peripheral vascular disease, researchers injected either EDTA or, as a control, saline alone. After treatment, there were no differences between the EDTA group and the control group in how long they could walk on a treadmill before developing leg pain.

A recent Canadian study of 80 angina patients reported this March at a meeting of the American College of Cardiology found no differences between the EDTA and control groups and how long they could walk on a treadmill before developing ischemic changes on an electrocardiogram.

But in all three studies, patients in both the EDTA and control groups had modest improvements in how long they could walk before they developed either leg pain or angina, and I think these findings emphasize the critical importance of including a control group in studies of chelation or any other CAM or conventional product or procedure.

In the Canadian study, at the end of one year of follow up, there were no deaths and one heart attack in the subjects in each group. Nine patients from the EDTA group and 6 from the control group had to be

hospitalized for treatment of angina.

On questionnaires, patients in both groups reported similar improvements in angina and a better quality of life after they had been treated, and chelation patients often will tell their doctors, and indeed feel, that they have been improved by the treatment, but I really suspect that anyone here, in front of me or behind me in the audience, would tell their doctors that they felt better after they had undergone 30 intravenous, two-hour injections and about $5,000 out-of-pocket expenses.

Most distressing to me is a statement that was made in response to this Canadian study by a past president of the American College for the Advancement of Medicine, who was quoted as follows: "I have been doing it for 18 years and have seen some dramatic differences. I have been really impressed with it." He also said that 75 percent of his patients respond and are able to walk further and to have less chest pain.

His reaction raises in my mind the terrible concern that CAM practitioners will not accept the negative results of scientifically valid studies, and use

those results to alter their practices appropriately. If that is true, then, properly conducted research by either CAM investigators or government-supported investigators at academic institutions will be a tremendous waste of time and money.

Quite frankly, I cannot believe how any practitioner who is truly interested in the welfare of his or her patients, given the available evidence about it, can continue to practice chelation therapy.

A second question we were asked to address is how can valid research study the complex issues inherent in CAM research. I would like to begin with a quote from an editorial in JAMA a few years ago which stated, "Advocates of alternative medicine argue that many alternative therapies cannot be subjected to the standard scientific methods, and thus, instead, must rely on anecdotes, beliefs, theories, testimonials, and opinions to support effectiveness and justify continue use."

Well, I disagree completely with the notion that CAM therapies cannot be subjected to valid testing, and I submit that the problems associated with CAM research are inherently no different than those faced in

other areas of clinical research. What is needed is some ingenuity, the design of carefully controlled studies, and the willingness of investigators to roll up their sleeves and go to work.

My recommendations to the Commission then. First, CAM research requires large, well-controlled studies which provide scientific evidence that either support or rejects the value of all CAM products, such as herbs and vitamins, as well as procedures like chelation and therapeutic touch.

Here, I will echo what has already has been said, and that is, that such studies on safety and efficacy must be done before marketing and before promotion of products, because it would be exorbitantly expensive, indeed impossible, for government agencies to fund such studies on every product or procedure that imaginative and entrepreneurial people can think of to sell to gullible members of the public.

I have heard, for example, that the NIH may feel compelled to use, I might even say waste, taxpayer money to fund yet another study on chelation therapy, despite the lack of any evidence to support it and the

completion of three studies showing no benefit.

The health food industry is doing well and can afford to carry out such studies before products and procedures are promoted and marketed.

The failure to carry out such studies means that the public will lose out on two scores. First, the public will continue to waste money using ineffective and possibly risky CAM products largely based on the widespread misinformation in the media and on the Internet.

Secondly, equally important, the public will not have widespread access through conventional physicians to products and practices that really are effective.

My second recommendation to the Commission is that you urge Congress to revise the Dietary Supplement Act of 1994, so that the Food and Drug Administration has some control over CAM products and procedures.

Finally, the Commission and CAM practitioners must accept and act appropriately when the results of sound studies prove that a CAM product or practice is either ineffective or dangerous.

Thank you for your attention.

DR. GORDON: Thank you very much.

Arthur Grollman.

Presenter: Arthur P. Grollman, M.D.

DR. GROLLMAN: Thank you for inviting me to appear before the Commission.

My background is as follows: I am a physician trained in internal medicine at Johns Hopkins, I have served on the faculty at the Albert Einstein College of Medicine and the State University of New York at Stonybrook.

As Chair of the Pharmacology Department for 25 years, I have been responsible for educational programs in pharmacology for medical students, other health professional students, and practicing physicians. I see patients in the role of attending physician in medicine, and I conduct NIH-supported cancer research in the area known as molecular toxicology.

You should also know that I have conducted research on the active principles of several herbal medicines, and I have served as a consultant to the Dahli Lama of Tibet regarding the use of Tibetan herbal

medicines.

Our panel was asked to discuss our concerns regarding CAM and CAM research. I will focus on the former, describing the dangers resulting from the unregulated use of herbal medicines.

Many are convinced that this is the Achilles' heel of alternative medicine. Many herbal medicines are safe, others available in health food stores or prescribed by herbalists may be harmful. A serious safety problem is the widespread adulteration of Chinese herbs with drugs and heavy metals, 40 percent in one study by the State of California.

