UNITED STATES DEPARTMENT OF JUSTICE

DRUG ENFORCEMENT ADMINISTRATION

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In the Matter of: :

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LYLE E. CRAKER, Ph.D. : Docket No. 05-16

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VOLUME I

Monday, August 22, 2005

DEA Headquarters
600 Army Navy Drive
Hearing Room E-2103
Arlington, Virginia

The hearing in the above-entitled matter convened, pursuant to notice, at 9:25 a.m.

BEFORE:

MARY ELLEN BITTNER
Chief Administrative Law Judge

APPEARANCES:

On Behalf of the DEA:

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Washington, D.C. 20537

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On Behalf of the Respondent:

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M. ALLEN HOPPER, ESQ.
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Drug Reform Project
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ALSO PRESENT:

MATTHEW STRAIT
Representative of the Government

Richard Doblin, Ph.D.
Representative of Respondent

C O N T E N T S

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E X H I B I T S

EXHIBIT NOS.	MARKED	RECEIVED
ALJ 1 - 9	6	6
RESPONDENT'S EXHIBITS		
3	14	14
11	84	84
43	51	51
44	68	Withheld
50	72	72
GOVERNMENT'S EXHIBITS:		
2	24	24
3	32	32

P R O C E E D I N G S

JUDGE BITTNER: This is a formal hearing before the United States Department of Justice, Drug Enforcement Administration, in the matter of Lyle E. Craker, Ph.D., Docket No. 05-16. The Administrative Law Judge presiding is Mary Ellen Bittner. Would counsel please state your name and address and phone number for the record? Mr. Bayly.

MR. BAYLY: Yes, thank you, Judge Bittner. Good morning. Brian Bayly. I'll spell the Bayly because nobody spells it the way I do. It's B-A-Y-L-Y, Department of Justice, Drug Enforcement Administration, Washington, D.C. 20537.

JUDGE BITTNER: Okay. And anyone else entering an appearance for the government?

MS. PAREDES: Good morning, Your Honor. Imelda Paredes with Drug Enforcement Administration. The same address as Mr. Bayly.

JUDGE BITTNER: Okay.

MR. TRANT: Good morning, Your Honor. Charles Trant, Associate Chief Counsel, Drug

Enforcement Administration, same address.

JUDGE BITTNER: Thank you. For Respondent?

MS. CARPENTER: Good morning, Your Honor, Julie Carpenter from Jenner & Block, J-E-N-N-E-R, B-L-O-C-K, 601 13th Street, N.W., Washington, D.C. 20005.

MR. HOPPER: Good morning, Your Honor. Also for Respondent, Allen Hopper. It's A-L-L-E-N H-O-P-P-E-R, and I'm with the ACLU's Drug Law Reform Project, and that's at 1101 Pacific Avenue, Suite 333, in Santa Cruz, California 95060.

JUDGE BITTNER: Thank you very much. And Dr. Craker is here?

MS. CARPENTER: He is, Your Honor.

JUDGE BITTNER: Thank you. The issue in this proceeding is whether a preponderance of the evidence establishes that granting Respondent's application for registration as a manufacturer of the Schedule I controlled substance marijuana would be in the public interest, as that term is used in 21 U.S. Code Section 823(a).

At this time, I would like to offer into evidence the Administrative Law Judge Exhibits. They are numbered 1 through 9. We prepared these on Friday before Mr. Trant entered his appearance so his appearance is not included in them, but he did enter it.

Is there any objection to any of these exhibits, Ms. Carpenter?

MS. CARPENTER: No, Your Honor.

JUDGE BITTNER: Mr. Bayly?

MR. BAYLY: No, Judge Bittner.

JUDGE BITTNER: Okay. Then the ALJ Exhibits 1 through 9 are received.

[ALJ Exhibits No. 1 - 9 were marked for identification and received in evidence.]

JUDGE BITTNER: I would have a few preliminary matters. First of all, on August 11, the Government filed a motion to file a third supplemental prehearing statement to which Respondent advised there was no objection. So I grant that motion.

On August 15, Respondent moved to file a second supplemental prehearing statement to which the Government has no objection, so that statement is deemed filed.

And on August 18, the Government moved to file a fourth supplemental prehearing statement, and, Ms. Carpenter, I understand that you have no objection.

MS. CARPENTER: That's correct, Your Honor.

JUDGE BITTNER: So it is deemed filed. I would also like to note that there is to be no recording in the courtroom other than that made by the official court reporter, and no cameras in the courtroom, at least not on, and I understand that the parties have agreed that we will not sequester the witnesses, and that Dr. Doblin will act as representative of Respondent for sitting at the counsel table, and Mr. Strait will act as representative of the Government.

Am I correct?

MS. CARPENTER: That's correct, Your

Honor.

MR. BAYLY: Yes, Judge Bittner.

JUDGE BITTNER: Okay. Ms. Carpenter, anything else before opening statements?

MS. CARPENTER: I don't think so, Your Honor.

JUDGE BITTNER: Mr. Bayly, anything else before opening statements?

MR. BAYLY: No, Your Honor.

JUDGE BITTNER: Okay. Ms. Carpenter?

MS. CARPENTER: Thank you, Your Honor. I really just have a very brief comment, a brief statement, and that is that as the proceedings go forward, there are three critical reasons that I would like Your Honor to focus on why it's in the public interest, as defined in 21 U.S.C. 823(a), for the DEA to grant Dr. Craker's application for registration as a bulk manufacturer of marijuana.

The first reason is the language of the statute and the regulation. The statute and the regulation specifically require, and I quote, "adequately competitive conditions."

Those are to ensure that there's an adequate and uninterrupted supply of whatever the Schedule I substance is, in this case marijuana, to meet the legitimate medical, scientific, research and industrial purposes.

Congress commonly uses the term "competitive conditions" when it's talking about markets. It uses it often in antitrust statutes, and it refers to those conditions existing between buyers and sellers in a particular industry or particular market.

And we would submit that because the evidence will show that there is one supplier of marijuana currently in the United States, and that one supplier is the government, so essentially a government monopoly, it is almost as a matter of law impossible for that to meet the statutorily required "adequately competitive" conditions.

The second point is that because the government monopoly can decide on its own when it will and will not provide marijuana to researchers and doctors without any market incentive to be

responsive to the needs of those researchers and doctors. The facts are that the current supply with the government monopoly does not provide an adequate and uninterrupted supply that's necessary to meet legitimate needs of researchers and medical and science.

The evidence will show here that NIDA has refused to provide medical marijuana for FDA-approved protocols and that they've refused to provide marijuana to researchers attempting to help develop new smokeless delivery devices to deliver marijuana in a way that's less harmful than smoking, and indeed the evidence will show that NIDA itself makes clear that it believes it is not its mission to further medical research into marijuana or to facilitate bringing it to market.

The third point that I'd like Your Honor to remember is that the statute also requires consideration of whether or not the license will promote technical advancements in the field. It will in this case, and the evidence will show that one of the primary purposes for which Dr. Craker

seeks this license or this registration is to assist researchers who want to develop a smokeless delivery device which is exactly what another branch of the government has called for in research in the medical marijuana issue.

So for those reasons--because it will further technical advancements in the manufacture of marijuana and the delivery of new substances, because the current supply is not adequate and uninterrupted, and because almost as a matter of definition, a supplier of one, a government monopoly, cannot constitute adequately competitive conditions--we believe the evidence will show strongly that it is in the public interest for DEA to grant the license to Dr. Craker in this matter.

JUDGE BITTNER: Thank you. Mr. Bayly.

MR. BAYLY: Your Honor, we are going to reserve our opening argument, and at the time that the Government puts on its rebuttal case, we will then present the opening argument.

JUDGE BITTNER: Okay. Ms. Carpenter, we're ready for your first witness.

MS. CARPENTER: Thank you, Your Honor. We would call Dr. Lyle Craker.

JUDGE BITTNER: Doctor, if you would come right up here, please.

DR. CRAKER: Thank you, Your Honor.

JUDGE BITTNER: Good morning. Stand and raise your right hand, please.

Whereupon,

LYLE E. CRAKER, PH.D.

was called as a witness and, having been first duly sworn by the Administrative Law Judge, was examined and testified as follows:

DIRECT EXAMINATION

BY MS. CARPENTER:

Q Good morning, Dr. Craker.

A Good morning.

Q Can you state your name and address for the record?

A Certainly. My name is Lyle E. Craker. I am a faculty member at the University of Massachusetts at Amherst, and that's located in Amherst, Massachusetts. My home address is 119

Mount Warner Road in Hadley, Massachusetts.

Q Thank you. Dr. Craker, can you tell me--you mentioned you were currently a faculty member, and what department are you a faculty member?

A I'm a faculty member in the Department of Plant, Soil and Insect Sciences.

Q Okay.

A The Insect Sciences was added this last summer.

Q And is that part of your specialty?

A What?

Q Is that part of your specialty?

A No, it's not.

Q Dr. Craker, could I ask you to turn in the book that's up there to Respondent's Exhibit 3?

A Yes.

Q Do you recognize that document?

A Yes, it's a resume that I've supplied.

Q Okay. And you prepared that and it explains your experience and publications?

A Yes, this is a record of my education, my duties at the university and part of the scientific

articles that I have been responsible for editing, writing, co-writing.

Q Okay.

A Editing, co-editing.

MS. CARPENTER: All right. I would move the admission of Exhibit 3 into evidence.

JUDGE BITTNER: Any objection, Mr. Bayly?

MR. BAYLY: No, Judge Bittner.

JUDGE BITTNER: Received.

[Respondent's Exhibit No. 3 was marked for identification and received in evidence.]

MS. CARPENTER: Okay.

BY MS. CARPENTER:

Q Dr. Craker, can you tell me a little bit about your education? Where did you get your undergraduate work?

A I did my undergraduate work at the University of Wisconsin in the Department of Agronomy.

Q And what is agronomy?

A Agronomy is the study of crop production.

Q Okay. And did you--
A And I did my doctorate degree at the University of Minnesota. I got that degree in agronomy also, studying crop production.
Q Okay. And what did you do your graduate work in, what particular project?
A My project had to do with the wheat and the absorption of radionucleotides into wheat because of the government concern about nuclear bombs contaminating our food chain.
MS. CARPENTER: Okay.
JUDGE BITTNER: What are radionucleotides?
THE WITNESS: The one we looked at was Strontium 89. It's a mineral, mineral element that has radioactive properties.
BY MS. CARPENTER:
Q What did you do after you got your Ph.D.?
A After I finished my doctorate degree, I did a postdoctorate in the Department of Horticulture where I worked on, studied the cold hardiness. That is the ability of plants to survive the winter and I worked there for six

months and then after that I was called to active duty in the United States Army Chemical Corps.

Q Okay. And what did you do in the Army?

A After training with the Chemical Corps in Alabama, I was assigned to work in research laboratories at the facility at Fort Detrick, Maryland.

Q And what did you study there?

A At Fort Detrick, Maryland, I studied the--we did work in the leaf abscission.

Q What is leaf--

A Abscission is the process by which plants lose their leaves and lose their fruit.

Q Why was the Army interested in wheat abscission?

A The Army was interested in this because of the use of foliage by enemy soldiers to hide themselves and if they could remove the leaves from trees, that would expose the enemy soldiers.

Q Okay. How long were you in the Army?

A I was in the Army for 25 months.

Q What was your rank there?

A Captain when I left.

Q Okay. And what did you do after you left the Army?

A After I left the service I was hired by the--I got a position at the University of Massachusetts, and I worked at the University Experiment Station in Waltham, Massachusetts.

Q What kinds of projects did you work on there?

A There my responsibilities were to study the effect of air pollution on plant growth and development.

Q Okay. And how long did you stay there?

A I was there from 1969 till 1976 when I went on sabbatical to Cambridge, England for six months and then I returned. I went to, they asked me to come to the campus at Amherst and I've been there since.

Q Okay. And are you a tenured professor?

A I'm a full professor, yes.

Q Okay. And what have you continued to do at Amherst when you moved to the main campus?

A In Amherst, I've worked on air pollution for, continued working on air pollution for five or six years, and have after that became interested in medicinal plants, looking at this for a potential crop for Massachusetts growers, and I've continued working in that area since that time.

Q Okay. Can you talk about some of the projects with regard to medicinal plants?

A With medicinal plants, we've worked with probably a number of plants over the years. We've had a study in Chinese medicinal plants. We've looked at Black Cohosh quite extensively, and currently we're working with spearmint.

Q Okay. And in those projects, did you grow those plants?

A Yes.

Q Right there at the University of Massachusetts?

A Yes, in the greenhouse, in environmental chambers, and some of those were grown in the field.

Q Okay. Who paid for that sort of work?

A Well, we've had money from some federal sources. We've had money from some foreign sources that help support this, foreign governments, and I think that's--some state money also, also goes into these type of things, yes.

Q And what federal agencies have supported your work?

A We've had money from the, well, for some of our studies, we've had money from the Environmental Protection Agency for our air pollution work. We've had money from the SARE grants which are federal money, sustainable agriculture grants. We've had money from the Experiment Station which comes through the Hatch Act, federal money.

