CHAIRMAN. Well, then, Senator Pell is recognized. [Laughter.]

OPENING STATEMENT OF SENATOR PELL

Senator PELL. At any rate, Mr. Chairman, I am very glad you are holding this hearing. I know I am glad to be a cosponsor of S. 784, Senator Hatch's bill, and agree with its central premise. The Food and Drug Administration has been a bit harsh in its regulation of dietary supplements, vitamins, minerals, and herbal preparations. My own rule of thumb would be as long as it does not hurt the individual, he ought to be permitted to take it, and that should be the premise that would guide us.

I would ask that my full statement be inserted in the record.

The CHAIRMAN. It will be so included.

[The prepared statement of Senator Pell follows:]

PREPARED STATEMENT OF SENATOR PELL

Mr. Chairman, I am delighted that you are holding today's hearing on issues related to the regulation of dietary supplements. This is an issue of great concern to many of my constituents, as it is to me—as a consumer and proponent of these products.

As you may know, Mr. Chairman, I am a cosponsor of S. 784, the Dietary Supplement Health and Education Act, Senator Hatch's bill. I agree with its central premise: that the Food and Drug Administration (FDA) has been too harsh in its regulation of dietary supplements, vitamins and minerals, herbal preparations, and related products. And I am very glad to see Commissioner Kessler here, because I would like to hear from him on this topic.

I must say, however, that I am well aware of concerns that have been raised about the Hatch bill. It is not my intention, in cospon-

soring this bill, to aid in the marketing of dangerous or fraudulent products. I have been much encouraged by Senator Hatch's comments along these lines, and know that we share an interest in the continued availability of safe, effective dietary supplements.

Mr. Chairman, I look forward to working with you, and with Senator Hatch and the other members of this committee, to reach a compromise on a matter of great concern to so many people in my own State and across the Nation.

Opening Statement of Senator Simon

Senator SIMON. Mr. Chairman, I think we have to protect the public with labeling, make sure they do not have contaminated products. We also have to protect the public, see that they have access to materials that are safe for them. Then, finally, one other area that is not covered here that I think at some point we have to cover, and that is, right now, for a company to get a drug approved, I understand it costs about $130 million. My——

Senator HATCH. About $360 million. Between $260 and $360.

Senator SIMON. Well, whatever; a lot of money.

One of my predecessors who served with Senator Kennedy, Paul Douglas, used to have a little bit of fish flour on the mantle in his room, and he said, "I think this really can contribute, but no one will spend the money to test this out because no one can have a monopoly on this." And there are other examples of that. Former Congressman Berkley Bedell believes he has other examples of this. This is an area that I think at some point—not in this bill, but at some point also needs to be examined.

Thank you, Mr. Chairman.

The CHAIRMAN. Thank you very much.

Senator Bingaman.

Opening Statement of Senator Bingaman

Senator BINGAMAN. Mr. Chairman, I will put my statement in the record. Thank you.

[The prepared statement of Senator Bingaman follows:]

Prepared Statement of Senator Bingaman

I want to thank the distinguished Chairman of the Senator Labor and Human Resources Committee, Senator Kennedy, for convening today's hearing. I also want to commend the distinguished Senator from Utah, Senator Hatch, and my colleague from New Mexico, Mr. Richardson, for their leadership on this issue. The regulation and availability of vitamins, herbs, and other dietary supplements is of tremendous importance to thousands of New Mexicans, so I appreciate the opportunity to participate in today's hearing.

Many New Mexicans are confused and concerned about the FDA's proposed dietary supplement regulations related to the Nutrition and Labeling Education Act (NLEA). I believe Senator Hatch's legislation, the Dietary Supplement Health and Education Act, has gone a long way toward alleviating these concerns. It is not a perfect bill—very few bills are—but S. 784 has given many New Mexicans the peace of mind that comes from knowing their

access to vitamins, herbs, and other dietary supplements will not be restricted by the FDA or its regulations. It is for this reason that I have agreed to cosponsor S. 784. Now, it is the duty of the members of this committee to work together to strengthen and improve the bill's provisions and enact into law a comprehensive solution to the problem of dietary supplement regulation.

I did not reach the decision to cosponsor S. 784 lightly, as many of my constituents know. In fact, since my election to the Senate, I have spent much more time and energy urging the administration to implement health and safety regulations than I have spent advocating delay or withdraw. I am proud to have been a cosponsor and strong supporter of the Nutrition Labeling and Education Act. I worked for 6 years to get the National Nutrition Monitoring Act signed into law and implemented. I founded "HealthNet New Mexico" several years ago to try to help New Mexicans improve their cardiovascular and physical fitness, stop smoking, and eat healthful foods. Earlier this year, Senator Cohen and I introduced the Healthy Students-Healthy Schools Act, a bill to help States and localities establish comprehensive, high quality health education programs in all schools, from kindergarten through 12th grade.

I care about the health status of all Americans, and I firmly believe that each and every one of us has the right to know whether the health claims we read in magazines and see on store shelves are truthful and valid. I believe every Member of Congress has a responsibility to do all he or she can to help protect the health and safety of all consumers. These should be our goals as we work to develop a compromise on the issue of dietary supplement regulation.

With the assistance of concerned and knowledgeable individuals in the Federal Government, the industry, and in our States, I am confident we can develop an effective, workable solution that meets the fundamental goal of consumer safety. I look forward to the day we reach that solution. Thank you.

The CHAIRMAN. Senator Wellstone.

OPENING STATEMENT OF SENATOR WELLSTONE

Senator WELLSTONE. Mr. Chairman, thank you for the half an hour here to explain my position. [Laughter.]

Let's go on and hear from the panel.

The CHAIRMAN. Senator Wofford.

OPENING STATEMENT OF SENATOR WOFFORD

Senator WOFFORD. I will put a statement in the record if I can edit it in such a way that my sympathies are shown as well as the striking of the balance that the statement now conveys. The chairman knows that nine other Senators and I have written him a letter setting forth the two conflicting interests and urging that we work together to get some action.

Senator Hatch knows that every time he talks to me, my sympathies are fully with him, so much so that he understood me 1 day to be a cosponsor. And I was not quite there for the very reasons you have stated. There are still some shortcomings in the bill. But my anti-bureaucratic spirit gets stirred every time I meet citizens,

some of whom came down and talked to me today. So I hope we do take action to assure access to dietary supplements.

[The prepared statement of Senator Wofford follows:]

PREPARED STATEMENT OF SENATOR WOFFORD

While there has been a dramatic increase in the use of nutritional supplements over the past several years, the issue of how these products are to be regulated by the Food and Drug Administration (FDA) has become a very difficult issue. Reasonable and legitimate concerns are in conflict.

I am well aware of general concern about the safety and the legitimacy of health claims for certain currently marketed nutritional supplements. A broad range of consumer organizations and government agencies have raised questions about whether consumers are receiving reliable information about nutritional supplements. There are also, however, questions about the proper role of the FDA in regulating these products. These concerns are all appropriate.

Over the past several months, I have been contacted by literally thousands of constituents about this issue. I have heard testimonials about the benefits of various nutritional supplements that would be regulated under the Nutritional Labeling and Education Act of 1990.

And I have repeatedly heard the fear that such regulation might make nutritional supplement products unavailable. Because the FDA has not been supportive of the nutritional supplement industry, these constituents have real concerns about the FDA's oversight of these products.

An article that appeared in the New England Journal of Medicine earlier this year reported that Americans spend over $10 billion on alternative medicine, including nutritional supplements. As Bill Moyers reported in his book, "Healing the Mind," people choose alternative therapies for a variety of reasons: frustration with conventional treatments, a desire to take more responsibility for their personal health.

I do not believe that the Federal government should reduce a person's ability to promote their personal health or seek a treatment of their own choosing.

All sides have reasonable concerns. I hope that I and members of this committee will be able to work with the relevant Federal agencies and interested parties to arrive at a creative solution. We need to respect the concerns and protect the interests of all involved, and support an individual's right to choose their health care treatment, including the use of nutritional supplements.

I have taken a personal interest in the issues that will be presented formally to the committee today. I look forward to working with the Chairman, Senator Kennedy, and Senator Hatch, to achieving a successful conclusion. That successful conclusion must assure safety of dietary supplements, but it also must assure the public that access to dietary supplements will not be compromised.

I welcome our witnesses and look forward to their testimony.

The CHAIRMAN. Thank you very much.

We welcome you, Commissioner Kessler. Have you got your bulletproof vest on today? [Laughter.]

Mitch Zeller and Mike Taylor, we are glad to have them, and we are very appreciative of the Commissioner's appearance here today.

Dr. KESSLER. If we can have just 1 minute here, Senator?

The CHAIRMAN. I think Senator Hatch and the other members of the committee know the battle of the charts. I think we are moving into a new phase here, I expect.

I think we have the idea, having admonished my good friends and colleagues to make brief statements. [Laughter.]

STATEMENT OF DR. DAVID A. KESSLER, COMMISSIONER, FOOD AND DRUG ADMINISTRATION, ROCKVILLE, MD; ACCOMPANIED BY MICHAEL TAYLOR AND MITCHELL ZELLER

Dr. KESSLER. Thank you, Mr. Chairman and members of this committee. First, may I ask that my written statement be included for the record, and also Dr. Philip Lee, who is the Assistant Secretary of Health, if we can submit a statement from him. Dr. Lee is in Houston, and he is very committed to working with this committee to resolve this very important issue.

What I need to do today, what I want to do today, is two things: one, to try to set the record straight; and, two, to pledge to you, this entire committee, that we stand ready to work with you to resolve this very important issue.

First, in setting the record straight, the industry's message is simple. It says: Write to Congress today or kiss your supplements good-bye. It is one of the reasons—it is not the only reason—that you are getting a lot of mail.

This message is absolutely false. We hear people claiming that FDA is trying to deny consumers the right to take vitamins and minerals or force them to go to a doctor to get a prescription for their Vitamin C. Nothing could be further from the truth.

Let me say it as clearly as I know how. FDA is not out to deny anyone access to dietary supplements. Our position can be stated in one sentence. FDA supports access to all dietary supplements as long as those products present no safety problems and make no unsubstantiated health claims. Anyone who tells you or your constituents something else is simply wrong.

Mr. Chairman and members of this committee, I am here to reaffirm FDA's commitment to maintaining the American consumer's access to dietary supplements. I support access to dietary supplements, and you should support that access, too.

I am here to pledge that the FDA will work with this committee to achieve the goal to which I believe we all can aspire: guaranteed access to a wide variety of supplements that consumers can trust, are safe, and are properly labeled.

Some say we are trying to put the health food industry out of business, that products will have to stop being sold. That is simply not correct. Any nutritional supplement currently on the market can be sold as long as it presents no safety problems. As long as these products are safe, manufacturers are not going to run into any problems from the FDA.

But there is a point at which I need to draw a line. It is the point at which one of those products on store shelves makes the claim that something is useful in treating diseases such as cancer, diabetes, or arthritis when it, in fact, does no such thing.

Manufacturers do not have to take the product off the market. They simply have to remove the unproven claim from the labeling or any promotional material. Sell whatever safe product you will, but do not say that it will prevent, cure, or treat a disease unless you have established affirmatively that it really will.

I have no problems with consumers taking supplements to improve their diets, but when supplements are really drugs in disguise, promoted to treat serious diseases, then I believe we have a problem. Recognize at the outset that the dietary supplement industry is essentially unregulated. When consumers pick up a dietary supplement today, they assume that the product is safe.

But the fact is that there has never been a systematic evaluation of the safety of dietary supplements. And when consumers see a health claim for a dietary supplement, they assume it will provide the benefit it touts. In fact, the marketplace is full of unsubstantiated claims.

Congress set the standard for health claims for foods in the Nutritional Labeling and Education Act. But you could not reach agreement on the standard for dietary supplements and asked the FDA to set that standard.

In November 1991, we proposed that dietary supplements should be subject to the same standard for health claims that you articulated so clearly for foods, not the standard for drugs, for foods; namely, that the claim be supported by significant scientific agreement.

We did not see why a health claim should be allowable for a Vitamin C tablet but not for the Vitamin C in broccoli or orange juice. We reaffirmed that position in a proposal we issued this past June.

Make no mistake, Mr. Chairman. There are many supplements on store shelves today making unsubstantiated health claims. The promotion of these products for serious health problems is a real problem. We issued a report, as Senator Hatch said, prior to Congressman Waxman's dietary supplement hearing on July 29th. It listed hundreds of products that claim to cure, treat, or reduce the risk of cancer, AIDS, diabetes, heart disease, arthritis, and other diseases. These claims appear in current catalogues, brochures, other advertising materials, and right on the label in certain instances.

In the absence of a clear standard, the best FDA can do to try to separate the good from the bad when it comes to dietary supplements is to go after products one by one. If there are people who want to go out and buy products such as this one—this one is named Nature's Response—let them do it. But no one should attach to this product this brochure making the claim that Nature's Response inhibits reproduction of the HIV virus and inhibits the growth of cancer.

Increasingly, scientists are uncovering important relationships between diet and health. But in the dietary supplement marketplace filled with unsubstantiated claims, for every legitimate product that may be of some value, there are many that are worthless. Some exciting advances, scientific advances, are being made, but unless something changes, products that provide real benefits—and there are products that provide real benefits—will be drowned out

by the hundreds of other products making unsubstantiated and sometimes downright fraudulent claims.

Congress confronted the issue in the 1990 under NLEA. Let's go back to what was happening in the supermarket before you passed NLEA. We had a proliferation of misleading claims and unfounded claims on food packages that undermined consumer's faith in the food label. When the marketplace is flooded with these products making unsubstantiated claims, the products that offer legitimate benefits are lost in the morass of those that offer nothing.

The food industry recognized it had a problem back then. The NLEA was a commitment to restoring credibility on the supermarket shelves. You, Congress, set a standard in NLEA that said preliminary, premature evidence was not an adequate basis for wholesale changes in the diets. You set the standard, significant scientific agreement.

Today, under current law, we have a standard for drugs, and we have a standard for foods. We believe that the standard you have already established for foods should be the standard for dietary supplements.

Some would have you create a standard for dietary supplements that is weaker than the standard for foods. But the implications of a weaker standard for dietary supplements deserve your full attention. Is weakening the standard what you really want to do at a time when millions of Americans, so many Americans, are taking supplements?

Believe me, I appreciate the promise of a simple cure. Of course, we would all rather take a miracle pill than undergo more arduous and sometimes uncertain treatments. But, unfortunately, cures do not always come packaged as neatly as we would hope. And patients who forsake therapies that offer some real benefit for the siren song of empty promises have a lot to lose.

Some would have you permit marketers to decide whether a health claim is appropriate without review by FDA. Remember that the proliferation of health claims on food labels in the 1980's occurred precisely because companies, rather than FDA, decided what claims could be made. This approach opens the floodgates to claims that have no scientific basis. It puts the consumer in an impossible situation because there is no way of telling what works from what does not work.

Furthermore, if companies are allowed to make claims without sound studies to back them up, there is no incentive to do those studies that will finally determine which products offer real benefits. It would be a sad loss if consumers were to turn their backs on all dietary supplements because their faith was undermined by the proliferation of misleading claims.

But there may be a higher price for consumers, a price greater than the cost of being victimized by worthless products or foregoing therapies with demonstrated usefulness. You know, there is a widespread perception that because something is natural it is safe. We have learned, sometimes the hard way, that equating safety with natural can be a costly equation.

Think about it. Half our prescription drugs in this country are derived from plants, and no one doubts for a minute that drugs can have toxic effects. Why, then, should we assume that all risks dis-

appear when plants are sold as dietary supplements for therapeutic purposes?

Dietary supplements have been linked to death, kidney and liver failure, nerve damage, psychosis, and we have only discovered it after the injuries have taken place. How can we work together to ensure the availability of safe dietary supplements that do not cross the line separating legitimate claims from bogus assertions?

We would ask you to consider doing three things:

First, guarantee access to dietary supplements. Write your constituents and tell them that Congress is working with the FDA to maintain access to dietary supplements. I guarantee that access.

Second, give the FDA an effective means to deal with demonstrable safety problems and to ensure that these products are properly manufactured.

And, third, hold manufacturers of dietary supplements to the same standard that you previously established for health claims on foods. Support that standard. Do not lower it. In the end, this approach will benefit consumers because it will keep insupportable health claims off the shelves, and it will give consumers access to meaningful choices, choices based on science and not salesmanship.

I know, when it comes to dietary supplements, the emotions are running very high. The time has come to lower the emotional tenor of that debate. And I know you are receiving more mail from constituents on this issue than seems imaginable.

The time has come to stem the floor of letters by acting decisively and responsibly to support access to dietary supplements, but not to allow unsubstantiated claims to be made for those products. It is time to sit down, to work things out, and to find a solution.

Thank you, Mr. Chairman.

[The prepared statements of Drs. Kessler and Lee follow:]

PREPARED STATEMENT OF DAVID A. KESSLER

Mr. Chairman and members of the committee, I am David Kessler, Commissioner of Food and Drugs. I am accompanied today by Michael Taylor, Deputy Commissioner for Policy; Gary Dykstra, Deputy Associate Commissioner for Regulatory Affairs; Mitchell Seller from the Office of the Deputy Commissioner for Policy; Dr. Elizabeth Yetley, Acting Director, Office of Special Nutritionals, and Dr. Lori Love, Director, Clinical Research and Review Staff, both in our Center for Food Safety and Applied Nutrition; Dr. Robert Temple, Director, Office of Drug Evaluation I, in our Center for Drug Evaluation and Research; and Margaret Jane Porter, our Chief Counsel.

Today's hearing focuses on one of the oldest public policy debates involving the Food and Drug Administration (FDA)—how should the Federal Government regulate the marketing and use of dietary Supplements? In Particular, the committee has expressed an interest in FDA's evaluation of a health claim for the supplement folic acid under the Nutrition Labeling and Education Act. I'll discuss this in more detail in a few minutes. First, I'd like to discuss some of the more general aspects of the dietary supplement debate.

FDA welcomes the open exchange of views on dietary supplements. As this debate unfolds, it is important for the Congressional community and all other interested parties to understand FDA's perspective on this significant public health issue and to recognize the precise focus of FDA's concerns.

The starting point of the debate is understanding how broadly the term "dietary supplement" is being used by consumers and the food industry. The term "dietary supplement" commonly is used to refer to everything from the traditional vitamin and mineral nutritional supplements to tablets or capsules that contain amino acids, herbs, and other substances. The traditional vitamin and mineral products comprise more than so percent of the multibillion dollar dietary supplement market and raise no serious concerns as long as they are sold without disease prevention or treatment claims, have potencies that do not raise safety concerns, and are manufactured

using appropriate quality control standards. These products are not what the current debate is about. Contrary to what Members of Congress may be hearing, FDA has no intention of forcing consumers to get a doctor's prescription to obtain Vitamins or minerals. Nor is the Agency intent on forcing health food stores out of business.

The remaining products on the market—products containing amino acids, herbs and other botanicals, and other substances—often raise questions about safety and labeling. Many of these products have no recognized role in nutrition, frequently bear express or implied disease prevention or treatment claims, and have been marketed for specific therapeutic purposes. Some of these products have been associated with serious, even fatal, adverse reactions.

The current debate is about the safety and proper labeling of these products, and any other Product that makes a scientifically unsubstantiated disease prevention or treatment claim aimed at vulnerable population groups. While today's debate is being shaped by some recent regulatory and Congressional concerns, the fundamental issue has been with us for decades. For example, as in the Laetrile controversy and other cases, the present controversy is the conflict between what marketers want to claim about unproven remedies and what is the extent of the Government's responsibility to ensure that those claims have a scientific basis.

The challenge to all participants in the dietary supplement debate—Congress, consumers, industry, FDA, and others—is to strike the right balance between ensuring the safety and proper labeling of all of these products while at the same time preserving consumers' freedom of choice. Freedom of choice means little unless consumers have meaningful and accurate information on Safety and effectiveness in deciding whether to purchase these products.

BACKGROUND AND HOW FDA SEES THE ISSUES

The nature of the dietary supplement debate has changed over the last 50 years. Immediately following the 1938 passage of the Federal Food, Drug, and Cosmetic Act (FDC Act), FDA's concern was to identify appropriate daily intakes of vitamins and minerals to ensure that minimum nutritional needs were being met.

In 1966, FDA Proposed new regulations regarding the labeling and content of special dietary food products and new definitions and standards of identity for vitamin and mineral substances. In addition to rules for food fortification, definitions for low-calorie foods, and a general condemnation of useless (but highly promoted) nutrients, FDA proposed that multi-vitamin and mineral product labels bear the following statement:

Vitamins and minerals are supplied in abundant amounts in the foods we eat. The Food and Nutrition Board of the National Research Council recommends that dietary needs be satisfied by foods. Except for persons with special medical needs, there is no scientific basis for recommending routine use of dietary supplements.

This so-called crepe label," in particular, met with uniform disapproval from not only the health food industry and vitamin manufacturers, but also from nutritionists and even from the Association of Food and Drug Officials of the United States.

FDA stayed its 1966 regulations and conducted public hearings on dietary supplements from 1968 until 1970.

By the early 1970's, FDA's interest and the Public debate—had shifted to high potency vitamin supplements and whether their potencies should be limited to "nutritionally rational" levels if they were to be marketed as "foods" rather than "drugs." Congress settled that debate in 1976 with the Proxmire Amendment, which permits FDA to limit potency only for safety reasons.

Moving back to 1966 for a minute, I'd like to illustrate the irony of the dietary supplement debate. In 1966, FDA proposed special treatment for dietary supplements—special treatment that would have disparaged their use. We were wrong in doing so, and we were told that we were wrong, not only by the health food industry, but by nutritionists and regulatory officials. Now the issue has come full circle, only it is not FDA that is proposing special treatment for dietary supplements but the dietary supplement industry itself. It would be equally wrong now as it was in 1966 to give special treatment to these types of products. FDA has held numerous meetings with the industry to explore what basis there is for such treatment, and quite frankly has been given none. Our scientists, and the scientists from outside the agency with whom we have talked, are not aware of any reason to treat nutrients differently depending on whether they are in a pill or in a conventional food.

Some may cite our health claim final rules as evidence to the contrary, but that is simply not correct. We have now approved or proposed to approve eight health claims, only two of which could appear on dietary supplements—this is where the science has led us so far. There are new scientific understandings of the links be-

tween diet and health, and there are some exciting possibilities, such as the possibility that high doses of certain antioxidant vitamins may lead to lower cancer rates.

As scientific evidence assessing the effects of diet and health accumulates, it is important that FDA carefully weigh the science and potential risks in order to protect the health of the American consumer and to allow appropriate claims when they are substantiated by scientific data. Equally important, FDA continues to have concerns about the safety of some products now sold as dietary supplements and about the scientific validity of therapeutic claims associated with many dietary supplement products.

THE ROLE OF DIETARY SUPPLEMENTS

The emerging knowledge about the potential role of diet, including specific nutrients, as well as behavioral changes, in promoting health and reducing the risk of certain diseases has enormous implications for public health.

FDA is dedicated to assisting health-conscious consumers to make informed choices about the role of nutritional supplements in their diet. The agency is carefully reviewing scientific data linking diet and disease and is making decisions as quickly as the available science allows.

FOLIC ACID

As you know, on October 8, 1993, FDA proposed to revise the food labeling regulations to authorize the use of a health claim about the relationship between folate and the risk of neural tube birth defects on labels or in labeling of foods in conventional food form or as dietary supplements. Unfortunately, the public has a perception that FDA took an unusually long time to recognize the benefits of folic acid in preventing neural tube defects. I'd like to be quite clear that FDA did recognize the benefits of folic acid early on but that there were other public health concerns that needed to be considered before FDA could authorize the health claim. In fact, the period of time from the U.S. Public Health Service (PHS) recommendation to the time that FDA proposed to authorize a health claim for folic acid was 9 months. Even though it took us until October to complete the preparation and clearance of the Federal Register documents for publication, FDA had announced in June of this year that it was our intention to approve the folic acid claim.

I would like to discuss briefly the series of events which led to the October 8, 1993, announcement that FDA was proposing a health claim for folic acid for both conventional foods and dietary supplements.

On November 27, 1991, the agency proposed as part of the implementing regulations for the Nutrition Labeling and Education Act not to authorize the use of a health claim relating to an association between folic acid and neural tube defects on the label or in labeling of foods, including dietary supplements. The agency quoted a recent CDC guideline for physicians recommending that high levels of folic acid be given to women at high risk of a neural tube defect-affected pregnancy because of a previous history of such a pregnancy. The guidelines also noted that this recommendation should be implemented under a physician's care. At the same time, the agency tentatively concluded that there was not significant agreement among qualified experts that intakes of folic acid at levels permitted under the food additive regulation would be protective against occurrence of neural tube defects in pregnancies of women in the U.S. population.

However, subsequently, in September 1992, while FDA's rulemaking was in progress, the PHS recommended, based on reviews of existing and newly available scientific data, that all women of childbearing age in the United States who are capable of becoming pregnant should consume 0.4 milligram (mg) of folic acid daily throughout their child bearing years to reduce their risk of having a pregnancy affected with spina bifida or other neural tube defects. The PHS recommendation noted that although all the effects of high intakes of folate are not well known, the effects do include the possibility of complicating the diagnosis of clinical vitamin B12 deficiency—by masking the anemia that is often associated with early stages of this deficiency. Data on the numbers of persons at risk of vitamin B12 deficiency are not available, but older adults and some younger Black women are at highest risk. There are no data available on the safety of high intakes of folic acid in young children. Therefore, the PHS recommended that care should be taken to keep total folate consumption from all sources at less than 1 mg per day except under the supervision of a physician.

On January 6, 1993, the agency published a final rule which concluded that a health claim for folic acid and reduced risk of neural tube defects should not be authorized at that time. The agency reaffirmed its support of the PHS recommendation that all women of childbearing age in the United States who are capable of be-

coming pregnant consume 0.4 mg of folic acid daily to reduce their risk of having a pregnancy affected with spina bifida or other neural tube defects. The agency noted, however, that the PHS had identified questions about the safe use of folic acid in food that remained unanswered, and the Agency concluded that it could not authorize a health claim for folic acid until these questions, among others, were satisfactorily resolved.

Given the seriousness of neural tube defects and the safety and other concerns expressed in the PHS recommendation, FDA convened a subcommittee of its Food Advisory Committee to consider the issues concerning folic acid. The Folic Acid Subcommittee met in November 1992 and in April 1993. FDA requested that the Folic Acid Subcommittee provide the agency with recommendations on several issues, including identification of the appropriate target population for a folate-neural tube defects health claim, the appropriate daily intake of folate to reduce the risk of neural tube defects, and safety concerns for the target population and the general population. One of the recommendations from the November 1992 meeting of the Folic Acid Subcommittee was that FDA attempt to design a fortification scheme that could not only provide 90 percent of women of childbearing age with at least 0.4 mg of folate per day from all sources, but would not result in excessively high folate intakes by nontarget groups.

At its April 1993 meeting, following expression of diverse opinions of the potential effectiveness of health claims as an educational tool and close votes by the subcommittee members, the Folic Acid Subcommittee voted to support FDA action to propose to authorize a health claim for folate and to propose fortifying cereal-grain products with folic acid. Based on the agency's discussion of the uncertainties in the food consumption database and the difficulties in predicting bioavailability factors under differing conditions, the Folic Acid Subcommittee supported 1 mg total folate as the safe daily upper limit for intake from all sources.

Based on the entirety of the available information, FDA has now concluded that there is significant scientific agreement supporting a relationship between folate and neural tube defects. The agency has also tentatively concluded that fortification of cereal-grain and breakfast cereals with folic acid is an appropriate means to increase the folate intake of women of childbearing age. In anticipation of this, the Centers for Disease Control and Prevention (CDC) is considering the establishment of a surveillance system to detect potential adverse effects of high folate intakes in high risk persons.

FDA believes that if a health claim for the folate-neural tube defect relationship is authorized, food manufacturers would have an incentive to add folic acid to a wide variety of foods, which could lead to a passive increase in the intake of folate both by women in the childbearing years and by other segments of the general population. For example, in the Federal Register of January 6, 1993, FDA Presented an analysis Showing that widespread fortification of the food supply with folic acid could lead to individual intakes in the range of 3 to 5 mg or more of folate per day. Because such an increase could bring with it certain risks, the Agency is proposing to amend the food additive regulation for folic acid so that authorization of a health claim can be safely implemented At the same time, FDA feels it is prudent public health to improve the nutriture of women of childbearing age in the United States within a safe range of intakes. Thus, FDA is also Proposing to require mandatory additive of folic acids to cereal grains labeled as "enriched." Dietary supplements and fortified breakfast cereals will also continue to be available.

OTHER CLAIMS

Also, on October 8, 1993, FDA proposed not to authorize health claims relating to an association between fiber and cancer, fiber and heart disease, antioxidant vitamins and cancer, omega-3 fatty acids and coronary heart disease, and zinc and immune function in the elderly on the label or in the labeling of dietary supplements of vitamins, minerals, herbs, or other similar nutritional substances. The agency has tentatively determined that there is not significant scientific agreement among experts that claims for these nutrient-disease relationships are supported by the totality of publicly available scientific evidence. The proposal, which FDA was required to publish by the Dietary Supplement Act of 1992, is based on the agency's tentative determination that there is not significant scientific agreement among experts about the nutrient-disease relationships, nor are the claims supported by the totality of publicly available scientific evidence. The proposal provides an opportunity for interested persons to submit new scientific data and comments on the five nutrient-disease relationships mentioned above. The agency will review all comments received and will conduct its own literature review to obtain recent scientific evidence.

In addition, on November 1–3, 1993, FDA is cosponsoring, with other research and health organizations, an open symposium on antioxidant vitamins to discuss the available science. FDA will consider the results of this symposium in making a final decision about whether to authorize a health claim on antioxidant vitamins and cancer.

There is much to be lost if we drift from the scientific base of our decisions and allow the marketplace to be filled with unsubstantiated claims on products of unproven safety. The public's health could be put at risk—both from unrecognized risks and from the potential for diverting patients from proven methods of treatment, including many that are lifesaving, and replacing them with unproven Products—and Scarce health care dollars would be wasted.

SAFETY CONCERNS

Amino acids, herbs, and a host of other supplement products are more likely to raise public health concerns than traditional vitamin and mineral supplements marketed at reasonable potencies.

FDA is concerned about safety even though there has not been a large number of reported adverse reactions reported for these products. The lack of reported injuries is not particularly surprising because there is not an adequate system in place to discover them and to link injuries with the ingestion of the substance. When injuries are not immediate and dramatic, they are often hard to link to their cause. This is true even for injuries from conventional drugs, which are given in the context of excellent physician recordkeeping and used in a conventional health care system that looks for such events; it is far more true of substances given outside a conventional health care system.

FDA efforts in the past to encourage reporting of adverse effects met with industry resistance. Moreover, physicians, in baking medical histories, usually do not inquire about dietary supplement use, and patients often do not volunteer this information. Thus, there is a significant possibility that many adverse reactions to dietary supplements go unrecognized and, as a result, unreported.

Nonetheless, increasing numbers of serious adverse reactions associated with the use of dietary supplements are being reported in the scientific literature and to public health officials worldwide. The first report of these reactions is usually not the first occurrence. These reactions were usually there—but not recognized.

During the last year, FDA's Center for Food Safety and Applied Nutrition (CFSAN) was reorganized and a new office was created to place greater emphasis on dietary supplements The Office of Special Nutritionals (OSN) now collects and evaluates information reported to FDA on the adverse effects from dietary supplements. With the help of OSN, FDA has begun to identify dietary supplements for which serious adverse effects have been documented.

As you know, on July 29, 1993, FDA released a four part report concerning the dietary supplement marketplace. One part of the report includes the most current information FDA has gathered on the health hazards associated with some dietary supplements.

Specific examples of safety concerns include:

AMINO ACIDS

FDA requested a voluntary recall of the amino acid L-tryptophan after published reports associated its ingestion with an epidemic of a connective tissue disease called eosinophilia myalgia syridrome (EMS). More than 1,500 cases, including 38 deaths, were reported to public health agencies, although the incidence of this disorder is thought to be much higher.

Despite recent intense research, the exact cause of EMS and an understanding of how it develops have not been established. Initial epidemiological studies implicated the L-tryptophan produced by a single Japanese manufacturer. Also, the studies noted that certain impurities were identifiable in batches of case-associated L-tryptophan. These findings suggested that some impurity or other component in these batches of L-tryptophan may have been responsible for EMS. However, both initial and subsequent epidemiological studies on the EMS epidemic have identified cases of EMS and of another related disease, eosinophilic fascitis, that occurred before the 1989 epidemic and that appear to be related to other batches or sources of L-tryptophan. Other data indicate that L-tryptophan, either alone or in combination with some other component in the supplement products, may be responsible for some of the pathological features in EMS. Taken together, these findings support previous suggestions that the L-tryptophan-associated EMS was caused by several factors and is not solely related to an impurity in a single source of L-tryptophan.

In 1990, following the L-tryptophan-associated EMS outbreaks, FDA contracted with the Federation of American Societies of Experimental Biology (FASEB) to review the available safety data on amino acids. FASEB reviewed the available scientific literature on the safety of each of the amino acids and gave special emphasis to metabolism, genetic influences on metabolism, and population groups at potentially higher risk for adverse health effects from use of amino acids in supplements. FASEB concluded that there was insufficient available information to establish a safe upper intake level for any amino acid supplement. FASEB also concluded, based on an evaluation of the limited data on patterns of amino acid use and adverse health effects, that the safety of unrestricted use of particular amino acids in dietary supplements cannot be assumed. FASEB made a number of recommendations including a systematic evaluation of certain effects of these substances. These experts also recommended that potentially vulnerable subgroups—the young, elderly, women of childbearing age, and people with chronic diseases use amino acids only under responsible medical supervision.

In the Federal Register of June IS, 1993, FDA issued an Advance Notice of Proposed Rulemaking (ANPR) to announce that we are reviewing the manner in which we regulate the safety of dietary supplements, and that we are requesting comment on approaches, consistent with the requirements of the FDC Act, for ensuring the safety of products offered as dietary supplements. The ANPR was published in response to the Dietary Supplement Act of 1992, recent developments and events in the marketplace, and to receive comment on the FASEB report.

FDA also announced in the ANPR the availability of a report by an internal FDA task force that was established in May 1991, following the EMS outbreak associated with the consumption of L-tryptophan containing dietary supplements. The FDA Task Force was asked to review to the agency's regulatory program for dietary supplements and to recommend improvements. Known as the Dietary Supplement Task Force, it was composed of agency staff with experience and expertise in regulatory, nutritional, legal, and medical issues related to supplements. The Task Force was asked to examine a number of issues, including whether safety concerns exist regarding dietary supplements, and, if so, to recommend a regulatory framework to distinguish supplements that raise safety concerns from those that do not. The Task Force completed its work in May 1992 when it submitted a report with recommendations to the Commissioner. It must be emphasized that nothing in the Task Force report represents Agency policy. FDA has made the recommendations of the Task Force available for public comment. The Agency will review the comments it receives and then decide what actions appear to be appropriate.

Also, the ANPR Contained FDA's announcement that we intend to bring amino acid-containing products into compliance with the law and requested that manufacturers of these products submit any additional information that may be available on the safety and use of individual amino acids or combinations of amino acids as ingredients in dietary supplements.

HERBALS

Many herbal and other botanical products are derived from familiar food-use herbs, but many others are derived from plants that have no traditional food use and no known nutritional value. Although many of these plant products are marketed as being "natural," "natural" is no guarantee of safety.

Some of our most potent drugs (morphine, certain cancer drugs, and many antibiotics) are natural plant derivatives, as are certain historic poisons (hemlock, strychnine, and belladonna). "Natural" products from plants come with the same full range of potential benefits and risks as synthesized materials. Furthermore, the dose of an active ingredient, whether from a "natural" or Synthetic product, determines its usefulness and safety or its toxicity. Manufacturing controls are important for both types of products. Adverse effects vary greatly depending on the particular species and strain of plant, when and how it is harvested, what plant parts are used, how the plant materials are processed.

Most herbal products, including many of those used traditionally, have not been subjected to routine safety testing, particularly for the effects of prolonged use. Indeed, given the variability in marketed products, and lack of standardized preparations, safety testing would be difficult. Despite these recognized difficulties with safety testing of botanical Products, serious adverse health effects have been recognized with the use of certain of these products in animals and humans.

Examples of risky herbals include:

1. Germander. Germander is the common name for a group of plants that are contained in medicinal teas, elixirs, capsules, or tablets, either singly or in combination

with other herbs, and marketed for the treatment of obesity and to facilitate weight loss.

Since 1986, at least 27 cases of acute nonviral hepatitis (liver disease), including 1 death, have been associated with the use of Commercially available germander products in France. These cases show a clear temporal relationship between ingestion of germander and onset of hepatitis, as well as resolution of symptoms when the use of germander was stopped. In 12 cases, re-administration of germander was followed by prompt recurrence of hepatitis. Recovery occurred gradually, in most cases approximately 2 to 6 months after withdrawal of germander. Analyses of these cases do not indicate a strong relationship between the dosage or duration of ingestion and the occurrence of hepatitis. On the basis of these cases, the French Ministry of Health has forbidden the use of germander in drugs.

2. Comfrey. Various Species of comfrey, including common comfrey and Russian comfrey, are used in herbal preparations. Comfrey is widely sold in the United States in teas, tablets, Capsules, tinctures, medicinal poultices and lotions. Since 1985, at least seven cases of hepatic veno-occlusive disease (obstruction of blood flow from the liver with potential scarring (cirrhosis)), including one death, have been associated with the use of commercially available oral comfrey products.

Comfrey, like a number of other plants, e.g., Senecio species, contains pyrrolizidine alkaloids. The toxicity of pyrrolizidine alkaloids to humans is well documented. Hepatic veno-occlusive disease, following ingestion of pyrrolizidine alkaloid-containing herbal products, has been documented repeatedly throughout the world. Hepatic veno-occlusive disease is usually acute and may result in fatal liver failure.

The United Kingdom, Australia, Canada, and Germany have recently restricted the availability of products containing comfrey, and other countries permit use of comfrey only under a physician's prescription.

3. Chaparral. Chaparral, commonly called the creosote bush, is a desert shrub with a long history of use as a traditional medicine by Native Americans. Chaparral is marketed as a tea, as well as in tablet, capsule and concentrated extract form, and has been promoted as a natural antioxidant "blood purifier," cancer cure and acne treatment. The most abundant component of chaparral is nordihydroguaiaretic acid (NDGA), which was removed from FDA's list of substances considered safe when it was determined to be nephrotoxic (harmful to the kidneys) in animal studies.

At least six cases (five in the United States and one in Canada) of acute non-viral hepatitis (rapidly developing liver damage) have been associated with the consumption of chaparral as a dietary supplement. Additional cases have been reported and are under investigation. In the majority of the cases reported thus far, the injury to the liver resolves over time, after discontinuation of the product. In at least two patients, however, there is evidence that chaparral consumption caused irreversible liver damage. One patient suffered terminal liver failure requiring liver transplant.

The first cases linking chaparral to liver damage in the United States surfaced in August and September 1992. By October, CDC had discussed the reported cases and the potential link between acute, non-viral hepatitis and chaparral in an article published in CDC's Morbidity and Mortality Weekly Report. And by December 1992, FDA had issued a health warning against using this product.

4. Yohimbe. Yohimbe is a tree bark containing a variety of pharmacologically active chemicals. It is marketed in a number of products for body building and "enhanced male performance." Serious adverse effects, including renal failure, seizures and death, have been reported to FDA with products containing Yohimbe and are currently under investigation.

The major identified alkaloid in yohimbe is yohimbine, a chemical that causes vasodilation, thereby lowering blood pressure.

Yohimbine is also a prescription drug in the United States. Side effects are well recognized and may include central nervous stimulation that causes anxiety attacks. Symptoms of overdosage include weakness and nervous stimulation followed by paralysis, fatigue, stomach disorders, and ultimately death.

5. Lobelia. Lobelia, also known as Indian tobacco, contains Pyridine-derived alkaloids, primarily lobeline. These alkaloids have pharmacological actions similar to, although less potent than, nicotine. There have been several reported cases of adverse reactions associated with consumption of supplements containing lobelia. Depending on the dose, lobeline can cause either autonomic nervous system stimulation or depression. At low doses, it produces bronchial dilation and increased respiratory rate. Higher doses result in respiratory depression, as well as sweating, rapid heart rate, hypotension, and even coma and death. As little as 50 milligrams of dried herb or a single milliliter of lobelia tincture has caused these reactions.

Because of its similarity to nicotine, lobelia may be dangerous to susceptible populations, including children, pregnant women and individuals with cardiac disease. Lobelia is nevertheless found in dietary supplement products that are marketed for use by children and infants, pregnant women, and smokers.

6. Jin Bu Huan. Jin Bu Huan is a Chinese herbal Product claimed to be good for "insomnia due to pain," ulcer, stomach neuralgia, pain in shrunken womb after childbirth, nervous insomnia, and spasmodic cough. Jin Bu Huan has been decently (August 1993) reported to be responsible for the poisoning of at least three young children (ages 13 months to 2½ years), who accidently ingested this product. The children were hospitalized with rapid-onset, life-threatening bradycardia (very low heart rate), and central nervous system and respiratory depression. One child required incubation (assisted breathing). All three ultimately recovered, following intensive medical care. Although the product label identified the plant source for Jin Bu Huan as polygala chinensis, this appears to be incorrect since preliminary analyses indicate the presence of tetrahydropalmatine (THP), a chemical not found in polyqala. THP is found, however, in high concentrations in plants of certain stephania species. In animals, exposure to THP results in sedation, analgesia, and neuromuscular blockade (paralysis). The symptoms of the three children are consistent with these effects. An additional case of THP toxicity, reported in the Netherlands, appears to be associated with the same product, and is being investigated. Just last week, three additional cases of toxicity associated with Jin Bu Huan have been reported to FDA—this time a pattern of toxic hepatitis occurred in adults unlike the overdose syndrome that occurred in the children.

7. Herbal Products containing Stephania and Magnolia species. A Chinese herbal preparation containing Stephania and Magnolia species that was sold as weightloss treatment in Belgium has been implicated recently as a cause of severe kidney injury in as least 48 women. These cases were only discovered by diligent investigations by physicians treating two young women who presented with similar cases of rapidly progressing kidney disease that required renal dialysis. Once it was determined both these women had used the herbal diet treatment, further investigation of kidney dialysis centers in Belgium found a total of 48 individuals with kidney injury who had used the herbal product. At the time that a report of these adverse effects was published in February 1993, 18 of the 48 women had terminal kidney failure that will require either kidney transplantation or life-long renal dialysis.

8. Ma huang. Ma huang is one of several names for herbal products containing members of the genus ephedra. Serious adverse effects, including hypertension (elevated blood pressure), palpitations (rapid heart rate), neuropathy (nerve damage), myopathy (muscle injury), psychosis, stroke, and memory loss, have been reported to FDA with products containing Ma huang as ingredients and are currently under investigation. The Ephedras have been shown to contain various chemical stimulants, including the alkaloids ephedrine, pseudoephedrine and norpseudoephedrine, as well as various tannins and related chemicals.

The concentrations of these alkaloids depend upon the particular species of Ephedra used. Ephedrine and pseudoephedrine are amphetamine-like chemicals used in over-the-counter (OTC) and prescription drugs. Many of these stimulants have known serious side effects. Ma huang is sold in products for weight control, as well as in products that boost energy levels. These products often contain other stimulants, such as caffeine, which may have synergistic effects and increase the potential for adverse effects.

9. Willow bark. White willow bark is marketed in products for use by children, and is often promoted as "aspirin-free." White willow contains an ingredient, salicin, that is converted in the body to the same active ingredient (salicylic acid) that is in aspirin. However, unlike aspirin, willow bark's label has no warning as FDA requires on aspirin labeling-that children should not take aspirin for chickenpox or influenza symptoms, because of an association with the serious illness Reye syndrome. Because willow bark shares many of the same chemical properties and the same side effects as aspirin, willow bark should also be avoided by aspirin-sensitive adults.

VITAMINS AND MINERALS

Even the more traditional vitamins and minerals, when marketed at potencies far higher than needed to prevent deficiencies, can pose safety problems. The margin of safety between the RDA and the toxic level varies greatly depending on the nutrient and is unknown for several nutrients. Also, ingredients that are naturally occurring in conventional foods often are concentrated in supplements, making it easy to greatly exceed the normal intakes from conventional foods. The bulk and calorie content of traditional foods somewhat limits the amount of these foods that can be

consumed and, thus, the intake of any one ingredient is limited. A single ingredient in excess may cause imbalances in other nutrients. Excess zinc, for instance, interferes with absorption of copper, an essential nutrient. It is common knowledge that most substances cause adverse effects at some level.

Some risks of nutrients taken at excessive potencies include:

1. Niacin. Niacin taken in high doses is known to cause a wide range of adverse effects. The RDA for niacin is 20 mg. Niacin is marketed in dietary supplements at potencies of 250 mg or higher in both immediate and slow-release formulations. Daily doses of 500 mg from slow-release formulations, and 750 mg of immediate release niacin, have been associated with severe adverse reactions, including gastrointestinal distress (burning pain, nausea, vomiting, bloating, cramping, and diarrhea) and mild to severe liver damage. Less common, but more serious (in some cases life-threatening), reactions include liver injury, myopathy (muscle disease), maculopathy (injury to the eyes resulting in decreased vision), coagulopathy (increased bleeding problems), cytopenia (decreases in cell types in the blood), hypotensive myocardial ischemia (heart injury caused by too low a blood pressure), and metabolic acidosis (increases in the acidity of the blood and urine).

2. Vitamin A. Vitamin A is found in several forms in dietary supplements. Preformed vitamin A (vitamin A acetate and vitamin A palmitate) has well-recognized toxicity when consumed at levels of 25,000 International Units (IU) per day, or higher.

The adverse effects associated with consumption of vitamin A at 25,000 IU or higher doses include severe liver injury (including cirrhosis), bone and cartilage pathologies, elevated intracranial pressure, and possibly birth defects in infants whose mothers consumed vitamin A during Pregnancy. Groups especially vulnerable to vitamin A toxicity are children, pregnant women, and those with liver disease caused by a variety of factors, including alcohol, viral hepatitis, and severe protein-energy malnutrition. There are some studies that suggest vitamin A toxicity has occurred at levels of ingestion below 25,000 IU.

3. Vitamin B6. Neurologic toxicity, including ataxia (alteration in balance) and sensory neuropathy (changes in sensations due to nerve injury), is associated with intake of vitamin B6 supplements at levels above 100 mg per day.

4. Selenium. Selenium is a mineral found in dietary supplement products. At high doses (approximately 800 to 1,000 micrograms per day), selenium can cause tissue damage, especially in tissues or organs that concentrate the element. The toxicity of selenium depends upon the chemical form of selenium in the ingested supplement and upon the selenium levels in the foods consumed. Human injuries have occurred following ingestion of high doses over a few weeks.

OTHER PRODUCTS

Germanium. Germanium is a non-essential element. Germanium has been marketed in the form of inorganic salts and novel organogermanium compounds as a dietary supplement. These products are promoted for their claimed immunomodulatory effects or as "health-promoting" elixirs. Germanium supplements, when used chronically, have caused nephrotoxicity (kidney injury) and death.

Since 1982, there have been 20 reported cases of acute renal failure, including 2 deaths, attributed to oral intakes of germanium elixirs. In surviving patients, kidney function improved after discontinuation of germanium, but none of the patients has recovered normal kidney function.

Germanium products have been the subject of an FDA Import Alert since June 1988.

Because of recognized risks of certain of these products (comfrey and germanium), the dietary supplement industry has recently taken steps to limit adverse effects associated with these products. FDA applauds these efforts.

LABELING ISSUES

Congress enacted the Nutrition Labeling and Education Act of 1990 (NLEA) in response to two developments. First, major scientific advances linking diet and disease prevention have taken place over the last 30 years. Second, throughout the 1980's food marketers tried to capitalize on the diet/disease connection and the supermarket shelves were filled with false and misleading health claims on food labels.

The NLEA expressly authorized FDA to permit explicit disease-related claims for nutrients on the labels of foods and dietary supplements.

In the NLEA, Congress said that health claims for conventional foods were appropriate if, based on the publicly available evidence, FDA determined there was significant agreement among experts regarding the scientific validity of the claim.

However, Congress asked FDA to determine the appropriate standard to be applied to health claims for dietary supplements.

In 1991, FDA issued a proposed rule to apply the NLEA standard of "significant scientific agreement" to health claims for dietary supplements. The agency's experts simply could not discern a public health reason to subject a claim for the health benefits of vitamin C in dietary supplements to a different standard from the one Congress mandated in the NLEA for vitamin C in broccoli or orange juice or for vitamin C added as a fortificant to foods.

FDA's 1991 Proposal generated an intense response from dietary supplement manufacturers and consumers. This reaction was based in part on misrepresentations about what the agency had proposed. FDA and many Congressional offices received angry letters and phone calls from consumers who had been told that FDA was trying to make vitamin and mineral products available only by prescription. The FDA has no such plans.

Another message communicated to Congressional offices was that FDA was trying to restrict the rights of consumers. In fact, FDA fully supports the right of dietary supplement consumers to exercise their "freedom of choice." However, Critical questions exist about how real or free that choice actually is when some of the health-related claims on product labels are not scientifically valid or are incomplete and misleading, and when some of the products themselves may be unsafe.

It is critically important to remember that the proliferation of false and unsubstantiated claims (such as "fat free," "cholesterol free") on conventional food labels in the 1980's occurred precisely because companies, rather than FDA, determined on their own what each claim meant. The promotion of unsubstantiated health claims associated with dietary supplement labeling has mushroomed. If FDA is not permitted to review health claims before they appear in labeling, this promotion of unsubstantiated claims will expand even more.

To illustrate the vastness of this problem, the four part report that I mentioned earlier provides examples of the pervasiveness of unsubstantiated claims currently being made for dietary supplements in the U.S. marketplace and, as I indicated earlier, reviews safety hazards associated with dietary supplements. We believe that the report illustrates a marketplace with a large number of products with unsubstantiated claims.

The report has four parts:

—a list, with more than 500 examples, of products and the unsubstantiated claims currently being made for those products;

—a representative list of recent FDA enforcement actions;

—a list of oral representations of specific products for hypertension, immune system problems, and cancer by employees of stores selling dietary supplements; and

—a narrative report describing serious adverse reactions associated with 16 ingredients marketed as components of dietary supplements.

Because of the vast number of products on the market with unsubstantiated claims or unproven safety, FDA has not been able to and cannot take regulatory action against every product. Even with our cooperative efforts with the States and other Federal agencies, the level of enforcement resources devoted to dietary supplements is relatively small given the size of the industry nationally. The program is administered under a Compliance Policy Guide (CPG) that was issued in June 1987.

The CPG describes FDA's two priorities for enforcement activities, in order of importance, as follows:

(1) products that are potentially harmful when used as directed or in a customary manner (a direct health hazard posing a risk of serious or life-threatening health effects); and

(2) products bearing misleading or deceptive claims posing a significant risk of adverse health effects (an indirect health hazard resulting from the delay or discontinuance of appropriate medical treatment).

Using the above criteria and on a case-by-case basis, FDA has successfully regulated many products as evidenced by the report I have released here today. It is easy to see, however, in a comparison with our report on products with unsubstantiated health claims, that FDA is unable to keep up. FDA just does not have the resources to investigate every product on the market with unsubstantiated claims. It is equally important to understand that there are many competing public health priorities facing FDA, and that the Agency must divide its scarce resources among all of the important issues that demand our attention.

S. 784

A final issue transcends label claims and the safety of dietary supplements. The dietary supplement legislation recently introduced in Congress, S. 784, would sig-

nificantly alter the safety and labeling standards in the FDC Act. For the last 35 years, Congress authorized FDA to place the burden of establishing safety on manufacturers. Current law requires that there be a reasonable certainty of no harm from food ingredients. This standard has given FDA the authority to act swiftly in cases of real harm.

Under the proposed legislation, the burden of proof, in most cases, would switch from the manufacturer to FDA. Ingredient safety would be presumed, and products could be sold until evidence of harm is identified. Exposing consumers to such untested products presents a real risk, especially when taking products for cancer or other serious diseases.

The proposed legislation also would eliminate the need for manufacturers to demonstrate to FDA the scientific validity of a nutrient-disease relationship before making a health claim for an ingredient of a dietary supplement. By contrast, the principal feature of the existing statutory framework is that FDA conducts a review of the scientific literature before authorizing claims about a particular nutrient-disease relationship.

For instance, under current law, if a substance is a food (because it is used for its taste, aroma, or nutritional value) this review is conducted under the NLEA health claims requirements If the product is intended to be used as a drug, Congress requires that the review be conducted under the drug approval provisions of the law.

All of this would change under S. 784. The proposed legislation would permit companies to make the initial judgment. A claim could be made as long as it accurately described the state of the Scientific evidence, which under the bill as written could include a complete lack of evidence. Thus, a claim could be based on mere belief or on one small preliminary study that in no way establishes the nutrient-disease relationship, as long as the label statements accurately portray the state of the evidence. Such a scheme was shown in the 1980's to not adequately protect Consumers against claims that are not Scientifically valid. This is exactly the situation that the NLEA was intended to address. The opportunities for false, misleading, or even fraudulent claims under this standard are obvious.

If this legislation is enacted, FDA would only be able to take action after a claim was already on the product label and in stores. Other provisions in the bill could tie FDA up in lengthy administrative proceedings and litigation before final action could be taken to protect consumers from false and deceptive claims.

CONCLUSION

FDA welcomes the dietary supplement debate. We understand and respect the consumer's right to choose dietary supplements that are safe and bear claims that are scientifically valid. Under these circumstances their ability to choose is well informed and thus truly free.

The explosion of knowledge over the last 30 years represents a public health opportunity of enormous potential value. FDA's responsibility, as always, is to ensure that Americans have access to products that are safe and that actually do what they claim to do.

Mr. Chairman, that concludes our testimony. We would be happy to answer any questions.

PREPARED STATEMENT OF PHILIP R. LEE

Thank you for the opportunity to submit this statement for the record at your hearing today on the very important issue of dietary supplements.

The Department of Health and Human Services (HHS) looks forward to working with all parties to craft a legislative solution ensuring that the public will have full access to dietary supplements that are safe and properly labeled. Preserving this form of access must be the hallmark of any legislative effort.

The Department is also committed to a legislative solution that maximizes the participation of experts in all disciplines of medicine as we resolve the safety and labeling issues related to dietary supplements.

Scientists have learned much over the last generation that has greatly advanced our understanding of the relationship between diet, nutrition, health, and disease. Health-conscious consumers want to be able to take advantage of this new knowledge about diet and health.

The legislative debate underway represents an opportunity to capitalize on these advances by providing consumers with health related information on dietary supplement labels. To assure that the information is scientifically valid, there must be a

clear and sufficiently rigorous standard to judge health claims for dietary supplements.

The CHAIRMAN. Thank you very much, Dr. Kessler. I want to indicate right away that we are interested in trying to find some common ground. I think as Senator Kassebaum and others have said, we are very hopeful that this can be achieved. That is certainly our intention.

For our questioning, we will do 7-minute rounds.

Two of the major concerns are the possible bias of the FDA against supplements—you have heard that argument made—and the long delays involved in approving health claims. If they have some health claims, given what happens in terms of the approval of pharmaceuticals, medical devices, and other products, delays in the approval process may be interminable and effectively deny access to some supplements.

Is FDA willing to open up the approval process to outside experts?

Dr. KESSLER. Absolutely. Mr. Chairman, we did it last week. It was the third Advisory Committee we had on folic acid. We had outside expertise, and we certainly are willing to get the best scientific expertise we can to make these decisions.

The CHAIRMAN. And what about meeting deadlines in deciding on these health claims? What can you tell us about that? That has been something that this committee has been very interested in.

Dr. KESSLER. We are certainly willing to work with this committee on coming up with reasonable deadlines. I need to point out, as you know, when NLEA was passed, and it asked us to evaluate a whole list of claims. Not one dollar was appropriated with that enactment. We have done what I think is a credible job, and I am sure we can do better.

The CHAIRMAN. We will be glad to pursue this issue with you. Isn't part of the problem that there is a great deal of uncertainty about what significant scientific agreement is? What do you think it means?

Dr. KESSLER. Senator, I did not set the term. It was a term that the Congress set in the Nutrition Labeling and Education Act. Let me give you our sense of how we have gone about trying to implement Congress' statutory request.

There is a standard for drugs. It is a very high standard. It requires in all instances adequate and well-controlled trials.

Significant scientific agreement is less than the standard for drugs. It is a much more flexible standard. It allows a much broader range of type of evidence to be considered.

Our Advisory Committee, our outside expert Advisory Committee, voted, for example, 6-5—it was a pretty close call—on the health claim for folic acid. It was certainly not 9 out of 10, 10 out of 10. It was 6-5. It was a pretty balanced panel, but I think the significant scientific agreement circling on that claim was enough with our colleagues in CDC to move forward, and that is why we have proposed allowing a health claim.

The CHAIRMAN. There has been concern over FDA's use of the food additive provisions to regulate supplements. My own sense—and I think there is general agreement—is that we ought to also

create a separate statutory category defining supplements. Would this, do you think, relieve some of the public's anxiety?

Dr. KESSLER. I think you are 100 percent correct, Mr. Chairman. The food additive section, Section 409, has been upheld for multiingredient dietary supplements. The issue is single-ingredient dietary supplements. I do not think the issue was ever clearly addressed by Congress, and I think it is worth addressing.

The CHAIRMAN. Many people, certainly including my colleague, Senator Hatch, feel that manufacturers should be allowed to make claims before FDA reviews them. On the other hand, the NLEA prohibits health claims until they have been reviewed and approved by FDA.

Why do you feel that we must have a pre-market review of health claims, and why is not a postmarket review adequate?

Dr. KESSLER. This is one of the key issues. This is the real hard issue that we need to grapple with.

My concern is that without a—if manufacturers can go to the market and put products like this on the market with these kinds of claims, then the FDA is forced to go chase after these products, and I have to litigate each one case by case. And we will never get—as you see, there are a lot of products on the market, and the murkiness of the current law and the difficulty of litigating these on a case-by-case basis really will open the floodgates.

The CHAIRMAN. My time is running out. What do these items on display represent?

Dr. KESSLER. There are many different products up here. These are products—these are some of 500. We have some more since we have done our report, about another 300 that we have been able to collate of just products that have on their brochures, have on their label, have on their promotional materials, claims.

These products, when our investigators walked into—just like any consumer, walked into a health food store and asked the questions—Do you have anything to treat cancer? Do you have anything to treat high blood pressure? Do you have anything that will bolster the immune system?—these are the products that were sold to them in response to those questions.

The CHAIRMAN. What is a health hazard?

Dr. KESSLER. We did not have a chance to put out all those products. But there are some products out there that do pose real safety problems. I think it is recognized by the dietary supplement industry—some of them are still out there—there are real hazards associated with some. I am certainly not saying all. I do not lose a lot of sleep about some of these, you know, in general. Certainly I do not lose any sleep about vitamins and minerals. But there are certain products out there that pose real significant risks, and they are still out there.

The CHAIRMAN. So if you take a certain amount of an item that may have a beneficial impact to your health, yet take too much or if you are an older person, for example, there might be some health hazard?

Dr. KESSLER. Exactly. Take niacin, for example, sustained release forms or above 500 milligrams a day. The industry itself warns against and tells its members not to sell those products, but unfortunately there are still sustained-release niacin products. Cer-

tainly under good care and monitoring of liver enzymes, a product could be helpful. But in certain forms that are out there without any warnings, there are also hazards that can be associated with them.

The CHAIRMAN. My time is up. Senator Kassebaum?

Senator KASSEBAUM. Dr. Kessler, I would like to ask you, given all the products that you have here, under the regulation as you have published it in the Federal Register, what would happen to all those products?

Dr. KESSLER. Very simple. This product can stay on the market. These products can stay on the market, just a label change. There has to be a label change to comply. That is it.

Senator KASSEBAUM. What about all those on top of the unsubstantiated box?

Dr. KESSLER. Again, those products can be sold. There is no problem. It would require some labeling changes either on the label itself or in the promotional brochures or catalogues that accompany it. That is it. You can still go buy these products if these regulations went into effect. The only change would be changes on the label with regard to disease or health prevention claims.

Senator KASSEBAUM. And that would apply to cancer and hypertension and the other products over there?

Dr. KESSLER. Do not make any promotional statements. That is all it would do. You can buy all these products. We have no problems with that.

I think we do have to think—and it is a small number of products. We have never had a systematic safety evaluation of these products, and I think that—I mean, that is not addressed in our regulations, but it is something that I would ask this committee to consider.

Senator KASSEBAUM. Well, so, when you say that, are you going to require—how are you going to monitor all of the products? Would you require that each——

Dr. KESSLER. Senator, it is very hard. That is why we need a clear standard because we never can monitor all the products. We cannot be out there all the time. We try to get some sense by going out to stores of what is in the marketplace. But I think by setting a clear standard and Congress agreeing and everyone getting together and behind that standard and how that standard should be interpreted—and if we are not interpreting the significant scientific agreement standard right, I am willing to go back and work with you to interpret that right. But I think if there is a coming together and there is a clear standard, then I would hope that everybody could live within those regulations.

Senator KASSEBAUM. But each product, then, each one of those would have to submitted for a clear——

Dr. KESSLER. No. Absolutely not.

Senator KASSEBAUM. Clear standard test?

Dr. KESSLER. No.

Senator KASSEBAUM. Just kind of walk me through this because I am not sure I understand.

Dr. KESSLER. We do not have to do—under NLEA, under the regulations, just as for food, you do not have to submit every cereal or every product that wants to make a claim. It would be on a class

of nutrients, or this class and this disease. That would be applicable to any product that had those nutrients. So we can approve one health claim in general for a nutrient and a disease, and there could be thousands of products or hundreds of products that go out and make that claim.

Senator KASSEBAUM. But I would think on all those products that you have there with immune system claims that there are a number of different nutrients—in each one of those bottles. I think applying a standard is different in many ways for these types of products which have a vast array of different combinations of nutrients in them, and that is what just puzzles me. How you do come up with a clear standard.

Mr. Taylor. If the regulations go into effect, as Dr. Kessler said, there will be a clear standard that says if you want to make a disease-related claim, that claim has to have been evaluated under the significant scientific agreement standard. But then the burden would rest on FDA still, under NLEA as it is currently constructed and our regulations, to go and find instances in which companies were making claims that had not been approved through that system.

There is no requirement for each label to be reviewed by FDA to see whether it is in compliance with all the regulations. The burden still rests on us to go ahead and find products that are not complying.

Senator KASSEBAUM. That is where, it seems to me, the regulatory process can get really very cumbersome and heavy-handed. But, again, you are monitoring the stores that sell the products, right? And at some point, it seems to me the burden of proof ought to rest on the manufacturer rather than the stores that are there with the product.

Dr. KESSLER. I agree with you, Senator.

Senator KASSEBAUM. Because certainly a lot of concern has been raised about heavy-handed tactics such as FDA going in to try and case a store to see what they can find. And that consumes a lot of your time in ways that I would wonder are very beneficial.

Dr. KESSLER. Knowing what is out there in the marketplace—that is why we went out there, to see what is actually in the marketplace. We were being asked by Members of Congress: What are the problems out there? What kind of claims are being made? So we went out to get a sense of what was in the marketplace?

Senator KASSEBAUM. Yes, but I think you would obviously want to find some way in which you are not out there as policemen.

Dr. KESSLER. Absolutely. But certainly if there is a regulation that is in place, there is always an enforcement component after that regulation. But we certainly want the most efficient and least burdensome way, and certainly I agree with you. The middle person certainly should not be having to bear the burden.

Senator KASSEBAUM. Well, my time is about up, but you said in response to Senator Kennedy on significant scientific agreement that the standard would be less than for drugs.

Dr. KESSLER. That is correct.

Senator KASSEBAUM. As I mentioned in my opening statement, what if there were an article in the New England Journal of Medicine, a very reputable journal, concerning a product health claim

that has not yet been FDA-approved, and that article was placed beside the product in the store under dietary supplements in the stores? Would that article be something that you would find be a substantiated enough message? How do we determine whether the claim is valid or not?

Dr. KESSLER. The claim would be subject—I mean, the standard for NLEA is to look at not simply just one study, but to require an evaluation based on the totality of evidence. So obviously you would want to look at all studies.

The issue of whether that New England Journal article—I wish we were dealing with New England Journal articles, New England Journal articles alone. That is one end of the spectrum. It is a very complicated question about what is available. I would certainly lose much less sleep with the New England Journal for which I have enormous respect. On the other hand, we deal with a whole spectrum where the New England Journal is on one side and promotional material is on the other side.

Senator KASSEBAUM. Thank you. My time is up.

The CHAIRMAN. Senator Pell.

Senator PELL. Thank you.

What is wrong with my query that I put before? Why is it not okay as long as the substances do not hurt you? If the consumer wants to take 10 Vitamin C pills or some bark off a tree or something, that is his privilege, as long as it does not hurt?

Dr. KESSLER. Absolutely. I have no problems with that. Where I draw the line, though—you want to take the Vitamin C or the bark off the tree or anything, put it in a bottle, as long as there is no demonstrable safety problem with it, please, feel free. My only problem is when the manufacturer makes a claim and associates a claim with that product. That is where I really draw the line.

Senator PELL. And how do you establish that that bark off the tree, to take that example, would be harmful?

Dr. KESSLER. Again, what we do is there is—we use the scientific tools we have. The problem is that the vast majority of products sold as dietary supplements have never been subject to a systematic safety evaluation. It has never been done. We have done it for a lot of other types of ingredients. We have done it for food ingredients. We have had what we call the Grass review where we have done a systematic review of everything. We have done it for over-the-counter drugs, for example. We have done a systematic safety evaluation.

You can look at the literature. You can look at the studies available. You can see whether there are any known risks. There are many ways to do a systematic safety evaluation.

Senator PELL. To be specific, going back to the bark off the tree which we pulled out of the sky, how do you show that that has harmed? Do you have prisoners eating it as an experiment, or do you try it out on human beings?

Dr. KESSLER. How do we determine the safety of all the other kinds of products that we regulate? There——

Senator PELL. That is not an answer to my question. How do you determine that it is unsafe?

Dr. KESSLER. Unless you look for the evidence, unless you look and see whether there are reported cases in the literature, whether

there are studies on this, there is animal data, there is human data that may be in the literature. Sometimes you have that data. We just did that study. We asked the Society for Experimental Biology to look at the safety of amino acids. It was the first time there was ever a general review of the safety of those. They go. They look at the literature. They see whether there are studies. Sometimes you are going to find studies; sometimes you are not going to find studies.

I certainly support, you know, the statement of we need to get more data so we can have that kind of answer. There are all ways to establish the safety. You can do animal studies.

Senator PELL. Excuse me. I do not mean to be too persistent. But what is the evidence of harm? How do you find out if it is harmful? In other words, you presume the bark off the tree is perfectly all right. How do you find out——

Dr. KESSLER. Again, with regard to safety, I believe that if it is bark off the tree, it should be available. I am willing to have the FDA bear the burden to only deal with those products that have a demonstrable safety problem, and that means if we know about a problem or there is a problem in the literature or it has been fed to animals or there are studies, I mean, we should have the burden on safety. If there is no known demonstrable problems, I mean, I think it—I have no problems. You want to put that bark in a bottle and label it as, you know, tree bark and sell it, and sell it for, you know, whatever price of money, that is fine. Where I draw the line is just do not put any claims on it. But it should be sold unless there is a demonstrable safety hazard associated with it.

Senator PELL. I thought your point was not that it should be sold with improper claims, it should not be sold if it was harmful. And my question to you is: How do you define the bark off the tree as being harmful? Do you try it out on individuals or how do you do it?

Dr. KESSLER. You normally start safety studies by using animal studies and getting preliminary data in animals. That is how we establish the safety of food and food additives.

Senator PELL. So if the dog gets sick, then you know it is harmful?

Dr. KESSLER. I am sorry?

Senator PELL. If the dog gets sick, you feed it to a dog, it will be harmful.

Dr. KESSLER. Pathological observations. That is what the whole field of toxicology is about. How do you determine the toxicity of certain substances when you cannot, when it would not be ethical to do experiments on humans?

Senator PELL. I am not sure you have answered the question, but thank you. [Laughter.]

Mr. Zeller. Senator, let me take a shot at it. If you are the manufacturer of a prescription drug and evidence comes to you of adverse reactions, you have a legal duty to report that information to FDA. If you are a manufacturer of a dietary supplement, you have no affirmative duty.

It makes it very difficult for the agency to get the individual cases of adverse reactions to any of the dietary supplements that we have been talking about. We call that a passive reporting sys-

tem. First of all, the injuries have to occur, and we do not find out about it until after the injuries occur. And then we have to hope that someone in the system—hospitals, doctors, the person who suffered the injury him- or herself—makes the connection between the injury and the supplement and somehow gets the information to FDA. That is very difficult. And we have not been doing a very good job of capturing that data. It is very hard for us to find out.

But for products that are on the market, that is really one of the only ways we have of finding out the cases of the injuries from the bark from the tree.

The CHAIRMAN. Senator Hatch.

Senator HATCH. Dr. Kessler, you have just described in very understandable terms the safety and efficacy process for approval of drugs. In essence, you have said here that the FDA just wants to prevent unsubstantiated claims, right, on food supplements?

Dr. KESSLER. That is correct.

Senator HATCH. Well, doesn't your regulatory scheme prohibit substantiated claims unless approved by the FDA? That is what you are saying, isn't it?