Since 1962, when the Harris-Kefauver Amendments were enacted in response to the thalidomide tragedy, the American public has taken FDA surveillance of commercially available medicines for granted. Most are unaware that since 1994, the Dietary Supplement Health and Education Act, DSHEA, allows herbs to be marketed as dietary supplements. Prior testing of dietary supplements is not required by law, and there is no premarketing safety approval by FDA.

Understandably, physicians, pharmacists,

researchers, and some leaders in the botanical industry have called DSHEA "an accident waiting to happen."

Now, in your briefing document, I cite three examples of serious toxic reactions associated with herbal medicines. Additional reports will surely appear before this Commission submits its report to President Bush next spring.

Importantly, the incidents I will discuss would not have occurred had the manufacturer been required to provide proof of safety. I will briefly summarize these events as a basis for the discussion, and then offer suggestions as to how such public health tragedies could be avoided in the future.

Aristolochia has been used in Europe and Asia for 2,000 years. For five centuries, women in Great Britain were given Aristolochia during childbirth, hence, its common name birthwort. In China, the herb is used to treat symptoms of arthritis.

A decade ago in Belgium, about 100 otherwise healthy young women were reported to have developed irreversible renal failure requiring dialysis or transplantation. This group had one thing in common.

They had attended the same weight reduction clinic in Brussels where they were given a cocktail containing the usual drugs plus several Chinese herbs including Aristolochia.

In addition to permanently losing kidney function, half of these individuals subsequently developed renal cancer. The syndrome, now known as a Chinese herb nephropathy, has been reported in countries throughout the world including the U.S.

What can we learn from this unfortunate event? First, that herbs used for centuries in folk medicine can have serious toxic effects including cancer. Aristolochia is hardly unique, comfrey tea, highly toxic to the liver; sassafras, which contains a carcinogen; and many other examples can be cited.

Second, the genotoxic properties of the major component of Aristolochia had been established at NIH 20 years before the tragic event in Belgium.

Third, stronger laws are needed to protect the American public from toxic substances sold as dietary supplements. Last month, nine years after the initial clinical report, and seven years after the herb was

banned in many European countries, the FDA finally sent warning letters to pharmacies, manufacturers, and consumers. Some voluntary recalls have been made. However, Aristolochia remains available.

Now, contrast this failure of the FDA to respond to reports of a serious herb-associated toxicity with the situation that occurred with the drug thalidomide in the sixties. Thalidomide, thalidomide, introduced as a sleeping medication, was taken by pregnant women whose children were subsequently born with disfiguring birth defects. FDA was alerted, thalidomide was not marketed in the U.S.

The public, however, was alerted and concerned, and major new laws requiring more substantial proof of safety and efficacy were enacted. Regrettably, basic safety regulations that apply to OTC and prescription drugs are not granted to herbal preparations under DSHEA.

Ephedra. Again we deal with an herb used in traditional Chinese medicine. Analogs of the active principal of ephedra, ma huang, known as sympathomimetic amines have been subjected to more studies by pharmacologists than any class of drugs in history.

These studies have shown that the structure, pharmacology and toxic effects of ephedra alkaloids are essentially similar to those of epinephrine, methamphetamines, speed, and phenylpropanolamine PPA.

Now, in the U.S., herbs containing ephedra are rarely used for its time-honored medicinal purpose, that is, to relieve bronchial congestion. Instead, ephedra has been adopted as a mainstay of weight reduction programs and as an energy pill.

Over time, tolerance rapidly develops and the toxic effects of higher doses on the cardiovascular system and the central nervous system are both predictable and profound.

In recent years, over 1,000 serious toxicities associated with ephedra use were reported to the FDA, far more than any other dietary supplement. Half of these were in individuals under the age of 40.

Now, since less than 1 percent of adverse effects resulting from dietary supplements are reported to the FDA, we can estimate that 100,000 individuals had suffered reactions to ephedra including cardiac arrhythmias, hypertension, psychosis, seizures, and

death.

Now, still focusing on safety, compare the FDA response to the toxicities associated with ephedra, an herb, with those associated with phenylpropalanolamine, a drug, knowing that the pharmacological properties of both agents are essentially the same.

In a recent issue of the New England Journal of Medicine, the adverse effects of these agents were independently analyzed. The use of PPA was associated with an increase in the number of strokes in young women. An FDA warning was issued and pharmacies promptly removed OTC drugs containing PPA from their shelves.

In contrast, although the simultaneously published study of adverse effects of ephedra confirmed the FDA's earlier analysis of those reports, no action to protect the public was taken.

The final example of preventable toxicity has enormous potential for harm. It has been alluded to several times today, but not specifically. I refer to herb-drug interactions as recently reported for St. John's wort, a widely used herb in the U.S. and even more widely used in Europe for symptoms of depression.

Essentially everything we take into our bodies including drugs are metabolized and herbal medicines are no exception. The pathway by which St. John's wort is metabolized is shared by approximately half of all drugs used by millions of Americans being treated for hypertension, heart failure, asthma, AIDS, and other chronic diseases.