Q The SARE grants, is that from the Department of Agriculture?

A Yes.

Q And the Hatch Act federal money would be from the--

A Yes.

Q --Department of Agriculture? Okay. And

the medicinal plants that you worked with, I think you mentioned Black Cohosh?

A Yes.

Q Would you tell us a little bit about what that is and what it's used for?

A Black Cohosh is a native American plant, and it has extensive use by women for relief of menopausal symptoms.

Q Okay. And what did you do with regard to that particular project?

A In the Black Cohosh we were concerned with a few things. Number one is that currently the Black Cohosh, primarily the Black Cohosh is collected in the wild, and we are worried about whether the wild population can sustain the market, so that we wanted to check where populations were growing and the size of those populations. So we did a field inventory of the natural range of Black Cohosh.

We wanted to in this think about bringing this plant into cultivation in the U.S. We made collections at all our populations. We brought

those back to the Amherst facility. We have looked at their DNA. We've looked at their morphology and we've looked at their chemistry.

We grew those at the university in a plot so they'd all have the same environment so when we checked the chemistry, any change in chemistry would be due to genetics as opposed to environment. We then submitted those plant materials to the germ plasm repository, at one of the germ plasm repositories for the United States in Ames, Iowa, where the populations we started are still being grown and available to other researchers.

MS. CARPENTER: Okay.

JUDGE BITTNER: How do you spell Cohosh?

THE WITNESS: C-O-H-O-S-H.

BY MS. CARPENTER:

Q Okay. And I think you also mentioned spearmint that you're working with? What are you doing--

A Yes. We're working with spearmint.

Q Can you tell a little bit about that work?

A The spearmint we're using as a model to

try and increase oil production, spearmint oil production. The thought process is that in plants there are two systems of metabolism, regular glycolysis and the pentose phosphate shunt, which is an alternative type of metabolism, and most of the ingredients of essential oil come off the shunt.

So if we could switch the plant from using the regular glycolysis to the shunt, we would supply more of the raw ingredients for the oil and theoretically produce more oil.

Q Okay. And who is funding the spearmint work?

A The spearmint work is being funded by--it's being funded partially by the Egyptian government and partially by USDA through the Hatch Act.

Q Okay. Dr. Craker, you have submitted a license, an application for registration to the DEA to become a bulk manufacturer of marijuana; have you?

A That's true.

Q Okay. If you would turn to--there are some loose exhibits up there.
A The what?
Q The loose exhibits there.
A Yes.
Q They're not in the book. But it's marked Government's Exhibit 2.
A Yes.
Q Do you recognize that document?
A Yes, this document is a memorandum from--it's a copy of a memorandum from me to Sharon Lick at the Registration Unit at the DEA.
Q Okay. And the next document that's attached to that?
A Yes. Yes, this is a memorandum from Carol Sprague who is the, was the associate director, I think now she's the Director of Office of Grant and Contract Administration at the University of Massachusetts Amherst.
Q Okay. And then the next two documents attached to that, or pages, I guess?
A Yes. This is the application for

registration that was submitted from the university to the DEA for the manufacture of marijuana.

MS. CARPENTER: Okay. At this point, I'd like to move the admission of Government's Exhibit 2 into evidence?

JUDGE BITTNER: Mr. Bayly, any objection?

MR. BAYLY: That's two and three?

MS. CARPENTER: Not three yet. This is just two. I'll get to three in just a few minutes.

JUDGE BITTNER: Okay. Let's see. What I have in two is an August 22, 2002 memorandum, a June 25, 2001 letter, and an application which I assume was double-sided originally; is that correct, Mr. Bayly? So I have three documents.

MR. BAYLY: Yes, Your Honor.

JUDGE BITTNER: Okay.

MR. BAYLY: That's what I have, and I have no objection.

JUDGE BITTNER: Okay. Received.

[Government Exhibit No. 2 was marked for identification and received in evidence.]

BY MS. CARPENTER:

Q Before we talk more about the application itself, Dr. Craker, can you tell me how you came to file this application?

A I filed this application after I had spoken with Dr. Doblin. He approached me about the possibility of growing marijuana for use in research trials.

Q Okay. Did he tell you why he wanted to grow marijuana for use in research trials?

A At that time, we discussed the reasons for the need for this material, the reasons for a need for alternative source, and during that time, I looked at this as something we did, grow medicinal plants.

Q Okay. Did you talk with anybody at the university about out?

A I'm sorry?

Q Did you speak with anybody at the--well, what did you tell Dr. Doblin after--

A Yes.

Q --you first met?

A At that time, after I had spoken with Dr. Doblin, I approached my administrative unit and asked them if they had an objection to this type of research and I spoke to my department head. I spoke to my dean and I spoke to the Office of Grants and Contracts, and I spoke to the Vice Chancellor for Research at that time, and asked if this was okay with all of them?

Q And what was their response?

A Their answer was that, yes, this was okay with them.

Q Okay. So what did you do next?

A Well, the next thing was that we filed the--I submitted the appropriate internal processing forms and the form that we just looked at to our Office of Grants and Contracts because all proposals need to go through the Office of Grants and Contracts at the university.

Q Okay.

A And for submission to the DEA.

Q Okay. And let me step back for just a minute.

A Yes.

Q And then we'll go back to where you were. But when you spoke with Dr. Doblin, did he indicate to you--what did he say to you why were the reasons why he was not able to get the marijuana that he needed to do research?

MR. BAYLY: Objection. I think that's been asked and answered.

JUDGE BITTNER: No, I don't think so. Overruled.

BY MS. CARPENTER:

Q Did he talk to you about particular reasons that he was unable to get other marijuana?

A He may have. I don't really recall. It's an initial meeting. It's a course of conversation which probably lasted an hour and a half or so.

Q Okay.

A And we exchanged pleasantries. We talked about the need. There may have been specific conversation, but I don't recall. That's five years ago or so. I don't recall.

Q Sure. Okay. So after you submitted the

application, do you recall roughly when that was?

A The initial application was submitted, as I recall, in the spring of 2001.

Q Okay.

A Late spring of 2001.

Q All right. If you would look at Government's Exhibit 2, the second page of that, the June 25, 2001 letter from Carol Sprague.

A Yes. That would be the cover letter that went with the application. So I assume that's the date that it was submitted.

Q Okay. And then if you turn to the next page and look at the date stamp on the long side of the page, not the short top.

A Yes.

Q What's the date stamp there?

A June 28, 2001, 3:51--

Q Okay. All right.

A --in the afternoon.

Q So after you submitted the application and sent it in, what happened next?

A Nothing.

Q Okay. So what did you do?

A Well, I, after some time had gone by, probably I would guess eight to nine months, I got in contact with the DEA and I don't remember who my initial contact, but I got referred to Ms. Lick, and I spoke with her on several occasions about my application.

At that time she told me that they had, the DEA had not received the application, that I should refile.

Q Okay. So what did you do?

A Well, I think that the memorandum in the Exhibit 2 was that I resubmitted the application as originally submitted.

Q At some point, did you receive something back from DEA?

A Well, before this, I received my application back from them after I talked to her, and she said that they had not received it. I did receive the application back from them.

Q Did it have anything attached to it?

A I got the application in a plain brown

envelope with no return address.

Q All right. So what did you do after you received the application back?

A After I received it, this was shortly after I had spoken to her, probably within two or three weeks after I had spoken to her, I called her and asked her--she said they had not received it, and I said that I had received it back from someone and that indeed it was stamped as having been received.

At that time, she told me that I had incorrectly filled out the form, and that I should submit a new form. I asked her to go through the form with me and tell me where I had made my mistake, and we went through the form line by line and at that time, it looked like to me that everything had been filled out correctly and I told her I was going to resubmit the same form.

Q So she didn't have any corrections for you to make on the form?

A Not that I recall.

Q Okay. So in the first letter on

Government's Exhibit 2 is dated August 22, 2002; is that--

A That's when it was resubmitted, yes.

Q Okay. So you resubmitted the same form, and then if you look at the form again, is there a new date stamp on there?

A I see a new date stamp that says August 28, 2002 at 6:37 in the morning.

Q Okay.

A I sent the second one registered mail so that I would be sure that they received it.

Q Okay. Great. Just to make sure this is a clear, I think you said earlier, but what's the date stamp, the first date stamp on the exhibit?

A The first date stamp was June 28, 2001.

Q Okay. Great. At the time that you spoke with Ms. Lick, did she have any additional questions for you from the DEA?

A She did have some additional, there were additional questions that came up, and I responded to those, yes.

Q Okay. And if you would look at what's

been marked for identification as Government's Exhibit 3.

A Yes.

Q It's a loose copy up there. Have you seen that before?

A Yes, this is the response to the bulk manufacture question. It appears to me that I submitted to the DEA.

Q Okay. This was in the response to questions from Ms. Lick?

A Yes.

MS. CARPENTER: So at this point I would move admission of Government's Exhibit 3 into the record.

JUDGE BITTNER: Mr. Bayly?

MR. BAYLY: No objection.

JUDGE BITTNER: Received.

[Government Exhibit No. 3 was marked for identification and received in evidence.]

BY MS. CARPENTER:

Q If you would look at that, Government's

Exhibit 3, Dr. Craker.

A Yes.

Q The first question says what is the purpose of bulk manufacturer of controlled substances. And then your answer follows that, I guess.

A Yes.

Q Can you--do you recall what the purpose was for your application for growing these? Can you summarize it there or we could read it if you prefer?

A Well, our purpose in growing, in asking for a license to manufacture the marijuana was to be able to supply a defined marijuana project, find a defined marijuana product to investigators that wanted to do clinical trials with marijuana.

Q Okay. And was this in particular to further the drug development process?

A Yes.

Q And who was the organization that was looking to do that?

A MAPS was the organization that Dr. Doblin

heads was the one that approached me and the one that was going to secure the funding for this, and I guess I would say looked for, look at or be the middle person for the clinical trials that would, he would interact with those initially.

Q Okay.

JUDGE BITTNER: Excuse me, doctor. Did you say defined or refined process?

THE WITNESS: I said defined.

JUDGE BITTNER: What does that mean?

THE WITNESS: Well, defined means if we want a particular level of in the case of marijuana cannabinoids or something else, and that we would supply a product with that level.

JUDGE BITTNER: So, in other words, is it like grow to suit or?

THE WITNESS: Like what?

JUDGE BITTNER: Grow to suit. That you could--

THE WITNESS: Yes, that's right.

JUDGE BITTNER: That you could grow it to meet certain criteria?

THE WITNESS: Yes.

JUDGE BITTNER: Okay.

THE WITNESS: Yes.

JUDGE BITTNER: Thank you.

BY MS. CARPENTER:

Q Was it your understanding that this research or the marijuana that you would grow, should the application for the registration be granted, would be used in research regarding vaporizer devices?

A Yes, this was new to me, a technology to me, but this was the understanding that it would be a new type of drug treatment.

Q Okay. Would it be a new type of drug treatment or a new type of delivery device?

A New type of delivery device for use of marijuana.

Q Okay. And what's your understanding of what the differences would be between smoked marijuana and vaporized marijuana, if any?

A Well, smoking marijuana has, in the literature you can see that smoking marijuana has

negative associations with the smoking in that the smoking itself, the burning of the material can cause adverse effects in patients. My understanding of the vaporizer technology is it will be below the threshold for burning, and so that we will not have the same effects as smoking.

Q Okay.

A Same negative effects.

Q So essentially a different product would be delivered through the delivery device?

A Yes.

Q In the second response to bulk manufacturing questions, the question was please describe the production process for these controlled substances from start to finish. Can you summarize generally what you would do to grow the marijuana under the application?

A Certainly. We looked at marijuana as we would do any other medicinal plant. The large difference here, of course, is the security requirements required for this type of plant material to be sure that it's not diverted into the

recreational market. So that we had extra security, things which we've talked to DEA agents about, but otherwise we generally grow plants within a--start plants--seeds in a media, and then transplant them into pots, and then we would grow them in a controlled environment facility, a greenhouse or a growth chamber, environmental controlled chamber as necessary.

Q So would this growing be inside a room?

A This would be inside a room, yes.

Q Not field--

A Locked room.

Q Okay. So it wouldn't be grown in a field, for example?

A No. This is not for field growing. Not under the current situation. It would be either--it would be a secure facility.

Q Okay. And would that allow greater environmental controls by growing it in a room?

A Yes, that's the idea here is to control the environment so that we can produce a defined product.

Q And I think you had mentioned before that you would be, anticipate using different selections or different strains of marijuana? What would be the purpose of that?

A Well, the plant material that is available varies quite considerably in the level of bioactive constituents, and so what we would want to do would be able to grow different strains of the plant material which have been previously characterized as to certain levels of the constituents.

Q Okay. And so you'd grow different types of plants for different testing?

A Well, it would be the same type of plant. It would be a little bit different strain of plant.

Q I understand. Get my botanical terms clear.

A Yes.