Dr. KESSLER. Senator, what I am saying is——

Senator HATCH. So they cannot make any claims unless you approve——

Dr. KESSLER. Senator, if I could just answer.

Senator HATCH. Sure.

Dr. KESSLER. What I am arguing is the same scheme that you set out, the same framework to evaluate claims for foods. That is the standard, that is the scheme——

Senator HATCH. What you are saying is that your regulatory approach would prohibit substantiated claims unless the FDA approves them. Isn't that right? Answer it yes or no, or else tell me why.

Dr. KESSLER. Senator, you submit the evidence. Just as you set out for foods, the evidence is submitted to the agency. The agency goes out and tries to gather that evidence and then makes a judgment.

Senator HATCH. But if the agency does not approve, then it cannot be substantiated, right? The claim could not be made under your——

Dr. KESSLER. If you have evidence of a substantiated health claim, then you submit that evidence to the agency——

Senator HATCH. I will come back to that.

Dr. KESSLER. OK. Thank you.

Senator HATCH. Because I will get to it when we get into folic acid.

Dr. Kessler, when you released the agency's report on dietary supplements at the House subcommittee hearing on July 29th, you confidently responded to Mr. Bliley's questions, if I recall correctly, about inaccuracies. You said there was a lot of material in boxes, something like you have done here today. Now we have learned that a substantial amount of material in the report should not have been included because the products simply do not exist. Claims were taken from reference books and the like. Now, today, I am releasing my own analysis which details why your report should be withdrawn.

Now, I would like to ask you—I am giving you one more chance to clean up the record, so I will ask you the same question posed by my colleague in the House. Are you aware that there are inaccuracies in the report and that products have been attributed to companies which they do not even manufacturer or sell?

Dr. KESSLER. For every item listed in that report, there is a catalogue or brochure or pamphlet that is available and that we have in house offering for sale that produce. We would be happy to show you the brochure we have or catalogue or pamphlet for each of those products and be happy to supply those brochures.

If we had the catalogue saying that the product is for sale, no, we did not go order the product.

Senator HATCH. Let me just go through a few things with you because I think it might help.

Dr. KESSLER. Sure.

Senator HATCH. Why was the ban on paper book, "The Miracle Nutrient, Coenzyme Q10," listed as a product on page 2, why was this ban on paper book and the authors listed as affirmed when they do not manufacture or even sell a product?

Dr. KESSLER. We would be happy to give you the reference.

Senator HATCH. I have the reference. I have the thing right here. I know exactly what I am talking about.

Dr. KESSLER. Senator, I would be happy to supply the actual document——

Senator HATCH. The fact is you have listed——

The CHAIRMAN. The witness is entitled to give the response without interruption.

Dr. KESSLER. We would be happy to supply the background material on each and every claim. Senator, I certainly—can products be withdrawn? Can products not be actually for sale, I mean, if they are in catalogues? That is possible. We went back, we have tried to update this. If there are some that are wrong, Senator, there is more here.

The point is—I mean, if you look at these, some of these, you know, trouble me and I am sure they trouble you.

Senator HATCH. We have seen these things. Let me just go through a few of them. You have listed a book as the firm. Let me just ask you this: Why was the product P4 on page 25 of the report, why was it attributed to the Herb Nook when the company does not make any product by that name?

Dr. KESSLER. Which product, Senator?

Senator HATCH. This is called P4 on page 25 of the report. It is attributed to Herb Nook.

Dr. KESSLER. Right. And there is a claim for diabetes.

Senator HATCH. But the company does not make any product by that name.

Dr. KESSLER. We would be happy to submit for the record the information that backs up that product.

Senator HATCH. OK. And on page 33——

Mr. Zeller. Could I——

Dr. KESSLER. Go ahead.

Mr. Zeller. All of the information that forms what we call the substantiation for our report was gathered in the weeks leading up to the House hearing.

Senator HATCH. Right. In preparation for the House hearing, right?

Mr. Zeller. That is right. We thought that it was very important——

Dr. KESSLER. And in response to questions by members.

Senator HATCH. Sure.

Dr. KESSLER. I mean, you asked us, for example, Senator, in writing to please explain what problems are out there, what kind of unapproved claims are out there. We needed a sense of the marketplace.

Senator HATCH. Let me list these, and you can provide the information later if you would like.

Dr. KESSLER. Sure, we would be happy to.

Senator HATCH. We asked your staff for all substantiation, and we reviewed everything that they gave us. But now let me just give you a couple of others.

On page 33 you list Vitamin C attributed to Crystal Star Herbal Nutrition. The company said it does not even make or sell that product. They do not even have pamphlets or brochures that advocate Vitamin C. Again, answer it later if you would like, but why include it?

In this so-called bombastic report on how lousy this industry is, Dr. Kessler, 141 of 528 products are wrongly attributed to Crystal Star. Now, I would like to know why these products are incorrectly included in the report and why you did not first contact the company and make known your concerns before you released this, I think, malicious report. Was your purpose to embarrass the company or to correct a perceived problem?

Let me go a little bit farther. And, by the way, we have our staff report criticizing this report, which we will give to the media right now. I think it will blow some of your minds that an agency of the Federal Government can be so incorrect in what they do and testify to before the Congress of the United States.

Now, Dr. Kessler, it is very odd that FDA sent employees undercover——

Dr. KESSLER. Can I just respond to that?

Senator HATCH. Sure.

Dr. KESSLER. I would also like to submit to the record some—I mean, we——

Senator HATCH. I would be glad to have your answer, too.

Dr. KESSLER. This has 500. I would like to submit to you another 300 products with their claims. There is a problem out there. Again, we have documents that show that it is attributable to that company, and there is a problem out there. And you know it and I know it.

What we need to do here, on the one hand there are dietary supplements that are going to have value. There are others that do not have value, and that is what we have to come to grips. How do we allow those that have value and claims that are supportable to do that? But to say there is not a problem here, Senator, I think defies what the reality is in the marketplace.

Senator HATCH. Well, let me just say this to you, that you have just acknowledged that you have no problems with vitamins and minerals.

Dr. KESSLER. That do not make claims.

Senator HATCH. OK. Well, I did not hear it that way, but that is okay if you want to add that to it.

Senator Metzenbaum says that there is no concern about any desire to make vitamins and minerals, herbal products, or amino acids prescription drugs. Your own regulations on page 38 say that the task force recommended that amino acids containing dietary supplements be regulated as drugs.

Am I wrong on that? Go ahead, Mike.

Mr. Taylor. There is a task force report which you have cited and which we have put out for public comment. But the agency has never proposed to regulate amino acids.

Senator HATCH. Not yet. Not yet you have not. But that is what is worrying people all over this country when you can say something like that.

Now, it is not even regulation of drugs. Of course, I do not think anybody at the FDA would dare do that to vitamins and minerals. What the problem is is an approval process that prices these products right out of the marketplace, and some of them, I suppose, might even be considered prescription drugs.

I think my time is up, but I will come back later in the next round.

The CHAIRMAN. Senator Metzenbaum.

Senator METZENBAUM. Dr. Kessler, I am not sure that in your exchange with Senator Pell it was made clear. Senator Pell was asking you, if somebody is attempting to sell tree bark, how you would make an evaluation of safety.

Am I not correct that somebody attempting to sell tree bark would be permitted to sell tree bark and there would be no interference with the sale of that tree bark unless on the label or in the literature the manufacturer or the selling company had said that tree bark can do this, that, or something else as far as your health, but other than that they can sell all the tree bark they wanted? Is that correct?

Dr. KESSLER. That is correct, Senator, unless there was evidence that existed—evidence that people were injured, there were studies in the literature that showed a demonstrable safety—that is the only other additional caveat.

Senator METZENBAUM. Absent that——

Dr. KESSLER. Absent that, you are correct. Absolutely.

Senator METZENBAUM. Anybody can sell tree bark any time if they want to.

Dr. KESSLER. Absolutely.

Senator METZENBAUM. Now, with respect to Senator Hatch's statements—and I think there are 500 and some odd items that you have listed here—he indicates that Crystal Star did not make certain products and certain other companies did not make certain products. How was this list compiled?

Mr. Zeller. Senator, we were able to go out into the field and get catalogues, brochures, books that recommended the use of specific products. We did not purchase the specific product mentioned in each catalogue and brochure, but the catalogues and brochures that any consumer could have gone into any store and gotten for free,

just the way we did, were available and were current at the time that we compiled the report.

If an individual company at the time that we were able to take a brochure off a shelf happened not to be manufacturing that product at that time, we could not have known. But the brochure was on the shelf in the weeks leading up to the Waxman hearing, and the claims being made were claims that any consumer would have been exposed to in these stores in early to mid-July.

Senator METZENBAUM. So in simple language, it is listed here either because a product was bought in a store and a claim was made in connection with that purchase at the time of purchase, or it was listed in a catalogue and the claim was made in the catalogue. Is that correct?

Dr. KESSLER. That is correct.

Senator METZENBAUM. Is that right?

Dr. KESSLER. That is correct.

Senator METZENBAUM. Thank you.

Now, Dr. Kessler, let me be unequivocally clear. Is the FDA going to force consumers to get a doctor's prescription in order to obtain any kind of minerals or vitamins?

Dr. KESSLER. No.

Senator METZENBAUM. Now, are there any if's, and's, or but's to that?

Dr. KESSLER. No.

Senator METZENBAUM. You have multiple entries in this list from the same company. Are we really talking about an industry-wide problem, or is this just a problem of certain companies?

Mr. Zeller. The report that was issued prior to the Waxman hearing and the update that we will provide for the record today, they are both intended as what we call snapshots in time. We did not intend them to be an exhaustive survey of every single health claim being made, either on the label or in the catalogues, for the universe of dietary supplement products. We thought that it would be of value to the Congress and to the public to get a flavor for the kinds of things that you could be exposed to if you walked into a store, either through oral representations, label claims, or catalogue and brochure claims.

We think that the presentation that we made in the report and the update that we have today gives you a flavor for the widespread nature of unsubstantiated claims.

Senator METZENBAUM. Why should we require the manufacturers of dietary supplements to meet the same burden of proof for establishing a health claim that we currently require food manufacturers to comply with?

Mr. Taylor. Because Congress asked us to evaluate the question of whether dietary supplements should be subject to the same standard as foods. We have examined that and thought about that a great deal. We are talking about, under NLEA, nutrients—whether it is in a food or in a dietary supplement form—and we are talking about conveying to consumers disease-related health claims about those nutrients.

We simply are unable to identify any scientific or public health reason why a company who is selling Vitamin C in a capsule should be enabled, empowered to make a disease-related health

claim on a different standard than a company that wants to make a claim about the Vitamin C in their orange juice or vegetable. Broccoli is a common example.

It is the same information about the same nutrient, and it seems to us that in the consumer's interest, so that they can make informed choices, they ought to have assurance that that claim is meeting the same standard, whether the nutrient is naturally occurring in a food or present in a dietary supplement.

Let me make one other observation about the burden here. One issue that has been raised is the expense of research, and if we are starting from scratch with a chemical or a substance we know nothing about and you want to begin to work it up for a disease-related benefit, then you have these significant research costs. There is a vast amount of scientific research being funded through the Government with respect to nutrients, with respect to components of the food supply. And, indeed, the evidence that we have relied upon in approving 8 of the 10 claims that were identified in the Nutrition Labeling and Education Act in 1990 was information out in the public domain, most of it supported by Government research.

So let's be clear that we are typically talking about situations in which we have publicly available literature that we can rely upon, and so supplement manufacturers are not necessarily going to have to bear that burden.

Senator METZENBAUM. Thank you. I think my time has expired.

The CHAIRMAN. Senator Harkin?

OPENING STATEMENT OF SENATOR HARKIN

Senator HARKIN. Thank you very much, Mr. Chairman. I am sorry I was late for opening statements. I just want to make a couple of comments before I get into questions.

Dr. Kessler, as you know, I have a long history of being interested in alternative medicine. I was the one, through my subcommittee on appropriations, that started the Office of Alternative Medicine at NIH 2 years ago because I have for a long time felt that we needed to take a look at alternative medical practices, therapies, and medicines; and also to break down the bias in medical research against the review of worthy treatments that are not in the mainstream of conventional medicine.

I also want to point out that our traditional health care system emphasizes high-technology medicine and I think too often dismisses approaches that may be less costly and more preventative in nature.

I just do not believe that conventional wisdom is always right and that mainstream medicine meets the needs or demands of everyone. I have had a lot of publicity in the last few months. I have been suffering from allergies for years. Doctors prescribed Seldane; they prescribed everything for me. Finally, they said, "You have to start getting shots, Harkin." Until finally someone said this spring to me, "Have you ever tried bee pollen?" I said, "No, never heard of it." I started taking bee pollen. I have not had any allergies since. [Applause.]

They can clap some more. I do not know what is wrong with that. [Laughter.]

But I have been taking this bee pollen, and it has taken care of my allergies. And I do not take any other drugs. And no doctor ever prescribed this to me. And it does not say on it anywhere that it will cure my allergies. Obviously the person that makes this said it would.

My point is that nothing in this product is going to hurt me. I read all the ingredients. As a consumer, I wanted to know what was included and there is nothing that is going to hurt me in this product. It is a food supplement. So why shouldn't I take it and try it?

I think there are a lot of people around this country that are looking for other things to take other than drugs to try to cure some of their ailments.

I point that out because I want to make sure that we are going down the right road. I want to make sure that people have access to these products. I also believe they should be informed and that is why I started the Office of Alternative Medicine because I want some of these things looked into, whether it is cancer therapies or a help with allergies. I want consumers to have a little bit more control over their own health care.

Consumers who take supplements have run into a bureaucracy that I believe has not been thoroughly objective and open to the growing body of evidence that indicates the values of dietary supplements and vitamins and other products. Consumers believe that the FDA wants to place unwarranted and arbitrary limits on vitamin and mineral dosage limits and regulate all amino acids and herbal products as drugs. Again, the FDA needs to clarify its position on this.

Last, let me just say this: We do need to strike a proper balance. We need to ensure access to safe products that show promising health benefits, but at the same time protect the public from harmful products and misleading claims.

My experience with the Office of Alternative Medicine at NIH tells me that overcoming institutional bias is very tough. Very tough. So, again, we need to find a solution to this problem that will not leave the decisions about health claims entirely up to a bureaucracy that has time and time again shown an unwillingness to objectively weigh the evidence and apply the standards set forth in the Nutrition Labeling and Education Act in an appropriate manner.

Having said all that, let me again say that I think that the NLEA, on which I worked for 10 years as a member of this committee and also the Agriculture Committee—is a good agreement.

Are you telling me that what you want to see happen with vitamins and supplements would comport with what we have done in NLEA?

Dr. KESSLER. That is correct, Senator.

Senator HARKIN. One of the problems we had with NLEA and with the FDA is the issue of significant scientific agreement. Is this standard less than the standard for drugs. Everyone agreed on that.

Now, maybe we did not do our job properly. We did not define what significant scientific agreement is. It has come to my attention from various sources that what you have applied thus far

under NLEA for significant scientific agreement is not 51 percent or 55 percent, but more like 80 or 90 percent, which is what you do for drugs.

Now, what I would like to know is: What standard will you apply for significant scientific agreement for dietary supplements and vitamins?

Mr. Taylor. As Dr. Kessler said earlier, we recognize the law is very clear that the significant scientific agreement standard is a more flexible standard than the drug standard. It is more flexible in terms of the kinds of evidence we can consider. We are not required to have adequate and well-controlled clinical trials to reach this finding under NLEA. I think it is also more flexible in terms of the degree of certainty.

When we approve a drug under the drug standard, we have a high degree of certainty about the efficacy of that product. Every single——

Senator HARKIN. Excuse me. Thank you. And I do not mean to interrupt you. I take the admonition of the chairman seriously that we should not interrupt. I guess what I am trying to get at is: Do we need to spell out for you—and perhaps we should—what we mean by significant scientific agreement? Should it be 51 percent? I ask you that: Should it be 51 percent?

Dr. KESSLER. Senator, I think it certainly would be worthwhile sitting down—and we are prepared to work with the committee—to come up with what was meant by significant. The problem ends up being 51 percent, you know, of what? In no two cases, 51 percent of the members of the National Academy of Sciences or the Alternative—it becomes hard to come up with a precise definition when you can plug it into a computer and an equation. That is the hard part.

Senator HARKIN. That is right. And that brings me to the second part of the question. Does the agreement, whatever we would agree on, does the agreement have to only reflect studies published in major medical journals which often have a bias against accepting studies about nutrition in general? How are we going to set this up?

One of the reasons I wanted to set up the Office of Alternative Medicine—and we set up a board, an advisory board—was to have lay people and medical people involved and who do not have an institutional bias against alternative medicines.

I guess my question to you is: Do you see this as a possible way for the FDA to approach this kind of problem? Is there a role for that kind of advisory board made up of nontraditional medical researchers? Is there a role for nontraditional medical journals?

Dr. KESSLER. Senator, NLEA does require, as written in statute, published studies. But on your point, I would welcome the Director of the Office of Alternative Medicine at the NIH to serve on an advisory committee to be able to do these kinds of——

Senator HARKIN. We can all clap for that.

Dr. KESSLER. I have no problems with that. I think the people should be grounded in science. I think the data should be in public view, not in private view. I think the data should be open to everybody.

Senator HARKIN. I also believe that you ought to have some lay people on that board, too, some people that are out there that maybe are not medical doctors but have valuable experience. I do not care whether it has been in homeopathic procedures or acupuncture or whatever it might be. But there are others out there that I think can bring a wealth of experience and knowledge to this kind of a process.

Dr. KESSLER. There are consumer representatives on every advisory committee, and there is no reason why a consumer representative should not be on this advisory committee.

Senator HARKIN. I cannot resist this, since Senator Pell brought up tree bark. I had an individual in my office a couple weeks ago from New Mexico, and I told him I had a sore throat that day. He reached into his pocket, and he brought this out. He got it from some Native Americans in New Mexico. I don't remember what he called it. He said, "Break off a piece and chew it," and sure enough, it was the best anti-sore throat medicine I have ever used. [Laughter/applause.]

So I am just telling you, there are things out there that people are using. Native Americans are using this treatment. I will break you off a piece if you ever have a sore throat. It will help you out. [Laughter.]

Senator METZENBAUM. Dr. Kessler, isn't it a fact that both that little piece and the pills that Senator Harkin is taking for—what is it?

Senator HARKIN. My allergies.

Senator METZENBAUM. For his allergies. You do not have any problem with that as long as there is no misrepresentation about it?

Dr. KESSLER. Absolutely. No problem.

Senator HARKIN. But there should be some way to provide information—now, I do not say that this is going to cure everybody, just like Seldane quit working for me.

Dr. KESSLER. It would be nice to get the data.

Senator HARKIN. But it would be nice for the manufacturer—to be able to say that in certain cases and in many instances, people who have taken this have been cured of allergies. What is wrong with that?

Dr. KESSLER. Senator, the problem is what is the level of proof you want to establish and whether you want to just allow everybody to make any preliminary claim on a product. What is the marketplace going to look like? What are the aisles going to look like?

Senator HARKIN. That is why I agree with you there should be significant scientific evidence. That is what we are trying to figure out here.

If you are going to set the same standard as drugs, I am not in favor of that. If it is the same as the NLEA, I think we can live with that, if, again, it is not as tight as what the drug is and if we have an advisory board or a group that can come up with this evidence that is not biased toward the traditional forms of medicine.

Dr. KESSLER. I do not disagree with that at all, Senator.

Senator HARKIN. Thank you very much.

The CHAIRMAN. Senator Bingaman?

Senator BINGAMAN. Thank you very much, Mr. Chairman.

Doctor, let me ask about some of your comments in your testimony, your written testimony, related to herbs. Some of them, you indicate that, for example, on—and I know nothing about these particular herbs. Let me just preface my statement that way, but it says "germander." I guess that is the way you pronounce it, "germander." You say there is a clear temporal relationship, these cases show a clear temporal relationship between ingestion of germander and onset of hepatitis.

Dr. KESSLER. Right.

Senator BINGAMAN. As you understand your authority right now, you do not have authority to do anything about the sale of unsafe herbs such as this that are on the market?

Dr. KESSLER. We can request a voluntary recall and have done that with a number of products.

Senator BINGAMAN. But you have no authority to do anything more than request voluntary action?

Mr. Zeller. That is right, without initiating case-by-case litigation. That is right. We cannot go in and wipe the shelves clean of——

Senator BINGAMAN. No, I understand. But why can't you initiate case-by-case action against herbs that you believe are causing hepatitis?

Mr. Zeller. Are you talking about litigation?

Senator BINGAMAN. I am talking about any kind of action. If, in fact, you believe that there is a relationship between ingestion of this herb and the onset of hepatitis, why aren't you out there going to court or going somewhere to deal with this problem?

Mr. Taylor. Under the laws that we work under, we can take enforcement action through the courts to try to remove those products from the market. The burden of proof that we bear in the case of an herb that is sold simply as an herb is that we must show that that product is ordinarily injurious to consumers, which means that there has to be a very high level of risk, a very high likelihood that people will be hurt.

That is one of the problems we have in this dietary supplement area where the courts are saying your food additives safety standard does not apply. We are left with this far less effective standard, and that is why we say we do not want to have—we are comfortable bearing the burden to identify products that present demonstrable hazards. Let's just be sure we have an efficient tool for doing that, and we have got some real concerns about the adequacy of that tool.

Senator BINGAMAN. Where is that standard that applies in the case of herbs found?

Mr. Taylor. It is in the food adulteration provision of our statute, Section 401(a)(1).

Senator BINGAMAN. And you have to show that it ordinarily causes health hazards?

Mr. Taylor. If it sold simply as a single-ingredients supplement, the courts are saying we have to show that it is ordinarily injurious.

Senator BINGAMAN. And it is not the same standard that you have to show in the case of broccoli? If, in fact, there were a bunch

of cases that showed there was a relationship between ingestion of broccoli and the onset of hepatitis, you would have an easier time going against the broccoli sales?

Mr. Taylor. The law distinguishes between substances that naturally occur in food and that are sold as a single food ingredient, like the herb or like the broccoli. And in both cases, we have to meet this very serious burden of proving that the food is ordinarily injurious.

If you add a substance to the broccoli, then it is a slightly easier standard for us to meet to prove harm. And if it falls within the legal definition of food additive, then we have the ability to shift the burden of proof to the company. So it is a very elaborate legal scheme, but in the herb case, the burden would be on us, your example, to prove the substance is ordinarily injurious.

Senator BINGAMAN. Well, it just seems to me it is disturbing to see testimony saying that there is a causal tie—I guess that is what I understand—a clear temporal relationship. I assume that means if you eat the one you get the other.

Dr. KESSLER. One happens after a period of time. It is not a necessary cause and effect, but it certainly goes toward that cause and effect.

Senator BINGAMAN. If, in fact, you said the same thing about broccoli that you are saying about germander, I would expect you to be out taking legal action to get broccoli off the shelves. If that meant going to court, that is what it would mean. But it just strikes me that there ought to be authority in the law—and I think there is today—for you to take action against unsafe herbs.

Dr. KESSLER. There is the authority, but under the "ordinarily render injurious" standard. The standard of "may render injurious," which we apply to any added substance in food, which is the possibility of risk, does not apply under recent court decisions to products such as single-ingredient herb products.

Senator BINGAMAN. And have you asked us to change that law?

Dr. KESSLER. I think the whole safety question—I mean, that is not—I mean, the whole safety question needs to be thought about so that we can have some kind of safety review, I mean, that is thoughtful, that leads products on unless there is a demonstrable hazard. You know, a number of other countries have been much more aggressive. I know there are members who say that we have done too much in dietary supplements. You have every right to say to we have not done enough. There are other countries that have acted against and banned whole classes of dietary supplements that we have not done in this country.

Senator BINGAMAN. Yes. I guess the only points I would make are I think there is a clear difference between action that you should take and be able to take to protect the safety of the public—that is on one side, where I think you should have clear authority and there should be no question about it—and then the other issue of whether or not labels about potential benefits are misleading.

Dr. KESSLER. I agree with that, Senator.

Senator BINGAMAN. Substances which we all agree do not cause any harm, but may not cause the benefits, may not bring about the benefits that they are advertised to bring about. I think that is another issue.

Now, on that, for example, there are a lot of folks in my State who drink chamomile tea on the theory that it helps them to sleep. In fact, you know, you can buy Sleepy Time Tea which Celestial Seasonings sells, and they say on the outside—or maybe they do not on that particular company's advertising, but the statement is generally made that this helpful for people sleeping.

I do not know if there is any scientific basis for that. I would not be surprised to find out there is not. It does not seem to me particularly harmful, though, to be telling people that this traditionally has been thought to help people sleep. In my State, there are a lot of folks who sleep better at night thinking that it helps them. [Laughter.]

Dr. KESSLER. Senator, the product should be available. There is no question about that. But if you allow products to be sold with claims, where is the incentive? You can just put claims on that do not have scientific evidence. Where is the incentive? Who is going to develop the evidence for where these products work? That is the issue.

If anyone could go put any claim on the product, then the issue is how are you going to get the evidence on what works and what does not work. And in the end, we would all like to know, whether it is allergies or sore throats or treatment of insomnia, we would like to get the data. There is no incentive, Senator, if you can just put anything you want on the label——

Senator BINGAMAN. Well, maybe I am slicing it too thinly, but, I mean, the main point that I am getting at, I guess, is that some of these traditional herbs that have traditionally been thought to have certain benefits, I do not see that it hurts to be able to say these have traditionally been used with the understanding that they cause these benefits or with the expectation that they cause these benefits. Maybe that is slicing it too thin. I do not know if they cause those benefits or not or bring about those benefits, but it would strike me that we are not doing any great harm to the folks in my State, as long as the herb is safe, allowing it to be sold as it always has.

Dr. KESSLER. What about an herb for diabetes?

Senator BINGAMAN. Well, I think that is a different business because there you are trying to cure a disease. In the case of suggesting that an herb helps with sleeping, that is not, in my view, trying to cure a disease. That is——

Dr. KESSLER. Senator, L-tryptophan was used for insomnia, and we saw real risks associated with that.

Senator BINGAMAN. But that was not because it was mislabeled. That was because it was improperly manufactured. And I support your claim or your desire to ensure that manufacturing processes are appropriate.

Dr. KESSLER. Senator, we just need to be careful on the fact that L-tryptophan was due to manufacture. The science is still out on that. There is a substantial body of science that questions that hypothesis that it was due to a contaminant and not also due to the L-tryptophan itself. We are seeing that kind of disease associated with other brands and, in fact, with other amino acids. So I think we just need to be careful whether it is associated with the manufacturing or not.

Senator BINGAMAN. My time has expired. I apologize to the chairman for going on too long.

Senator Harkin [presiding.] I am not the chairman. Senator Wofford had a question, but he had to leave.

I just had a couple of follow-ups, Dr. Kessler. Again, I think we got it cleared up on the NLEA, and I do believe that we are going to have to give some guidance and direction on what we mean by significant scientific agreement. Second, in terms of who does the studies, this has to be opened up, and I am happy to hear you say that you would be receptive to people from the Office of Alternative Medicine, that you would be open to having people who are involved in alternative therapies and alternative drugs serve in that capacity.

Am I misunderstanding that?

Dr. KESSLER. Not at all, as long as they have a strong scientific base, Senator.

Senator HARKIN. I did not know there was a vote on. The last thing I had was the time period. If we do not put time limitations within which the FDA would have to make a decision about a health claim, I think we are going to have significant and unwarranted delays. I think you responded to that earlier.

Are you willing to go on record in support of a reasonable and specific time period?

Dr. KESSLER. As long as there are resources to meet those times frames.

Senator, the answer is yes, but you enacted NLEA, asked us to evaluate claims. There was not one additional dollar appropriated. I cannot promise you something that I do not have the resources for.

Senator HARKIN. Would 6 months be a reasonable time period?

Dr. KESSLER. If the resources are there to be able to do that so that we have people who can evaluate those claims. But there has been nobody added to do that. So the question comes to resources.

Senator HARKIN. Well, I have to go vote. There is a vote on. We will stand in recess until the chairman returns, the real chairman returns. Thank you.

[Recess.]

The CHAIRMAN. We will come to order.

We apologize to our witnesses. We had to vote. They are expecting others. We want to give a full opportunity. I want to recognize Senator Hatch. I guess Senator Wofford, too, who had to interrupt his questions. We want to give an opportunity to hear some of the other witnesses.

I am a member of the Armed Services Committee. We have Secretary Deutsch who is coming up to speak to us on a C-17 issue somewhat after 6:00. So we will try and do the best we can in terms of the time constraints.

I will recognize Senator Hatch now to get started, and then when Senator Wofford comes back, since he is in the midst of his, we will go to Senator Wofford and then return to Senator Hatch.

Senator HATCH. Well, thank you, Mr. Chairman.

Dr. Kessler, I am disturbed by the last exchange because I feel like you missed the point. You already have given me the documentation for your report. It is about 2 feet high. My staff has gone

through each document that you gave us. Your own documentation just simply does not substantiate the allegations in your report, and that is the point I am making.

To resolve those difficult issues, you know, we need accurate information from the FDA, and your report fails that simple test. So I would like to move on, but I would like you to take——

Dr. KESSLER. Senator, can I ask a question on that? Maybe we can——

Senator HATCH. Let me just finish making this one statement.

Dr. KESSLER. Sure.

Senator HATCH. I would like you to take this staff report to me on false and misleading and read it yourself. I think you are going to be alarmed at the amount of errors that really are in that report that you represented as true to the Congress. Now, I know you personally believed it to be true, so I am not finding any fault with you except that it bothers me that we had to go through that. It is just that simple.

Go ahead.

Dr. KESSLER. Senator, I just want to understand. Maybe I did misunderstand you. What you are saying is that there is a product listed in a catalogue, we reported that it is in a catalogue with a claim, but the company no longer sells it? Is that the problem?

Senator HATCH. I am saying a lot more than that. I am saying that 34 out of 528 products on the list simply do not even exist. I am saying that 142 were assigned to companies that neither manufacture nor even sell the product. Twenty-five products are listed more than once. One of the alleged dietary supplements is not a product, but a paperback book. Three products are listed more than once for the same claim. And 17 of the products on the list were removed from the marketplace prior to the release of the report. And there is a whole raft of other things.

We are saying your report was very flawed, very false, presented to the Congress as true, and people have to say, well, what else is false and not true?

Then I also brought out the other aspect that I felt is an important one. You are talking about substantiation as you view it, but your regulatory scheme would prohibit substantiated claims unless you approve that. And that means an approval system that runs up the cost of these substances.

It comes down to risk. Look, you are talking about 1 in 30 million for somebody to die from a vitamin. You know, you have got a better chance of dying from tripping down the stairs than you do of dying from a vitamin. But if you talk about pharmaceutical products, you are talking about some fairly high risks. That is why we have that very onerous, burdensome, expensive, and difficult safety and efficacy process. But this is not the pharmaceutical industry. These are dietary supplements that basically you have a power right now to take off the marketplace if they happen to be toxic or unsanitary.

Now, let me just go a little bit further. I have asked repeatedly on various occasions why FDA does not use its existing authority to remove products that you claim are false or misleading, such as those you claim are false and misleading in front of you. I am not sure you claim all of them are, but I think that is the implication.

I have never received a satisfactory response from the FDA or from you either.

Now we have a false and misleading report before us, at least as I view it, and I think anybody else who looks at it. Are you going to withdraw that report?

Dr. KESSLER. Senator, I stand by that report. I would be happy to go through your comments.

Senator HATCH. I am asking you to do that.

Dr. KESSLER. I would be happy to go through those comments, but I believe there is substantiation that a claim has been made for each of those products.

Senator HATCH. Fine.

Dr. KESSLER. I would be happy to go through your report, and I would be happy to be back and forth——

Senator HATCH. I am asking——

Dr. KESSLER. And if the number is not 500, Senator, I mean, if it is 300 more, if the number is 450, I mean, there is a problem out there. That is my point.

Senator HATCH. Well, out of 40,000 products, you know, you are going to—there is no question that the industry itself wants to make sure that bad actors are out. But I think if you look at it carefully, the vast majority of all these products are worthwhile and decent products.

I was very interested in the last section of the report, which is the description of the illnesses and injuries associated with selected dietary supplements. For example, you make it clear that the herb comphrey is toxic. Now, would you explain to me why the FDA has not removed that herb from the marketplace? If it is toxic and you know it is toxic, why haven't you removed it?

Mr. Zeller. Senator, we have been examining the safety of comphrey, and the industry—at least it is our understanding that some segments of the industry and trade associations agree and have taken steps on their own to remove comphrey from at least some shelves. So there is agreement within industry of the potential for comphrey to do some harm.

Senator HATCH. Well, if it is toxic, I think you have an obligation to take it off, and you certainly have the authority to remove it. Nobody is asking you to not remove products that are toxic or unsanitary or deleterious or poisonous, or whether it is false and misleading advertising.

Dr. KESSLER. But, Senator——

Senator HATCH. You have that power now.

Dr. KESSLER. Well, let's talk about what power we do have.

Senator HATCH. All right.

Dr. KESSLER. If you take away the food additive authority, then we can only take off a product if it is "ordinarily render injurious" to health. That is the standard, not the "may render injurious." It is a very high standard. It is a "bodies in the street" kind of standard that we have to meet.

I think the "may render injurious" standard probably would be more appropriate, and I think it is something we need to look at. We do not have all the authority. We certainly do not have the authority to look at good manufacturing practices.

The CHAIRMAN. Well, if you do not have the authority, how come you never come up here and ask us for it?

Dr. KESSLER. Senator, I would be happy to work with you on making sure that we have a thoughtful, fair system in place.

Senator HATCH. OK. Let me move on to another subject. It is no secret that I have been very critical of the FDA for its handling of the health claim for folic acid. I think this is a case in point to show how FDA's interpretation of the NLEA "significant scientific agreement" standard is too strict. I think it also points out why your rulemaking process is too cumbersome to allow the public to have speedy access to accurate scientific information about the benefits of dietary supplements. And I think it is no less tragic that 100 babies a month are born per month with preventable birth defects which could have been prevented by the use of 0.4 milligrams of folic acid in early months of pregnancy.

Now, a week before this hearing, FDA finally published a proposed regulation on folic acid, and I want to ask you a little bit about that proposal and the process which led to the proposal.

How long has FDA known that folic acid could help prevent neural tube defects? You told me the other day, you criticized my use on television that you have known about it for 11 years.

Dr. KESSLER. Right.

Senator HATCH. OK. I will give you that opportunity.

Dr. KESSLER. Senator, I went back, and I looked at those studies 11 years ago, and I reviewed all the studies. There was a study 11 years ago, but there was no statistical significance. There was a study back in 1983. It was on multivitamins. It was not on folic acid alone. There has been a hypothesis for many years, but there has been inconclusive animal and human data.

In 1991, there was a published study, an MRC study in England, that showed that women who were at high risk for recurrences—not the general population, the certain segment of women—could benefit. That was the first study that we believe conclusively—that established a link that we thought was sufficient. And the CDC and us the PHS recommended high doses—only high doses were involved in those studies—for high-risk women because there was no evidence at that time that the general population, that women in general, certainly on their first pregnancy, would benefit.

In August 1992, there was a Hungarian clinical trial and also a case-controlled study done by Werler that showed for the first time that the general population of women, at food-level doses, could benefit.

In September 1992, the PHS—the study was in August 1992, and in September 1992 the PHS issued a recommendation that we were a part of that all women of child-bearing age have adequate folic acid throughout their child-bearing years. We convened folic acid experts, a subcommittee, in November 1992, in April 1993, and October 1993. We have proposed adding folic acid to the entire food supply. The problem, as you know well, is the—I wish this were simple, but the margin of safety on folic acid is not very wide. At 400 milligrams it is fine—micrograms, excuse me. When you get to 1,000 micrograms, people start being concerned about the elderly and certain groups at risk for peripheral neuropathy.

Getting this right, when you add something to the food supply—I mean, you are right. I do not lose an enormous amount of sleep about the safety of dietary supplements, but I do lose sleep—if I get the folic acid wrong, the dose wrong, people are going to be consuming both from dietary supplements and from the natural content of folic acid in the food supply, and what we would fortify, we have got to get that right, and we have got to get that right the first time.

It was August 1992 where the Hungarian study was available. We have gone and proposed adding folic acid to the food supply, of allowing a health claim. I think with all due—that we have considered this responsibly.

Senator, I have taken care of these kids. I have taken care of kids born with neural tube defects. Our advisory committee of outside experts voted 6-5 to support that health claim. That was good enough for me.

I think there is good evidence, I think there is a link here. But I cannot promise you, and I do not think anyone could promise you, that there really—that neural tube defects are going to disappear in this country or that, in fact, there are going to be 100 less babies that are born with that. I certainly would hope because I have taken care of these kids.

Senator HATCH. Well, that may be, and I have seen these kids. Frankly, according to the CDC, FDA participated in the CDC workshop in August 1982, 11 years ago, to determine what research should be undertaken to confirm promising studies indicating that folic acid could help prevent birth defects.

We know that 2 years ago CDC recommended that 0.4 milligrams, or 400 micrograms, of folic acid be used in early pregnancy to prevent neural tube defects. You know as well as I that there are 200 babies per month born with neural tube defects, half of which, these scientists seem to estimate, probably could be prevented by this folic acid dosage. And yet FDA still has not approved it. You filed the regulations, but it is going to take another 90 days, plus another 30 days, to be able to have those regulations. And you have five people on your advisory group who voted against it, anyway, 6-5.

To me, how can anybody in this industry make any claims ever? You have only had—well, I will get——

Dr. KESSLER. Senator, please do not look—I mean, it is very important. I know the benefits look great, but please understand with folic acid that there are risks, and there are risks to——

Senator HATCH. I do understand.

Dr. KESSLER. And we have to get the dose right. Obviously, we want to get rid of those 2,500 cases of neural tube defects, but the risk of peripheral neuropathy—and it is real, of nerve damage. If we do not get the dose right——

Senator HATCH. OK. But——

Dr. KESSLER. It is very important to do this right.

Senator HATCH. OK. But was anybody questioning in the whole scientific field that 0.4 milligrams of folic acid would be beneficial in early months of pregnancy? I do not know of anybody.

Dr. KESSLER. Senator, I would be happy to submit the transcripts of our advisory committee. There are certainly those who

question whether there is one magic single ingredient, bullet, that is going to stop neural tube defects. The studies in Hungary and the United Kingdom may not be comparable to the diet of the American public.

Senator HATCH. That was not my question. My question was not whether it will absolutely stop neural tube defects. There are those who believe it will, and they are fairly substantial scientists, if not very substantial scientists. My question was: Is there anybody questioning the dose as a seriously bad dose of 0.4 milligrams of folic acid to work against neural tube defects?

Dr. KESSLER. There has been a lot of work trying to get the dose correct.

Senator HATCH. Well, that may be, but nobody questioned that that dose was safe, that that dose was adequate, that that dose might do something to neural tube defects. And here we are 2 years—actually, 11 years later from when it started. That is pretty substantiated. Now, forget all that. Two years later from when CDC says, my gosh, this will do it.

Dr. KESSLER. Eleven years ago there was a hypothesis; there was an idea. Is that what you want me to act on?

Senator HATCH. If I can say, it was just pointed out by staff that the director of the Hungarian study confirmed that he was going to—their data demonstrated a significant protective effect—that is, zero cases on occurrence with the use of a preparation that contained both a low-dose of folic acid of 0.8 milligrams per day, or 800 micrograms per day, and multiple vitamins.

Now, I do not mean to work this over. It is just how difficult—I think what I am trying to establish is not that you are not doing your job as the Commissioner, but that the FDA, it is almost impossible to get a health claim through the FDA. And here we have something that could have—could have—prevented 100 neural tube defective babies in this country a month.

Dr. KESSLER. And that is why I stood up with the CDC——

Senator HATCH. Two years later.

Dr. KESSLER. No. I stood up in 1992 with the CDC. FDA was part of that announcement and that advisory to all women of childbearing potential. But before I go fortify the food supply and put folic acid—I mean, Senator, the weightiest decisions I have, when you add something to the food supply of 200 million people, which is what, in fact, we are going to have to do if we are going to try to get this number of neural tube defects, because the issue is getting folic acid in the first 6 weeks, I mean, of conception. So you cannot—and with the number of unplanned pregnancies, you cannot always just start the pill or the dietary supplement when you know you are pregnant. So if we want to deal with this, the best way to deal with this is to do this with a combination of dietary supplements and fortification. But getting it right—if we get it wrong, a lot of people can be injured here.

Senator HATCH. I understand. But, Dr. Kessler, why did you link folic acid supplements, that claim, with the fortification policy? Why didn't you just allow food supplements to solve the doggone problem?

Dr. KESSLER. Because you cannot get it right without doing both. Low-income women, the first 6 weeks, women have to be on this

and have folic acid in this intake throughout their years of childbearing potential.

Senator HATCH. Agreed. You can do both.

Dr. KESSLER. And that is what we are proposing.

Senator HATCH. Well, yes. But it is still not going to be effective for another 3, 4, 5 months even if it is approved, those regulations.

Dr. KESSLER. Senator——

Senator HATCH. Listen to me. I know your intentions are good. I know you personally. I think you are a terrific human being. I am mad as hell at you on this particular subject, but that does not stop my friendship. I may seem unfriendly here today, and maybe I am to a degree. But the fact of the matter is that here is an important illustration of something that I do not think is all that unclear, where the FDA could have moved a long time ago, and there might be a number of kids who would not have neural tube defects today who do. And these study results were based on supplements, and no claim can be made to this day in the eyes of FDA.

Let me just move on a little bit because we could go on and on about that. But let me just say this: I understand that prior to the NLEA, FDA was not authorized to approve health claims. Now, isn't it true that prior to the enactment of NLEA you had the authority to require fortification as you do for other supplements in food? Is that right?

Dr. KESSLER. It was 1990 that you gave us the authority to do health claims for food.

Senator HATCH. Why didn't you use that back then to propose fortification for folic acid years ago, even before the NLEA?

Dr. KESSLER. Again, Senator, I think that a fair reading of the science will show that an MRC trial was published in 1991. It was high doses for high-risk women. The August 1992 Hungarian study and the Werler study I think was the evidence that certainly led me to believe, stand up as a pediatrician and say women of childbearing potential should have it. I do not think that evidence was real. There were hypotheses before that. I just do not think——

Senator HATCH. All right. I will accept that. I just say the folic acid thing really makes me angry. I wish Bill Proxmire were here today. I think he would give the Golden Fleece Award to the FDA for its slowness in approving a claim that almost everybody else in the world accepts.

Now, speaking of awards, I do have something for you here today, so you are not going to go away from here poorer than when you came in. I have a beautiful tie for you. I really do. This tie shows folic acid. It shows folic acid, how it looks under the microscope, and I am going to give it to you. [Laughter.]

Here, somebody take that over.

The CHAIRMAN. I thought you were giving him the tie you were wearing. [Laughter.]

Senator HATCH. That tie is still with question marks as to why the FDA cannot act on this process. [Laughter.]

Now, that is folic acid.

Dr. KESSLER. Senator, am I allowed to accept this under the Ethics Act?

Senator HATCH. Sure you are.

The CHAIRMAN. I think it is below $125. [Laughter.]

Senator HATCH. It is right out here in the public. I will take the responsibility, let me tell you.

Now, I have another tie for you—not for you. This one is the way Vitamin E looks under the microscope. Now, I am not going to give this to you. I am pretty sure you are one of the——

Dr. KESSLER. You are going to give that to Senator Kennedy?

Senator HATCH. No. I have been trying to get him to take Vitamin E. As much as we disagree, I would like him to last for a long time. [Laughter.]

The reason I am not going to give this to you is because I am sure you are one of the two doctors out of ten who don't take Vitamin E. But I do know your boss. I know your boss down there at HHS who has indicated in his excellent statement today that he wants to work with us, and he is a great believer in Vitamin E. He is like eight out of ten doctors who know that Vitamin E will cut the risk of cardiovascular disease, something that apparently the FDA does not know. But the New England Journal of Medicine knows, and almost everybody else. But I am going to give this to you to present to your boss because I think he deserves that one.

Now, let me just go a little bit further here. The FDA's use of the food additive theory to remove dietary supplements from the marketplace has been thoroughly repudiated in the courts, and one court likened your approach, as we have said, to Alice in Wonderland. And despite these decisions, is it the agency's intention to continue to use the food additive provisions of the law to remove single-ingredient supplement products from sale?

Dr. KESSLER. No.

Senator HATCH. OK.

Dr. KESSLER. For multiple ingredients, but you asked single ingredients.

Senator HATCH. I said single.

Dr. KESSLER. Single. That is right.

Senator HATCH. OK. Is the agency intending to use the food additive theory to remove multiple ingredients from the marketplace?

Dr. KESSLER. That has been upheld by the courts. That allows us to use the "may render injurious" test, which I think is a reasonable test.

Senator HATCH. OK. Now, on numerous occasions, Dr. Kessler, you and other senior FDA officials have stated that you have no intention of removing dietary supplements from the market and that the dietary supplement industry is using scare tactics to confuse and mislead the public.

Yet in your proposed regulations published on June 18th, you State that, "FDA considers all other uses of amino acids in food"—that is, dietary supplement use—"to represent unapproved and therefore unlawful food additives." Also, your dietary supplement task force report recommended that all amino acid-containing dietary supplements be regulated as drugs and that your intention is to "bring amino acid-containing supplements into compliance with the law."

Now, I will go to Mr. Taylor. Do you intend to regular amino acids as unsafe food additives and/or as drugs?

Mr. Taylor. Let me clarify exactly what we are saying about amino acids. In multiingredient supplements, they fall within the

food additive definition if they are not, as you know, generally recognized as safe. And so that legal theory remains available for multiingredient amino acid supplements. It does not remain available for single-ingredient amino acid supplements.

But let me just be crystal clear about FDA's current State of thinking about amino acids and the whole array of products that were addressed in the Federal Register notice. We have asked questions in that notice. We have asked for the industry to submit information that they believe supports the safe marketing of these products. We have no interest, as Dr. Kessler said, under current authority—indeed, we would favor new statutes that would make this clear. We have no interest in taking any of these dietary supplement products off the market unless there are demonstrable safety concerns.

We have asked the industry to come sit down, give us evidence, help us understand, in the case of amino acids particularly, if there are products that ought to be of concern. An outside group of scientists, the Federation of American Scientists for Experimental Biology, convened a group of scientists, and they evaluated the evidence on the safety of every amino acid supplement on the market today. Some are of low concern; some are of potential concern. But the bottom-line finding was that they were unable for any of those supplements to identify the upper intake level that is safe.

We think it is in the industry's interest for products that are being marketed for very high intake consumption, often by athletes and body builders, to have the science so that we know what the comfortable upper limit is so people will not take too much. But we are not looking to take those products or any supplement products off the market unless there are demonstrable safety hazards.

Senator HATCH. But the quotes that I quoted were accurate, right?

Mr. Taylor. Unfortunately, there is a context for each of those quotes that makes the ADC's position a little different than implied.

Senator HATCH. Well, you can understand why the supplement——

Mr. Zeller. Senator, could I ask for one clarification?

Senator HATCH. Sure.

Mr. Zeller. That is, if you are reading from quotes from the summary of the task force report that does appear in that document, we have to State for the record that the task force—anything in the task force report does not stand as the official position of the Food and Drug Administration on the regulation of any category of dietary supplements.

Senator HATCH. I accept that. I accept that, but you can understand why the dietary supplement industry is alarmed and concerned about having anything in this industry treated as prescription drugs.

Dr. KESSLER. Absolutely. Senator, we want to work with you on the amino acid issue. Canada has taken some very strong, aggressive steps to bring these products under control. We have not. We proposed to do that in 1972. Those never went into effect. I certainly would welcome working with you so that we can make sure that the products on the market are safe.

Senator HATCH. Well, Mike, what is your definition of a demonstrable problem as you have defined it? How do you define that?

Mr. Taylor. Again, you have to use the evidence that is available, and if there is evidence that suggests there is a certain level——

Senator HATCH. Which means they are going to have to make the case.

Mr. Taylor. At a certain level of intake there is a reasonable possibility that someone will be harmed, if we have that affirmative evidence, then we ought to do something.

Senator HATCH. I see. That could take another 11 years.

Mr. Taylor. Well, in the meantime, those products are on the market, Senator Hatch.

Senator HATCH. Yes, I understand. They have been on the market for centuries, to be honest with you. In fact, most of these have been on the market for 4,000 years, and the real issue is risk. And there is not much risk in any of these products, even though you do not like the claims on some of them.

Now, Dr. Kessler, FDA's proposed regulations for health claims for dietary supplements set out four tests of pre-conditions that must be met before a dietary supplement manufacturer can petition the agency to approve a health claim. These pre-conditions are:

One, the dietary substance must be associated with a disease or health-related condition for which the general U.S. population is at risk, or the relevance of the claim must be explained within the context of the daily diet;

Two, the supplement must be a food. A food is a substance that must contribute taste, aroma, or nutritive value and retain that attribute when consumed at a level necessary to justify the claim;

Three, the substance must be safe and lawful under applicable U.S. food safety provisions of the Food, Drug, and Cosmetic Act;

Four, the health benefits must come from the nutritive value of the substance and not from the physiological process provided by the substance.

Now, please give me an example of any herbal dietary supplement that you believe could meet all four of those pre-conditions? Are there any? I do not see any.

Mr. Taylor. Senator Hatch, these conditions that you have described are inherent in the current law as Congress has passed it, and the——

Senator HATCH. My point is: Can any of them meet that?

Mr. Taylor. That is a question that those who would want to submit claims to us under NLEA for an herbal product would address. Some no doubt——

Senator HATCH. Well, you can see why they are concerned, can't you? If they cannot meet all four of those, they are dead, according to you.

Mr. Taylor. Well, that is why——

Senator HATCH. And there is no way they can meet——

Dr. KESSLER. But no one is talking about any of these products going off the market. The issue is whether they can make certain health claims and labels on the product, I mean, that are associated with the products. None of these products we are talking about, Senator, has to go off the market.

Senator HATCH. That is precisely the issue. There is no question about it.

Dr. KESSLER. Right.

Senator HATCH. And if these were pharmaceutical drugs, I can see your point. These are not. These are products that have been in existence for centuries that people have benefited from.

It is my understanding that the agency's policy is to send warning letters to prevent dietary supplement companies from providing information on their labels such as cautions, warnings, or specific dosage recommendations because such information makes these products new drugs. Is that correct? Mr. Taylor?

Mr. Taylor. Well, under the current laws that exist, a product is either a food or a drug. And if you make a disease-related claim for a product that does not fit within the food part of the statute, then under current law the available remedy is the drug authorities. And we have used those authorities.

But this is precisely why Congress is interested, and we agree that there ought to be an effort to recognize that dietary supplements have attributes that, as a practical matter, place them somewhere between what people think of as foods and what people think of as drugs. But under the current statute, we have those two choices to make.

Senator HATCH. OK. Dr. Kessler, the agency recently gave 60 FDA employees awards for their role in attempting to remove evening primrose oil from sale. Now, what safety hazard was the FDA addressing that warranted such intensive use of agency resources and personnel?

Dr. KESSLER. Senator, I can read you the claims made for oil of evening primrose. The list starts with cancer, Raynaud's syndrome. I mean, the list is about 20 or 30. Let me submit those for the record.

Senator HATCH. Remember, the issue is safety I am talking about.

Dr. KESSLER. The claims——

Senator HATCH. Do you know of any unsafe——

Dr. KESSLER. Gamma linolenic acid, and the courts that have looked at that have concluded that the agency's concern about safety was valid. My real concern, though, my real concern is the types of diseases for which oil of evening primrose is promoted, and I would be happy to submit that list for the record.

Senator HATCH. But my question is: What proof do you have that this substance is unsafe? I did not ask you what speculations you have. I asked what proof do you have. I mean, I had a Nobel Prize winner come in from Great Britain and tell me that this has been a very beneficial product.

Dr. KESSLER. For what disease, Senator?

Senator HATCH. He could not even meet with you.

Dr. KESSLER. Again, I mean, this is being promoted for a lot of different diseases, anywhere from hypertension to atopic dermatitis.

Senator HATCH. Safety, Doctor, safety. That is the question. It is not——

Dr. KESSLER. I would be happy to submit for the record the evidence that we submitted in court in animal studies that raised cer-

tain questions. But my major concern about these products are the types of claims that are being made.

Senator HATCH. All right. Let me go to claims, but just one final question on safety. Is an American citizen more likely to die from an adverse reaction to a drug approved by the FDA or a dietary supplement?

Dr. KESSLER. Senator, I am amazed. What do you think—what are in pharmaceuticals? I mean, half our pharmaceuticals come from natural—from plants.

Senator HATCH. What are in dietary supplements?

Dr. KESSLER. Many come from plants, too.

Senator HATCH. Right.

Dr. KESSLER. The origin—I mean, there are chemicals in pharmaceuticals, and those chemicals are found naturally. There are naturally occurring substances in dietary supplements. There is the assumption, you know, that all pharmaceuticals are toxic and natural substances are not, and I think that that belief—I mean, I just think we have been proven wrong on a number of occasions.

Senator HATCH. It sounds to me, though, like you are saying dietary supplements are the same, they are drugs. And, see, that is what worrisome to a lot of people in this industry, too.

Well, let me go to claims because that is a very important part of this.

Dr. KESSLER. Senator, the issue——

Senator HATCH. That is what you are concerned about.

Dr. KESSLER. The issue is, I mean, they are molecules. And you asked me about what kind of harm things can occur from dietary supplements. And there are instances of real harm. I agree with you——

Senator HATCH. I would like you to document them for me because I do not share that same overall, over-riding concern that you do.

Dr. KESSLER. The industry, Senator, agrees that there are risks with certain dietary supplements.

Senator HATCH. Sure, and they are very careful in the industry, by and large, to solve——

Dr. KESSLER. And, Senator, I would appreciate—I mean, we have seen instances where the industry is not following its own guidelines on niacin, selling sustained release where the industry association is saying it should not be sold, selling Vitamin A in doses above what the industry sold, selling Vitamin B6 at above what the—I mean, I would be happy to submit that for the record.

I am not saying—I do not want to exaggerate the safety concerns here. I said earlier I do not lose a lot of sleep. There are certain areas where I have certain concerns. We have some concerns about the amino acids, and I think we have to work it out.

Senator HATCH. Let's work on it together and see if we can do something about it. I share your concerns about dietary supplement products that make claims that they can cure diseases without any or even sufficient scientific evidence or history to validate those claims.

On the other hand, to give the other side of the coin, FDA has only approved a single health claim for a dietary supplement in 30

years, and that is, of course, calcium in osteoporosis in women, white and Asian women.

Dr. KESSLER. Senator, the authority, as you said, was given us to approve health claims for foods. It was given to us in 1990.

Senator HATCH. But our problem is that the agency also tries to prevent companies from making statements of general nutritional fact, and the agency apparently wants even to ban health food stores from distributing a variety of books, Government documents, and even medical reports.

Now, it is my understanding that when promotional literature is making an unsubstantiated claim, the FDA believes that such literature containing the claim should be removed from the marketplace. It is also my understanding that the term "labeling" could include everything from pamphlets, books, brochures, to oral statements made by sales people. Am I incorrect on that?

Dr. KESSLER. The definition of labeling is an expansive one, as upheld by the courts in the last 50 years of food and drug law.

Senator HATCH. Well, if that is so, do you believe that the book, "The Miracle Nutrients, Coenzyme Q10," which is listed in your report as a product making an unsubstantiated claim, should be removed from the marketplace?

Dr. KESSLER. Senator, there is a spectrum. Senator Kassebaum and I talked about that spectrum of information. On the one hand, you have, you know, the New England Journal. On the other hand, you have promotional materials. I think that is something that we need to look at and talk about independent, third-party, peer review information, if it is not promotional in disguise.

You and I see a lot of stuff that is presented and it is made out to be independent, thoughtful evidence, thoughtful documentation, and it is nothing more than promotion in disguise. So it is a difficult question, and we need to be able to deal with that question.

Senator HATCH. All right. Could a dietary supplement product use literature which makes the following claim, "An increased intake of chromium could increase the glucose tolerance of many individuals, and thus might reduce the risk of heart disease"?

Dr. KESSLER. Senator, I was told yesterday—I would be happy to submit it for the record. There are some safety concerns, as I understand it, with chromium that I would be happy to submit. I am not an expert on chromium.

Senator HATCH. I am talking about the claim. Can they make that claim? Would they be able to make that claim?

Dr. KESSLER. If you could just restate it?

Senator HATCH. The actual quote that I gave you was, "An increased intake of chromium could increase the glucose tolerance of many individuals, and thus might reduce the risk of heart disease."

Dr. KESSLER. That is a disease-related claim, on the surface of it.

Senator HATCH. They cannot make it in your eyes?

Dr. KESSLER. That looks like a disease-related claim.

Senator HATCH. What about the following: "Persons with rheumatoid arthritis have a negative nitrogen and calcium balance. To control the progress of this disease, it is important to enhance protein and calcium ingestion"?

Dr. KESSLER. Senator, I would have to look at that language. I could not comment on that.

Senator HATCH. Well, these two statements come from a Department of Agriculture report on human nutrition. Now, should that literature be banned?

Dr. KESSLER. Senator, the Department of Agriculture is not selling dietary supplements, and I have no problems with independent parties making statements that are based on science. The issue is when the manufacturer uses statements to promote a product. That is where 50 years of food and drug law separates the third-party, the independent statements based on science from the manufacturer using something to promote it.

Senator HATCH. Well, as you know, the Centers for Disease Control and Prevention has issued a recommendation for folic acid. Could a manufacturer of folic acid or health food store use this recommendation in conjunction with the sale of folic acid today?

Mr. Taylor. Again, where the law draws the line today—and I think we believe the law should draw the line—is when companies want to link a claim to a particular product and use it to promote and sell the product. It simply needs to meet the significant agreement standard.

Senator HATCH. But you did not answer the question, as far as I am concerned. I am saying, could they make that recommendation in conjunction with the sale of folic acid today? You are saying yes or not?

Mr. Taylor. I am saying——

Senator HATCH. You are saying they cannot, right?

Mr. Taylor. If they are using that claim to sell the product, the law today says—and NLEA stands for the principle that they have to have met the scientific standard.

Dr. KESSLER. And we propose to approve that statement.

Senator HATCH. Six months from now, if we are lucky.

In other words, the point I am making is that the poor little health food store owner could not even hand out a Government pamphlet from Centers for Disease Control or from the Agriculture Department.

Dr. KESSLER. Senator, we have not said that. We have not said that. You asked me whether—you asked me if it is used to promote a specific product, if it is used to accompany a product. If there is independent literature and it is not associated with individual promotion, and it is really true independent literature, I think that is something—there is a spectrum, and I think that is something that we need to sit and consider.

Senator HATCH. In your report on unsubstantiated claims by store employees, several of those employees first consulted a book entitled "Prescription for Nutritional Healing" by James F. Bolch, M.D.—I do not know if I am pronouncing that name right—and Phyllis A. Bolch, C.N.C. The book is based upon their experience using dietary supplements in patient care.

Does the FDA believe that this book should not be available as a reference tool for employees or customers of health food stores?

Dr. KESSLER. The FDA, what we tried to do in that list was to tell you exactly what our experience was. We are not saying one

way or the other whether that is appropriate. We have not taken enforcement actions on those particular areas.

Senator HATCH. That still does not answer the question. Can they use that book? Can they refer to it?

Dr. KESSLER. I would be happy to study that book, Senator.

Senator HATCH. All right. I would like you to do that. I think you might add to your store of medical knowledge if you would. [Laughter.]

The CHAIRMAN. We will have order in the audience now. These witnesses are responding to various questions, and we will ask that the audience be courteous in their response and not demonstrate either approval or disapproval. That is the way this institution has worked and will continue to work.

Senator HATCH. Thank you, Mr. Chairman.

Let me give you a hypothetical that is important. A customer walks into a store and says that he has heard in the news that he should take Vitamin E. The employee quotes a recent article in CSPI's October health letter which suggests that while researchers will not know for sure for several years whether antioxidants can help prevent heart disease, it makes sense to take antioxidants like Vitamin E, beta carotene, and Vitamin C every day.

On the basis of that testimonial, the customer buys products which provide the dosage as recommended by CSPI. Would the employee's use of CSPI's newsletter constitute an "unsubstantiated claim"?

Dr. KESSLER. I would be happy to provide you with an analysis of that.

Senator HATCH. But what is your feeling?

Dr. KESSLER. Senator, I am trained as a lawyer, and you know I am not going to give you a legal opinion. First of all, I am not going to give you a legal opinion anyway because I——

Senator HATCH. I want you to put your legal head aside and tell me as the head of the FDA if you think that is an unsubstantiated claim.

Dr. KESSLER. I think that the oral representations—I mean, I happen to agree with Senator Kassebaum. I am less concerned about, you know, the stores than I am about the information coming from manufacturers. And I think that oral discussions of what is in the New England Journal—I mean, I think that we would like to get it right. I think that CSPI may be wrong on the Vitamin C in that instance. The New England Journal study showed no effect of that. It did shown an effect of Vitamin E.

But I do not have a lot of—I mean, I think oral representations that are done in good faith, that try to capture stuff in the New England Journal, we are not going to go after that, Senator. I have not gone after——

Senator HATCH. I understand. Just two last thoughts, because we have kept you a long time and I have appreciated your patience and the patience of my colleagues.

In your testimony, you refer to the importance of allowing consumers to make informed choices about dietary supplements. But the only information that you would permit these consumers to have is that white and Asian women might take calcium for osteoporosis. While Harvard Hospital releases a study showing that

Vitamin E may help prevent heart disease, a manufacturer or retailer could very easily violate the law, as you are interpreting it, for telling its customers about the study. And that does not make any sense to me, and I am sure it does not to you if you really think about it.

One final observation. Consumers need information to make informed choices, but the current regulatory arrangement impedes instead of educates. It seems absurd to me that Americans have to sneak copies of Government reports, medical journals, scientific treatises to educate themselves on how to lead healthier lives and help protect themselves and their families from spiraling medical costs.

It is time for the FDA to work with Congress to develop a more intelligent approach. I would like to do that. And let me just say this to you: There is nobody that would exceed me in wanting to keep false and bad products off the marketplace. You know that. I know that.

Dr. KESSLER. Absolutely.

Senator HATCH. But, you know, Senator Pell in his comments, if it does not hurt them, why are you giving them such a rough time about it? The fact of the matter is that many people get well because they take placebos, because in a large sense they believe they are doing something that helps them, and psychosomatically it does. A lot of doctors feel that 80 percent of all illness is psychosomatic, or at least psychosomatic-related.

This is an industry where there is a very low incidence of risk. I do admire you and appreciate your efforts in trying to make sure the American consumers are protected. But it is an industry where you really cannot show much in the way of risk from a percentage standpoint, a statistical standpoint, or even an actuality standpoint. And the few times that you do, there are good answers for it, very good answers. And this is not the pharmaceutical industry. This is not the chemical industry. And I think there has got to be a more open mind toward these.

Now, I would like to have you examine the products you brought here today, and really, if you do not mind, I would like you to leave those with us so that we can review them. I would like to examine them and just see what we think about them, if you do not mind. We will take a good look at them as well. And when there are false and misleading things, you have the total authority right now to take them off the marketplace. Where things are unsanitary or toxic or poisonous or deleterious, you have the total power right now to take them off the marketplace.

But what a lot of people out there feel you have been advocating for, especially if you listened to your testimony before the House committees, is basically that they have got to prove every claim that they make before they can put the claims out there. And if they do not, they cannot do it. Therefore, a lot of products that basically are helping people like Senator Harkin—I remember when he started to take bee pollen. You know, I am a believer in bee pollen, but the number of pills that they were telling him to take every day was kind of exciting to me. I thought it was really something. But he did. And I knew he suffered tremendously from that, and he just got better.

Now, you know, when there is not much risk, I think there ought to be a little more leeway. And, frankly, what the FDA has been arguing for over the last number of years has been a lot less leeway. And I do not think your record is a good record with regard to approving claims, and I can see why nobody in this industry would want to leave it up to the FDA to approve claims when you have only approved 1 in 30 years and then one that is so clear-cut it is not even funny, and only 6 out of 11 approved of folic acid supplementation or fortification. You know, that has to bother anybody.

So these are some of the things that are bothering me. Now, I do want to sit down and work with you, with Mr. Taylor and you, and try to resolve this problem. I do not want bad products out there any more than the industry does. The industry has been tainted because of some of the accusations, frankly because of some of these displays that we have had at some of these hearings. And this is a good industry that does an awful lot of good for people, and there are millions, 100 million people who take these substances that feel that they are healthier and better. And I know doctors here in this room right now who are helping patients with AIDS with nutritional therapy to a much more beneficial effect than some are with the known pharmaceutical therapies. And that is not knocking the pharmaceutical therapies. I am just saying nutritional therapy can help in a wide variety of ways. I am sure of it. And I think others would back that up in the scientific community as well.

Well, I thank my——

Dr. KESSLER. Senator, we would be happy to make copies of the labels and give you those.

Senator HATCH. You are afraid we will use those? [Laughter.]

Dr. KESSLER. No, Senator. I think that we stand ready to work with you. Our goals are the same.

Senator HATCH. I hope they are. Thanks, Mr. Chairman.

The CHAIRMAN. Thank you very much, Dr. Kessler. Listening to all the comments here, I think there is some opportunity, at least I believe so—I know perhaps others might not—that we can make some progress.

I think you are going to really have to take a look at those documents. I think you get into a situation in published reports, even by independent medical people, we get into a situation where we are into First Amendment kinds of issues. I am sure you have given a lot of thought to that. I was unfamiliar with exactly what all of that was about, though I think Senator Hatch brought that out. But I am sure you have given this some thought, and I think if we can, we certainly ought to see what guide we ought to have on that type of issue, because it runs into a lot of very, very significant and important First Amendment issues as well.

We thank you very much for your presence.

Dr. KESSLER. Thank you, Mr. Chairman.

Senator Harkin [presiding.] The chairman had to leave for a previously scheduled engaged and asked me to take over, and I am honored to do so.

Our next panel is Dr. Michael Janson, a Massachusetts physician specializing in nutrition and holistic medicine; Patricia Hausman is

a nutritionist who has written several books on supplements; Tim Dyk, representing Nutritional Health Alliance. It says here you have to catch a plane a 6 o'clock, but you are not going to do that, are you? Is 7 o'clock? OK. Good

We will go ahead here, and since Mr. Dyk has to catch an airplane, if you do not mind, we will start with Mr. Dyk. Again, I am sure the chairman has already said that your written statements are made a part of the record in their entirety. Mr. Dyk, please proceed.

STATEMENTS OF TIMOTHY DYK, JONES, DAY, REAVIS & POGUE, WASHINGTON, DC; DR. MICHAEL JANSON, PRIVATE PRACTITIONER, CAMBRIDGE, MA; AND PATRICIA HAUSMAN, NUTRITIONIST AND AUTHOR, GAITHERSBURG, MD

Mr. DYK. Senator Harkin and members of the committee, thank you very much for allowing me to testify here today, and thank you in particular for allowing me to go earlier than the schedule provided for.

I am a partner at Jones, Day, Reavis & Pogue, a former clerk to Chief Justice Warren. I have taught constitutional law subjects at Yale, Virginia, and Georgetown law schools, and I am here today representing the Nutritional Health Alliance, a nonprofit coalition of consumers, health care professionals, natural-products retailers, and dietary supplement manufacturers. With me today is Mr. Jerry Kessler—I understand no relation to Commissioner Kessler—who would be able to answer any questions if you have any.

My testimony is going to be limited to a single subject, and that is the First Amendment implications of the proposed regulation of dietary supplements by the Food and Drug Administration. The question arises because, as Commissioner Kessler said earlier, there is no question as to most of these products that they are safe for sale and can be sold, and the question is how can they be labeled. And what the FDA proposes is to have a pre-clearance procedure which would mean that every health claim would have to be approved in advance, every piece of literature that was distributed in connection with the sale would have to meet the advance approval standards of the FDA, including any Government publication or New England Journal of Medicine publication that was handed out at the point of sale.

Now, there is no question that the First Amendment protects commercial speech. That has been clear since at least 1976. And in particular, it protects commercial speech dealing with health claims.

For a long time, since at least 1931, when the U.S. Supreme Court decided Near against Minnesota, it has been clear that the heart of the First Amendment doctrine in this country is the doctrine barring prior restraint. What the FDA is proposing to do here is to create a regime of prior restraint with respect to these health claims, and it would be no defense to a charge that a health claim had been made that the health claim was accurate. You could go to jail even though the health claim was entirely accurate if you did not get pre-clearance.

The problem is, as this hearing has shown today, that the pre-clearance procedure can take a very long time. Only one claim has

been approved. Only one other claim has been proposed to be approved. And in each case, it took 2 or 3 years to accomplish that.

No regime of prior restraint that the U.S. Supreme Court has ever considered could survive with that kind of procedure. Procedural safeguards are essential in terms of a prompt decision by the administrative agency and prompt judicial review, and the scheme here that the FDA proposes provides neither for a prompt decision by the administrative agency nor prompt judicial review.

The agency has many other weapons in its arsenal to deal with false and misleading claims. No one is suggesting that it should not use those weapons in its arsenal, and those include the seizure provision, which is a very draconian remedy for seizing misbranded products; injunctions; criminal penalties; a whole host of remedies which are perfectly adequate to deal with these problems.

The Hatch-Richardson bill would alleviate these First Amendment problems that are presented by this pre-clearance procedure. The Richardson bill, indeed, would give the FDA 30 days in which to consider and go after any misleading claims using these various procedures—seizure, injunction, criminal penalties, other methods—which it has at its disposal without imposing this regime of pre-clearance.

Thank you very much.