Thus, this herbal remedy, apparently innocuous when taken alone, has ability to inactivate the effects of life-saving drugs on which many patients with chronic diseases depend. You saw the data presented to you by Dr. Eisenberg this morning.

Because herbal medicines contain many chemicals, they are much more likely than pure drugs to be involved in drug interactions, and the scope of this problem could be significantly reduced simply by requiring premarketing safety testing.

What should the Commission recommend to the President to reduce the clear dangers associated with the unregulated use of herbal medicines? I suggest the following:

Echoing Dr. Eisenberg's strong plea and first

and foremost as a matter of highest priority, Congress should amend DSHEA, so that manufacturers of dietary supplements, including herbs and other botanicals, would be required to obtain premarketing approval by demonstrating safety to FDA.

Two. All recommendations contained in a recent report by the Office of the Inspector General, I sent the executive summary to you, with respect to reporting adverse reactions to dietary supplements should be implemented. Among other things, OIG recommends that the manufacturer should report all adverse drug reactions to FDA.

Third. NIH should conduct randomized, double-blind, placebo-controlled clinical trials designed to test, not only efficacy of selected herbal medicines, but also to record their adverse effects. This essential information recently obtained for St. John's wort, will establish the all-important risk-benefit ratio.

Finally, if resources are limited, only after the major safety issues have been addressed, basic research on the mechanism of action and toxicities of commonly used herbal medicines should be conducted as

this approach can provide leads to new drugs and help to anticipate toxic effects.

Thank you.

Panel Discussion

DR. GORDON: Thank you. Thank you all for your thoughtful comments and suggestions.

Tom.

MR. CHAPPELL: Thank you all very much for your concern for consumer safety and good science. I am a manufacturer of herbal-based wellness products that qualify under DSHEA and OTC drugs with the FDA.

I share your concern and join you in wanting to bring greater safety to consumers, and the route of doing that is more knowledge, more science. I do want you to be aware, however, of the options that are available to us manufacturers at the present time, because it really gets to my question that I have for Dr. Margolis and Dr. Grollman.

We can do a responsible search of available literature on the safety data of a given herb, and that search can provide very clear indication of sufficient clinicals or trials that have been conducted on an herb,

and that search will indicate whether there are problems in history.

That search can also keep very current with ongoing trials that are going on, so I think the first responsible action is to do a sufficient search of available information.

The second responsible action would be test the safety and efficacy. That, too, is a possible course for any of us in this business.

Now, having done both steps, a secondary search and specific testing, the options available to us do not change. They are: market under the DSHEA law, marked as an over-the-counter drug, or apply for a new drug application that is a long and expensive process.

What I am suggesting is that in the case of plants, such as our herbs, commonly known herbs, that the public wants to have access to, there is very little proprietary data available because there are no patents for such work.

The search, the motive to do the research is very limited because it is not patentable, and I am not recommending patentability of these herbal substances,

but I am suggesting that there is a far vast open area of a middle ground of simply doing safety and efficacy testing of herbs that does not require a new drug application or does not require hitching the formulation to an over-the-counter drug, monograph-approved item like pseudoephedrine.

So, what would you recommend given the options, because all I am saying to you is that for us to do the secondary research, for us to do the clinical research, the options don't change, they are still the same - DSHEA, over-the-counter drug, or new drug application, and it is extremely limiting.

So, if you want more evidence, what kind of evidence, and the FDA does not have the time, is not staffed to pass judgment on the tests that are done. That is why postmarket is the best course they have.

They have testified here that safety is the best they can keep up with. Efficacy is on, at best, a chance or a crisis basis. So, the middle ground, it seems to me, is just doing, as you say, use some ingenuity, some basic evidence-based research, six-month clinicals, 150,000 bucks or 250,000 bucks, whatever is

involved, and those are not small numbers to the people in the health food industry. They are back-breaking numbers to most of them.

At the moment, there is no middle ground, and that is why even responsible manufacturers seek the umbrella of either DSHEA or OTC drugs.

Now, for me --

DR. GORDON: Tom, excuse me. Do you have --

MR. CHAPPELL: I do have a question, would you put this burden of testing -- but, of course, I had to provide this background information --

[Laughter.]

MR. CHAPPELL: Would you put the burden of testing, as you say in Item 3, Dr. Grollman, back to the NIH for these commonly held or these common herbs for the basic research, or would you put the burden on the manufacturers? So, that is my question.

We are dealing with publicly available herbs and drugs. You don't need a prescription for these things. So, where do we place the burden of proof of a publicly available plant, with the government or with the manufacturer?

DR. GROLLMAN: I am very clear on this. I definitely would place it with the manufacturer, and I would point out -- but I think that some of the special aspects have been taken care of in a document which I am sure you are familiar with, that the FDA put out on advice for botanical products.

They allowed you to take information from abroad and from other things. In other words, use this great, wide use and you could bring this. You can't do this with a regular drug. I think this is very important to be able to bring the evidence you have. From every point of view, because of the diversity in your profession, not all of the manufacturers particularly where herbs are brought from abroad, and they can't be checked, they actually can't be checked, they can't be checked as to whether they have the right name on them, et cetera, so the burden must be placed on the person to do that.