Q The next question was what material would be used to manufacture the controlled substances and what quantities will be used? Can you just briefly summarize? Maybe you've already said that.

A Yes, well, we're going to--we said we're

going to grow them in some type of controlled facility.

Q Okay. And you mentioned a growth chamber; can you tell the Court what that is?

A Environmental growth chamber, yes. That's a metal box where we can control the levels of light, the temperature, humidity in order to ensure the uniform plant growth around the year.

Q Okay. And why would it be important to ensure uniform consistency between plants?

A Well, there are two things that affect the active constituents in a plant, and that is the genetics of the plant and the environment in which the plant grows. As I mentioned before, with the Black Cohosh study, we wanted to determine the differences in genetics. We had to grow them in all the same location with the same environment so that any differences would be due to the genetics as opposed to the environment.

Q Okay. And the question number six on Exhibit 3 is what quantities of controlled substance does your company anticipate producing

and who are the interested customers? What's your answer to that question?

A Well, in conversations with Dr. Doblin, it was calculated approximately 25 pounds would be needed in the first year.

Q Okay. And how much table space do you think it would take to grow 25 pounds of marijuana?

A Well, since I'm not experienced in growing this plant, I'm not exactly sure. I have talked with other licensed growers and we have said that I will talk with them to further determine the number of plants we need.

Q Okay. But it would all fit in one room; would it?

A I'm sure it will fit in one room, yes.

MS. CARPENTER: Okay.

JUDGE BITTNER: Doctor, when you say dry weight, do you mean after it's been dried or--

THE WITNESS: Yes, after it's been dried.

JUDGE BITTNER: Okay.

BY MS. CARPENTER:

Q Now, Dr. Craker, at some point, did you

receive an opportunity from the DEA to bid on a government contract to grow marijuana?

A Yes. I received the notice from the government that they were taking bids on growing marijuana, yes.

Q Okay. Were you interested in that opportunity at all?

A I looked at the prospectus on it and decided that there was little chance of the university successfully bidding on this.

Q And why was that?

A Well, they were, first of all, we had essentially no experience in producing the material and whereas the current successful bidder has had lots of experience. There was call for and analyzing material that's brought off the street. We were not exactly interested in that.

Q Okay.

A And in looking at it, I thought if I was, you know, that it was not for us at that time.

Q Okay. So after you submitted the answers to the questions, and resubmitted your original

application in August of 2002--

A Yes.

Q --what happened next?

A We had, next thing that came after we resubmitted, I would say approximately--again, the dates are approximate because I don't have them.

Q That's fine.

A But I would say probably within six to eight weeks after that submission, we had, I had two DEA agents visit the campus.

Q Okay. And what happened during that visit?

A In the initial contact with the agents, they asked that I come to a meeting along with my department head, my dean, the Vice Chancellor for Research, and the chancellor of the campus.

Q So all you all gathered together and met and what did they have to--

A The chancellor did not come, but the department head, the dean, and the Vice Chancellor for Research did attend along with me. We met with the two agents.

Q Okay. And what happened in that meeting?
A During that time, we met with the agents. The agents, the primary purpose of the meeting to me seemed to be that the agents were trying to discourage the university from participating in the research. They asked the, they asked especially the Vice Chancellor for Research and my dean whether this is something that they really wanted the university working in, that the university could get a bad reputation from growing this plant material.
Q Okay. And what was the response from the university?
A The response from my department head, my dean and my Vice Chancellor for Research said this was a research university and these are the type of problems that we worked on.
Q Okay. Did those DEA investigators ask questions at all about security or any issues like that?
A Not that I recall.
Q Okay.

A Not that I recall at that time. I had a second visit by DEA agents to talk about security.

Q Okay. So the first visit focused solely on whether or not the university would proceed with this?

A Well, we, again, it's been--

Q Okay. Primarily.

A --three years ago or so. That was the primary focus of the meeting. We did not visit any facilities. We did not walk around campus. We met in a room and around a table and that was the conversation as I recall.

Q Okay. And what happened at the second DEA meeting?

A At the second DEA meeting when the agents came to, one of the original and another agent came to visit me from the DEA, we walked around campus; we talked about where the material would be growing, grown. They indicated some of their requirements for growing the material. They wanted to, I think, be sure that I understood the need for security of this plant material, which I assured

them that I did. We looked at--we looked at one room where I had secured from the department, had an agreement to use for growing the material. They thought that room could be made secure with no problems.

They wanted to know where I'd be drying the material. I told them there was a small room next which we would connect the growth room to the small room where the plant would be dried so it would all be contained in one facility.

Q Okay. Did any state investigators play a role in this?

A The state investigators were the first to come and see me. They came in 2001 immediately after I had submitted the application. They walked around campus with me at that time, discussed their security requirements, and at the time they told me that a state permit would depend upon a federal permit being granted.

Q Did they indicate that if the federal permit was granted, the state permit would be granted?

A That's what they indicated to me, yes.
Q Okay. So after these visits from the DEA, what happened after that?
A Well, as I talked with the agents and asked them what the next step would be, they said a decision was going to be made. I expected shortly but heard nothing for awhile, and so then we filed a request or whatever it is for them to come to an answer.
Q Okay. So let me just be clear. I understand that you filed in August of 2002, and the DEA agents came out within six or eight weeks after that, so that would be--
A No, we got, we got a response, final response from the DEA, a negative response in 2004.
Q Right. I'm not there yet.
A Yes.
Q Back when you filed, you filed, you refiled the application--
A Yes.
Q --in August of 2002. Then I think you said six or eight weeks after that, DEA agents came

to visit?

A Yes.

Q So that would be fall of 2002?

A That's correct.

Q And then you didn't hear anything from the DEA?

A I heard nothing from the DEA.

Q Until?

A Until 2004 essentially.

Q After you filed the lawsuit?

A I think the second DEA visit came probably in the spring of 2004, summer of 2004. I can't recall it at this time.

MS. CARPENTER: Okay.

JUDGE BITTNER: Summer of 2004 or 2003?

THE WITNESS: 2004.

JUDGE BITTNER: Okay. So some time after the first visit?

THE WITNESS: Yes. Something like that as I recall.

BY MS. CARPENTER:

Q All right. And did a point come when you

filed a lawsuit to try and get an answer from DEA?

A Yes, that was in 2004.

Q Okay. In the summer?

A Yes.

Q And let me just step back for one minute, and do you recall whether in July 2003, notice was published in the Federal Register of your application?

A I'm sorry. I do not understand the question.

Q Do you recall that in July of 2003 that DEA published in the Federal Register a notice of your application finally?

A Well, I knew that they did--

Q Okay.

A --because of publicity that comes and newspaper people calling and things like that.

Q Okay. So that in July 2004, you filed a lawsuit?

A Yes.

Q And what was the result of that lawsuit?

A The result of that lawsuit was a decision

to deny the license.

Q Okay. And do you recall when you received that?

A In the fall of 2004.

Q Okay. Does December 2004 sound about right?

A Sounds about right, yes.

Q All right. The lawsuit that you filed, was that with the Court of Appeals in the District of Columbia? You don't recall what court it was?

A I don't recall the court.

Q Do you recall whether the court ordered the DEA to give an answer?

A Yes.

Q Okay. So basically about three and a half years after you first applied, you got the denial; does that sound about right?

A Well, the initial application was in 2001. We got an answer, a denial in 2004.

Q Okay. Let me ask you to turn in the notebook up there, after you get a drink, to Exhibit 43.

JUDGE BITTNER: And this is your Exhibit 43?

MS. CARPENTER: Respondent's Exhibit 43. We're back to Respondent's Exhibits.

THE WITNESS: Yes.

BY MS. CARPENTER:

Q Okay. Do you recognize that document, Dr. Craker?

A Well, this looks like a copy of a memorandum that I must have gotten from the Drug Enforcement Agency.

Q Okay. This is dated--what's the date on there?

A December 10, 2004.

Q Okay. And to your knowledge, is this the order that denied your application for registration as a bulk grower of marijuana?

A Yes.

MS. CARPENTER: Okay. I would move the admission of Respondent's Exhibit 43 into evidence.

JUDGE BITTNER: Mr. Bayly?

MR. BAYLY: Judge Bittner, it's already an

ALJ exhibit so I don't know. I think it's like redundant and superfluous so I don't--

JUDGE BITTNER: I think the problem, though, is that where we have redundant exhibits, it usually turns out that either the witnesses or counsel are used to referring to them by the numbers that their counsel assigned them. So I've tended to leave them in. So--

MR. BAYLY: Okay.

JUDGE BITTNER: All right. No objection then?

MR. BAYLY: No.

JUDGE BITTNER: Okay. Respondent 43, which is extremely similar to ALJ-1, is received.

[Laughter.]

[Respondent's Exhibit No. 43 was marked for identification and received in evidence.]

MS. CARPENTER: Thank you, Your Honor.

BY MS. CARPENTER:

Q Dr. Craker, I know it's been probably awhile since you read this document, but if you

could turn to page four of that document. And there's three paragraphs there. Do you understand those paragraphs (a), (b) and (c) at the top of the page to be essentially the reasons why your application for registration was denied?

A Yes, those are the three reasons that the, as I understood, that the license was denied.

Q Okay. Could you read that first paragraph there, paragraph (a)?

A Yes. Current marijuana research has not progressed to Phase 2 of the clinical trials because current research must utilized smoked marijuana which ultimately cannot be the permitted delivery system for any potential marijuana medication due to the deleterious effects and difficulty in monitoring the efficaciousness of smoked marijuana.

Q Okay. So is your understanding of that paragraph that they're saying you can't have a license because smoked marijuana cannot be a permitted delivery system?

A Yes. When I received this, this was

curious to me because I don't think we had ever asked about smoked marijuana. We had asked about an alternative delivery system, the vaporizer.

Q And that was clear in your application; was it?

A That was clear in my application.

Q That part of the reason to do this was for--

A Yes.

Q --working with the vaporizer?

A To do away from the smoked marijuana.

Q Okay. Could you read the second paragraph there, paragraph (b)?

A As of January 2004, FDA has not received any new drug application for the development of a prescription drug containing marijuana or a constituent of marijuana. Since the new drug application process cannot take many years--

MR. BAYLY: Sorry. I--

THE WITNESS: Can take many years DEA should not register another marijuana manufacturer at this time on such a speculative basis.

BY MS. CARPENTER:

Q Okay. And in the information that you had, was it clear to you that there had to be an FDA new drug application pending before you could get a license?

A No, I saw nothing about that in the guidelines of following the application.

Q Okay. And if you could read paragraph number (c) on that same page?

A In accordance with the Single Convention, the federal government has to limit marijuana available for clinical research to one source. Based upon this mandate of the Single Convention, HHS through NIDA submits a contract to open bidding every five years to determine which one enterprise will be allowed to cultivate marijuana. Since this HHS policy is consistent with the Single Convention, DEA has no authority to overturn this policy. Moreover, DEA agrees with HHS policy inasmuch as DEA's interpretation of the Single Convention, as noted previously, is that marijuana available for clinical research must be limited to

one source.

Q Okay. I'm just going to ask you--I think you probably don't have any experience--but do you have any experience with the Single Convention that it refers to here?

A No.

Q Okay. Doctor--just a minute, Your Honor. If you'd just turn to the next page there, page five.

A Yes.

Q And it's paragraphs (a), (b) and (c) of paragraph 10.

A Yes.

Q If you look at paragraph (c), could you just read that into the record, if you would?

A Starting with "This system"?

Q Yes, sir.

A This system has not unduly limited clinical research with marijuana. Since the year 2000, there have been or are 11 approved clinical trials utilizing smoked marijuana, three approved clinical sub-studies on side effects of marijuana

and four approved pre-clinical trials in laboratory and animal modes. Current registered marijuana researchers administer marijuana to almost 500 human subjects. Research with other Schedule I controlled substances is not as extensive as it is with marijuana at this time.

Q Okay. Do you understand what Phase 2 studies are, FDA Phase 2 studies?

A That's not in my specialty area.

Q Okay. All right. I'll move on. Dr. Craker, are you familiar with the statutory factors that help determine the public interest in terms of whether or not your application is granted?

A Determine what?

Q That determine whether or not your--

A Am I familiar with the statutes that do that?

Q Let me start over. Are you familiar with the statute that lays out the factors the Court will consider in determining whether or not your application for a registration will be granted?

A Only from a lay point of view.

Q Okay.

A Again, that's not my specialty.

Q Okay. All right. The first factor, do you recall that it is to ensure an adequate and uninterrupted supply under adequately competitive conditions?

A Well, I understand that--

MR. BAYLY: Your Honor, excuse me. I'm going to object. First of all, this is not within the scope of the prehearing testimony of Dr. Craker, and that would be in the Respondent's Supplemental Prehearing Statement, pages, it looks like the third through the fourth page. I don't see where he's talking about the statutory factors.

Secondly, Dr. Craker has already informed us on the stand that this is not something that he's familiar with. He certainly has been testifying about his qualification as a professor, botany and growing, but certainly not in law or in interpreting statutes. So I would say for all those reasons, we shouldn't be allowing his testimony.