Senator HARKIN. Thank you very much, Mr. Dyk.

[The memorandum of Mr. Dyk follows:]

MEMORANDUM ON REGULATION OF HEALTH CLAIMS FOR DIETARY SUPPLEMENTS

This memorandum addresses the First Amendment implications of the Food and Drug Administration's ("FDA's") regulation of health claims for dietary supplements, as reflected in its proposed regulations under the Nutrition Labeling and Education Act of 1990, and the legislation pending in Congress to alter this regulatory approach.

We have concluded that the FDA's proposed scheme to regulate truthful, non-misleading health claims for dietary supplements presents serious First Amendment concerns. The FDA intends to allow only those health claims that it has approved in advance through a process that may take years to complete. This regulatory approach constitutes a classic "prior restraint" of constitutionally protected speech, which fails to provide those procedural safeguards, such as prompt agency action and judicial review, that the Supreme Court has demanded in similar contexts.

The constitutional deficiencies in the FDA's proposed regulatory scheme for dietary supplement health claims would be substantially reduced by the proposed legislation (S. 784 and H.R. 1709) sponsored by Senator Hatch and Representative Richardson. Other pending legislation on dietary supplements, however, fails to deal with these First Amendment concerns.

1. The FDA's Proposed Regulation of Dietary Supplement Health Claims: The FDA has for some years restricted the ability of manufacturers, distributors and retailers of dietary supplements to engage in truthful speech about the health benefits of their products. In the past, for example, if a health claim appeared on the label of a dietary supplement, the FDA could seek to regulate the product as a drug, and thus to impose sanctions for its failure to conform to the more stringent branding and substantiation requirements applicable to drugs.[1]

In 1990, Congress enacted the Nutrition Labeling and Education Act ("NLEA" or "the Act"),[2] which directed the FDA to promulgate new standards and procedures for evaluating dietary supplement health claims. The Act also directed the FDA to consider authorizing a number of specific health claims concerning the roles of various nutrients and dietary supplements in preventing or reducing the risk of disease.

In response, the FDA issued proposed regulations that would bar all health claims for dietary supplements unless the FDA had expressly approved the claim in ad-

[1] See Food Labeling, 52 Fed. Reg. 28843, 2884 (1987).
[2] Pub L. No. 101–535, 104 Stat. 2353 (1990).

vance.[3] A health claim could thus be made in connection with the marketing of a dietary supplement only if the FDA had previously both (i) chosen to evaluate the merits of a given health claim, which it is not statutorily required to do, and (ii) then concluded that "there is significant scientific agreement, among experts qualified by scientific training and experience to evaluate such claims, that the claim is supported by (the totality of publicly available scientific) evidence."[4] A party who made an unauthorized health claim in connection with the marketing of a dietary supplement would continue to be subject to criminal prosecution.[5]

The proposed regulations were to apply to health claims on labels of dietary supplements, in package inserts, and in literature that is made available with dietary supplements. The FDA's regulation was to extend to "implied" health claims, and to endorsements and other statements by "third parties" that are distributed with dietary supplements.[6]

After the FDA issued its initial proposed regulations to implement the dietary supplement provisions of the 1990 legislation, Congress imposed a moratorium on FDA regulation in this area until December 31, 1993.[7] The FDA issued a new set of proposed regulations on June 18, 1993, which reflected the same regulatory approach as the earlier proposed regulations. The comment period closed on August 17, 1993, but no final regulations have yet been issued. According to the statute imposing the moratorium, if no final regulations are issued by December 31, the proposed regulations will become effective.

In addition, as noted above, Congress directed the FDA in the NLEA to consider six health claims concerning nutrients found in both foods and dietary supplements[8] and an additional four health claims concerning nutrients in dietary supplements.[9] Seven of these claims concerned nutrients with a potentially positive effect on health (e.g., the role of folic acid in preventing neural tube defects), while three of the claims concerned nutrients with a potentially detrimental effect on health (e.g., sodium and hypertension).

The FDA did not issue its proposed regulations on any of these specific health claims until November 27, 1991—more than 12 months after the enactment of the NLEA—and did not issue any final regulations until January 6, 1993. And of the seven positive health claims that Congress directed the FDA to consider concerning the role of particular nutrients in preventing or reducing the risk of disease, the FDA has approved only two such claims applicable to dietary supplements: calcium for the prevention of osteoporosis, and folic acid for the prevention of neural tube birth defects. It took the FDA more than a year to issue the proposed regulation authorizing the calcium health claim.[10] The proposed regulation authorizing the folic acid health claim was not issued until October 14, 1993—some three years after Congress directed the FDA to examine the issue——even though the U.S. Public Health Service and the Centers for Disease Control had long recommended the use of folic acid in foods or dietary supplements to prevent birth defects.[11]

2. The Hatch-Richardson Legislation Concerning Health Claims: Congress is presently considering several measures that would affect the FDA's regulation of dietary supplements, including its treatment of health claims.

The substantially similar legislation offered in the Senate by Senator Hatch and in the House by Representative Richardson would allow health claims for dietary supplements without prior FDA approval in two circumstances:

(i) If a health claim has already been allowed by the FDA for a nutrient when contained in conventional foods, then the same health claim must be allowed for the nutrient when contained in a dietary supplement. There is an exception for circumstances in which the FDA determines, "through rulemaking based upon the totality of publicly available scientific evidence," that consumption of the nutrient in a dietary supplement would not have the same health benefit as consumption of the nutrient in food.

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[3] Food Labeling, 56 Fed. Reg. 60537, 60539–40 (1993).

[4] Id. at 33710. The FDA has also indicated that nutrients intended to be used "in the diagnosis, cure, mitigation, treatment, or prevention of disease," may be regulated as drugs rather than dietary supplements, and this required to meet an even higher standard to permit a health claim. Id. at 33712.

[5] See 21 U.S.C. Secs. 333, 334.

[6] Food Labeling, 58 Fed. Reg. 2478, 2483 (1993).

[7] Pub. L. 102–571, 106 Stat. 4500 (1992).

[8] These claims are: calcium and osteoporosis, dietary fiber and cancer, dietary fiber and cardiovascular disease, lipids and cardiovascular disease, lipids and cancer, sodium and hypertension.

[9] These claims are folic acid and neural tube defects, antioxidant vitamins and cancer, zinc and immune function in the elderly, and omega-3 fatty acids and heart disease.

[10] Food Labeling, 56 Fed. Reg. 60689 (1991).

[11] Food Labeling, 58 Fed. Reg. 53254 (1993).

(ii) A health claim must also be allowed for a dietary supplement if, in the words of the Richardson bill, the claim "accurately represents the current state of scientific evidence." That determination is to be based on "the totality of scientific evidence (including evidence from well-designed studies conducted in a manner consistent with generally recognized scientific principles)." The Richardson bill requires those who intend to make such health claims to notify the FDA at least 30 days before the claim is to be made (e.g., at least 30 days before a label or package containing the claim is introduced into interstate commerce).

Accordingly, a manufacturer, distributor or retailer of dietary supplements would not have to obtain advance approval from the FDA in order to make a truthful health claim. The FDA would, however, have the power to bring suit against those who make or intend to make a health claim, as well as to seize their products under the libel of information procedures of 21 U.S.C. sec. 334, if the FDA determines that the claim is not supported by current scientific evidence.

3. Health Claims Are Protected by the First Amendment: It is clear that truthful speech concerning the health benefits of dietary supplements is protected by the First Amendment.

The Supreme Court has unequivocally held that commercial speech is entitled to First Amendment protection.[12] As the Court has recognized, "significant societal interests are served by such speech," because even commercial advertisements "often carry information of import to significant issues of the day."[13] In addition, commercial speech "serves to inform the public of the availability, nature, and prices of products and services, and thus performs an indispensable role in the allocation of resources in a free enterprise system."[14] The Court has thus observed that "the consumer's concern for the free flow of commercial speech often may be far keener than his concern for urgent political dialogue."[15]

That may be particularly so where, as here, the commercial speech relates to matters of health. Indeed, the Supreme Court and the lower federal courts have specifically acknowledged the protected status of commercial speech on a variety of health-related topics, including prescription drugs,[16] contraceptives,[17] dental services[18] and weight-loss programs.[19]

Although commercial speech may be regulated more extensively than non-commercial speech, the First Amendment imposes significant constraints on such regulation. So long as commercial speech concerns lawful activity and is not misleading, the government may regulate it only to serve a "substantial" interest.[20] Moreover, the regulation must "directly advanc[e]" the government's interest and be "narrowly tailored" to serve that interest.[21] The Supreme Court and the lower federal courts have applied this standard to prevent commercial speech regulations from being applied in circumstances where "truthful and nonmisleading expression will be snared along with fraudulent or deceptive commercial speech."[22] The Supreme Court has recognized, for example, that the states may regulate advertising by lawyers and other professionals. But the states cannot place an "absolute prohibition" on advertisements that contain truthful but "potentially misleading" information, at least where "the information also may be presented in a way that is not deceptive," such as with "disclaimers or explanation."[23]

Some of the speech that the FDA proposes to reach in its regulation of dietary supplement health claims may merit an even greater degree of First Amendment protection. As noted above, not only does the FDA intend to regulate the distribution of materials written by manufacturers, distributors and retailers of dietary supplements, but the FDA also intends to regulate the distribution of materials written by independent third parties. For example, if the owner of a health food store reprints and distributes an article from The New York Times or the New England

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[12] See, e.g., Bolger v. Youngs Drug Prods. Corp., 463 U.S. 60 (1983); Central Hudson Gas & Elec. Corp. v. Public Service Comm'n of N.Y., 447 U.S. 530 (1980).

[13] City of Cincinnati v. Discovery Network, Inc., 113 S. Ct. 1505, 1512 n.17 (1993) (internal quotations omitted).

[14] Id.

[15] Id.

[16] Virginia State Board of Pharmacy v. Virginia Citizens Consumer Council, Inc., 425 U.S. 748, 761(73 (1976).

[17] Bolger, 463 U.s. at 64–69.

[18] Parker v. Commonwealth of Kentucky, 818 F.2d 504, 509–13 (6th Cir. 1987).

[19] Better Business Bureau of Metropolitan Houston, Inc. v. Medical Directors, Inc., 681 F.2d 397, 404–05 (5th Cir. 1982).

[20] Board of Trustees of State Univ. of N.Y. v. Fox, 492 U.S. 469, 475 (1989); Central Hudson, 447 U.S. at 566.

[21] Fox, 492 U.S. at 475, 480; Central Hudson, 447 U.S. at 566.

[22] Edenfield v. Fane, 113 S. Ct. 1792, 1799 (1993).

[23] In re R.M.J., 455 U.s. 191, 203 (1982).

Journal of Medicine about a particular nutrient found in dietary supplements, he may be deemed to be making health claims subject to FDA regulation and even criminal prosecution.

Newspaper and journal articles and similar materials written by persons not engaged in the marketing of a commercial product serve the same important First Amendment interests, regardless of whether they are distributed by the original source (e.g., The New York Times) or by those who sell dietary supplements (e.g., Mary' s Health Food Shop). In Bolger v. Youngs Drug Products Corp.,[24] the Supreme Court recognized that the commercial speech label could not automatically be applied to "informational pamphlets" distributed by a contraceptive manufacturer that concerned birth control and sexually transmitted diseases. The Court allowed the pamphlets to be treated as commercial speech only after considering a variety of factors, including whether the pamphlets were "advertisements," as the manufacturer conceded that they were, and whether the pamphlets made reference to "a specific product."[25] These criteria may be difficult to satisfy in the case of informational materials concerning the properties of particular nutrients—especially where, in contrast with Bolger, the materials are written by third parties who are unaffiliated with those marketing the dietary supplements.

4. The FDA's Proposed Regulatory Scheme Does Not Satisfy Constitutional Standards: The FDA's proposed regulation of dietary supplement health claims is constitutionally suspect because it would amount to prior censorship of presumptively protected speech.

The Supreme Court has emphasized that "(a)ny system of prior restraints of expression"—that is, where the government decides in advance whether or not to allow particular speech——"bear(s) a heavy presumption against its constitutional validity."[26] According to the Court, this special aversion against prior restraints reflects the view that "a free society prefers to punish the few who abuse rights of speech after they break the law than to throttle them and all others beforehand."[27]

The Court has thus held that the First Amendment mandates "rigorous procedural safeguards" whenever the government seeks to impose such prior restraints.[28] These safeguards include prompt administrative adjudication of whether or not the speech is to be permitted, as well as prompt judicial review of any administrative decision to prohibit the speech.[29] The Court has explained that such safeguards are essential when a government official or agency is given the unusual authority to censor speech:

Because the censor's business is to censor, there inheres the danger that he may well be less responsive than a court—part of an independent branch of government—to the constitutionally protected interests in free expression. And if it is made unduly onerous, by reason of delay or otherwise, to seek judicial review, the censor's determination may in practice be final.[30]

While the Supreme Court announced these procedural safeguards in the context of prior restraints on sexually explicit materials,[31] the lower federal courts have recognized that such safeguards are also necessary in the context of prior restraints on commercial speech.[32] For example, in Space Age Products. Inc. v. Gilliam,[33] a state agency issued a cease and desist order against a home products company that was accused of operating an unlawful "pyramid distribution scheme." The court held that the company had a First Amendment right in these circumstances to "a prompt determination of whether the speech involved is within the gambit of the prohibition (against such schemes) ."[34] The court suggested that the company's rights may well

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[24] 463 U.S. at 66–67.

[25] Id. at 66.

[26] Bantam Books, Inc. v. Sullivan, 372 U.S. 58, 70 (1963); accord Freedman v. Maryland, 380 U.S. 51, 57 (1965).

[27] Southeastern Promotions, Ltd. v. Conrad, 420 U.S. 546, 559 (1975).

[28] Bantam Books, 372 U.S. at 66; accord Freedman, 380 U.s. at 58.

[29] Southeastern Promotions, 420 U.S. at 560; Freedman, 380 U.S. at 58–59; Bantan Books, 372 U.s. at 70–71.

[30] Freedman, 380 U.S. at 57–58.

[31] The Supreme Court has not yet applied these standards in the context of commercial speech. See Posadas de Puerto Rico Assocs. v. Tourism Co., 478 U.S. 328, 348 n.11 (1986); Central Hudson, 447 U.S. at 557 n.13. In Posadas, while the majority did not reach the prior restraint issue, Justices Stevens, Marshall and Blackmun would have applied the prior restraint doctrine to commercial speech. 478 U.S. at 359, 361 (Stevens, J., dissenting).

[32] See, e.g., United States Postal Serv. v. Athena Prods., Ltd., 654 F.2d 362, 367–68 (5th Cir. Unit B 1981), cert. denied, 456 U.s. 915 (1982); Space Age Prods., Inc. v. Gilliam, 488 F. Supp. 775, 782–85 (D. Del. 1989).

[33] 488 F. Supp. at 782–85.

[34] Id. at 785.

have been violated when the state agency did not make its determination until six months after its issuance of the cease and desist order.[35]

It cannot be disputed that the FDA's proposed regulations would establish a system of prior censorship by forbidding health claims for dietary supplements. Manufacturers, distributors and retailers would be barred from engaging in speech about the health benefits of these products—unless that speech had been specifically approved in advance by the FDA. This is precisely the sort of "licensing schem(e) requiring speech to be submitted to an administrative censor for prepublication review" that the Supreme Court regards as a classic prior restraint.[36]

The FDA's proposed regulation of dietary supplement health claims would not assure the prompt agency action and prompt judicial review that the First Amendment demands of regulatory schemes involving prior restraints. The NLEA itself merely directs the FDA to promulgate "a procedure and standard, respecting the validity" of health claims for dietary supplements. The NLEA thus does not require the FDA to complete its consideration of health claims for dietary supplements within any particular period of time. Indeed, after Congress directed the FDA to consider several specific health claims in November 1990, the FDA did not issue final regulations concerning any of those claims until January 1993.[37] It did not issue proposed regulations authorizing a health claim for folic acid (or folate) until October 1993.[38] The NLEA likewise does not require that FDA decisions denying health claims be subjected to prompt judicial review.

The NLEA does prescribe some procedures, including timetables, for FDA consideration of health claims for foods.[39] The FDA has said in its latest proposed regulations that the same procedures are to be applied to health claims for dietary supplements.[40] These statutory procedures allow "(a)ny person" to submit a petition requesting that the FDA authorize a health claim. The FDA must either deny the petition or "file the petition for further action" within 100 days after receiving it. (The statute imposes no constraints on the FDA's discretion to deny a petition.) If the petition is filed "for further action," the FDA then has another 90 days in which to either deny the petition or "issue a proposed regulation to take the action requested in the petition."

These procedures thus allow the FDA to take up to 190 days—that is, six months—to decide whether to issue a proposed regulation granting or denying a health claim. And they provide no timetables for issuance of a final regulation or for judicial review of the regulation. It could thus take years for a particular health claim to be finally resolved by the FDA and the courts. To put this in perspective, the Supreme Court in Kingsley Books, Inc. v. Brown[41] upheld a scheme of censorship that ensured a final judicial determination within three days, and in Southeastern Promotions, Ltd. v. Conrad[42] struck down a scheme in which a final judicial determination occurred within five months.

The FDA's proposed regulatory scheme for dietary supplement health claims thus presents serious First Amendment problems, given the absence of any of the procedural safeguards for prompt administrative action and judicial review that the Supreme Court requires when the government engages in prior censorship. This scheme poses a very real danger that, as the Supreme Court has warned in its prior restraint decisions, "the censor's determination may in practice be final."[43]

5. The Hatch-Richardson Legislation Would Significantly Reduce These Constitutional Concerns: The Hatch-Richardson legislation would limit the FDA's authority to impose prior restraints on truthful, non-misleading health claims for dietary supplements. In contrast to the FDA's proposed regulatory scheme, which would prohibit all health claims unless specifically approved in advance by the FDA, the proposed scheme would allow all claims consistent with current scientific evidence without advance FDA approval.

To be sure, the FDA could seek to silence health claims once they had been made, or during the 30-day notice period provided by the Richardson bill, if the FDA determined that those claims did not reflect current scientific evidence. But the FDA could prevent such a health claim only by taking some affirmative act, such as by causing libel of information and condemnation proceedings to be initiated under 21

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[35] Id.
[36] Alexander v. United States, 113 S. Ct. 2766, 2773 n.2 (1993).
[37] See Food Labeling, 56 Fed Reg. 2537-2846 (1993).
[38] Food Labeling, 58 Fed. Reg. 53254 (1993).
[39] See 21 U.S.C. sec. 343(r)(4)(A)(i).
[40] 58 Fed. Reg. at 33706.
[41] 354 U.S. 436 (1957).
[42] 420 U.S. at 560.
[43] Freedman, 380 U.S. at 57–58.

U.S.C. sec. 334. This process would assure reasonably prompt agency action and judicial review of disputed health claims.

In contrast to the Hatch-Richardson legislation, the dietary supplement bill introduced by Representative Collins (H.R. 2923) does nothing to rectify the First Amendment deficiencies in the FDA's proposed regulatory scheme. Rather, the Collins bill would continue to bar all health claims for dietary supplements——regardless of the amount of scientific evidence in support of those claims—unless they had been approved in advance by the FDA. Moreover, the Collins bill provides no new procedures for timely administrative or judicial review of FDA determinations concerning dietary supplement health claims.

In addition to restricting the FDA's ability to engage in prior censorship of dietary supplement health claims, the Hatch-Richardson legislation would promote First Amendment interests in other ways. The legislation would focus the FDA's regulatory attention on only those health claims that are not consistent with current scientific evidence. This standard would be more "narrowly tailored" to serve the government's only "substantial" interest in this area—to prevent false or misleading health claims—without also barring those health claims that are truthful and thus constitutionally protected.

The legislation would also advance First Amendment interests by providing for timely administrative and judicial review of adverse FDA determinations on health claims and other dietary supplement issues. The legislation prescribes procedures for manufacturers, distributors and retailers to seek initial review of such FDA determinations within the Department of Health and Human Services. If the administrative appeal is resolved in the FDA's favor, the party could then seek review in federal district court, where any factual issues would be decided de novo. In addition, the legislation would clarify that the government's institution of a libel of information to condemn a dietary supplement would constitute final agency action for purposes of judicial review.

In sum, the Hatch-Richardson legislation would significantly reduce the First Amendment concerns posed by the FDA's proposed regulation of dietary supplement health claims. The legislation would prevent the FDA from imposing this system of constitutionally suspect prior restraints, without the necessary procedural safeguards for prompt agency action and judicial review. And the legislation would institute a new system of FDA regulation of only those health claims that are not supported by current scientific knowledge—a system that is more "narrowly tailored" to target those false or misleading health claims that the government has a "substantial" interest in preventing. It would thus promote all Americans' right under the First Amendment to engage in truthful speech about the value of dietary supplements.

Respectfully submitted,
JONES, DAY, REAVIS & POGUE
Timothy B. Dyk
Barbara McDowell

Senator HARKIN. Next, Dr. Michael Janson.

Dr. JANSON. Thank you, Senator Harkin. I am delighted to be here, and I am not going to bore you with all the things that I have submitted in writing, which are only going to take away from time. I have great respect for your encouragement of the kind of medicine that I practice.

Based on the testimony today, I am the only other physician on this panel testifying today, as far as I know, besides Dr. Kessler. And I am really disturbed by a number of the things he said which were erroneous scientifically. There is no danger of folic acid being toxic, which is something that he put out, in any dose that I have been aware of in 17 years of clinical practice. I have been out of medical school for 23 years. There is a chance that folic acid intake can mask a Vitamin B12 deficiency, but we have good methods of evaluating that now which would probably not allow for that as a problem. It does not have any direct toxicity. I am also convinced of the same thing with chromium, which he said has some toxicity questions concerning it.

Based on the testimony I have heard today, I have a great fear that there is no possibility that the FDA will be able to regulate

this industry in an unbiased fashion. And I think they need strong controls on the way they are going to do that if they are, indeed, given that authority, more so than perhaps the dietary supplement bill would allow.

As you know, I am a fellow and member of the Board of Directors of the American College for Advancement in Medicine and the chairman of their Scientific Advisory Committee. I am also the vice president of the American Preventive Medical Association. I know many of my colleagues are concerned with the way the FDA has been behaving in terms of dietary supplements, and that is, I believe, why I was invited here today. I thank you for that invitation.

Half of all Americans take dietary supplements, and they have done so for many years quite safely. The safety issue that the FDA brings up with the supplements that are specific in their testimony are really spurious most of the time with their long history of bias against dietary supplements and the more recent evidence of it with their removal of black currant oil capsules from the market. When in court Dr. Kessler said that the court confirmed their suspicion of toxicity, and that is not true. The court found that there was no suspicion, and, in fact, the FDA's own scientists and toxicologists testified that they were unaware of any safety problems with this product. So I think it is very misleading, and I think there is no way for Dr. Kessler not to have known that that statement was not correct.

He also mentioned L-tryptophan, and I know I have articles here from the New England Journal of Medicine and from the Journal of the American Medical Association in 1990 showing that the L-tryptophan problem was not an L-tryptophan problem but a contaminant. And he must know that more recently, within the past month, Dr. Clue at Georgetown University reported at a rheumatology meeting that the EMS occurs without supplements and also his conclusion that it was not related to tryptophan but a contaminant. This month the CDC reported in the Archives of the Contaminants and Environmental Toxicology that only a contaminant could be linked to EMS, and "A Contaminant in L-tryptophan" was the title of the article. That was published in 1993, Volume 25, page 134, by Dr. Hill. There is just no reason to believe that this continued diatribe against tryptophan is really honest.

If I had a half-hour with the three of you, and I am sure with many other people on the committee who are not here at the moment, at the end of a half-hour you would be taking a lot more dietary supplements than you are now, and you would probably be taking things that the FDA has ever intention of either regulating strictly, taking them off the market, or have already done so, and I take them myself. Coenzyme Q10 is a good example. They have no provision for a supplement in their regulations, and in their testimony in the summer, they said that they plan to regulate these things. Now, they said today they do not plan it, and the fact that within a couple of months, with all the public outcry, they have changed their position, apparently changed their position, I have a great fear that they are not going to be able to be consistent and that when the hearings are over they will go back to the other position. And I am just not satisfied that they are going to be doing the things as provided by law.

In 17 years of clinical practice, I have seen almost no side effects from dietary supplements and no serious side effects at all. FDA-approved prescription drugs kill more people every year than car accidents, and they also claim that they are concerned for safety and for efficacy. In their own report in "New Developments"—and this is 1990 in March—they talk about an herbal product called Serenoa repens, which is a saw palmetto berry extract which shrinks the prostate gland in adult middle-aged men. And saw palmetto and Coenzyme Q10 are perhaps some of the things that the committee members would consider taking at some point in their lives—not all of the committee members, but some of them. [Laughter.]

In this report, they showed statistically significant improvement from the saw palmetto berry extract in prostate enlargement in every parameter of urinary flow, which is the problem related to prostate enlargement, and they said that this was statistically significant but not clinically significant. But in every case, in every parameter that they measured, it was better than the drug that they finally approved for the same purpose. The drug has known side effects, and in fact, so severe that women who are partners of men who are taking this drug are cautioned not to contact the semen of these men and not to handle the crushed pills because they might be exposing their potential fetuses to birth defects. So the FDA approves a drug that is dangerous compared to our herb, and they deny the value of the herb when the studies show that it is better than the drug. Now, to me, that is a pretty clear bias, and they say they are not biased against supplements. They just need to see the evidence.

A colleague of mine, Dr. Rimland, said: "You can show the FDA all the evidence in the world. They are not going to buy it because they do not believe dietary supplements are valuable." So you cannot substantiate any claim according to their standards, and Dr. Rimland, the colleague I mentioned, said, "You could more easily convince a shark to become a vegetarian." It is just not fair that products that I have used for so long—and I really could not practice without them—might be removed from the market, and the information about them might be unavailable to me because I cannot always do all this research in the literature. I am happy when suppliers and purveyors of nutrients send me scientific articles. I do not consider that labeling, and I do not consider these products safe. And I really—even if they were mislabeled, that is not a real public health risk. The real public health risk is not having the information available that is going to prevent disease and not having the ability to purchase supplements with accurate information.

The reason people in health food stores give inaccurate information sometimes or unapproved information is because people have no way of legitimately getting this information. So that is one of the reasons that there is such a serious problem, and obviously you have my written testimony. I made a number of specific points. I could not really practice medicine responsibly without these substances that the FDA, I know, has already removed from the market. I have had trouble getting some of them.

Why they suggest that a combination product could be controlled under the food additive provision because Vitamin E is mixed with

gamma linolenic acid, yes, it could be under the provision, but why would it be since both products are perfectly safe? And yet using that provision, they have attempted to regulate even in primrose oil because it contained Vitamin E. It is totally inappropriate, and it really speaks unfortunately about what the FDA is doing. They misrepresent the dangers of supplements, and it would really be ridiculous in America to have restrictions on the availability of dietary supplements or information about them, but ready access to alcohol, tobacco, Big Mac's with all their known problems. And I really strongly support the Dietary Supplement Health and Education Act as it is written.

Thank you.

Senator HARKIN. Thank you, Dr. Janson.

[The prepared statement of Dr. Janson follows:]

Prepared Statement of Michael Janson

My name is Michael Janson. I am a physician in Massachusetts with offices in Cambridge and on Cape Cod. I received my M.D. from Boston University twenty-three years ago in 1970, and then did a four-year residency in pathology. I developed an interest in nutrition, preventive medicine and vitamin therapy after graduation, and proceeded to found the Cambridge Center for Holistic Health in 1976 and more recently, the Center for Preventive Medicine, in Barnstable, on Cape Cod.

I am a charter member of the American Holistic Medical Association. I am a Fellow and member of the Board of Directors of the American College for Advancement in Medicine, and the Chairman of their Scientific Advisory Committee. I am a Fellow of the International Academy of Nutrition and Preventive Medicine. I have a weekly Boston area call-in radio show reporting the latest in nutrition and preventive medicine. I am also the Vice President of the American Preventive Medical Association.

I want to thank Senator Kennedy and the members of this committee for the opportunity to clarify some of the important issues regarding dietary supplements and the FDA. I am particularly eager to relay the concerns of many of my patients and radio listeners in and around Massachusetts about their continued ability to purchase all forms of dietary supplements and to have information about their use. Many ideas relating to this form of medical care and self care are coming out of Massachusetts. You are no doubt familiar with the reports on alternative health care, by Massachusetts physician Dr. David Eisenberg, from the recent programs with Bill Moyers.

One-third of all Americans are choosing to visit alternative health care practitioners and one-half take dietary supplements because they are willing to take personal responsibility for their own health. This costs the government nothing, and it can be clearly demonstrated that it will save the government a large amount of money while enhancing the health of most Americans with no significant risks.

The FDA has a long and clear history of bias against dietary supplements, recently evidenced by their unwarranted removal from the market of black currant oil capsules, claiming that it was an unsafe food additive, and that the food to which it was being added was the gelatin capsule in which it was packaged. This was thrown out of court by three judges who said that the FDA was using "Alice-in-Wonderland reasoning in an effort to make an end-run around the law." FDA's own experts testified that this oil is perfectly safe. Following FDA guidelines, the Texas Department of Health confiscated Coenzyme Q10 from health food stores. Coenzyme Q10 is a remarkable, harmless substance that helps so many patients that I could hardly practice conscientiously without it. I have no doubt that it would be unavailable without passage of S. 784.

The FDA has helped to block the dissemination of information about Serenoa repens, a standardized extract of the saw palmetto berry, that can help shrink enlarged prostate glands in middle-aged men. Meanwhile, they endorse Proscar, a more expensive, more toxic, and less effective drug, for the same purpose. They knew that the published evidence showed the superiority of the Serenoa, but their action exposed 10 million men to unnecessary risks.

CSPI has referred to this bill as the "snake-oil promotion act." This is offensive to me and thousands of my colleagues who have used supplements safely and effectively for many years. In fact, I started using them because of the vast medical literature substantiating their benefits. I have seen these benefits in seventeen years of clinical practice. I have seen almost no side effects from these products in all these years, and no serious side effects. FDA approved

prescription drugs, when used as directed, continue to kill and injure many people annually. Dietary supplements are incredibly safe. I have been taking large amounts of them myself for many years. FDA's stated concerns about the safety of such products is not justified. Supplements are probably safer than the water that you drink to take them.

The case of L-tryptophan is important, because the FDA continues to use it as an example. It was published in both the New England Journal of Medicine and in the Journal of the AMA, in 1990, that the eosinophilia myalgia syndrome was due to a contaminant in a particular company's product. In fact, L-tryptophan has not been removed from the market, but only from the health food stores. It is still used in intravenous feeding and in infant formulas. The FDA has adequate safety data to permit it as an ingredient in these products.

No one wants to be the victim of fraud, and labels need to be accurate. S. 784 vigorously addresses fraudulent labelling. However, misleading labels are not as serious or dangerous a problem as the potential loss of health-enhancing dietary supplements. But FDA's proposed regulations, which essentially ban all health claims for dietary supplements, violate the intent of the NLEA. A textbook about supplements, or scientific studies, cannot be provided by a health food store, according to FDA. Last year the New York Times published an article supportive of the value of dietary supplements, but a manufacturer cannot send that article, nor any supportive scientific article, to its customers.

FDA's spokesmen mislead by carefully selecting their words when testifying before Congress in order to avoid saying what they really intend, as evidenced by their position papers. They say the debate is not about vitamins and minerals when sold in what they call reasonable potencies. What they call reasonable is far too low to be used as a guideline for health. FDA considers higher potencies of vitamins or minerals, or dietary supplements that have no essential requirement in human nutrition, or products consumed for health enhancement or therapy to be drugs. Again, the real public health danger is from restricting access to dietary supplements, not their potential side effects.

Specific Points:

1. Without the passage of S. 784, the FDA will increase its inappropriate enforcement of misinterpreted regulations to eliminate a number of safe, effective health products from the marketplace, decreasing the available health choices of Americans and raising health care costs.
2. The Dietary Supplement Health and Education Act would allow these products to remain on the market with substantiated health claims based on scientific data. FDA and CSPI do not speak for or protect the public on this issue, and their comments are usually unsubstantiated opinion.
3. I couldn't practice medicine responsibly without many of the substances that the FDA, based on its own position papers, has every intention of severely restricting.
4. The vast majority of the population do not want the FDA to restrict dietary supplements. To call this bill simply an industry attempt to avoid regulation belittles the enormous grass roots movement in its favor and the intelligence of the many constituents who take and depend on dietary supplements for their continued good health.
5. The FDA blatantly misrepresents the dangers of supplements when it reports to Congress that there have been deaths from vitamin A or toxicity from essential oils, which is contrary to fact.
6. It would be ridiculous in America to have restrictions on dietary supplements, but ready access to alcohol, tobacco, sugar and "big Macs," with all their known dangers.

If I could spend a half hour with each of you, I am convinced that you would want to take at least two or three dietary supplements that the FDA has either already tried to restrict, or will without passage of S. 784. Serenoa for the prostate and Coenzyme Q10 for the heart are good examples.

In my practices in Massachusetts over the past 17 years, I have seen over ten thousand patients, and I have thousands of listeners to my radio shows. I have reached thousands more from around the country through lecturing, TV appearances, writing for magazines and newspapers and through a computer network. It is clear that many people are willing and competent to make their own choices regarding health care, including dietary supplements. They are willing to spend their own money, not federal or state money, for the right to improve their health and prevent disease. They will not be able to continue to do this without the passage of this bill, which I strongly support.

Some of my colleagues and various researchers have also expressed similar sentiments, and I would like to report some of these to you. For example, Gladys Block, Ph.D. has made the following points:

1. The evidence of a beneficial role for [antioxidant] nutrients is extraordinarily extensive.
2. Many Americans are not consuming even minimal, let alone excessive, amounts of nutrients.
3. There is no evidence that supplement users neglect their diet or other health care -- quite the contrary.
4. The evidence of benefit is increasing explosively, and conclusions formed a decade ago are insufficient to inform us.
5. FDA's role in protecting public health would be much more valuable if focused on ensuring quality of supplements, and providing consumers with information.

In the reviews of the Serenoa repens extract studies published by the FDA in New Developments, of March 5, 1990, they gave their reasoning for not allowing claims for prostate improvement. Although they admitted that there was "statistically significant" improvement, they considered it not to be "clinically significant," even though it was better in all parameters than Proscar (finasteride), the drug that they did approve. Proscar is potentially dangerous, and women who may get pregnant, who are partners of men taking the drug, are cautioned to avoid exposure to this partner's semen and to avoid handling the crushed tablets of the drug. It also has other side effects (impotence, decreased libido, ejaculation dysfunction). There are no side effects from the herbal product.

The FDA does not only consider the value and safety of dietary supplements in deciding what to approve. It has other motives, including "...what steps are necessary to ensure that the existence of dietary supplements on the market does not act as a disincentive for drug development." Also, Deputy Commissioner for Policy David Adams said that the establishment of a separate regulatory category for supplements "...could undercut the exclusivity rights enjoyed by the holders of approved drug applications."

In a letter to the New York Times, September 8, 1992, Dr. Bernard Rimland said "...Dr. Kessler tells us that the FDA doesn't want to block the sale of vitamins. All we have to do is convince him and his fellow bureaucrats that they have been wrong for many decades in saying that vitamins are useless. Just provide the FDA with the evidence that will make them change their minds and they will let us buy all the vitamins we want. Fat chance! The FDA's stonewalling of any and all evidence favoring the use of vitamins is legendary. We could more easily convince a shark to become a vegetarian."

The evidence does not support the FDA claims that nutrients, including amino acids, are in any way a significant risk. These baseless claims mislead Congress and the public, and make it dangerous to give such regulatory power to the FDA. The attached chart documents the safety of supplements.

In case there is doubt about the regulatory intentions of the FDA, let me include some quotes from FDA officials pinpointing their position:

From the Task Force Report on Dietary Supplements

"...the task force recommends that the agency adopt a 'Dietary Supplement Limit' which would be the maximum daily intake of a given vitamin or mineral that the agency deems safe" – e.g. "the highest RDA levels listed by the National Academy of Sciences." "The Agency should take regulatory action against those supplements that exceed the above guidelines as 'unsafe food additives'..."

"Amino acids should be regulated as drugs"

"If a potency is listed on the label for any non-essential substance (a dietary supplement for which there is no RDA) action would be taken against those products."

One has to question the rationale behind the FDA's proposal to redefine amino acids as "drugs." Using such an approach should suggest that sugar (sucrose) refined from beets or sugar cane, a food extraction product, should be regulated as a "drug." In fact, sugar in the American diet poses far more risks than amino acids.

Other quotes from Dr. Kessler:

"It has become fashionable in some quarters to argue that women ought to be able to make such [breast implant] decisions on their own. If members of our society were empowered to make their own decisions about the entire range of products for which the FDA has responsibility, however, the whole rationale for the agency would cease to exist." (From the New England Journal of Medicine-Wall Street Journal 6/24/92)

"The American public does not have the knowledge to make wise health care decisions...FDA is the arbiter of truth...Trust us. We will tell you what's good for you..." (From The Larry King Live Show, 1992.)

Well, I don't trust them, and I do trust that the American public is not as ignorant as the FDA bureaucrats suggest.

COMPARATIVE CAUSES OF DEATH

Annual Average in the US

Adverse Drug Reactions	60,000-140,000
Heart Attacks preventable w/VitaminC	75,000
Automobiles	39,325
Food Contamination	9,100
Boating Accidents	1,064
Birth Defects, preventable w/Folic Acid	500
Charcoal Briquettes (Carbon Monoxide)	34
Household Cleaners	24
Lawn Mowers	15
Acute Pesticide Poisoning	12
Hair Dryer Accidents	10
Accidental Iron poisoning	6
All Plants (house plants etc.)	1
All Vitamins	0
Uncontaminated amino acids	0
Commercial Herbal Products	0

Sources: Calculations based on data from the American Association of Poison Control Centers, National Center for Health Statistics, Journal of the American Medical Association, Centers for Disease Control, March of Dimes, Consumer Product Safety Commission, FDA Reports.

The Well Street Journal
Cambridge, Massachusetts June 1, 1993

Nutrients Restricted; Big Macs Freely Available

System Change No Solution to Health Care Crisis

by Michael Janson, M.D.

The twisted reasoning of some of our regulatory agencies has become even more bizarre in recent months, as they are threatened with the loss of some of their control. The Food and Drug Administration (FDA) has reacted violently at times to the continued availability of harmless nutritional supplements. They have tried to close manufacturers and they have attacked distributors and doctors who use nutritional alternatives.

No health claims are made for products such as candy, sodas, alcohol, fast foods, cakes, pies, ice cream, cookies and the like. Nor could they be. These are clearly damaging to health and, along with smoking, significant contributors to the high cost of health care. These products are freely available to the American public, and indeed are spreading around the world with no restriction on their distribution or sale.

On the other hand, we have nutritional supplements and herbs. They have a long history of contributing to health in general, and to the prevention and treatment of many diseases. In many cases they can decrease the need for drugs and surgery, and can thereby decrease health care costs.

Over the years there have been some unscrupulous purveyors of nutritional products who have made unfounded claims of their miraculous benefits. In spite of this, almost no one has been injured by nutritional products. However, some credulous people have lost some of their money to these salesmen. Because of this there is a hue and cry in the regulatory agencies and in some political circles. There is a significant risk of harm to the public health if nutritional supplements and herbs are restricted by the FDA in their grab for increased power under the guise of protecting the public.

The tragic joke would be if beneficial supplements become unavailable because of a few false claims (and many true ones that the FDA also wants to restrict). Then we would have the ridiculous scene of freely available toxic imitation foods, alcohol and tobacco and no vitamin C or E or Coenzyme Q10; no chamomile; no L-carnitine.

A further tragedy would be the continually worsening health and increasing costs of disease care that Americans already cannot afford. The real problem is that people continue to abuse themselves with harmful health habits and little clear guidance from their professionals or government.

For example, a healthy diet has less than 15% fat, common in many developing countries and in the native diets of Africa, China and Japan. But authorities in the United States are unwilling to suggest such a diet (ignoring the scientific merits) because they feel that no one will comply. What they fail to realize is that most people will aim at a target but not always hit it.

If you make the target too broad, most people will hit it but it won't win them the prize. And with human nature, if you say 30% people will think that 35% is OK. If you say 20% they will aim at 25. And so on. If we fail to reveal the ideal, no one will have the opportunity of achieving it.

Prescription drugs kill more people per year than auto accidents. Nutritional supplements and herbs have a spectacular record of safety in comparison to any other method of treatment. Even if they did not work (and they do) they would pose little risk to the public. The only reason that the FDA and others want to regulate them is based on their need to extend their political influence.

Doubts Raised about CSPI: Who really supports them?

The Center for Science in the Public Interest claims to have over 400,000 supporters in their campaign to give the FDA more regulatory power over nutritional supplements. They are suggesting a bill that, if proposed and passed in Congress, would lead to severe restrictions on the right of the public to choose and purchase nutritional supplements. They claim their entire list of newsletter subscribers as supporters of their position.

This is probably a misrepresentation. It is likely that many of their subscribers do not support their position on supplements. I, for one, subscribe to their newsletter for nutrition information, with which I sometimes agree, but not always. CSPI has always had a difficult time accepting the benefits of nutrient supplements. Only recently have they started to admit, with great reluctance, that they may have a place in the health care of the entire population. They are not being scientific, nor are they serving the public interest when they try to give the FDA more regulatory powers. This is especially true since the FDA has a long history of bias against nutrients compared with their attitude toward drugs.

If you are a subscriber to their newsletter, let them know that you disagree with their position on supplements. We all agree that they need to be pure and safe, and live up to their potency claims, but they do not need to be regulated as dangerous substances. There is a greater danger to the public health from restriction of supplement availability. Although I urge people not to smoke or drink excessive alcohol, those substances are freely available to the public. It is called freedom of choice. Nutrients should be at least as readily available.

Write or call your senators and representatives to let them know that you support the Dietary Supplement and Consumer Education Act of 1993, that you disagree with CSPI, and you want access to supplements. It is urgent that we all do this now. Call 202-224-3121 and give them your zip code for connection to your representatives.

Center for Preventive Medicine

Michael Janson, M.D.

The FDA and Dietary Supplements

The use of large doses of food supplements in the practice of medicine, and, indeed, in the frequently self-administered programs of many consumers, is virtually non-toxic, and has many potential benefits. To allow unlimited access to alcohol, caffeine, tobacco, sugar, aspirin and other proven harmful substances, while restricting access to nutrients, is ludicrous.

We expect people to make informed judgements and to be responsible for their decisions. Most manufacturers, especially of repeatedly consumed products, have no interest in harming their current and future customers. Liability laws offer protection from negligence and fraud through civil and criminal penalties. Our freedom to choose depends on informed consent and personal responsibility, yet the FDA would like to treat adults as if they were naughty or easily misled children.

An FDA that is organized as a research body that tests for purity is one thing, just like Underwriters Labs (UL). An FDA that is an independent enforcement body that has a history of using tactics like the KGB is quite another. Adding to their enforcement powers and creating them as the sole arbiters of what is substantiated health information is irresponsible. It is detrimental to the health of individuals and it will perpetuate the rising cost of health care.

The FDA, through unwarranted and arbitrary interpretation of the NLEA, has created its own authority to prevent what they call "unsubstantiated health claims" being made by manufacturers or sellers of nutrients. Unfortunately, without scientific rationale, they define any health claim as unsubstantiated, even those that are substantiated in the medical literature. This leads to the ridiculous situation where a scientist can write an article on the benefits of vitamin E in immunity (an article already published) but a reprint of that article distributed with or without bottles of vitamin E would make the distributor a criminal. They create the description of unapproved food additives, and use it to confiscate or ban substances with no evidence of dangerous side effects (e.g. Efamol brand of Evening Primrose Oil).

Almost every week in the medical and lay literature there are articles reinforcing the older information that nutritional supplements are beneficial in a wide range of illnesses. The illnesses range from heart disease to cancer, from acne to PMS, from arthritis to infections to asthma and allergies. The list goes on and on, and it is growing daily.

This is not meant to ignore that the foundation of good nutrition is a proper diet. The sad fact is that Americans do not eat a healthy diet. This is evidenced by simple observation of what people put in their carts at the supermarket, as well as by some statistics. For example, the average American diet derives nearly two-thirds of calories from fat and sugar! In Japan, with the lowest heart disease rate of the developed nations, the incidence of obesity and heart disease is rising with the Westernization of the food supply. The growth of McDonald's (now Japan's number one food retailer) parallels this increase in disease.

To start making inroads in the cost of health care, some vitamin "enforcement" money needs to go into the education of the public about healthy nutrition and the value of supplements. With the historical bias of the FDA, we must protect supplements from their strongarm tactics. We cannot allow the FDA to ban educational information about supplements, even though it comes from manufacturers or distributors of nutrients. We need responsible education, from all sources, about the growing body of evidence for the benefits of nutrient supplements in health care. People are willing to spend their own, not government, money on these health enhancing substances.

Support S. 784 and HR. 1709, the Dietary Supplement Health and Education Act of 1993

275 Mill Way, P.O. Box 732, Barnstable, MA 02630
Tel. (508) 362-4313 Fax. (617) 661-8651

Center for Preventive Medicine

Dietary Supplements or the FDA, Which is the Real Fraud?

by Michael Janson, M.D.

On the surface, it seems reasonable that the FDA should force dietary supplement manufacturers to prove their marketing claims. No one wants to be the victim of fraud or to waste money on useless or potentially dangerous products. Unfortunately, if you are expecting the FDA to protect you, you may be surprised to learn that FDA approved drugs, both prescription and over-the counter, are far more dangerous than any dietary supplements. It may also be a surprise to find out that dietary supplements are extremely safe, even without FDA endorsement. They often have significant scientific documentation supporting their value in the prevention and treatment of a wide range of health problems.

People want dietary supplements. They want them to be more readily available than alcohol or tobacco. They want them at least as easily as fast foods, sugar or caffeine, all known to be harmful to health. More than half the population take supplements with almost no side effects, and no serious side effects in decades. If so many people were taking dangerous substances, the FDA would be able to cite numerous examples of harm, but with dietary supplements they cannot. They have, however, conducted armed raids on health food stores, legitimate manufacturers and doctors, and confiscated harmless B-vitamins and herbs. Sometimes these raids have appeared to be in retaliation for complaints against prior FDA actions.

The FDA repeatedly cites the neurologic damage from L-tryptophan to support their claims of risk. However, it has been known since 1980 that this side effect resulted from a contaminant in a batch from a single manufacturer of this otherwise safe amino acid. In fact, L-tryptophan is used routinely in infant formulas and in intravenous feeding with FDA approval. It is approved because it is not dangerous, but after 4 years you still cannot find it at health food stores.

The FDA has a long history of strong bias against nutritional supplements. Even now, they make baseless claims of toxicity to mislead Congress and the public. In the 1970's, Senator Proxmire had an amendment passed that prohibited the FDA from regulating supplements as dangerous drugs. It was because of the FDA bias that such a law was necessary. Since that time, the FDA has made every effort to avoid, misinterpret and misapply the law. Some of their actions are so ludicrous that a judge was prompted to refer to them as "trying to make an end run around the law, with 'Alice-in-Wonderland' reasoning." Their current effort at further control is dangerous to your health.

The FDA commissioner, David Kessler, cites "more than 500 examples of fraudulent claims" for dietary supplements. But just what are some of these claims? An example would be the recent removal from health food store shelves in Texas of Sleepytime Tea. The FDA considered the very name to be an unsubstantiated (fraudulent) health claim! They have removed black currant oil capsules from the market on the grounds that it was an "unsafe food additive." The oil has been in safe use for 1000 years. Since it was not being added to anything, the FDA called the gelatin capsule the "food" and the black currant oil the additive! This was thrown out in court, prompting the above comments from the judge.

You must also consider on what grounds the FDA finds fraud. If the FDA has not approved a health claim, manufacturers of a product cannot even distribute scientific literature that

275 Mill Way, P.O. Box 732, Barnstable, MA 02630
Tel. (508) 362-4343 Fax. (617) 661-8651

supports the claim. For example, an article in the American Journal of Clinical Nutrition, by researchers at Tufts University, showed that vitamin E in high doses enhances immunity in the elderly. Enhanced immunity is very valuable, and may save lives by reducing pneumonias and other infections. A company marketing vitamin E is violating FDA rules by copying that article to send to purchasers. According to the FDA, this could be one of their 500 frauds. Getting this information out is important to the health of all Americans, and manufacturers should be able to send this information without being accused of fraud. We need to control real fraud without wasting time and money going after legitimate companies.

No doubt there are some truly fraudulent claims, but the FDA considers any health claim as fraudulent, even if there is scientific data behind it. In addition, if research shows that an herb or supplement compares favorably to a drug for the same use, they will favor the drug, in spite of higher cost and greater risks. This is true of the Saw palmetto berry extract which is safer, cheaper and more effective for prostate enlargement than the drug Proscar. In an industry as large as alternative health care ($14 billion), there is bound to be some fraud, but the FDA already has adequate power to regulate real fraud. They are abusing the power they already have to control preventive medicine, and they want more. They are reluctant to admit that they have adequate regulatory power, and that the supplement industry is responsive to their complaints about false or misleading advertising.

The FDA proposals for regulation would virtually eliminate 80% of supplements, with no evidence of risk from them. They would limit potencies to what they consider "reasonable" doses -the new Reference Daily Intake (RDI), a level lower than the minimal Recommended Dietary Allowance (RDA). That would mean if you wanted to take 1 gram of vitamin C you would have to take 17 tablets. The dose of vitamin E in the Tufts study was 800 I.U. Under FDA proposals it would take more than 26 pills to get that dose. Amino acids, essential fatty acids, and food co-factors that have no established RDA would be unavailable. Long established herbs would be considered "unsafe drugs" and removed from the market until proven otherwise.

A new bill before the Congress addresses the issues of fraud and safety while maintaining ready access to dietary supplements. The Dietary Supplement Health and Education Act of 1993, introduced by Senator Orrin Hatch and Representative Bill Richardson has been endorsed by 59 senators, including Senator Claiborne Pell of Rhode Island, and at least six Massachusetts representatives-- Barney Frank, John Olver, Richard Neal, Peter Blute, Marty Meehan and Peter Torkildsen. They would take control of dietary supplements away from the FDA bias and give it to a new Office of Dietary Supplements under the control of the National Institutes of Health.

For the right to choose the kind of health care that many people want, the power of the FDA must be reigned in and properly directed, not extended.

Center for Preventive Medicine

Michael Janson, M.D.

Senate Labor Committee Hearing October 21, 1993
On the Dietary Supplement Health and Education Act of 1993
Follow-up Testimony of Michael Janson, M.D.
For Inclusion in the Hearing Record
Submitted October 22, 1993
by MICHAEL JANSON, M.D.

During the testimony at this hearing of Dr. David Kessler, Commissioner of the Food and Drug Administration, he made a number of misleading and false statements, and a number of confusing points. I addressed some of those points in my testimony, but due to a lack of time I did not address all of them nor did I respond adequately to reflect my concerns.

First of all on the issue of the safety of nutrients. The FDA has asked that dietary supplements meet the same standards of safety as OTC drugs. Using their own data and according to all the records of the American Association of Poison Control Centers, dietary supplements are 2550 times safer than OTC drugs.

Dr. Kessler said that there was potential toxicity from chromium, folic acid, gamma-linolenic acid (GLA) and L-tryptophan. I am sure that he feels there is a problem with other nutrients in spite of their long record of safety based on animal and human studies and traditional use. If Dr. Kessler feels there is a risk, he can avoid taking these products, but only if he can reasonably prove a risk should the FDA be allowed to remove these from the market.

I would like to state categorically that there is no known risk from the ingestion of any of the above products at anywhere near the amounts that are typically used. In fact, you would probably have to take enough GLA-containing oil to get obese, from the calories, before it would do any other harm. No one is recommending such high doses.

Folic acid does not cause any side effects. What Dr. Kessler calls a side effect, the masking of the anemia which is an early sign of a B12 deficiency, is actually a therapeutic benefit. However, I recognize that a B12 deficiency, if prolonged may lead to peripheral neuropathy, but this is not a side effect of the folic acid. There are now easy ways to measure B12 in the blood, so a physician would not have any difficulty in recognizing a deficiency. You might argue that you need to see a physician to determine this even if people are taking folic acid on their own. However, that is moot, because a person would need a physician to recognize the anemia also. Although the dispute revolves around the dose of 400 to 1000 micrograms (mcg), folic acid is safe at doses measured in milligrams (mg). I have seen no side effects in patients taking up to 100 milligrams (100,000 micrograms). This dose has been used to treat gout, because as a xanthine oxidase inhibitor folate works like the drug allopurinol. Inhibition of xanthine oxidase may also reduce the risk of heart disease.

Chromium is a perfectly safe nutrient that can lower cholesterol and help to regulate insulin, thus improving sugar control in diabetics and hypoglycemics. Doses that I have recommended, again with no clinical or laboratory signs of toxicity range up to 1000 micrograms. It is safer than the drugs that are approved to lower cholesterol (e.g. lovastatin), and they have side effects such that their effect on mortality is neutral or negative.

Lovastatin actually inhibits the production of another substance, coenzyme Q10, which is very impor-

275 Mill Way, P.O. Box 732, Barnstable, MA 02630
Tel. (508) 362-4313 Fax. (617) 661-8651

tant for a healthy heart, immune function and energy production. Since coenzyme Q10 protects against heart disease there is theoretical evidence, and also clinical studies showing, that this is a risk of taking the drug. And, as an aside, coenzyme Q10 is a substance that the Texas Department of Health following FDA's lead tried to remove from the health food stores in Texas.

The case of L-tryptophan deserves more comment. Dr. Kessler repeated in his testimony the claim that "they" were not sure that the eosinophilia myalgia syndrome (EMS) was due only to a contaminant. As I stated in my testimony, the New England Journal of Medicine and the Journal of the AMA both concluded that it was from a contaminant back in 1990. In the past month there have been two reports, one from the CDC by Robert Hill published in the Journal of Contaminants and Environmental Toxicology, and one from Dr. Cluew, a professor at George Washington University reported at a rheumatology meeting. They both concluded that the EMS was the result of a contaminant, and not L-tryptophan itself.

If the FDA and Dr. Kessler do not know the older literature on the subject and they do not know the more recent literature on the subject, they are the wrong agency or the wrong personnel to be involved with the enforcement of dietary supplement regulations. There are many other reasons that I have come to this conclusion. Either we change the agency, change the personnel or specifically limit their power with strict Congressional guidelines such as mandated in S. 784.

Dr. Kessler also revealed his true intentions inadvertently when he stated that FDA was within the law to regulate dietary supplement products that were mixtures, as food additives. There is no scientific rationale for removing two safe products from the market if they happen to be mixed together, just because you have the legal authority to do so. Some products are better when they are mixed, such as GLA and vitamin E. The product lasts longer on the shelf without oxidizing because of the presence of the vitamin E. Sometimes mixtures are cheaper and sometimes they are more effective. The FDA attitude is to "blow up Mount McKinley because it's there!" There is no reason to expect that the FDA, with its current personnel make up and level of authority, will suddenly start to treat dietary supplements more equitably than they have for decades.

Dr. Kessler left the impression that all the bottles of products that he displayed, in his grandstanding gesture, were labeled with false claims. He presented only one that had a false claim on the label. (No one at the hearing actually examined the label, but I have no doubt that there are occasional false claims, which generally are not a great risk to the public health.) Most of those products were properly labeled, but FDA agents were able to cajole someone at a health food store to suggest to them that the product would be useful for a specific health problem. The manufacturers or distributors are inappropriately being held liable for the actions of retail clerks. If a clerk in a market said to take prunes for constipation, that would be an unsubstantiated health claim according to the FDA, and they could put a box of prunes on the table with all those bottles.

When confronted with the toxicity of FDA approved drugs, which kill so many people annually, Dr. Kessler replied with his "canned" comment that "half of our drugs are derived from plants." This is a clear misrepresentation and designed to mislead. Many pharmaceuticals are plant extracts that have been significantly altered so that they can be patented, and this alteration usually increases their toxicity. Also, many of them are synthetic analogs of plant products, not the plants themselves. You might as well say that they are made from carbon, nitrogen and oxygen, which we encounter every day! Further, many of the most widely used and most expensive drugs are totally synthetic and have nothing to do with plants. Anti-ulcer drugs, anti inflammatory drugs, anti-anxiety drugs, newer cardiac drugs and anti-hypertensives are not plant products. They cost many Americans lots of money and have numerous side effects. They are necessary for many patients, but are widely overused. This is partly because physicians have no access, in the normal course of their work, to the information about dietary supplements that should be disseminated widely. This would lessen the need for drugs and enhance the health of all Americans while reducing the medical care crisis that we are now facing.

Dr. Kessler decried the variety of health claims being made for evening primrose oil. He is perhaps unaware of the hundreds of studies in the literature supporting most of those uses. It is not surprising that a physician would be skeptical of something that seems to help so many illnesses. But it is a mistake to be blinded by skepticism from seeing the scientific evidence. Because GLA is a precursor to regulatory substances known as "prostaglandins" it has wide-ranging metabolic effects. It does help to lower blood pressure, reduce or cure atopic dermatitis, relieve PMS, reduce cholesterol and inflammation and help asthmatics and allergic patients. These are the many effects of the prostaglandins that are made from this important fatty acid. It is therefore not "incredible" to someone who bothers to look up the scientific documentation and who understands the metabolic rationale.

I want to reaffirm that these claims were <u>not</u> on the labels of these products, but they <u>are</u> in the medical literature. Also, I have observed in my practice the above stated clinical effects, and have reviewed many of the studies substantiating some of the claims that the FDA agents heard from health food store clerks. The FDA should be doing everything in its power to disseminate this information and encouraging manufacturers to disseminate it also, as long as it is in the medical literature and not misleading. Instead they are an obstacle to information exchange, and are themselves misleading. This

can only be changed if the FDA stops confusing its role of regulating real danger and fraud with the role of being the arbiter and promoter of truth as they see it. Passage of S. 784 will ensure a more sane approach to regulation, availability of dietary supplements and truthful health claims.

When Dr. Kessler says that they "plan to take no products off the market," that is a dramatic shift from what they have proposed in all their written material until now. With such waffling, confusion and misleading testimony, the FDA cannot be expected to take an honest and human approach to regulating such an important component of our health care.

I have read Dr. Linus Pauling's letter to the committee supporting the Dietary Supplement bill. I hope it is included in the record because it is an eloquent statement that combines common sense, science, reason and compassion.

Sincerely,

Michael Janson, M.D. (via FAX)

Senator HARKIN. Patricia Hausman.

Ms. HAUSMAN. Thank you, Senator. It is an honor to be here.

As you know, I am a nutritionist and author of books about nutrition. I also spent 7 years on the staff of the Center for Science in the Public Interest. I have submitted my full testimony for the record and would like to summarize it here as briefly as I can.

The best known of my seven books is about supplement safety. It was based on my study of virtually every case of adverse effects from vitamin or mineral supplements reported in NIH's data base of scientific literature. Because of the warnings of supplement dangers I had heard in graduate school, I had expected to find volumes of evidence about toxicity. Much to my surprise, I found compelling evidence of safety instead.

Perhaps I should digress here because of my concern about the comment made by the Commissioner about chromium, because the evidence of benefits is so compelling and I would not want to leave without comment the possible suggestion that there is a safety problem with chromium. Chromium had the best safety record of any mineral studied in the book, and the reason for this is that it is so poorly absorbed that it is extremely difficult for it to become toxic.

Unless something has happened dramatic in the last few months, I would say, I think that that comment about chromium being potentially dangerous is probably based on confusion between occupational exposure to chromium on the job, which is a problem, and ingestion of chromium supplements, which I have never seen a single report of toxicity on.

I am not trying to say that there are no safety concerns about supplements, only that, as I explain in my written testimony, the facts are often distorted. What we heard here today, that FDA has essentially no safety concerns with vitamins and minerals, is sharply at odds with the comments in its recent publication, "Unsubstantiated Claimed and Documented Health Hazards in the Supplement Marketplace." That report says, for instance, that 800 to 1,000 micrograms of selenium can cause harm. I have never recommended a dose this high, but I only know of one mild case in that dose range, and so I called FDA for references.

I was told that the statement was based on selenium intakes in parts of the world where signs of selenium excess have been reported. In other words, these intakes were from eating food grown in selenium-rich soils. This is what FDA has called "an injury associated with supplement use."

This and other examples cited in my written comments make me wonder what standard FDA is using to assess supplement safety. Clearly it is not significant scientific agreement; it is not the totality of the evidence. It seems to me that what the agency is doing is using whatever anecdote or idiosyncratic reaction it can find to paint supplements in the most unsafe light.

Yet properly designed scientific studies ranging from dozens to hundreds in number have not been enough for FDA to acknowledge any benefit of supplements other than the calcium claim. It seems that for this category of products only, FDA is more concerned with avoiding a few adverse reactions, most of them quite reversible, than with preventing thousands of deaths.

This report also makes numerous charges of unsubstantiated claims which Senator Hatch has addressed in detail. Reading down the list confirms something that I have suspected for a long time: that to FDA health fraud is anything that it has not heard of. It is simply inconceivable that an effort by FDA, even a modicum of effort to find scientific support for some of the claims listed in that document would have yielded nothing.

I chose several of the claims, ran simple literature searches on them—this is from my home, with a mere computer and modem—and compiled some supporting studies for the record. Here there are. These are just four of the claims: garlic, Vitamin C and the immune system, chromium.

I think that you will see in this document that substantiation does exist for some of the relationships listed in that report, and more importantly, that these findings are important ones that can not only improve public health but greatly reduce our health care costs. Needless to say, it is much less expensive to lower cholesterol with chromium than with some of the cholesterol-lowering drugs that people must see a physician first to obtain.

I would like to make a comment about the health claims issue. We keep using this term "health claims," and I think the expressing is misleading. Much of what FDA is currently restricting is not the claim but a statement of fact. A phrase such as "cures AIDS" is what I would consider a claim. But disclosing, for instance, that 14 out of 20 studies show a condition is less common among people who have ample intakes of a nutrient to me is more a statement of information. I do not really think it is fair to call that a claim.

Consumers can consider this information in the context of their own circumstances, which are going to vary from one person to another, and decide whether to wait or act now. And I am hopeful that a distinction along these lines might help resolve this controversy over messages about dietary supplements.

Why consumers should continue to be deprived of information such as this truly mystifies me, because what we have right now with these current prohibitions against health information in the marketplace is a privileged class——

Senator HATCH. Excuse me just a second, Ms. Hausman.

I know you have a 7 o'clock plane and you want to go. I just wondered if anyone had any questions for Mr. Dyk.

Senator HATCH. We are appreciative of your testimony.

Mr. DYK. Thank you very much. I appreciate the committee's courtesy.

Senator HARKIN. Thank you for your testimony and also your many endeavors in this field, and your patience.

Mr. DYK. Thank you. I will just offer my full statement for the record.

Senator HARKIN. Thank you very much.

If you could hurry up and wrap it up, we would be appreciative.

Ms. HAUSMAN. Very quickly.

What we have right now with these current prohibitions on health information in the marketplace is a privileged class of insiders. These are scientists and affluent Americans who are privy to findings that the general public is not. Admittedly I am one of them, and I can assure you that many members of this group are

not waiting for all the evidence. We are taking antioxidant supplements to reduce our risk of cancer, heart disease, cataracts. These are all diseases that exact a huge price from our health care system. The idea that the rest of our citizens are not entitled to this same opportunity is so alien to me it is frightening.

Let me close by saying this: FDA has been attributing the outpouring of support for legislative reform to a misinformation campaign. It seems to be unable to accept that the loss of public trust is of its own making. My own decision to spend the last 4 months volunteering my time on this issue was prompted by FDA seizing products that I use myself and that I know to be backed by scientific research.

The idea that some aspect of the supplement industry has fooled me into doing its bidding just simply renders me speechless. FDA needs to take steps to regain the public trust that it has lost with its own regulatory actions and proposals. Meanwhile, I feel too much hangs in the balance for us to sit and wait. Senate bill 784 is a sound solution. Its passage will ensure that the FDA does not interfere with the right of all citizens to learn about and implement some of the most important scientific findings of our time.

I appreciate this opportunity to testify and would, of course, be happy to answer any questions.

Senator HARKIN. Thank you very much.

[The prepared statement of Ms. Hausman follows:]

PREPARED STATEMENT OF MS. HAUSMAN

Mr. Chairman and members of the committee, good afternoon, It is an honor to be here. I am Patricia Hausman, a professional nutritionist and author of seven books about nutrition. I also spent 7 years on the staff of the Center for Science in the Public Interest. The appendix includes a detailed summary of my career.

The best known of my books is *The Right Dose.* It was based on my study of virtually every case of adverse effects from vitamin or mineral supplements reported in NIH's database of scientific literature. Because of the warnings of supplement dangers I had heard in graduate school, I had expected to find volumes of evidence about toxicity. Much to my surprise, I found compelling evidence of safety instead.

This is not to say that there are no safety concerns about supplements—only that the facts are often distorted. Rare harms are made to sound common, and adverse effects life-long. In fact, most reactions end in full recovery. Critics often do not mention that a large percentage of cases involve abuse or illnesses that make people more vulnerable to unwanted effects. And a surprising proportion of reactions come from doctors using very high doses to treat disease. These effects are hardly "hazards in the marketplace," though they are often described as such.

Finding that the real facts were not what I learned in graduate school changed my perspective. It taught me that sometimes science is neither objective, nor rational. The current debate illustrates this all too well. There is more scientific evidence to support use of certain supplements than for much of our conventional wisdom in nutrition. But many would rather resist change than face facts. That is why such a massive smokescreen—composed of exaggerated claims about supplement hazards—has been built here on Capitol Hill.

FDA's recent publication, *Unsubstantiated Claims and Documented Health Hazards in the Dietary Supplement Marketplace* has done much to exaggerate safety issues. for example, it says that 800–1000 mcg of selenium can cause "tissue damage." I do not recommend doses this high, but knowing of only one case in this dose range, I called FDA for references. The statement, I was told, was based on estimated selenium intake in regions where signs of selenium excess have been reported. Such intakes were from eating food grown in selenium-rich soil. Yet FDA calls this an "injury associated with supplement use."

When I asked if FDA knew of any supplements providing this allegedly harmful level of selenium, the answer was no. My questions about alleged hazards of vitamin A also brought responses that defy fair-mindedness. FDA's comments about the safety of niacin are likewise exaggerated. And its concerns about the amino acid

phenylalanine are remarkable in view of its vigorous defense of aspartame. Foods sweetened with aspartame can also provide large doses of phenylalanine in an isolated form similar to that in supplements.

This makes one wonder what standard FDA uses to assess supplement safety. Clearly, it it not "significant scientific agreement" or the "totality of the evidence." Rather, the agency appears to use whatever anecdote or idiosyncratic reaction paints supplements in the most unsafe light possible. Yet, well-designed studies ranging from dozens to hundreds in number are not enough for FDA to acknowledge most benefits of supplements. For this category of products alone, FDA seems more concerned with avoiding a few adverse reactions among millions of consumers than with preventing thousands of deaths.

This report also makes numerous charges of "unsubstantiated claims" in the supplement marketplace. Reading this confirms something I have suspected for a long time: that to FDA, health fraud is anything that it hasn't heard of. It is inconceivable that an effort by FDA to find scientific support for some of these claims would have yielding nothing. I chose some of these claims, ran a simple literature search, and compiled some supporting studies for the record. Brief excerpts from these studies are attached. I think you will see that substantiation does exist for these claims, and that the findings not only offer the potential to improve public health, but to reduce health care costs as well.

Though the term "health claim" is widely used, I think that this expression can be misleading. Much of what FDA restricts are not "claims" but statements of fact. The phrase "cures AIDS" is a claim. But disclosing that 14 of 20 studies show a condition to be less common among those who have ample intakes of a nutrient is more a statement of information than a claim. Consumers can consider such information in the context of their own circumstances and decide whether to act or to wait for more findings. Perhaps a distinction along these lines could help revolve the controversy over this aspect of S. 784.

Why consumers should be deprived of information such as this is a mystery to me. One could even argue that they own it. After all, most medical research in the United States is funded by taxpayers. Is it fair for them to be charged for research, then denied ready access to the results because of a paternalistic belief that scientists should make decisions for them?

[Editor's note—The appendix and submissions are retained in the files of the committee.]

Senator HARKIN. I would yield to Senator Hatch.

Senator HATCH. I would just like to thank both of you for being here. Ms. Hausman, you are world-renowned for some of your writings, and I think people ought to pay attention to what you are saying.

And, Doctor, I have to tell you, I am meeting more and more doctors who are utilizing nutritional therapy and having much greater results than they are—not that pharmaceutical therapy does not have a role. It does. But if they can use nutritional therapy rather than pharmaceutical therapy, they would always opt for that. Frankly, if we had more doctors like you, we would have a lot more healthy people in this society.

Dr. JANSON. Luckily, we do have a lot more doctors like me. We teach 125 of them every 6 months at one of our groups, and I am teaching them quite frequently.

Senator HATCH. Well, that is terrific, and I am finding more and more coming out of the woodwork all the time who are saying, hey, this works. And they are not nearly as concerned about claims or safety as Dr. Kessler has been. They know that there is virtually a negligible risk to the use of these products. And it has been going on for 4,000 years.

Frankly, this is not the pharmaceutical industry, and I have to say that that is the issue. It is a question of risk, and there is really very little risk here, even in spite of some of the things that Dr. Kessler was saying. Nobody wants to do 100 milligrams of folic acid. I do not know of anybody who wants to do that, and I do not

think there are many instances where niacin is prescribed above what is reasonable. And you will not find many other instances like that. I do believe that this industry is very sophisticated, and based upon years and years of helping people with their dietary and health problems.