Dr. Eisenberg put it very well this morning - safety trumps efficacy. Safety is what we all owe the people. It has nothing to do with the size of the industry, the money, and actually a $5 billion herb

industry is pretty good and is growing.

So, I think that an industry --

MR. CHAPPELL: It is declining at the rate of 25 percent a year currently.

DR. GROLLMAN: Last year, yes, but a $5 billion industry can certainly afford to do the testing that the American people expect to have. The FDA obviously can't do the testing, nor do I believe it should be shifted to the taxpayer, which is basically what you have suggested as the other possibility, shifting to the NIH.

So, I do feel strongly about that, but I think that accommodations need to be made because of their long history, and that document that I referred to, that you know of, I think tries to do that, and I think they ought to work with industry to further work within that.

DR. MARGOLIS: I agree completely that the burden of proof, certainly for safety and hopefully for efficacy, lies with the promoter or the manufacturer. I am really impressed with your statement putting clearly the problems that you face, but you say that these herbs are widely available to the public, but they are only widely available because they are widely promoted.

The public would never have heard of these herbs if it weren't for the fact that they are advertised all the time. So, that is what brings the public's desire to have them, but they are unaware of the fact that they either have potential risks or that they are not beneficial.

So, I think the burden does have to fall on the manufacturer, but there ought to be, and I would be in favor of -- I am not familiar with the document you mentioned -- but I would be in favor of alternative ways to allow herbs that have proven safety and studies that show efficacy to be marketed. That is the desirable goal, not some rule that has to be passed, but that these products are proven to be safe and effective.

MR. CHAPPELL: Well, thank you for your concern and your suggestions.

DR. GORDON: Dean.

DR. ORNISH: I also want to thank the panel for your thoughtful comments which were very helpful, and I certainly agree with the position for the need for evidence-based approaches. I think most of us on the panel would agree with that.

I guess I just wanted to make two points. One is certainly, Dr. Margolis, I share your concerns about chelation and I thought you did a very good job about critiquing that, but particularly I guess with the National Council Against Healthcare Fraud, and so on, why aren't you equally vigilant with conventional therapies in terms of holding them to the same standard.

I think there is a concern among many of the people that we have heard testifying that there is a double standard, that the same rigorous scientific evidence-based approach, which we all agree on, certainly I do, isn't applied equally, I mean in the same vein -- or artery I should say -- as chelation, the same standard to angioplasty or radioactive stents.

There was an article that was presented to the American College of Cardiology just six or eight weeks ago showing that radioactive stents actually increased complications, atherosclerosis, and yet the use of radioactive stents has increased since that time.

I don't see anything in the National Council Against Healthcare Fraud journal -- I guess it's the Scientific Review -- are you affiliated with the

Scientific Review of Alternative Medicine?

DR. LONDON: We are a separate organization completely.

DR. GORDON: I'm sorry, I couldn't hear.

DR. LONDON: We are completely separate.

DR. ORNISH: But are you also working with that journal, too, or not?

DR. LONDON: I think I am a contributing editor.

DR. ORNISH: I would say that is some affiliation.

DR. LONDON: But that is me personally, and I am a volunteer for both.

DR. MARGOLIS: Can I address that first? The reason I would like to is the last thing I did before I came here today was review about six articles on brachiotherapy for stent placements, and there is some disagreement among them, but studies have been done. Sincere efforts have been made to see if they work, to test various doses.

They found that the first doses they used didn't work, so they are trying different doses. They

are using different radioactive compounds. Some are using beta, some gamma emitters.

So, I think the difference is not that there is a double standard, but that there has to be at least an effort, a sincere effort to study things, and there will be disagreements, but at least they must be studied and carefully evaluated, and that is a situation with angioplasty and brachiotherapy.

DR. ORNISH: We are all in agreement with that, but the difference is that you are also saying, and certainly the journal is saying, that unless something has been proven to be effective and safe in double-blind, randomized trials, it shouldn't be used, and that is not the case here, and yet it is still being used.

I am only making the point that I think that your impact might be greater -- and this is just a personal thing, not speaking so much as a commissioner -- if you applied the same rigorous standards equally to conventional and other approaches, both in terms of evaluation and the standard of what should be out there and what should be made available, and as you say, people may be using supplements because they are being pushed by

advertising, but they are using radioactive stents because they are being pushed by people who have other economic incentives, as well as a genuine desire to help. I think you find that mixture of motivations on both sides.

I just think that to the degree that those standards could be applied equally, I think there might be a better dialogue. I am also curious why -- just two last points -- why you don't vigorously support increasing the research budget for, say, the National Center for Complementary and Alternative Medicine if the goal is to have more good scientific research, which certainly I think we both agree with.

The problem has been that the other double standard is that until recently, it has been very difficult to get those studies funded. You may say, well, industry should be funding supplements, and that is certainly one position, but many of these alternative interventions have no industry as such, and I am just curious to know what your position is.

This is directed both to Dr. Margolis and to Dr. London on increasing funding for good quality

scientific research, because part of our recommendations are going to be dealing with issues like that.