MS. CARPENTER: Your Honor, may I respond?

JUDGE BITTNER: Yes.

MS. CARPENTER: On the third paragraph, first line, Dr. Craker will further testify that he meets all the criteria for issuing a DEA license, and then it proceeds to discuss. It doesn't say specifically he'll talk about each factor, but it clearly--obviously that's our burden of proof, and if our applicant can't testify as to why he meets his factor, I think we're not able to meet our burden.

It says--

JUDGE BITTNER: Okay. Did you have more?

MR. BAYLY: No.

JUDGE BITTNER: Okay. First of all, I think, and we are just--make sure we're all literally on the same page. We're talking about Respondent's Supplemental Prehearing Statement which was filed on July 26; right?

MS. CARPENTER: That's correct, Your Honor.

JUDGE BITTNER: Page?

MS. CARPENTER: Page three.

JUDGE BITTNER: Okay.

MS. CARPENTER: I'm sorry that those pages are not numbered. But it's subsection four.

JUDGE BITTNER: Yeah. I think that reference to testifying that he meets the criteria is sufficient given that there was no request to expand upon it.

However, I have a different problem, and that is that I think rather than have the statutory factor described to the witness, he should have it in front of him because that particular one is rather long and involved and has subparts.

MS. CARPENTER: All right.

JUDGE BITTNER: Would you like a copy of the statute?

MS. CARPENTER: I was going to say I don't have one.

JUDGE BITTNER: Why don't you take mine. Nicole, would you please give this to the witness?

MS. CARPENTER: I was cutting down on the number of books I was bringing in and I should not

have left that one.

JUDGE BITTNER: And I don't think he needs to read it into the record. We're all familiar with it.

MR. BAYLY: I need to find the reference to--if we're going to go through all six criteria, I need to find the reference, too, Judge Bittner, if I may have a moment.

JUDGE BITTNER: Okay. Let's go off the record.

[Discussion held off the record.]

JUDGE BITTNER: Back on the record.

BY MS. CARPENTER:

Q Dr. Craker.

A Yes.

Q If you would look at 21 U.S.C. Section 823(a), subsection (1).

A Yes.

Q And just read that to yourself, if you would.

A Yes.

Q Do you see the language in there that

refers to "adequately competitive conditions for legitimate medical, scientific research"--

A Yes, the last sentence there.

Q Yes--"and industrial purposes."

A Yes.

Q As far as you know, would granting your license in your application for registration, would that as far as you know improve competitive conditions in manufacturing marijuana?

MR. BAYLY: Your Honor, I need to object for the record. Again this is asking a question of a witness that's not qualified to answer this.

JUDGE BITTNER: Ask him if he knows and let's get a foundation here.

MS. CARPENTER: Okay.

BY MS. CARPENTER:

Q Dr. Craker, do you know how many people or how many people currently hold a license to bulk manufacture marijuana?

A In the United States--

Q In the United States.

A --only one that I'm aware of.

Q Okay. And so do you know whether, as far as you know, granting your application would improve competitive conditions in the field of, in the area of growing bulk marijuana?

MR. BAYLY: Your Honor, again, I don't think that predicate question has covered the scope of the objection.

JUDGE BITTNER: I'm sorry. I missed the question. What was it?

MS. CARPENTER: He testified--

MR. BAYLY: Well, the predicate question was simply asking do you know how many other manufacturers are and the answer I believe was yes, just one, but that is--that's a fact. That's true, but that kind of doesn't give you, I don't believe, the necessary predicate to make a ruling on whether this witness is qualified to answer such a question.

MS. CARPENTER: Your Honor, this is a question any lay witness. It's not a matter of expertise. The question is whether adding one to a field of one would improve competition?

JUDGE BITTNER: Well, but, well, actually I had a case about that once.

[Laughter.]

JUDGE BITTNER: It was really quite interesting. Doctor, do you have any background in economics or competition or any of these issues?

THE WITNESS: Well, only to the extent that every college student takes a course in economics and I do have an associate's degree in business that I took on the GI bill.

JUDGE BITTNER: Do you know the arrangements under which the one current manufacturer of marijuana is manufacturing it and the cost associated with it and the prices associated with supplying it to researchers and so on?

THE WITNESS: I have no idea on the costs or the prices. The only thing I know that it's produced under contract to NIDA.

JUDGE BITTNER: In that instance, then, I think I'll sustain the objection.

MS. CARPENTER: Okay.

BY MS. CARPENTER:

Q Dr. Craker, can I ask you to turn to Exhibit 44 in the book in front of you? That's Respondent's Exhibit 44.

A Turn where?

Q I'm sorry. Respondent's Exhibit 44.

A Yes.

Q Have you seen that letter before?

A Yes, I have.

Q Okay.

A This is a copy of a letter that I received a copy of the letter sent to by Senator Kennedy and Senator Kerry to the Drug Enforcement Administration.

Q And what's the date on that letter?

A The date on that letter was October 20, 2003.

Q Okay. Dr. Craker, could you read the second and third paragraphs of that letter into the record?

JUDGE BITTNER: I don't think he needs to read it into the record.

MS. CARPENTER: Okay.

JUDGE BITTNER: Because if it's received in evidence, I'll read it.

MS. CARPENTER: Okay. That's fine. Let me just move the admission of Respondent's Exhibit 44 into evidence.

JUDGE BITTNER: Is there a signed copy somewhere?

MS. CARPENTER: I don't have one, Your Honor. I think it was at the DEA.

JUDGE BITTNER: Do we know if it was sent and signed?

MS. CARPENTER: It was sent and signed, Your Honor, is my understanding.

JUDGE BITTNER: Okay. Mr. Bayly?

MR. BAYLY: Yeah. Just, well, a couple of things, Judge Bittner. First of all, the copy I have, and maybe this can be cleared up with Dr. Craker's counsel, but I've got October 20, 2003 as the date, as one date, and then the very top, it's got October 20, 2004.

JUDGE BITTNER: So does mine. Did you

receive a copy of it at the time, Doctor?

THE WITNESS: I received a copy of it. I would say it was probably 2003.

JUDGE BITTNER: But you're not certain?

THE WITNESS: No, I'm not certain.

JUDGE BITTNER: Okay.

THE WITNESS: All dates are approximate. I did not bring my calendar with me when various things happened.

JUDGE BITTNER: Okay.

MS. CARPENTER: I pulled this off a Web site, as you can see at the bottom of the page.

JUDGE BITTNER: Uh-huh.

MS. CARPENTER: And I believe that that line at the top is just, it's a mistake. It was a title for the document on the Web site, and I think they just typed the date wrong.

JUDGE BITTNER: Okay. I think before I receive it, I'd like to know the date.

MS. CARPENTER: Can we get the original?

JUDGE BITTNER: So can I just withhold ruling on this until we can determine the date and

perhaps reach a stipulation on it?

MR. BAYLY: Yeah. I'm not going to object. I think we can clear this date issue up.

JUDGE BITTNER: Okay.

MR. BAYLY: So that's not a problem.

JUDGE BITTNER: So I'll allow you to question the witness about it. I just don't want to receive it when I don't know when it was written.

MS. CARPENTER: Right.

MR. BAYLY: But I will object to having this letter used as a predicate for the witness because this letter is, yes, maybe the witness has seen it, but that doesn't necessarily mean it's a predicate for it.

JUDGE BITTNER: Okay. Right. We're not there yet.

MR. BAYLY: If the defense wants to admit this on its own for whatever worth they think it has, then I would not object on any other basis.

MS. CARPENTER: That's fine, Your Honor.

JUDGE BITTNER: Okay. So I'll just

withhold ruling pending--I'll receive it once we know when it was sent.

[Respondent's Exhibit No. 44 was marked for identification.]

MS. CARPENTER: That sounds fine.

JUDGE BITTNER: Okay.

BY MS. CARPENTER:

Q So just to back up for a moment, you received a copy of this at the time it was--

A Yes, I did.

Q Okay. And what's your understanding of the reason that letter was written?

A Well, my understanding was that this was--

MR. BAYLY: I'm sorry. I have to object again. I don't think this is covered in the prehearing statement as to why this letter was written. There's no predicate that Dr. Craker has contacted Senators Kennedy or Kerry.

JUDGE BITTNER: Well, and the witness also said that it was his understanding. Do you know? Did you talk to the senators or their staff about

this?

THE WITNESS: I have not talked to the, I have not talked directly to either the two senators about this. I have talked to staff of one of them. I think it was Kennedy's staff, but I--

JUDGE BITTNER: Okay.

THE WITNESS: Again, it's one of those things that have fogged over.

JUDGE BITTNER: I think the letter has to stand on its own.

MS. CARPENTER: That's fine.

JUDGE BITTNER: Okay.

MS. CARPENTER: That's fine.

THE WITNESS: Their staff called me and talked about the content of the letter.

BY MS. CARPENTER:

Q Okay. About this letter?

A Yes.

Q Okay. So you did have discussions with them about the content of the letter?

A I had discussions with staff of one of the two senators and I think it was Senator Kennedy's

staff that contacted me.

Q Okay. All right. And do you know if they wrote this letter in support of your application?

A I considered it in support of my application, yes.

Q All right. Thanks. Do you know if in the letter they referred to the necessity for adequate competition in the field of manufacture?

MR. BAYLY: I have to object again.

MS. CARPENTER: I'm simply asking him whether it's in the letter?

JUDGE BITTNER: Yeah, but the letter speaks for itself. I'll read it.

MS. CARPENTER: Okay.

JUDGE BITTNER: So--

MS. CARPENTER: That's fine, Your Honor.

JUDGE BITTNER: I really do read all this stuff.

MS. CARPENTER: I take your word on that.

JUDGE BITTNER: Well, I'm not sure I'm going to read the entire Single Convention. I take that back.

[Laughter.]

BY MS. CARPENTER:

Q Dr. Craker, if I could ask you to turn to Exhibit 50. Hopefully this exhibit will have fewer issues.

A Yes.

Q Have you seen that letter before?

A Yes, this looks like a copy of the letter that was sent to the Drug Enforcement Administration by members of Congress from Massachusetts.

Q Okay. And do you recall whether you saw this letter at or around July 26, 2005?

A Again, the answer to that is yes, I received a copy of this letter. The exact date I cannot be sure, but somewhere around that time.

MS. CARPENTER: Okay. I move the admission of Respondent's Exhibit 50 into the record.

JUDGE BITTNER: Mr. Bayly?

MR. BAYLY: No objection.

JUDGE BITTNER: Received.

MS. CARPENTER: Okay.

[Respondent's Exhibit No. 50 was marked for identification and received in evidence.]

JUDGE BITTNER: Doctor, do you know how many--I'm embarrassed that I don't know this--how many members of the House of Representatives Massachusetts has?

THE WITNESS: I think there are ten or 11.

JUDGE BITTNER: Do you know if any others took a position on your application?

THE WITNESS: Not that have communicated with me, no.

JUDGE BITTNER: Okay.

BY MS. CARPENTER:

Q If you would look back at the statute again, Dr. Craker, in that big thick book. That would be 21 U.S.C. 823 Subsection (a), the second factor there.

A Yes.

Q Which reads "Compliance with Applicable State and Local Law."

A Yes.

Q Do you intend to comply with applicable state and local law should you be granted the registration you're seeking here?

A Certainly.

Q Will the cannabis grown under this license be available to anyone other than those allowed to obtain it in FDA approved research?

A No.

Q With regard to clinical studies, FDA approved clinical studies?

A Yes, FDA approved clinical studies that have permission to use this material in clinical trials.

Q Okay. Would it also be available in some circumstances to scientific users who do not intend to use it in clinical trials but have legitimate scientific, for example, vaporizer testing techniques?

A Well, if they have the appropriate federal permits.

Q Okay.

A Just sending us a letter saying we'd like some is not going to work.

Q Okay. So will you comply with state and federal laws relating to the growing of any cannabis that you're allowed to grow?

A Yes. We are prepared to meet those.

Q If you would look at factor number three.

A Yes.

Q And that refers to the promotion of technical advances in the art of--

JUDGE BITTNER: Actually I have--wait a minute. It would help if I read the right section of the statute. I'm sorry.

MS. CARPENTER: Okay.

BY MS. CARPENTER:

Q That refers to the promotion of technical advances in the art of manufacturing these substances and the development of new substances? Do you believe that your application will further promote the technical advancement of these substances?

MR. BAYLY: Objection. This is leading.

I think we need to get a little more open questions.

MS. CARPENTER: That's fine, Your Honor. Are there any ways--

JUDGE BITTNER: Yeah, would you rephrase it?

MS. CARPENTER: Sorry. I beg your pardon?

JUDGE BITTNER: Would you rephrase the question?

MS. CARPENTER: Yes, I will.

BY MS. CARPENTER:

Q Do you understand what promotion of technical advances means?

A Well, I think I do. I mean it means making scientific advances or technical advances in something.

Q Okay. Do you think your application would further technical advances?