Thank you both. I really appreciate it.

Senator HARKIN. Senator Kassebaum.

Senator KASSEBAUM. Just one brief question. Dr. Janson, you mentioned, regarding scientific information that is published in various articles and so forth, that it is hard to disseminate that to the stores and those who carry health food products and dietary supplements. Is there some better way—this is really to both of you—to be able to have that information pulled together? Could this be something that an independent commission should be set up to do—review some of this information and make it available?

Ms. HAUSMAN. I personally find nothing wrong with manufacturers supplying copies of papers from the New England Journal of Medicine to professionals, and I have actually received a letter from one of the wholesalers that I buy from telling me that they can no longer give me those papers because FDA has come down on them.

Now, I personally feel the idea that professionals cannot evaluate these papers properly is without any basis at all, and that this is just another effort to cut off the information flow about supplements, even supplements that doctors need to know about in order to best help their patients.

I think having the manufacturers distribute these papers is the most efficient way to do it, the most cost-effective way to do it, but right now the only choice I have is to go to the library and do the research myself. Part of my reason for being here today is, frankly, FDA has made it much harder for me to do my job because I cannot get this information from manufacturers.

Dr. JANSON. The problem is partly the difference between professionals and the public. I see no reason that a dietary supplement manufacturer could not send professionals literature on how best to use that product if it is accurate literature, or if they could—but that does not go to the public, and the public cannot evaluate all the time—although they are not as ignorant as some people in the FDA seem to think—an actual article from the New England Journal or JAMA. It is very complex and very difficult. But a reasonable summary of that article that is accurate in its reflection, there is no reason that could not be distributed to health food stores and let people read the accurate summary; and if it is inaccurate, prosecute the company that sends an inaccurate statement.

FDA could do that according to that kind of a regulation, but I have a fear that they will not. Therefore, I believe another office or someone that consists of a panel of experts that include physicians like myself could evaluate those claims and say what the percentages are, what the possibility is.

Remember, these things are not dangerous, and if people do take them with the claim that Vitamin E helps heart disease and we prove 10 years from now that CSPI is wrong that their suggestion for that dose is inaccurate, nobody has been harmed because Vitamin E is not going to harm anybody. And if they do not get their

money back, well, that is the risk people take in life. There are many products that they take freely and many drugs that are over the counter that are much more risky and they also do not work.

You know, the cold remedies are the only approved substances that companies can market with claims that they help with colds. But the only documented effects of those products are side effects. So there is no purpose in criticizing dietary supplements when cold remedies are more risky and not as effective. And I can tell you that Vitamin C is effective from tons of studies. And if you just do a meta analysis or a study of studies, you will find a statistically significant number of studies that have varying levels of benefit from Vitamin C.

This information should come out either through the FDA or through another agency that can, in a fair way, evaluate them. And do not call it a health claim; just call it dissemination of information.

Senator HARKIN. Thank you both very much. I have a lot of things I could go through with you but time will not permit. Again, thank you.

Dr. JANSON. Call me in the office.

Senator HARKIN. Well, I might. [Laughter.]

Senator HATCH. What is that number?

Senator KASSEBAUM. I am a local call.

Dr. JANSON. It is in the back of my book which I have distributed to each of you.

Senator HATCH. I see it.

Dr. JANSON. Which the FDA, of course, would not allow at health food stores, possibly, because it recommends and evaluates some dietary supplements that may be of benefit.

Senator HARKIN. May I get a copy of that?

Dr. JANSON. Yes. There is a copy available for you.

Senator HARKIN. I appreciate that very much. Thank you both very much.

Senator HATCH. Could I just ask Ms. Hausman one question? You worked with CSPI for 7 years?

Ms. HAUSMAN. Yes, I did; 1974 through 1981.

Senator HATCH. All right. Thank you.

Senator HARKIN. Just one last thing before you go. You said that if you spent a half-hour with us, we would take more supplements.

Dr. JANSON. It is complimentary.

Senator HARKIN. You do not know how many I take right now. [Laughter.]

Dr. JANSON. I can guarantee you you might take more.

Senator HARKIN. I have been studying this for some time.

Dr. JANSON. Good. Well, we will have a good conversation then.

Senator HARKIN. I take mine every day. Anyway, the other issue that everyone here should be thinking about is whole health care reform bill. I am sort of wearing two hats—one on vitamin and supplements but another on the therapies and medical practices that are the focus of the Office of Alternative Medicine.

Again, as we reform the medical care system in this country, we have got to open it up more and make it more consumer-driven and let people have more choices as to the kind of health care paths that they want to take. I think we are going to have a big debate

on that because I want to open it up more and give people more choices.

I am sure that there will be those that will not want to do that.

Dr. JANSON. The only way to have that consumer-driven is to educate the public, and that is something that the FDA regulations for dietary supplements and, of course, alternative medicine itself has made it very difficult to do. I do that all the time, on my radio show, my lectures, coming here.

Senator HARKIN. When was RDA established?

Dr. JANSON. Thirty years ago. The last review was about 10 or 12 years ago, 15 years ago.

Senator HARKIN. I think it was even before that.

Dr. JANSON. It was established longer ago, but it is reviewed every 10 years. But recently they have had trouble with coming to some agreements.

Senator HARKIN. Exactly. Thank you both very much.

Dr. JANSON. Thank you.

Senator HARKIN. Our last panel is Mr. John Bode, legislative counsel of the National Food Processors Association; Steve McNamara, Hyman, Phelps & McNamara, representing the Utah Natural Products Alliance; and Bruce Silverglade, director of legal affairs for the Center for Science in the Public Interest.

I am sorry, but I have to leave. I forgot that I have another engagement for which I am already late. Again, I apologize. I will read over your testimony.

John, good to see you again.

Mr. BODE. Thank you, sir.

Senator HARKIN. So I will turn over the chair to Senator Kassebaum.

Senator Kassebaum [presiding.] Thank you.

Thank you very much. Again, we all appreciate your patience in waiting this long. It is late, but it is obviously a subject of great interest to many. So I guess we will start with Mr. Silverglade.

STATEMENTS OF BRUCE SILVERGLADE, DIRECTOR OF LEGAL AFFAIRS, CENTER FOR SCIENCE IN THE PUBLIC INTEREST, WASHINGTON, DC; JOHN BODE, LEGISLATIVE COUNSEL, NATIONAL FOOD PROCESSORS ASSOCIATION, WASHINGTON, DC; AND STEPHEN H. MCNAMARA, HYMAN, PHELPS & MCNAMARA, REPRESENTING UTAH NATURAL PRODUCTS ALLIANCE, WASHINGTON, DC.

Mr. SILVERGLADE. Thank you and good evening. I appreciate this opportunity to present the views of the Center for Science in the Public Interest as well as the American Cancer Society, the American Heart Association, and 10 other public health, consumer protection, and professional organizations. I also have with me a written statement by the American Association of Retired Persons. It is in agreement with the joint statement I am presenting, and I have been asked to submit it for the record.

Senator KASSEBAUM. All the statements and your full statement will be submitted for the record if you wish to summarize.

Mr. SILVERGLADE. Thank you, Senator.

All of our organizations support the right of consumers to have access to safe and efficacious dietary supplements. The question before us is: Is S. 784 the best way to accomplish this goal?

Now, we do agree in principle with several key aspects of the legislation, and, Senator Hatch, we want to congratulate you for opening up this issue and bringing it to the forefront of Congress' attention.

First, we support the creation of a new specific regulatory framework to ensure the safety of dietary supplements, and that is a concept in your bill.

Second, we also support attempts to ensure that dietary supplements are manufactured in a manner that ensures potency and purity, and that is also addressed in your bill.

Third, we support the creation of a new office devoted specifically to matters pertaining to dietary supplement regulation, and again, that is a concept in your bill.

We are concerned, however, that other portions of S. 784 would provide consumers with less protection against unsafe supplements and misleading labeling claims than is currently provided under the Food, Drug, and Cosmetic Act. We are also concerned that S. 784 would make it more difficult for the FDA to take prompt enforcement actions against manufacturers of unsafe or improperly labeled products. And for these reasons, we unfortunately cannot support the bill overall.

We note that several cosponsors of S. 784, including Minority Leader Dole, have raised similar concerns and have stated that their continued support for this legislation is contingent upon these matters being addressed. We stand ready to work with you, Senator Hatch, and this committee to come to an acceptable resolution of these issues.

Let me just spend another minute or so talking about health claims and safety. Under S. 784 health claims would be allowed so long as manufacturers disclosed the State of the evidence supporting the claim, even if it was minimal. Such claims would explicitly be permitted by S. 784, and the FDA could not prohibit them under its authority, under the agency's authority to control misleading labeling.

If 784 became law in its current form, manufacturers could hype products on the basis of preliminary, shaky, and inconclusive scientific evidence that would preclude consumers from making an informed choice, and a uninformed choice is tantamount to no choice at all.

Now, some of the members of the committee have asked: What is the harm in letting the consumer err in making a mistake in buying a product that does not deliver? There are really at least three major types of harm that have not been discussed yet at this hearing. The most egregious type of harm is that the consumer who makes a mistake and buys a product based on a preliminary health claim might be avoiding something else that would really work. There might be something else out there: another type of dietary modification, a prescription drug, some other medical treatment that would work.

The second harm is that if the consumer finds out eventually, based on new scientific evidence, that the health claim on the label

did not pan out, they are going to be very disillusioned. And as an organization that recommends that consumers use certain supplements, we are very frightened, frankly, that the public may throw their hands up in the air and start disregarding all dietary advice, including advice to use supplements, if preliminary claims are allowed on labels and they turn out to be untrue.

Third, let's not forget the economic harm. Consumers will be paying premium prices for products that they believe deliver a special health benefit, and if the claim turns out not to be true, no one is going to get their money back.

Now, it is true that the Center for Science in the Public Interest makes a number of health recommendations in our newsletter. We would like to see the FDA allow the types of claims that we are suggesting in our newsletter. FDA has been too slow in allowing health claims. But the problem is that there are other newsletters out there. Some of them recommend consuming shark cartilage to cure cancer. And so, therefore, we believe there needs to be a Government clearinghouse, and the FDA has to serve this clearinghouse function so that it reviews the claims and helps consumers sort fact from fiction.

Last, I just wanted to make a note on the safety issue. It is not the major issue here, but it is difficult to pass Federal public health policy on the sole assumption that because a product has been used for many years that it is safe. Most of our work actually involves food safety, and Congress was involved a number of years ago with FDA's regulation of sulfiting agents, a preservative used in foods. And sulfites had been used for hundreds of years in wines. Since the Middle Ages, wines have been preserved with sulfites. They were assumed safe.

The FDA, in fact, was going to reaffirm them as safe. But as it turned out, a new problem had been discovered. Asthma sufferers were particularly allergic to sulfites, and people who had been drinking wine in restaurants and then choking on the appetizer were actually found to be suffering an allergic reaction from sulfites.

My point is that the problem was not discovered until people looked for the problem, and just because a substance is natural and has been used for hundreds of years does not mean that it is definitely safe.

Thank you.

Senator KASSEBAUM. Thank you very much. I was remiss perhaps in saying that you are the director of legal affairs for the Center for Science in the Public Interest.

[The prepared statement of Mr. Silverglade follows:]

PREPARED STATEMENT OF BRUCE SILVERGLADE

On behalf of: The American Cancer Society, American College of Physicians, American College of Preventive Medicine, American Health Foundation, American Heart Association, American Institute for Cancer Research, American Nurses Association, Association of State and Territorial Public Health and Nutrition Directors, Citizens for Public Action on Cholesterol, Consumer Federation of America, Public Voice for Food and Health Policy, and Society for Nutrition Education.

Good afternoon, we appreciate this opportunity to present our views regarding federal regulation of dietary supplements.

We support the right of consumers to have access to safe and effective dietary supplements In light of new scientific evidence indicating the potential benefits of supplements, it is especially important that this right be preserved.

A majority of the members of this committee are co-sponsors of S. 784, the "Dietary Supplement Health and Education Act of 1993." This legislation raises important public health issues and we congratulate Senator Hatch and the other members of this committee for addressing them. We agree in principle with several key aspects of the legislation.

First, we support the creation of a new, specific regulatory framework to ensure the safety of dietary supplements. Currently, the Food and Drug Administration (FDA) is forced to regulate these products as either foods, food additives or drugs. This approach has been cumbersome and has created uncertainty and controversy.

We also support attempts to require dietary supplements to comply with regulations ensuring that these products are manufactured in a manner that ensures a quality product. As more and more consumers come to rely on dietary supplements, it is all the more important that such products be pure and potent.

We further support the creation of a new office devoted specifically to matters pertaining to dietary supplement regulation. This step will help ensure that dietary supplement issues receive adequate attention and that pressing matters are addressed in a timely fashion.

S. 784 contains provisions that address each of these matters. While we have concerns about specific aspects of these provisions, we support the objectives of these portions of the legislation.

We are concerned, however, that other portions of S. 784 would provide consumers with less protection against unsafe dietary supplements and misleading labeling claims than is provided under current law. We are also concerned that S. 784 would make it more difficult for the FDA to take prompt enforcement actions against manufacturers of unsafe or improperly labeled products. For these reasons, we are unable to support the bill. We note that several co-sponsors of S. 784, including Minority Leader Dole, have raised similar concerns and have stated that their continued support for this legislation is contingent upon these matters being addressed.

At issue is not an effort to impose the excesses of government bureaucracy on a small industry, but rather to ensure the safety of millions of unwary consumers whose health—and in some cases, whose very lives—may be at risk due to false or misleading health and nutrition claims on vitamins, herbs and other diet supplements. While problems have been rare in the past, the potential harm to consumers from toxicity, impurities, and unsafe dosages alone—not to mention the cost to consumers in outright fraud—cannot be overlooked.

We are concerned specifically about the following matters:

Safety provisions for Dietary Supplements: S. 784 would make it more difficult for FDA to take action against a dietary supplement product of questionable safety by placing the burden of proving risk on the FDA and weakening the safety standard currently in the Food, Drug and Cosmetic Act (FDCA).

The bill would exempt dietary supplements from the FDCA's definition of "food additive" and "drug," thereby preventing the FDA from invoking its authority under these provisions when it might be appropriate. While the legislation grants the FDA authority to adopt rules that declare specific ingredients to be unsafe, the standard that the FDA must meet—"substantial and unreasonable risk of injury or illness"—is too stringent. Moreover, we believe that the amount and type of evidence needed by a supplement manufacturer to substantiate safety is insufficient.

Health Claims for Dietary Supplements: We continue to believe that health claims for both food and dietary supplements should be supported by "significant scientific agreement." S. 784 would allow supplement manufacturers to make health claims supported by a single, inconclusive study. As a result, supplement products would continue to carry confusing and misleading labels, and the nutrition education efforts being conducted by the Department of Health and Human Services, the Department of Agriculture, and private health and consumer organizations would be undermined.

Furthermore, the FDA simply does not have the resources to adequately survey the marketplace and take individual enforcement actions against misleading claims as would be required by S. 784. A regulatory approach similar to the approach set forth in this legislation was utilized by the FDA from 1984 to 1990 for both food and supplements with disappointing results, which led eventually to the enactment of the NLEA.

Enforcement: The enforcement provisions of S. 784 would make it extremely difficult for the FDA to take prompt action to protect the public from deceptive or fraudulently marketed dietary supplements. Supplement manufacturers would be allowed to delay FDA enforcement action by making administrative appeals and by

bringing untimely challenges. We support efforts to strengthen, not weaken, the FDA's enforcement authority.

We welcome the opportunity to work with the committee to produce supplement legislation that all concerned parties can support. We would like to thank the committee ounce for the opportunity to testify and we would be pleased to answer any questions.

Senator KASSEBAUM. Mr. Bode, who is the legal counsel for the National Food Processors Association.

Mr. BODE. Thank you, Senator. In light of the many previous statements made today and the testimony already offered, I will try to be very brief.

I would like to make three points. First of all, the National Food Processors Association greatly appreciates the statement that Senator Hatch made at the outset today making clear that he feels certain modifications are warranted in his legislation. Those modifications would be most helpful in addressing the concerns that we have identified. In particular, to have a consistent statutory standard for the regulation of foods and dietary supplements is most appropriate, both to provide nutrients for an increasingly health-conscious public—and there is simply not basis for permitting a claim on dietary supplements and then prohibiting it on foods that have the same or even better nutritional characteristics.

Second, a point that has not been mentioned is we are concerned that, as currently drafted, S. 784 has a provision regarding dietary intake standards that would compel a change in the daily value amounts used in food labeling, thus requiring another mass change in almost all food labels. We had been advised this is not an intended result of the legislation, and we would greatly appreciate attention being given to that provision, sir.

Third, I would just note that with respect to health claims, there has been much discussion today. The National Food Processors Association enjoys being together with the dietary supplement industry and CSPI and virtually everybody else in expressing concerns about the very restrictive regulatory approach that the Food and Drug Administration is taking to health claims. We are greatly troubled that FDA is preventing truthful and nonmisleading statements from being made. And Chairman Kennedy's comments along that line earlier today were greatly appreciated. And we are troubled when the Commissioner's response to questions about some of those statements is not to defend his role, but to simply say that actions that are violative of the regulations are not an enforcement priority. That is not the kind of reasonably, consistently applied regulatory standard that makes for a sound marketplace.

In conclusion, we feel that dietary supplements have a role in the marketplace and believe that consumers should have access to dietary supplements as well as truthful and nonmisleading information about both foods and supplements.

Senator KASSEBAUM. Thank you very much, Mr. Bode.

[The prepared statement of Mr. Bode follows:]

PREPARED STATEMENT OF JOHN W. BODE

Mr. Chairman and members of the subcommittee, thank you for this opportunity to provide testimony. I am John W. Bode, a partner with Olsson, Frank and Weeda. I serve as legislative Counsel for the National Food Processors Association (NFPA). Accompanying me today is Regina Kildwine, Director of Technical Regulatory Affairs for the National Food Processors Association.

NFPA is the science-based association of the food industry, whose 500 members manufacture the nation's processed-packaged fruits and vegetables, juices and drinks, meat and poultry, seafood and specialty products. NFPA maintains three food science laboratories which conduct an array of important research related to food processing. We very much appreciate this opportunity to testily today on the issue of dietary supplements regulation.

My testimony provides NFPA's views on the dietary supplement regulations proposed by the FDA, issues related to health claims and safety on dietary supplements, and some perspective on the competitive environment for dietary supplements and foods.

NFPA members are now in the process of developing new nutrition labels, to comply with FDA regulations implementing the Nutrition Labeling and Education Act of 1990 (NLEA). Processors of meat and poultry products are also adopting a new nutrition label to comply with regulations of USDA's Food Safety and Inspection Service, which were promulgated under existing authority, and which conform closely to the FDA mandatory nutrition labeling rules. This is a challenging activity for the food industry, but it is also an endeavor which NFPA and the food industry both support. Studies have shown that consumers want clear and believable nutrition information on food labels, and these new rules will deliver that information.

The food industry also supported the authorizing legislation, the NLEA, and expended much time and effort in working with Congress so that labeling legislation would provide a level playing field among competitors. Once the NLEA was passed, NFPA expended considerable scientific and regulatory expertise during the rulemaking process to help assure that this complicated law was implemented in an effective and reasonable fashion. NFPA now is helping to educate both the food industry and consumers about the new nutrition label. On May 8, 1994 the mandatory nutrition labeling requirements of the NLEA become effective, and mandatory nutrition labeling for meats and poultry becomes effective shortly thereafter, but already we are seeing new food labels that will over time become a significant part of the education of American consumers on nutrition and healthful dietary choices.

In June of this year, FDA proposed three rules, under the NLEA, to regulate dietary supplement labeling and claims in closely comparable terms to foods. At the same time, FDA announced its intention to regulate the safety of amino acids, herbs, and other nutritional substances.

NFPA supports the FDA proposed rules. It is the view of NFPA that dietary supplements should be regulated in the same manner as foods. Dietary supplements figure prominently in the dietary and nutrient decisions of Americans. As such, it is crucial that dietary supplements—vitamins and minerals, herbal substances, and other nutrients such as amino acids—be regulated in a manner consistent with foods under the NLEA to achieve the over-arching purposes of the Act. We can not expect to educate and empower consumers to make sound dietary choices if supplements are not brought within the regulatory regime of the NLEA.

NFPA believes there is no scientific basis to consider dietary supplements, which deliver vitamins, minerals, and other nutrients, as any different from foods, which deliver the same nutrients to consumers through slightly different means.

By way of illustration, food processors often supplement foods with vitamins and minerals through enrichment or fortification. Enriched flour contains the added nutrients thiamine, niacin, riboflavin, and iron, according to the specifications in its standard of identity. Many manufacturers of juices and drinks add ascorbic acid to fortify the food with vitamin C. These vitamins and minerals—vitamin C, iron, thiamine, riboflavin, and niacin—are the same food chemicals used in many dietary supplements. Both food manufacturers and supplements manufacturers obtain these chemicals from the same commercial sources. The examples I've noted do not even illustrate the most obvious point of comparison: fortified breakfast cereals, often considered to be dietary supplements in food form, and marketed occasionally as "crispy, crunchy vitamins."

In FDA's NLEA regulations for food labeling, published this January, there are strict provisions for assuring that the label declaration of nutrients accurately represents the nutritional qualities of the food. There are thorough regulations for claims—both nutrient content claims and health claims—for foods containing these nutrients. Also, the rules contain misbranding provisions, which prohibit a food from stating that, because it contains or is absent certain dietary properties, it is adequate or effective in the prevention or treatment of any disease or symptom. Health claims regulations permit certain statements on specific diet-disease relationships.

New food labeling regulations assure a level playing field for conventional foods. The food industry believes firmly that dietary supplements must be held to the same standards as foods. Conventional foods and dietary supplements compete for

consumers' vitamin and mineral dollars, and this reason alone demands that the competitive playing field must be level.

The issue of the level playing field raises the question of the basis of health claims for dietary supplements. Conventional foods now are held to the NLEA standard of "significant scientific agreement among qualified experts" prior to securing FDA approval for health claims. This standard provides a high degree of confidence that the accuracy of claims will be borne out over time and the nutrition education function of labeling reinforced, though FDA's implementing regulations are inappropriately restrictive. There is no rationale of merit to justify a less exacting standard for health claims on dietary supplements.

NFPA believes firmly that all dietary supplements must be held to the same standards of safety as other foods. Without adequate FDA regulation, consumers may be enticed into over consumption of certain nutrients contained in dietary supplements, and thus run the risk of suffering from acute or chronic toxicity. There are many identifiable examples of nutrient toxicity: excessive zinc intake can interfere with the body's ability to absorb another necessary nutrient, copper, which may lead to severe anemia and death, and there are indications that consumption of zinc can have a negative effect on total cholesterol by decreasing HDL cholesterol levels without reducing other cholesterol component levels; over supplementation of iron in the diet poses a special risk to children and to those with genetic tendencies to hemochromatosis; selenium can be very toxic at low doses and a mislabeled supplement containing this nutrient resulted in the deaths of thirteen individuals in 1984; excess consumption of vitamin B6 can cause neurotoxicity; and people with undiagnosed abnormalities of calcium metabolism who consume high calcium intakes could develop hypercalcemia, which can prevent the normal repair of microfractures in bones and lead to fragility. From a health perspective the greatest concern may be the over consumption of amino acids. The Federation of American Societies for Experimental Biology (FASEB) concluded that the current state of scientific understanding does not permit the establishment of safe upper limits on the consumption of amino acid supplements, and that certain population groups should only consume these products under explicit medical supervision.

It is important to the food industry that supplements and the components of supplements be regulated in a manner similar to foods and their ingredients. Many nutrients in dietary supplements also occur naturally in foods, or are added to food products during the manufacturing process. If misused or over consumed due to inadequate safeguards, these normally safe substances can lead to acute or chronic toxicity. Such events could tarnish the value of specific nutrients or other substances in the eye of the consumer. Likewise it is important that, like foods, supplements be manufactured under good manufacturing practices to assure that impurities or other contaminants do not render a product injurious to human health.

The food processing industry fears that highly publicized episodes of injury or illness resulting from inadequately regulated supplements may turn consumers away from foods bearing safe and beneficial quantities of the same substances. For example the addition of dietary fiber to foods can substantially enhance the nutrient profile of a particular food for the benefit of consumers. However, ingesting isolated fiber in the absence of food can reduce the intake of essential nutrients. of even greater concern is the possibility of immediate injury that can result from consumption of soluble fiber that is not fully hydrated: soluble dietary fiber supplements can be especially dangerous. If a soluble fiber supplement is not fully hydrated before consumption, then the fiber once consumed can expand dramatically in the stomach and intestine as it becomes hydrated. This increased bulk can lead to intestinal obstruction and excess fermentation. Recently the use of guar gum supplements, also a common constituent of many processed foods, produced severe gastrointestinal illness for several consumers, and resulted in the recall of the product.

It has been NFPA's experience over 85 years that a high degree of safety in food products enhances consumer confidence in foods, and serves to build trade in those foods. Adverse episodes undermine consumer confidence, often affecting entire segments of the industry—not to mention the consequences for the company involved. Because conventional foods and dietary supplements compete directly for consumers' nutrient dollars, it is imperative that both industries maintain the same images of safety and credibility in the eyes of consumers. Any loss of credibility, or failure of public confidence, can mean literally hundreds of millions of dollars in market disruptions to the food industry.

Advocates for the dietary supplement industry may contend that supplements are distinct and apart from foods, and certainly marketing strategies for supplement products may try to create the illusion of such differences. Nonetheless consumers expect and believe that FDA regulation of dietary supplements is as comprehensive and effective as it is for conventional foods. The consumer has no reason to know

or expect that supplements may represent a class of products manufactured and sold under a regulatory regime that is less rigorous or effective than that which governs food products.

All of the issues that are present in the dietary supplement rulemakings and a few others, arise in connection with S. 784, the Dietary Supplement Health and Education Act of 1993. Permit me to address the issues that S. 784 raises.

In several respects, S. 784 would impose a lower regulatory standard for dietary supplements than applies to foods. In particular, lower standards are proposed with respect to substantiation of health claims, regulation of potency, and safety of ingredients. We know of no substantive basis for permitting a lower regulatory standard for dietary supplements than foods and respectfully suggest that a strong policy bias against such a distinction should exist because foods and dietary supplements compete as nutrient sources.

Certainly with respect to health claims, a lower standard of substantiation is inappropriate. There is 00 basis for a food with nutritional characteristics similar or identical to a dietary supplement to be prohibited by law from making the same health claim as the supplement. Such a distinction would undermine the nutrition education function of the NLEA The objective of common definitions and standards, already a complex field, would be rendered unintelligible by the groundless distinction between regulation of claims on supplements and foods. That situation would be further confused as there would be great incentive to present products that are now regarded as fortified foods as dietary supplements. Finally, public health concerns arise in connection with the health claims standard proposed in S. 784 when viewed in the context of hobbling FDA's ability to regulate potency and the safety of ingredients used in dietary supplements. In such circumstances, aggressive health claims on dietary supplements can invite significant problems with nutrient toxicity and interactions, particularly with respect to amino acids.

S. 784 would establish a lower regulatory standard for dietary supplement ingredients than for foods. Foods, of course, must have ingredients that, before marketing, are determined to be generally recognized as safe (GRAS) or approved by FDA for safety as a food additive. Under S. 784, substantiation of the safety of an ingredient bears a lighter standard than for foods and, once made, would require that FDA determine through rulemaking that the ingredient presents a "substantial and unreasonable risk of illness or injury." Requiring FDA to undertake a rulemaking to determine an ingredient poses substantial risk probably means at least a two-year decision-making process. There is no basis for this distinction in standards of ingredient safety, and in light of the grave limitations of FDA resources, it is difficult to overstate the effect of the procedural burden this approach would place on FDA.

Of course, food remains subject to the fortification policy of FDA S. 784 would prohibit the agency from regulating the potency of dietary supplements despite a clear record of problems with nutrient toxicity and interactions—a public health threat that could be heightened in the presence of inappropriate health claims.

In short, Mr. Chairman, NFPA generally supports the standards of public health protection enumerated in current law because of the importance of assuring a high degree of confidence in public health protections. There is no basis for lowering regulatory procedures and standards for dietary supplements while holding foods to the current exacting standards. To do so would lower public health protections, as well as create an unlevel field of play for competitive industries.

Mr. Chairman, beyond the level playing field issues, S. 784 would create another major issue for the food industry. Section 6 of the Act, dietary intake standards, among other things, specifies that daily values used in food labels should generally be no less than the "United States Recommended Daily Allowances established by the Food and Nutrition Board of the National Academy of Sciences for the age and sex group most at risk of nutritional deficiencies of any particular nutrient." This apparent reference to the Recommended Dietary Allowances would compel FDA to change daily value amounts and thereby compel yet another mass change in food labeling to reflect the new daily value amounts. NFPA sees no deficiency in FDA's promulgation of current daily values. Indeed, it appears to be a more appropriate method than the "highest possible" level S. 784 would require. Above all, an additional change in food labels would be a significant expense that largely would be passed on to food consumers for modest changes in Daily Values that would offer no real benefit to public health.

Mr. Chairman, we appreciate this opportunity to present testimony, and respectfully urge revisions in S. 784 to accommodate the problems we have identified.

Thank you.

Senator KASSEBAUM. Mr. McNamara, who represents the Utah Natural Products Alliance, is a member of the firm Hyman, Phelps & McNamara.

Mr. MCNAMARA. Thank you, Senator. I appear here today as legal counsel for the Utah Natural Products Alliance which has been working together with Senator Hatch now for quite some time on behalf of a rational reorientation of the laws concerning regulation of dietary supplements because we strongly believe that the current system that the FDA administers is not fair and that the industry needs some legislative relief.

The UNPA has prepared a detailed brief which provides exhaustive discussion of various issues as well as citations and copies of FDA documents that ought to be a matter of concern to members of this committee. We will submit that for the record. That will then leave me a moment or two to reflect on some of the frustrations that I heard and felt in the back of the room as members of the Utah Natural Products Alliance and their colleagues elsewhere in the dietary supplement industry listened to the FDA presentation. Because in our hearts and experience, we know that the very reassuring depiction of FDA behavior that was conveyed to this committee does not reflect the real world that our members have experienced.

It is terribly difficult to get the same degree of time and attention from the Senate to have our side heard as directly. I would like to just mention a couple of examples.

First of all, let's talk about safety. The Commissioner here asserts in front of yourself and others that his real concern is only with potentially dangerous products; that if things are safe, they are not really chasing around after that, and that all they are doing is applying the law that you have already passed in a fair and reasonable manner.

Well, the existing cases that this Commissioner and this agency have been bringing right up until the present time show that that is not really a fair characterization of what has been going on.

Now, attached to the testimony that we have submitted are copies of two United States Courts of Appeals decisions. They have been referred to by others briefly here, but I think it becomes important to think about what FDA was doing. It is an example of the real world. People were selling a substance called a dietary supplement of black currant oil. What is black currant? Black currant is the same stuff you put on your toast in the morning for breakfast.

Rational people, including Sir James Black, who has won the Nobel Prize for medicine, believe that gamma linolenic acid, which is provided by black currant oil and also by certain other oils, is a useful, rational, safe dietary supplement.

The FDA goes out gangbusters after this material to prevent it being available at all. Now, you need to understand that this food additive definition is not just a semantic game where we argue whether something is a food or a food additive. The consequence of being a food additive is that you are deemed to be illegal until FDA issues an approving food additive regulation, which our footnote will show to you here typically takes somewhere in the neighborhood of 5 years and more than $1 million to get approved.

Now, two U.S. Courts of Appeals, with two separate panels, six Federal judges, reviewed this year the FDA's actions against dietary supplements of evening primrose oil. Unequivocally, they both agreed with each other. The second court cited the first as being an outstanding finding with which they agreed. What we get is a statement first that FDA had not shown that the product was unsafe in any way. FDA had not shown, this Commissioner, this same people sitting at the table before you today, who profess that they do not have any desire to take away safe products, had failed to show that this product was unsafe in any way.

They then attempted to say, but it is deemed automatically to be illegal because you put it in a gelatin capsule, and that makes it a food additive; and because it is a food additive, it is deemed to be unsafe.

One of the Courts of Appeals noted that that was an Alice in Wonderland construction of the law. The other said it was nonsensical. Do not take my word for it. Have your staff read the United States Courts of Appeals decisions that are attached here. They both rejected the FDA position.

Then this year, this Commissioner encouraged the Solicitor General to take those cases up to the U.S. Supreme Court, and only because the Solicitor General of the United States had enough wisdom to refuse to do that are we not now faced with the defense of that proposition in front of the U.S. Supreme Court.

Let's talk about labeling. Here is another thing. The concept seems to be that we are talking about a claim that this product will cure cancer, but let's talk about the real world as an honest dietary supplement company has to deal with it when they are trying to sell product.

You have got a dietary supplement with certain vitamins and minerals in it. You would like people to know something about what it is good for. If you are a dietary supplement company in Utah, you might go to the University of Utah and say, look, let's hire the professor from the department of nutrition to prepare a quarterly summary of the latest literature that has recently been published about the usefulness of nutrients. FDA's position is that you may not do that. Why? Because the newsletter that you publish will be deemed by law to be labeling, since it is written, printed, or graphic matter that accompanies product within the meaning of the definition, even if you mail it separately. So it is labeling. And under their proposed regulations, you may not say anything, regardless of whether it is truthful and not misleading, unless the FDA has first approved it in a regulation insofar as it is a health claim. And their concept of a health claim is anything that either explicitly or implicitly links a nutrient either to a disease or to a health-related condition.

The bottom line is they do not believe you can truthfully summarize the recent scientific literature and distribute that information because they have to approved it first, God help us, in a regulation, which will take years.

Take a look at another aspect of this significant scientific agreement concept. I have quoted it here, but the company in this country that has the largest fleet of fishing ships. The Zapata Haynie Company, obviously quite interested in oil and in fish, filed com-

ments with FDA in the proceeding on health claims about omega-3 fatty acids. They said to FDA in that proceeding, look, what we propose to do is to be able to say in literature a summary of the current State of the scientific literature. We do not want to say that it has been proven that fish and fish oil will prevent cardiovascular disease, but we want to have a truthful, balanced statement about the current State of scientific opinion. And I have quoted in the brief exactly the position that they wanted to State. I do not think anybody denies that it was a truthful and nonmisleading summary.

FDA's response was, no, we cannot allow that kind of thing because the only thing that significant scientific agreement will permit is ultimate proof of the ultimate question; i.e., the day that you get around to having finally proved that something will cure, treat, or prevent a disease by a great preponderance of the evidence, then we will consider entertaining a new regulation which will take us 3 years to allow you to make that statement.

There is even one terribly surprising example in here of FDA's abusive concept of what is misleading labeling. They are telling dietary supplement companies that put in the same product vitamins and minerals and other things that FDA does not think are vitamins and minerals, like rutin or bioflavenoids that they may not tell the customer on the label how much of the rutin or the bioflavenoids is in the product. Their assertion is that it is inherently illegal to tell somebody how much of an ingredient is in a product. And then they come here and want Government money and our very precious purse to be expended on allowing them to pre-clear labeling so that one would not be free to say anything until they had decided that it was good enough.

In a free society, one of the things we ought to have and particularly need when we are talking about the FDA and dietary supplements is a situation where there is not prior restraint on free speech. We need the freedom to be able to make truthful and nonmisleading statements and be prepared to have the FDA whack us in court if we make a false or misleading claim or if we have in some other manner violated the law.

The final thing that Senator Hatch's bill would do that no one today has mentioned that is really very important to the industry—and I hope no one is forgetting as one gets around to talking about resolutions and accommodations—is the way FDA currently regulates allows it to disparage your company without accountability. The FDA issues warning letters to members of the industry telling them, for example, they are selling adulterated products because they have got an unapproved food additive consisting of black currant oil, and threatens in the letter to bring a court case, a civil seizure action, or an injunction, and then makes a public record of that letter, places the letter on public display at FDA headquarters where it is routinely picked up on by the trade press, by the Wall Street Journal, by investors, by bankers, by your competitors. Your children read about it in the newspapers and ask you about it at night.

And if you do not agree with them and you want to get judicial review, they argue that there is no judicial review available to you, that you are denied any judicial review when they behave that

way. I think that among the many other things we need is to have that situation corrected.

Thank you. I hope that anyone who is interested in this and has not already been long ago persuaded by Senator Hatch's bill and its merits will take the time to have their staff at least look at the brief that the Utah Natural Products Alliance has submitted to the record.

Senator KASSEBAUM. I am sure they will, and thank you, Mr. McNamara.

[The prepared statement of Mr. McNamara follows:]

PREPARED STATEMENT OF STEPHEN H. MCNAMARA

Mr. Chairman and members of the committee on Labor and Human Resources, the Utah Natural Products Alliance (UNPA) appreciates the invitation to testify at this hearing to review the regulation of dietary supplement products by the U.S. Food and Drug Administration (FDA). UNPA is an association of Utah companies that manufacture or distribute dietary supplement products. These companies have been working closely with the senior Senator from their state, Senator Orrin Hatch, a Member of this Committee, on behalf of appropriate legislation for dietary supplement products. UNPA strongly endorses the concepts underlying S. 784, the "Dietary Supplement Health and Education Act of 1993," which was introduced by Senator Hatch, for himself and Senators Reid and Murkowski, on April 7 of this year, although UNPA members hope for certain refinements in S. 784 during the legislative process. We note that there are now more than 55 cosponsors of S. 784.

We have been asked to explain why UNPA members believe that dietary supplements are in need of legislative relief from excessive FDA regulation. We are pleased to have the opportunity to do so.

I. NEED FOR NEW LAW TO STOP FDA FROM TRYING TO IMPOSE "FOOD ADDITIVE" STATUS ON SAFE SUPPLEMENTAL FOOD SUBSTANCES

UNPA believes that Congress should amend the Federal Food, Drug, and Cosmetic Act (FDC Act), 21 U.S.C. (301 et seq., to make it clear that a food substance provided by a dietary supplement is not subject to regulation as a "food additive" by the FDA. This provision is needed because FDA has tried to prevent consumers from obtaining supplemental amounts of food substances that they want to consume by asserting that such substances are subject to the technical definition of "food additive." FDA has asserted that, as "food additives," food substances are banned from being included in dietary supplements without the prior issuance by FDA of a food additive regulation.[1]

UNPA believes food additive status for ingredients in dietary supplements should be reserved for chemical preservatives, solvents, processing aids, or other such technical or functional agents[2] FDA should not be permitted to assert "food additive" requirements to prevent consumers from obtaining safe vitamins, minerals, herbs, or other similar food substances that they knowingly want to consume and to add to their diets by means of a dietary supplement.

This is not just a theoretical concern. In recent years FDA has tried—sometimes successfully—to deprive dietary supplement consumers of a number of food substances——including black currant oil, linseed/flaxseed oil, evening primrose oil, co-enzyme Q10, chlorella, calcium acetate, and even orotic acid (a substance found in milk) by arguing that the substances—food substances, desired by consumers in dietary supplement form—were "food additives."

A. CHROMIUM

Indeed, in the recent past FDA even suggested that compounds of chromium were unapproved food additives and thus illegal[3] when added to dietary supplements, even though it is clear that chromium is (1) a nutritionally essential mineral, (2) extremely safe (in the trivalent form commonly used in dietary supplements), and (3)

[1] It can cost from $1 to $2 million for a petitioner to prepare and pursue a food additive petition, and FDA approval of a food additive petition typically takes from 2 to 6 years. Kutak, Rock & Campbell, "FDA Safeguards Against Improper Disclosure of Financially-Sensitive Information: The Product Approval Centers," Final Report (November 14, 1991) at 162; 33 Food Chem. News 67 (November 4, 1991).

[2] Indeed, these kinds of additives are often not used at all in dietary supplements.

[3] E.G., see 56 Fed. Reg. 60382 (November 27, 1991) ("Dietary supplements of—chromium—are not permitted").

not present in optimum amounts in all American diets.[4] Instead of raising doubts about the legality of chromium, FDA should have been encouraging its inclusion in multimineral dietary supplement products.

This year, after Senator Hatch had spoken out on the floor of the Senate in 1992 about FDA over-regulation of chromium supplements (Congressional Record, S. 7983, June 11,1992), FDA implied that it was no longer so concerned about chromium (58 Fed. Reg. 2212, 2170, January 6, 1993); but there is no guarantee that FDA will not revert to its former attitude with respect to this essential nutrient. UNPA believes that FDA should not be allowed to prevent consumers from obtaining supplements of chromium or other safe supplemental food substances by asserting that such substances are "food additives."

B. BLACK CURRANT OIL

FDA has asserted to Congress that in pursuing "food additive" allegations against dietary supplement ingredients, it is simply applying the current law in a reasonable manner and is restricting its actions to products that present serious safety concerns. Two very recent federal judicial decisions, however, show that in fact FDA has been distorting the law in its actions to try to prevent the marketing of safe dietary supplement substances. We attach to this statement copies of unanimous decisions by three-judge-panels of two different United States courts of appeals, rejecting efforts by FDA to ban safe dietary supplements of black currant oil by means of the legal ruse of asserting that the black currant oil was a "food additive." United States v. Two Plastic Drums—Viponte Ltd. Black Currant Oil—Traco Labs, Inc., 984 F.2d 814 (7th Cir. 1993) ("Traco") (Attachment A); United States v. 29 Cartons of—an Article of Food—Oakmont Investment Co., 987 F.2d 33(1st Cir. 1993) ("Oakmont") (Attachment B).

Both of these cases involved the same product, i.e., black currant oil intended to be used as a dietary supplement in gelatin capsules. As the Seventh Circuit noted, "FDA has not shown that BCO [black currant oil) is adulterated or unsafe in any way." (Traco, page 820.) Nevertheless, FDA attempted to cause this safe supplemental substance to be banned by asserting that it was a "food additive" (apparently, on the basis that the substance would be "added" to gelatin capsules). If the substance were a "food additive, " it would become illegal by operation of law because the food additive provisions of the FDC Act provide that a food additive is "deemed to be unsafe" if it is not the subject of a regulation issued by FDA approving its use. 21 U.S.C. Secs. 342(a)(2)(C), 348(a)(2).

Fortunately, both courts unanimously rejected this FDA "food additive" interpretation, which was clearly an effort by FDA personnel to ban a safe dietary supplement by stretching the legal definition of a "food additive" beyond all reason. The decision by the Seventh Circuit Court of Appeals describes the FDA's effort as an "Alice-in-Wonderland" approach. (Traco, page 819.) The decision by the First Circuit describes FDA's approach as "nonsensical." (Oakmont, page 37.)

We understand that FDA recommended to the Department of Justice that petitions for certiorari be filed with the United States Supreme Court to try to have these decisions overturned. Fortunately, it appears that the Solicitor General declined to file such petitions. Nevertheless, we also understand that FDA personnel are now asserting: (1) that they may not regard FDA as bound by the Traco and Oakmont decisions in other circuits, and that at some point in the future FDA may once again seek to enforce the view that even a single supplemental food substance sold in a gelatin capsule may be regulated by FDA as a "food additive"; and (2) that, notwithstanding Traco and Oakmont, if a company were to add an additional substance to black currant oil, e.g., vitamin E (a combination that dietary supplement products have sometimes provided in the past), such an addition of another substance would create a different set of facts and would enable FDA to assert all over again that the black currant oil in such a product is an unapproved, "illegal" food additive.

It is this sort of FDA action in using and abusing the food additive definition to try to stop the sale of safe dietary supplement products that has caused persons interested in dietary supplements to ask Congress to pass a law that would explicitly provide that FDA may not regulate supplemental substances as food additives. Such a provision is included in S. 784. UNPA strongly encourages all Members of this Committee to support such legislation.

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[4] E.G., see National Academy of Sciences, Recommended Dietary Allowances, 10th ed. 1989, pp. 241–243.

C. EVENING PRIMROSE OIL

I have had a striking personal experience with what I believe is FDA misuse of the food additive definition in the case of dietary supplements. This concerned evening primrose oil. A few years ago, I accompanied Sir James Black, the highly respected British physician-researcher (who has won the Nobel Prize for Medicine), to a meeting with senior personnel at the FDA Center for Food Safety and Applied Nutrition. At that time, Sir James wanted to explain to FDA personnel why he believed that dietary supplements of evening primrose oil were both clearly safe and useful, as a source of gamma linolenic acid (GLA). In what was one of the most surprising and disturbing meetings that I have ever attended at FDA, Sir James was not allowed to explain to FDA personnel why he believed evening primrose oil was safe and appropriate for supplementation; instead, he was told that FDA would not permit such a presentation and that the agency had already decided that evening primrose oil was an "unapproved food additive" and should not be sold as a dietary supplement.

The extent of FDA's subsequent determination to eradicate all dietary supplements of evening primrose oil from the United States market has also truly surprised me. The most recent (1993) FDA Annual Awards Ceremony provides some instructive insight in this respect: At this ceremony the FDA Commissioner presented a special award to more than 60(!) FDA personnel for pursuing regulatory actions against evening primrose oil. (See Attachment C.) Note that this crusade was taken against a product that I understand is readily available, with a substantial record of safety, to the general public in most of the rest of the modern world——including, for example, in Canada, Great Britain, Germany, Scandinavia, and Israel. Why should FDA be so determined to deprive American citizens of such a supplemental food substance that they want to consume?

I am a lawyer and not a scientist, so I cannot, of course, speak as an expert about safety. However, FDA assertions that there are safety-related concerns about dietary supplements of evening primrose oil at reasonable potencies appear to me to be incredible. I have heard Nobel Prize-winner Sir James Black express just the contrary view; and, as noted above, the substance is widely available with a substantial record of safety in other sophisticated nations. The fact that FDA would give a major award to its personnel for preventing American consumers from obtaining a dietary supplement that is readily available elsewhere in the modern world is both instructive about FDA's attitude concerning dietary supplements, and, I believe, disturbing.

D. Preventing FDA From Regulating Food Substances In Dietary Supplements As "Food Additives" Would Not Deprive FDA Of Ample Authority To Protect Consumers From Unsafe Products

It is important to note here that preventing FDA from regulating food substances in dietary supplements as "food additives" would not deprive FDA of ample authority to protect consumers from unsafe products. Section 402(a)(1) of the existing FDC Act, 21 U.S.C. Sec. 342(a)(1), would continue to apply to dietary supplements. This section prohibits a food (including a dietary supplement) from bearing or containing any "poisonous or deleterious substance which may render it injurious to health." Under this section of the FDC Act, however, FDA must at least have some realistic basis to believe and show that a food substance is poisonous or deleterious and "may" render a product injurious to health before the agency can deprive consumers of foods that they want to purchase and consume—and that is just as it should be in a free society.

E. FDA Disregard Of Its Previous Statements To Congress

There is another point that UNPA wants to mention here because it should be of special interest to the Committee—since it concerns the matter of adherence by a regulatory agency to laws enacted by Congress.

One of the problems that the dietary supplement industry faces when FDA asserts that an ingredient in a dietary supplement is an "unapproved food additive" is that FDA has interpreted the law in such a manner that, in most circumstances, such an assertion by FDA becomes a necessarily-self-fulfilling prophecy. In general, FDA asserts that the only way for the proponent of such a substance to avoid food additive status, and illegality, is to show that the substance is "generally recognized as safe" ("GRAS")—but FDA then asserts that if its experts state that a substance is not GRAS,then, as a matter of law, the substance cannot be "generally recognized" as safe and therefore must be deemed to be a food additive. E.g., FDA asserts that once a court is presented with affidavits by FDA witnesses stating that a material is not GRAS, there is not even any reason for the court to hold a trial on the subject, and that summary judgment should be granted for FDA.

We raise this matter here because such an argument by FDA—although it may meet with favorable acceptance in a court that does not particularly want to hear a long trial involving a battle of scientific witnesses who disagree about GRAS status—is, UNPA believes, in flagrant disregard of the interpretation of the food additive definition that FDA conveyed to Congress that it would abide by when the Food Additives Amendment was enacted in 1958. At that time, the representatives of the Department of Health, Education, and Welfare who testified for FDA before Congress about the proposed legislation explicitly stated that no matter what definition of "food additive" was adopted, in an enforcement action the burden would be on FDA to prove that a substance was not GRAS! (See Attachments D and E.) Current FDA practice essentially renders that testimony a nullity. Instead, FDA argues that the burden of proof is on anyone who disagrees with FDA to prove that a substance is GRAS, and that a substance cannot be GRAS, as a matter of law, if FDA says it is not. FDA's ability to manipulate the burden of proof and the meaning of the food additive definition in this respect is one more reason why the dietary supplement industry needs a clear statutory exception from food additive status for food substances provided as dietary supplements.

II. NEED FOR EXPLICIT LEGISLATIVE RECOGNITION THAT LABELING FOR A DIETARY SUPPLEMENT MAY PROVIDE TRUTHFUL HEALTH-RELATED INFORMATION WITHOUT FDA PRECLEARANCE

As Senator Hatch observed when the Nutrition Labeling and Education Act (NLEA) was passed in 1990, "By their very nature, the dietary supplements must be marketed so that the consumer is informed of the health or disease-prevention benefits that may be conferred." Congressional Record, S. 16611 (October 24, 1990). Nevertheless, since passage of that Act, FDA has repeatedly tried to impose severe restraints on the freedom of dietary supplement manufacturers efficiently to provide truthful health-related information in labeling. 56 Fed. Reg. 60537,60583 (proposed 21 C.F.R. 1101. 14(a)(1)) (November 27,1991); 58 Fed. Reg. 33700, 33714 (proposed 21 C.F.R. 1101. 14(a)(2)) (June 18, 1993). The dietary supplement industry needs enactment of legislation that clearly permits dietary supplement products to include in their labeling truthful information, including truthful information about the physiological properties or other health-related aspects of the products.

Of particular concern here is the matter of a prior restraint on free speech, which should be regarded as anathema by Americans: FDA has repeatedly proposed regulations that would not allow truthful health-related information to be included in labeling for dietary supplements until after FDA first issues a final regulation approving the information—a process that can be expected to take years to complete. 56 Fed. Reg. 60537, 60563 (November 27, 1991); 58 Fed. Reg. 33700, 33714 (June 18, 1993).

Let us be very clear here that UNPA is not arguing that companies should be free to make false or misleading claims. If a labeling claim is made that is false or misleading, or the claim otherwise violates a proper legal standard, FDA already has, should have, and would continue to have, ample authority to take action against the product, as a "misbranded" food. 21 U.S.C. 1343. FDA can initiate a civil seizure action, an injunction action, or a criminal prosecution in response to the marketing of a misbranded dietary supplement, 21 U.S.C. 331-334, or it can request a recall of the product. 21 C.F.R. secs. 7.40-7.59. However, UNPA strongly believes that a dietary supplement distributor should not be required first to obtain FDA permission, including the issuance of a new regulation, before the company may begin to provide health-related information in labeling that the company is prepared to defend in court, if necessary, as truthful, not misleading, and supported by valid scientific evidence. Petitions to FDA to issue regulations can be extremely time-consuming and costly to prepare, and it typically takes FDA years to issue a new regulation. Labeling information about food substances should not be subject to such burdensome and delaying prior restraints. (Furthermore, enforcement convenience for FDA should not be given priority over freedom of speech!)

The extent to which FDA has been willing to go to try to prevent dietary supplements from providing truthful and nonmisleading information in labeling is instructive here. Let's consider just three examples:

A. NUTRITION NEWSLETTERS

FDA regards a company newsletter that reviews the recent scientific literature on health-related effects of nutrients as "labeling" for company products that contain those nutrients. Under the terms of FDA's NLEA regulations, such a newsletter, as "labeling," could not be published without the company's first obtaining FDA ap-

proval (by means of the issuance of a new regulation) for every report in the newsletter about a study that would link a nutrient to a health-related condition.[5]

The pragmatic "bottom line" of all of this is that, it appears, FDA's intentions for regulating the labeling of dietary supplement products would effectively prevent a company even from issuing a regular, timely newsletter that provides a truthful and nonmisleading review of the recent scientific literature concerning nutrients that the company sells. This would not only prevent the rendering of a valuable consumer service, it would be a serious breach of the freedom of speech.

B. LABELING STATEMENTS ABOUT EVOLVING SCIENCE

In the course of FDA's rulemaking proceeding on whether to allow health-related claims for omega-3 fatty acids in food labeling, at least one manufacturer filed comments with FDA in which it asked that food companies be permitted to make a truthful and nonmisleading, balanced statement in labeling about the nature and extent of evolving knowledge concerning possible benefits of fish and omega-3 fatty acids in the diet. The model labeling statement that the company's comments proposed reads as follows:

There is considerable scientific interest in the subject of whether fish, or certain nutritional substances found in fish, including omega-3 fatty acids, may, when included in the diet on a regular basis, reduce the risk of coronary heart disease. At the present time, there is no established consensus that omega-3 fatty acids definitively have such an effect, but a number of researchers believe that such a relationship may exist, and research is underway to obtain further information.

(Comments by Zapata Haynie Corporation, dated February 20, 1992, filed in FDA Docket No. 91N-0103.)

So far, at least, FDA has refused to permit a statement of this type about omega-3 fatty acids to be used in food labeling—in part, it seems, because the agency appears to be opposed to any labeling at all, even truthful labeling, about evolving health-related knowledge that has not reached the point of (what FDA regards as) significant scientific agreement that a nutrient will inhibit a disease (as distinguished from significant scientific agreement about the current state of evolving knowledge concerning whether a nutrient may have that effect). See generally 58 Fed. Reg. 2478, 2682 (January 6, 1993). I am a lawyer and not a scientist, but I understand from some highly-qualified experts that the model labeling quoted above is a fair and reasonable brief summary of the current state of scientific knowledge and opinion on its subject. It saddens me to realize that my government has tried to put in place a new requirement of law that would prevent a food company from being able to provide truthful and balanced labeling information about evolving scientific knowledge.

If a company wants to make such a statement in labeling, on the premise that the statement is truthful and not misleading, and the company is prepared to defend the scientific validity of the statement, and is willing to assume the risk that FDA might bring regulatory action against the company in court if the agency should conclude that the company has made a false or misleading statement, why should the company not be free to make such a statement on its own responsibility? UNPA believes that a company should not need to wait, first, for the wheels of government at FDA slowly to grind out concurrence that such a statement is truthful and not misleading, and then, for FDA to publish an authorizing regulation (which, inevitably, takes FDA years to accomplish) before such a statement may be made in labeling. Such prior restraints on speech should not be tolerated by Congress.

Moreover, UNPA believes that companies should not be subjected to a regulatory system where (as appears to be the situation here) FDA may even acknowledge that a proposed labeling statement is truthful, but nevertheless refuse to permit the statement because the agency takes the position that the only health messages it will approve for use in labeling are ones where the described nutrient has been proven to have disease-preventive benefit. Why should a company be denied the freedom to provide a truthful summary of evolving scientific knowledge about whether the nutrient may have such benefit? Is this the kind of law—restriction on truthful speech about evolving scientific knowledge—that we want to have in a free society? What kind of country are we creating for ourselves in the future?

UNPA believes that, in addition to the mandatory basic label information (e.g., statement of identity, net quantity of contents, list of ingredients, and name and ad-

[5] Furthermore, it appears that FDA would probably not be willing to issue a regulation approving such a newsletter at all because the recent scientific literature, even if truthfully reported, would probably net yet have reached the state that FDA would regard as "significant scientific agreement" about matters described therein!

dress of the responsible company), and subject to the need to conform label statements to any pertinent definitions of terms that have been established by law (e.g., in a valid FDA regulation), in general, (1) any truthful and nonmisleading statement should be allowed, so long as it is not a drug claim (and we do not believe the model statement proposed by Zapata Haynie, for example, amounts to a drug claim), (2) such labeling should be subject to government policing and enforcement actions for violations (e.g., for false or misleading statements) but not to preclearance, and (3) a regulatory process that would chill truthful speech should not be tolerated.

C. LABELING STATEMENTS ABOUT QUANTITATIVE CONTENT

As a third example of the extent to which FDA has been willing to go in trying to prevent dietary supplement companies from providing even truthful information in labeling, consider the fact that recent FDA regulatory correspondence has actually told some companies that they should not state in labeling how much of a supplemental substance is provided by a tablet. For example, in correspondence issued on July 16, 1992, FDA told one company that a label text that the company had proposed to FDA was improper because "[i]nositol[,] choline bitarate, para-aminobenzoic acid, citrus bioflavonoids and betaine hydrochloride are declared in milligram amounts on the label of this vitamin and mineral tablet." (See Attachment F.) FDA did not want the company to tell its customers how much of each of these substances was present in the product!

Do we really want the public's limited resources being spent by IDA on preventing a dietary supplement company from truthfully telling how much of a substance is present in a dietary supplement?

All of the foregoing examples underscore a continuing concern of the dietary supplement industry. The industry needs to be able to provide truthful and nonmisleading information to its customers. UNPA is full-willing for the industry to be held to a high standard of truthfulness in providing information, but companies should not be required to obtain FDA issuance of an approving regulation before using new labeling. Such a prior restraint on free speech would delay, or effectively prevent entirely, the communication of truthful information about products, and it would also build the size of an additionally-expensive regulatory bureaucracy.

D. THE PROPOSED LEGISLATION WOULD NOT AUTHORIZE FALSE OR MISLEADING CLAIMS

We emphasize that the desired legislation would not authorize false or misleading claims. Whenever FDA believes that a false or misleading claim has been made in labeling for a dietary supplement product, or that a claim has been made that goes so far in providing health-related information that the product should be deemed to be a drug, the agency has ample power to take action in court—under the authority that it already has under existing law—to obtain seizure and condemnation, or to obtain an injunction, or to pursue criminal prosecution—subject to the burden, which FDA properly should bear, to show that the product is indeed in violation. 21 U.S.C. 11331-334; 343(a)(l). The federal courts, including even the United States Supreme Court, have affirmed FDA's power to stop improper claims for dietary supplements under existing law by initiating seizures or taking other punitive action when such claims have been made. E.g., Kordel v. United States, 335 U.S. 345 (1948) (criminal prosecution for improper claims for vitamin/mineral products).

Accordingly, if FDA should present to this Committee some extreme or gross examples

of products that appear to bear false or misleading claims, or improper drug claims, FDA should be told to exercise its existing authority to take regulatory actions against improperly-promoted-products; but it should not be allowed to set in place new rules, as now proposed, that would require honest distributors of dietary supplements to obtain a new regulation from FDA approving each new health-related statement before the statement may appear in labeling. Such a prior restraint on truthful speech is unnecessary and inappropriate. An agency that has not properly exercised its ample existing authority to take action against wrongdoers should not be given new authority that would have the effect of restraining free expression of truthful information by honest citizens as well as the wrongdoers.

III. NEED TO BE ABLE TO OBTAIN JUDICIAL REVIEW OF FDA WARNING LETTERS

UNPA's third legislative goal is a simple request for fundamental procedural fairness in FDA regulation. FDA's primary form of initial regulatory action against allegedly improper dietary supplement products is the issuance of a "warning letter." Such a letter, usually addressed to the president of a company, is put on public display by FDA; and it routinely asserts that a particular product is in "serious violation" of the law—either because the product allegedly bears false or misleading la-

beling, or because it allegedly contains an "unapproved food additive," or because it allegedly bears labeling that constitutes an unauthorized drug claim. The warning letter also routinely threatens an action in court against the product or company. These letters are promptly put on public display at FDA headquarters, and they are frequently the subject of reports in the press or other media.

Such a warning letter can have a devastating impact upon a company, causing the business community, customers, stockholders, and others to believe that the company is in "serious violation" of law and in danger of an enforcement action in court.

If the points raised by FDA in a warning letter have merit, usually the addressee company will promptly take corrective action. However, in circumstances where a company believes that FDA's letter is in error, a most unreasonable situation currently applies. Even though the letter has been made public by FDA and states to the world that the agency has concluded that the company is in serious violation of law, nevertheless, FDA will not agree that the company can obtain judicial review of the merits of such a letter in court. Instead, FDA argues that such a letter is not technically "final agency action" (because the agency might possibly change its mind—although the letter contains no hint of that). The effect is that a dietary supplement company can receive from FDA a formal public warning telling the company that it is in serious violation of law, and demanding that it cease marketing a certain product, and yet FDA will not allow the company to obtain judicial review of the merits of the assertion.

Such a situation is fundamentally unfair. FDA should not be allowed to issue threatening ad disparaging warning letters, which are made available to the press and the public generally, without having the warning letter be subject to judicial review. UNPA believes that legislation is urgently needed to authorize a dietary supplement company to obtain judicial review of any public warning letter that is issued to it by FDA, asserting that the company is in violation of law. S. 784 would have this favorable effect.

IV. CONCLUSION

UNPA hopes the foregoing comments are helpful. We will be pleased to try to answer any questions you may have.

The record supports the district court's finding that Rem did not actually intend to rush to the incoming Chicago train to quickly regain possession of the suitcase before the police found it. Notably, Rem arrived in Chicago and went to a motel to change his clothes and make several telephone calls. The district court stated: "I'm very puzzled in view of his explanation of what happened here that if he was concerned, as I believe he certainly would have reason to be concerned, about his safety that he would have stopped on the way from Midway airport to the Amtrak station and taken the time to check into a motel based on his explanation. I find that incredible."

In addition, when the police approached him, Rem *denied* having been on the train from Los Angeles—or on any train at all. He had been in Chicago two weeks; could not remember the name or location of his hotel; and was merely "visiting" and "looking around" at the train station. This is the equivalent to an oral disclaimer of ownership. *See Tolbert*, 692 F.2d at 1044–45 (court found the oral disclaimer showed abandonment). Aside from any issue of standing, at the very least, Rem's statements indicated that he had no expectation of privacy in the suitcase which did not have his name on it, and which was found on a train that defendant had never been aboard.

III.

The district court did not err in finding that Rem had abandoned the suitcase and as a result had no legitimate expectation of privacy in it or its contents. The district court's denial of Rem's motion to suppress the evidence found is

AFFIRMED.

UNITED STATES of America, Plaintiff-Appellant,

v.

TWO PLASTIC DRUMS, MORE or LESS OF AN ARTICLE OF FOOD, LABELED IN PART: VIPONTE LTD. BLACK CURRANT OIL BATCH NO. BOOSF 039, etc., and Trnco Labs, Incorporated, Defendants-Appellees.

No. 92-1172.

United States Court of Appeals, Seventh Circuit.

Argued Oct. 21, 1992.

Decided Jan. 27, 1993.

Rehearing Denied March 31, 1993.

The Government, acting through the Food and Drug Administration (FDA), commenced an in rem seizure action against drums of black currant oil (BCO). The United States District Court for the Central District of Illinois, Harold Albert Baker, J., 791 F.Supp. 751, granted the processor's motion for summary judgment. The Government appealed. The Court of Appeals, Cudahy, Circuit Judge, held that encapsulated BCO, with a single active ingredient, was not a "food additive" and, thus, the processor did not have burden of proving that BCO was generally recognized as safe (GRAS), even if BCO was merely a component of BCO dietary supplement capsules.

Affirmed.

1. Food ⇐5

Generally, component of food is "food additive," and processor has burden of proving that it is generally recognized as safe (GRAS), even if component is principal component or ingredient sought when food is purchased. Federal Food, Drug, and Cosmetic Act, § 201(s), as amended, 21 U.S.C.A. § 321(s).

See publication Words and Phrases for other judicial constructions and definitions.

2. Food ⇐5

Even substances ordinarily considered "food" in common usage may become food

ATTACHMENT A

additives for which processor has burden of proving that they are generally recognized as safe (GRAS). Federal Food, Drug, and Cosmetic Act, § 201(s), as amended, 21 U.S.C.A. § 321(s).

3. Food ⇐½, 5

Black currant oil (BCO) is dietary supplement itself, not component of dietary supplement and, thus, is "food" and not "food additive," for which processor would have burden of proving that it is generally recognized as safe (GRAS), when BCO is combined with gelatin and glycerin in capsule form; dietary supplement is BCO combined with inactive ingredients used to market BCO in capsule form. Federal Food, Drug, and Cosmetic Act, § 201(f, s), as amended, 21 U.S.C.A. § 321(f, s).

See publication Words and Phrases for other judicial constructions and definitions.

4. Food ⇐5

For substance to become food additive, for which processor would have burden of proving that it is generally recognized as safe (GRAS), substance must not only be added to food, but must have purpose or effect of altering food's characteristics; it is not enough for substance to become component of food. Federal Food, Drug, and Cosmetic Act, § 201(f, s), as amended, 21 U.S.C.A. § 321(f, s).

5. Food ⇐5

Encapsulated black currant oil (BCO), the single active ingredient of a dietary supplement, was not "food additive" and, thus, processor did not have burden of proving that BCO was generally recognized as safe (GRAS). Federal Food, Drug, and Cosmetic Act, § 201(f, s), as amended, 21 U.S.C.A. § 321(f, s).

6. Food ⇐5

Congressional purpose of protecting public health did not permit Food and Drug Administration (FDA) to interpret "food additive" within meaning of Federal Food, Drug, and Cosmetic Act as including every component of food, even single active ingredients, in order to shift burden to processors in all cases to prove that component is generally recognized as safe (GRAS). Federal Food, Drug, and Cosmetic Act, § 201(f, s), as amended, 21 U.S.C.A. § 321(f, s).

7. Food ⇐5, 24(1)

Fact that black currant oil (BCO) was marketed in capsule form, rather than as bottled liquid, did not permit Food and Drug Administration (FDA) to treat BCO as food additive and require processor to prove that it was generally recognized as safe (GRAS); no difference existed between encapsulated BCO and BCO in bottled form. Federal Food, Drug, and Cosmetic Act, § 201(f, s), as amended, 21 U.S.C.A. § 321(f, s).

Douglas Letter, Robert D. Kamenshine (argued), Dept. of Justice, Civ. Div., Appellate Section, Washington, DC, Leslie Kux, Food & Drug Admin., Rockville, MD, for plaintiff-appellant.

Robert Ullman (argued), Jacob Laufer, Steven Shapiro, Bass & Ullman, New York City, Marc Ansel, Erwin, Martinkus, Cole & Ansel, Champaign, IL, for defendants-appellees.

Before CUDAHY and EASTERBROOK, Circuit Judges, and WILL, Senior District Judge.*

CUDAHY, Circuit Judge.

The Food and Drug Administration ("FDA") brings this *in rem* seizure action under the Food, Drug and Cosmetic Act, 21 U.S.C. §§ 301 *et seq.* ("Act"), seeking to condemn and destroy two drums of black currant oil as adulterated under 21 U.S.C. § 342(a)(2)(C) for being a food additive not recognized as safe. The district court granted summary judgment against the FDA, and the government appeals. We affirm.

* The Honorable Hubert L. Will, Senior District Judge for the Northern District of Illinois, is sitting by designation.

I.

Black currant oil ("BCO") is extracted from the seeds of the black currant berry and is marketed as a dietary supplement for its unique fatty-acid structures. The FDA argues that BCO is a food additive not generally recognized as safe ("GRAS") and seeks to seize and condemn two drums of BCO pursuant to sections 334 and 342 of the Act. A food is adulterated and subject to seizure under section 334 "if it is, or it bears or contains, any food additive which [the Secretary has not recognized as safe pursuant to section 348]." 21 U.S.C. § 342(a)(2)(C). The determination of whether a substance is a food additive is critical in establishing the safety of the substance because, if the substance is deemed a food additive, it is presumed to be unsafe, and the processor has the burden of showing that the substance is GRAS. On the other hand, if a substance is not a food additive, but food in the generic sense,[1] then the substance is presumed safe and the FDA has the burden of showing that the substance is injurious to health. *United States v. An Article of Food ... FoodScience Labs.*, 678 F.2d 735, 739 (7th Cir.1982).

The Act defines "food additive" as

> any substance the intended use of which results or may reasonably be expected to result, directly or indirectly, in its becoming a component or otherwise affecting the characteristics of any food (including any substance intended for use in producing, manufacturing, packing, processing, preparing, treating, packaging, transporting, or holding food; and including any source of radiation intended for any such use), if such substance is not generally recognized, among experts qualified by scientific training and experience to evaluate its safety, as having been adequately shown through scientific procedures ... to be safe under the conditions of its intended use....

21 U.S.C. § 321(s). The FDA contends that BCO is a food additive because it is a "component" of food when it is combined with the gelatin and glycerin used to market the BCO in capsules. The gelatin and glycerin encase the BCO to prevent it from becoming rancid. The FDA concedes that if the BCO alone was marketed in bottles for teaspoon consumption, it would not be a food additive, and the FDA would bear the burden of proving that BCO is injurious to health. But the combination of BCO with glycerin and gelatin, the FDA maintains, creates a food consisting of three components, and thus, three food additives.[2] In this instance, therefore, the FDA would require the processor to prove that the substance is safe—something that Traco Labs, the claimant of the two drums of BCO, has not done.

The district court granted summary judgment against the FDA, holding that the FDA's definition of food additive "would obscure any distinction between 'foods' under § 321(f) and 'food additives' under § 321(s)" contrary to the intent of Congress. *United States v. Two Plastic Drums, More or Less of An Article of Food ... (Traco Labs)*, 791 F.Supp. 751, 754-55 (C.D.Ill.1991); *see also* 761 F.Supp. 70, 74 (C.D.Ill.1991) (order denying FDA's motion for summary judgment).

II.

[1, 2] We review the grant of summary judgment de novo. *Overton v. Reilly*, 977 F.2d 1190, 1191 (7th Cir.1992). Summary judgment is appropriate when there is no genuine issue of any material fact and the moving party is entitled to judgment as a matter of law. *Anderson v. Liberty Lobby, Inc.*, 477 U.S. 242, 250, 106 S.Ct. 2505, 2511, 91 L.Ed.2d 202 (1986). The sole issue presented in this action is whether BCO, when combined with glycerin and gelatin, is a food additive pursuant to section

1. Because food additives can be thought of as a subset of food in the broadest sense, *see Nutrilab, Inc. v. Schweiker*, 713 F.2d 335, 337 (7th Cir.1983), reference to food in the generic sense refers to articles of food not considered food additives.