DR. MARGOLIS: Well, having served on several NIH study sections, I can only say that I truly believe that peer review of a well-designed study in alternative medicine would be funded. That was always an opportunity, and I don't remember in the years I was on the study section that there was ever such a proposal made.

Secondly, it happens that at Hopkins we have just been given a large amount of money by the NIH to study alternative medicine based on four proposals that I was involved in, in some advisory way, four proposals to carry out what we hope are scientifically valid studies of alternative medicine.

DR. ORNISH: I am familiar with that because I reviewed that for the NIH. I was on the study section. But the point is that until this year, that was the first year there was a study section to specifically look at grants in NCCAM.

DR. MARGOLIS: I think that there needs to be more provision of funds by the NIH for truly valid

studies, but at the same time, as I said earlier, the government cannot possibly study every herb or procedure that is being promoted, there just isn't enough money, so they are going to have to be very selective in picking the ones for which there is at least reasonable evidence that they might be effective.

I think St. John's wort is a good example where there was some reasonable evidence that it was helpful in mild to moderate depression, and so they have chosen to support that, and I hope they will continue to pick and choose among the best options to provide support that would give real evidence.

DR. GORDON: Joe first, and then Tieraona.

DR. FINS: Dr. Grollman, in your role as a toxicologist, could you tell us about the level of preparedness of the poison control centers in the country to handle toxic events and any recommendations that you might make to increase their level of awareness about the toxicities related to supplements that they are encountering as you demonstrate, and also any strategies for tracking these events in a systematic way, so we can understand the extent of the public health issues related

to these agents.

DR. GROLLMAN: I would be glad on, and you should get from the national head of the Poison Control Center, if you really want, you should have her, Ms. Liebowitz, I think it is, should actually come here, but here is the essence of what she would say.

They get calls from people who are taking supplements. There is no way that the individual knows from the label, nor is there any connection with the manufacturer, so they are really operating in the dark. So, they would urge you in the strongest way to make sure the manufacturers, number one, are known and that there is a listing, so that they would be able to do it because you know how a poison control center, they have to act quickly.

Now, with other chemicals and things, they have that information. They do not have it. There are 17,000 cases related to dietary supplements this year. They don't break them down into herbs. They have herb homeopathic remedies. They don't break them down up until now. Next year they will break them down.

I am sure you are going to find the biggest

section is with the herbs, but they don't have the information to do it. That would be a very important thing for you to put into it, and I would suggest that you get a true poison control center, particularly the executive director, who I think can do it.

Now, that report that I cited, I hope that you have all taken advantage of it, the Inspector General's Report addresses several of those as to how to do it, and, in fact, the FDA should actually contract with the poison control centers, so they can find out what is going.

FDA gets a thousand reports. There is 17,000 of them out there, at least putative ones out there, so they could contract with them, but you don't help the FDA by starving it, and if they don't have the money to even get a trivial contract, to get the information, so you can help this whole process by suggesting that the small amounts that the FDA is requesting -- you know, it is 2/10ths, 3/10ths of a percent that is not receiving attention on the Hill, which would allow them to make contracts with poison control centers, to get adverse drug action, that would be a tremendous help.

DR. FINS: Of the people who staff these centers, even if they had that information, you know, in the next iteration, what is their educational preparedness for handling the drug-drug interactions? They know about insecticides and things like that, but how much do they know about the supplements and what kind of educational strategy would you recommend for their CME?

DR. GROLLMAN: Well, remember herb-drug interaction would be the kind like I described. You have an older person who is taking, and all of a sudden he goes into heart failure. Well, you really need an internist, a trained family physician who puts it together and says, gee, they are either not taking their digitalis or something was interfering with it, but certainly poison control centers would never, with any education, couldn't handle that.

What I would really like to do is cut it off at the beginning and have industry -- we spoke about the cost of doing it. It doesn't cost a lot to test for drug interactions, $10- $15,000. They give them a cocktail and you could test your herbs. That is a very small

expense and done as a Phase I thing on volunteers, and that is something the manufacturers could do with an herb, and if you did that, then, maybe the problem would disappear rather than taking care of it after the fact.

DR. FINS: Before that happens, we could probably do this before that --

DR. GROLLMAN: Yes.

DR. FINS: Thank you very much.

DR. GORDON: Thank you. I also wanted to share with you that we have heard a lot of testimony about helping the FDA move ahead with their efforts especially to monitor adverse events, and that is something the Commission feels very strongly about, as well, so we appreciate your recommendations and also about the Office of the Inspector General Report. Thank you.

Tieraona.

DR. LOW DOG: I want to appreciate all of you. Thank you for all of your comments. Mine are really focused on the botanicals, and it is the Achilles' heel, there is no question, and they range from foods and spices to dilute drugs to potent substances, and so we tend to just talk about them as herbs, and they are just

vastly different. You cannot compare comfrey to garlic, I mean, so there is just huge differences there.

DSHEA is going to be difficult to overturn. I mean we are seeing that. There is a lot of industry fighting for an overthrow of that bill, of that act.