A Well, I think there is two answers to that as far as I'm concerned. One is that, yes, it would make an advance in the understanding any possible clinical use of marijuana if we were able

to supply this to investigators to run trials, and, secondly, as I've explained to DEA agents that visited, that we would learn more about how the environment affects the constituents in the plant material which would enable, if this does become at some stage down the road here, becomes a useful drug, and that the manufacturer of it has to be controlled under security conditions, they would know the environment it needs to be grown under to produce a clinical marijuana, medical marijuana.

MS. CARPENTER: All right.

JUDGE BITTNER: Could I just ask--

THE WITNESS: Yes.

JUDGE BITTNER: Because I want to make sure I understand things. Doctor, would you distinguish for me between cannabis and marijuana?

THE WITNESS: Well, the cannabis is the Latin name for the marijuana plant.

JUDGE BITTNER: So can you use the two terms interchangeably?

THE WITNESS: It can be used interchangeably and they are.

JUDGE BITTNER: Okay. Is there a connotation of using one over the other?

THE WITNESS: I don't--there would have been probably in the beginning, but I don't think there is anymore. I think in the street, they're accepted as the same. To me they are accepted as the same thing.

JUDGE BITTNER: Okay. Thanks. Go ahead, Ms. Carpenter.

THE WITNESS: The only different distinction I would make is between medical marijuana and marijuana, marijuana being associated with recreational use and medical marijuana being restricted to use for helping people.

JUDGE BITTNER: Okay.

BY MS. CARPENTER:

Q And you mentioned earlier that part of the work that Dr. Doblin had asked you all to help with was to develop a vaporizer. Do you think that work would lead to any technical advances?

A Well, whenever, I think whenever we can talk about advances in drug delivery, we're talking

about advances. I mean that's why clinical trials need to be run. I'm not qualified at this time without something that I can--a study that's been run by medical doctors under appropriate conditions to judge whether the vaporizer is better than anything else. I don't have that expertise.

I assume that the purpose of manufacturing this medical marijuana is to be able to test various delivery systems and to determine if they are effective and will help patients.

Q And in your opinion would that be a technical advancement in medical marijuana?

A That would be an advance over smoking the marijuana, yes.

Q Okay. If you would look at statutory factor number four, prior conviction record of applicant?

A Yes.

Q Have you ever been convicted of any offenses, federal or state?

A I had a speeding ticket once.

Q That's it?

A Yes.

Q Okay. Factor number five is past experience in the manufacture of controlled substances and the existence in the establishment of effective control against diversion. What do you understand that factor to mean?

A Well, I think what it means if I've had any experience in the manufacture of these or effective controls, and the answer is no, I have not had any experience in that.

Q Okay.

A I've never grown marijuana or any other controlled substance. We have not--I have no experience in the control against diversion. That's why we've been working closely with the DEA agents that came to visit campus to set up appropriate security conditions.

Q And have you agreed to meet all those appropriate--

A We've agreed to meet all of those.

Q So the fact that they're not there now wouldn't mean that they wouldn't be there should

you get the license?

A No, and the university understands that we'd have to have appropriate security.

Q Okay. To your knowledge, is there anybody in the country other than one person who has an experience growing medical marijuana for clinical use?

A Well, in growing, there are other people that are growing it, but for manufacture purpose, only one that I'm aware of for supplying product.

Q Okay.

A Other studies that I'm aware of have to do with detecting marijuana fields, but those are just for that type of purpose.

Q Okay. So to your knowledge, would there be anybody else in the country who would have that experience except for one person?

A No, I think that probably only the one current under contract has any experience in manufacture of this product.

Q Okay. All right. And factor number six is such other factors as may be relevant to and

consistent with the public health and safety. Do you think that your application would further any other factor that would fit into that category?

A Well, only that, you know, I'm looking for--as a scientist, I'm looking to forward advanced science in the study of this product and that's what our contribution would be, to determine if this material could be used clinically and if it would help patients and our part would be as the beginning part of being able to manufacture the product which could be tested.

MS. CARPENTER: Okay. Could I have the Court's indulgence for one moment? Your Honor, we have no further questions at this time.

JUDGE BITTNER: Okay. Let's go--oh, yes, Doctor.

THE WITNESS: I have one correction I'd like to make.

MS. CARPENTER: Okay.

JUDGE BITTNER: Okay.

THE WITNESS: Okay. In reference to the dates, in the second DEA visit as I was thinking

about as we were going through here, and I had mentioned it was in 2004 summer, but it could have very well been the fall of 2003. Those dates are merging on me here, the second visit by the DEA, and I just want to be sure that we understand.

JUDGE BITTNER: You don't know how long after the first visit it was?

THE WITNESS: Well, the first visit was in 2002. So it was probably over a year since the first visit and that's about all I can--I recall it was in the summer because we walked across campus, and it was very beautiful weather. It was a beautiful day and I remember talking about that, but it could have been the fall of 2003 or the spring of 2004, and I cannot, I cannot place it exactly at this time.

JUDGE BITTNER: Okay. Okay. Thank you.

MS. CARPENTER: Thank you, Dr. Craker.

JUDGE BITTNER: Let's go off the record.

[Discussion held off the record and a short recess was taken.]

JUDGE BITTNER: We are on the record. Ms.

Carpenter, your next witness.

MS. CARPENTER: Thank you, Your Honor. We'd like to call Dr. Irwin Martin.

JUDGE BITTNER: Doctor, raise your right hand, please.

Whereupon,

IRWIN G. MARTIN, PH.D.

was called as a witness herein and, having been first duly sworn by the Administrative Law Judge, was examined and testified as follows:

JUDGE BITTNER: Please be seated.

DIRECT EXAMINATION

BY MS. CARPENTER:

Q Would you state your name and address for the record, please?

A Irwin G. Martin, Ann Arbor, Michigan, 3812 Michael Road, North Ann Arbor, Michigan.

Q Thank you. What do you do, Dr. Martin?

A I'm currently retired.

Q Okay. What did you do before you retired?

A I was an executive in the pharmaceutical industry and after that worked--did some consulting

for a few years and then was an executive in the nonprofit world as well.

Q Okay. Let me ask you to turn in one of those big fat books up there to Respondent's Exhibit 11.

A Okay.

Q Do you recognize that document?

A Yes.

Q What is it?

A It is my CV as posted on my Web site.

Q Okay. And did you create that document?

A Yes, I did.

MS. CARPENTER: I would move Respondent's Exhibit 11 into evidence?

MR. BAYLY: No objection.

JUDGE BITTNER: Received.

[Respondent's Exhibit No. 11 was marked for identification and received in evidence.]

JUDGE BITTNER: Could I ask what is the date of the document, Doctor? Do you know when you prepared this?

THE WITNESS: When I prepared this?
JUDGE BITTNER: Yes.
THE WITNESS: I constantly change it as I add and subtract things. So it's sort of a fluid document.
JUDGE BITTNER: So it's current?
THE WITNESS: It is current except that I've recently taken off the picture because the picture no longer applies, as you can probably tell.
[Laughter.]
JUDGE BITTNER: I don't know. I thought it was pretty good. I like the tie.
THE WITNESS: Thank you.
JUDGE BITTNER: So are you still the acting President of the DIA Foundation?
THE WITNESS: No, the new document has a through 2005 there.
JUDGE BITTNER: Okay. Okay. Go ahead, Ms. Carpenter.
MS. CARPENTER: Thank you, Your Honor.
BY MS. CARPENTER:

Q Let's talk a little bit about your education first.

A Sure.

Q Where did you receive your degrees?

A I have an undergraduate degree in biology and environmental studies from Brandeis University and a doctorate in zoology from the University of Massachusetts.

Q Okay. Have you taken any other courses along the way?

A I've taken a number of business courses at Drexel University School of Business and the Wharton School at University of Pennsylvania.

Q Okay. And what did you do after you graduated, got your doctorate?

A I had a post-doc position at the Monell Chemical Senses Center at the University of Pennsylvania.

Q And what did you do there?

A I studied olfaction in guinea pigs.

Q Okay. And where did you go from there?

A I was hired by SmithKline Beckman

Corporation into a management training position.

Q And what were you training to manage?

A Regulatory affairs and pharmaceuticals.

Q So when was that?

A When was that?

Q When did you start at SmithKline?

A In 1982.

Q Okay. And what did you do in that position?

A Well, if for that six year period at SmithKline and French, and I believe it was SmithKline and French for most of those six years--we kept changing names--I was in regulatory affairs responsible in various levels of responsibility, increasing levels of responsibility. At all levels, however, my primary role was to represent the company at the FDA, be the liaison for the R&D division to the FDA as well as advise internally my colleagues in R&D on FDA issues, policies, et cetera.

Q Okay. And were you working with regard to a specific new drug that was being developed?

A Yes, a number of new drugs, yes.
Q Okay. When you left SmithKline, where did you go from there?
A I had a short stint at Squibb, the Squibb Institute, and left there after they were acquired by Bristol-Myers.
Q And what did you do at Squibb?
A Similar position. I was the Director of Regulatory Affairs.
Q Director of Regulatory Affairs. And so what did that involve at Squibb?
A Again, the same type of responsibilities, just a larger portfolio of products representing the company at the FDA and then providing internally--my customer was the R&D Division to whom I gave advice similar to what the FDA would be.
Q Just be clear. R&D stands for?
A Research and development.
Q Okay. And that would be for pharmaceutical products?
A Right.

Q Okay. And after you left Squibb, where did you go?

A To Parke-Davis which was the pharmaceutical research division of the Warner-Lambert Company.

Q All right. And how long did you stay there?

A That was ten years.

Q And what did you do while you were there?

A Again, similar responsibilities. At this point, I was now heading first the U.S. Division for Regulatory Affairs and then my last year there I headed International Regulatory Affairs.

Q Okay. And so did you continue to work with liaison with the FDA in those positions?

A Up until that last year, yes.

Q Okay. And that was with regard to new drugs being developed?

A Again, new drug development; right.

Q Was it also in regard to other new indications for previously developed drugs or?

A It was drugs in development, marketed

drugs, which would include developing drugs for new indications, new formulations, responsible for the regulatory advice related to the advertising and promotion of drugs as well.

Q Okay. So can you just--take your experience at Parke-Davis, what would be the experience, what would be the steps you would go through as the representative for Parke-Davis in terms of getting a new drug developed? How would that start out?

A The Research Division discovers a compound. It would be within the research end of things before we move into development. They would come forward with an idea. The molecule would be synthesized. Initial animal testing would be done to show that it seems to have some, that it's pharmacologically active, that it actually does something.

Once the research scientists have what they think is a viable product, it comes forward to a management team, who agrees or not agrees that we can move forward towards testing in humans, at

which point a project team is assembled. Regulatory affairs is part of that project team. The team works together towards an IND, an Investigational New Drug Application, which would allow the company to study the drug for the first time in humans.

Q So after you've done the animal research, would you meet with the FDA to propose the IND or how does that happen?

A Depending on the type of drug and whether it is a completely new pharmacologic class, if that were the case, indeed we would be meeting with the FDA well before the IND. If it's another drug of a well-known class, we might not meet with the FDA until after we submit the IND.

Q Okay.

A But there is constant dialogue with the agency throughout the drug development process.

Q And again if you could just state, what is an IND again?

A Investigational New Drug Application.

Q Okay. And what does that do? What does

getting an IND do?

A Well, technically, by statute, it allows you to shift drug across state lines for clinical testing.

Q Okay. So you met with the FDA, you've submitted an IND; do they have to approve an IND?

A An IND goes into effect in 30 days unless the FDA objects and puts it on hold.

Q Okay.

A So they review INDs very quickly.

Q So after the IND is--

A In effect.

Q --in effect, what happens next in that drug development process?

A Phase 1 studies are conducted. Phase 1 studies are typically in healthy volunteers. This basically is to show obviously the initial safety of the drug, whether there is some very quick unpleasantry that is discovered, but most importantly--well, that's important, but in addition, how the drug is handled by the body, the biopharmaceutics of the drug, if you will.

So, how much drug you take in a tablet or in a solution and how much gets into the bloodstream, how that's excreted, how long it lasts in the blood. Those are all the Phase 1 studies.

Q Okay. And are you dealing with the FDA during the Phase 1 study?

A Absolutely.

Q Okay. And what happens next?

A Once the company feels they have sufficient data to proceed to patients, both safety and biopharmaceutical data, they move on to Phase 2, Phase 2A would be small patient studies. You pick a patient class that is your intended patient group when the drug is actually marketed, and this is your first test of efficacy.

If you have a blood pressure drug, does it lower blood pressure. If you have a lipid lowering drug, does it lower lipids? This is really your first test in patients.

Q So the difference between Phase 1 and Phase 2, they're both in people, but Phase 2 is the first time you're studying whether the drug does

what it's supposed to do; is that accurate?

A Right. It's the first time it's actually in patients.

Q Okay.

A As opposed to healthy volunteers.

JUDGE BITTNER: At what point are you looking at what the impact of the drug on the body is? Both or do you start that in Phase 1?

THE WITNESS: Well, always.

JUDGE BITTNER: Okay.