2. Because gelatin and glycerin are GRAS, they are not formally considered "food additives" under the statute.

321(s). In determining what is a food additive, we look first to the language of the statute itself, *Consumer Product Safety Comm'n v. GTE Sylvania, Inc.*, 447 U.S. 102, 108, 100 S.Ct. 2051, 2056, 64 L.Ed.2d 766 (1980), and if the language of the statute is plain, then it is conclusive absent contrary legislative intent *United States v. Ron Pair Enters., Inc.*, 489 U.S. 235, 109 S.Ct. 1026, 103 L.Ed.2d 290 (1989). Section 321(s) defines a food additive as "any substance the intended use of which results ... in its becoming a component or otherwise affecting the characteristics of any food...." This language is very broad, and thus, the general rule is that a component of an article of food is a food additive, even if the component in question is the "principal component," i.e. the ingredient sought when purchasing the food. *Food-Science*, 678 F.2d at 738. Moreover, even substances ordinarily considered "food" in common usage may become food additives in some circumstances. *National Nutritional Foods Ass'n v. Kennedy*, 572 F.2d 377, 391 (2d Cir.1978) (vitamins and minerals may be food additives when added to food) In addition, this court has held that DDT found naturally in fish is a food additive under the broad language of the Act. *United States v. Ewig Bros. Co.*, 502 F.2d 715, 721–24 (7th Cir.1974) (Stevens, J.), *cert. denied sub nom., Vita Food Prods. of Illinois, Inc v. United States*, 420 U.S. 945, 95 S.Ct. 1324, 43 L.Ed.2d 423 (1975).

[3] The FDA argues that the statutory language clearly indicates that any and every component of an article of food is a food additive. Although we are mindful of the deference due the FDA in construing the statute it administers, *Young v. Community Nutrition Inst.*, 476 U.S. 974, 981, 106 S.Ct. 2360, 2364–65, 90 L.Ed.2d 959 (1986); *Chevron U.S.A., Inc v. NRDC*, 467 U.S. 837, 843–44, 104 S.Ct. 2778, 2782, 81 L.Ed.2d 694 (1984); *United States v. 25 Cases, More or Less, of An Article of Device*, 942 F.2d 1179, 1182 (7th Cir.1991), deference here is unwarranted since its interpretation is contrary to the language and intent of the Act. *Demarest v. Manspeaker*, 498 U.S. 184, 111 S.Ct. 599, 112 L.Ed.2d 608 (1991) (administrative interpretation of statute contrary to plain language is not entitled to deference). As an initial matter, we question whether BCO can even be considered a "component" under the Act. The term "component," commonly understood and defined as a "a constituent part" or "ingredient," Webster's Third New International Dictionary 466 (1976), loses its meaning when applied to foods used in conjunction with inactive ingredients, as this case amply evidences. Here, the dietary supplement (the food) is nothing but BCO combined with glycerin and gelatin—two inactive substances used for marketing the BCO in capsule form. The gelatin and glycerin do not interact with or change the character of the BCO, but merely act as a container comparable to a bottle containing liquids marketed for teaspoon consumption. The BCO in question is the dietary supplement and the dietary supplement is the BCO. Therefore, to hold that BCO is a component of the dietary supplement would be to find that BCO is a component of itself. Such an interpretation would defy logic and common sense.

[4] But even assuming that a single active "ingredient" of food can be considered a component of the food, the statutory language does not indicate that every component of food is necessarily a food additive. The Act defines "food additive" as a substance "becoming a component *or otherwise affecting the characteristics of any food.*" 21 U.S.C. § 321(s) (emphasis added). The FDA interpretation of this provision implies that the language "or otherwise" is used disjunctively in such a way that a substance is a food additive if it (1) is a component of any food, *or* (2) affects the characteristics of a food. We think that this interpretation, however, distorts the plain meaning of the provision. The phrase "or otherwise," as employed here, is not used to express two alternative definitions of a food additive. Rather, it is used in a way to clarify or elaborate, such that "otherwise" is correctly read as "similarly." This view comports with established principles of statutory construction holding that courts should rein in broad and general statutory language when such language is

immediately coupled with more limiting language or a specific enumeration. 2A Norman J. Singer, Sutherland on Statutory Construction §§ 47.16, 47.17 (5th ed. 1992) (reviewing doctrines of *noscitur a sociis* (coupling of words denotes an intention that they be understood in same general sense) and *ejusdem generis* (general words coupled with statutory enumeration are construed only to embrace objects similar in nature)); *see also Toilet Goods Ass'n v. Gardner*, 278 F.Supp. 786, 790 (S.D.N.Y. 1968) (employing doctrine of *ejusdem generis* to limit expansive application of color additive provision), *aff'd in relevant part, rev'd in part sub nom., Toilet Goods Ass'n v. Finch*, 419 F.2d 21 (2d Cir.1969). The phrase "becoming a component" in section 321(s) is immediately followed by more descriptive language relating to the substance's effect on food. Moreover, the examples of food additives then enumerated in the Act describe the substances by their function or by their effect on food. 21 U.S.C. § 321(s) (listing as examples of food additives "any substance intended for use in producing, manufacturing, packing, processing, preparing, treating, packaging, transporting or holding food; and including any source of radiation intended for any such use"); *cf.* 104 Cong.Rec. 17,417 (remarks of Rep. Williams) ("substances which are used to improve the characteristics of our food are illustrative of the kinds of things this legislation deals with."); Harry A. Toulmin, Jr., Treatise on the Law of Foods, Drugs and Cosmetics §§ 22.5–22.10 (2d ed. 1963) (grouping food additives according to function). Therefore, simply becoming a "component" of food does not, in and of itself, satisfy the definition of a food additive. To be a food additive, a substance must not only be added to food, but it must also have the purpose or effect of altering a food's characteristics.[3]

[5] When two or more active ingredients comprise a food, each component is arguably different from the food in such a way that the addition of each has affected the characteristics of the other components and of the food. Thus, courts faced with foods involving two or more active components have held that each component is a food additive. *See United States v. 45/191 Kg. Drums of Pure Vegetable Oil*, 961 F.2d 808, 812 & n. 3 (9th Cir.) (Evening Primrose Oil ("EPO") held food additive when encapsuled with Vitamin E, since "EPO is not a single ingredient"—distinguishing the case of BCO encapsuled alone), *cert. denied sub nom., Efamol, Ltd. v. United States*, — U.S. —, 113 S.Ct. 375, 121 L.Ed.2d 287 (1992); *Food Science*, 678 F.2d at 738 (principal ingredient of food a food additive if combined with another active ingredient); *United States v. 41 Cases, More or Less, etc.*, 420 F.2d 1126, 1130 (5th Cir.1970) (medicated poultry feed found adulterated as containing two-three active ingredients held to be food additives); *United States v. 42/30 Tablet Bottles*, 779 F.Supp. 253 (E.D.N.Y.1991) (two active non-chemical ingredients of dietary supplement held food additives); *United States v. 21 Approximately 180 Kg. Bulk Metal Drums*, 761 F.Supp. 180 (D.Me.1991) (BCO held food additive when encapsuled with fish oil and various vitamins and minerals). But when there is only one active component, as is the case here, that single component does not affect the characteristics of the food in question—rather, it constitutes the food. Thus, even if we were to find that BCO was a component of the BCO dietary supplement capsules, the language of the Act indicates that it is not a food additive because, as the single active ingredient, it does not affect the characteristics of any food.

This interpretation is buttressed by the structure and history of the Act. The language of the Act must be read in the light of the statute as a whole: its design, objectives and policy. *Crandon v. United States*, 494 U.S. 152, 110 S.Ct. 997, 108 L.Ed.2d 132 (1990); *Illinois EPA v. United States EPA*, 947 F.2d 283 (7th Cir.1991).

3. Although certainly not controlling, our interpretation also reflects the common understanding of an additive, defined by Webster as "a substance added to another in relatively small amounts to impart or improve desirable properties or suppress undesirable properties." Webster's, *supra*, at 24.

[upon reviewing the structure and evolution of food regulation under the Act, it is clear that Congress intended to distinguish food additives from food in the generic sense. The original Food and Drug Act of 1906 required the government to prove that foods containing poisonous substances were unsafe. The addition of deleterious substances alone would not necessitate a finding of adulteration. *United States v. Lexington Mill & Elevator Co.*, 232 U.S. 399, 34 S.Ct. 337, 58 L.Ed. 658 (1914). The Act was revamped in 1938, adopting a "per se" approach: It prohibited the use of poisonous or deleterious substances unless the industry proved that the addition of the substances was safe. *See Ewig Bros.*, 502 F.2d at 720; Toulmin, *supra*, §§ 1.5, 2.1, 2.3. The 1938 Act itself proved inefficient and Congress took steps to amend the Act in the early 1950's. Congress perceived essentially two flaws in the regulatory scheme. First, the government had the burden of first proving that a food additive is poisonous or deleterious before it could prevent the industry from using it. This required substantial time, during which the industry could market the potentially injurious additives to the consuming public. The second problem was that the law prevented processors from using certain additives in harmless amounts that, if used, would increase and improve the food supply. S.Rep. No. 2422, 85th Cong., 2d Sess. (1958), *reprinted in* 1958 U.S.C.C.A.N. 5300, 5301; Toulmin, *supra*, § 22.3.

After six years of extensive hearings, Congress passed the Food Additives Amendment Act of 1958. The thrust of the amendments was to put upon processors rather than the government the burden of proving that a newly discovered substance added to food is safe if used within specified quantities. The Act, however, did not require processors to prove that all of their marketed food was safe, although Congress would have been free to enact such a requirement. Rather, the burden imposed upon processors applied only to food additives, and the government retained—as was the case prior to the 1958 amendment—the burden of proving that a given food was unsafe.

[6] Consequently, the Act distinguishes between food additives and food in the generic sense, and this distinction is critical in allocating the burden of proof. The FDA's food additive definition is so broad, however, that it would blur this distinction. It would classify every component of food—even single active ingredients—as food additives. Thus, it would seem, even the addition of water to food would make the food a food additive. The only justification for this Alice-in-Wonderland approach is to allow the FDA to make an end-run around the statutory scheme and shift to the processors the burden of proving the safety of a substance in all circumstances. To be sure, the paramount objective of the Act is to protect the public health. But "[i]n our anxiety to effectuate the congressional purpose of protecting the public, we must take care not to extend the scope of the statute beyond the point where Congress indicated it would stop." *62 Cases of Jam v. United States*, 340 U.S. 593, 600, 71 S.Ct. 515, 520, 95 L.Ed. 566 (1951).

[7] The FDA's interpretation would also arbitrarily classify a substance as either food or food additive by how it is marketed rather than by the nature and use of the substance itself. The FDA concedes that BCO marketed in bottles instead of in capsule form is not a food additive, and that it would in that event have the burden of proving that the BCO is harmful or deleterious. Yet there is no difference between the BCO bottled for teaspoon consumption and the encapsuled BCO but for the way it is marketed. How a product is marketed is not a rational way of determining whether a substance is a food additive and which party—the FDA or the processor—bears the burden of proving its effect, if any, on the consuming public.

Therefore, although a component of food is generally a food additive, when the "component" is the single active ingredient and thus in all material respects is identical to the food of which it is supposedly a component but for certain inactive additions, such as the gelatin and glycerin used for encapsulation here, the substance in

question is not a food additive. Our holding today is not inconsistent with *FoodScience*, the case on which the FDA relies. In that case, this Court held that the substance N,N-dimethylglycine hydrochloride ("DMG")—the lesser by weight and volume of two active components of the tablet Aangamik 15—was a food additive even though DMG was the "principal ingredient" of the tablets. 678 F.2d at 738. The DMG, even though it was the reason consumers would purchase Aangamik 15, comprised only 4 percent of the tablets' weight, and was mixed with another active ingredient (calcium gluconate) to form Aangamik 15. We did not reach the question presented here where the substance at issue is the single active ingredient of a marketed product. The district court in *FoodScience* enjoined the use of DMG "except when offered as a single ingredient for food use." But because the government did not cross-appeal from the exception, we refused to consider that question. *Id.* at 737 & n. 2. Indeed, if the majority opinion had held what the FDA alleges it held, the concurrence in that case, on which the district court below relied, would have been a dissent. The concurrence states:

> I believe ... as did the district court, that this would be a far different case if DMG were being marketed as a single food ingredient. In that case, the FDA would not be entitled to rely on the "food additive" presumption to condemn plaintiff's product but would instead be obligated to shoulder its normal burden of proving, by a preponderance of the evidence, that DMG was an "adulterated food"....

Id. at 741 (Cudahy, J., concurring) (footnote omitted). In short, this case is different from *FoodScience* and other cases in which the substance in question was mixed with other active ingredients to form an arguably distinct article of food. *See 45/194 Kg. Drums of Pure Vegetable Oil*, 961 F.2d at 812 & n. 3; *41 Cases, More or Less*, 420 F.2d at 1130; *42/30 Tablet Bottles*, 779 F.Supp. at 253; *21 Approximately 180 Kg. Bulk Metal Drums*, 761 F.Supp. at 180. In fact, the rule enunciated today is supported by every court that has addressed the precise question involved here. *See United States v. 29 Cartons of An Article of Food ... Oakmont Inv. Co.*, 792 F.Supp. 139 (D.Mass.1992) (encapsuled BCO not food additive); *United States v. Vitality Systems, Inc.*, Food Drug Cosm.L.Rep. ¶ 38,251 (D.Or. August 6, 1991) (holding that methylsulfonylmethane ("MSM") marketed in pure form not food additive but MSM held food additive in multi-ingredient products containing other nutrients such as Vitamin C); *United States v. Undetermined Quantities of Articles of Food ... Blue-Green Algae*, No. 83-1180-FR, 1984 WL 1981 (D.Or. November 8, 1984) (encapsuled Aphanizomenon flos-aquae (blue-green algae) not food additive because it was not intended to affect the characteristics of another food or become component of another food); *United States v. An Article of Food ... L-Tryptophan*, No. 77-687 (D.N.J. January 23, 1979) (L-Tryptophan tablets not food additive).

III.

Accordingly, we hold that BCO encapsuled with glycerin and gelatin is not a food additive. Because the FDA has not shown that BCO is adulterated or unsafe in any way, there is no basis to condemn the two drums at issue. If BCO is injurious to health, the statute requires the FDA to prove as much. Meanwhile, the Act's labeling requirements protect the consuming public to the extent mandated by Congress by enabling persons to weigh for themselves the benefits and risks of consuming BCO. The judgment of the district court is therefore

AFFIRMED.

judge's added statement that premeditation "excludes action which is taken so spontaneously that there is no time to think," was appropriate only because the judge earlier stated that premeditation "may occur within seconds." The trial judge in this case did not imply that premeditation could be formed in seconds. In this case, Watkins argued with the victim in the hallway outside the apartment, went to the kitchen to get a knife, and returned to the hallway where he fatally stabbed the victim. Watkins had time to reflect.

The jury focused on the critical distinction necessary to find guilt beyond a reasonable doubt of the crime of first degree murder. It chose to convict Watkins. Again, we do not find Watkins' arguments compelling and discern no "gross miscarriage of justice" *Hernandez-Hernandez*, 904 F.2d at 763. Thus, we are not required to considered the *McCleskey* exception. As a final matter, we note that Watkins has not made "a colorable showing of factual innocence," making the likelihood of success on the exception exceptionally slim.

Because the district court properly dismissed Watkins' new arguments as an abuse of the writ, we affirm.

Affirmed.

UNITED STATES of America, Plaintiff, Appellant,

v.

29 CARTONS OF [illegible] AN ARTICLE OF FOOD, ETC., Defendant.

Claim of OAKMONT INVESTMENT CO., INC., Claimant, Appellee.

No. 92-1915.

United States Court of Appeals, First Circuit.

Heard Feb. 1, 1993.

Decided March 3, 1993.

Government sought to condemn cartons of encapsulated black currant oil, alleging that oil was "food additive" of questionable safety. The United States District Court for the District of Massachusetts, Joseph L. Tauro, Chief Judge, 792 F.Supp. 139, dismissed government's complaint, and it appealed. The Court of Appeals, Selya, Circuit Judge, held that encapsulated oil, which was "food" in its liquid form, in two inert substances did not render oil "food additive."

Affirmed.

1. Food ⇐5

Food and Drug Administration (FDA) can prevent sale of "food" only if it proves by preponderance of evidence that it is injurious to health as substances classified as "food" are presumed safe. Federal Food, Drug, and Cosmetic Act, §§ 201(f), (f)(1), 402(a)(1), as amended, 21 U.S.C.A. §§ 321(f), (f)(1), 342(a)(1).

2. Food ⇐5

Purpose of statute governing "food additives" is to protect consumers against introduction of untested and potentially unsafe substances, such as flavor, texture, or preservative agents, into food. Federal Food, Drug, and Cosmetic Act, § 409, as amended, 21 U.S.C.A. § 348.

3. Food ⇐5

Food and Drug Administration (FDA) can prevent sale of products containing "food additive" unless and until processor shows that substance, when added to food, is generally recognized as safe (GRAS). Federal Food, Drug, and Cosmetic Act, § 409, as amended, 21 U.S.C.A. § 348.

4. Food ⇐5

Any substance that meets statutory definition of "food additive" is presumed to be unsafe until Food and Drug Administration (FDA) has promulgated regulations prescribing conditions assuring safe use. Federal Food, Drug, and Cosmetic Act, § 409(a)(2), as amended, 21 U.S.C.A. § 348(a)(2).

ATTACHMENT B

5. Food ⇐5

To be labeled as "food additive," substance must be intended, or reasonably expected, to become component of food or to otherwise affect characteristics of food, and not be generally recognized as safe (GRAS). Federal Food, Drug, and Cosmetic Act, § 201(s), as amended, 21 U.S.C.A. § 321(s).

See publication Words and Phrases for other judicial constructions and definitions.

6. Food ⇐5

Only component which, when added to food, effects, or could be expected to effect, some change in food, rather than any component of multicomponent substance, active or inactive, is "food additive;" phrase "becoming a component or otherwise affecting the characteristics of any food" in statutory definition of "food additive" indicates that definition targets only those components that have purpose or effect of altering food's characteristics. Federal Food, Drug, and Cosmetic Act, § 201(f, s), as amended, 21 U.S.C.A. § 321(f, s).

7. Food ⇐5, 24(1)

Black currant oil encapsulated in glycerin and gelatin for easy ingestion as dietary supplement was not "food additive" within meaning of Federal Food, Drug, and Cosmetic Act, even though it was one of three edible ingredients in capsules; black currant oil in its liquid form was "food," whether substance is food additive depends on its use for its effect on food, oil was only active ingredient in capsules, and it was not being used for its effect on glycerin and gelatin. Federal Food, Drug, and Cosmetic Act, § 201(f, s), as amended, 21 U.S.C.A. § 321(f, s).

8. Food ⇐5

Food processor's subjective determination of what constitutes "food" is not determinative of whether particular substance is "food" or "food additive." Federal Food, Drug, and Cosmetic Act, § 201(f, s), as amended, 21 U.S.C.A. § 321(f, s).

9. Statutes ⇐219(6.1)

Purely legal question of statutory construction concerning whether particular substance was "food additive" within meaning of Federal Food, Drug, and Cosmetic Act, did not require court to defer to Food and Drug Administration's (FDA) expertise in interpreting Act. Federal Food, Drug, and Cosmetic Act, § 201(f, s), as amended, 21 U.S.C.A. § 321(f, s).

10. Statutes ⇐219(1)

True measure of court's willingness to defer to agency's interpretation of statute depends on persuasiveness of that interpretation given all attendant circumstances.

Robert D. Kamenshine, Atty., Civil Div., U.S. Dept. of Justice, with whom Stuart M. Gerson, Asst. Atty. Gen., Washington, DC, A. John Pappalardo, U.S. Atty., Boston, MA, Douglas N. Letter, Atty., Civil Div., Margaret J. Porter, Chief Counsel, and Leslie Kux, Associate Chief Counsel, U.S. Food & Drug Admin., Washington, DC, were on brief, for appellant.

Robert Ullman, with whom Jacob Laufer, Steven Shapiro, and Bass & Ullman, New York City, were on brief, for appellee.

Before SELYA, Circuit Judge, ALDRICH, Senior Circuit Judge, and CYR, Circuit Judge.

SELYA, Circuit Judge.

The government seized, and seeks to condemn, twenty-nine cartons of undiluted black currant oil (BCO), in capsule form, owned by claimant-appellee Oakmont Investment Co. (Oakmont), alleging that BCO is a food additive of questionable safety. Because we believe that encapsulated BCO, intended to be ingested as purchased, cannot properly be termed a food additive as defined in the Federal Food, Drug, and Cosmetic Act (the Act), *as amended*, 21 U.S.C. §§ 301 *et seq.* (1988), we affirm the district court's dismissal of the government's *in rem* complaint.

I. BACKGROUND

On October 11, 1988, the United States Food and Drug Administration (FDA) seized 200 bottles of encapsulated BCO, packed in twenty-nine cartons, and brought

an *in rem* action contending that, under 21 U.S.C. § 342(a)(2)(C), the capsules should be condemned as "adulterated" food because they contain a "food additive," the BCO, that Oakmont had not proven to be safe.

At the ensuing bench trial, certain facts were uncontradicted. BCO is a liquid obtained by squeezing black currant berry seeds. It is composed of polyunsaturated fatty acids. In its pure liquid form, it can be ingested by the spoonful as a dietary supplement. However, Oakmont markets BCO in capsules which are to be swallowed whole. The capsules contain pure BCO—nothing more. They are made from gelatin and glycerin (or an equivalent plasticizer) and have no independent nutritional value. Rather, a capsule serves a dual purpose as a container (enabling consumers to ingest predetermined quantities of BCO in solid form) and as a prophylactic (protecting the BCO from rancidity).

On these and other facts, the district court dismissed the government's complaint and ordered the capsules released. *See United States v. 29 Cartons, Etc.*, 792 F.Supp. 139, 142 (D.Mass.1992). The court reasoned that when, as in this case, BCO comprises the only active ingredient within a gelatin capsule, it can properly be classified as a "food," but not as a "food additive." *See id.* at 141–42. Accordingly, the FDA erred in seizing the bottles on the ground that they "allegedly contain[ ] an unsafe food additive." *Id.* at 142.

When the FDA appealed, the district court stayed its release order.

II. THE REGULATORY LANDSCAPE

[1] To put this case into workable perspective, we first review the relevant statutory provisions. The Act defines "food" as:

> (1) articles used for food or drink for man or other animals, (2) chewing gum, and (3) articles used for components of any such article.

21 U.S.C. § 321(f). The FDA concedes that pure BCO (sold, say, as a bottled liquid) falls within section 321(f)(1) and is, therefore, "food." Substances classified as "food" are presumed safe. Thus, the FDA can prevent sale of bottled BCO or any other "food" only if it proves by a preponderance of the evidence that the food is "injurious to health." 21 U.S.C. § 342(a)(1); *see, e.g., United States v. Lexington Mill & Elevator Co.*, 232 U.S. 399, 411, 34 S.Ct. 337, 340, 58 L.Ed. 658 (1914); *United States v. An Article of Food [FoodScience Labs., Inc.]*, 678 F.2d 735, 741 n. 8 (7th Cir.1982) (Cudahy, J., concurring). Although the FDA suspects that BCO may be unhealthful, it is unable at the present time to translate this suspicion into legally competent proof.

[2–4] In addition to regulating the sale of food *per se*, the Act contains provisions anent food additives. These provisions are designed to protect consumers against the introduction of untested and potentially unsafe substances, such as flavor, texture, or preservative agents, into food. A gloss was added to the treatment of food additives in 1958. *See* Pub.L. No. 85–929, 72 Stat. 1784 (1958) (codified in scattered sections of 21 U.S.C.). Unlike section 342(a)(1), which places the burden of proving injuriousness upon the government in respect to foods, the food additives amendment allocates the burden quite differently: the FDA can prevent the sale of products containing a food additive unless and until the processor shows that the substance, when added to food, is generally recognized as safe (in the vernacular, "GRAS"). *See* S.Rep. No. 2422, 85th Cong., 2d Sess. (1958), *reprinted in* 1958 U.S.C.C.A.N. 5300, 5301–02 (explaining the processor's burden "of proving that a newly discovered substance which ... [is] add[ed] to the food we eat is safe"). Thus, in contrast to the Act's treatment of "food," any substance that meets the Act's definition of a "food additive" is presumed to be "unsafe" under 21 U.S.C. § 348 until the FDA, or more particularly, the Commissioner of Food and Drugs, has promulgated a regulation prescribing conditions assuring safe use. *See* 21 U.S.C. § 348(a)(2); 21 C.F.R. § 5.10(a)(1) (1992).

[5] The 1958 amendment defines a food additive in pertinent part as:

> any substance the intended use of which results or may reasonably be expected to result, directly or indirectly, in its becoming a component or otherwise affecting the characteristics of any food (including any substance intended for use in producing, manufacturing, packing, processing, preparing, treating, packaging, transporting, or holding food; and including any source of radiation intended for any such use), if such substance is not generally recognized, among experts qualified by scientific training and experience to evaluate its safety, as having been adequately shown through scientific procedures ... to be safe under the conditions of its intended use....

21 U.S.C. § 321(s). To be labeled a food additive, then, a substance must (1) be intended, or reasonably expected, to become a component of food or to otherwise affect the characteristics of food, and (2) not be GRAS.

The Act thus creates a distinction between foods and food additives which has meaningful consequences for purveyors and for the public. The distinction also significantly affects the ease with which the FDA may regulate a substance's sale.

III. THE ISSUE

This appeal revolves around the question of whether the FDA or Oakmont must carry out the research necessary to show that BCO is, or is not, GRAS. The issue reduces to whether pure BCO, when sold in encapsulated form, must be regulated as a "food" within the meaning of section 321(f) or as a "food additive" within the meaning of section 321(s).

The meat of the parties' disagreement lies in their differing interpretations of that portion of the Act which states that a substance can be a food additive if its intended use results, or may be expected to result, "in its becoming a component or otherwise affecting the characteristics of any food." 21 U.S.C. § 321(s).[1] The FDA reads the quoted language as creating two independent and disjunctive standards: to satisfy the first prong of the food additive definition, a substance must either (1) be a component of food, or (2) otherwise affect the characteristics of food. Because each constituent part or element of a food (that is, each "component") necessarily affects the food's characteristics, the FDA considers every component, at least potentially, *see infra* note 3, to be a food additive.[2] Drawing on this interpretation, the FDA asserts that the seized capsules are composed of three consumable components—BCO, gelatin, and glycerin—and that, therefore, each of these three ingredients is subject to potential regulation as a food additive.[3]

As Oakmont parses the statute, it creates only a single, unitary food additive standard. The phrase "or otherwise affecting the characteristics of any food" signals that a component is potentially a food additive only if it affects the characteristics of some food to which it is added. Unlike the FDA's interpretation, Oakmont's interpretation attaches no significance to a substance's mere presence as a component of a whole. It focuses instead on the substance's affirmative use in a way that affects food.

Applying its interpretation of the statute to the facts at bar, Oakmont argued below, as it does here, that the BCO contained in the seized capsules is itself a food and not a component of some other food, that it is intended so to serve, and that its sale in a convenient carrier medium does not transmogrify it into a food additive. In holding

1. The district court bifurcated the trial and, during the initial phase, determined only that BCO does not meet the first prong of the bipartite food additive definition. Thus, the district court had no occasion to reach the second prong, viz., whether BCO is GRAS. Hence, that issue is not before us.

2. In the FDA's view, the second of the two independent standards confers potential food additive status on substances that, while they are not constituent parts of a food, may nevertheless have deleterious effects on food. One example might be chemicals used in packaging food.

3. We use the adjectival modifier "potential" because gelatin and glycerin are concededly GRAS. Hence, these components cannot be classified as food additives because neither can fulfill the definition's second prong.

that food is defined "by its 'use[ ] for food,'" *29 Cartons*, 792 F.Supp. at 141 (quoting 21 U.S.C. § 321(f)), whereas a food additive is defined by its effect on another substance, *see id.*, the district court substantially adopted Oakmont's reading of the law and its focus on a substance's intended function.

In specific terms, then, we must determine whether, as the FDA would have it, *any* element of *any* substance that has more than one component may be branded a food additive, or, rather, whether, as Oakmont urges and the court below believed, such treatment should be reserved for elements which, when so added, effect a change (or, at least, could be expected to effect a change) in some other active ingredient.

IV. FOOD FOR THOUGHT

[6] The Seventh Circuit has recently grappled with a factually similar case presenting this very issue. *See United States v. Two Plastic Drums, Etc.*, 984 F.2d 814 (7th Cir.1993). Employing a perspicacious analysis of the Act's text and legislative history, the court rejected the FDA's notion that *all* components of a substance are necessarily food additives. The court observed that the "'or otherwise'" phrase contained in the statutory definition of a food additive targets only those components that "have the purpose or effect of altering a food's characteristics." *Id.* at 818. The subsequent enumeration of sample food additives, describing each substance by its "function or by [its] effect on food," makes it clear that an additive must stimulate some change in a food to which it is added. *Id.* at 818. Turning to the legislative history, the court observed that the FDA's broad definition of a food additive, which would apply to all components, even a substance which comprises the only active ingredient of the whole, subverts congressional purpose. Blurring the distinction between food additives and food in this way would permit the agency to tilt a delicately balanced statutory scheme that allocates the burden of proving an additive's safety to the processors while leaving the burden of establishing a food's safety with the FDA. *See id.* at 819.

[7] The Seventh Circuit also recognized the incongruity of categorizing a food's single active component as an additive. Because "that single component does not affect the characteristics of the food in question—rather, it constitutes the food," *id.* at 818, it has no place within "the common understanding of an additive, defined by Webster as 'a substance added to another ... to impart or improve desirable properties or suppress undesirable properties.'" *Id.* at 818 n. 3 (citation omitted). Thus, in order to qualify as a food additive, a component must be added to a food in order to change that food's properties. *See id.* at 819. On that basis, pure BCO, in capsule form, is not a food additive. *See id.* at 820.

Judges should hesitate to write lengthy opinions merely for the sake of committing their own prose to posterity. Given the existence of a cogent, well-reasoned, eminently correct opinion closely on point, we embrace it. We will, therefore, affirm the judgment below for substantially the reasons elucidated in *Two Plastic Drums*. We pause, nevertheless, to essay a few additional observations.

First: We are reluctant to believe that Congress traffics in absurdities. Since it defies common sense to say that a substance can be a "food additive" when there is no (other) food to which it is added, we think that the FDA's reading of the Act is nonsensical, and, hence, must be incorrect. Moreover, classifying BCO as a "component" merely because it is combined with two totally inert substances serving collectively as a carrier medium would itself create a bizarre paradox: as the Seventh Circuit noted, "to hold that BCO is a component of the dietary supplement would be to find that BCO is a component of itself." *Two Plastic Drums*, 984 F.2d at 817.

[8] *Second:* In the FDA's estimation, a processor's "subjective intent" that only one of a product's components constitutes the food is irrelevant because "it is the *objective* intended use, *i.e.*, the intent to combine two or more components, that

counts." Appellant's Brief at 11. But, this harangue misses the mark. We fully agree that a processor's subjective determination of what constitutes a food is not determinative in cases of this stripe—but neither is the naked fact that more than one component has been combined. In the final analysis, what counts is the use of an ingredient for its effect on food. Here, from an objective standpoint, BCO is not being used for its effect on gelatin and glycerine. Thus, contrary to the FDA's loudly expressed fears, eschewing its rendition of the statutory text will not supplant objectivity with subjectivity.[4]

Third. The FDA also maintains that because "the ingredients of multi-ingredient food products, such as cake mixes," indisputably fall within the food additive definition, the statute could not possibly contain a "requirement that a substance must be added to a *preexisting* food, which it must be shown actually to affect." Appellant's Brief at 9. We disagree. Cake mixes are foods composed of many interacting food additives, each with its particular effect on the whole.[5] Absent any one ingredient, the concoction remains a cake mix, albeit one that may be short on sweetness or lumpy in texture. In that sense, cake mixes and products of that ilk are a far cry from a dietary supplement composed of a single active ingredient. What differentiates this case is that, if the BCO is removed, one is left with nothing but an empty capsule.

[9] *Fourth:* We think it advisable to mention the FDA's insistence, citing *Chevron U.S.A. Inc. v. NRDC, Inc.*, 467 U.S. 837, 843, 104 S.Ct. 2778, 2782, 81 L.Ed.2d 694 (1984), that we must obey its interpretation of the Act. In our estimation, the purely legal question facing us in this case presents no occasion for deference. In this realm of judicial expertise, the courts, not the agency, have the last word. *See id.* at 843 n. 9, 104 S.Ct. at 2782 n. 9 ("The judiciary is the final authority on issues of statutory construction...."); *BATF v. FLRA*, 464 U.S. 89, 98 n. 8, 104 S.Ct. 439, 445 n. 8, 78 L.Ed.2d 195 (1983) (observing that "deciding what a statute means" is "the quintessential judicial function"); *FTC v. Colgate-Palmolive Co.*, 380 U.S. 374, 385, 85 S.Ct. 1035, 1042, 13 L.Ed.2d 904 (1965) (holding that "legal standard[s] ... must get their final meaning from judicial construction"); *Wilcox v. Ives*, 864 F.2d 915, 924 (1st Cir.1988) (quoting *BATF v. FLRA, supra*).

[10] At any rate, the true measure of a court's willingness to defer to an agency's interpretation of a statute "depends, in the last analysis, on the persuasiveness of the interpretation, given all the attendant circumstances." *Massachusetts Dep't of Educ. v. United States Dep't of Educ.*, 837 F.2d 536, 541 (1st Cir.1988). "The simple fact that the agency *has* a position, in and of itself, is of only marginal significance." *Mayburg v. Secretary of HHS*, 740 F.2d 100, 106 (1st Cir.1984). When, as now, a court is persuaded neither by "the validity of [the agency's] reasoning," nor by the interpretive fit between the agency's rendition, on the one hand, and the language and structure of the statute, on the other hand, a court should not defer.[6] *Skidmore*

4. Moreover, if the FDA worries that processors may muck the statutory classifications with convenient recitals of subjective intent, we question the agency's espousal of a rule that would "arbitrarily classify a substance as either food or food additive by how it is marketed rather than by the nature and use of the substance itself." *Two Plastic Drums*, 984 F.2d at 819. In the words of Sir Francis Bacon, the FDA's suggested "remedy is worse than the disease."

5. We do not quarrel with those courts that have held, when confronted with multi ingredient products containing two or more active ingredients, that each active ingredient is potentially a food additive. *See, e.g., United States v. 45/194 Kg. Drums, Etc.*, 961 F.2d 808, 812 n. 3 (9th Cir.), *cert. denied*, — U.S. —, 113 S.Ct. 375, 121 L.Ed.2d 287 (1992); *FoodScience*, 678 F.2d at 738; *United States v. 41 Cases, Etc.*, 420 F.2d 1126, 1130 (5th Cir.1970).

6. The longevity of an agency's position is often significant in assaying the degree of deference owed to it. *See Bowen v. Georgetown Univ. Hosp.*, 488 U.S. 204, 212, 109 S.Ct. 468, 473, 102 L.Ed.2d 493 (1988) (refusing to apply *Chevron* deference to "agency litigating positions that are wholly unsupported by regulations, rulings, or administrative practice"); *Skidmore*, 323 U.S. at 140, 65 S.Ct. at 164 (acknowledging the value of "consistency" in respect to gauging persuasiveness). Here, the FDA's position is of recent vintage. Indeed, the original complaint in this

v. Swift & Co., 323 U.S. 134, 140, 65 S.Ct. 161, 164, 89 L.Ed. 124 (1944).

V. CONCLUSION

We need go no further. The proposition that placing a single-ingredient food product into an inert capsule as a convenient method of ingestion converts that food into a food additive perverts the statutory text, undermines legislative intent, and defenestrates common sense. We cannot accept such unfractuous reasoning.

Affirmed.

UNITED ELECTRICAL, RADIO AND MACHINE WORKERS OF AMERICA (UE), et al., Plaintiffs, Appellants,

v.

163 PLEASANT STREET CORPORATION, et al., Defendants, Appellees.

No. 92-1865.

United States Court of Appeals, First Circuit.

Heard Dec. 8, 1992.

Decided March 3, 1993.

Union and retirees brought suit against employer and related Scottish corporations, alleging that planned cessation of health care payments after plant closing would violate Commonwealth and federal labor laws. After remand by the Court of Appeals, 960 F.2d 1080, which vacated injunction and contempt order based on lack of personal jurisdiction, the United States District Court for the District of Massachusetts, A. David Mazzone, J., dismissed for lack of personal jurisdiction. On appeal, the Court of Appeals, Stahl, Circuit Judge, held that: (1) allegations by unions were sufficient to make prima facie showing of "purposeful availment" of privilege of conducting activities within commonwealth, so that exercise of personal jurisdiction would not violate due process clause, and (2) union made prima facie showing that corporation's activities during negotiations of collective bargaining agreement were "transaction of business" within Massachusetts, and that causes of action arose from such transaction of business, so that corporations fell within reach of Commonwealth's long-arm statute.

Vacated and remanded.

1. Federal Courts ⇐562

Although resolution of plaintiff's motion for reconsideration by margin order contravened separation of documents requirement, plaintiffs' appeal, which was timely when viewed against the date order was entered, would be deemed waiver of separate document requirement. Fed. Rules Civ.Proc.Rule 58, 28 U.S.C.A.

2. Federal Courts ⇐792

Where district court elects to dispose of motion for lack of personal jurisdiction without evidentiary hearing, "prima facie standard" governs review, under which it is plaintiff's burden to demonstrate existence of every fact required to satisfy both forum's long arm provision and due process clause. U.S.C.A. Const.Amends. 5, 14.

See publication Words and Phrases for other judicial constructions and definitions.

3. Federal Civil Procedure ⇐1829

Prima facie showing of personal jurisdiction on motion to dismiss, being resolved without evidentiary hearing, must be based upon evidence of specific facts set forth in

action planned food additive status not on BCO but on gamma linolenic acid, BCO's fatty acid constituent. And, in a prior case involving blue-green algae in gelatin capsule form, the FDA argued that the blue green algae was an additive because it was to be consumed with water or other foods or liquids, not because of its placement in gelatin capsules. *See United States v. Articles of Food (Blue-Green Algae)*, No. 83-1180-FR, 1984 WL 1981, at *3-*4 (D.Or. Nov. 8, 1984).

FDA
1993 Annual Awards
Ceremony Program

61 persons at FDA recognized for all of their efforts against evening primrose oil!

ATTACHMENT C

COMMISSIONER'S SPECIAL CITATION (Continued)

Evening Primrose Oil Litigation Team

For outstanding performance in the investigational and evidentiary seizure proceedings concluding EPO litigation in California and Maine.

From the Centers for Drug Evaluation and Research, and Food Safety and Applied Nutrition, the Atlanta, Boston, Buffalo, Chicago, Denver, Kansas City, New Orleans, and Orlando Districts, the Winchester Engineering and Analytical Center, the Offices of the Commissioner, Regulatory Affairs and the General Counsel:

Marvin G. Appleton
A. Joel Aronson
R. Daniel Benz, Ph.D.
Joseph J. Bulas
Robert A. Chamberlin
Isabel S. Chen, Ph.D.
Timothy J. Couzins
Philip S. Derfler
Jane E. Easttey
Ralph A. Erickson
Anne Fabiszewski
David Firestone
Donald G. Gordon
Jnhn D. Harris
Sara H. Henry, Ph.D.
S. Steven Hotta, M.D.
Hiltje Irausquin, Ph.D.
Stanton W. Johnson
James M. Kewley
Camilla K. Kintner
Jean Knight
Charles J. Kokoski
Michael R. Kravchuk
Leslie Kux
Margaret M. Laski
Ronald R. Laski
Marijane C. Lawson
Lawrence J. Lin, M.D.
Shelly L. Maifarth
Barbara Marcelletti
Gerad L. McCowin
Francis G. McNerney
Daniel L. Michaels
Edith D. Miller
Richard C. Nelson
Louisa Nickerson
Frances V. Noyes
Janice F. Oliver
Mary K. Pendergast
Richard H. Penta
Antoinette M. Pusatier
Ruth E. Rubino
James P. Reavey
Robert J. Reina
Peter A. Salsbury
Emil G. Siegmund
Manjeet Singh
Solomon Sobel, M.D.
John J. Stamp
Linda M. Stewart
Cynthia Stofberg
Donald W. Stresser
Pearl M. Tanjuaquio
John M. Taylor
Edward W. Thomas
John E. Thomas
Richard W. Thornton
George D. Tilroe
Gloria J. Troendle, M.D.
Michael D. Wirth
Edward J. Wojtowicz

Amanda B. Tedersen
Chief Mediator and Ombudsman

For outstanding skills and exceptional performance as the Food and Drug Administration's Chief Mediator and Ombudsman.

FEDERAL FOOD, DRUG, AND COSMETIC ACT

(CHEMICAL ADDITIVES IN FOOD)

HEARINGS

BEFORE A

SUBCOMMITTEE OF THE COMMITTEE ON INTERSTATE AND FOREIGN COMMERCE HOUSE OF REPRESENTATIVES

EIGHTY-FOURTH CONGRESS

SECOND SESSION

ON

H. R. 4475

A BILL TO PROTECT THE PUBLIC HEALTH BY AMENDING THE FEDERAL FOOD, DRUG, AND COSMETIC ACT SO AS TO PROVIDE FOR THE SAFETY OF CHEMICAL ADDITIVES IN FOOD

H. R. 7605, H. R. 7606, H. R. 8748

BILLS TO PROTECT THE PUBLIC HEALTH BY AMENDING THE FEDERAL FOOD, DRUG, AND COSMETIC ACT TO PROHIBIT THE USE IN FOOD OF NEW FOOD ADDITIVES WHICH HAVE NOT BEEN ADEQUATELY TESTED TO ESTABLISH THEIR SAFETY

H. R. 7607, H. R. 7764, H. R. 8271, H. R. 8275

BILLS TO AMEND THE FEDERAL FOOD, DRUG, AND COSMETIC ACT FOR THE PROTECTION OF THE PUBLIC HEALTH, BY PROHIBITING NEW FOOD ADDITIVES WHICH HAVE NOT BEEN ADEQUATELY PRETESTED TO ESTABLISH THEIR SAFE USE UNDER THE CONDITIONS OF THEIR INTENDED USE

JANUARY 31, FEBRUARY 1, 2, 3, AND 14, 1956

Printed for the use of the Committee on Interstate and Foreign Commerce

UNITED STATES
GOVERNMENT PRINTING OFFICE
WASHINGTON : 1956

must uphold the finding of the Administrator. You could change that act in many other fields, and perhaps make it work. But to select this highly technical field as an innovation, as a departure from the administrative act, it seems to me would be unwise. If we are going to experiment and try to improve it—and I think we can improve the administrative act—I much prefer to try on something else, and something that is not so highly technical and does not involve the safety of so many people.

There is one question here about this standard that troubles me. As I interpret the act, the standard of whether a man has obeyed the act or not—the test whether has has violated a criminal statute—is not whether the additive is safe or not safe. The test is whether it is generally recognized by the experts to be safe.

If this were a purely simple matter, there might be some justification for that sort of a test. But where a man is put in jeopardy, it seems to me that he is entitled to some standard that is much safer and much more certain than that. In order to determine whether he is committing a violation of the penal code, he has to pass on the question of whether the experts generally recognize.

Mr. GOODRICH. Yes, sir.

Mr. DIES. He goes into the field of opinion and conflicting opinion and highly technical matters. I just don't think that is good, even though it is in the Drug Act. I can't believe that is good legislation. I am wondering why we simply don't make the test the safety of the matter. Then he can certainly make his decision. He is a manufacturer. He has his experts. Whenever he makes his decision, then he will have to accept the consequences of it. I am wondering what difference that would make if we substituted and changed that language and struck out the "generally recognized."

Mr. GOODRICH. We have in general language "generally accepted," because the committee over the years has never been willing to give the Food and Drug Administration the authority to make a list to specify which products are in and which are out. This is what has been called here an objective standard.

We have the burden, no matter how this bill goes, of proving that a product is not generally recognized as safe among experts in the courts.

Let us assume that this bill came out as we recommended it and company X had a chemical which had not been adequately tested, we thought it was not generally recognized as safe, the applicant thought it was generally recognized as safe. We would have the burden of going to court to seize, prosecute, or enjoin to prove that fact, that it was not generally recognized as safe.

We have in this food and drug law some general language. "Prepared under unsanitary conditions," "if it consists in whole or in part in filth," "if it is a poisonous or deleterious substance which may be injurious," all those generalities have been to the courts, and we have not had difficulty with vagueness knocking down the law. We have been singularly successful, I think.

Mr. DIES. Under the present law, what happens if a man does put on the market—I am not talking about civil liability, but criminal—a deleterious substance, something that causes great damage. Can he be criminally prosecuted?

FOOD ADDITIVES

HEARINGS

BEFORE A

SUBCOMMITTEE OF THE COMMITTEE ON INTERSTATE AND FOREIGN COMMERCE HOUSE OF REPRESENTATIVES

EIGHTY-FIFTH CONGRESS

ON

BILLS TO AMEND THE FEDERAL FOOD, DRUG, AND COSMETIC ACT WITH RESPECT TO CHEMICAL ADDITIVES IN FOOD

JULY 15, 16, 17, 18, 19, 22, 23, 24, AUGUST 6, 7, 1957, AND APRIL 15, 1958

Printed for the use of the Committee on Interstate and Foreign Commerce

ATTACHMENT E
SEE P. 455 (617)

UNITED STATES
GOVERNMENT PRINTING OFFICE
WASHINGTON : 1958

courage the adoption of reasonably uniform laws. We need all the help they can give in controlling chemical additives, for the task is so big that combined Federal-State-city interest is imperative.

Last year the State of Utah enacted a new food, drug, and cosmetic law that contains an approach to the control of chemical additives not too different from the basic principles in some of the bills you are considering. The State of New York is considering new additives legislation now. New York City is considering a revision of its sanitary code with respect to food additives. And we understand that food-law enforcement officials of other States are considering the steps they should take to deal with residues of additives. If the Federal Government fails to enact legislation that can serve as a guide, the result may be the adoption of varying methods of State and local control.

In conclusion, the problem, the real hazard of the use of inadequately tested chemicals in food is very clear and is with us today. It is not, as some of the testimony last summer suggested, merely a theoretical problem. Inadequately tested chemicals are being used in food today and their use constitutes a real hazard to the public health.

(The information referred to follows:)

SUPPLEMENTAL STATEMENT OF THE DEPARTMENT'S VIEWS TO ACCOMPANY STATEMENT OF GEORGE P. LARRICK ON CHEMICAL ADDITIVES LEGISLATION

1. SCOPE OF THE LEGISLATION

(a) *Definition of "chemical additive"*

The witness for the Grocery Manufacturers Association questions the definition of "chemical additive" suggested in the administration bill. He states:

"The food additive definition under review is principally obscure, because of its governing 'generally recognized' clause."

The so-called generally recognized clause here referred to is the provision (p. 2, lines 8–14) under which a substance which otherwise would be regarded as a chemical additive is nevertheless to be considered as such only if—"not generally recognized among experts qualified by scientific training and experience to evaluate its toxicity or other potentiality for harm, as having been adequately shown through scientific procedures or through prolonged use in food to be safe for use under the conditions of its intended use."

All the bills, including those supported by industry, contain a "generally recognized" clause in one form or another. It stems from the similar provisions of the Federal Food, Drug, and Cosmetic Act with respect to new drugs (sec. 201 (p) and pesticide chemicals (sec. 409)).

The clause is designed to exclude from the bills those substances which according to the general consensus of competent scientific opinion are safe under the conditions of their intended use. While in all the bills this exclusionary provision is an integral though negative part of the basic definition, it could with the same effect, and no less logic, have been placed in section 409 (a)—in analogy to section 408 of the present act—which states under what circumstances a chemical additive shall be deemed to be unsafe. It is important to note that under all the bills, as drawn, the burden would be on the Government in an enforcement proceeding, to prove that a substance is not generally recognized by experts as safe and is therefore within the scope of the bill.

The concept of scientific consensus is, to be sure, not susceptible of reduction to a mathematical formula, but it is not obscure as a governing rule. Neither the industry nor the Government has encountered any material difficulty in determining under the present act whether new drugs or pesticide chemicals are generally recognized by appropriately qualified experts as safe.

At any rate—assuming that (in addition to the Secretary's exempting authority) some provision is desirable for automatically excluding from the bill those additives which may safely be used without submission for official safety evalua-

July 16, 1992

JUL 2 0 1992

Dear Mr.

Your letter written in response to the referenced Warning Letter has been reviewed by the Agency.

We note the corrective actions which has taken regarding the inconsistencies noted between the immediate bottle label and carton. However, as stated in our Warning Letter, we do not agree that the product is labeled in accordance with §411 of the FD&C Act. Inositol choline bitartrate, para-aminobenzoic acid, citrus bioflavonoids and betaine hydrochloride are declared in milligram amounts on the label of this vitamin and mineral tablet. Such declarations give prominence to these ingredients which are not vitamins, minerals, or sources of vitamins and minerals in violation of §411(b)(2)(B).

Also, we are unable to concur with your proposal that this issue be deferred until NLEA regulations become final since §411 has been in effect since 1976.

Sincerely,

Eugene C. Schultz
Compliance Officer
Philadelphia District

ECS/bgp

ATTACHMENT
F

Senator KASSEBAUM. I also want to assure you that I think all Senators are very aware of this issue, particularly those on this committee, but others as well. And as Senator Hatch said, it is a fascinating subject—it really is—and I think the dimensions of it are really very important. So it has been an interesting hearing, I believe from all sides, and I know Senator Hatch may have some questions.

Yes, Mr. Silverglade?

Mr. SILVERGLADE. If the Senator has questions, I will defer.

Senator HATCH. Well, thank you, Senator Kassebaum. I really appreciate your remarks.

Mr. Bode, we appreciate your remarks. We want to work with you and hope we can get this resolved. We have to get it resolved before the end of this legislative session.

Mr. McNamara, you used to be counsel at the FDA, didn't you?

Mr. MCNAMARA. A long time ago, sir.

Senator HATCH. That is right.

Mr. MCNAMARA. I am past my 50th birthday now.

Senator HATCH. What made you see the light? [Laughter.]

Mr. MCNAMARA. I had 8 very good years there. It was a long time ago.

Senator HATCH. Well, I want to thank you for your compelling remarks. Time is short, but I would like to underscore just how important this issue is to my home State of Utah. And you have pointed that out pretty capably. We have a lot of very fine companies out there who put out very fine products, and in all honesty this is a very, very important issue. But it is an important issue to the whole country at a time when we are trying to save health care costs. I have seen estimates where just if people would take Vitamin E that we would save about $25 billion a year in health care costs on the reduction of cardiovascular disease.

You could just extrapolate that out with Vitamin C, beta carotene, Vitamin A. You could just go right through it. The American people would be much better off.

Now, Mr. Silverglade, we have had our differences in the past, as you know, but I think your statement indicates you want to reach an agreement and try and resolve this in an appropriate way. And I agree with you that your claim on antioxidants should be allowed. But FDA says no. I am not trying to misinterpret your statement, but it almost sounds like, well, as long as you make the claim, CSPI, it is okay; but if somebody else makes another claim, it is not.

Mr. SILVERGLADE. No, we did not mean to say that.

Senator HATCH. I know. I know.

Mr. SILVERGLADE. It is just that there are other newsletters out there that we do not have much respect for, and you cannot write a law that allows any newsletters to have their claim on labels. We support a Government clearinghouse that decides which claims are really bona fide.

Senator HATCH. I understand.

Mr. SILVERGLADE. And we are willing to submit our claims to the Government and let them evaluate them. We wish the industry would, too.

Senator HATCH. Let me rephrase that. CSPI's claims are going to be always considered exactly right, but others, we will have to really subject them to more scrutiny.

Mr. SILVERGLADE. No. All claims, whether they are in the newspaper, magazines, or health letters, or by the manufacturer, need to be run through a Government clearinghouse to see which are really well supported. And we are willing to submit our advice to the Government, and we hope to see it ends up on labels.

Senator HATCH. I think the reason I am doing this to you is because how do we get these claims reviewed. How do we do that? Because you can see I think we have made a pretty strong case here today that the FDA is not used to approving claims. One claim in 3C years, and then a very narrow claim only for white women and Asian women, and it is ridiculous.

Mr. SILVERGLADE. I agree with you, and I think Senator Kennedy or Senator Metzenbaum suggested putting some deadlines on the agency, setting up an advisory panel to get the agency moving a little bit more quickly, and those are certainly good starts, and we are willing to work with your office on additional suggestions.

Senator HATCH. Good, and I appreciate that. You are looking at the Senator who went along with user fees last year because they were going to speed up the safety and efficacy process. Now, I had told the industry, you know, 3 or 4 years before, I said: You are going to get hit with user fees. Why don't we use them to build the FDA a central campus with a completely unified campus that has all the scientific instrumentation and computerization that really would make it possible to do the safety and efficacy process a lot faster than it is?

They have been hit with user fees, and I do not see a heck of a lot of results coming out of FDA this year that benefit the consumers. But I guess what my final question would be: Would you be opposed to having another Government body besides FDA to approve the claims? Since I do not have a lot of confidence in FDA approval of claims. And anybody who listened to Commissioner Kessler and Michael Taylor and others here today I think has to draw that conclusion, that really there is no justification to have confidence in the FDA approving claims, especially in this industry. And if that is the case, then would you be willing to work with another Government body that would be more fair and would in an expeditious way approve or disapprove claims with an expedited right of appeal in the case of disapproval, or either way?

Mr. SILVERGLADE. Well, I certainly think that is a very constructive idea. The FDA itself prior to the passage of the Nutrition Labeling and Education Act issued a proposed rule in February of 1990 that would have set up a Public Health Service committee to help evaluate claims for FDA approval. And it could be that that type of interaction between several agencies might be the answer here.

Senator HATCH. Well, I am not sure getting several agencies involved is the way to do it. If I had my way, I would move medical devices right out of FDA and have a full scientific agency very equipped to approve those devices, because our medical device industry is going to move off—they are moving offshore because FDA cannot approve claims. They just cannot act. And it is not because

they cannot. I think they will not. And part of the reason is they are paralyzed by the Congress because if they make a mistake we criticize them so strongly that they are just afraid almost to move.

We have to have a Government agency that is pure science, that gets these things done in a reasonable and fast and expeditious way that benefits the consumers. And I am convinced it should not be the FDA.

So help us on this, and give us your good advice. We know you are a very intelligent man in this area. Wrong a lot of the time, but nevertheless, I have a great deal of respect for you. [Laughter.]

We want to thank all of you for being here. This has meant a lot.

Senator KASSEBAUM. Thank you very much.

Senator HATCH. And thank you, Senator Kassebaum.

[Additional statements and material submitted for the record follow:]

LINUS PAULING, PH.D

October 25, 1993

Bill Clinton
President of the United States
The White House
Washington, D.C. 20500

Dear Mr. President:

Congratulations on your efforts to guarantee every American access to health care. You have taken on major obstacles that have prevented millions from receiving adequate health care for too long. You have made prevention of illness a priority. Your plan to improve the nation's health will be even more successful if Congress passes *The Dietary Supplement Health and Education Act (S. 784 and H.R. 1709).*

Educating the public about the benefits of vitamins and other dietary supplements can save thousands of lives and millions of health care dollars.

Studies in the respected journals of medicine have documented not only that vitamin C can help prevent the common cold, but that a whole range of vitamins, known as antioxidants, can also prevent chronic illnesses including the nation's two largest killers, heart disease and cancer. Folic acid, an important nutrient, is proven to prevent the most common form of birth defects. And science is uncovering new discoveries about dietary supplements every day. Unfortunately, government regulators at the Food and Drug Administration remain locked in a virtual Cold War against vitamins and minerals and will not allow information about these exciting findings to be put on product labels where it might do some good.

Mr. President, during the campaign you expressed interest in legislation that would reform the FDA so that the government can do a better job of educating people on the benefits of vitamins and other nutritional supplements. Now you have the opportunity. *The Dietary Supplement Health and Education Act* is supported by over half the Senate and more than one-quarter of the House of Representatives.

This legislation will help reinvent a government agency that has resisted change. It will allow the public to have important information and will protect consumers from risk.

Mr. President, help the government meet the challenge of scientific progress and support *The Dietary Supplement Health and Education Act.*

Sincerely,

Linus Pauling

Linus Pauling, Ph.D

STATEMENT OF CLINTON RAY MILLER
HEALTH FREEDOM LEGISLATIVE ADVOCATE

SENATE HEARING ON S. 784,
OCTOBER 21, 1993
BEFORE THE COMMITTEE ON LABOR AND HUMAN RESOURCES

Mr. Chairman, and distinguished members of the Committee:

Thank you for giving me the opportunity to submit this statement.

My statement is a 12 page history of the Food and Drug Administration's (FDA) continuing hostility to the use of herbs or other dietary supplements to treat, prevent, mitigate, or cure dietary related diseases. It was written by Annette Dickinson and is submitted with her approval.

If we understand the attached history of FDA's continuing opposition to the "Proxmire" Vitamin Bill of 1976, we can easily see FDA's refusal to honestly enforce it.

The Proxmire Bill was enacted unanimously in 1976 by both the Senate and the House, in spite of opposition by the Center For science and the Public Interest (CSPI), Ralph Nader, and the same groups that are presently opposing S. 784.

The Proxmire Vitamin Bill was one of the most popular bills ever enacted by Congress. We should learn from history and repeat this great miracle.

CONTACT MILLER: 703-754-0228, Box 528, Gainesville, VA 22065

TEMPEST OVER TABLETS

Few people know that the House Health Subcommittee played a critical role in the passage of the so-called "Proxmire" vitamin bill, that the legislation enacted was not the legislation originally supported by Proxmire, or that two competing vitamin bills created extreme controversy within the ranks of the vitamin lobby. The following is a worm's-eye view of the struggle as seen by one who was deeply involved.

My new employer, a vitamin manufacturer, suggested I make a courtesy call on Clinton R. Miller, legislative advocate for the National Health Federation. When I called for an appointment, Miller suggested I come right over, since he had someone in his office he wanted me to meet. He greeted me at the top of the stairs to his townhouse office on Capital Hill and ushered me into a large cluttered room where his guest was seated. The Admiral, from his vantage point behind a battered desk, surveyed me solemnly and informed me that, if I ate cooked food, I was by definition insane. I cackled (only a little insanely), but he was quite in earnest.

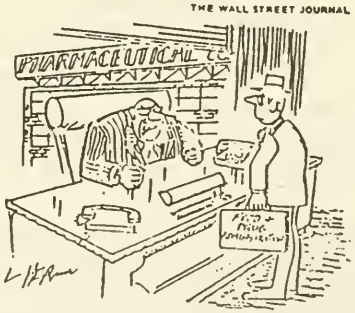
After a while, Miller steered the conversation around to the life and death struggle in which we were embroiled. He related how he had labored for decades virtually alone, fighting off the Food and Drug Administration with whatever meager resources he could command, singlehandedly mobilizing Congressional support for our cause, while prominent manufacturers in the vitamin industry had declined to lend their full moral and financial support to the battle. He urged me to persuade my company to take a more active role in lobbying for the vitamin bill, and I promised to have a look at it.

After two years of tilting at windmills with consumer advocate Robert B. Choate, I had in 1972 felt the need for some "inside" experience in the food industry and had landed a job as Washington Representative for a new health food conglomerate, Archon Pure Products Corporation. The company planned to ride the wave of consumer interest in natural foods and to introduce scores of new products into supermarkets as well as health food stores. I soon learned, however, that before we got on with making the world safe for natural foods, there was another problem which required our immediate attention. One of the company's subsidiaries made vitamin products, and the Food and Drug Administration was expected momentarily to finalize regulations which would outlaw at least 90% of them. By 1972, FDA had been working at these regulations for ten years.

Vitamins had hit the market with a bang in the 1930's during the heyday of nutrition research, when the magical properties of vitamins were being trumpeted in the usually staid medical journals. As early as 1931, for example, Dr. H. C. Sherman had extolled the virtues of "vitamin G" (now known as vitamin B-2 or riboflavin) in the Journal of the American Medical Association: "Most emphatically I do not offer vitamin G as a panacea for the prevention of premature senility and the falling of hair! But just as a lack of this factor brings about a condition of malnutrition which may contribute to premature senility, so a liberal intake of vitamin G contributes to a better than average nutritional condition and this to...'the preservation of the characteristics of youth.'" Inevitably such paeans of praise found their way into newspapers and magazines and ultimately into advertising copy and onto product labels. Health lecturers took up the hue and cry, blanketing the country with their tales and their wares; cigarette girls in New York nightclubs hawked vitamins along with the noxious weed; and in the 40's patriotic companies provided free vitamins to industrial workers to boost productivity. Higher and higher doses were packed into every pill, and vitamins were said to prevent or cure everything from colds to cancer.

The medical community looked on askance. In the 50's FDA went after vitamin promoters with a vengeance, FBI style, crawling through air ducts to eavesdrop on public lecturers, burning books, and occasionally throwing people in jail. But it was guerilla warfare; ten zealots took the place of every one who was squelched, and their persecution only added to their fervor.

In 1962, FDA proposed to put a stop to the vitamin explosion by the direct means of outlawing the most popular products. Under the regulations, which were finalized in 1966, products would be permitted to contain only certain vitamins and minerals, and then only at levels within the range of officially recommended daily allowances. All other products (namely most of the ones actually available) would be prohibited. Even the approved products would be branded as useless, for the front label would have to proclaim that ordinary foods provided "abundant amounts" of vitamins and minerals and that there was "no scientific basis" for the routine use of dietary supplements.



"Those pills have made us a profit of five million dollars and you people call them worthless?"

The industry screamed bloody murder, and FDA was deluged with more than 50,000 letters and postcards from an irate public devoted to its vitamins. The regulations were stayed while all sides of the controversy were endlessly aired during two solid years of hearings from 1968 to 1970. As a result of the hearings, FDA dropped the idea of the derogatory front label, but stuck to its intent to severely limit the products available in the marketplace. The final order was expected to come down early in 1973.

Clinton Miller had not been sitting idle all these years, waiting to hear what FDA would finally decide to do. The National Health Federation had helped to generate the impressive flood of letters to FDA, and had similarly been encouraging a steady stream of letters to Congress. In particular, the letters supported and Miller tirelessly urged the passage of the Hosmer vitamin bill, which would prevent FDA from limiting any ingredient of a food supplement unless it was "intrinsically injurious to health."

The Hosmer bill seemed a bit drastic to us; but while we were still evaluating it, Miller persuaded us to circulate petitions in the health food scores visited by our company salesmen. A couple of months later, I received half a dozen shipping crates full of signed petitions, which I sorted into Congressional districts with the help of my Congressional Staff Directory and then personally delivered to the appropriate offices.

On my rounds, I learned that for literally years every Representative had been inundated with mail from constituents demanding to be saved from FDA interference with their vitamins. In many offices, more mail was eventually received on vitamins than on Watergate or Vietnam. Staffers were harrassed by the continual onslaught of letters, particularly in offices where every form letter and even every petitioner had to be answered, but I was repeatedly assured that "the boss" sympathized with the constituents' frustrations and had proved it by cosponsoring the Hosmer vitamin bill. Some felt that cosponsoring was an empty gesture; it gave them something to tell the voters, but in reality it accomplished nothing, since everyone knew the Hosmer bill wasn't going anywhere. The bill was introduced in every session of Congress, scores of Representatives leaped on it as cosponsors, and then it languished for the rest of the session in the Health Subcommittee, which refused even to hold hearings on it. The Health Subcommittee was chaired by Congressman Paul G. Rogers of Florida, a knowledgeable and powerful Congressman who was said to be adamantly opposed to the Hosmer Bill. What most surprised me was that, one after another, staffers told me we could surely get some kind of vitamin bill passed, if we could just come up with one Mr. Rogers could tolerate. The public pressure was there, and Congress would love to get the monkey off its back.

Archon meanwhile was having other problems. Its stock had plunged from nearly $20 to about $2 per share with stunning rapidity, and the company was beginning to wonder whether it could afford to keep even a token Washington office, let alone commit itself to a major lobbying effort.

Enter William T. Thompson, another California vitamin manufacturer. Bill had long dreamed of creating a real trade association for vitamin manufacturers, which were dispersed among several existing associations, depending on their chosen marketing strategy. The companies that sold their products in drug stores and supermarkets belonged to the Proprietary Association. The companies that sold their products door-to-door belonged to the Direct Selling Association. And the companies like Thompson that sold their products in health food stores belonged to the National Nutritional Foods Association, an association of health food retailers (store owners).

The imminent threat of the vitamin regulations provided just the sense of crisis needed to spawn a new organization, and by June of 1973, three companies--the W. T. Thompson Company, Archon Pure Products Corporation, and Plus Products Corporation--had founded a new vitamin manufacturers' association with a name guaranteed to attract attention. They called themselves the Council for Responsible Nutrition (affectionately, the Council or the CRN). As their legal advisor they chose Archon's Washington counsel Dan Marcus of Wilmer, Cutler and Pickering. As their government relations advisor and

PR man they picked Larry Zoeller of Burson Marsteller. Bill Thompson was elected President, his associate Peter Semper was appointed Executive Director, and I was hired as Director of Government Affairs.

The FDA meanwhile had laid its cards on the table. The basic plan was the same as in 1966, but FDA's imaginative General Counsel Peter Barton Hutt had come up with one new fillip. In the 1966 version of the regulations, all products that didn't fit FDA's prescribed design would simply have been banned. Hutt offered us a theoretical opportunity to salvage some of these products. All vitamins and minerals in excess of the approved levels for food supplements would be classified as drugs and would be reviewed by an FDA expert panel. If the panel determined that these higher doses of vitamins and minerals were "safe and effective" for some particular use as drugs, then they could be sold to the general public. For example: The regulations decreed that any vitamin C product sold as a food supplement must have between 30 mg and 90 mg of vitamin C. No more, no less. Under Hutt's scheme, our hottest products, having 250 mg or 500 mg of vitamin C, would be classified as "drugs" and we could sell them only if the FDA's expert panel found them to be effective for some specific purpose such as the prevention of colds. It took us about ten seconds to calculate the liklihood of FDA's panel approving any such thing: zero, at the 99% confidence level.

The National Health Federation (NHF) and the National Nutritional Foods Association (NNFA) saw this as a transparent attempt to classify all vitamins and minerals as prescription drugs. FDA protested that it had no such intent, but it was fairly typical of its bad timing throughout this affair that at that very moment FDA was in fact proposing to classify high doses of vitamin A and vitamin D as prescription drugs.

We were anxious to make known the existence of our fledgling Council for Responsible Nutrition, and we seized on FDA's vitamin A and D regulations as a vehicle for demonstrating how "responsible" we intended to be.

FDA's main vitamin regulations were meant to impose sweeping restrictions on vitamin and mineral products, not because higher doses were unsafe, but because FDA did not consider higher levels to be nutritionally rational. In contrast, the vitamin A and D regulations were based squarely on a concern for safety. We called a press conference to announce the formation of the Council and also to announce, somewhat self-consciously, that our Council would not challenge the A and D regulations because we recognized the need to act conservatively in matters of safety. (Our conservatism exceeded the Court's in this case, since the A and D regulations were ultimately overturned.)

Our earthshaking announcement was broadcast to an almost empty room, so our "responsible" gesture was completely lost on the regulators and the nutrition community. We made sure, however, that it wasn't lost on the health food community. Burson Marsteller had designed us a classy newsletter called OPTIMUM, and the first issue was sent to all the health food stores trumpeting the news of our "responsible" decision to accept the A and D regulations. Now, as it happened, the NNFA had already decided to fight the A and D regulations tooth and nail. Our capitulation was judged premature, to say the least, and within days a long letter went out to all health food stores from NNFA headquarters, heaping abuse on our heads for failing to toe the party line. It was a shaky debut.

We turned our attention to the legislative arena, where we saw a golden opportunity to play a catalytic role. Since the CRN members all planned to attend the 1973 NNFA annual convention and trade show in San Diego, we met there in Thompson's suite to design our legislative strategy.

We proposed to act on the assumption that the time was ripe for a reasonable alternative to the Hosmer vitamin bill, and we believed the alternative should accomplish two goals: prevent FDA from limiting vitamins and minerals for reasons other than safety, and prevent the agency from arbitrarily classifying nutrients as drugs. Our counsel Dan Marcus outlined some of the ways the Food, Drug and Cosmetic Act might be amended to accomplish these goals, but reminded us that Mr. Rogers wasn't likely to be enthusiastic about a bill, however reasonable, which simply served our vested interest. After all, Mr. Rogers was "Mr. Health", and if a vitamin bill was passed, it

would be the first time the Act had ever been amended to reduce rather than increase FDA's power.

Dan suggested a tradeoff. As we curtailed FDA's authority over the actual products on the one hand, we might on the other hand beef up the agency's authority to control misleading or exaggerated claims. Specifically, Marcus suggested we tell Mr. Rogers we would support a bill which gave FDA authority over the advertising of dietary supplement products. The silence was palpable as the assembled company presidents digested this little bombshell. The discussion began haltingly, but quickly a feeling of excitement began to grow. We knew we had something. The idea was certainly "responsible", and we knew it would appeal to Mr. Rogers because it responded directly to one of FDA's most consistent complaints, namely that claims were out of control. It was agreed that we should return to Washington and set up a meeting with Rogers' subcommittee staff to discuss the feasibility of drafting a new vitamin bill. If necessary, we would agree to support new advertising authority for FDA over vitamin products.