I know that the USP, which I work with, we are in the middle of a pilot program right now that will be available for people who want to participate, it is voluntary, this fall, and it will assure the consumer that that herb company has undergone an GMP inspection meaning that it has shown how it can identify, quarantine, look at the plants, it is free of heavy metals, it is free of pesticides in accordance with the law, that it is the right genus species, et cetera.

It is amazing how some support we are getting from the industry and how much also resistance we are getting from the industry for that.

The safety data is there for many of these plants - ginseng, ginkgo, St. John's wort. They didn't do mostly drug testing, p450, they didn't do those.

The problem that I think we are going to have in this country, though, is that the German companies who

spent that money on doing that safety and toxicity research, did it on their particular extract and product, so the ginkgo is free of ginkgolic acid, but if you are doing a different ginkgo, it may have it in there.

The black cohosh may not have the estrogenic substance in it, black cohosh, Remifemin, but you might in a product here.

So, I am curious, given the state of where we are with DSHEA now, do you believe that the federal government -- I believe the manufacturers need to step up to the plate, too -- but do you believe that the federal government has a role to play from a public health point of view to take the top 20 to 25 herbs that make up 80 percent of the sales in this country and do the safety studies on them?

I mean if they are not that expensive and we take the major herbs that are being sold, is that something that we should step up to the plate for as a government or as an agency, one of the agencies from a public health point of view?

DR. GROLLMAN: What the government should do is not to overthrow. Overthrow is a word you don't use in

Washington. Just amend it. Just make the simple amendment to put the burden on the manufacturers the safety. That's all. So, that's a smaller, smaller change. It addresses the point that was so discussed in the very beginning, but I think that is -- and I think the manufacturers should also attend, and they would, to standardization is what you are bringing out in the difference between the Germans.

Now, just being careful and just being standard and having a commission and monograph isn't enough. Look how many Germans have been taking St. John's wort for how long for this, they didn't pick up the drug interaction at all, so remember that just writing a nice monograph never makes up for -- but I think that your specific question was or the option was should the NIH or some government agency take in the testing.

I think that would be going down a slippery slope. I don't think they are going to do it, and while the other, I think is a way of professionalizing and actually saving the wonderful things that could be done with herbal medicines is just get Mr. Hatch to let the question be raised, and I think that we should look at it

again.

DR. GORDON: I just want to ask the Commissioners if you would please focus on questions. We have a significant but limited time with the panel.

DR. LOW DOG: The question about the amendment, would you require safety and toxicity data for everything, peppermint, chamomile, and would we take them off the market? I mean I guess my question is, because we have argued with this dilemma, what would the amendment be, have you thought through that and how we would do it?

DR. GROLLMAN: Well, I haven't thought through as well as this letter that the FDA -- and they have thought through, and it is treated very differently from a drug. They are open to the information, not just from this country, but it is a big step to say we would take the information from abroad.

So, you could provide the information from the -- commission the monographs, so that is going to simplify it a great deal. Simpler, straightforward cellular studies and testing for drug interaction, which have never been done, just need to be done.

So, I think that new document offers a real opportunity for a discourse for people who want to make this happen.

DR. GORDON: Wayne.

DR. JONAS: Thanks. I think we heard from a number of groups including the manufacturing industry, that there should be some modifications of DSHEA, and I, myself, am going to suggest that that be one of our recommendations in some form. Clearly, that needs to be addressed.

I am rather saddened actually by the lack of interest there is in evidence. We talk about it, for all the number of times we use the word evidence-based medicine, I don't think people seriously are interested in evidence. The reason evidence-based medicine, the term and the whole process came about, was not because the public wasn't using it, the public wasn't even involved in the discussion, it was because professionals weren't doing it, and every new technology that came up got into practice before --

DR. GORDON: Wayne, could you come to the question, please.

DR. JONAS: Yes -- and now we are just adding on top of that the public and the manufacturing. I guess the question is, is there a standard that most reasonable people can agree? For example, would you agree that what was discussed on the last panel, the Cochrane type of work, is the type of evidence evaluation that we need to be doing? Would everybody agree with that, Dr. London, would you agree with that?

DR. LONDON: Since I walked in right as that was ending, I am not --

DR. GORDON: Could you come a little closer to the mike, please.

DR. LONDON: I didn't get to hear those presentations.

DR. JONAS: Any others on the panel?

DR. MARGOLIS: I think it is a very good first step. The problem is, as you heard, for most of the studies they have done, they come to the conclusion that they can't reach any conclusion, and that gets back to the point that it is fine to do these literature searches, but if there is no good data, they don't help very much.

DR. JONAS: The next question is really what you all are addressing, is all right, let's say we now know what we do know or what we don't know, how do we get that out into actual recommendations and practice, and I think maybe that is where the government has not, and in the past they have gotten into recommendations, but they have pulled back from that, and now most government agencies that I have dealt with are very loath to make recommendations one way or another, positive or negative.

AHRQ actually had some trouble because they got into make those kinds of recommendations, and now they no longer do that anymore. So, I am wondering if there are some suggestions from you all as to how evidence can get better disseminated into practice and also to the public, is there anything that we and the government can do to recommend that, are there some suggestions that you have assuming we can come up with agreements on what is good evidence or what is at least a good methodology as to how to really make communication, should there be a center that is sanctioned, if you will, that then disseminates that in some way, or are there any ideas about how to do that?