THE WITNESS: Any time you put it in people, you're clearly measuring what the drug is doing. For instance, lipid lowering drugs while you may not be looking at a patient class, Phase 1 studies, you can see whether the lipids are lowered because the drug would have the effect even in healthy people.

JUDGE BITTNER: Okay.

THE WITNESS: So you're always measuring those sort of endpoints.

JUDGE BITTNER: I also have an irrelevant question that's been bothering me.

THE WITNESS: Okay.

JUDGE BITTNER: That is why are the initials for an Investigational New Drug Application IND without the "A" at the end?

THE WITNESS: It's actually a long story that has an answer.

JUDGE BITTNER: Okay.

THE WITNESS: The initial law or the initial regulation was written exemption for blah-blah-blah-blah. It was like a really long thing, and IND was picked out of that. It was only later that they changed the name of the application to an Investigational New Drug Application, but by that time, the IND term had been so ingrained that people just kept calling it IND. Sort of like the CDC.

JUDGE BITTNER: Okay.

THE WITNESS: You know people still call it the CDC, but it's actually the CDC and whatever the other letter is, you know.

JUDGE BITTNER: Okay. So the acronym IND stands for Investigational New Drug Application.

THE WITNESS: Application, yes.

JUDGE BITTNER: Okay. I just kept wondering why.

THE WITNESS: Yeah, it's--

JUDGE BITTNER: I'm sorry. Go ahead, Ms. Carpenter.

MS. CARPENTER: That's quite all right. I had that question myself. I just didn't have the nerve to ask it.

BY MS. CARPENTER:

Q So I think you were describing the Phase 2 studies.

A Right.

Q And again, is the FDA involved with those?

A The FDA reviews every--well, the FDA certainly has the ability to review every protocol that is submitted. You need to submit a clinical protocol before conducting any study in humans. So the FDA is supposed to look at every protocol submitted. I have no reason to think they don't because, again, their highest priority review--they only have 30 days to object.

Initially, they don't have any time to object. If you submit a new protocol, technically you can go ahead and start that protocol immediately. So typically they're looking at these things fairly readily. So there's dialogue back and forth, formal, informal. FDA will provide comments on protocols if they think it's a safety issue.

So if they think that you're taking undue risks with patients you will get a formal reply. If they think you're doing something silly and simply wasting your own money, you're not likely to get any formal reply.

MS. CARPENTER: Okay.

JUDGE BITTNER: You were on Phase 2A, I think, before--

THE WITNESS: Right, right.

JUDGE BITTNER: --got off my on my question.

THE WITNESS: Yeah.

JUDGE BITTNER: Okay

BY MS. CARPENTER:

Q And what would Phase 2B be?

A Phase 2B is the larger proof of efficacy studies. So now you actually power the study with enough patients so you can meet a statistical p-value. You can actually say with some statistical certainty that indeed the drug shows efficacy. So these are--

Q And what--sorry. Go ahead.

A So you're moving from tens of patients to hundreds of patients.

Q And what is efficacy just to be clear?

A Does the drug have the clinical effect that it was intended to? Does it lower blood pressure? Does it lower lipids? Does it, you know, slow the growth of a tumor or whatever your intended clinical endpoint is.

Q Okay. And is there a Phase 2C?

A No.

Q Okay.

A Then there is Phase 3. And Phase 3 are the large safety studies so you've moved from tens of patients to hundreds of patients, and now you're

into thousands of patients. So you're once again proving your efficacy, but at this point collecting safety data. You're always collecting safety data, but now in thousands of patients you have a safety database that is a lot more reliable than simply a few hundred patients.

So Phase 3 is what you complete and then you're ready to go to the FDA with a package of thousands of patients and saying we think this drug is suitable for marketing.

Q Okay. And so after you take that package in, is that called something else?

A I wish you could just take it in. You have to actually write a New Drug Application, an NDA, which summarizes all these thousands of patients as well as all the, how the drug is made and manufactured and the controls there, all the preclinical, all the animal testing, so everything you ever know about the drug. And basically the NDA regulations are written, you know, tells A, tells B, it tells C, and then the last one is basically and tells everything else.

So anything you know about the drug, you assemble into a coherent document. Today, this is done electronically and send it into the FDA as a New Drug Application.

Q Okay. And what does the FDA then do?

A The FDA has by agreement ten months to review the document. That doesn't mean approve it or reject it, but they have to at least complete the review within ten months. They provide comments or they provide an approval, and then there is discussion about what other data are requested or how can I interpret these data; they don't seem to make sense? And then hopefully the company and the agency discuss labeling and the drug is hopefully then approved.

Q Okay. And what happens after it's approved?

A Companies often, usually because they want to, sometimes because the FDA asks them to, conduct Phase 4 studies, and these are studies in marketed products either to gather additional safety information, to gather efficacy information in a

new patient population, maybe for a new indication. If you have a heart failure drug, maybe you're going to test it in, you know, blood pressure, you know, similar types of indications, but yet those were not done in the initial NDA. So those are called supplemental NDAs.

Q Okay. And then once it's approved, it's marketed as it's been approved, I presume?

A Right. And there is obviously data collected post-marketing on safety and always submitted. So the dialogue with the FDA is constant throughout the life of a drug.

Q Okay. Dr. Martin, do you have any academic affiliations or have you had them in the past?

A I've had an adjunct professorship at University of Michigan in the College of Pharmacy as well as at Eastern Michigan University in their School of Allied Health, I believe, is the title.

Q And did you give talks or teach classes on drug development issues?

A I lectured on regulatory affairs and drug

development as well as was a preceptor for pharmacy students within Parke-Davis.

Q Okay. And what professional associations do you have?

A I've been a long-time member of the Drug Information Association.

Q Can you tell us what that is?

A Drug Information Association, or DIA, is a nonprofit neutral organization that provides primarily educational and networking opportunities for people within the pharmaceutical and related health care fields. Members are from academia, from the industry, from the regulators themselves, from governments, and there are meetings, workshops.

We just had an annual meeting here in Washington back in June where we had approximately 8,000 people. So it is a large, very respected, I believe, organization. Again, neutral. We take no positions. I keep saying "we" even though I'm no longer with them so forgive me for that. It should be "they" at this point.

Q And what were the positions that you held at the DIA?

A As a volunteer, while I was still in industry, I was, again, moved up through the ranks, became a member of the board and then was president of the association. And after I left the industry and I was consulting, DIA then offered me a full-time job and I was Associate Executive Director and then Acting Executive Director up through the beginning of this year.

Q Okay. What other professional associations are you affiliated with?

A I had been a member of the Food and Drug Law Institute. When I was a consultant I was a member of that. I've been a long-time member of the Regulatory Affairs Professional Society and I was a, when I was in industry, I was an active volunteer for PhRMA which is the trade organization of the pharmaceutical industry and did a lot of work with them, for them.

Q Have you done presentations for those organizations relating to drug development?

A I've done a number of presentations, worldwide for a number of organizations relating to primarily regulatory affairs, drug development, submitting NDAs and, you know, new technology related to that.

Q Okay. Have you also made presentations to the FDA?

A Yes, actually I was, I had the honor of being the first industry lecturer at the FDA new reviewer training course. They wanted to have someone from the other side of the table come and speak to their new reviewers. That was probably one of my favorite things to do.

Q Okay. Can you give us an estimate as to--well, let me ask first. How long does it take to get a new drug through the very beginning stages through market approval, just a ball park?

A Well, a lot depends on how you define "beginning" because there may be a ten year research program before the first compound is even discovered, but once you have a compound that you say is a lead candidate and you want to actually

bring that to the market, I think the average tends to be seven, eight years now, something like that.

Q Okay. And so over the course of your career, can you ball park how many new drugs that you've shepherded through this new drug development process?

A Well, in a 20 plus year career, I'm guessing it was on the order of ten or 12.

Q Okay. And were there other drugs that you helped develop for new indications?

A Oh, yeah, many. I have no idea, but it was more in the dozens.

Q Okay. And you would shepherd that through the process at FDA in a similar way?

A Right, right.

MS. CARPENTER: Okay. Your Honor, at this time, I would tender Dr. Martin as an expert in new drug development.

JUDGE BITTNER: Mr. Bayly?

MR. BAYLY: No objection.

JUDGE BITTNER: Granted. Could I just ask, the DIA Foundation you reference, is that an

affiliate with the Drug Information Association?

THE WITNESS: Right.

JUDGE BITTNER: And it's a 501(c)(3)?

THE WITNESS: Yes, they're both 501(c)(3)s.

JUDGE BITTNER: Oh, okay. So what's the difference between what they do?

THE WITNESS: Oh, how much time do we have? The foundation was set up to provide grants and right now the foundation's main mission is to provide grants that no one else can provide and that is to actually governments. So that developing countries can send their regulators to the FDA, to the EMEA, to the TJA in Australia, to learn from their colleagues. Where their country doesn't have enough money to actually spend, you know, for travel and room and board where they get there, the foundation will provide grants on the order of $50,000 or so.

JUDGE BITTNER: So it's really to provide training to potential regulators?

THE WITNESS: Right.

JUDGE BITTNER: Okay.

THE WITNESS: That's the primary purpose. We also have given academic grants, modest research grants on the 15, $20,000 range, but right now the thrust is to do those things that no one else can do, and the reason DIA can do it is, again, because it's that neutral forum that the FDA and other governments will accept money from.

JUDGE BITTNER: Okay. Go ahead, Ms. Carpenter.

MS. CARPENTER: Thank you.

BY MS. CARPENTER:

Q Dr. Martin, we've talked a little bit about how you would take a drug through the process, but we haven't talked about the FDA looks at the drug. So when a new drug or IND comes through the door, what is it that the FDA is evaluating?

A The primary thing--I should say once they receive a document, they create a parallel group to the industry group. The industry has a project team. The FDA then creates a review team which has

technical experts from all their disciplines. Their primary responsibility is to assure public safety, not to assure new drugs are developed.

That is part of their mission, but their primary mission is to protect the public. So they review particular INDs for safety issues.

Q Okay.

A And again object within that 30-day period if they see something.

Q All right. Do they also--what else do they review for, for efficacy or any other?

A Well, as you move through the drug development process and eventually towards an NDA and then ask for marketing approval, the main criteria upon which drugs are approved is basically safety, efficacy and quality. Those are the international terminology.

Safety being not just the clinical safety but all the animal data would be reviewed by their safety experts. So this is short term as well as long term. Carcinogenicity studies in animals.

Efficacy is all the clinical data to

assure that indeed the drug does do what it is alleged to do, and then quality is all the manufacturing controls to assure that indeed the tablet that was tested or the dosage form that was tested in the clinic is the same as the patient takes in his or her doctor's office as well as two years later, it's exactly the same product.

So that those three things is what determines whether a drug can be approved.

Q Okay.

A And the control of the formulation is a very important part of that.

Q Okay. Let's talk a little bit about quality. How would a company go about assuring the quality that you're talking about of making sure that what is tested in the clinical studies is the same thing that's delivered to a patient?

A You have to test for consistency. You have to test batch to batch whether the product is exactly the same. You have to test for potency so that, again, what was tested in Phase 1 is the same as tested in Phase 2 as eventually on the

marketplace. This is done by a number of techniques, very complex analytical tools to assure that you're actually testing the formulations, you're testing the bulk drug before it's formulated. It's a fairly rigorous thing.

Q Okay. And I presume that would vary somewhat from product to product, what would be required for quality?

A Well, what would be required doesn't really vary, but how one meets those requirements varies greatly. If you have a simple small molecule that was designed to affect a particular receptor, it is fairly easy to know whether the tablet that tested here is the same as the tablet you tested here because your analytical analysis will show you the exact same amount of that particular single small molecule because you know that is the active component.

Some products are much more complex. Botanicals is a great example. Biotechnology derived products where you have proteins and all other things that are being made at the same time

as that protein.

One of my favorite examples is a very well-known drug called Premarin which actually stands for pregnant mare urine, and this is a naturally derived product from pregnant horses, and the active component is a whole combination of equine estrogens and the FDA was able to review that and approve it and it is a remarkably complex product. So the answer to the question I guess is the requirements are the same, but how you meet those requirements, yes, is remarkably variable.

Q Okay. You mentioned botanicals. Can plants or botanicals ever be approved as a matter of quality?

A Well, last year, and while I wasn't active in the industry, I do know that they did issue a guidance document for how to submit an application, a new drug application for botanically derived material, and at a quick review of it, the standard seemed fairly similar.

So it seems that the FDA is willing to accept a botanically derived product and hold it to

the same standards as any other product.

Q And did you happen to notice whether that review mentions marijuana at all?

A There was--

MR. BAYLY: Objection, Your Honor. There is absolutely nothing in this prehearing statement where there's a proffer of the witness talking about a particular botanical, particularly marijuana.

JUDGE BITTNER: Let me look. I think this was in your original prehearing statement?

MS. CARPENTER: I believe it was the same in the supplemental, Your Honor. I tried to make it all one document for ease of reference.

MR. BAYLY: As I recall, the supplemental incorporated the initial--

JUDGE BITTNER: Okay.

MS. CARPENTER: It did.