We soon learned that Mr. Rogers was interested, since he genuinely believed FDA had overstepped its authority in the vitamin regulations and since his constituents in the geriatric strongholds of southern Florida had been particularly vocal in demanding that he intercede. As for FDA control of dietary supplement advertising, it became the sine qua non of the bill and eventually caused no end of grief. At the time, however, we were euphoric.

Rogers scheduled three days of hearings on vitamin legislation in October of 1973. In addition to the usual complement of lobbyists and the press, the hearing room was packed with vitamin enthusiasts wearing pink and green lapel stickers provided by NHF, proclaiming CONSUMER PROTECTION YES from one shoulder and NUTRITIONAL TYRANNY NO from the other.

HERMAN

"We'll take you off the vitamins for a couple of days."

On the first day of the hearings, Mr. Rogers led the witnesses through their paces, steering the discussion away from the particular merits of the Hosmer bill and concentrating instead on the basic issues: Could vitamins be adequately regulated as foods, without resorting to the drug authority? Were product limits really necessary, in cases where safety was not an issue? Was dietary supplement advertising adequately regulated? We did our song and dance and pledged to submit draft legislation of the type we could support. Our show was on the road!

On the second day of the hearings, a very different show played for the standing-room-only audience. The witnesses for the second day included panels assembled by NNFA and NHF, plus representatives of several other organizations, but the two most memorable incidents centered around Dr. Carlton Fredericks and Clinton Miller.

Dr. Fredericks--a nutrition lecturer, radio personality, and author--was interrupted in mid-presentation by a very angry Dr. Tim Lee Carter, the ranking minority member of the Health Subcommittee, who attacked the witness in a bitter and personal manner. The air was thick with tension and anger, and the careful moderation that had characterized the first day's hearing was swallowed up in a morass of hostility. This performance, for which Dr. Carter apologized in part the following day, was followed soon after by a lengthy exchange between Clinton Miller and the other doctor on the Subcommittee, Dr. Bill Roy of Kansas. Dr. Roy had been provided with a poop sheet citing the various instances in which NHF leaders had been charged with violations of the Food, Drug, and Cosmetic Act, and he wanted Miller to comment on the charges. One by one, the names were read and the charges were recited. Miller responded articulately and with humility, playing his role to the hilt. Miller granted that the men were charged as stated, and that in some cases they had been convicted of selling electronic devices or vitamins or herbs (or in Miller's case Swiss whey) for the treatment of various diseases or conditions. FDA regarded the claims as "false" and the products as "worthless", but Miller argued that FDA was in the wrong and that these men were martyrs to a cause. He closed by reminding the Subcommittee that when Emerson had found Thoreau in jail and asked what be was doing there, Thoreau had responded that "at a time when the government imprisons righteous men, the place for every righteous man is in prison."

As theater, it was riveting. As political strategy, it was the pits. What had begun as a scholarly discussion of the proper regulation of vitamin products had ended as a discourse on unorthodox medical treatments, from unapproved cancer cures to little black boxes. And we, the heralds of a new era, were up to our armpits in the skeletons of the old.

Well, in due course we submitted draft legislation to Mr. Rogers, and he received it cordially. As far as we could see, the plan seemed to be moving right along. Miller, however, was distraught. The sudden emergence of the idea of giving FDA control over dietary supplement advertising was completely unexpected, and he viewed it as the deathknell of the industry. Accordingly, while we were sitting on our laurels and congratulating ourselves on our breakthrough in the House, Miller was busily at work in the Senate.

In early December 1973, Senator Proxmire and an unbelievable galaxy of powerful cosponsors introduced a Senate vitamin bill virtually identical to the old Hosmer bill. (Initial cosponsors included Eastland, Humphrey, Goldwater, Church, Thurmond, Moss, Tower, McGovern, Schweiker, and Helms. Others were added later.) We shopped around for a Senator willing to sponsor our version of the bill, but soon learned that other Senators did not rush to take a stand against something Proxmire really got his teeth into, and Proxmire's published attack on the vitamin regulations, the FDA, the National Academy of Sciences, and the medical profession made it clear that he had sunk his teeth into this one. Miller, an old friend of Proxmire's aide Howard Shuman, had brought off a stunning coup, and I thought it only polite to compliment him on his brilliant maneuver.

After gloating for a couple of days, Miller got down to the serious business of getting rid of our legislative proposal and its advertising provision. He called our company presidents, collect, to summon them to meetings in Washington, in New York, in California. And they answered his summons. They went, time and again, to submit to Miller's harangue: the advertising provision would destroy the industry more surely than FDA's regulations; the Hosmer/Proxmire bill was the only true salvation; and moreover he would make their lives miserable if they didn't straighten up and fly right. One company executive, after a particularly bitter confrontation in New York, came away shaken and declared that he knew for the first time--after a career spent in the health food industry, attending its conventions and rubbing shoulders with his fellow converts--that he knew for the first

time what it was to encounter a true radical. For the most part, our members stood firm, but Miller made some headway.

At a meeting late in December, CRN leaders agreed that, although we would not support the Proxmire bill, we would not oppose it and would cease any efforts to generate Senate support for our alternative. At a meeting in the spring of 1974, CRN leaders agreed to go to Rogers in the company of representatives of NNFA and NHF and attempt to persuade him to give up the advertising provision. Rogers knew the pressure we were under and interpreted our actions accordingly; we ended by reaffirming that if Rogers thought the advertising provision was necessary, we would stand by it. We were utterly convinced that no vitamin bill would ever become law without Rogers' support.

For months, the NNFA bombarded health food stores (our customers, I remind you) with letters and memos detailing in the most outraged terms the latest activities of the CRN. When our member companies' salesmen went to call on stores, they found themselves backed up against the wall and lectured about the vitamin bill. I am genuinely touched by this image, although it was a pain the neck at the time. Imagine Pop leaving his cash register and shaking his finger in the face of some poor salesman, demanding that he account for his employer's activities in Washington. It has elements of the ludicrous and yet...and yet...

The 1974 NNFA annual convention was in Houston, and once again our members turned out in force to show their wares in the exhibit halls and to plan strategy in the hospitality suites. A few weeks before the meeting, Miller informed us that he planned to debate our legislative position at an early morning session. Peter Semper and I agreed to participate, and at the appointed hour several hundred very earnest, very interested store owners gathered to receive Miller's instruction on manipulating the Congress. We made a few points, but Miller was obviously the man of the moment, and these good people simply took his word for it that it made no difference whether or not Chairman Rogers was willing to accept the bill they were trying to shove through.

Back in Washington, Congressman Rogers was preparing to hold a markup session on the vitamin legislation. At a markup session, a Committee may of course attempt to reconcile all the existing bills into a single compromise document, or it may start from scratch and write its own bill. The Rogers Subcommittee chose to write its own vitamin bill, and over a period of four days it created the official House vitamin bill. The bill prohibited FDA from limiting product formulation except for reasons of safety; it prohibited FDA from classifying nutrients as drugs unless therapeutic claims were made; and it granted FDA authority over the advertising of dietary supplements. During the markup session, Congressman Peter Kyros of Maine took a particularly active role in debating with FDA counsel Peter Hutt, who was present for the entire time. After four days of wrangling, one of the Subcommittee members suddenly announced that he was leaving to catch a plane and that, since he was needed for a quorum, the vote on the bill had to be now or never. Debate ended, the vote was taken, and Mr. Rogers directed the staff to be sure that Mr. Kyros was listed first among the sponsors. By this fateful order, the House vitamin bill became the Kyros bill.

Just a month later, Senator Kennedy's Senate Health Subcommittee, under mighty pressure from Senator Proxmire, finally deigned to hold hearings on Proxmire's vitamin bill. We testified that we preferred the Kyros bill; the NHF and the NNFA testified that they could not tolerate the Kyros bill; and the nutrition societies and medical associations appeared as usual to praise the FDA regulations and to decry the need for any legislation.

The very day after the hearings, the Second Circuit Court of Appeals acted on fifteen combined petitions for judicial review and overturned key portions of the FDA regulations. The judges held that FDA had no legal authority to declare that nutrients above a certain limit were automatically drugs, unless the products were promoted for therapeutic purposes. The court found other aspects of the regulations to be unreasonably restrictive, and commented on the "all or nothing attitude adopted by both sides in this long

and bitter controversy." The regulations were stayed and FDA was instructed to rewrite them, permitting higher levels of some nutrients and a wider variety of products.

While the August 1974 court decision was a big psychological victory, it bad strong pyrrhic potential. The FDA could not automatically declare high levels of nutrients to be drugs, but with few exceptions the agency was not required to permit their sale as foods. The net effect of this victory was, in the words of the FDA counsel, to create a large class of "illegal foods". Before we could fully evaluate the impact of the decision, the legislative situation exploded.

In September 1974, Senator Proxmire grew tired of waiting for Kennedy to act and decided to attach his vitamin bill as an amendment to one of Kennedy's major health bills. The amendment passed by a whopping 81-10, partly because no one wanted to argue about vitamins at home during an election year, and partly because Senator Kennedy assured his colleagues that the House would never let the Proxmire amendment become law. "Aye" was the safe vote. With this Senate victory in hand, NHF pulled out all the stops in the House.

Our situation then became very complicated. We knew there wasn't time to get the Kyros bill passed in 1974, except by some unlikely parliamentary fluke. In the meanwhile, the NHF was assuring our members that, with their help, the Hosmer/Proxmire bill could become law before the end of the 1974 session. The entire industry was thrown into a higher frenzy and new avalanches of letters fell upon the Congress. We had to make a judgment call, and our best guess was that neither vitamin bill would make it through the 1974 session. Since we wanted to be in a strong position to renew our efforts with Mr. Rogers at the opening of the 1975 session, we decided to continue to support the Kyros bill through the end of 1974.

Some of our members couldn't go along with us in this judgment. A handful of our supporters (and we only had a couple of handfuls at that time) split off and sent a telegram to all the members of the full Committee, withdrawing their support from the Kyros bill and urging passage of the Proxmire bill. Two of those members, Rodale Press and General Nutrition Centers, jumped wholeheartedly into the letter-writing fray, blanketing all of the districts represented by members of Rogers' subcommittee. The two key targets, however, were Kyros and Rogers himself.

Peter Kyros was, in the view of the NHF, in an anomalous position. At one time, he had been a cosponsor of the old Hosmer bill, and his action had been hailed with glee by NHF because he was one of the few members of the Health Subcommittee to agree to cosponsor. And now here he was, not only consenting to the House subcommittee bill and its advertising provision, but actually carrying the banner for it. NHF chose to view this change of position as a venal one, declaring that Kyros had been "bought off" the true vitamin bill by the American Medical Association. AMA protested that they opposed any vitamin legislation, including the Kyros bill, but their protestations fell on deaf ears. Clinton Miller and Dr. Carlton Fredericks held a press conference in the headquarters of Kyros' opponent, at which they "presented" the absent Kyros with an anti-consumer award for his "switcheroo" on the vitamin bills. The Maine papers, which had long been hostile to Kyros, ran a substantial article complete with picture.

Kyros was being bombarded with irate postcards, thoughtfully provided to the voters by our former members. Kyros asked us to get him the Rodale Press mailing list, which we did, and he proceeded to send out a long letter of response to his constituents. Unfortunately, a new campaign law made it illegal to use the franking privilege to send mail to constitutents within a few weeks of the election, and Kyros' opponent promptly filed a suit for violation of the Fair Campaign Practices Act. In the election, he beat Kyros by a margin of only a few hundred votes and became the youngest member elected to the new Congress that November.

Mr. Rogers came in for equally heavy personal attack, although his seat was never in danger. Like Kyros, Rogers was repeatedly summoned to "debates" in his district, sponsored by the NHF; like Kyros, he repeatedly declined and the "debates" proceeded without him. In addition, Rogers received

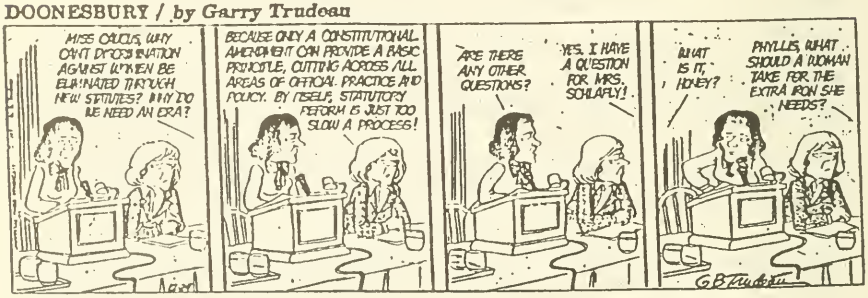
tens of thousands of UN THANK U GRAMS from his Florida voters, accusing him of selling out to the AMA and of disregarding the clear instructions of his constituents in the matter of the vitamin bill. Mr. Rogers, whose integrity was simply never questioned, was livid. He inserted lengthy statements in the Congressional Record, itemizing his campaign contributions and outlining the "true facts" about the vitamin bills, describing the Hosmer/Proxmire bill as the industry bill and the Kyros bill as the consumer bill. Ralph Nader's Public Citizen was even prevailed upon to write a letter more or less endorsing the Kyros bill, which was said to "inflict less damage to consumer principles than the Proxmire-Hosmer bill."

Having fought to a stalemate, both Rogers and Proxmire were anxious to avoid more needless confrontation, but were still committed to the need for a vitamin bill. Their staff members, together with staffers from Senator Schweiker's office, began to meet regularly to hammer out the details of a compromise. In May of 1975, Rogers and Proxmire introduced identical vitamin bills simultaneously in the House and Senate. The new Rogers/Proxmire bill incorporated parts of the old Proxmire and Kyros bills, and we had no qualms about supporting it. The new bill did grant FDA control over dietary supplement advertising, although some provisions were added to protect retail store owners who might simply display promotional materials provided by a manufacturer. NHF and NNFA remained adamant in their opposition, despite Senator Proxmire's agreement to the compromise. They held a rally at the Capitol and fanned out all over the Hill carrying lists of "non-negotiable demands" and urging other Senators and Representatives not to cosponsor the new bill.

With Rogers and Proxmire united at last, the role of our little health food lobby quickly waned. It became evident to Washington's serious lobbyists that the heretofore latent vitamin bill had become a viable reality which must be dealt with, and the big boys proceeded to deal with it. The Proprietary Association, representing manufacturers of "patent medicines" (mostly over-the-counter drugs) viewed the advertising provision with alarm. They saw it as a dangerous precedent for FDA control of all food and drug advertising and set out to squelch it. Several national advertisers' associations joined in this effort and began to tap their own multitudinous sources of letters to Congress.

Fortunately, the J. B. Williams Company, makers of Geritol, broke ranks with the Proprietary Association at this crucial juncture and began to lobby actively for the Rogers/Proxmire bill, turning out in force and with great good humor under the leadership of the company's Vice President and General Counsel, Roger (Tony) Schultz. Another Proprietary Association member, Vitaminerals, Inc., had been on the scene all along and continued to support the low-key but effective efforts of its Washington counsel on behalf of the Rogers bill. We adopted a very low profile, since our visible presence set off renewed outbursts from the NHF and NNFA.

DOONESBURY / *by Garry Trudeau*



With deplorable timing, FDA issued its revised vitamin regulations, as instructed by the Court of Appeals, in late May of 1975, just about two weeks after the introduction of the joint Rogers/Proxmire bill. The revision was impressive. As ordered by the court, FDA dropped the idea of classifying vitamins as drugs above the approved limits. The agency would accept industry petitions for new formulas that should be approved and would remove all upper limits on single vitamins and minerals which were Generally Recognized as Safe (GRAS). It was a generous offer, in the true spirit of compliance with the Court of Appeals' direction, but it came at the wrong time to head off the legislation. Besides, we could not be sure FDA would finalize regulations which carried through on the promise clearly inherent in this proposal. We submitted the petitions called for by FDA but continued to support the legislation. FDA took no further action for a year and a half.

As 1975 slipped into 1976, Kennedy's Health Subcommittee agreed to accept the Rogers/Proxmire bill as an amendment to another major health bill, and despite a last-ditch effort by the Proprietary Association to have the advertising portion stripped out during floor debate, it sailed through the Senate intact. In the House-Senate conference committee, the Proprietary Association finally succeeded in emasculating the advertising provision but was unable to get rid of it entirely. The vitamin bill became Public Law when it was signed by the President on April 22, 1976.

Five years later, that is essentially where the matter stands. The new law directed FDA to amend, within 180 days, any regulations inconsistent with its provisions. In October 1976, precisely 180 days after the law was signed, FDA re-issued the regulations. The generous approach proposed in May 1975 was abandoned and FDA essentially reverted to the pattern of the 1973 regulatory proposal, cutting loopholes where the law required them. These patchwork regulations were invalidated by the Court of Appeals in February 1978, and in March 1979, FDA revoked the entire package of regulations--the basic labeling provisions which had been repeatedly upheld by the courts and which had not been undermined by the legislation, as well as the Standards of Identity which had created so much controversy. No further proposal has been issued.

From my worm's-eye perspective, it seems that FDA has abandoned its responsibility in a fit of pique. Unable to defend its sweeping plan, it has declined even to finalize basic labeling regulations, and the industry is, for all practical purposes, adrift.

Written and distributed by Annette Dickinson; 1707 N Street, N.W.; Washington, D.C. 20036. 202-872-1506. Dickinson is a government relations consultant and Executive Director of the Basic and Traditional Food Association. She was Director of Government Affairs for the Council for Responsible Nutrition from 1973 to 1979. Her academic training is in food science. (M.S., University of Maryland, 1975).

Statement of Kenneth M. Rosenberg
Chairman & Chief Executive Officer
of Pharmavite Corporation

PHARMAVITE

We feel compelled to report to this Committee on but one of many issues related to the regulation of dietary supplements, i.e., folic acid and its role in preventing neural tube birth defects such as spina bifida.

FDA's recent folic acid health claims proposal and attendant food additive and food fortification proposals are yet the latest example of the agency's bias against nutritional supplements and emphasize the urgent need for passage of legislation that will finally force FDA to establish reasonable and evenhanded policies with respect to dietary supplements in the public interest.

Although FDA has finally recognized the appropriateness of a health claim concerning the relationship between folic acid intake and reduced risk of neural tube defects, the agency has required such lengthy and cumbersome language as to make it virtually impossible to print a helpful consumer claim on a dietary supplement label. As proposed, any health claim for folic acid would have to include information on numerous factors related to folic acid consumption, sources of dietary folate and other required statements that do not reasonably need to appear on a dietary supplement label and can't physically be placed there. Of FDA's five model health claims for folic acid, the shortest claim which includes essentially the minimum language necessary to satisfy the regulation, requires 82 words and nine lines of text. This is clearly far too much copy to print in readable fashion on a supplement label, which typically measures about 2" by 6". In order to accommodate the practical realities of supplement labeling, a much more concise and simplified health claim is critically needed without further delay.

The food additive proposals also place flawed and unrealistic expectations on a highly controversial scheme of food fortification that, at best and by the agency's own estimates, provides less than adequate folic acid intake for large numbers of women of childbearing age. Combined with the de-emphasis on dietary supplements by requiring lengthy, qualification-laden language, the agency has effectively ruled out health claims on supplement labels. The end result is a totally ineffective and contradictory policy that cheats the public out of the opportunity for a simple, safe, economical and effective means of combating this terrible disease.

In addition, the Food and Drug Administration has jeopardized the approval of any health claims at all for folic acid supplements, by tying in as a condition the approval of the food fortification policy. The agency insists that they cannot approve a health claim unless it can be "safely implemented." If the safety issues (presented only by the fortification policy) cannot be satisfactorily answered, the agency may then ultimately reject all health claims for folic acid. This is clearly unacceptable. The irony is that the studies proving folic acid's beneficial effects in preventing birth defects have all been conducted with dietary supplements, not foods. For FDA to sacrifice or even compromise a health claim for folic acid supplements on the basis of their desire to introduce an untested and unproven food fortification solution is unconscionable. There is no justification for further delays in approving an appropriate health claim for folic acid supplements independent of any of the issues raised by the food fortification proposal.

Summarizing our concerns:

- FDA has, instead of focusing on an abbreviated health claim that would be useful and consumer friendly for supplements of folic acid, issued a lengthy, contorted two-part plan mainly focusing on fortification of the food supply

- The fortification policy does not provide the targeted population with a high enough level of folic acid intake to achieve the intended prevention effect.

- The health claim for supplements is too long and convoluted to be put on a package and, therefore, is not usable by manufacturers and will not be effectively communicated to consumers.

- The end result is to have nobody satisfied and the public cheated of the opportunity to simply, economically, and safely protect against this terrible disease.

- There is simply no justification for not "uncoupling" the fortification policy from the supplement health claim and permitting a rational, brief phrase that will fit on product labels immediately, with no further delay or confusion.

- FDA should be held accountable for its position on this and the fact that it has been stalling while the preventative steps could have been taken over a year ago.

We comment on this subject not only because of its importance in saving and improving lives and saving health care costs; but also because this is a prime, current example highlighting the need for Congressional action and oversight to mandate that FDA act with public health policy considerations foremost in mind and to eliminate the beaucratic bias that it has continuously demonstrated against dietary supplements.

October 21, 1993
Washington, D.C.

Respectfully submitted,
Kenneth M. Rosenberg

Release date:
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Citizens For Health is a national non-profit health advocacy membership organization of consumers and health professional.

National Office:
P.O. Box 368
Tacoma, WA 98401
206-922-2457
Facsimile 206-922-7583

Washington, D.C. office:
601 Pennsylvania Avenue, NB #1407
Washington, D.C. 20004
202-737-1909
Facsimile 202-737-1913

Amino Acid, L-Tryptophan: Safe or Unsafe?

Background

Since the early 1970's a growing body of research suggested that L-tryptophan, an essential amino acid, might be useful for the treatment of behavioral disorders (e.g. depression) and other conditions such as insomnia. By the early 1980's it was apparent that a number of behavioral disorders could benefit from L-tryptophan supplementation since the brain's serotonin content could be altered by changes in the plasma tryptophan levels. Aside from very rare reports of mild yet reversible side effects, consumers reported numerous beneficial effects and no adverse effects from consuming L-tryptophan supplements at suggested ranges of intake. Various sources estimate that during the 15 years L-tryptophan was commercially available between 14 to 20 million Americans consumed L-tryptophan supplements. Prior to 1989, two surveys found that between two to four percent of all households had some person who consumed L-tryptophan on a daily basis. In fact, by late the late 1980's L-tryptophan supplements had begun to receive wider support in the medical community as a viable alternative to benzodizapines in mild to moderate sleep disorders, and as an effective mood stabilizer and alternative to such drugs as Prozac®.

In early October, 1989, physicians in New Mexico reported on three women with clinical symptoms of eosinophilia-myalgia syndrome (EMS). The doctors suspected an association between the EMS and the women's consumption of L-tryptophan supplements. Soon thereafter other cases began to be reported in other parts of the country, resulting in the Center for Disease Control (CDC) initiating a national

surveillance program. Based on the CDC's epidemiological findings, on November 17, 1989, the FDA issued a national consumer advisory to discontinue the use of L-tryptophan supplements, followed by a voluntary recall of all over-the-counter L-tryptophan supplements above 100 mg. This action limited the number of additional cases. Exempt from this voluntary recall were protein supplements, infant formulas, intravenous and oral solutions, and special dietary foods. By late 1990, a total of 1,531 cases of EMS had been reported to the CDC, including 27 deaths. It should be noted that in Germany, where single amino acids were sold under prescription, the same outbreak occurred, requiring similar regulatory action.

In an effort to explain the unexpected cases of EMS, two hypotheses were proposed to explain the association. The first hypothesis suggested that L-tryptophan itself triggered EMS in susceptible individuals, owing to possible abnormalities of L-tryptophan metabolism. The other hypothesis claimed that the EMS was triggered by a contaminant present in the lots of L-tryptophan supplements. The former hypothesis was not consistent with the sudden appearance of the outbreak, since there had been no apparent ill effects reported prior to 1989, particularly of EMS-like symptoms. No EMS-like symptoms were reported in any of the American Association Poison Control Centers' annual reports for the six year period of 1983-1988. In 1992, it was concluded by researchers at the Departments of Immunology and Medicine, Mayo Clinic, and the Acute Disease Epidemiology Section of the Minnesota Department of Health, that "Epidemiologic investigations subsequently demonstrated that EMS was not triggered by tryptophan per se, but rather by exposure to a contaminant in tryptophan manufactured by one company."(2)

The evidence for a tryptophan contaminant was provided by several case-control studies and animal studies. There was also a striking resemblance to the clinical findings of EMS reported associated with contaminated L-tryptophan and the toxic oil syndrome (TOS) outbreak that occurred in Spain during 1981. In the TOS cases in Spain, nearly 20,000 people were affected, including 315 who died. Epidemiological investigations of TOS implicated denatured industrial rapeseed oil illegally sold to consumers. This prior experience with TOS in Spain urged scientists to identify potential contaminants in the lots of L-tryptophan associated with EMS in the United States.

To determine if EMS was caused by the implicated contaminated L-tryptophan, researchers at the Mayo Clinic conducted a study involving Lewis rats given either the implicated L-tryptophan or pure L-tryptophan. Muscle biopsy specimens of the animals showed that after 38 days, 7 of 9 animals receiving the implicated contaminated L-tryptophan developed fascial thickening and perimysial inflammation associated with EMS, compared to 0 of 10 rats receiving pure L-tryptophan ($p<.001$). Subsequent studies demonstrated that when one of the isolated contaminates, 1,1'-ethylodenebis[tryptophan] (EBT), was given Lewis rats, the same EMS-like symptoms developed in experimental animals but not in those rats treated with pure L-tryptophan. These findings were the first to demonstrate that a contaminant present in the implicated L-tryptophan lots were associated with EMS. Obviously, ethical considerations prevented testing these animal findings in humans.

By 1992 it was the conclusion of researchers at the Mayo Clinic and the Minnesota Department of Acute Disease Epidemiology that,

> "Epidemiological studies indicate that EMS is triggered by one or more contaminants in tryptophan that was manufactured by one company. The chemical that has been most strongly implicated is 1,1'-ethylodenebis[tryptophan] (EBT), a molecule that is structurally similar to tryptophan. Results from animals studies suggest that EBT may cause pathologic changes in fascia that resemble EMS. Epidemiologic investigations have shown that the presence of EBT was associated with changes in the tryptophan manufacturing process."

It is also important to mention that in the Mayo Clinic report cited above the researchers stated that, "There is no convincing evidence that any EMS cases were caused by consumption of tryptophan by companies other than [the single implicated Japanese company]."

The implicated company, according to the Mayo Clinic's authors, utilized a biofermentation process employing biogenetic engineering incorporating a strain of *Bacillus amyloliquefaciens* used to synthesize tryptophan. Between December, 1988, and June, 1989, and possibly earlier, the company introduced a newer strain of *B. amyloliquefaciens* (strain V) which had been genetically altered to increase the synthesis of intermediates identified in the biosynthesis (production) of L-tryptophan. At the same time the company modified some of its filtration and purification processes which possibly enhanced the likelihood of contaminants finding there way into the finished product.

That this single company was the source for the implicated contaminated L-tryptophan was further supported by "fingerprinting" of all known bulk sources of L-tryptophan through chromatographic patterns that provide distinctive signature peaks upon analysis. The "fingerprint" for the implicated manufacturer was distinctive and included five signature peaks that were found in those manufactured lots epidemiologically linked to the EMS cases. This included several contaminant peaks, including the more culpable EBT contaminant.

Since 1990, the FDA has used the EMS-contaminated L-tryptophan link as an opportunity to expand its regulatory control of the entire dietary supplement and herbal market. In fact, the FDA's Dietary Supplement Task Force was launched following comments in April, 1991, by FDA Commissioner David Kessler, in which the Commissioner prefaced the introduction of the Task Force by saying: "The recent problems with L-tryptophan...unequivocally demonstrates that dietary supplements, who regulatory status has been in limbo, can harm people." Since that public address, both the Commissioner and his staff have refused to qualify their statements concerning L-tryptophan by saying "contaminated L-tryptophan", thereby continuing to imply that pure L-tryptophan was responsible for the EMS cases, which has not only not been proven, but disproven both experimentally and epidemiologically.

Further, the FDA kept from public knowledge the association of the implicated manufacturer's use of biogenetic engineering technology in producing contaminated L-tryptophan until August, 1990, when Michael Osterholm, one of the original investigators in the Minnesota Department of Public Health, publicly admitted what Federal investigators had known for months, namely that the contaminant was associated with a genetically-engineered bacteria. Citizens For Health was able to confirm this through its securing lots of conversations between FDA, CDC and various investigators obtained in the summer of 1993 through the Freedom of Information Act. Some believe that this information was not made public to protect the biotechnology industry.

Nevertheless, Dr. Kessler's comments, and the recommendations of the FDA Task Force and Advanced Notice of Proposed Rules in the *Federal Register* of June 18th not only ask that L-tryptophan be made a prescription drug, but that all amino acids sold as supplements be reclassified as drugs.

Citizens For Health concludes that the FDA's regulatory proposals for amino acids are not only unnecessary but eliminate many safe and effective uses of amino acid supplements in the mitigation and treatment of various conditions.

Should L-tryptophan Be Classified a Drug or Withheld From the Over-the-Counter Market Place?

If only one company was responsible for inculcating the L-tryptophan market place with a contaminant that placed consumers at risk of EMS, why then is L-tryptophan still off the market as an over-the-counter dietary supplement?

The FDA's response to this question has been that they believe that L-tryptophan itself may have a role in EMS.

As a consumer health advocacy organization, Citizens For Health would be concerned with restoring L-tryptophan to the market place if in fact uncontaminated L-tryptophan would contribute to additional cases of EMS. That this may be possible is extremely doubtful.

To support their cause, the FDA cites a March, 1993, paper they published in the *Journal of Clinical Investigation*.(3) In that paper the FDA claims that dosages of L-tryptophan representing a human dose of 5-6 grams a day, resulted in pathological signs similar to contaminated L-tryptophan and EBT. A careful review of the paper's methodology section however reveals that the amount of L-tryptophan actually administered was closer to 2,000 mg/kg body weight per day, corresponding to a human dose of 140 grams per day for an average 147 pound individual. An amount that is 30 times the human dose of 5 grams in a 147 pound man. Yet even at these excessive levels of consumption, only the EBT and contaminated L-tryptophan produced immune reactions characteristic of earlier EMS cases in humans who consumed contaminated L-tryptophan. A number of investigators familiar with L-tryptophan research have written strong letters of protest to the journal requesting that the paper be retracted and corrected.

Recently, Citizens For Health contacted two professors of biochemistry and nutrition who had conducted a comprehensive literature search on L-tryptophan as part of their on-going studies into the safety of L-tryptophan. The search found 13,542 citations on L-tryptophan published during the period of 1966 to the present. Listed under "toxicity" of L-tryptophan were 65 papers. Each of these papers were reviewed by the researchers. No adverse findings or deleterious effects were reported in any of these 65 papers in either healthy animal or human feeding studies. Adverse effects were only reported in animals that had been compromised in some way (i.e. prior induced liver pathologies, suffered protein-deficient, or were given cancer causing agents such as nitrosamines).

This literature search covering a period of nearly thirty years in addition to the absence of adverse cases reported prior to 1989 suggests that uncontaminated L-tryptophan has a remarkable history of safety and absence of adverse effects at levels commonly consumed by humans.

Conclusion

In light of present evidence on the clinical and epidemiological safety of the amino acid L-tryptophan, Citizens For Health urges the FDA to return L-tryptophan supplements to the marketplace and reject the recommendation of its task force panel to reclassify the product a drug.

References

1. *Dietary Supplement Task Force: Final Report*. DHHS-PHS, FDA, May 1992, p. 38.
2. Belongia, E.A., Mayeno, A.N. and Osterholm, M.T. The eosinophilia-myalgia syndrome and trytophan. *Ann Rev Nutr* 1992: 12:235-256
3. Pathological and immunological effects of ingesting L-tryptophan and 1,1'-ethylidenebis[L-tyrptophan] in Lewis rats. *Journal of Clinical Investigation*, 1993: 91; 804-811.

ACT UP SAN FRANCISCO
ALTERNATIVE TREATMENT COMMITTEE
84 Castro Street, Suite 135
San Francisco, Ca. 94114
PH. (415) 392-4055

October 20, 1993
Senator Orrin Hatch
and Members of the Labor and Human Resources Committee
U.S. Senate
Washington, D.C.

Dear Senators,

I request that the attached comments sent to FDA Documents Management Branch concerning the Dietary Supplement Task Force Report be placed on the official record of the hearing on S 784.

Sincerely,

Michael Onstott

Michael Onstott

Alternative Treatment Committee
ACT UP San Francisco

Dockets Management Branch (HFA 305)
Food and Drug Administration
Room 1-23
12420 Parklawn Drive
Rockville, MD 20857

Re: Docket No. 93N-0178, 21 C.F.R. Ch. 1, Regulation of Dietary Supplements

Dear Commissioner Kessler:

Following are comments of the ACT-UP San Francisco, Alternative Treatments Committee, with respect to the above-referenced U.S. Food and Drug Administration ("FDA") proposal, and with respect to the Task Force on Dietary Supplements Final Report ("the Task Force Report").

1. Introduction and Summary.

The ACT-UP San Francisco Alternative Treatments Committee is committed to the battle against AIDS. In this struggle, as in the struggle against other life-threatening illnesses, we must maintain the right to pursue all viable treatment options. It is vitally important that people with AIDS, and other life-threatening diseases, are consulted, empowered and allowed a basis for continued hope in the selection of available options, including natural and alternative options utilizing nutritional supplements. We regard the current access to natural, traditional and alternative options as an absolute right, which activists, patients and consumers are prepared to defend. The FDA's proposals do not give sufficient weight to the important consumer and patient interest in freedom of choice and access, since the proposals would result in serious limitations on access to nutritional supplements without adequate justification in safety or otherwise.

We also believe that the FDA's proposals--contrary to the Commissioner's direction--ignore or unreasonably minimize the important potential public health benefits from the current availability of nutritional supplements. Especially in light of the Concorde Study and other research indicating that anti-retroviral drugs are less efficacious than previously believed, there is a profound public health benefit in ensuring that alternative and natural options utilizing nutritional supplements remain available and can be pursued, whether for AIDS or other life-threatening diseases. Only clear, specific and compelling safety concerns could be sufficient to outweigh this important benefit, and such concerns are not identified. Accordingly, the FDA's proposals would seriously impact potential public health benefits from availability of nutritional supplements, and would do so without an adequate justification in safety concerns or otherwise.

As we explain in more detail below, these two vital interests--freedom of choice and access for patients and consumers, and public health benefits from nutritional supplements--are systematically ignored or understated by the Report and proposals. Less restrictive options that would serve these vital interests are not seriously considered. An exclusive and exaggerated focus on "safety" (which does not even apply to most nutritional supplements) is used to displace the required evaluation of these important interests. Since the Task Force Report and regulatory proposals are thus fundamentally deficient in their analysis of basic policies, we believe the proposals should be withdrawn until such time as an adequate and unbiassed analysis can be conducted.

2. The Task Force Report fails to accord sufficient importance to freedom of choice and public health benefits.

Despite at some points offering "lip service" to these important policies (Report, p. 9), the Task Force Report fails to provide analysis that reasonably recognizes their importance. A great deal of careful analysis indeed would be required to justify the serious impingements on interests in free choice and health benefits that the FDA is proposing. The absence of the required analysis, and the biassed analysis that is offered instead, shows clearly the FDA's unsupported assumption that "safety" concerns justify stringent regulation of all dietary supplements.

A. The Report attaches no weight to public health benefits from taking dietary supplements.

Among the primary charges from the Commissioner to the Task Force was to consider the benefits and advantages of dietary supplements, and what approaches would best serve the public health. See Appendix 1. The Report is grossly deficient in carrying out this charge.

For example, in reviewing the "issues" considered by the Task Force, the following are mentioned: ensuring safety, limiting potential for fraud, and taking steps to ensure that the existence of dietary supplements does not act as a disincentive for drug development (a clearly improper motive). Exec. Sum., pp. 1-2. There is not even an acknowledgement that serious public health benefits might result from availability of supplements. While the Report notes that the public has various "reasons" for taking supplements (Report, p. 9), it does not appear to take seriously the possibility that these reasons may be valid.

The only public health benefit of dietary supplements that

the Report appears to recognize is that of ensuring a balanced diet. Exec. Sum., p. 2. However, the Report appears to endorse the view of Dr. Olsen that even for this purpose supplementation is not needed. Report, pp. 24, 26. The Report also adopts the extraordinary view that supplementation with amino acids has "no known nutritional use." P. 25. Thus the Report effectively rules out any serious public health benefits from supplementing the diet with amino acids. However, the brief and superficial analysis offered is clearly inadequate to support this important conclusion.

The Report does acknowledge that certain population groups may have a need for increased intake of certain nutrients (Report, p. 25) and that certain health conditions may also lead to deficiencies of nutrients (p. 24). We emphasize that an important such group are people with AIDS or HIV infections. It is well-established that deficiencies of certain nutrients tend to arise in these individuals, and nutritional replacement strategies have been recommended to address these. People with AIDS or HIV infections also very often have greater difficulty in absorbing adequate nutrition from the "balanced diet" theoretically available to all Americans, and supplementation is necessary for them to ensure adequate nutrition.

The Report appears to concede that "safe" vitamin and mineral supplements should be available to such individuals. Report, pp. 25-26. However, the exaggerated and unjustified requirements for "safety" that the Report would impose make this concession meaningless. If supplements are not available until some far-distant time when they have been demonstrated to the FDA's satisfaction to be "safe" according to standards as yet unknown, then important potential public health benefits for people with AIDS and many others will be irretrievably lost for an indefinite period of time. These potential public health benefits require that supplements remain available for free choice by affected consumers, unless compelling and specific safety concerns have been demonstrated by the FDA to require otherwise.

We note that there are many other potential public health benefits from the availability of dietary supplements, which we do not address here. There is an increasing volume of scientific evidence that various nutrients can be of use in preventing or ameliorating health problems. While the FDA cannot seem to bring itself to accept evidence of these benefits, which millions of common sensical Americans, as well as many scientists, do accept, that does not mean that these benefits are not real. The proposals would unjustifiably result in loss of many of them.

B. <u>The Report effectively negates freedom of choice by an exaggerated and unjustified requirement to demonstrate safety</u>.

While we acknowledge that the safety of dietary supplements is an important and valid concern, we oppose the Report's approach to this issue, since it effectively results in a negation of freedom of choice and other policies. By making the undefined "safety" of supplements an "overriding concern" (Report, pp. 2, 15), and placing a burden on the supplements industry to demonstrate to FDA's satisfaction that supplements (in any amount) are "safe" before they may be made available, the Report eliminates any real role for consumer free choice.

Although the Task Force purports to have given consideration to freedom of choice, its decision to adopt this overstated requirement of "safety" clearly suggests otherwise. We note, for example, with respect to vitamins and minerals, that a larger portion of the Report is devoted to developing a "regulatory scheme" (pp. 26-36) than is devoted to discussion of the important policy concerns that must precede the decision to regulate at all. This clearly illustrates the Report's biassed approach, which has pre-ordained that stringent regulation on the basis of "safety" should be proposed.

We note also the Report's extraordinary concession that it is treating dietary supplements as over-the-counter ("OTC") drugs, and perhaps requiring greater safety. Report, pp. 17-18. Relying on an unspecified concern that the relative absence of regulation of supplements creates a "disparity in the relative risk to the consumer," the Task Force feels compelled to close this regulatory gap. Notably absent here is any requirement that specific safety concerns attaching to specific supplements need be shown. The fact that supplements have a long history of use and are naturally occurring substances found in foods is ignored, and they are assumed to be more dangerous than OTC drugs. See also Report, p. 23 (there is a "high presumptive risk" from intake levels exceeding RDAs). The Task Force sees the mere absence of regulation as creating a risk, and would impose regulation whether or not a real danger to safety exists. Again, this is clearly a biassed approach, and one which effectively negates any real role for consumer choice.

Apart from the Report's "assumption" that dietary supplements pose safety risks, we do not find any demonstration that such potential dangers require the stringent regulation proposed. While with respect to a few substances--such as Vitamin A--there may be risks from excessive intake, the experience with these cannot justify wholesale restrictions with respect to other substances. The safety concerns identified in the Report are for the most part vague and general, and do not even apply to many of the substances for which regulations are proposed. In addition, where genuine safety concerns with specific substances are identified, the Report should consider other regulatory approaches such as warnings. The failure to seriously do so again shows the lack of real weight attached to freedom of choice (as well as the apparent "assumption" that the public is too stupid to heed such warnings, Report, p. 17).

We also wish to emphasize that the "consumers" who have called for stringent regulation of dietary supplements at the FDA's hearings (Report, pp. 7, 14) do not speak for us. Nor do we believe that they speak for the majority of consumers who purchase and consume dietary supplements. We question whether many of these purported "consumers" are truly independent of the FDA.

We assume that other commenters will address in detail the legal objections to requiring industry to demonstrate the safety of dietary supplements. With respect to vitamins and minerals, the Report concedes that the Proxmire Amendment places on the FDA the burden of showing the unsafety of certain potencies. Report, p. 6. The Report's basic approach to the safety issue appears to stand this requirement on its head, and thus to be legally indefensible (at least with respect to vitamins and minerals, and perhaps other supplements). Nor does the Report's reliance on regulation of supplements as "food additives" provide a legally adequate basis for placing such a burden on industry; the notion that dietary supplements are "food additives" is clearly unreasonable, as the courts have ruled.

C. The Report endorses a clearly improper policy: encouraging drug development at the expense of the availability of dietary supplements.

We find absolutely outrageous the Task Force's indication that one of its primary concerns is "what steps are necessary to ensure that the existence of dietary supplements on the market does not act as a disincentive for drug development." Report, p. 2. Perhaps more clearly than any other portion of the Report, this statement shows the bias of the Task Force against the use of dietary supplements.

This "policy" implies, first, that consumers have only a very limited right to choose dietary supplements over "drugs" and that the FDA must take away access to supplements if consumers threaten to use them too much, to the exclusion of the drugs that

FDA has approved. This is insulting to consumers, and shows the lack of importance really attached by the Report to free choice and access. This policy ignores the fact, second, that the use of dietary supplements may have benefits that are entirely independent of those derived from taking FDA-approved drugs; for no good reason the benefits of taking drugs are to be achieved at the expense of potential benefits derived from taking supplements. The Task Force apparently thinks that consumers and the nation generally must be forced to spend their money on the (generally more expensive) drugs approved by the FDA rather than on the (generally cheaper) preventatives offered by dietary supplements; and it is willing to forego the benefits obtained from supplements if that is necessary to achieve this end. This way of thinking is entirely unreasonable and biassed, and must be unequivocally rejected.

3. The Task Force Recommendations regarding regulation of vitamins and minerals are unjustified.

We have already described many of the deficiencies in the Report's approach to regulating vitamins and minerals. As noted, the Report depreciates or denies without adequate discussion, the potential public health benefits of vitamin and mineral supplements. Report, pp. 24-26. The Report also gives short shrift to the public's interest in free choice and access to these supplements; a requirement of demonstrating safety according to undefined standards is to be made "a prerequisite before products are made available to consumers." Report, p. 26. Thus, whether or not specific safety concerns have been identified with vitamins and minerals, access will be allowed only if the FDA has been convinced that the potencies in which they are available are "safe."

The Report certainly does not demonstrate the existence of safety concerns sufficient to justify the FDA's broad-brush approach to regulating vitamins and minerals. The only toxicity concerns even mentioned in passing are those concerning vitamins A, D and B-6, and even these are not documented or discussed at any length. No specific safety concerns with respect to potencies of other vitamins and minerals are even mentioned, although the Report recommends an onerous program of regulation premised on purported safety concerns. Although the Report refers to a "high presumptive risk" from intake of vitamins and minerals in excess of RDAs, it does not document any specific safety concern; obviously there may be risk from consumption of such products at sufficiently high levels, but a demonstration of what risk and from what levels is necessary to justify such onerous regulations.

Rather than offering a genuine analysis of safety concerns and benefits of supplements, the bulk of the Report's discussion of vitamins and minerals is occupied by exposition of a "regulatory scheme," implementation of which appears to be an Agency goal in itself. The "scheme" is introduced at some length, and without any real pretense that it can be justified by specific safety concerns. Less onerous regulatory options for addressing supposed safety concerns--such as required warnings--are not considered. The "scheme" includes counter-intuitive "definitions" of "vitamin" and "mineral," (e.g., Vitamin D is not a vitamin since it can be synthesized in the body). These definitions appear to be designed to limit the applicability of the Proxmire Amendment and have little else to recommend them. Alleged "corollaries" to these definitions are also offered, although their significance is not made clear.

While the Report purports to distinguish between "dietary supplements whose use is safe and have a reasonable rationale" and those whose "use creates public health concern" (Report, p. 35), it does not in fact do so. The Report actually assumes that for potency levels of vitamins and minerals in excess of RDAs "there is high presumptive risk" (p. 23), and by this means

attempts to shift from the FDA the Proxmire burden of demonstrating that levels in excess of the RDAs are unsafe (p. 35).

We do not believe that legally this attempt at burden-shifting can succeed; for simply because the FDA affirms that certain potencies of vitamins and minerals are GRAS, it does not follow that higher levels have been demonstrated to be "unsafe," and the latter is the agency's burden under the Proxmire Amendment to justify regulating potencies. Since the FDA would not have met its regulatory burden, no burden can "shift to the commenters" to show that potencies in excess of the RDAs are "safe." Report, p. 35. The fact that such an approach might make the Agency's job in reaching its pre-determined goals easier, and "focus the work of agency scientists," (p. 35) is certainly not sufficient to justify ignoring the clear constraints of the Proxmire Amendment.

Since the Task Force has not in fact even attempted to draw the appropriate distinctions among dietary supplements (Report, p. 35), and has proposed instead an approach that would implicitly classify all vitamins and minerals in excess of RDAs as "unsafe" without any specific evidence, we believe that consumers and people with AIDS or HIV infection are more than justified in continued "opposition to the agency's actions." P. 36. On behalf of people with AIDS and HIV, and consumers generally, we strongly oppose the Task Force recommendations with respect to vitamins and minerals. These proposals are unjustified by genuine safety concerns, contrary to important public health benefits, and in violation of consumer rights to access and choice. They should accordingly be withdrawn.

4. <u>The Task Force Recommendations regarding regulation of amino acids are also unjustified</u>.

We believe that for many of the same reasons the Task Force proposals for regulating amino acids as drugs are also unjustified. Potential public health benefits from availability of amino acids are ignored, freedom of choice of consumers is not considered, and safety concerns are inadequate to justify the onerous approach recommended. Apart from the experience with L-Tryptophan, the Report does not identify any specific safety concerns with amino acids. The supposed concerns about imbalances or excesses from consumption of specific amino acids are described briefly and in only the most general terms (Report, pp. 43-44), and do not in any event apply to all amino acids.

As with vitamins and minerals, the Report does not appear to take seriously the Commissioner's charge to evaluate public health benefits from availability of amino acids. There is simply no discussion of this important issue. Instead, the Report appears to assume that if consumers have the temerity to choose to use individual amino acids for their physiological or therapeutic effects, then they must obviously be prevented from doing so without regard to whether health benefits might be achieved or whether serious and specific safety concerns are raised. This total disregard by the FDA of vital health issues is patronizing, insulting to consumers and obviously unwise as a policy matter. While the FDA may be so biassed that it believes without analysis that there are no public health benefits from availability of amino acids, this sort of bias must not be allowed to serve as the basis for the nation's policy.

The Report even attempts to turn potential public health benefits from availability of amino acids into safety concerns. The Report notes that an excess of one amino acid (such as lysine) could inhibit functions of another (such as arginine). Report, p. 44. Such an effect is indeed exactly what is sought by consumers who take lysine as a natural means of controlling activity of the herpes virus, which requires arginine for its functioning. While the Task Force may not approve of such approaches, and may not believe that they are effective, this is

not an adequate basis for ignoring potential benefits from such natural therapies; especially since no serious or specific safety concerns with taking lysine have been identified.

Another serious public health benefit ignored by the Task Force is the benefit of N-acetyl cysteine ("NAC") for the enhancing of cell function and immunity in people with AIDS and others. NAC is of potential benefit in raising cellular levels of glutathione in HIV-infected individuals, who have been shown often to suffer from glutathione deficiency. Such a nutrient replacement strategy for avoiding or minimizing the effects of glutathione deficiency is being pursued by many people with AIDS or HIV infection. To deprive such individuals of this potential benefit without so much as considering it, is the height of arrogance and unwisdom.

The Report also makes the extraordinary assertion that there is "no known nutritional use" for amino acids. Report, p. 45. We have already noted at least one such use. In addition, since amino acids are the basic building blocks of life this statement is absurd on its face. Consumption of amino acids clearly does have nutritional use.

The Report also fails to provide any importance to the consumers' right of free choice and access to amino acids. This issue is simply not seriously addressed. The Task Force's assumption appears to be that if consumers are employing amino acids for their physiological or therapeutic effects then they must be prevented from doing so until such time as the FDA has reviewed and approved such uses, regardless of whether any real safety concerns exist. Given the FDA's attitude toward nutritional approaches to therapy, and the absence of financial incentives for companies to make such showings for substances in the public domain, it will be a far-distant time indeed before the FDA approves such uses of amino acids. The effect of the Report would be to deprive consumers of any right to pursue such uses in the meantime.

As with vitamins and minerals, the Report describes supposed safety concerns with amino acids only in vague and general terms and again those are grossly overstated. The Report, for example, quotes the statement that "any products which are believed by competent scientists to carry the risk of significant harm if taken in isolation or in excessive dosages" should be available only as prescription drugs. Report, p. 39. This overbroad description would apply to virtually any dietary supplement, as well as ordinary foods or plain water; to require a prescription in all such cases is an obvious overreaction, and would also amount to a total denial of the policy favoring free choice. Relying on the mere "potential" for adverse effects from excess intake of individual amino acids, the Report follows the same strategy of requiring a guarantee of "safety" before access may be allowed; options such as warnings are again ignored.

With respect to the L-Tryptophan experience, the Report concedes that the instances of eosinophilia-myalgia syndrome ("EMS") may be due to a contaminant in certain products. Report, p. 38. If it is so, then regulations permanently depriving consumers of access to contaminant-free L-Tryptophan are unreasonable. The Report also maintains that L-Tryptophan in itself may have a role in EMS. We note, however, that use of L-Tryptophan is allowed in other contexts, such as infant formulas and total parenteral nutrition, and indeed that L-Tryptophan is conceded to be an essential amino acid, that is, one of the basic building blocks without which life is not possible. We thus suspect that the Report's concern with the potential safety hazards of non-contaminated L-Tryptophan in itself is questionable.

However, even if there are genuine safety concerns with non-contaminated L-Tryptophan, these are insufficient to demonstrate serious safety concerns with all other amino acids. Since the

Report proposes to deny consumer access to all single amino acids in capsule, tablet, liquid, powder or other form, the safety concerns regarding L-Tryptophan are too limited to justify such measures.

In the end, the Report makes amply clear that safety concerns are not the real basis for the proposal to deny all consumer access to amino acids. Rather, the Task Force's perception that these substances are being marketed and used for physiological or therapeutic purposes that render them "drugs" is the real basis driving these proposals. However, this perception rests upon a conception of "drug" that is so overbroad that it would encompass not only drugs and dietary supplements, but ultimately all foods as well. Such an overextended notion of "drug" cannot serve as the basis of a factual record supporting a finding that amino acids may be removed from the market as drugs.

The Report relies on review of "articles published in popular periodicals" that conclude that consumption of amino acids are effective in alleviating various medical conditions. Report, pp. 48-49. Based on such evidence--and the absurd claim that amino acids have no known nutritional use--the Report concludes that amino acids are "being consumed for drug purposes." Report, p. 50. Yet numerous articles in the popular press could be found recommending, for avoidance or amelioration of health problems, consumption of a low-fat or high-fiber diet, or drinking of eight glasses of water daily. By the Task Force's logic, foods low in fat or high in fiber, or water, would also be drugs. While the FDA may believe that it has the legal discretion to deprive consumers of such basic items as food and water, we find this result to be totally absurd.

We note that the Report also relies on use of so called "drug claims" by manufacturers on labels of amino acids. Report, p. 47-48. These claims are presumably to be dealt with by the FDA's proposed labelling regulations. We do not agree with the wisdom of the proposed labelling regulations, and plan to submit comments on those regulations separately. Here we are primarily concerned with the FDA's proposal to deprive consumers of access even to amino acids not labelled with so called "drug claims." If consumers wish to read health-oriented literature, and to purchase and consume dietary supplements which they believe will achieve various benefits for them, then we believe that they should have an absolute right to do so, unless specific safety concerns exist. To label any such substances "drugs" because the objectives sought by consumers are therapeutic in nature is obviously grossly overbroad and would overstep the legal bounds of the FDA's authority.

On behalf of people with AIDS and HIV, and consumers generally, we strongly oppose the Task Force recommendations with respect to amino acids. These proposals are unjustified by specific and genuine safety concerns, contrary to important public health benefits, and in violation of consumer rights to access and choice. They derive from a biased and pre-determined Agency agenda, which is not adequately supported by the analysis contained in the Report or otherwise, and should be withdrawn.

Very truly yours,

Michael Onstott

Michael Onstott

ACT UP SAN FRANCISCO
BOX 14844
SAN FRANCISCO, CA 94114
PH. (415) 292-4055

October 20, 1993

Senator Orrin Hatch
Labor and Human Resources Committee
U.S. Senate
Washington, D.C. 20510

Dear Senator Hatch,

In the battle against AIDS, as in all struggles against life-threatening illnesses, we must pursue a course which includes all potentially viable options for treatment. People with AIDS and other life-threatening illnesses must be consulted, included, and empowered during the process of developing new or individualized therapies. Given the results of the Concorde Study and other research indicating that anti-retrovirals are less efficacious than previously believed (especially with regard to early intervention) alternative options such as anti- oxidants, amino acids, and herbs become even more crucial.

Access to natural, traditional, and alternative treatments is an absolute right which activists, patients, and consumers will not give up. On June 15, 1993, the Food and Drug Administration released the final "Dietary Supplements Task Force Report" which calls for regulating amino acids, herbs, and other supplements in ways that could dangerously restrict access. Although many of the task force's proposals are rational and reasonable, some recommendations will lead motivated PWA's and other consumers to seek products and treatments in the underground market place.

Under FDA proposed guidelines all medicinal herbs could potentially be classified as "unapproved food additives". Further, a recommendation that the agency adopt a "Dietary Supplement Limit" (DSL) could ultimately lead to restrictions on vitamin and mineral potencies which would jeopardize access to optimal nutrient replacement therapies for People with AIDS and drive up costs for all consumers of nutrients. All amino acids are to be regulated as drugs including NAC (N-Acetyl Cysteine) and L-glutathione which are used to raise deficient levels of glutathione for people with AIDS\HIV; thus, FDA policy jeopardizes and increases the costs of nutrient replacement therapies utilizing amino acids. FDA proposals would hand free form amino acids over to the medical pharmaceutical industry and individuals who hold "use patents" on these same nutrients which will then become lucrative sources of excessive profits.

Many FDA employees are recruited from and retire to the pharmaceutical industry and many come from the law enforcement field. Over the years the Agency has developed a negative and combative kind of "drugs and guns" philosophy. In its attempts to "protect" consumers, the Dietary Supplement Task Force considered "what steps are necessary to ensure that the existence of dietary supplements on the market does not act as a disincentive for drug development". The Task Force is blatantly promoting drugs over nutrient and botanical therapies at the expense of the public.

Act Up San Francisco, in coalition with other AIDS, Cancer, and Alzheimer's groups fighting for access to alternative and holistic therapies, opposes all FDA proposals which seek to redefine amino acids, herbs, or other dietary supplements as unapproved drugs or "unapproved food additives" Further, Act Up San Francisco supports the passage of legislation which protects the right of all citizens to choose their own health care. The Dietary Supplement Health and Education

Acts S. 784 (the Hatch bill) and HR 1709 (the Richardson bill) attempt to protect consumer-patient access to anti-oxidants, vitamins, minerals, amino acids, herbs, and other products which FDA has chosen to restrict in ways which can and probably will compromise the health of people with AIDS who seek alternative treatments. We will not give in to bureaucratic or Congressional paternalism in the name of corporate profit or even in the name of "consumer protection". Nutrient and herbal prohibition is no solution. We will continue the fight for the right of all People With AIDS to choose their own treatments.

Sincerely,

Rebecca Hensler
Women's Caucus

Michael Onstott
Alternative Treatments Committee

Jim Lewis
Prison Issues Committee

Paul Fertig
People with Immune System Disorders [PISD] Caucus

ACT UP SAN FRANCISCO
ALTERNATIVE TREATMENT COMMITTEE
584 Castro Street, Suite 135
San Francisco, Ca. 94114
PH. (415) 292-4055

October 20, 1993

Senator Orrin Hatch
And Members of the Labor and Human Resources Committee
U.S. Senate
Washington, D.C.

The following is a statement submitted by ACT UP San Francisco Alternative Treatment Committee. We request that this statement be included in the record of the hearings.

In speaking for the Food and Drug Administration, Commissioner David Kessler says that the Agency does not intend to remove dietary supplements from the market except for reasons of safety. This is the same agency which tried to make an "end run" around the statutory scheme by improperly shifting the burden of proof in the **Food and Drug Administration vs. Traco Labs Inc.** case (Seventh Circuit Court of Appeals, no . 92-1172, the quote is from page 9). The FDA argued that black currant seed oil was an unapproved food additive and therefore presumptively unsafe. It was regarded as an "unapproved food additive " because it was to be enclosed in a gelatin capsule which could be regarded as a "food substance". Given FDA's past actions, it appears likely that the Agency will use "safety concerns" to make an "end run" around the Proxmire Amendment, using the proposed Dietary Supplement Limit. (See page 33694-33695, **Federal Register**, June 18, 1993, for an explanation of the DSL to be used in limiting vitamin potencies). Can we trust this agency to deal properly with "safety concerns" when it so improperly misused the food additive theory?

As an example of FDA's presumable bias against dietary supplements, Commissioner Kessler, in his testimony before the House Subcommittee on Health and the Environment, July 29 (page 20-21) says "...Ingredients that are naturally occurring in conventional foods often are concentrated in supplements, making it

easy to greatly exceed the normal intakes from conventional foods..." and thus raising safety concerns. We tend to forget that such products as butter, lard, and salt fit the description Kessler gives above of "supplements". Butter, lard, sugar and salt are concentrated ingredients which naturally occur in much less concentrated form in conventional foods. In the case of butter and lard, at least, we have an example of concentrated ingredients that are known to be harmful. These are concentrated sources of saturated fatty acids which raise blood cholesterol levels and lead to cardiovascular disease. By Kessler's own logic, these concentrated "food supplements" of saturated fatty acids that are known to be harmful should be removed from the market. They are by implication harmful drugs. A drug is defined as a substance which alters the physiological functioning of the body. Concentrated sources of saturated fatty acids alter the functioning of the liver, causing it to increase production of blood cholesterol. Obviously no one, including the FDA is demanding that butter and lard be removed from the over the counter market. The Agency is proposing to limit choice in the area of dietary supplements but not with regard to concentrated foods. FDA is employing a double standard here.

The contrast between the Federal Government's treatment of the dietary supplement industry and of the tobacco industry is both obvious and outrageous. Dietary supplement products arguably have killed no one, except as the result of contaminants or accidental overdose. Tobacco annually kills over 400,000 consumers. And yet the Federal Government wants to remove dietary supplements from the market because of "safety concerns", whereas tobacco products are rapped on the knuckles with warning labels. Although we are not calling for the removal of tobacco from the market, this situation is intolerably hypocritical and Congress had better resolve it one way or the other. Warning labels allowing "informed choice" are appropriate for tobacco products. They *may* be appropriate for a limited number of dietary supplements which are alleged to be harmful.

The FDA exploits the tragedy of EMS victims in calling for the removal of so-called "unsafe" amino acids. Apart from the FDA, there is significant scientific agreement that EMS is caused by a contaminant or contaminants, and not by pure l-tryptophan. Currently, the FDA allows pure and safe doses of l-tryptophan to be administered intravenously to patients who cannot digest and assimilate certain nutrients. Tryptophan is added to infant formulas and to animal feed. For these uses to be authorized, the FDA must legally have determined that pure l-tryptophan is safe. Even more ironic is the fact that a use patent (# 5,185,157) has been issued for the treatment of EMS with one to three grams of pure l-tryptophan. The FDA seems more concerned with control than with safety. The Agency has formed a partnership with the medical/pharmaceutical industry to exert full control over all health choices.

On the matter of claims, we in the AIDS community are constantly exposed to claims concerning possible treatments for AIDS related conditions. There must be some reliable mechanism whereby plausible claims can be separated from implausible claims. The FDA's "significant scientific agreement" standard does not accomplish this. The FDA has only two categories concerning claims: substantiated and unsubstantiated. We in the AIDS community and all consumers want to know which claims within the "unsubstantiated" category are plausible. After all, every claim is unsubstantiated before it is substantiated. Unsubstantiated

is not the equivalent of "false", and therefore not the equivalent of "snake oil". "Snake oil" had no support in the medical literature of its day. We would like to know which claims, within the category of "unsubstantiated", nevertheless have support in the scientific community. In this way we can begin to distinguish them from claims which are totally unsupported. The FDA's "snake oil" rhetoric is not helpful in this regard. S 784 will allow claims which have scientific support, even though they are not yet sanctified by the FDA. The Agency must not be the sole gatekeeper for health information. The FDA asserts that allowing accurate information concerning scientific support for health claims is too confusing to consumers or too expensive to taxpayers. It is the equivalent of admitting that the FDA cannot afford to be honest about scientific support for claims, presumably because FDA does not respect the intelligence of consumers. Apparently the Agency, in its paternalism, is asserting that honesty is not the best policy. If the FDA believes this, what reason do we have to trust it?

The system of FDA substantiated-unsubstantiated claims is simple and retains absolute Agency control over health information, but it can ultimately lead to the untimely deaths of people with chronic and life-threatening illnesses. Some recent examples are: folic acid and neural tube defects, antioxidants and cancer, fiber and colon cancer.

Sincerely,

Michael Onstott

Michael Onstott
Alternative Treatment Committee
ACT UP San Francisco

STATEMENT OF

JULIAN M. WHITAKER, M.D., PRESIDENT

AMERICAN PREVENTIVE MEDICAL ASSOCIATION

"The functionaries of every government have propensities to command at will the liberty and property of their constituents."

Thomas Jefferson

For functionaries of the FDA, that propensity, has become a mission.

I am Julian M. Whitaker, M.D. I received my undergraduate education at Dartmouth College, I graduated from Emory University Medical School in 1970, had a medical-surgical internship at Grady Memorial Hospital in Atlanta, Georgia, and completed two and one-half years of surgical training at the University of California in San Francisco.

I have not pursued a surgical specialty, and over the last 20 years I have treated close to 20,000 patients with a variety of ailments, using low fat diet, exercise and a wide variety of vitamins, minerals, herbs and other nutritional supplements.

I was a founding member, along with Dr. Linus Pauling, of the California Orthomolecular Medical Society, a founding member of the American Holistic Medical Society, a member of the American College of Advancement in Medicine, a previous board member of the American College of Advancement in Medicine and a founding member and current president of the American Preventive Medical Association.

I have written three books, *Reversing Heart Disease* and *Reversing Diabetes*, published by Warner Books, and *Reversing Health Risks*, publishing by Putnam, outlining dietary, exercise and nutritional supplement regimens that are helpful for both heart disease and diabetes and for preventing major degenerative diseases.

I am the writer and editor of Health and Healing, a newsletter that currently has 475,00 paid subscribers. The subject matter includes diet, exercise and the reasonable and rational use of supplements to enhance health.

I appreciate the opportunity to comment at these hearings. However, it is difficult for me to articulate in a rational manner. I feel as if I've been asked to debate nonsense. The recent actions and positions of the FDA are so obviously contrary to the public good that "debating" the "issues" is decidedly unpleasant.

First, how can a federal agency be trusted if it's leaders openly lie to the American people?

On a nationally broadcast "Larry King Live" television show in July of 1992, Mary Pendergras, senior advisor to FDA commissioner David Kessler, responded to a caller who asked, "How many people are on record of having died from either vitamins or minerals?"

She stated, "I couldn't tell you the total number of people who have died from vitamin and mineral overdoses, but it certainly happens every year. For the records, we had from poison control agencies in 1988, 16,000 people with overdoses of lead. Six of them died. Vitamin A kills a dozen or so people every year - overdoses. At overdoses it's a toxic drug - a toxic product."

Lead is hardly part of a vitamin and mineral supplements. Secondly, there have been no deaths recorded from vitamin A.

Neither Ms. Pendergras nor the FDA have made any effort to correct this obvious misstatement of the fact.

On the same show, when discussing the FDA's guns drawn raid of Dr. Jonathan Wright's clinic in Kent, Washington, Ms. Pendergras stated, "He was also selling and dispensing to his patients injectable drugs which could also kill you. When we tried to find out what was going on at Dr. Wright's clinic and in this clandestine manufacturing facility, Dr. Wright would not let us in. So when we followed up on these moldy injectables, we learned they were being made in a room in part of Dr. Wright's clinic.

1. As Dr. Wright clearly pointed out, the FDA never tried to contact him or his lawyer with any questions regarding any of his activities before his offices were raided.

2. In the affidavit and search warrant signed by Seattle judge John Weinberg, no drugs of any kind were mentioned. There was no mention of any "clandestine manufacturing operation" or "manufacturing room" in the offices of Dr. Jonathan Wright.

3. The moldy injectable that Ms. Pendergras referred to was not a drug but an injectable form of magnesium. It was not mentioned in the affidavit, nor was it obtained during the raid. It was found by FDA agents six months before the raid in a trash bin used by Dr. Wright's clinic and also by a pharmacy. The FDA has no idea where it came from or even when it "got moldy."

In October 1993, Michael Taylor, also on the "Larry King Live" show stated that prior to the raid on Dr. Wright, "The FDA had clear evidence that Dr. Wright was manufacturing illegal drugs in his facility." Again, this statement is contrary to the affidavit and search warrant signed justifying the raid, and it is contrary to what has transpired since the raid.

18 months following the raid, Dr. Wright has not been charged with any crime. This would hardly be the case if, indeed, there was "clear evidence" of illegal drug manufacturing.

Prior to the guns drawn raid of his offices, Dr. Wright had been in medical practice for over 20 years. He had treated tens of thousands of patients from all over the world and was and still is highly respected as a competent and responsible physician specializing in nutritional therapy. There had been no complaints of any impropriety on Dr. Wright's part to any government or regulatory agency during this entire time.

It is inexplicable that the FDA would choose to use the forced entry, guns drawn tactic. They knew that the facility was a medical office of unarmed health professionals. The affidavit contained the written statement of FDA agent Victor Meo. Using an alias, agent Meo had been treated in the

clinic on two occasions as a patient. He clearly describes the facility as a medical office where unarmed and licensed health care professional quietly and efficiently dispense health care.

That a productive professional member of our society would be treated in this manner by a government agency is one thing. That that individual would then be publicly, dishonestly vilified by the leaders of that agency is reprehensible beyond words.

The FDA is also being dishonest about L-tryptophan. L-tryptophan is an essential amino acid and a precursor to the neuro transmitter seratonin. Taken alone it can have beneficial effects on mood, anxiety, pain and sleep. From the mid-1960s until 1989, millions of Americans took L-tryptophan and experienced no negative side effects at all.

In 1989 some consumers of L-tryptophan imported from Japan experienced a serious inflammatory reaction. It was quickly determined to be caused by a contaminant from a single manufacturer, Showa Denko, who had changed its manufacturing processes without safeguards. In both the New England Journal of Medicine as well as the American Medical Association Journal, it was stated clearly that the cause of EMS (eosinophilia myalgia syndrome) was this contaminant in the L-tryptophan produced by Showa Denko. Later, in a certified letter from the FDA dated February 20, 1991, the FDA wrote, "CDC concludes and FDA agrees, based on the recent study and the previously reported studies, that it appears that virtually all EMS patient associated L-tryptophan was produced by Showa Denko K.K. Further evidence from recently published animal studies suggested that L-tryptophan from Showa Denko K.K. resulted in specific pathologic changes characteristic of EMS."

The continual band on L-tryptophan is an obvious fraud. It covers only capsules or tablets of the substance. The same L-tryptophan that should be available in capsules is freely added to baby foods, tube feeding and pet products. To justify this ban on L-tryptophan, David Kessler, under oath, told Congress in July of 1993 that "despite recent intense research, the exact cause of EMS and our understanding of how it develops has not been established." This is a direct contradiction of published studies and FDA published and written comments, and it was presented to Congress without one shred of significant or legitimate evidence.

In addition, it has been shown that uncontaminated L-tryptophan would have therapeutic benefit on patients currently suffering from EMS.

Yet uncontaminated L-tryptophan is still banned which eliminates a useful therapy for EMS patients.

The ban on L-tryptophan has nothing to do with public safety. It is testimony to the dishonesty and arrogance of the FDA and its entrenched bias against all nutritional supplements.

In its "Dietary Supplement Task Force" report, as well as its proposed rules published in the Federal Registry in June 1993, the FDA writes that "The agency should insure that the existence of dietary supplements on the market does not act as a disincentive for drug development." Consequently, if a nutritional supplement competes with a drug, the FDA arbitrarily disallows dissemination of information about the supplement and often tries to take it from the market, even if the supplement is superior to its drug competition.