DR. GROLLMAN: The gentleman from the Public Health, working closely with NCCAM, he is developing those, so clearly, people can do that. The German experience is clear. You can get intelligent people working together with information, and you can do that. I think it is very important to do.

Now, the public gets it from the Internet, and that is an impossible thing to sort out. I can't sort it out, they certainly can't sort it out. So, I think that that should be a strong recommendation to get the information, but we certainly ought to be able to communicate, and that certainly is a government responsibility.

DR. JONAS: I think Bill during the break recommended that what we really should be doing is getting PubMed to work with AOL on line because they actually are the main ones where most people get their information, health information in some way.

DR. MARGOLIS: I am not sure I think it is a good idea to have government do this, because if it comes from government, there is always the question in the minds of practitioners whether that is a regulation, a

requirement, or a recommendation.

So, I think it might be better to come from the various groups, internal medicine groups or others who could take this information and make recommendations to internists, family physicians, surgeons, and so on.

But coming from the government, I am a little concerned that it would be suspect.

DR. JONAS: [Off mike.]

DR. MARGOLIS: Except they don't have any information, and I think the idea would be if these Cochrane Reports or other studies would put together the information, and it were credible, that a product or a procedure should be used, then, I suspect those organizations would recommend their use.

DR. JONAS: [Off mike.]

DR. MARGOLIS: That would be my thought, to have them make the guidelines.

DR. GORDON: Don.

DR. WARREN: I was kind of interested in your comment about the $5,000 not being able to speak up. I believe that people, no matter what they spend, if they think they have been done wrong or they think they have

been scammed --

DR. GORDON: Don, could you come a little closer.

DR. WARREN: -- I think they are going to say something one way or the other. We can differ about that, and that's okay.

We talk about a lot of things here with CAM. We also have a problem with drugs in that we have off-label use of drugs. We are talking about having the manufacturers of all CAM products prove their efficacy and safety.

Should we then have the drug manufacturers prove the efficacy and safety of the off-label use of their drugs? And then I have got one more thing after that.

DR. MARGOLIS: That sounds like a question to be answered by a pharmacologist.

DR. GROLLMAN: That is not a bad idea. Certainly, that has not been the case. I think it is a very reasonable proposition to do so.

DR. WARREN: And these off-label uses of the drugs are promoted. Does that mean they are fraud?

DR. MARGOLIS: No, no, no.

DR. GROLLMAN: That is not correct.

DR. MARGOLIS: If a pharmaceutical representative is in your room and you mention an off-label drug use, they will say we can't talk about that. They really do not promote that.

DR. GROLLMAN: They can't promote the off-label.

DR. WARREN: Then, I have one other question. Dr. London, who funds your organization?

DR. LONDON: Mostly members and subscribers to our newsletter and people who occasionally buy a book or a T-shirt or something like that.

DR. WARREN: Any drug companies?

DR. LONDON: No.

DR. WARREN: Any medical organizations?

DR. LONDON: No.

DR. WARREN: I just wanted to know.

DR. GORDON: Thank you.

I have a question, particularly for Dr. London, but really for any of you. In your recommendations, there is sort of a theme saying that if there is

information, if information is gained, that a practice is either ineffective or fraudulent, that information ought to be disseminated, or that some kind of regulation ought to happen.

Do you have any thoughts about how that would be implemented? How would we gather the information? And then, who would gather it? And then, how would you suggest getting that information out to the public and practitioners, as well?

DR. LONDON: I am not sure how you would do that. My concern is with an imbalance that is set up when methods are studied that don't necessarily have a plausible rationale to support them.

Just the fact that things get studied lead reasonable people to think some experts must think there is something there to base that on. I don't know, with all the investment and studying a variety of methods, that might not get funded on the basis of the strengths of its rationale, what we have learned at this point.

I am kind of stumped, but I think it all sends a message that raises expectations, and I think something needs to be done to temper them, perhaps messages, clear

messages, that, just because something is under investigation doesn't necessarily mean it is something that is promising.

DR. GORDON: I think it is a bind because we have to find out, get some answers. I think that what is happening is, for example, the St. John's wort study that was recently published in JAMA showing it was not particularly effective for serious depression is an example of studying an herb and coming out with a negative result, and publishing it and letting people know.

So, I think we are in a quandary. We need the information, just as the other two panelists have said, and since we need the information to make recommendations, yes or no, we are really open to figuring out when something is not effective or is dangerous. We would like to know how to better get that information out, just as we would like to get information out if something is beneficial. That is where we are at this point.

DR. MARGOLIS: I will reiterate the point that I made, that even if the public isn't informed, then at

least the practitioners should be informed and follow appropriately. I would like to cite what was a recommendation. It says, "Resolved, that pending the results of thorough, properly controlled studies, the American Osteopathic Association does not endorse chelation therapy as useful for other than its currently approved and medically accepted uses, which is for heavy metal, like lead poisoning."