MR. BAYLY: --and then added, which I think is a pretty good idea really.

JUDGE BITTNER: Actually I agree with you.

MS. CARPENTER: Your Honor, the only thing

I would point out is he does talk about the requirements, simply the requirements for the approval of new drugs and biologics, and I assumed, but I may be wrong that biologics included botanicals. I may have--

JUDGE BITTNER: Let me just find it. Let' see.

MS. CARPENTER: It may be my linguistic fault. That line is--it's the first line of the second paragraph.

JUDGE BITTNER: I'm lost.

MS. CARPENTER: It's under the proposed testimony of Irwin Martin which is--

JUDGE BITTNER: Right.

MS. CARPENTER: --the second one under the summary of testimony. Second paragraph, first sentence.

JUDGE BITTNER: Will discuss the fact that the major developed regions of the world. That's what I have.

MS. CARPENTER: Have unified their requirements for the approval of new drugs and

biologics.

JUDGE BITTNER: Oh, I see.

MS. CARPENTER: This is not extensive testimony, Your Honor, but--

JUDGE BITTNER: Okay. I'll overrule the objection.

MS. CARPENTER: Thank you.

MR. BAYLY: Judge Bittner, then in that event, we have proffered Dr. Ouslander. I don't know if he's going to come or not. It looks more like he's going to come and I'm going to ask that he be able to testify about marijuana if Dr. Martin is going to get into that. I just don't think that biologics--it may--really stretching it--talk about, give us a slight hint about maybe talking about botanicals in general, but particularly not marijuana.

So we simply, this is not simply notice that we have to take this on, so the best we can do is to have Dr. Ouslander come in here and rebut it even though I will admit that on our supplemental prehearing statement, we didn't mention this issue.

JUDGE BITTNER: I think that's fair.

MS. CARPENTER: I think that's fair, too, Your Honor, and I would say it's one question about marijuana which is simply--and I don't think he's even answered if he knows.

BY MS. CARPENTER:

Q So it's do you know if this botanical guidelines that you mentioned mentions marijuana at all?

A I believe there is a parenthetical, for example.

Q Okay.

A And that was it. It was certainly not directed towards marijuana.

Q Thank you.

A And that's all I'm going to say about marijuana.

[Laughter.]

BY MS. CARPENTER:

Q So given these requirements to meet safety, efficacy and quality, as a company is thinking about developing a new drug, what are some

of the first steps a company has to take before it even decides to move to the IND process?

A Well, it's a very complex decision. One of the most important meetings that are held in a research and development company is whether to move forward with a new drug candidate and there's a number of questions that management asks. One, does it seem to work? And two, does it, how safe does it seem to be?

And one of the most important is can we make it and can we make it at a reasonable price and can we assure ourselves that we'll continue to be able to make it at a reasonable price.

Q Okay. So I guess you need a source for the product?

A Right. Where are we getting it? Are we making it? Are we buying it? Can it be made again reasonably? You don't want to market drugs that are going to cost thousands of dollars to the patient when they can then take an aspirin instead, for instance.

Q Okay.

A It doesn't make sense.

Q And when they're deciding on what source they're going to use to obtain the either raw ingredients or the product itself, what are the things that you would think about?

A Well, I would think one of the most important decisions management has to make is do we have a consistent source, can we control that source? For again, small molecules that we can synthesize, the company controls that. If they are more complex molecules or these mixtures, you know, when Wyeth was making Premarin, you know, can we continue to have pregnant mares to produce enough urine for us? And they therefore went and built huge farms so that they could control that raw substance.

So any company would be unlikely to give a positive development recommendation if they're not assured that they will have a drug supply that is unchanging and reliable.

Q So it needs to be reliable in terms of its quantity or in terms of its make up or what?

A Well, reliable in that can we assure that we can get it? Can we assure that it won't change? Can we assure that it's consistent? One of the biggest problems in drug development is the unfortunate need sometimes to repeat studies. If you have a new formulation or your drug source has changed, you may need to repeat years worth of data because you can no longer assure that the data you developed with this earlier version of this drug will actually be the same drug as you now have.

So companies go out of their way to assure at Phase 1 or certainly at Phase 2A that that drug substance is what they will develop throughout drug development. Repeating studies is a very costly, both in money and time, endeavor.

Q And having a reliable and a consistent source would prevent that or at least come as close as possible?

A You would hope so. Right.

Q Is it important to be able to choose as a drug developer exactly what components are in the product?

A Are in the?
Q In the product that you're developing?
A Well, it's important to be able to control it. You may not always be able to choose. Again, if it's a naturally derived product, you may not have all those answers. I keep coming back to Premarin, but, you know, again Wyeth did not necessarily choose which of those equine estrogens to develop, but they had to assure that once they had that mixture, that that stated consistent, so it's not necessarily the choice, but it's the ability to control once you've made--once that choice has been handed you.
Q Okay. And if there were differences in a product, that different sorts of mares produced different sorts of urine, for example, would it be important for Wyeth to be able to choose which mares were going to produce the urine it was going to use?
A Yeah, I think the analogy isn't quite working, but--
Q Probably not.

[Laughter.]

BY MS. CARPENTER:

Q Having not much familiarity with mare's urine and happy that way.

A Yeah. I don't want anybody to think that women are actually taking urine. You know it's a little bit more synthesized, purified than that. But it is important to be able to control the source, especially any naturally derived product because there are variations, yes.

Q Okay. And what would be the effect on the development of a new drug, in your opinion, if a developer cannot be sure that they have a reliable and consistent supply, as you've described?

A Well, if you know from the beginning of development that you're not going to have a reliable consistent source, the impact is there is no development. No company, no reasonably business-oriented company would ever develop a product.

If during the course of development, something changes because there is something out of

your control or that a change was made because it may actually work towards a better product, then there's two things you do. One is you try and show biopharmaceutically--in other words, pharmcokinetically like you do in Phase 1, is this new product equivalent? Does the body use this new product the same way it used the old product?

If that can't be done because of the complexity or the lack of analytical technique, then you basically start over. So those are your two choices.

Q Okay. Just a couple of other quick questions. One is do you know what orphan drug status is?

A Yes.

Q Can you explain to the Court what that is?

A I can explain very broadly, not being an expert, but I have submitted one or two orphan drug applications in my life. Basically the orphan drug statute was passed to give some financial incentive to companies to develop drugs that seem to be effective or at least have been alluded to be

effective for very small patient populations, and I believe the number is 200,000 patients or less in the U.S. so that these patients typically would not have had the benefit of a potentially efficacious drug because the economics were not there for the company.

It costs hundreds of millions of dollars to develop a drug, and develop a drug for 200,000 people, no company would ever get the return on that investment. So a law was passed to allow companies to recoup tax credits as well as get research grants to develop drugs for small populations.

Q Okay. So if a company had an orphan drug status, it would have a financial interest in developing that drug?

A It would not have a financial disadvantage. How is that?

Q Okay.

A I think that's a more accurate way of saying it.

MS. CARPENTER: Okay. That's fine.

JUDGE BITTNER: Doctor, what happens if there's a small population in the United States, but a large population someplace else, is that considered?

THE WITNESS: I believe, for malaria, for instance, let's say, I believe you could get orphan drug status in the U.S., but most companies would be developing it overseas anyhow because you wouldn't be getting tax credit for clinical studies in the U.S. since you wouldn't be doing your clinical studies in the U.S. because there would be so few patients. You'd be doing your clinical studies elsewhere.

JUDGE BITTNER: So it just becomes irrelevant?

THE WITNESS: I believe so. Again, I'm not an expert in that.

JUDGE BITTNER: Okay.

BY MS. CARPENTER:

Q Can a drug developer develop an orphan status drug without similar concerns about source and consistency and availability of the product

that you discussed earlier?

A If a drug is a true orphan, I would think those sort of decisions are even more important because you're sort of on the edge of profitability or at least maybe not even profitability. You're sort of on the edge of losing a lot of money, and if indeed drug development is going to cost you even more, then that might be a way to make that decision to stop development even earlier if the market is so small to start with.

This is in answer to a question about the reliability of the source.

Q Thank you.

A I want to make sure I tie this long-winded answer back together.

MS. CARPENTER: Okay. Thank you. The Court's indulgence for one minute. Okay. I think we have no further questions, Your Honor.

JUDGE BITTNER: Okay. Mr. Bayly.

MR. BAYLY: Thank you, Judge Bittner.

CROSS-EXAMINATION

BY MR. BAYLY:

Q Good morning, Dr. Martin.
A Good morning.
Q I'm Brian Bayly. I'm, as you probably may have heard, I'm one of the Government attorneys, and I just want to ask you a few questions about the testimony that you just gave.
You said you retired. When did you retire?
A I left DIA at the end of March of this year.
Q Oh, okay. And I think you already talked about or you indicated you're very familiar with an NDA, or New Drug Application?
A Right.
Q Okay. Are you familiar with what I would term an abuse liability assessment in terms of marking a potential drug?
A I know that's part of the NDA.
Q Okay. All right. Would you explain what that is to us, Dr. Martin?
A Well, I can tell you that of all the drugs I've developed I've never had to complete that

portion.

Q You never had what?

A I never had to complete that part because we didn't develop drugs that had abuse potential.

Q Okay.

A I know it's one of the boxes one has to check on the NDA form. Having, I've never needed to complete that.

Q Well, would, then does that mean that you didn't have to deal with marketing a drug that would be controlled?

A That's correct.

Q I just want to make sure I got what you said on direct correctly here, but I think you indicated that in your career, you were responsible for getting ten to 12 drugs on the market; is that correct?

A The numbers are difficult to remember.

Q I'm not going to hold you to any specific numbers, but it's--

A I believe that's approximately the number of NDAs that I've worked on, I've been responsible

for, yes.

Q And what I'm interested in, Dr. Martin, is that number you're talking about the drugs that actually got approved and launched for marketing; is that correct?

A I think all but one of those NDAs was actually approved.

Q All but one?

A Yeah.

Q Okay. And how many, can you say approximately how many drugs did you look into that--well, let me put it this way. Can you say how many INDs you were involved in?

A I have no way. Many, many.

Q A lot?

A Yeah. I think the numbers tend to be ten NDAs to one--ten INDs to one NDA, in that order. So if my career is representative of the industry, then you might multiply that by ten.

Q So would you then represent that's roughly the ratio of INDs to NDAs?

A For drugs that are actually submitted and

go into clinical testing, I believe the number is about ten percent wind up actually on the market. I don't know exactly but that's certainly the order of magnitude.

Q Ball park figure?

A Yeah.

Q And of those, just to make sure now, of the ten percent of the NDAs that get approved then, of those how many actually get marketed, and I think you said in your experience, one did not?

A Let me restate that if you don't mind.

Q Sure.

A Of the ten percent that get submitted as an IND, they get studied in humans. Ten percent get marketed.

Q Okay.

A That's a different question, and the one out of ten or so that was not approved was an NDA. It simply was withdrawn before it was approved. Okay. Do you understand?

Q Well, was an NDA submitted--

A Yes.

Q --and then withdrawn?
A Yes.
Q Okay.
A Yeah.
JUDGE BITTNER: So that was a kind of sport case?
THE WITNESS: It was kind of--sorry?
JUDGE BITTNER: Sport case? It was an unusual situation?
THE WITNESS: We like to think so. I mean it was withdrawn for a business decision.
JUDGE BITTNER: Okay.
BY MR. BAYLY:
Q But that happens? That's not unusual?
A Yes, yeah, clearly. Well, I wouldn't say it's unusual. It's unusual, not unheard of. Companies tend not to develop compounds and then decide not to pursue them. That's not a smart thing to do.
Q Dr. Martin, you've testified about the source of supply for marketing a drug and the consistency, but as based upon your experience and

your education, are there other factors that a pharmaceutical company would consider before launching or getting an IND, before they would, and simultaneously consider the source of supply?

A Oh, of course. There's many factors. I'm saying three of the most important are the ones I identified.

Q Okay.

A I'm not sure--well, I'll let you ask the question.

MR. BAYLY: Right. Judge Bittner, I would request that we can give Dr. Martin Respondent Exhibit No. 1.

JUDGE BITTNER: Okay.

BY MR. BAYLY:

Q Maybe you're way ahead of me. You have that already?

A I think this is it, yeah.

Q Is that the--it's the IOM report?

JUDGE BITTNER: Right. Let's find it.

THE WITNESS: This is says "Marijuana in Medicine." Is that the one you're talking about?

BY MR. BAYLY:

Q Yes.

A Okay. Which I have not seen before.

MR. BAYLY: I'll make sure everybody has got it before I--

BY MR. BAYLY:

Q Dr. Martin, I'm referring to this exhibit as a point of reference, but just let me ask you, is this exhibit something you're familiar with or not?

A No.

Q Okay. If you would please turn to page 213 of Exhibit 1, and I know this is going to--I'll explain this right up front so we don't get confused by the record. It's the page numbers I'm referring to looks like Bate stamps, and they are on the very bottom so that it will actually read 0213.

A Right. Okay.