For example, the extract of saw palmetto berries has been shown by scientific studies to be about three time more effective than the Merck drug, Proscar, for alleviating symptoms of prostate enlargement, such as poor urinary stream, urinary retention and nighttime urination. In addition, the extract has no toxicity, whereas Proscar causes impotence, ejaculation dysfunction and decreased libido, and it is so toxic for women of childbearing age that they are told not to have contact with the semen of men on the drug or even handle the drug. Proscar can cause birth defects in male children.

The FDA clearly knew that the extract of saw palmetto berries was safer and more effective than Proscar and stated so in the Federal Register. Nonetheless, it refused to allow a truthful health claim for the herb and recommended that it be taken off the market. The FDA shortly thereafter gave the green light for Merck to market Proscar, and as a result, 10 million men have been robbed of a safer, more effective therapy.

Last spring, two studies in the New England Journal of Medicine reported up to a 40% reduction in the risk of heart disease for users of vitamin E. If everyone took 100 to 400 units of this inexpensive, completely safe supplement, there would be a 23% reduction in the nation's heart disease rate and a savings of $25.1 billion in health care costs. There are numerous drugs on the market aimed at lowering the risk of heart disease by reducing the LDL cholesterol fraction. These drugs have a definitive toxicity ban and with wide usage will damage tens of thousands, if not millions, of people.

Yet not in the wildest dreams of any statistician could the so-called

benefits of these drugs even come close to the published benefits of supplemental vitamin E. Yet the FDA won't allow any health claim on any bottle of vitamin E, even though out health care costs are out of control.

There are numerous examples of this tyranny disguised as public service, but the best example is the FDA's "regulatory approach" to Coenzme Q10 (CoQ10).

Co Q10 was first isolated from beef heart in 1957 by Professor Fred Crane at the University of Wisconsin. In 1958 Professor Karl Folkers, a PhD biochemist at Merck, Sharpe and Dohme, defined the formula and shortly after that discovered how to synthesize Co-Enzyme Q-10. Merc could not patent this remarkable substance, and thus had no interest in it. They sold the technology on how to make CoQ10 to Japan, who currently, makes all the CoQ10 used worldwide..

In spite of Merc's disinterest, Dr. Folkers knew that, like insulin or antibiotics, he was working with a bonafide medical breakthrough, a substance that could enhance that energy production throughout the body and thus could prevent and alleviate suffering of many diseases. He was sure that Co Q10 would open up an a new medical specialty, the study of bioenergetics.

Dr. Folkers left Merck in the late sixties to study ÇoQ10 full time and in 1970 the FDA granted him an Investigational New Drug License (IND#7013) authorizing him to conduct human studies with CoQ10.

With research funds coming exclusively from Japan, Karl Folkers authored, co-authored or helped with of over 1,000 scientific articles by over 200 collaborating scientists world wide Most of the work was done under the authority of the IND issued to him by the FDA. These studies all showed the same thing:

In both subtle and dramatic ways, it would improve the health of almost all who took it and save millions of lives. Also, it had no toxicity.

CoQ10 was a specific and highly beneficial therapy, for congestive heart failure. It is to congestive heart failure what antibiotics are to bacterial infections. All that is needed is to take enough of the supplement to elevate the blood levels.

Dr. Folkers and researchers from all over the world have organized 7 international scientific conferences on CoQ10 with the 8th scheduled for this November, in Stockholm, Sweden. Over the last two decades, between 30 and 40 million people mostly in Japan and Europe, have been studied

and/or treated with CoQ10 with excellent results and no reports of any toxicity.

After 30 years of working with the nutrient, Dr. Folkers felt that he and others had produced more than enough data to support a label on Co Q10 as a safe and beneficial treatment for heart ailments. So in August of 1991, with suitcases of published material, he and cardiologists Per Langsjoen, M.D. traveled to Washington to meet with the FDA.

They were not prepared for what happened. Essentially, the FDA stated that none of the research produced under Dr. Folkers IND or any of the extensive world literature "was relevant." To the FDA, it didn't exist. If Folkers and Langsjoen wanted a new classification and labeling for CoQ10, they would have to produce "additional" research costing between $50 and 100 million taking another decade to complete.

In addition, as Dr. Folkers related to me, the FDA told him that he would have a better chance getting a label on this substance if he returned as a representative of a drug company. Since CoQ10 cannot be patented, stimulating the interest of a pharmaceutical firm is next to impossible.

It has been two years since that visit, and Dr. Folkers is still hoping to open the eyes of the FDA. However, the FDA had other plans for Co Q10.

Having just been presented data showing that the CoQ10 was incredibly safe, used by millions of people, including 25% of the country of Denmark, and that it was necessary for survival for many patients taking it for congestive heart failure, the FDA decided to move against the supplement. They classified CoQ10 as "actionable" and "as unsafe, an adulterant, and illegal in this country," and that "to the FDA;s knowledge, CoEnzyme Q10 is not generally recognized as safe and effective for treating disease."

On February 11, 1992 under FDA directions, the Texas Department of Health invaded health food stores and swept from the shelves 51 separate items, including bottles of Co-Enzyme Q10.

Betty Dwyer had been diagnosed with cardiomyopathy in 1981 and was near death in 1983 before Per Langsjoen, M. D., started her on Co Q10. Today 10 years later, her heart is virtually normal and she has been off all medication except Co Q10 for 6 years She states thta "she does not appreciate the FDA or Texas Department of Health trying to kill her in order to protect her from CO Q10."

Tom Miller from Tyler, Texas another heart patient dependent on CoQ10 refers to the FDA as the 'phantom board,' and stated that "as far as I can tell, what they were going to do was kill a bunch of people and ruin a good doctor's practice, and that makes me mad as the devil."

Patricia Sharp, reporting on the episode for the Texas Monthly noted that "everyone was furious that their lives seemed to count for nothing in the machinations of a bureaucracy they could neither comprehend nor affect."

The magnitude of the public reaction caught the Texas bureaucratize off guard and Co Q10 was returned to the shelves. They stated, however, that it was only temporary and that Co Q10 was still "actionable" as outlined by documents suppled to them by the FDA.

The FDA is relentless in its persecution of the nutritional supplement industry. In July,1993, FDA commissioner David Kessler, under oath, presented to Congress, a document entitled *Unsubstantiated Claims and Documented Health Hazards in the Dietary Supplement Marketplace.* It contains 500 unsubstantiated claims for nutritional supplements.

This document is an disgrace to human civilization. It reads like a dark ages manifesto on heresy. It simply listed a nutritional supplement, the company, and the "unsubstantiated" claim. The FDA disallows all positive claims for a nutritional supplement, yet it never supports its opinions with scientific references. It cites no science at all. It simply "decrees" the claim unsubstantiated.

Kessler attacked Co Q10 eight times decreeing all health claims for the nutrient "unsubstantiated." Even though it was not a supplement manufacturer, David Kessler cited a book, "The Miracle Nutrient CoEnzyme Q10" by Emile G. Bliznakov, M.D., as an unsubstantiated claim for a Co Q10.

Dr. Bliznakov cited 165 scientific references to substantiate the comments made, many of them published by Karl Folkers under authority of the IND issued by the FDA to Karl Folkers.

Under oath, David Kessler assures congress that the book and all of its references are a fraud.

The FDA, in order to move against nutritional supplements that do not make a drug claim, often classifies them as "unsafe food additives." The theory is that the nutritional supplement is a "food additive" to the gelatin

capsule which is a food.

In two court cases the FDA lost in its argument that nutritional supplements were food additives. In fact, the FDA was strongly rebuked by the judges. Some of the published rebukes were:

"Contrary to the intent of Congress...."

"If marketed in bottles for teaspoon consumption, it would not be a food additive..."

"Unwarranted since its interpretation is contrary to the language and intent of the Act."

"Such an interpretation would defy logic and common sense."

"Distorts the plain meaning of the provision."

"It is clear that congress intended to distinguish food additives from food in the generic sense."

"Because the FDA has not shown that BCO is adulterated or unsafe in any way, there is no basis to condemn the two drums at issue."

"The only justification for this Alice in Wonderland approach is to allow the FDA to make an end run around the statutory scheme and shift to the processors, the burden of proving the safety of a substance in all circumstances."

"How a product is marketed is not a rational way of determining whether a substance is a food additive...."

"In fact, the rule enunciated today is supported by every court that has addressed the precise question involved here."

"Enabling persons to weigh for themselves the benefits and risks of consuming BCO."

"Accordingly, the FDA erred in seizing the bottles on the ground that they allegedly contained an unsafe food additive."

"Unable at the present time to translate the suspicion into legally competent proof."

"As the FDA would have it, any element of any substance that has more than one component may be branded a food additive...."

"The FDA's broad definition...subverts congressional purpose."

"We are reluctant to believe that congress traffics in absurdities. Since it defies common sense to say that a substance can be a food additive when there is no (other) food to which it is added, we think the FDA's reading of the Act is nonsensical, and, hence, must be incorrect."

"But this harangue misses the mark."

"What differentiates this case is that, if the BCO is removed, one is left with nothing but an empty capsule."

"The simple fact that the agency has a position, in and of itself, is of only marginal significance."

"In the words of Sir Francis Bacon, the FDA's suggested 'remedy is worse than the disease'."

"We need go no further. The proposition that placing a single ingredient food product into an inert capsule as a convenient method of ingestion converts the food into a food additive perverts the statutory text undermines legislative intent, and defenestrates common sense. We cannot accept such anfractuous reasoning."

Even after these decisions, the FDA still confiscates nutritional supplements as unsafe food additives. In the proposed rules published on June 18, 1993, the FDA wrote that BCO, Evening Primrose Oil and other nutritional supplements "are subject to the food additive provisions of the act (sections 201(s) and 409 of the act)." And for a whole wrath of nutritional supplements also including BCO and Evening Primrose Oil, the FDA writes: "The Task Force recommended that the agency find an effective means of ensuring safe use of this "other" category of ingredients. Among the possible options suggested by the Task Force were to continue regulating these ingredients as food additives...."

Is it a reasonable allocation of government resources to fund a city of lawyers to argue FDA reasoning before federal judges that deem them Alice in Wonderland schemes? And what about the American citizens who are forced to spend their own money defending themselves from a hostile, irrational agency?

Finally: nutritional supplements are not drugs, are not food additives, and are not food.

People use nutritional supplements to enhance their health in the same manner that they use food selection and exercise.

The nutritional supplement industry has the best safety tract record of any industry in the free world. Adverse reactions to prescription drugs kill about 140,000 to 160,000 people a year and harm close to 10,000,000. With this degree of public safety concern, it is ludicrous for the FDA to be spending so much time "looking" for "potential" toxicity of nutritional supplements. SB 784 provides for reasonable protection of the society from potential harm of nutritional supplements.

With respect to labeling and claims, it is high time for a different system. The FDA has proven themselves incapable of acting in the public interest when it comes to arbitrating what constitutes truthful claims, and what should be allowed.

The premise that the FDA and its supporters expouse is that if it is not approved, it is not legal. This is the standard premis of all tyranny and is contrary to the Bill of Rights. It is time for a change.

SB 784 is an appropriate and overdue step to right some of the wrongs that continue to exude from the FDA.

It is my hope that the members of this committee will see the obvious and vote for passage of this badly needed legislation.

Sincerely,

Julian M. Whitaker, M. D.

STATEMENTS REGARDING AMINO ACIDS
for
SENATOR WOFFORD and/or OTHER LEGISLATORS

1. Amino acid supplements *have never killed anyone*, have many positive nutritive values, and can be compared to *aspirin's upward of 600 deaths per year.*

2. FDA's whole case against amino acids goes back to the 1988-89 contaminated batches of L-tryptophan from Showa Denko KK.

3. FDA has had a 30-year vendetta against the food supplement industry, for no good reason beyond its unreasonable drive for control.

4. A seriously flawed animal study of pure and Showa Denko-contaminated L-tryptophan in rats is FDA's main weapon in its fight to gain control of amino acids in specific, and by implication therefrom of all food supplements.

5. The *real* issues are bureaucratic control *vs* American freedom of choice -- which freedom of choice can vastly improve the health of this nation *and* vastly decrease national health costs, *if it is not taken from us.*

6. If FDA will but abandon its illogical stand that amino acids are *not* foods and admit that they *are* foods, then FDA has all of the authority it needs to ensure purity and safety.

FDA already has all of the powers it needs to enforce standards of purity and labeling in the $37 billion food supplement industry, but it is not using them properly. No additional powers are needed nor should they be granted to the FDA.

WHAT EFFECT DOES THE AVAILABILITY OF OVER-THE-COUNTER AMINO ACIDS AND OTHER NUTRIENTS HAVE ON PUBLIC HEALTH?

Introducing his bill "DIETARY SUPPLEMENT HEALTH AND EDUCATION ACT OF 1993" on April 7, 1993, Senator Hatch made the following statements:

> "In the United States, more than a hundred million Americans purchase and use, either regularly or occasionally, vitamins, minerals, herbs, amino acids, and other nutritional substances to supplement their diet and improve health... Many Americans understand that dietary supplements can help promote health and prevent certain diseases, a fact substantiated by an ever-growing body of scientific studies and other evidence. They understand that at a time when America spends over $2 billion a day on health care, prevention is the best and most effective form of cost control."

WHAT EFFECT DOES THE AVAILABILITY OF OVER-THE-COUNTER AMINO ACIDS AND OTHER NUTRIENTS HAVE ON PUBLIC HEALTH?

Left to its own devices, the American public is smart enough to take steps, with or without direct, individual medical advice, that can have a profound effect on public health. The most outstanding example that supports this view is the steady decrease in deaths from cardiovascular disease that has occurred since the 1950s. In the past three decades, there has been a decrease in annual death rates from heart attack, stroke, and aneurysms by about 35%. This figure is conservative, based on 1990 figures, and may now be over 40%. Surely, medical science can take credit for a portion of this largess, with new, more effective medications and better techniques for diagnosis and treatment (e.g. coronary angiograms and angioplasty). But epidemiological experts have noted that the decrease is much greater than can be accounted for by these factors, even when reduced smoking among adults is factored in. This has caused them to ask collectively, "What is happening?"

One thing that has been happening for sure is that the American public has become aware of the possibility that their diets are probably not well balanced and key nutrients might be in short supply. One easy way to insure against nutritional deficiencies might be to supplement their diets with a few cheap, simple, safe substances that can be taken daily to assure that enough of most vitamins and nutrients are consumed. The most commonly consumed extra nutrients are Vitamin C, Vitamin E, calcium, and recently Vitamin A. It would seem to be more than coincidental that the increase in consumption of these substances has been paralleled by the percent decrease in deaths from cardiovascular disease. The three vitamins happen to be antioxidants, and increasingly, studies in humans and animals are finding that antioxidants are protective against cardiovascular disease, some forms of cancer, and other diseases. This was explained in plain language in the June 7, 1993 issue of Newsweek. Under the headline "Vitamin Revolution" the sub-head states: "The good news: nutrients from food or supplements help us prevent heart disease, cancer, and other chronic ailments."

In regard to the amino acids, the literature is replete with well-done studies that show unequivocally the benefits to human well-being of the judicious use of amino acid supplements. There same studies have demonstrated the very high degree of safety of these simple substances when consumed in greater-than-normal amounts by humans. It would therefore be tragic indeed to unreasonably restrict their availability by classifying them as prescription drugs. That action would deprive the public of a valuable natural resource, would increase the burden on the health care system, and add enormously to the cost of maintaining public health. Because of the FDA requirements regarding New Drug Applications (NDAs), no amino acids in any form would be available for many years, while each of the 20 or

more amino acids is carried through all of the stages of testing and approval. The added burden on the FDA would be truly staggering, to say nothing of the added costs to the manufacturers* of testing along with years of delay. And the end product would be prescription drugs, which would then cost between 100 and 1,000 times the present costs of the current o.t.c. preparations. If and when amino acids actually made it through this whole process, they would still be virtually unavailable to the public.

It is seen therefore that FDA's demand to regulate amino acids as drugs is inappropriate and totally unjustified by the facts.

* Hugely added costs, because the FDA is now empowered to charge "user fees" to the manufacturers to pay the FDA to review their NDA submissions! This alone could drive nearly all of the amino acid manufacturers out of business.

Questions and Answers Regarding Amino Acids. An Information Resource.

In the interest of providing general information about amino acids, how they relate to daily life, and what the interests of Congress, the FDA, and the general public may be in regard to them, the following group of Most Frequently Asked Questions and their Answers is provided.

Q What are amino acids?
A Amino acids are simple chemical compounds made of carbon, hydrogen, nitrogen, oxygen, and sometimes sulfur.

Q What do they do for us?
A They are the basic building blocks of protein. We eat animal or vegetable protein, and our digestive system breaks it down into a mixture of amino acids. The amino acids are then absorbed into our bloodstream, where they are used in the construction of structural and functional components of all living cells; to build new proteins for our body tissues, and important metabolic products like insulin and thyroid hormones, while others are stored for future use or used directly as fuel to operate our muscles and brains.

Q Where do they come from?
A All amino acids in proteins are made by natural processes. All plants make protein. Animals eat the plants and, by digestion and absorption, rearrange the amino acids into new proteins. People get amino acids from both animal and/or vegetable proteins by eating meat and/or vegetables.

Q How much weight of amino acids does a person eat every day?
A A well-nourished adult eats a little over three ounces, or about 100 grams of protein every day. It is digested into about 100 grams of the mixture of amino acids that made up the protein.

Q Since there are about twenty-one different amino acids in a typical protein, how much of each are we getting each day? That is, what sort of a range of intake are we talking about ?
A The scarcest amino acid in protein is called tryptophan. We get about one gram (1/30 of an ounce) of it per day. The most abundant one is called glutamine, a close relative of the familiar MSG, Monosodium Glutamate (a flavor enhancer), and we get nearly 1/3 of an ounce (10 grams) of it. The amounts of the others fall in between these extremes.

Q Compared to the amounts we already get in food, how much can the body handle safely?
A The human (or any other mammal) body is very flexible. It possesses the machinery to deal with up to at least thirty times the normal intake of many of the amino acids, on a short-term basis, so utilizing something like two to ten times the usual intake of most of them poses no problem.

Q What happens if you get too much of any particular amino acid by ingesting the pure amino acid?
A Most often, you will get an upset stomach. In extreme cases, it can progress to nausea, vomiting, or diarrhea. This will only happen if a very large dose — on the order of 1/3 to about 2 ounces — is swallowed all at once, on an empty stomach. This is actually a safety feature, since the body will purge a truly excessive quantity before any harm can be done. With smaller doses, the amino acids will be absorbed into the blood stream and processed for building materials or fuel, just as if the person had eaten an equal amount of protein.

Technically, the intestine has a limited capacity to absorb amino acids, and can only absorb a certain amount of any particular amino acid at any one time; and the specific limit is different for each amino acid. The capacity is several times the normal daily intake of each amino acid. When the ingested excess is very large, it can cause a stomach ache or upset, nausea, and vomiting, just like eating too much of any one food can do.

Q Has anyone ever died from taking too much of any amino acid?
A In all of the known literature on amino acids, *there is no known case where a normal person has been injured or died as a result of taking a large oral dose of an amino acid.*

Q Are some people likely to become allergic to some amino acids?
A The following statement appears on page 211 of the LSRO/FASEB Report "Safety of Amino Acids Used as Dietary Supplements":

> "There are clinical reports of idiosyncratic and adverse reactions to amino acids; however, there are no data to suggest that these have an immunologic origin. Based on the [small] molecular size of the amino acids and their ubiquity in intermediary metabolism, there is little scientific rationale to predict that hypersensitivity would be expected." In plain terms, they are saying that amino acids are so small and, since they are already everywhere in our bodies, it is practically impossible for them to cause allergy.

Q How can you really say what is a safe dose or a safe daily intake?
A It isn't possible to say how <u>high</u> a dose of any amino acid would be tolerated safely. The reason is that the amino acids are so very benign that no one has yet looked for a <u>maximum</u> safe dose. After all, we have been eating amino acids since the beginning of time and our bodies have evolved all the necessary mechanisms and enzymes to handle them. That is why the LSRO/FASEB Report "Safety of Amino Acids Used as Dietary Supplements" correctly concluded that they could not recommend any maximum safe doses. Such data do not exist because it is exceedingly difficult to ingest an unsafe dose.

It is quite a different matter to decide from all of the published studies on each amino acid what daily dose in excess of the normal daily intake, would be entirely safe for any person not suffering from some particular illness such as PKU syndrome or cirrhosis of the liver. For each amino acid there is ample dosing data from studies done in people for various reasons, which show the amounts which can be taken without any problems, even on repeated long-term dosing. Depending on the particular data for any amino acid, it is then possible to judge what dose can be depended upon to cause no problem for anyone. That turns out to be

supplemental levels of from about 1.5 times the normal daily intake for some amino acids to as much as about ten times the daily intake for others.

Q What is an LD_{50} and how does it apply to amino acids?

A The LD_{50} is defined as the amount of any particular substance, that when introduced (by ingestion or injection, e.g.) into an animal will cause 50% of the test population to die. It is determined for any substance by giving increasing doses of the material to groups of test animals such as mice, rats, rabbits, guinea pigs, hamsters, gerbils, etc., until the animals begin to die. The Lethal Dose (LD) that causes half of a group of animals to die is called the LD_{50}. It is a test that the FDA requires for any new prescription drug, in order to give an idea of what a toxic dose in a human might be, compared to the dose that will be used to treat an illness or condition. If a certain compound has an LD_{50} of 10 milligrams and is effective at 1 milligram, it is said to have a therapeutic ratio or safety factor of 10. Many prescription drugs have a therapeutic ratio in the range of 2 to 50. The LD_{50} values for amino acids, except tryptophan and tyrosine, have not been determined, because they are so innocuous that it is virtually impossible to find toxic doses! Tryptophan has an LD_{50} of 1.6 grams per kilogram in rats, equal to a 112 gram dose (4 ounces — a whopping amount) to an adult human. This value is only extrapolated from the rat to the human; it does not mean that such an amount was actually given to a human in any study! Tyrosine has an LD_{50} of 1.4 g/kg in rats, or about 98 grams (3.5 ounces) in an adult human. Other than the one report for tyrosine, the Expert Panel that wrote the LSRO/FASEB Report "Safety of Amino Acids Used as Dietary Supplements" found no information on LD_{50}s of amino acids, nor are we aware of any others that they did not find.

Q We keep hearing that some special groups of people shouldn't take supplements of some particular amino acid. If that is really true, why shouldn't the FDA put all amino acids on prescription? And who decides what the special groups are for any particular amino acid?

A It is true that there are special groups of people who should not be taking large amounts of amino acid supplements, but the affected people will all be under a doctor's care because they could not live normal lives otherwise. It will be clear from the following brief list that the affected persons will be advised by their physicians what they should avoid, just as a person with food allergies is advised by an allergist (or by experience) what foods and/or drugs to avoid.

- Schizophrenics, people with homocysteinuria (an inborn error of metabolism), alcoholics, and persons with cirrhosis of the liver or impaired liver function should avoid the sulfur-bearing amino acids: methionine, cysteine, and cystine.

- People, especially children, with phenylketonuria or PKU disease (an inborn error of metabolism) should avoid phenylalanine. That is why soft drinks and other foods that contain aspartame™ carry a warning that the foods contain phenylalanine. But aspartame™ is not banned just because a small segment of the population is at risk if they ingest it.

- It is recommended that women with breast cancer should not take supplemental arginine, because a single study found that an arginine supplement given for three days before breast surgery apparently stimulated protein synthesis by the tumors. Ordinarily, a single unconfirmed study of this sort would only be taken as an alert to a possible problem, but a prudent approach requires that such women not take arginine, until more is known about this unusual, and very recent, finding.

• The LSRO/FASEB Report suggests that infants, children, adolescents, and pregnant women should not take extra aspartic or glutamic acid; this recommendation, however, is not based on any actual findings of problems in people.

So the answer to the question "... why shouldn't the FDA put all amino acids on prescription?" is pretty clear:

1. Very small, well defined groups of people need to be cautious about *some* amino acids.
2. Those people know who they are and what to avoid because they are receiving medical advice; and
3. By its approval of the wide use of aspartame™ and appropriate labeling, the FDA has already recognized that small at-risk groups of people can be adequately protected by appropriate warnings.

"And who decides what the special groups are for any particular amino acid? "

Once the biochemical problem is medically identified, the affected people generally become knowledgeable about what it is they must avoid.

Q If it is eventually agreed that FDA should not regulate amino acids as drugs, what controls do we or should we have over what is sold to the public?
A The public has a right to expect that whatever is offered as a dietary supplement should be truthfully labeled as to its contents' identity and purity, and directions for usual and prudent use. Production lot identity and shelf life should be given in plain language. Unsubstantiated or poorly supported claims for a particular biological action should not be permitted. In addition, cautionary statements to the special groups of people who should not take the particular amino acid supplement should be printed on the label in much the same way that products with Nutrasweet™ advise PKU people against their use. These are reasonable requirements, to which no reputable manufacturer could object. Such enforcement would seem to be a proper function of the FDA.

Q How are amino acids taken as nutritional supplements?
A They are usually taken as tablets or capsules containing one or more amino acids, sometimes in combination with vitamins and minerals. Some are also available as bulk powders that the users stir into water and drink. They may be taken before, during, after, or between meals, but are not customarily added to ordinary foods.

Q Are amino acids foods?
A Amino acids, biochemically, are THE protein-derived compounds which are essential to life. All foods are just the packages in which the essential nutrients — in this case, amino acids, are "wrapped". Since foods are digested and the protein is broken down to amino acids which then go on to perform their required functions, it would seem logical to categorize amino acids as foods. Since amino acids are absolutely essential — and they come from the foods we eat — how can we not call them foods?

Hospitals recognize amino acids as foods for people who must be fed intravenously. A full range of amino acids is added to the intravenous fluids to replace the amino acids that would ordinarily come from food that the person would normally eat. They are not administered for any medicinal purpose; amino acids are used to provide balanced nutrition when food cannot be eaten. Therefore there should be no question about their status: amino acids <u>are</u> foods.

Q How are amino acids different from drugs?
A Nearly all modern drugs are synthetic organic chemical compounds. They have very complex chemical structures that are totally unknown to the human system and are therefore foreign substances. That is why they are all toxic at some dose. They have been, and are being, developed as ways to correct or cure health problems, often very successfully (e.g. antibiotics for serious infections), but they all possess toxicity which must be judiciously balanced against their benefits. Formally, they are said to produce Side Effects (SE) and Adverse Experiences (AE) — in addition to performing valuable functions. Some drugs are natural products, which means that they are made by plants or microorganisms, like digitalis or penicillin G, but still, these drugs are certainly not "natural" to the human system. They possess the same liabilities as the synthetic drugs.

Amino acids are entirely different. They are completely natural substances which are thoroughly recognized and used by the human body. Because they are and must be present at all times to maintain health, they are virtually devoid of SE and AE, even when ingested at many multiples of the normal daily intake.

Q Are amino acid supplements added to foods?
A Except for special circumstances, such as the supplementation of specific amino acids to amino acid-deficient foods in the developing countries of the world, we are not aware of any manufactured foods (in the United States) to which free amino acids are added. Only MSG is deliberately added to foods, and that use is already thoroughly covered by FDA actions and policies. The negative gustatory aspects of most of the other free amino acids, except for the BCAA (branched chain amino acids) which are exceptionally benign and mildly sweet, would mitigate against their addition to foods during preparation at home or elsewhere.

Q Can or should we think of amino acids as drugs?
A No! An amino acid used to alleviate a deficiency is no more of a drug than is Vitamin C a drug because it happens to cure scurvy. Whether the Vitamin C comes from drinking lime juice or taking a tablet is totally irrelevant to the outcome of the treatment. In this case, Vitamin C corrects an imbalance due to its lack, but that does not make it a drug. Vitamin C is a vital nutrient. A deficiency of it causes scurvy. A Vitamin C supplement ends, or "cures" the scurvy. Similarly, a dietary shortage of tryptophan is well known [literally hundreds of papers have been published] to lead to depression, insomnia, and even chronic, intractable pain. Simply replacing the missing tryptophan relieves these conditions, but that does not make it a drug any more than replacing the missing Vitamin C made it a drug. Supplementation has merely replaced a natural material, tryptophan, which was in short supply in the individual.

AMINO ACIDS - THE IND-NDA ROUTE TO APPROVAL AS DRUGS

The FDA has indicated its intent to consider all amino acids (AAs) to be drugs (Fed Reg/ Vol 58, No. 116/ Friday, June 18 1993, p. 33697) and require that they go through the same clearance and approval procedure as any other prescription drug. An understanding of the required testing procedures alone, quite aside from the lengthy and expensive review process for each NDA submitted to FDA, will demonstrate the impracticability of such a regulation.

Toxicity Testing of Candidate Prescription Drugs

Since all such candidates have toxicity because all are not natural components of our body or diet, they must be put through animal toxicology studies[1], and human Phase I, II, and III clinical studies to demonstrate that the benefits clearly outweigh the risks. Phase I simply investigates the range of doses that are expected to be used in Phases II and III, to see that they are tolerated without unacceptable Side Effects (SE) or Adverse Experiences (AE). In Phases II and III human clinical

studies the actual range of doses necessary to treat the target illness or condition is identified, and patients are carefully observed for the occurrence of SE or AE, as well as the desired efficacy. Once the dose is known, then the dose that produces similar effects in animals can be compared with that species' LD_{50} to arrive at a Therapeutic Ratio, or T.R., where T.R. equals the toxic dose, mg/kg, divided by the effective dose, mg/kg. T.R.s for marketed drugs are usually in the range of 10 to 50, but are sometimes as low as 2! In other words, twice the [1] effective dose of some drugs is toxic!

Toxicity Testing on Amino Acids

The situation with AAs, compared to prescription drug candidates, is entirely different.

Since AAs are normal (in fact obligate) components of our diets and of our bodies, then under any conceivable conditions of oral ingestion of them, it is extremely difficult to produce or demonstrate any toxic effect. Indeed, the usual toxic effects of synthetic drugs, such as poisoning of the nervous system (causing convulsions and death) or of the cardiovascular system (e.g., causing heart failure or arterial inflammation and blockage) or causing various types of tumors, CANNOT be produced at all by oral doses of any AA.

As the result of the inability to demonstrate toxicity of AAs by oral dosing of laboratory animals, it will be nearly impossible to suggest doses of the individual AAs that should be investigated in human Phase I, II, and III clinical trials. Based upon animal data, the Phase I safety study doses would be enormous - of the order of 10 to 50 grams as single doses - with two principal consequences:

[1] Acute dosing, to calculate the LD_{50}; chronic dosing at fractions of the LD_{50} for 4 weeks to 1 year in 2 species; and carcinogenicity testing for up to 2 years, usually in 2 species. 29

(1) No IRB would allow such studies to be done, because in order to obtain useful information, the people would have to be deprived of nearly all dietary protein, putting their health at unreasonable risk.

(2) If such oral doses were actually given, some AAs would cause vomiting and diarrhea in some subjects, due simply to the excessive stomach load of one concentrated substance (the "little green apples" syndrome), and that would not provide any useful or meaningful data on actual "toxicity".

It is obvious that the obligatory drug-testing of AAs cannot actually be done. The impossibility of demonstrating toxic levels of AAs could be used as a means to remove them from the shelves. The fact that toxic doses are impossible to demonstrate would be irrelevant.

CHART 1
ESTIMATED SAVINGS IN DISEASE CARE COSTS
From Improved Nutrition/Prevention Information Dissemination

Kellog Report Estimates:

Respiratory	1.4
Arthritis	0.9
Mental Illness	1.4
Alcoholism	14.5
Digestive Disease	1.0
Kidney & Urinary	1.3

$20.5 Billion

Health Studies Collegium:

Cancer	7.0
Stroke	23.0
Cardiovascular	15.0
Adult Diabetes	29.0
Gingival & Dental	43.0
Neural Tube Defects	45.0
Hip Fracture	4.0

$166 Billion

With Use of Natural Therapies including Supplemental Nutrients & Herbal Remedies

Townsend Letter for Doctors:

Prostate	2.8
Asthma	3.0
Heart Attack	1.0
Osteoarthritis	1.0
Ear Infections	.5
Ulcer	1.3

$9.6 Billion

TOTAL, SELECTED CONDITIONS = **$196.1 BILLION**

CHART 2
RELATIVE PRODUCT "TOXICITY"
ANNUAL AVERAGE

DEATHS:

Adverse Drug Reactions:	**60,000-140,000**
Food Contamination:	**9,100**
Charcoal Briquettes (Carbon Monoxide):	**34**
Household cleaners:	**24**
Pesticide poisoning:	**12**
Hair Dryers:	**10**
Iron poisoning:	**6**
All Plants (house plants, etc.):	**1**
All vitamins:	**0**
Uncontaminated amino acids:	**0**
Commercial Herbal Products:	**0**

Sources: Calculations based on data from the American Association of Poison Control Centers, National Center for Health Statistics, Journal of the American Medical Association, Centers for Disease Control, U.S. Consumer Product Safety Commission.

Since 1936
NNFA
National Nutritional Foods Association

Backgrounder #5

FDA Authority

Contrary to recent reporting in the national media, which has claimed that the dietary supplement industry is "virtually unregulated" (CBS News, Dr. Bob Arnot, May 24, 1993), the FDA has a host of statutory authorities under current law to use against unsafe products or false claims. The source of this statement: the FDA.

In its May 1993 Enforcement Report to the Congress, which was required by the Dietary Supplement Act of 1992, the FDA states that it has initiated 669 judicial enforcement actions against dietary supplements between 1989 and 1992. The FDA cites as its authorities several sections of the Food, Drug and Cosmetic Act: 402(a)(1) relating to poisonous or deleterious substances added to foods; 402(a)(2)C pertaining to foods containing unsafe food additives within the meaning of section 409; 403(a) covering false or misleading labeling; 501(a)(2)(B) regarding drugs not produced under good manufacturing practices; 502(a) prohibiting drugs with false or misleading labeling; 502(f)(1) covering products failing to bear adequate directions for use; 503 baring the dispensing of prescription drugs without a prescription; and 505(a) banning the marketing of new drugs without FDA approval.

All these authorities are supplemented by non-judicial but very powerful remedies including the issuing of warning letters, import detentions and requests for voluntary recall. When the FDA challenges a claim on a label, the manufacturer usually withdraws the claim without the necessity of judicial action.

Under the Hatch and Richardson bills, the power of the FDA to act against products that are or may be harmful or mislabeled would be preserved, and new requirements would be added that would require supplement labels to contain greater and more uniform information regarding their ingredients, purity and dissolution properties. What the FDA could not do would be to misapply the food additive provision of the statute against dietary supplements.

Projections for Health Food Stores

Serving approximately 10.5 million customers per week, health food stores are staffed by 116,000 employees (58,600 full-time and 57,400 part-time.)

The annual wages paid by all stores projects to $1.8 billion.

In 1991, these nearly 12,000 stores had projected total sales of over $6.5 billion. Sales covered a wide range of products as follows:

Vitamins/supplements	$2,532,915,000
Packaged foods	778,855,000
Bulk foods	320,705,000
Refrigerated/dairy foods	294,525,000
Frozen foods	242,165,000
Produce	209,440,000
Meat/poultry/fish	85,085,000
Snacks/confections	248,710,000
Herbs/teas	602,140,000
Appliances	130,900,000
Beverages	235,620,000
Personal care items	327,250,000
Books/tapes	215,985,000
Exercise equipment	19,635,000
Other products and services	301,070,000
	$6,545,000,000

In order to help generate these sales, retail health food stores spend $190 million annually on advertising.

Projections for Manufacturers/Distributors

Based on our projections, the nearly 4,300 manufacturers and distributors of health food items had total sales of $37.4 billion in 1991.

These firms employ 167,100 full-time and 60,800 part-time employees, with their total annual wages equaling $3.2 billion.

They have a present inventory valued at $2.6 billion.

In the past 12 months, manufacturers and distributors that service the health food industry spent over $1 billion for equipment, buying the following:

Packaging equipment	$525,005,000
Manufacturing equipment	349,440,000
Laboratory equipment	65,917,000

Office equipment	59,122,000
Transportation equipment	38,394,000
	$1,037,878,000

The estimated market value of the real estate owned by those manufacturers/distributors that own their property is $4.5 billion.

Council for Responsible Nutrition
1300 19th Street, N.W., Suite 310
Washington, D.C. 20036-1609
(202) 872-1488
Telefax (202) 872-9594

NEWS

September 22, 1993

Contact: Mary Burnette
(202) 872-1488

VITAMIN SUPPLEMENTS COULD CUT BILLIONS IN HEALTH CARE COSTS

The U.S. health care system could save $8.7 billion annually from reduced hospitalizations resulting from five major diseases if Americans consumed optimal levels of the antioxidant vitamins C and E and beta-carotene. The $8.7 billion figure implies a five-year savings of more than $43.5 billion.

These numbers were part of an economic analysis released today at the Council for Responsible Nutrition's 20th anniversary annual conference in Washington, D.C.

The study by Pracon, Inc., a Reston, Virginia economic analysis firm, concluded:

- For coronary heart disease-related hospitalizations, vitamin E supplements have the potential to save:
  - $1.5 billion for Medicare; $7.7 billion for the United States annually
- For breast, lung and stomach cancer hospitilization avoidances, diets optimal in antioxidant vitamins, C and E and beta-carotene may yield:
  - $196.4 million in savings for the Medicare program; $1.0 billion or more in savings for the entire United States annually.
- By preventing 50 percent of cataract hospitalizations, optimal intake of vitamins C and E and beta-carotene may save:
  - $7.1 million for the Medicaid program; $49.3 million for the United States annually
- In addition to hospitalization savings, of the estimated $108.9 billion in total health care expenditures for coronary heart disease, optimal intake of vitamin E of between 100-400 IU may save $27.2 billion annually.

"These figures represent only one portion of the potential savings since hospitalizations represent only a piece of the total

medical costs of the diseases studied," said Steven Pashko, Ph.D., Pracon senior director and project leader on the study.

The Pracon study, which was commissioned by CRN, estimated national costs from Medicare and select state hospital records for cardiovascular disease, cataracts, breast, lung and stomach cancers.

Then, using data published in scientific literature, the study estimated how many cases of each disease might be prevented if all Americans consumed optimal levels of the antioxidant vitamins C and E and beta-carotene.

The Pracon study used, for example, information reported in two studies of health professionals from Harvard Medical School on the role of vitamin E in preventing heart attacks. The studies were published in the *New England Journal of Medicine* earlier in 1993.

Most people find it difficult to get protective levels of some antioxidant vitamins from diet alone. The National Cancer Institute recommends eating five servings of fruits and vegetables a day to help prevent cancer. A 1990 analysis of the National Health and Nutrition Examination Survey (NHANES II) showed that less than 10 percent of Americans actually consumed two servings of fruits and three of vegetables a day.

Another analysis of NHANES II data showed that on any given day 50 percent of Americans ate no vegetables, 70 percent ate no fruit or vegetable rich in vitamin C and 80 percent ate no fruit or vegetable rich in carotenoids such as beta-carotene.

"The science supporting the role of supplements in improving health is becoming stronger every year," said Annette Dickinson, CRN's technical director. "We now have compelling data showing that vitamin supplements can not only improve health but save our country billions of dollars".

"We need to reorient our health care system to focus on prevention," said Alexander Leaf, emeritus professor of clinical medicine at the Harvard Medical School. Leaf had earlier addressed

the CRN annual conference on the need to change the American medical approach from treatment to prevention.

"The analysis demonstrates why prevention is needed," Leaf added. "This data will be terribly important for the long term."

U.S. HOSPITALIZATION EXPENDITURES

	Total Expenditures ($ mil)	Percentage Preventable from increased Antioxidants (C, E, Beta-carotene)	Estimated Medicare Cost Savings ($ mil)	Estimated Total Savings ($ mil)
Cancer				
Breast	$ 1,088.3	16%	$ 27.4	$ 174.1
Lung	$ 3,263.7	21%	$ 125.4	$ 685.4
Stomach	$ 538.0	30%	$ 43.6	$ 161.4
Cardiovascular Disease	$ 30,823.7	25%	$1,500.0	$ 7,705.9
Cataracts	$ 98.5	50%	$ 7.1	$ 49.3
TOTAL	$ 35,812.3		$1,676.6	$ 8,776.1 annual

Source: Pracon economic analysis data

STATEMENT SUBMITTED by

ALVIN B. SEGELMAN, Ph.D.
VICE PRESIDENT
CORPORATE HEALTH SCIENCES
NATURE'S SUNSHINE PRODUCTS, INC.
PROVO, UT

NATURE'S SUNSHINE PRODUCTS INC.
75 E. 1700 S. • P.O. BOX 19005 PROVO, UTAH 84605-9005
TEL: (801) 342-4100 • FAX: (801) 342-4305

Introduction:

Mr. Chairman and Members of the Committee on Labor and Human Resources, I am grateful for the opportunity to present my statement today. My remarks will deal with safety issues as they apply to dietary supplements, with special emphasis on herbs and herbal dietary supplements.

- FDA has recently listed a number of herbs as being partially hazardous to health (*Unsubstantiated Claims and Documented Health Hazards in the Dietary Supplement Marketplace, Department of Health and Human Services, Food and Drug Administration, July 1993, pp.100-105*).

- At the dietary supplements hearing held 20 July 1993 before the Subcommittee on Human Resources and Intergovernmental Relations of the Home Government Operations Committee, Dr. Fred Shank, the Director of the FDA's Center for Food Safety and Applied Nutrition stated that the most important FDA priority in terms of enforcement action will involve those "products that are potentially harmful when used as directed or in a customary manner (a direct health hazard posing a risk of serious or life-threatening adverse health effects)".

Purpose:

I wish to state that herb-containing dietary supplements do not present a major problem with regard to safety. Furthermore, we support the notion that people should be allowed free access to self-use of herbal supplements when safety can be established on the basis of the following criteria:

1. **Published information reveals a past history of safe human use for any particular herb, and**

2. **Published information reveals no cases of significant toxicity when a particular herb or herbal product is taken in the amounts normally used.**

Comments:

- With regard to Criterion #1, that is, history of long and continued safe use, there is a vast amount of documentation showing that with very few exceptions, most of the herbs used as dietary supplements (foods) have long been employed extensively and safely by humans. Is Point #1 above valid? We believe it is and there is precedence for it. Thus, the validity of using historical use as a criterion for proof of food safety

was indeed earlier endorsed by a former FDA Associate Commissioner [*104 Cong. Rec. 17, 420 (1958)*]:

> *Our Department believes that it is not necessary to good public health protection to have chronic toxicity studies conducted of common food chemicals, such as salt, sugar, vinegar, baking soda, and a great many other materials that have been in common use for a long time. As a matter of fact, these substances have been established as suitable food ingredients through feeding to generations of human beings.*

• With regard to Criterion #2, that is, no reported cases of significant toxicity, I should first mention it is noteworthy that for the several hundred herbs which have been used as dietary supplements by people all over the world, only very few cases of toxicity have been reported But there are problems with most of these case reports. For example, it turns out that the majority of the "toxic case reports" have not withstood careful scientific scrutiny. Indeed, most reports which suggest herb toxicity and serious adverse effects, have eventually been proven to involve not the herb itself, but instead to be due to various other factors, including the following:

- A different herb was used instead of the intended herb.

- The intended herb was adulterated or contaminated with some other toxic herb.

- The intended herb was adulterated or contaminated with potent. pharmaceutical-type drugs or with toxic, non-herbal materials like lead and arsenic.

In connection with Criterion #2, I would like to chose a few examples from the recent FDA's list of potentially harmful herbs and show that toxicity concerns in these cases may be unwarranted.

1. Herbal Products Containing *Stephania* and *Magnolia* Species

" A Chinese herbal preparation containing *Stephania* and *Magnolia* species that was sold as a weight treatment in Belgium, has been implicated recently as a cause of severe kidney injury in at least 48 women" (*Unsubstantiated Claims and Documented Health Hazards in the Dietary Supplement Marketplace, Department of Health and Human Services, Public Health Service, Food and Drug Administration, July, 1993, pp. 100-105).*

However a critical evaluation of this problem, including the original report (*Lancet,341 387, 1993*) as well as previously published information, showed the following:

- The herb *Stephania tetrandra* that is used in traditional Chinese formulations was not present in the formulas used by the women who suffered kidney damage. Quite possibly some other plant was involved.

- Previously published information shows that *Stephania tetrandra* has a history of continued use as a dietary supplement; there are no case reports of human toxicity.

- Previously published information shows that *Magnolia officinalis* has a history of continued use as a dietary supplement; there are no case reports of human toxicity

- Finally, the authors of the *Lancet* report state, " we cannot identify the precise causal factor ".

2. Jin Bu Huan (*Polygala chinensis*)

Jin Bu Huan is a Chinese herbal product manufactured in China and the stated ingredients are the herb *Polygala chinensis* L. (alkaloid 30% and starch). [*Morbidity and Mortality Weekly Report 42, 633 (1993)*] This case report involved serious side effects in 3 children who ingested from 7 to 60 tablets of Jin Bu Huan. However , a critical evaluation of the problem shows the following:

- *Polygala chinensis* is not the plant normally used in traditional Chinese herbalism; *Polygala tenuifolia* is the plant commonly used.

- Previously published information shows that *Polygala tenuifolia* has a history of continued use as a dietary supplement; there are no case reports of human toxicity.

- However, a chemical substance, namely an alkaloid (which can be toxic in high doses) known as tetrahydropalmitine (THP) was found to be present in Jin Bu Huan tablets; this alkaloid is not known to occur in members of the genus *Polygala*, including *Polygala tenuifolia*. Therefore a *Polygala* herb was probably not present in the tablets and accordingly, *Polygala tenuifolia* can be ruled out as a suspect herb. Regretfully, the tablets were not even analyzed to determine the presence of plant material.

- THP does occur in some members of the genus *Stephania*, but THP has not been found in *Stephania tetrandra*, the herb mentioned in Case #1 above.

Conclusions:

- In both of the two case examples, one can only conclude that there is no substantial evidence that the three suspect herbs, namely, *Stephania tetrandra*, *Magnolia officinalis* and *Polygala tenuifolia*, are hazardous to human health.

- The so-called "toxicity problems" here are actually quality control issues and do not involve any inherent toxicity of the named herbs.

- Finally, to put the herb safety issue into proper perspective, I would like to briefly describe some of my unpublished experimental results (1979) using the common carrot. To the best of my knowledge, there have been no reported cases of serious carrot toxicity in humans. Prompted by a published report which indicated the presence of a toxic substance (carototoxin), an extract was prepared from ordinary carrots. This extract was highly toxic when administered to mice. Since the extract contained a mixture of substances, the experiments were not continued. But the results raise the question, "Should carrots be considered potentially hazardous to health?" We think not, based on a long history of safe carrot ingestion in the amounts normally used by humans. But interestingly, a scientific report appeared last year [*Phytochemistry 31, 3621 (1992)*], indicating that the mixture of substance components of carrots had been separated and purified and will be studied for biological effects. So the story on carrots is still open!

In closing, I would like to point out that the Dietary Supplement Health and Education Act of 1993 quite adequately addresses "herb safety issues" (Sec. 2 (a) (13), and Sec.4 Safety of Dietary Supplements.)

Summary:

1. **Herbs should be considered safe if: a) they have a history of continued safe use as dietary supplements by humans and b) if there are no published reports regarding human toxicity cases.**

2. **Published information regarding case reports of herb toxicity should be carefully and critically evaluated because many such reports do not clearly provide substantial evidence for actual serious toxicity problems.**

Respectfully submitted,

Alvin B. Segelman

Alvin B. Segelman, Ph.D.,
Vice President
Corporate Health Sciences
Nature's Sunshine Products
Date: October 21, 1993

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5 August, 1993

SPENCER-JONES INC
TECHNOLOGY TRANSFER CONSULTANTS
19 Donegani Avenue, Suite 302
Pointe Claire, Quebec
Canada H9R 2V6
Tel: (514) 783-6569
(514) 453-2170
Fax: (514) 453-8974
Telex: 05-822549

DISCUSSION NOTES:

Dietary supplements; an opinion relating to Regulatory treatment with maximal benefits for all parties concerned.

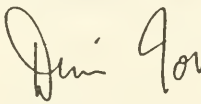
This document has been prepared by Dr. Dennis Jones at the request of a number of interested parties.

Dr. Jones studied Medical Sciences and Chemistry at the University of Cambridge, specializing in Pathology. After obtaining his first Cambridge degree and an external degree in Chemistry in 1963, he remained in Cambridge to conduct research in Nutritional Pathology and Histochemistry which resulted in his Doctorate. In 1966, he was appointed to a University position with responsibilities for teaching and research in Nutrition, and played a fundamental role in helping to establish one of the first Nutrition courses for Medical Students.

In 1971, he moved to Holland, initially as a sector research Director for a Dutch pharmaceutical company, whose origins were based on natural products. His responsibilities in this company were subsequently expanded to include development projects ranging from neuromuscular blockers and psychoactive drugs (including appetite control agents) through to natural substances, synthetic hormones and low calorie diets.

After leaving Holland in 1979, he spent some time in France as Director of Research and Development for a French pharmaceutical company, moving to Canada late in 1980 as President of a semi-government Food Engineering Research Institute. More recently, after a couple of years with a pharmaceutical company in Montreal, he started his own consultancy operation, and now includes major dietary health care and dietary supplement manufacturers among his clients.

Dr. Jones is a Member of two Canadian Government Committees, the Expert Committee on Human Nutrition and the Expert Committee on Plant Products, and has served on various other official Government Committees in this general area in both North America and Europe.



Dr. Dennis Jones,
M.A., Ph.D., C.Chem., FRSC,
C.Biol., M.I.Biol., MCIC, MBIM.

Preamble:

Dietary supplements can broadly be defined as substances other than "food" which are ingested for a variety of reasons related to maintenance or improvement of health. They have traditionally included herbs, spices, micronutrients such as vitamins and minerals, semi-micronutrients (essential fatty acids, free amino-acids), and materials such as bacterial cultures.

The use of many of these materials, particularly herbs, is motivated by a long history of tradition, in some cases going back 20,000 years or more. In other cases, such as the essential fatty acids, unknowing use by primates and, more recently, man has occurred for millions of years, but current deliberate use is based on findings from relatively recent scientific research. Though the use of herbs is frequently based on tradition, many herbs have been studied scientifically, and research performed not only frequently validates the opinions concerning their health benefits, but often indicates new areas of interest.

In most countries, legislation has been implemented which acknowledges the value of dietary supplements. Such legislation protects the rights of the public to exercise their freedom of choice, provides them with a reasonable assurance of safety, and also protects them from fraud and misrepresentation, in all cases without being unjust, unwieldy, excessively bureaucratic or subject to arbitrary whims of the regulatory agency concerned.

In the United States, however, most dietary supplements fall into a legislative limbo which serves neither the best interests of the consumer (public) nor those of the regulatory authorities (FDA, FTC, State Authorities). Currently, dietary supplements can be sold freely, provided their labelling does not contain any information that could be construed as making drug-like claims. Thus the public can purchase a wide variety of dietary supplements but cannot access information on their properties and use, having to rely instead on word-of-mouth or reports carried by the media, that are frequently sensational and inaccurate.

It has been contended, both in the media and in official circles, that safety is a major issue, and that dietary supplements must therefore be stringently regulated. The FDA contention, that herbs and other supplements may be unsafe, savours of "wishful thinking" and is not borne out by the facts; other than isolated, sensational and somewhat apocryphal articles in the media, exhaustive study of the international medical and scientific literature has failed to reveal any evidence of toxicity problems.

Similarly, a thorough investigation of the reports of the American Association of Poison Control Centers, performed by the Herb Research Foundation, likewise failed to reveal any evidence that herbs were unsafe!

In this context, it should be noted that the toxicity potential of some common culinary spices exceeds that of any of the herbs available as dietary supplements (see Appendix), yet the FDA has expressed no concerns about such spices, nor made any proposal to prohibit their sale!

Thus there is a lack of convincing evidence that herbs and dietary supplements are unsafe, or are a hazard to the American public. If dietary supplements were even intrinsically unsafe, then the current conditions under which they are sold would certainly reveal this; provide any article or material to an untrained lay person without simultaneously providing the information relating to its use, and accidents will happen! The legal ban on putting information about the product on the label of a dietary supplement causes more harm than does the rational use of the product, and the isolated "events" reported by the media, noted above, would in most cases not have occurred if the users had been informed about the products!

The current legislative framework also fails to protect the public from fraud and misrepresentation; legitimate products with well-established health benefits are seized, while misbranded and fraudulent products whose very composition contravenes various requirements of several Federal Acts are ignored, even when their nature has been revealed through publications in scientific journals and their existence is well known to the FDA.

Finally, current legislation contributes to arbitrary and illogical decisions about dietary supplements by the FDA, which sometimes appear unfounded and unsupported by evidence, without creating any real opportunity for these decisions to be fairly contested and discussed. For example, recent internal correspondence of the FDA characterized a certain herb as "unsafe", without defining why it was considered unsafe, or referring to any scientific or medical literature. FDA officials questioned about this were unable to provide information other than to confirm the herb was considered unsafe. In this particular case, some 400 scientific publications and a 20,000 year history of use (including several hundred years of use in North America) had failed to reveal any health hazard associated with use of this herb, and a recent history of use by more than 100,000 Americans, far from demonstrating a lack of safety, has shown that the herb in question is not only remarkably free from side effects but also confers very significant health benefits with quantifiable effects on health care costs (reduction)!

The alternative approach:

The diversity of types of dietary supplements renders an all-encompassing Regulatory scheme almost impossible to achieve, and it is probably better to view it from the perspective of the objectives to be achieved.

Firstly, the public has a right to continued access to traditional remedies, use of which predates FDA authority in this sphere by hundreds or even thousands of years. Not only do many ethnic groups believe strongly in the virtues of "herbal" medicine, but many Americans of other origins also believe in the healing powers of herbal products and exercise their rights in purchasing them. There is little doubt that use of such products is frequently effective, and both cheaper and safer than the alternative of administration of synthetic drugs, often requiring visits to physicians and hospitals.

Secondly, the public has a right to access dietary supplements that, by virtue of more recent research findings, are known to have positive health benefits in either a therapeutic or prophylactic sense.

Thirdly, the public has a right to "full disclosure" with respect to any dietary supplement offered for sale, thus the labelling and product information should contain accurate information about possible health benefits and potential adverse effects.

Fourthly, the public should be protected against fraud and misrepresentation, and should be guaranteed authenticity, quality and purity. An important aspect of this objective is that both labelling and advertising material should be based on the principle of "the truth, the whole truth, and nothing but the truth", and that where there are varying scientific opinions about a particular dietary supplement, all informative material should reflect these varying opinions in a balanced fashion.

Finally, in the event of any dispute of interpretation or differences of opinion between manufacturers and authorities (FDA), there should be opportunities for discussion and resolution of the dispute or differences, in discussion forums which would permit both parties to present their arguments, and the authorities (FDA) should be prohibited from unilateral and arbitrary action. This would not preclude disputes which could not otherwise be resolved from being presented to appropriate third parties for arbitration, and measures could be included to permit unilateral FDA action in the event of verified, obvious and serious health hazards, or lack of cooperation from a manufacturer.

To avoid creating excessive costs and delays in the implementation of a regulatory scheme that would initially have to cope with many thousands of existing products, and numerous new products each month, it is preferable that the legislation to be enacted not require any form of prenotification or approval process, but would rather place the onus on the manufacturer to be in compliance. Manufacturers could optionally be required to file Monographs on their products, summarizing the features of their products, their justification for labelling and advertising copy, and the Quality Assurance and Control aspects of their manufacturing procedures. These Monographs could be reviewed, and comments could be addressed to the manufacturer. Though such a review procedure would, ipso facto, occur after the product concerned had been marketed, it would serve to restrict products which had no logical, scientific or traditional justification, or products for which there were valid concerns about long-term safety. For example, such reviews would be useful for the elimination of products containing free amino-acids, which have the potential of unfavourably altering the balance of neurotransmitters in the brain but for which otherwise no rationale exists.

Additionally, Monograph reviews would identify products which, though valid dietary supplements for certain purposes, are marketed on claims for which no scientific basis exists, such as chromium picolinate as a "weight loss" pill (chromium picolinate is a valid and bioavailable source of chromium, but its metabolic actions are inconsistent with the metabolic needs of the obese).

Products which would automatically be deemed valid dietary supplements and thus would be permitted in the marketplace would be:

1) Traditional remedies of herbal or other nature, for which there is a history of use for certain indications. There would be no geographical or temporal limitation on this history of use, and labelling and advertising for such

products would refer to the traditional use and to any contraindications (for example, warnings about use of Arctostaphylos in pregnancy).

Such products would be assumed safe based on their history of use, unless there was valid, published scientific data casting doubt on their safety. Subjective concern about safety which was not based on scientific evidence would be ignored, irrespective of source. Products falling into this category could be single or multi-component; if the latter, the rationale for combination should be either historical or scientifically valid for the claims made.

For example, the presence of both Herba Ephedrae and Chromium in a single product intended to assist weight loss would be invalid because of their antagonistic effects on adipose tissue, but would be valid for a product marketed for "fitness" purposes.

2) Traditional remedies of herbal or other nature, for which there is a history of use for certain indications, but for which other scientifically acceptable indications have been identified. Labelling and advertising for such products would refer to the use identified and to any contraindications, and could optionally refer to the traditional uses.

The indications claimed would require justification, either directly (through appropriate published or unpublished scientific documentation) or indirectly, by reference to studies of active principles or closely related substances. It would not be the intention to impose a costly burden of experimentation and documentation on the manufacturer or sponsor of the product concerned, since the traditional herbs used have already been deemed safe (see 1) above), but there should be a reasonable and acceptable scientific basis for claims made (for example, an appropriate review of literature).

In the case of both 1) and 2), there is a further desirable labelling requirement, and that is uniform nomenclature. Currently, many herbs have multiple common names, and manufacturers are free to use whichever appears most attractive or glamorous. This is confusing to the consumer, who, for example, may think the "bissé nut" is a new and exotic herb, without realising that this is simply the cola nut (of Coca Cola fame) in disguise!

3) Nutrient substances, such as vitamins, minerals and essential fatty acids, to be used to prevent deficiency, or where scientifically justifiable, to be used for identified purposes associated with health benefits.

Such products would automatically be deemed safe when used within a normal dosage range, or when used in larger dosages if no evidence to the contrary exists. However, high dosages of these substances, putatively 3 or more times the official RDA where an official RDA exists, would have to be substantiated by direct or indirect scientific evidence. For example, there is adequate evidence that large dosages of the antioxidant vitamins (C, E) and β-carotene are beneficial, and may safely be consumed over long periods of time, thus these substances would be permissable, but there is less justification for large doses of pyridoxine, and some evidence of toxicity, when this vitamin (Vitamin B_6) is consumed in large dosage.

4) Other substances, not falling into any of the preceding categories, for which adequate scientific justification exists, such as inulin, other novel dietary fibres, and bacterial cultures.

In many cases, safety can be deduced by inference based on presence of such materials in conventional and traditional foods, and claims would require justification either directly (through appropriate published or unpublished scientific documentation) or indirectly, by reference to studies of related substances.

Further requirements:

It seems logical that manufacturers of dietary supplements should be required to follow the principles of Good Manufacturing Practice, as it applies to the pharmaceutical industry, but with some relaxation in certain respects relating to analytical requirements (except for vitamins and minerals, where analytical certification of batches would be required). The ability to guarantee the authenticity, quality and purity of a product is paramount. In addition, manufacturers should be able to mount a recall procedure effortlessly if required.

It is also desirable that manufacturers and marketers have programmes for Post-Marketing Surveillance, and carry liability insurance.

Enforcement aspects:

The dietary supplement industry behaves in general in an ethical fashion, but as with any other business, does contain those who operate in a slick and fraudulent fashion. Regrettably, these few are generally successful in accumulating large profits, are rarely "brought to book" for their misdeeds, and often bring the industry into disrepute. It would be beneficial to both public and the industry if the FDA were to diligently pursue those who, within the framework outlined:

1) Persist in making outrageous and unsubstantiated claims, exploiting the gullibility of their target groups.

2) Manufacture sham or fake products, which either do not contain the claimed ingredients, and thus are unlikely to have the claimed properties, or are laced with pharmaceutical grade substances intended to give profound effects that will ensure repeat sales.

Conclusion and Post Scriptum:

Despite the stated, but subjective, beliefs aired in some quarters, the dietary supplement industry does not endanger the health of the American public. On the contrary, it has a major and positive impact on the health and wellbeing of over 100 million Americans who believe in the curative or preventative properties of dietary supplements, and who purchase and use them. If deprived of their right to buy (at their own expense) and use these dietary supplements, many of these believers would have to resort to conventional channels to obtain relief for their ailments, with a consequent increase in the health care burden and costs, while the negative impact in terms of loss of preventative effects can scarcely be calculated.

At the same time, the death knell would sound for many small and medium sized companies across the country, resulting in a loss to the economy of more than $ 4 billion a year and many thousands of unemployed.

Comments made in some quarters that dietary supplements are "virtually unregulated" are also deliberate misinformation; under the current regulations, dietary supplements are regulated as foods, and must meet the same standards. In fact, they generally meet higher standards, since many manufacturers conform more

closely to the stricter requirements of pharmaceutical GMP! The major frustrations in the industry at present are:

a) Dietary supplements have to be totally presented as "food" if they are to avoid unwelcome attention from the FDA, and thus neither their properties nor the precautions associated with their use can be communicated to the user.

b) The presence in the market of scam artists who seem never to attract FDA attention, while legitimate companies with genuine products suffer frequently from FDA actions.

c) The perception that the FDA is itself spreading incorrect information about dietary supplements with the intent of enlisting public support to "regulate the industry out of existence".

Legislation such as that proposed in the "Dietary Supplement Health and Education Act of 1993" (S.784; Senator Hatch) would make a major contribution to the health and wellbeing of the American public, guaranteeing their rights to access authentic, safe and effective dietary supplements, ensuring their rights to accurate and full information about these products, giving the FDA realistic authority to eliminate fake and misbranded products, and safeguarding the survival of an important industry on whom many millions of Americans rely.

APPENDIX: Hazardous products in the kitchen spice cupboard!

The contention that dietary supplements can be unsafe pales to insignificance when the potential of common culinary herbs and spices for exaggerated pharmacological effects and true toxicity is revealed.

Proven or suspected carcinogens occur in some culinary herbs and spices; for example, safrole and related compounds occur in black pepper, basil, cinnamon leaf, cocoa, mace, nutmeg, carrot seed, celery seed, parsley and star anise oil. Sassafras, which has officially been banned, also contains safrole, but its presence in common herbs and spices apparently carries other connotations!

The long-term toxicity associated with such compounds may or may not be a concern, but the acute pharmacological effects of other spices and herbs are definitely interesting! Nutmeg is a typical example; it meets all the criteria for a narcotic hallucinogen! It has a powerful hallucinogenic effect, inducing a hypnotic trance accompanied by golden dreams and euphoric bliss. Various authorities have classified it as up to 4 times as powerful as marijuana, and it is suggested that the effects are in part due to the presence of substances which break down into amphetamines in the body.

An interesting paradox; possession of marijuana is a criminal offence, while a more powerful narcotic hallucinogen is not only freely available, but actually has official GRAS status!

The list could go on, but the purpose of this Appendix is merely to emphasize the inconsistency of attitude; none of the herbs available as dietary supplements are as potentially toxic or as potentially subject to abuse as several spices which are deemed risk free and are readily available to the public!

If the spice cupboard is not sufficient, there are many ornamental flowers and shrubs which are even more hazardous.

File: HSF190C3
(8 pages)

19 October, 1993

SPENCER-JONES INC
TECHNOLOGY TRANSFER CONSULTANTS

10 Donegani Avenue, Suite 902
Pointe Claire, Québec
Canada H9R 2V8

Tel.: (514) 693 0556
(514) 458 2170
Fax: (514) 458 4574
Tlx: 06 823830

Safety aspects of Ma huang, also known as Ephedra or Herba Ephedrae.

Refererence is made in this Report to the review document entitled:

> EPHEDRA (MA HUANG) IN NUTRITION AND HEALTH. A review of the facts as reported in the literature, with Executive Summary and Conclusions. Reference HSA-30C3, 28 pages.

This brief report specifically addresses the topic of the safety of Ma huang, or Ephedra herb, and has been motivated by comments and statements made by FDA officials, in writing or verbally (as reported in newspaper articles), that Ma huang is "toxic" (FDA Import Bulletin 66-B62, 26 June, 1992), that serious adverse effects with products containing Ma huang as ingredients have been reported to the FDA (Report "Unsubstantiated Claims and Documented Health Hazards in the Dietary Supplement Marketplace", FDA, July, 1993), and that the FDA is *worried about its increased use as a diet aid because it could cause heart attacks in certain overweight people* (New York Times, 14 July, 1993).

Despite an exhaustive search of the literature, and detailed investigation of the use of Ma huang-based products, no evidence can be found that Ma huang is toxic or causes serious adverse effects. Based on the pharmacology of ephedrine, there is no evidence that the relatively small amounts of this substance found in Ma huang is likely to cause heart attacks in overweight people. Reports of serious adverse effects appear to be associated with use of fake products (products that contain added substances of pharmaceutical grade, deliberately added for economic or other reasons), and the effect of the Import Bulletin cited above may have been to increase the number of fake products available, by restricting availability of genuine Ma huang.

The Import Bulletin is further inaccurate in a number of respects, including its classification of ephedrine, and its claim that there is "no known food use" for Ephedra. In fact, there are well-documented food uses for Ephedra dating back 150 years in North America and several hundred years elsewhere.

Prepared by:

Dr. Dennis Jones,
M.A., Ph.D., C.Chem., FRSC(UK),
MCIC, C.Biol.,M.I.Biol., MBIM.

Concept of safety:

The concept of safety needs to be defined, since it appears to depend on context and the opinion of the person or persons uttering comments on safety. For example, ritual suicide is committed in several nomadic desert tribes by consuming ½ lb of salt. It is also possible to die by doing any of the following within a short period of time (say 5 minutes): drinking a little in excess of one gallon (Imperial measure) of water, consuming several teaspoons of various spices that are common in most kitchens, drinking upward of ½ bottle of whisky (or other strong drink), consuming 30 or more acetaminophen tablets (500 mg), or by abnormal use of a variety of other common items. However, none of these "toxic" materials would be considered unsafe!

Thus many of the commodities that are a normal part of our life are unsafe when used in a way that is not intended by the manufacturer or by the regulatory authority that permits them to be part of our environment. Accordingly, the concept of safety must be modulated by reference to "normal conditions of use". To exemplify this concept, legislation recently adopted in Denmark, permitting the free sale of traditional herbal remedies, specifically states "safe under normal conditions of use" (Executive Order on Natural Remedies, Danish Ministry of Health Executive Order No. 790 of 21 September, 1992).

A major prerequisite for the concept of "safety under normal conditions of use" is that the normal conditions of use must be defined, implied or otherwise be obvious to the consumer. Thus in the extreme examples cited above, consumption of ½ lb of salt, one gallon of water, ½ bottle of whisky or several teaspoons of spices is obviously an abnormal use to the consumer, and (except for whisky) poisonings or fatalities due to these agents are rarely seen. In the case of acetaminophen, the normal conditions of use and some warnings are printed on the label (and even so, there a number of fatalities each year, estimated at 50 or more, as well as several hundred cases of severe poisoning).

In the case of products containing Ma huang, it is not permitted, under current legislation, to put the normal conditions of use on the label, and yet despite this limitation, and despite the fact that at least 500,000 people in the United States use products containing Ma huang each year, there are no reports of fatalities, and very few reports of serious adverse effects in general. Such reports of serious effects as there are are anecdotal and poorly investigated, which topic will be dealt with in detail later in this report.

Concept of toxicity:

It is inappropriate and unscientific to title a document "Toxicity of . . . . . " when what is actually referred to is the pharmacological activity. Toxicity implies, and is defined as, damage caused by a toxic agent, such as, for example, the liver failure due to hepatic necrosis that might be seen when a toxic dose of acetaminophen was given. Pharmacological activity, on the other hand, could be defined as the reversible effects on the physiology and/or metabolism that can be observed when a reasonable dose of an agent is given (see, for example, Turner and Richens, 1978, Clinical Pharmacology, 3rd Edition, Churchill Livingstone, or any other textbook of pharmacology). It would also be desirable to make a distinction between adverse effects and side effects, though this distinction is vague in the minds of many scientists. However, it is extremely important to distinguish between an exaggerated pharmacological effect, which, though it may cause discomfort to the person using the causative agent, will disappear when the agent is reduced in dosage, a true adverse effect which causes some physical or measurable damage that persists after administration of the causative agent, and a side effect that is pharmacological in nature due to properties of the agent that are not desired within the context of use.

As an example, consider ephedrine itself. Ephedrine is, of course, one of the alkaloids present in genuine Ma huang. It is considered to be non-toxic or of low toxicity (HSA-30C3, page 17), thus does not cause any organ changes or damage to the metabolism. The only note of caution in the medical literature is that the pharmacological effects may become apparent to the patient (in a daily dose of 150 mg given intravenously, side effects are rare; HSA-30C3, page 17). For example, patients using ephedrine as a decongestant may sometimes experience difficulty in urinating. This is not a toxic effect, nor is it an adverse effect (though the user may perceive it as a side effect); it is simply an expression of the pharmacological activity of ephedrine that occurs at slightly higher dosage, due to increase of tone in the bladder sphincter! In fact, this property of ephedrine is used to advantage in the treatment of nocturnal enuresis (otherwise known as bedwetting) in children. The same applies to the cardiovascular effects of ephedrine. One use of ephedrine is to stabilise patients with threatened circulatory collapse; given intravenously in quite high dosage (25 - 50 mg), it will restore a reasonable cardiac function (increasing the heart rate and the blood pressure to normal levels). In most patients who take ephedrine tablets for some reason, such as appetite control or as a decongestant, there is no significant effect on cardiodynamics (HSA-30C3, page 12 et sequens), but a few patients perceive "palpitations"; in fact, they perceive either a slight increase in heart rate or a slightly stronger beat: Thus a pharmacological effect.