So, here is a statement made in 1985, again in 1990 and 1995. It apparently has had no effect on the osteopaths or other physicians who do chelation therapy. So, evidently that approach doesn't work.

DR. GORDON: Yes.

DR. GROLLMAN: Just to sort of tidy up on two points that I wanted to comment. One was the question of the double standard, a very good point being made, but I want to differentiate in terms of my own presentation. I don't think there is -- this is to your question -- a double standard for new chemical agents.

There clearly is a double standard for procedures, and they are not controlled, but for new chemical agents, drugs, I think we do have a method that

works, and we could apply it to the other.

The second was, there has been a lot of speaking about the public, and protecting the public, but the public is pretty smart. My reading of the 25 percent fall -- by the way, I thought it was only 15 percent. That is what I read in Herbalgram, anyway. At any rate, it is leveling off.

I think the public is now concerned about the herbal things. They have heard. They are not waiting for the Commission report. They are certainly not waiting to hear from pharmacologists. So I think that they are on to that, and another reason why I think your recommendations will get some urgency, particularly if we can address a safety aspect of herbal medicine.

DR. GORDON: I just want to share with you that we have consistently heard, a major concern of public and responsible manufacturers is, that what is said to be in the bottle is not in the bottle in the strength or the appropriate form. So, this clearly, I think, just confirms everything that we have heard over the last nine months of hearing testimony. That is a major concern.

Tom.

MR. CHAPPELL: Dr. Grollman, I would just to clarify your position and your recommendations. Your third recommendation is that the NIH should conduct randomized, double-blind, placebo-controlled clinical trials.

DR. GROLLMAN: On selected herbs, just as they are doing. The NCCAM is doing just what I would like them to do.

MR. CHAPPELL: And the object of those tests is what?

DR. GROLLMAN: That is for efficacy, and that is for benefit, because if we have something that has a risk, and we know that it has no benefit or the benefit is placebo, we need to know that.

We don't have both sides of the equation. We certainly don't have the risk. That is the safety side, and although I didn't address efficacy, others have, it would be nice to have the risk and the benefit.

So, doing the proper studies, as has been said over and over again, and having them done under NCCAM with the funding, on those that seem to have promise, is, I am just saying, more of the same.

MR. CHAPPELL: So, public dollars.

DR. GROLLMAN: Public dollars absolutely.

MR. CHAPPELL: Your fourth recommendation is that basic research should be conducted on the mechanisms of action. Now, as you know, that is even more complicated a study than safety studies.

DR. GROLLMAN: You have dozens of very excited pharmacologists, like myself, who would love to do these sort of studies, both on the toxic and on the therapeutic things. Don't forget, although there is no published data on this, but those of you who have a connection with industry, the pharmaceutical companies have been exploring botanicals for the last 40 years.

Now, they don't publish when they don't work, or when they do work, but there is no better source of an unusual molecule, and there are wonderful screens now that they can put them in. Chemists don't think that way. They still don't think as complicated as that.

So, they are a wonderful source, the pharmaceutical industry, academics, to look at their mechanism of action and toxicity. Academics have to get their funding from NIH. The pharmaceutical companies are

driven by themselves. I am suggesting more of that.

MR. CHAPPELL: That is consistent with what I was saying, as well.

DR. GROLLMAN: Yes, absolutely.

MR. CHAPPELL: Very good. Thank you.

DR. GORDON: Effie.

DR. CHOW: I don't have a question. I just really have a comment, that I really appreciate this panel's discussion because it has brought forth and confirmed our discussions in our groups about the safety. We are really concerned about safety. You have brought up some very good suggestions and some ideas, and I just want to say thank you for that.

DR. GORDON: Did you want to say something?

DR. LONDON: I did want to answer your question again about how to get the information out. It seems to me that if you can call a method "alternative" or "complementary," that is categorizing it in some way, and I have questioned the meaningfulness of those terms.

What is to stop characterizing various methods as unproven. If you can label it one way, why not label it in a way that is meaningful. I think, in my remarks,

I suggested three ways you can look at alternatives or complements: one, genuine; two, experimental but hopeful.

My concern about experimental is that they should be things that have a promising, plausible rationale. The third, was genuine.

It seems to me if you can call things complementary and alternative, you can just as easily call them --

DR. GORDON: So, in fact, those categories transcend complementary, alternative, and conventional.

DR. LONDON: I don't buy into the notion of categorizing things as alternative and unconventional, or complementary and conventional. I don't buy into it, period.

DR. GORDON: I appreciate that. Thank you very much. Thank you all three, and, please, if you have any further thoughts, let us know.

[Applause.]

DR. GORDON: We will adjourn now and convene again tomorrow morning at 8:00.

[Meeting recessed at 5:30 p.m., to reconvene Wednesday, May 16, 2001, at 8:00 a.m.]

CERTIFICATION

This is to certify that the attached proceedings

BEFORE THE: White House Commission on Complementary and Alternative Medicine

HELD: May 14-16, 2001

were convened as herein appears, and that this is the official transcript thereof for the file of the Department or Commission.

DEBORAH TALLMAN, Court Reporter