Safety and toxicity of Ma huang:

Based on the concepts of safety and toxicity discussed, Ma huang is a very safe herb. The literature reviewed in HSA-30C3 failed to reveal any publications about either toxic effects or side effects of Ma huang, and pivotal reviews, such as that of Kalix (1991; see HSA-30C3, page 20) indicate that adverse effects need not be expected. This agrees with other significant literature on the safety of ephedrine itself (HSA-30C3, page 17 et sequens).

It also agrees with the "clinical" experience acquired over a period of 2½ years by about 30 companies selling genuine Ma huang-based products for use as an aid to weight loss. Statistics on both safety and efficacy (in helping weight loss) are being compiled with a view to publication, but the preliminary evaluation shows the following:

A total of 31,040,420 capsules were used from several sources, but in all cases the "genuineness" of the Ma huang was confirmed analytically. This corresponded to 10,346,806 user days, or expressed in terms of the average duration of use (6 weeks), the products were used by 246,000 persons for 6 weeks each.

During this period, there were no formal adverse effects reported. Several patients using one particular product noted that they seemed to bruise easily; the causal relationship with the product they were using was obscure, but this particular product was found to contain another Chinese herb, Bai zhu, which according to Chinese sources and some literature references may on rare occasions after longer use cause some ease of bruising. No further complaints of this nature were heard when the Bai zhu was eliminated.

There were a number of occasions when dosage had to be adjusted or the administration scheme changed because users perceived typical ephedrine effects. This usually related to difficulty in falling asleep at night, which was rectified by taking capsules earlier in the day, for example at 4:00 pm. Occasionally, dosage was reduced because users noticed their heart beating more strongly! The blood pressure was measured regularly in many users, and few changes were seen. One volunteer invariably responded with a headache when given one single capsule! This was attributed to absolute intolerance to the product being tested, and was considered to be a food-type allergy rather than an ephedrine effect.

The evaluation has also indicated that the products improved the success rates of the various weight loss programmes being followed.

Thus conservatively, observation of over 200,000 users of products based on genuine Ma huang has failed to reveal any concern that Ma huang is unsafe or toxic, and results in terms of efficacy confirm those reported in numerous studies performed with ephedrine itself, alone or in combination with methylxanthines (HSA-30C3, pages 11 - 16). In short, Ma huang is a valuable aid to weight loss; it improves compliance with dietary programmes and results in a greater rate of short and long term success.

The fake products:

A number of products supposedly containing Ma huang are, in fact, fakes (see, for example, Pardoe et al., 1993, cited in HSA-30C3). These fake products usually contain ephedrine (in pure form), sometimes with other substances (e.g. phenylpropanolamine). The motivation for these scams is economic; genuine Ma huang is expensive, and a kilogram of ephedrine mixed with an innocuous cheap herb can make 50 kilograms of fake Ma huang for less than the price of 5 kilograms of genuine material! A further economic motivation arises from the FDA Import Bulletin of June, 1992, which has considerably restricted the imports of genuine Ma huang, but which has had no effect whatsoever on the profusion of products available in the marketplace.

The knowledge of how easy it is to convert ephedrine into methcathinone has also gradually trickled down to the less scrupulous "entrepreneurs" in society! Even a minor degree of conversion of the ephedrine used in a fake Ma huang product into methcathinone would give a product with dramatic effects, not necessarily displeasing to the user, and certain to result in repeat sales for the enterprise selling the product. It would also be certain to result in abuse syndromes!

To date, and to our knowledge, there are only two reports of serious adverse effects that are sufficiently documented to have some degree of credibility, and one of them, which related to an incident of cerebral haemorrhage, occurred in a person who was using a fake product that contained pharmaceutical grade ephedrine, phenylpropanolamine and caffeine (though labelled as containing Ma huang).

This case is *sub judice* and cannot be discussed, but it should be noted that though phenylpropanolamine is freely sold "over-the-counter", it appears to represent a significant degree of risk, having been implicated in a number of cases of cerebral haemorrhage associated with drug-induced vasculitis (HSA-30C3, page 21).

The second case that has a degree of credibility was reported in the New York Times of 14 July, and the facts given in the article have been confirmed; a user of a product termed Lite and Rite Formula No. 1 did indeed develop a psychotic syndrome, similar to the syndrome frequently seen in amphetamine users, after a relatively short period of time.

The product concerned was not analysed; since it stated "Ma huang" on the label, it was assumed to contain Ma huang! However, in a search of the scientific literature, covering the period up to late 1992, there were only 23 cases of psychosis due to ephedrine itself (HSA-30C3, pages 18 - 20). The syndrome that all had in common was characterized as a paranoid psychosis with delusions and auditory hallucinations in a setting of clear consciousness. A prevailing factor was long-term use of ephedrine (up to 30 years) with a recent history of increasing dosage; the daily dose prior to development of the psychotic episode averaged 880 mg (calculated from the original cited publications) and was as much as 5400 mg in one case!

The entire scientific literature for Ephedra herb, going back to the 19th Century, and the traditional literature (to 3100 B.C.), reveals only one vague report of a similar adverse effect with Ma huang, which is so anecdotal, missing all pertinent facts, that it can be discounted (HSA-30C3, page 17 et sequens).

It appears to be just about physically impossible to abuse Ma huang in such a way that a psychosis could develop. In the first place, genuine Ma huang contains a mixture of alkaloids with dissociated effects; ephedrine and pseudoephedrine predominate in ratios that are characteristic of the species and the area grown, and while pseudoephedrine has more pronounced peripheral effects, it has much less central effect. The other alkaloids, up to 10 in number, generally only constitute about 10% or less of the total. In the second place, the dosage regimen required for Ma huang to produce similar effects would be several ounces per day for a long period of time, not the 6 capsules per day reported!

Theoretically, of course, use of a mono-amine oxidase inhibitor simultaneously with one of the stronger Ma huang products could result in some adverse effects, but there are no literature reports of such incidents. Furthermore, yohimbe (active principle yohimbine) has also been used in weight loss products, and yohimbine does have some MAOI activity. No competent herbalist or pharmacognosist would, however, consider using Ma huang and yohimbe in combination.

While the fakeness of the product implicated in the first case has been documented, no effort was made to sample and analyse the product implicated in the second case, which is regrettable, since the case history is consistent with the presence of either amphetamines, methamphetamine or methcathinone.

A final point on fake products is that the biological behaviour is different; they show more rapid absorption and greater initial effects, even when they only contain ephedrine. In terms of pharmacodynamics, genuine Ma huang has a very acceptable profile.

Availability of ephedrine:

Ephedrine tablets (25 mg) are freely available OTC products in the United States. Ephedrine is also a constituent of numerous OTC cough and cold remedies. During 1991 and 1992, a total of 555,215 kilograms of ephedrine were imported, of which 360,352 kilograms was ostensibly converted into pseudoephedrine. Thus leaving 194,863 kilograms of ephedrine available for direct use as such. Based on 100,000 kilograms per year, and an average daily dosage of 150 mg, this corresponds to 666,600,000 patient days of therapy, or placed in terms of treatment periods of 6 weeks per patient, nearly 16 million treatments.

It is, of course, known that a significant proportion of the ephedrine traded in the United States is eventually used for illegal purposes, namely the conversion to methamphetamine and, more recently, methcathinone. However, a large proportion of the material which is imported and not used industrially for manufacture of pseudoephedrine must still be used as the product itself, either as a bronchodilator or as a cheap and freely available nonaddictive stimulant. It is therefore surprising that there are few reports of adverse effects due to this major use of ephedrine, and that no concerns have been expressed about its use (the only concerns noted have been about the illicit use of ephedrine purchased in tablet form to make the controlled substances identified above).

Furthermore, no proposals have been made to restrict the sale of OTC ephedrine at Federal level, though several States have limited its availability, not on grounds of its abuse potential (which is considered negligible) but in connection with its use as a precursor for synthesis of methamphetamine and methcathinone.

Import Bulletin 66-B62, dated 25 June, 1992, revised 26 June, 1992:

It can be contended that this Import Bulletin, by restricting the imports of Ma huang, has caused a proliferation of fake products; such fake products are not necessarily faked by the actual manufacturer of the capsule or tablet, since there is also a considerable amount of fake Ma huang traded, and purchasers without sophisticated equipment and expertise may be unable to distinguish between a genuine and a fake Ma huang.

However, the Import Bulletin was also grossly inaccurate in a number of respects:

1) Joint fir is not Ephedra sinica, but an indigenous North American Ephedra (usually E. nevadensis). Since USDA sponsored efforts some 60 years ago to introduce Ephedra sinica and other foreign Ephedra species in South Dakota, it is likely that some hybridization has occurred.

2) The Import Bulletin incorrectly states that there is no known food use for this herb. In fact, there is a long history of food use in both North America and elsewhere, predating 1958 (see HSA-30C3), and at one time, teas prepared from Ephedra were more popular in the Western United States than coffee. It is significant that the Import Bulletin fails to mention "Mormon tea" as another name for Ephedra.

3) The Import Bulletin incorrectly states that ephedrine is obtained from the stems and roots. Ephedrine is obtained only from the stems (which also provide pseudoephedrine); the roots are used to lower blood pressure in Chinese medicine. They contain ephedradines and similar substances, but no ephedrine.

4) The Import Bulletin fails to mention the fact that Ma huang contains a mixture of alkaloids.

5) The Import Bulletin refers to ephedrine as a strong, reactive alkaloid; the correct term is mild and non-addictive (HSA-30C3, page 17).

6) The Import Bulletin states that ephedrine should only be used on the advice of a physician. This is at variance with the label directions in CFR 341.76, which are clearly directed at those who wish to self-medicate.

This Import Bulletin should be withdrawn. It is not based on demonstrable facts, is pertinently untrue in several respects, and it does not conform to the consensus of scientific opinion.

File: HSA-30C3
(Revision and expansion
of file HSA28SE3)

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SPENCER-JONES INC
TECHNOLOGY TRANSFER [illegible]

13 Donegani Avenue, Suite 30[illegible]
Pointe Claire, Quebec
Canada H9R [illegible]

Tel (514) 383 5555
(514) 453 [illegible]
Fax (514) 453 [illegible]
[illegible]

EPHEDRA (MA HUANG) IN NUTRITION AND HEALTH.

A review of the facts as reported in the literature, with Executive Summary and Conclusions.

NOTE: Literature available on this topic extends to well over 1000 scientific publications and reports. For the sake of simplicity, only a small selection of these publications has been cited, but further references on specific topics can be provided on request.

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Motivation:

A risk:benefit evaluation of the known facts about Ephedra herb and ephedrine in synthetic and natural forms for use in weight loss programmes indicates negligible risks and substantial benefits, both in terms of health and in terms of health care costs. Approximately 30% of the health care costs of the nation go to cover the expenses involved in treating diseases caused by, or associated with, excess body weight. Reduction of these expenses by as little as 1% represents savings of billions of dollars.

EPHEDRA HERB IN NUTRITION AND HEALTH

Executive summary and conclusions:

Ephedra, also known as Herba Ephedrae and *Ma huang*, has been known to mankind for at least 20,000 years, and it has at various times been used as food, in beverages and for healing purposes. The benefits attributed to this herb have been many, but they all relate to health and wellbeing in a positive sense.

Ephedras are among the oldest and most primitive of plants, scientifically described as gymnosperms, and are leafless

except for tiny scales at the joints. The genus includes more than 40 species world-wide. They grow by preference in arid regions, and possibly by virtue of their widespread distribution, almost every culture has a history of their use which persists to the present day. They are also important in animal nutrition in several areas of the world, both for livestock and for wild animals, and thus may occupy an important position in the food chain in areas where they are indigenous.

Their use in traditional medicine goes back at least 5000 years, the main geographical area for these uses being the Far East, particularly China and India, but even in North America there are several hundred years of tradition underlying the use of Ephedra as healing herbs or in refreshing drinks. Though their main historical healing virtues have been associated with respiratory disorders (they were specifically used as decongestants and mucolytic agents), they have recently been found to possess considerable value as adjuncts to *healthy eating* and aids to weight loss. In this respect, medical research into the properties of ephedrine, the main alkaloid present in the Ephedras, has revealed the scientific basis for their use and has done much to explain the quite startling efficacy of herbal remedies based on Ephedra in induction of weight loss.

In particular, recent research has substantiated the view that ephedrine, whether in pharmaceutical form or in the natural form as a herbal remedy, is quite possibly the most appropriate, most effective and safest aid to weight loss. In fact, in the form of the natural herb, ephedrine appears to possess the intrinsic pharmacokinetic properties of slow and smooth absorption which go even further to enhance efficacy and safety.

As noted, ephedrine, and by both extension and directly herbs containing this substance (the Ephedras), has been shown to possess considerable merit as a treatment which facilitates weight loss. The efficacy is increased by combination with other natural substances termed methylxanthines, particularly caffeine, without concomitant increase in the risk of side effects.

Though the best results have been reported when this treatment is administered together with a low calorie diet, use of ephedrine in patients who are free to select their own food (the unrestricted diet) also results in weight loss at a moderate rate.

The action of ephedrine and herbs which contain this substance is shown to be an increase in thermogenesis with increases in Resting Metabolic Rate, increased lipolysis, and in some cases, particularly at higher doses, suppression of hunger and sensations of increased wellbeing. In practical terms, patients losing weight who use ephedrine show significantly increased rates of weight loss, and a greater proportion of the weight lost is from stored fat. The corollary to this, which has also been shown clinically, is that such patients retain lean body mass, and the administration of ephedrine thus has a protein sparing effect. Though it has not been specifically investigated, it also appears that patients on low calorie diets who use ephedrine or herbs containing ephedrine exhibit better compliance, in that there are fewer drop-outs, and are also more likely to reach their target weight.

The dosage levels at which effects are obtained is low, and doses high enough to result in central stimulation do not appear to improve the rate of weight loss, though they may improve the subjective sense of wellbeing of the patients. Since the effects are obtained through modulation, or normalization, of existing mechanisms in the human body, and at dosage levels at which ephedrine itself has no direct actions, the use of ephedrine for this purpose may be considered physiological and not pharmacological, and can be compared to the modulating and

normalizing effects of many micronutrients. In fact, the effects of ephedrine at the levels used compare with the effects of high protein diets, and if herbs containing ephedrine were more widely distributed in nature, arguments could be mounted for classification of ephedrine as a beneficial, if not essential, nutrient. The widespread consumption of Ephedra herbs by wild animals and the postulated beneficial effects of these herbs when used as fodder by farm livestock could also indicate an important role of the Ephedraceae in various ecosystems.

No concerns have been expressed about the safety of ephedrine under normal conditions of use; the only reports in the literature of unusual effects relate to the development of psychoses in patients who abused ephedrine-containing products by taking massive doses over long periods of time. Such occurrences cannot be considered as true adverse effects, and it is noteworthy that all symptoms associated with these events rapidly disappeared after the abuse ceased, without any lasting psychological or physical damage. None of the studies reviewed in this document (or those examined but not included) have reported any undue hazard associated with use of ephedrine in reasonable dosages. Concerns of theoretical nature have been discussed and eliminated as of no practical significance, and a number of scientists quoted have stated that though ephedrine is safe, even the theoretical concerns about it could not apply to herbs containing this substance naturally. This latter point has been substantiated by a literature review of references to Ephedra herb, which likewise failed to reveal any safety hazards associated with use of this herb in an appropriate fashion.

The beneficial effects seen with ephedrine in the treatment of obesity and weight problems are achieved at low dose levels, and for this reason, use of herbs containing natural source ephedrine is not only a logical alternative to pharmaceutical forms of ephedrine, but may even be more desirable.

The rationale for this statement lies in the need to maintain levels of ephedrine at the active sites (mainly the synaptic gaps) for long periods. Most pharmaceutical forms are designed to rapidly release their active constituents, so that levels at the active sites fluctuate with the periodicity of the administration. However, active components of herbs are generally released only slowly, and over long periods of time. While a rapid release of ephedrine is undoubtedly desirable for the relief of congestion of the upper respiratory tract, which is the indication for which OTC ephedrine tablets are marketed, it is not desirable for the stimulation of thermogenesis and lipolysis in patients who wish to lose weight. Thus in the latter case, a genuine herbal product which smooths the absorption over a longer period is preferable and could be much more effective.

That this is not only theoretical may be adduced from studies of fake and genuine herbal products, where the onset of action with a fake product (that is, a product which was claimed to contain Ma huang, but actually contained pharmaceutical grade ephedrine, caffeine and phenylpropanolamine) was rapid and dramatic, but short-lived, in comparison with a genuine product.

Historical perspectives:

Ephedra . . . . . has been used for thousands of years in the East (Stuart, 1979).

The oldest current record of man's interest in Ephedra dates back approximately 20,000 years, to the burial of a Neanderthal individual in what is now Iraq (Lietava, 1992). This early ancestor of ours was buried with a number of plants, including Ephedra altissima, and knowledge of the customs of the Middle Paleolithic period, sparse though it is, indicates that this Ephedra must have had considerable significance during life to have merited being interred with the deceased.

Under the name Ma huang, Ephedra has traditionally been used as an invigorating tea or infusion with beneficial effects on respiration in China for more than 5000 years (Stuart, 1979), and the earliest written reference to its use and properties is attributed by some experts to the Emperor, Shen Nung (circa 3100 B.C.) in what may have been the first ever Pharmacopoeia, the *Ben Cao Chien* (others claim that the Shen Nung Ben Cao Chien did not appear until about 100 B.C.). This work was substantially revised and enlarged by Li Shih-Chen (1596). Chinese use of Ma huang (which is correctly the stems of the plant) presently encompasses relief of dyspnoea, the exploitation of the thermogenic properties, the promotion of diuresis and the decongestant properties (Ou Ming, 1989). The roots of the plant also have specific uses, which are distinct from those of stems and leaves.

The Indo-Aryans knew Ephedra as an edible plant that gave strength and happiness, and combated exhaustion (Mahdihassan, 1981). Though Indo-Aryans traditional believed that substances conferring longevity were mainly inorganic, Ephedra was considered as a food with similar beneficial properties (Mahdihassan, 1984), and there is strong evidence that the Rigveda references to *soma* actually describe Ephedra juice (Mahdihassan and Mehdi, 1989). If the Shen Nung Ben Cao Chien was indeed not written until about 100 B.C., then the honour of being the first written reference to the use of Ephedra may fall to the Rigveda (circa 1500 B.C.).

Soma, according to the Rigveda, was the drink of longevity which was even given to newborn infants; this Aryan custom was later to be followed by the Romans, and is still practiced among the Parsee of Bombay and in parts of Iran. Lewis and Elvin-Lewis (1977) also report a long history of use of the dried stems of Ephedra gerardiana in Northern India and Pakistan.

Ephedra was wellknown to the Romans, and was clearly described by Gaius Plinius Secundus in 77 A.D. (see Rackham et al., 1956 - 1966) in his *Natural History*, a work that encompassed 37 volumes, of which 12 dealt solely with the healing properties of plants! It was apparently not widely used in Europe after the times of the Romans (Moritz, 1953), though sporadic references do occur in medieval European literature; Gerard (1597), for example, refers to Herba Ephedrae (presumed to be Ephedra fragilis) as the "Great shrubbie sea Grape".

However, in North America, historical Amerindian use of Ephedra species is well-documented (Moerman, 1986), and includes use of the roots to make bread (Rose, 1972) as well as the stems to make tea (Tyler, 1982). The early settlers may have adopted the latter custom from observation of the Indians, or may have learnt the virtues of such teas from early Chinese immigrants, since during the last 150 years, various Ephedra species have enjoyed use in North America as herbal teas, under names as varied as Mormon Tea, Teamster's Tea, Settler Tea, Squaw Tea, Cowboy Tea, Canutillo, Popotillo, Desert Herb and Ma Huang (Saunders, 1920; Kowalchik and Hylton, 1987). To quote from Saunders (opus cit.):

> *Throughout the arid and semi-desert regions of the Southwest from New Mexico to Southern California, a peculiar plant called* **Ephedra** *by the botanists is abundant. There are several recognized species but all have so strong a family resemblance that in popular parlance they are lumped as one and spoken of as Desert Tea or Teamster's Tea. . . . . Desert Tea was first adopted by the white explorers and frontiersmen as a medicinal drink, supposed to act as a blood purifier and to be especially efficaceous in the first stages of venereal diseases; but its use at meals as an ordinary hot beverage in substitution for tea or coffee is by no means*

uncommon, and cowboys will sometimes tell you they prefer it to any other.

Though Ephedra was also used conventionally as a herb or dietary supplement, or even as food, the pleasant, piney tea, frequently prepared from Ephedra trifurca (Lewis and Elvin-Lewis, 1977) was widely used by Mexicans, Indians and settlers alike, even to the extent of regularly being served in brothels ("Whorehouse Tea")!

In conclusion, therefore, one may safely say that the Ephedra herb has a long and well documented history of use, both in food applications and for its healing properties. These uses have not given rise to any cautionary notes on adverse effects, and none of the historical documents that are still available make any reference to negative aspects related to ingestion of Ephedra in either native state or processed form.

Comparative nutrition:

Ephedra not only has a long history of use as a food and a traditional healing plant, but it has also played important roles in animal nutrition. According to the USDA, in the 1930's (USDA, 1937), Ephedra nevadensis and Ephedra viridis were the most important forage ephedras in the United States, and they were described as palatable to all classes of livestock. There are no reports that consumption of Ephedra has adverse consequences for livestock, even at high levels, and in Yugoslavia consumption of Ephedra campylopoda by sheep is considered to increase yields of milk (Kovacevic et al., 1974). Investigation of this particular plant revealed only 6% crude protein but high digestible energy (opus cit.), and with our current understanding of the mode of action of the ephedrine-group alkaloids found in the Ephedraceae, there is little doubt that use as animal fodder would increase the Food Conversion Efficiency of domestic livestock. This would improve milk yields, and also give better rates of weight gain, with leaner carcasses, in meat animals.

Wild animals also consume various species of Ephedra freely. For example, Neotoma devia, a species of woodrat indigenous to Northern Arizona, eats predominantly Ephedra epidermis (Dial, 1988), while paleozoological studies have shown that the diet of the Shasta ground sloth, Nothrotheriops shastense, an extinct species from Arizona, contained large amounts of Ephedra nevadensis (Mormon Tea) and was thus not vastly different from the diets of extant desert herbivores (Hansen, 1978). Other studies have shown that the population dynamics of certain rodents in Mongolia correlate directly with changes in growth patterns of indigenous Ephedra species, denoting the importance of these plants as a food source (Knyazev et al., 1991).

An interesting curiosity is that when given free choice, the honey-bee (Apis mellifera) prefers pollen from Ephedra mellifera (Schmidt and Johnson, 1984). Pollen analysis has also shown reliance of bees on Ephedra species in other arid parts of the world (Riciardelli d'Albore, 1980).

Ephedra in modern times:

Though we know nothing of the uses to which Stone Age man put Ephedra, we may assume that he used it for some healing or nutritional virtue, since these two facets of its use are reflected in the Chinese and Indo-Aryan traditions respectively.

The Indo-Aryans viewed Ephedra as a food that vitalized, and this attribute of the herb was also the main reason why the value of Ephedra as an enervating tea-like drink was recognized in 19th Century North America. Amerindians, though they also recognized, and utilized, this aspect of the herb, pragmatically used the roots as a staple food with no particular virtues

implied. Both these nutrition-related aspects are seen in current food uses of the herb. For example, Tanaka (1976), who classifies the Ephedras as edible (food) plants, summarizes the various ways in which they are used as preparation of drinks from the stems, use of seeds to make flour and use of the fruits as such. More recently, Ephedra (as Ma huang) became popular as a non-toxic and non-addictive substitute for caffeine in energizing drinks and products (Dharmandra, 1984), and over the last 15 years hundreds of Ephedra-based products have entered the marketplace for use as such products.

Despite the fact that most users of Ephedra-based products consume them for the energy and vitality boosting effects, as an alternative to tea or coffee, other nutritive uses have not been neglected, and Ephedra continues to be regarded as a conventional food in various parts of the world. For example, the CSIR (1952) identified Ephedra gerardiana as one of the resource plants of India, and noted the food uses of the fruit, while Katiyar et al. (1990) also report that the berries from Ephedra gerardiana are normal dietary constituents for tribes in the North-Western range of the Himalayas. Certain types of regional foods rely on Ephedra (Beketaeva et al., 1979), and the herb has also been characterized as possessing a harmonious combination of trace elements, vitamins and other biologically active substances in ratios optimal for a human organism (Gerasimova and Barelko; 1980). Interestingly, among desert plants, Ephedra species have extremely high Vitamin C levels (150 mg/100 grams), which make them a major contributor to vitamin requirements of humans subsisting on the local food flora (Grebinskiĭ and Yaroshkin, 1953).

Thus the Indo-Aryan attitude to Ephedra has persisted through to modern times, and this herb continues to be widely used for its food aspects alone. In fact, it could be postulated that use of Ephedraceae as food may favour survival in harsh climates (Vallerand, 1993), firstly because of the thermogenic effects (protection against cold) and secondly because of protein-sparing effects (improved utilization of available food).

The Chinese viewed Ephedra solely as a healing herb with merit in the treatment of respiratory conditions (though they also used the roots, which contain anti-hypertensive substances, for other purposes), and this aspect of the Ephedra herb finally drew the attention of scientists in the late 19th Century. By the mid 20th Century, Ephedra, mainly of Chinese and Indian (now Pakistan) origin, had become an important source of the alkaloids ephedrine and pseudoephedrine, much used in cough and cold remedies.

The medical uses of these alkaloids can thus trace their development back to the original isolation of ephedrine itself from Ma huang towards the end of the 19th Century, and the subsequent thorough investigation of its properties in the early 20th Century (Chen, 1925; Gaignault et al., 1982).

Ephedrine and pseudoephedrine are now mainly manufactured synthetically, since their use in a variety of over-the-counter remedies requires amounts of raw materials that could never be produced from natural sources; in fact, pseudoephedrine and ephedrine together rank close to the top of pharmaceutical raw material manufacture in terms of tonnage, which may serve to illustrate the extent of their use. However, much is known about the compositions of the various members of the genus from research performed at about the time of the Second World War (see for example, Alberti, 1939), and from more recent studies in a large number of countries (see for example Abdel-Wahab et al., 1961) where extraction of natural products remained a viable alternative to chemical synthesis.

The exigencies of the early half of the 20th Century also stimulated attempts to cultivate Ephedra species in North America, and the acquisition of considerable amounts of agronomic and compositional data (Christensen and Hinde, 1936, 1939). These attempts were successful, but also revealed that Ephedras growing in the wild generally give higher yields of alkaloids. Another result of the studies was the naturalization of foreign Ephedras in North America, so that in addition to the indigenous American Ephedras, Ephedra sinica and other exotic Ephedras may also now be found in the wild in North America.

The situation changed significantly in the early 1980's. Up to that time, Ephedra was viewed in two distinct ways; the protagonists of the Indo-Aryan tradition, knowingly or unknowingly, merely used Ephedra as an invigorating food, without really being aware of the properties of the ephedrine-group alkaloids, while the supporters of the Chinese tradition either viewed Ephedra as a potential phytopharmaceutical plant to be processed into sources of raw material for the pharmaceutical industry or as a gentle, natural and non-toxic alternative to ephedrine and pseudoephedrine when a decongestant was required.

In fact, though Ephedra as a herb is practically devoid of toxicity (Dharmandra, 1984; Minamatsu et al., 1991) and can only be abused under the most bizarre circumstances, both ephedrine and pseudoephedrine are themselves of low toxicity, and when presented in pharmaceutical dosage forms they act much more rapidly. Since self-medication sufferers from respiratory disorders generally require rapid relief for acute episodes, the pharmaceutical products have gradually overwhelmed the natural alternative in this particular marketplace.

However, a new use for Ephedra herb was perceived at this time, and far from being a disadvantage, the slower absorption but longer lasting duration of effect from the natural product proved to be a major advantage for this particular use, namely the use as a natural aid to promote weight loss, either alone or as and adjunct to diet programmes. The extremely low incidence of unwanted reactions (estimated in retrospect at less than 20 per 100,000 patients), which were furthermore never of serious nature, also favoured the use of the natural herb for this indication.

Ephedrine in pharmaceutical presentations had been used as an anorexic agent in the 1970's (Sapeika, 1974; Stauffacher, 1975), and though it proved safer than phenylpropanolamine and the amphetamines (Glick et al., 1987; Forman et al., 1989), it was not superior in terms of appetite (hunger) suppression, which was the only mechanism that was thought, at that time, to be of importance. It was therefore little used, until a major research group showed that it possessed pronounced thermogenic properties and became particularly effective when combined with caffeine (Malchow-Moller et al., 1980, 1981; Roed et al., 1980; Stockholm and Hansen, 1983). It was later shown that the thermogenic effect, far from fading away with time (tachyphylaxis), actually became more pronounced (Astrup et al., 1985, 1986).

Though it took some time for these findings to cross over from the strict world of pharmacology to the distinct world of the herbalist, their significance was eventually realized, and a new use for Ephedra herb developed (Bergner, 1993; Jones and Egger, 1993).

Currently, much of the literature and research findings supporting the use of Ephedra herb as an adjunct to weight loss programmes is based on studies with the active principle, ephedrine itself, and these studies also provide the explanation for the synergistic effects seen when Ephedra is taken together with one or more herbs containing caffeine and/or salicylates. Thus, though explanations of mechanisms and actions are derived from studies of

the pure constituents, they can logically be extrapolated to the use of the constituents in the form of the natural herbs. This also applies to evaluation of safety, and the only rider to be applied is that absorption of active constituents from the natural herbs is generally slower and shows a smoother pattern.

Ephedra and ephedrine in weight loss:

Malchow-Moller et al. (1980, 1981) published reports of the first study in which a product containing ephedrine was shown to significantly increase weight loss in patients on a diet, in comparison to patients who received only a placebo product. Their double-blind study encompassed 132 patients who were 20% - 80% over their ideal weight, randomized to 3 groups receiving either ephedrine with caffeine, diethylpropion, or placebo. All patients were also given a 1200 kilocalorie diet. A total of 108 patients completed the study, which lasted 12 weeks, and median weight loss in the two treatment groups was significantly better ($p < 0.01$) than in the placebo group:

Placebo - - - - - - - - - - - 4.1 kg in 12 weeks (n = 31)

Ephedrine plus caffeine - - - 8.1 kg in 12 weeks (n = 38)

Diethylpropion - - - - - - - - 8.4 kg in 12 weeks (n = 39)

Interestingly, there were more drop-outs in the placebo group, and no serious adverse effects were seen in the treatment groups.

The clinical applications of ephedrine were followed, *inter alia*, by Pasquali and his team. An initial study in unselected patients (Pasquali et al., 1985), failed to show significant differences in weight loss between patients receiving placebo and those receiving ephedrine (75 or 150 mg per day), but indicated that ephedrine could be of value under certain conditions. The investigators therefore performed a double-blind cross-over randomized study (Pasquali et al., 1987) in 10 selected adult overweight and obese (body mass index greater than 27) women who had been adapted to low-energy intake for a long period of time and who had plateaued (shown difficulty in losing weight with conventional hypocaloric treatment). Combined with diet therapy (1000-1400 kcal/day), L-(-)-ephedrine hydrochloride (50 mg three times a day per os) or placebo were administered daily before each meal, after a period of stabilization with diet only for 1 month. Each pharmacological treatment lasted for 2 months. Weight loss was significantly greater during the ephedrine treatment period than during the placebo period (2.41 ± 0.61 kg vs. 0.64 ± 0.50 kg, $p < 0.05$). None of the patients presented clinically important side-effects.

In a further study (Pasquali et al., 1992), performed in 10 obese subjects on a 6-week very low calorie diet programme (1965 kJ, 60 g of protein, 45 g of carbohydrates). L-(-)-Ephedrine hydrochloride (50 mg three times a day by mouth) or placebo were administered during 2-week periods (weeks 2 - 5 of the VLCD programme) in a randomized, double-blind, cross-over design.

Five subjects began with ephedrine and five with placebo. The results were analysed separately in the two groups. Though differences in rates of weight loss were not significant, ephedrine therapy induced a significantly lower daily urinary excretion of nitrogen (and, consequently, a better nitrogen balance) with respect to placebo, independently of the drug sequence. The resting metabolic rate (oxygen consumption, ml STP/min) fell significantly during the very-low-calorie diet in both groups, but this effect was partially and significantly prevented by administration of ephedrine. Diet therapy significantly reduced 24 hour urinary levels of vanillylmandelic acid and homovanillic acid,

which, however, increased to pretreatment values during ephedrine treatment. No significant effects were shown on 24 hour urinary concentrations of adrenaline, noradrenaline and dopamine during the very-low-calorie diet and/or ephedrine treatment. Both the diet and the ephedrine therapy were well tolerated and no adverse effects were seen.

The results of the reported studies have been interpreted to mean that ephedrine can play an important role in the treatment of patients in whom a reduced capacity for energy expenditure may complicate, or have contributed to, their obese state (Pasquali and Casimirri, 1993). The nitrogen-sparing effect is, however, also seen in patients who do not respond with significantly increased rates of weight loss, and this in itself may be sufficient argument for adjunctive ephedrine treatment.

The topic of reduction of capacity for energy expenditure in the obese was also investigated by Geissler (1993), who compared the effects of ephedrine with and without caffeine or aspirin in lean and obese volunteers. The obese subjects, who initially had poor thermic response to food, showed improvement or normalization when given any of the treatments. In a restricted subpopulation, Molnar (1993) also showed that some subjects fail to respond to thermogenic drugs; metabolic studies with ephedrine alone (1 mg/kg lean body mass) or with aminophylline (3 mg/kg lean body mass) in obese children showed that some children did not respond to treatment with an increase in resting energy expenditure.

Though it had previously been shown (Astrup et al., 1985, 1986) that the thermogenic properties of ephedrine did not exhibit tachyphylaxis, but actually increased with time, the clinical significance of this finding was uncertain. However, Toubro et al. (1993) administered ephedrine (3x20 mg per day), caffeine (3x200 mg per day), ephedrine with caffeine (same dosages), or placebo to groups of 45 patients on 1000 kilocalorie diets for 24 weeks. All treatments improved weight loss over placebo, and were well tolerated. There were no withdrawal symptoms when treatment ceased. These authors also confirmed the conservation of lean body mass in a separate double-blind 8-week study.

In volunteers, Astrup and Toubro (1993) showed that the combination of 20 mg ephedrine with 200 mg caffeine produced a better thermogenic response than ratios in any other combination, or the active substances separately. The combination also had pronounced effects on glucose metabolism, increasing plasma glucose, insulin and C-peptide concentrations. In acute studies, systolic blood pressure showed small increases, though diastolic blood pressure was unaffected, as originally noted by Martin et al. (1971). However, during chronic administration, thermogenic effects persisted while haemodynamic and metabolic effects subsided.

The potential for use of synergistic mixtures of ephedrine with methylxanthines (such as caffeine) or with inhibitors of prostaglandin synthesis (such as aspirin) in the treatment of obesity has also been examined from the safety aspect, both in the short term and the long term. For example, Daly et al. (1993) gave a mixture of ephedrine (75 or 150 mg/day), caffeine (150 mg/day) and aspirin (330 mg/day) to obese humans (mean BMI 37.0) on unrestricted diets in both randomized double-blind cross-over placebo-controlled studies lasting 8 weeks and in open studies lasting 7 - 26 months. These investigators, in a very comprehensive study, failed to find significant changes in heart rate, blood pressure, blood glucose, insulin or cholesterol levels in any subject, and the incidence of subjective side-effects was identical for the treatment and the placebo groups. With regard to efficacy, though the volunteers used were not placed on diet, mean weight losses in the 8-week treatment periods of the double-blind study exceeded 3 kg for the treatment group, and were significant in

comparison with the placebo group. In the open study, weight losses averaged 1 kg per month, except for one volunteer who lost 66 kg in 13 months.

The mode of action of ephedrine, and its synergistic effects with caffeine and aspirin, have been reviewed or postulated by various scientists. Landsberg and Young (1993) adopt the position that since the activity of the sympathetic nervous system may be reduced in obesity, improvement of the activity to normal levels is physiological, rather than pharmacological, and use of ephedrine, an indirect-acting sympathicomimetic, does nothing more than restore normal catecholamine function. In this respect, therefore, it differs in no way from the effects of high protein diets, or consumption of foods containing natural thermogenic substances. These authors also note that ephedrine may be particularly useful in combatting the weight gain that usually follows cessation of smoking, since this is also associated with impaired catecholamine function.

Dulloo (1993) concurs with this point of view, and notes that at levels compatible with therapeutic doses, ephedrine has little or no direct agonist activity, but mediates its effects via endogenous release of noradrenaline and adrenaline, thus essentially doing nothing more than increasing the efficiency of the system already in place in the body. He notes that this has potential positive implications for its use in the treatment of obesity, and also explains some of the obscure clinical observations reported:

1) The fact that tolerance rapidly develops to the very mild cardiovascular effects of ephedrine, but not to its thermogenic effects, suggests that adrenaline and noradrenaline released by ephedrine activate the β_3-adrenoceptors.

2) The adrenaline released is a preferential agonist for the β_2-adrenoceptors, which stimulate protein synthesis, and thus can counteract loss of lean body mass during use of low calorie diets.

In this respect, it has already been shown (Pasquali et al., 1992) that ephedrine enhances fat loss in diet-restricted fat patients and reduces loss of nitrogen.

3) Chronic stimulation of postsynaptic α-adrenoceptors by the adrenaline and noradrenaline released in response to ephedrine therapy may activate thyroxine deiodinases, leading to peripheral conversion of T_4 to T_3, which in turn may increase adrenoceptor sensitivity to the thermogenic effects of the catecholamines.

This mechanism may also partially explain why the thermogenic effect of ephedrine is increased after chronic administration.

4) Single dose studies have shown that skeletal muscle and visceral organs contribute most of the thermogenic activity after ephedrine administration, with a minor contribution from brown adipose tissue. These tissues can all be reactivated and even proliferate in response to chronic catecholamine activation.

This is a further explanation for the fact that long-term ephedrine therapy in obese women enhances the thermogenic effect.

Thus ephedrine, by exerting its effects indirectly via adrenaline and noradrenaline, generates a certain selectivity for the receptors with desirable anti-obesity effects.

Dulloo also explains the suprasynergistic effects of mixtures of ephedrine with methylxanthines (such as caffeine) and salicylates. Under normal conditions, negative feedback controls tend to inhibit catecholamine release via adenosine and prostaglandin release in the synaptic gaps, via activation of presynaptic α_2-adrenoceptors, and through stimulation of phosphodiesterase (which degrades cyclic AMP) within the cell. Inhibition of any of these feedback controls will thus enhance the thermogenic effects of ephedrine. Thus caffeine and aspirin, both of which are mildly thermogenic in their own right, and do induce lipolysis, interfere with one or more of the catecholamine control systems: caffeine inhibits cyclic AMP and reduces release of adenosine into the synaptic gap, aspirin reduces release of prostaglandins of the PG_2 family into the synaptic gap. The net result is increased catecholamine availability.

In this respect, it is interesting to note that reports of increased thermogenesis after administration of essential fatty acids have also been published (Cunnane et al., 1986; Jones and Schoeller, 1988); such administration also modulates prostaglandin metabolism (Jones, 1990), in the sense of normalizing it, which may indicate that essential fatty acid deficiency plays a greater role in causing obesity than hitherto suspected.

Arner (1993) approaches the mechanism of action of ephedrine from the lipolysis aspect. He notes that catecholamines have both lipolytic and antilipolytic effects, so that at any time there is a balance. However, it has been suggested that lipid metabolism in man is mainly controlled by inhibitory modulators, and that adenosine has been shown to reduce the sensitivity of lipolytic ß-adrenoceptors, particularly in subcutaneous fat depots. Several prostaglandins of the E-type are also potent antilipolytic agents, as are inhibitors of phosphodiesteraae. Thus the potentiation of the ephedrine effect by caffeine and aspirin may not be restricted to the synaptic gap, but may also extend into the actual fat-mobilizing mechanism.

It is noted (Dulloo, 1993) that in early investigations of the use of ephedrine as an anti-obesity agent, attention was concentrated on the central action of ephedrine in reducing appetite (the anorexic effect), but that the thermogenic and lipolytic effects now appear to be the main properties that make this substance so suitable for use as a weight loss aid. Indeed, significant improvements of rates of weight loss occur at dosage levels far below those required to achieve detectable central effects, and increasing dosage to the level at which central effects occur does not give better rates of weight loss (Daly et al., 1993).

The synergistic effects of low dosage ephedrine with caffeine are particularly impressive (Dulloo, 1993), and optimal dosage appears to be 60 - 150 mg ephedrine with 150 - 600 mg caffeine per day (Daly, 1993; Astrup and Toubro, 1993). At such levels, unwanted effects on the cardiovascular system are minimal or non-existent, central effects do not occur (other than a mild and desirable increase in alertness), and classical side effects (headache, dryness of the mouth, agitation, tremors) are not reported. Whether a slowing of gastric emptying (Jonderko and Kucio, 1991) makes a meaningful contribution to overall efficacy seems doubtful, but cannot be excluded.

While ephedrine was initially investigated in weight loss as an anorectic agent, the most recent studies have focussed on its thermogenic effects, and have shown that these are sufficiently pronounced to cause weight loss even in the absence of a formal low calorie diet plan. There has been little attention paid to the behavioural modification aspects of ephedrine therapy, though indications of increased patient compliance (fewer drop-outs) in some clinical studies suggest that the behavioural effects can be quite important. Zgourides et al. (1989) conclude that ephedrine

should be tested in a multi-dimensional programme for the treatment of obesity, with full integration of psychtherapeutic procedures of cognitive-behavioural nature. There are also strong indications that positive behavioural changes contribute to the efficacy of herbal products containing Ephedra when used as an integral component of diet programmes (Jones and Egger, 1993). For example, these latter authors, using Linear Rating Scales, showed considerable improvement in some behavioural parameters in dieting patients given supplemental Ephedra herb.

In conclusion, ephedrine, whether as the pure substance in pharmaceutical form or as a genuine herbal product based on Ephedra herb, has considerable merit as an adjunct to weight loss programmes. Part of this merit undoubtedly lies in the prevention of the decline of Resting Metabolic Rate that generally occurs with low calorie intake, but the direct thermogenic cost to the body and the stimulation of true fat loss with sparing of lean body mass is also a valuable property. The role of the central anorexic effect is uncertain, but may also be of considerable importance, since even patients not on formal diets report weight loss with ephedrine or herbal Ephedra products. This may relate as much to improved mood as to direct hunger suppression.

The safety of ephedrine and Ephedra herb:

> *Ephedrine, ... is non-toxic (Dharmandra, 1984).*
>
> *Ephedrine, mild, non-addictive drug . . . (The American Spectrum Encyclopedia, 1991).*
>
> *Side effects: Rare in therapeutic doses . . . (Gahart, 1985)*

According to Gahart (opus cit.), a normal therapeutic dose of ephedrine, intravenously, would be 150 mg per 24 hours, and at this level, side effects are rare. Those that are reported at such dose levels are, in fact, not side effects in the true sense of the word, but manifestations of pharmacological activity. Thus Gahart lists appetite suppression as a possible side effect, whereas many of the authors cited previously in this review would consider such an anorexic effect as a highly desirable main effect!

There is little doubt that overdosage of ephedrine can give an exaggerated pharmacological response, and a variety of sypmtoms may appear that are characteristic of increased tone in the sympathetic nervous system. Various Monographs and standard reference works, not cited, list these effects as usually being an extension of the pharmacological effect and thus an indication of overdosage or, in isolated cases, excessive sensitivity to the product. Such effects can include headache, restlessness, insomnia, anxiety, tension, tremor, weakness, dizziness, confusion, delirium, hallucinations, pallor, respiratory difficulty, palpitation, precordial pain (occasional) or tightness in the chest, sweating, nausea, vomiting, syncope and difficulty in micturition.

The various standard works also note that these effects are usually not serious, are transient, minimized by rest and recumbency, and that they indicate the need for adjustment of dosage.

In short, ephedrine is actually one of the safest drugs available, if not used in excessive dosage, and the few cases of exaggerated pharmacological effects that may be seen cause discomfort but no harm. The various scientists (cited in the previous section) who have studied ephedrine as a potential aid in treatment of obesity concur that side effects are minimal or non-existent at dosage levels where significant effects on weight loss, and beneficial effects on the composition of the weight

lost, are seen. If more evidence was required, there is the fact that ephedrine has now been available as a drug for more than 60 years, most of this time as an "over the counter" drug that is cheap and freely available, and that it is used annually by many millions of people world-wide on a self-medication basis.

In the United States, ephedrine is classified as a bronchodilator drug for over-the-counter human use under CFR 341.16, and the dosage which must be stated on the label, according to CFR 341.76, is 12.5 - 25 mg every 4 hours, with a maximum not to exceed 150 mg every 24 hours. Thus it is also the official opinion that 150 mg ephedrine per day is safe, and can be used without any form of medical supervision, that is, for self-medication.

Bättig (1993) has reviewed the potential for side effects with, and abuse of, caffeine, aspirin and ephedrine if widely available for self-medication as a treatment for obesity. Caffeine when used incidentally has mild cardiovascular effects (increase in heart rate and blood pressure), but these are not considered significant, and furthermore disappear on regular use. Similarly, the central stimulant effects are mild and beneficial except at excessive doses. Aspirin may act as a very mild central depressant, but again, there are no theoretical or practical obstacles to its widespread use in low dosages. Ephedrine has been contrasted with amphetamine in terms of both immediate central nervous system effects and cardiovascular effects, and was 5 - 10 times less potent in all respects. In particular, there was dissociation between the central anorexic effect and the peripheral cardiovascular effects to the extent that cardiovascular effects such as increase in heart rate and diastolic blood pressure may be minimal or non-existent at doses that show reasonable hunger suppressing effects.

However, though the amphetamine-like properties indicate a theoretical potential for abuse, animal studies have failed to demonstrate any potential for abuse or addiction, including a lack of potentiation of preferences for other substances. A review of the clinical literature likewise reveals no significant practical concern for ephedrine, with only 23 cases of abuse syndromes covering the period up to 1990. Most of these cases were reviewed by Whitehouse and Duncan (1987), and the syndrome that all had in common was characterized as a paranoid psychosis with delusions and auditory hallucinations in a setting of clear consciousness. A prevailing factor was long-term use of ephedrine (over 1 year in 80% of cases) with a recent history of increasing dosage; the daily dose prior to development of the psychotic episode averaged 510 mg!

Typically, symptoms disappeared completely within a few days of ceasing use of ephedrine, and this can be illustrated by reference to 2 cases noted by Whitehouse and Duncan (opus cit.) but originally reported by Herridge and a'Brook (1968):

Case 1 was a 65 year old truck driver who presented with a florid paranoid psychosis of two months duration. He was ostensibly receiving 3 x 60 mg ephedrine per day for chronic bronchitis. This medication was stopped while he was hospitalized, and his psychosis resolved completely within 4 days.

He then revealed that he had been taking up to 200 ephedrine (60 mg) tablets per week for some years (corresponding to 1700 mg per day), and had recently increased this dose even more. He was discharged under instructions not to take any more ephedrine and remained symptom-free.

Case 2 was a 54-year old woman, who had a 10-year history of recurrent paranoid psychosis. On questioning, she admitted to using large amounts of ephedrine for 20 years, and was currently taking 75 tablets of 30 mg per day (2250 mg per day). Ephedrine was discontinued, and the psychosis resolved in 4 days, leaving the patient a little lethargic. She was discharged, but had to be

re-admitted 4 weeks later with a recurrence. She strongly denied taking ephedrine again, but a sample of urine was positive for ephedrine.

Loosmore and Armstrong (1990) report 3 further cases from abuse of Do-Do tablets; per tablet, these contain 222 mg ephedrine hydrochloride, 30 mg caffeine and 50 mg theophylline sodium glycinate. Their first case was a 33-year old man who had been taking 30 Do-Do tablets a day for 15 years (5400 mg ephedrine per day). His symptoms resolved when he ceased using Do-Do tablets.

The second case was a 46-year old man who had been taking 9 - 12 Do-Do tablets per day for 30 years (1600 - 2200 mg ephedrine per day). His symptoms were very mild, and he had no intention of stopping!

The third case was a 36-year old woman who had taken 15 - 30 Do-Do tablets per day (2700 - 5400 mg ephedrine per day) for 15 years. She claimed that when she stopped, she became depressed and lethargic.

The occurrence of so few cases of abuse, taken with the statistics on the widely popular use of ephedrine over many decades, leads Bättig (1993) to conclude that ephedrine is essentially very safe, and could freely be used as an aid to the treatment of obesity without significant risk of either adverse effects or of abuse syndromes. In fact, the reported abuse cases serve to stress the safety of ephedrine; despite use of this substance at doses up to 36 times the normal maximum daily dose, there was no evidence of permanent harm in any of the cases described, and the symptoms resolved completely within a very short space of time. Herridge and a'Brook (1968) also note that recovery was much more rapid than that usually seen with amphetamine psychoses.

Abuse of any medication can, of course, occur, and laxative abuse is said to be not only much more common, but biologically far more hazardous for health in the long term.

It should also be noted that the mean dose level required to cause an abuse syndrome with ephedrine, at 510 mg per day, is approximately five times the mean daily dosage of Vitamin B_6 (pyridoxine) that causes neurological damage (Dalton and Dalton, 1987).

Kalix (1991) reviewed the pharmacology of the alkaloids from Ephedraceae and Catha edulis. Though he notes the compilation of cases by Whitehouse and Duncan (vide infra), he comments:

> *Due to its stimulant effect, ephedrine has some abuse potential, which, however, is considered as negligible. Therefore, ephedrine is generally a non-controlled drug . . . . . As far as the Ephedra herb is concerned, it is not used for obtaining a stimulating effect, the ratio between the concentration of the alkaloid in the plant and its potency being so low.*

A simple calculation can put this opinion in perspective:

According to various pharmacopoeial entries (such as: British Herbal Pharmacopoeia, 1983; British Pharmaceutical Codex, 1954; Martindale. 27th Edition), Ephedra contains not less than 1.25% total alkaloids, calculated as ephedrine. The pattern is characteristically 80% - 90% ephedrine and pseudoephedrine, in proportions which vary with species and geographical origin, and lesser amounts of related alkaloids. Generally, 60% or more of the total alkaloid content consists of ephedrine, except for some indigenous North American species which contain larger amounts of pseudoephedrine.

At a content of 1.25%, to achieve an intake of 510 mg, the mean daily dose of ephedrine shown to be associated with reported cases of psychotic manifestations, the abuser would have to consume 41 grams of Ephedra. Even with a 1:4 dry extract, the amount needed would still be in excess of 10 grams, and this amount would have to be consumed for considerable periods of time.

However, this calculation does not allow for the dissociation in properties between ephedrine and pseudoephedrine. The latter has much less stimulant effect, and thus larger amounts of Ephedra herb would actually be required. The exact amounts that would be needed have never been ascertained, and are likely to remain hypothetical, since there are no confirmed reports in the literature! In fact, the scientific literature contains only one negative reference to Ephedra, comprising several lines of a letter to the Editor (Siegel, 1980) which also includes references to caffeine tablets causing stomach cramps and diarrhea, and to tobacco snuff products causing sneezing and nausea. In fact, the main theme of this letter appears to be the opinion that snorting cocaine is actually safer than use of legal alternatives, and it must be considered anecdotal and unconfirmed.

A further reason for dismissing this report, which applies equally to a recent newspaper article (Burros, 1993) is that there was no product verification; the allegation was not supported by the minimum of scientific investigation required for confirmation, namely an accurate case history, full clinical findings, and most important of all, analysis of the product concerned or other confirmation of composition.

This latter point is particularly important, since it is known that "fake" products are present in the marketplace (Pardoe et al., 1993). Such products are labelled as containing Ma huang (Ephedra) but generally contain pharmaceutical grade ephedrine, caffeine and phenylpropanolamine. The motivation for vendors to deliberately misbrand is quite clear; there is a very receptive market, the fake products have rapid and perceptible onsets of action (appreciated by users), and ephedrine, caffeine and phenylpropanolamine are much cheaper than genuine Ephedra, so profit margins are attractive. However, though so far the only verified fakes have contained ephedrine and phenylpropanolamine, it cannot be excluded that some fake products actually contain controlled substances in the guise of harmless Ephedra!

It is also of concern that some fake products contain phenylpropanolamine. Though this drug is an "over-the-counter", it appears to represent a degree of risk that is unacceptable, since it has been implicated in a number of cases of cerebral haemorrhage associated with drug-induced vasculitis (Glick et al., 1987; Forman et al., 1989).

From the foregoing, it is obvious that ephedrine itself is scarcely a substance of concern with respect to either acute toxicity (effectively exaggerated pharmacological response rather than true toxicity) or long term abuse. Being freely available, it could readily be obtained by those wishing to abuse it over the long term, and it has the advantage of being cheap. On grounds of potency and pharmacokinetics alone, Ephedra herb appears immune from both acute adverse reactions and long term abuse. It is furthermore expensive, and mostly has only limited availability, both of which would restrict access by potential abusers.

References:

Abdel-Wahab, S.M., Hilal, S.H. and El-Keiy, M.A., 1960, Phytochemistry of Ephedra species growing in Egypt. Egypt. Pharm. Bull., 42, 9 - 21.

Alberti, C., 1939, Italian ephedras. Boll. chim. farm., 78, 477 - 481.

Arner, P., 1993, Adenosine, prostaglandins and phosphodiesterase as targets for obesity pharmacotherapy. Int. J. Obesity, 17, S57 - S60.

Astrup, A., Lundsgaard, C., Madsen, J. and Christensen, N.J., 1985, Enhanced thermogenic responsiveness . during chronic ephedrine treatment in man. Am. J. Clin. Nutr., 42, 83 - 94.

Astrup, A., Madsen, J., Holst, J.J. and Christensen, N.J., 1986, The effect of chronic ephedrine treatment on substrate utilization, the sympathoadrenal activity, and energy expenditure during glucose-induced thermogenesis in man. Metabolism, 35, 260 - 265.

Astrup, A., 1986, Thermogenesis in human brown adipose tissue and skeletal muscle induced by sympathicomimetic stimulation. Acta Endocrinol. Suppl., 278, 1 - 32.

Astrup, A. and Toubro, S., 1993, Thermogenic, metabolic, and cardiovascular responses to ephedrine and caffeine in man. Int. J. Obesity, 17, S41 - S44.

Bättig, K., 1993, Acute and chronic cardiovascular and behavioural effects of caffeine, aspirin and ephedrine. Int. J. Obesity, 17, S61 - S64.

Beketaeva, L.I., Alchimbaeva, A.T., Chipurin, M.M., Drboglav, E.S., Nurlanov, T.N., Vinichenko, V.I. and Yakimenko, V., 1979, [Formulation for "Meruet" apple wine]. Patent No. 644828, USSR.

Bergner, P., 1993, Botanical Medicine, The Nutrition & Dietary Consultant, June issue, page 8.

Burros, M., 1993, With some dietary supplements, what you don't know can hurt you. The New York Times, 14 July, page C4.

Chen, K.K., 1925, A pharmacognostic and chemical study of Ma huang (Ephedra vulgaris var. Helvetica). J. Am. Pharm. Assoc., 14, 189 - 194.

Christensen, B.V. and Hinde, L.D., 1936, Cultivation of ephedra in South Dakota. J. Am. Pharm. Assoc., 25, 969 - 973.

Christensen, B.V. and Hinde, L.D., 1939, Cultivation of Ephedra sinica in South Dakota. J. Am. Pharm. Assoc., 28, 199 - 209.

CSIR, 1952, Council of Scientific and Industrial Research, The Wealth of India, 11 vols., New Delhi, (published 1948 - 1976).

Cunnane, S.C., McAdoo, K.R. and Horrobin, D.F., 1986, n-3 Essential fatty acids decrease weight gain in genetically obese mice. Brit. J. Nutr., 56, 383 - 393.

Dalton, K. and Dalton, M.J.T., 1987, Characteristics of pyridoxine overdose syndrome. Acta Neurol. Scand., 76, 8 - 11.

Daly, P., Krieger, D., Dulloo, A., Young, J. and Landsberg, L., 1993, Ephedrine, caffeine and aspirin: safety and efficacy for treatment of human obesity. Int. J. Obesity, 17, S73 - S78.

Dharmandra, S., 1984, Ma hunag: the "Energy Herb". Bestways, September 1984, 32 - 35.

Dial, K.P., 1988, Three sympatric species of Neotoma; dietary specialization and coexistence. Oecologia (Berl), 76, 531 - 537.

Dulloo, A.G. and Miller, D.S., 1987, Aspirin as a promoter of ephedrine-induced thermogenesis: potential use in the treatment of obesity. Am. J. Clin. Nutr., 45, 564 - 569.

Dulloo, A.G. and Miller, D.S., 1989, Ephedrine, caffeine and aspirin: "over-the-counter" drugs that interact to stimulate thermogenesis in the obese. Nutrition, 5, 7 - 9.

Dulloo, A.G., Seydoux, J. and Girardier, L., 1991, Peripheral mechanisms of thermogenesis induced by ephedrine and caffeine in brown adipose tissue. Int. J. Obes., 15, 317 - 326.

Dulloo, A.G., 1993, Ephedrine, xanthines and prostaglandin inhibitors: actions and interactions in the stimulation of thermogenesis. Int. J. Obesity, 17, S35 - S40.

Forman, H.P., Levin, S., Stewart, B., Patel, M. and Feinstein., 1989, Cerebral vasculitis and hemorrhage in an adolescent taking diet pills containing phenylpropanolamine: case report and review of literature. Pediatrics, 83, 737 - 741.

Gahart, B.L., 1985, Intravenous medications; a Handbook for Nurses and other allied health professionals. 4th Edition, The C.V. Mosby Company, 200 - 201.

Gaignault, J.C., Marchandeau, C. and Koertge, D., 1982, Some examples of long-used medicinal plants having led to drugs still used, Part II. Actual. Chim., (5), 7 - 15.

Gerasimova, L.K., and Barelko, I.B., 1980, [Trace elements in medicinal food plants of the Kirgiz-SSR, USSR]. Fiziol. Biokhim. Kul't Rast., 12, 186 - 188.

Gerard, J., 1597, The Herball or Generall Historie of Plantes, John Norton, London. Second Edition enlarged and amended by Thomas Johnson, 1633, and reprinted 1636 [Note: translation of Dodoens' Stirpium Historiae Pemptades Sex, Antwerp, 1583].

Geissler, C., 1993, Effects of weight loss, ephedrine and aspirin on energy expenditure in obese women. Int. J. Obesity, 17, S45 - S48.

Glick, R., Hoying, J., Cerullo, L. and Perlman, S., 1987, Phenylpropanolamine: an over-the-counter drug causing central nervous system vasculitis and intracerebral hemorrhage. Case report and review. Neurosurgery, 20, 969 - 974.

Grebinskiĭ, S.A. and Yaroshkin, B.I., 1953, Vitamin C in desert plants. Dopovid L'vov. Derzhav. Univ. im I. Franka, 4, 30 - 31.

Hansen, R.M., 1978, Shasta ground sloth food habits, Rampart cave, Arizona. Paleobiology, 4, 302 - 319.

Herridge, C.F., and a'Brook, M.F., 1968, Ephdrine Psychosis. Br. Med. J., II, 160 - 161.

Ikezono, E., Takahashi, G. and Ikezono, T., 1993, A trial of thermogenic agents for further weight reduction in obese patients with weights that have plateaued. Int. J. Obes., 17, S80.

Jonderko, K. and Kucio, C., 1991, Effect of anti-obesity drugs promoting energy expenditure, yohimbine and ephedrine, on gastric emptying in obese patients. Aliment. Pharmacol. Ther., 5, 413 - 418.

Jones, P.J.H. and Schoeller, D.A., 1988, Polyunsaturated:saturated ratio of diet fat influences energy substrate utilization in the human. Metabolism, 37, 145 - 151.

Jones, D., 1990, Neglected nutrients in dietary weight reduction programmes: the essential fatty acids! The Bariatrician (Am. J. Bar. Med.), Fall 1990, 11 - 15.

Jones, D. and Egger, T.E., 1993, Use of herbs containing natural source ephedrine alkaloids in weight loss programmes. Int. J. Obes., 17, S81.

Kalix, P., 1992, The pharmacology of psychoactive alkaloids from *Ephedra* and *Catha*. J. Ethnopharmacol., 32, 201 - 208.

Katiyar, S.K., Sharma, K. and Bhatia, A.K., 1990, Composition of some unconventional Himalayan wild fruits. J. Food Sci. Technol. India, 27, 309 - 310.

Knyazev, A.V., Kiseleva, N.K. and Sokolovskaya, V.T., 1991, [Changes in the size of the population and diet of Alticola stolizkanus Blandford 1875 and Eolagurus luteus Eversman 1840 in the foothills of the Transaltai Gobi Mongolia during the last 900 years]. Ekologiya, 0, 51 - 59.

Kovacevic, J., Cizek, J. and Kurjakovic, V., 1974, [Ligneous forage plants with special reference to Euphorbia spinosa L., Ephedra campylopoda C.D. Mey and Ulmus campestris L.]. Veterinaria Yugoslavia, 23, 541 - 545.

Kowalchik, C., and Hylton, W., 1987, Rodale's Illustrated Encyclopaedia of Herbs. Rodale Press, Emmaus, Pensylvania.

Krieger, D.R., Daly, P.A., Dulloo, A.G., Ransil, B.J., Young, J.B. and Landsberg, L., 1990, Ephedrine, caffeine and aspirin promote weight loss in obese subjects. Trans. Assoc. Am. Physicians, 103, 307 - 312.

Landsberg, L. and Young, Y.B., 1993, Sympathoadrenal activity and obesity: physiological rationale for the use of adrenergic thermogenic drugs. Int. J. Obesity, 17, S29 - S34.

Lewis, W.H. and Elvin-Lewis, M.P.F., 1977, Medical Botany. John Wiley & Sons, New York.

Li Shih-Chen, 1596, Ben Cao Kong Mu, Peking, China.

Lietava, J., 1992, Medicinal plants in a Middle Paleolithic grave, Shanidar IV. J. Ethnopharmacol., 35, 263 - 266.

Loosmore, S. and Armstrong, D., 1990, Do-Do abuse. Br. J. Psychiatry, 157, 278 - 281.

Mahdihassan, S., 1981, The tradition of alchemy in India. Am. J. Chin. Med., 9, 23 - 33.

Mahdihassan, S., 1984, Outline of the beginning of alchemy and its antecedents. Am. J. Chin. Med., 12, 32 - 42.

Mahdihassan, S. and Mehdi, F.S., 1989, Soma of the Rigveda and an attempt to identify it. Am. J. Chin. Med., 17, 1 - 8.

Malchow-Moller, A., Larsen, S., Hey, H., Stokholm, K.H., Juhl, E. and Quaade, F., 1980, Effekten af Helsingor-pillen i behandlingen af adipositas. En kontrolleret klinisk undersogelse. Ugeskr. Laeger., 142, 1496 - 1499.

Malchow-Moller, A., Larsen, S., Hey, H., Stokholm, K.H., Juhl, E. and Quaade, F., 1981, Ephedrine as an anorectic: the story of the 'Elsinore pill'. Int. J. Obes., 5, 183 - 187.

Malecka-Tendera, E., 1993, Postheparin lipoprotein lipase activity in obese children treated with hypocaloric diet supplemented with ephedrine or theophylline. Int. J. Obes., 17, S80.

Martin, W.R., Sloan, J.W., Sapira, B.S. and Jasinski, D.R., 1971, Physiologic, subjective, and behavioral effects of amphetamine, methamphetamine, ephedrine, phenmetrazine, and methylphenidate in man. Clin. Pharmacol. Therap., 12, 245 - 258.

Minamatsu, S., Kobayashi, Y., Kobayashi, N., Fujii, Y., Aburada, M. and Yamashita, M., 1991, Acute Ephedrae Herba and ephedrine poisoning in mice. Jpn. J. Toxicol., 4, 143 - 149.

Moerman, D.E., 1986, Medicinal Plants of Native America. Tech. Rep. Univ. Mich. Museum of Anthropology, 1, 160.

Molnar, D., 1993, Effects of ephedrine and aminophylline on resting energy expenditure in obese adolescents. Int. J. Obesity, 17, S49 - S52.

Moritz, O, 1953, Einführung in die algemeine Pharmakognosie. 2nd Edition, Jena, 305 - 306.

Ou Ming, 1989, Chinese-English Manual of Common-Used in Traditional Chinese Medicine. Guangdong Science & Technology Publishing House and Joint Publishing (H.K.) Co., Ltd., Hong Kong, 492 - 493.

Pardoe, K.E., Gorecki, D.K.J. and Jones, D., 1993, Ephedrine alkaloid patterns in herbal products based on Ma huang (Ephedra sinica). Int. J. Obes., 17, S82.

Pasquali, R., Baraldi, G., Cesari, M.P., Melchionda, N., Zamboni, M., Stefanini, C. and Raitano, A., 1985, A controlled trial using ephedrine in the treatment of obesity. Int. J. Obes., 9, 93 - 98.

Pasquali. R., Cesari, M.P., Melchionda, N., Stefanini, C., Raitano, A. and Labo, G., 1987, Does ephedrine promote weight loss in low-energy-adapted obese women? Int. J. Obes., 11, 163 - 168.

Pasquali, R., Casimirri, F., Melchionda, N., Grossi, G., Bortoluzzi, L., Morselli Labate, A.M., Stefanini, C. and Raitano, A., 1992, Effects of chronic administration of ephedrine during very-low-calorie diets on energy expenditure, protein metabolism and hormone levels in obese subjects. Clin. Sci., 82, 85 - 92.

Pasquali, R. and Casimirri, F., 1993, Clinical aspects of ephedrine in the treatment of obesity. Int. J. Obesity, 17, S65 - S68.

Rackham, H., Jones, W.H.S. and Eichholz, D.E., 1956 - 1966, translation of *Natural History* of Pliny the Elder, volume 8, Harvard University Press, Cambridge, Massachusetts.

Ricciardelli d'Albore, G., 1980, [Identification of the nectariferous flora of Morocco from microscopic analysis of honeys]. Rivista di Agricoltura Subtropicale e Tropicale, 74, 57 - 72.

Roed, P., Hansen, P.W., Bidstrup, B., Kaern, M., Helles, A. and Petersen, K.P., 1980, Helsingor-slankepiller. En kontrolleret klinisk undersogelse i almenpraksis. Ugeskr. Laeger., 142, 1491 - 1495.

Rose, J., 1972, Herbs and Things. Grosset & Dunlap, New York.

Sapeika, N., 1974, Drugs in obesity. S. Afr. Med. J., 48, 2027 - 2030.

Saunders, C.F., 1920, Useful Wild Plants of the United States and Canada. Robert M. McBride & Co., New York, page 158 (Dover unabridged republication of the revised edition published in 1934, under the title "Edible and Useful Wild Plants of the United States and Canada").

Schmidt, J.O. and Johnson, B.E., 1984, Pollen feeding preference of Apis mellifera, a polylectic bee. Southwestern Entomologist, 9, 41 - 47.

Siegel, R.K., 1980, Cocaine substitutes. N. Engl. J. Med., 302, 817 - 818.

Stuart, M., 1979, The Encyclopaedia of Herbs and Herbalism. Orbis Publishing Limited, London.

Stauffacher, W., Wirkungsweise und Indikation der Appetitzugler in der Therapie des Ubergewichts. Schweiz. Med. Wochenschr., 105, 461 - 466.

Stokholm, K.H. and Hansen, M.S., 1983, Lowering of serum total T3 during a conventional slimming regime. Int. J. Obes., 7, 195 - 199.

Tanaka, T., 1976, Tanaka's Cyclopedia of Edible Plants of the World. Keigaku Publishing Co., Tokyo.

The American Spectrum Encyclopedia, 1991, The American Booksellers Association, page 362.

Toubro, S., Astrup, A., Breum, L. and Quaade, F., 1993, Safety and efficacy of long-term treatment with ephedrine, caffeine and an ephedrine/caffeine mixture. Int. J. Obesity, 17, S69 - S72.

Tyler, V.E., 1982, The Honest Herbal - A sensible guide to the use of herbs and related remedies. George F. Stickley, Philadelphia.

USDA, 1937, Forest Service, Range Plant Handbook, U.S. Department of Agriculture, Washington, D.C.

Vallerand, A., 1993, Effects of ephedrine/xanthines on thermogenesis and cold tolerance. Int. J. Obesity, 17, S53 - S56.

Whitehouse, A.M. and Duncan, J.M., 1987, Ephedrine psychosis rediscovered. Br. J. Psychiatry, 150, 258 - 261.

Zgourides, G.D., Warren, R. and Englert, M.E., 1989, Ephedrine induced thermogenesis as an adjunct to cognitive restructuring and covert conditioning: a proposal for treatment of obese individuals. Percept. Mot. Skills, 69, 563 - 572.

Senator KASSEBAUM. That concludes the hearing.
[Whereupon, at 6:33 p.m., the committee was adjourned.]

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