Q And it's chapter five of this exhibit, this book here. And I want to take you down to the second full paragraph, Dr. Martin. Do you see

that?

A Yes.

Q And since it's short, I'll read it for the record and then just ask you if you agree or disagree, just to get your thoughts on this statement.

Drug development is a long and financially risky process. For every drug that ultimately reaches clinical testing through an IND, thousands of drugs are synthesized and tested in the laboratory, and only about one in five drugs initially tested in humans successfully secures FDA approval for marketing through a new drug application, NDA.

A Right.

Q Do you agree with that or what is your reaction to that--

A Yeah, I think that's correct.

Q --short paragraph?

A I was guessing one in ten. They're saying one in five. I mean it's the same order of magnitude. That's correct.

Q And then I'd like you to look down at the bottom of the page 213 and I'm just going to read you one or two sentences here, but it skips over to 215, Dr. Martin. If you see, there's like a chart in between.

A Okay.

Q So the statement I want you to recess here, it starts at the very bottom of 213, quote: "With respect to the cost of a single drug's development, a number of recent studies have provided a range of estimates of about 200 to 300 million depending on the method and year of calculation."

And what I'd like to ask you about that statement, Dr. Martin, is that estimate roughly true or is it somewhat obsolete in light of when this report was written back in the late '90s?

A Yes, I was just looking up references 33 and 44 and those are indeed late '90s. The latest out of Tufts which is the Tufts Center for Drug something or other, it's the drug development research group at Tufts University. They're the

ones who have been conducting or analyzing the cost of drug development. I believe their latest number is about 800 million.

Q Is there a range in there or is it just roughly 800 million?

A Oh, 800 million is like a very rough estimate. You know you take the cost of all of R&D and how many NDAs come out of that. So it includes everything that was never developed. It includes, it actually includes the price, the cost of the opportunity, so, you know, if you have $100 million, is it best to put it in new drug or can you put it in a money market and, you know, earn two and a half percent or something. So it's the loss of the what they would have made if they simply invested the money somewhere else. It is not actually out of pocket costs.

Q Okay. So you're talking about opportunity costs?

A Yeah, yeah. So the 800 million estimate is across the entire industry for all new drugs including opportunity costs.

Q Now, Dr. Martin, in your experience with drugs, have you also had to deal with drug devices, the delivery system?

A I've never dealt with devices. I've been in pharmaceuticals only. I've dealt with delivery systems, but not as a drug device.

Q Well, at least let me ask you then this question, though.

A Right. Are we done with this?

Q Your experience, is it with only dosage units or some of the drugs that you developed that got through the NDA process and were launched, were some of those drugs delivered by other methods other than just your normal dosage unit tablet pill?

A Well, I'm trying to answer this without being--well, I'll try and answer it politely. There are a number of chemists who would say that there is no such thing as a simple tablet pill. I mean I know what you're trying to say, but there's some fairly sophisticated things that go on inside of some of those little capsules, and I've had

experience in some fairly sophisticated pharmaceutical work, all within a tiny little capsule.

There is actually pump mechanisms, osmotic pumps and things like that. So the consumer looks at it and it's a simple capsule, but it's a very complex delivery system. So that experience I have had. I have not had experience in medical devices per se.

Does that answer your question?

Q Well, yes, it does, but then as a follow up, though, in the industry, are you familiar with the fact that a device would need the FDA approval as well as the drug? In other words, if you're marketing a drug and you want to deliver it through a syringe or something like that, would that need to be approved?

A If it is indeed a drug device combination product like a pre-filled syringe, basically the centers, the Center for Drug Review and the Center for Device Review, determine which has the primary responsibility. These are called combination

products.

So if the centers feel, and there's a committee they have that work together, if the centers feel that it is primarily a drug, such as a pre-filled syringe, we know very well what a pre-filled--what a syringe is. We don't need to do an extensive review of that. Then the responsibility would be within the Center for Drugs.

If it is primarily a device, and I can't frankly think of one at this point--maybe even--see, even the drug-coated stints, I believe--I'm not sure who has primary review for that. I would bet it was the drug side. But I'm not sure. So there are mechanisms within the FDA review to jointly review drug device combinations.

Does that answer your question?

Q Yes.

A Okay.

Q But on follow-up to that, then in certain cases, the drug manufacturer would have to consider developing the drug itself as well as the device? I mean that would be two separate issues or at

least two separate expenses. Let me put it that way.

A It would be a parallel development and it would all be part of the same NDA. It may not be any more expensive than the capsule that I was describing, for instance. Some devices are very inexpensive. Some formulations are very expensive. I wouldn't take the next step and therefore conclude it's more expensive to develop a combination that a non-combination. I don't think that's a cause and effect there.

Q Well, it depends then on the device.

A Sure.

Q As one factor?

A Right.

Q Are you familiar with any of the safety devices that have to be overcome with the delivery system? Any safety issues?

A That have to be overcome with a delivery system?

Q I mean, yeah, as a drug company anticipates a certain delivery system, are there

safety issues that they have to consider?

A There are safety issues on everything the company considers. I'm not trying to be smart, but I'm not sure what you're getting at. I mean everything is, there is nothing done in drug development that is not with patient safety in mind. So what are you--can you ask your question differently?

Q Well, could you tell us some of the safety issues that have to be overcome with a delivery device or does it depend on a particular delivery device?

A Well, it clearly depends on the delivery device. One of the more common questions for time release products, most folks are familiar with drugs that used to have to be taken six times a day and now you can take one a day. Well, that's basically done through some fairly sophisticated pharmaceutics, and one of the things that one must show to oneself as well as to the agency, to the FDA, is that all that drug indeed is delivered over time.

So dose dumping is what's that called. One has to assure that that doesn't happen. So there are extra questions when you have a new device or any device that is part of a drug delivery system. But I wouldn't say it's anything terribly unusual or a hurdle terribly high to jump over.

Q If you could turn, please to page 220, 221.

A Okay.

Q Yeah. Let me back up here. That would be page 219, Dr. Martin. The bottom paragraph. Again, I'll read it.

It says: The possibility of scheduling is a major detriment of whether a manufacturer proceeds with drug development. In general, pharmaceutical firms perceive scheduling to be a detriment because it limits their ability to achieve market share for the following reasons: restricted access, physician disinclination to prescribe controlled substances, stigma, the additional expense for abuse liability studies, and

expensive delays in reaching the market due to federal and state scheduling processes.

Do you agree with that?

MS. CARPENTER: Sorry. Could I just make one quick objection just because there were two mistakes in the reading, and I wanted it to be clear. The first line, I think you said a major detriment, but it's actually a major determinant.

MR. BAYLY: Yeah, you're right.

MS. CARPENTER: Is that correct? And then the second time you said detriment, it was in general pharmaceutical firms perceive scheduling to be a detriment, but it's actually deterrent. Just wanted to be clear on the record.

JUDGE BITTNER: All right.

MS. CARPENTER: Thank you.

BY MR. BAYLY:

Q Dr. Martin, discount my reading. Just look at that paragraph that I read and ask you if you could assess that, if you're in agreement with that?

A That sentence, yes, not that paragraph?

We've only read the sentence; yes?

JUDGE BITTNER: Uh-huh.

THE WITNESS: Yes, right.

BY MR. BAYLY:

Q Okay.

A Because I haven't read the rest of the paragraph and I don't know what the rest of the paragraph says. So I'm just being clear here.

MS. CARPENTER: And, Your Honor, let me just object quickly. I think he already testified he had no experience with controlled substances.

JUDGE BITTNER: He said that, I believe, that he had not brought any controlled substances to market.

THE WITNESS: Right.

JUDGE BITTNER: So I don't know. Can you answer the question? I think the question was do you agree with that sentence?

THE WITNESS: Yeah, I can answer the question, and that would certainly, I would agree with the assessment that drug companies are not keen to develop scheduled drugs because of the

reasons outlined here.

BY MR. BAYLY:

Q Okay. Well, Dr. Martin, let me ask you just a few more general questions on your testimony here. Would another consideration to launch an IND, would that be based on, would you assess whether there are already competing drugs on the market that address the same medical problem?

A Sure.

Q Would you assess the potential drug market? I know it sounds rather cold, but if you're marketing such a drug--would you see a difference between wanting to market a drug such as Lipitor, which is going to be a drug that you keep taking indefinitely, as opposed to a drug where you know the population has a terminal problem? Would that be a consideration?

JUDGE BITTNER: Terminal problem as in the population is going to die or terminal problem as in the problem is going to go away?

MR. BAYLY: Well, actually it could be both. I guess the problem goes away--

JUDGE BITTNER: Okay. In other words, taking for an indefinite duration as opposed to--

THE WITNESS: Right.

JUDGE BITTNER: --something like a pain killer that you hope would not have to be taken forever.

THE WITNESS: If I may digress--thank you for the Lipitor example. Having developed Lipitor, I just like to hear that name out there.

[Laughter.]

BY MR. BAYLY:

Q A lot of us use it.

A I have a tee-shirt that says--to answer your question directly, no. Market share clearly or market size is clearly considered, but not whether it's short-term versus long-term use. In other words, you could have a painkiller, for instance, that is a huge market even though people may only take it, you know, when they have a headache once a month.

That's still a huge market. Or you can have a relatively small market, but people take it

for the rest of their lives. So it's not how long the patients take the drug; it's the size of the market is clearly considered.

Q So it depends then? It's going to vary as to the people that need it as well as how long they take it?

A All of those things are taken into account and you know clearly part of every management team is a marketing person who helps to figure out just how large the potential market is, and that's drug companies are indeed businesses. And they need to make those smart business decisions.

Q Is a market analysis done before the IND is submitted?

A Well, there's certainly an informal market analysis done of every, you know, research program. It's unlikely that companies would want to be researching things for which there is no market.

I mean I've had too much experience in drugs looking for indications, you know, where scientists come up with a drug that inhibits this particular enzyme perfectly or this receptor

perfectly, yet it doesn't do anything. You know there's no clinical indication for that. We try not to do things like that. So clearly before any decisions in research are made and clearly before any decisions in development are made, market potential is assessed, again initially informally and then much more formally as you move to the bigger dollar costs.

Q Could you tell us what a market analysis would entail generally when you're assessing the possibility of doing an IND?

A I can give you some general, you know, a few key things that would be included.

Q Well, let me back up here.

A Okay.

Q And let me withdraw that just for a second, Dr. Martin.

A Sure.

Q And ask you in your experience, were you the one that or were you one of the ones that participated in the market analysis or did they do the market analysis and say, okay, Dr. Martin, here

we've got this; now you take the ball?

A Well, everything is done as a team. I never carried the ball on my own, if you will. You know I worked very closely with the drug development folks, with the clinical folks, with, you know, clinical development is a huge discipline. So there's hundreds of people that work on drug development.

There's a management team on the order of about 20 that might make that decision on whether to move forward. Did I conduct market analysis? No. I mean nor did the marketing person conduct the regulatory analysis. Everyone comes with their own area of expertise, brings it to the team and then the team makes a recommendation to senior management.

Does that answer that question?

Q Well, then I want to make--you're saying you did participate in the market analysis somewhat being a member of the team?

A I would say that as a member of any project team--we're not just talking about Lipitor

now; right? We're talking in general terms; right?

Q Right.

A Okay. As a member of any project team, the team receives information on the potential market and then people with expertise and people without expertise put in their two cents, but hopefully those with the expertise formulate the team's opinion, if you will, the consensus opinion and that goes to senior management.

So in that regard, I've certainly heard enough market proposals and my expertise was not in marketing, so I would be on the listening end and not on the participating end of, you know, the size of that market.

Does that answer the question?

Q Well, yeah, if I could follow it up, Dr. Martin.

A Okay.

Q And at least if you were engaged in some of the market proposals, could you tell us what that entailed in your experience?

A In very general terms. How many patients

have the disease or the symptom that the product is to help to treat or cure, whatever the type of product is. So it's a size of the population. Again, how long the drug would be used. Clearly that's part of it.

Who else is on the market? You know what other companies with whatever products? And how good those products are versus what we think the profile of our product would be? And then whatever we can find publicly about what other companies are doing as well in this particular field? How many new beta blockers does one need? After awhile you don't need anymore. There's more than enough out there.

So it's the incremental benefit of your drug versus the competition and it may be smaller, it may be huge, and then the size of the market. I mean that's basically how those decisions are made.

Q Is the interaction with other drugs also a factor in the market prospects or market analysis?

A Now your question was specific to before the IND, so we really wouldn't have much

information about interaction with other drugs, but as you move into drug development and you're starting to get potential drug interactions, sure, companies stop development for a number of reasons, one of which may indeed be newly discovered drug interactions that makes the product no longer competitive. That's a potential thing.

Or you continue with development, but now you simply warn your investigators and then the prescribing physicians about that drug interaction.

Q Okay. So an IND can be derailed perhaps because of side effects?

A That's the primary--well, yes. Safety or efficacy or lack of ability to make the drug consistently. Any of those things could cause a drug company to decide to discontinue development; yes.

Q How about patents and the need for patents; is that another factor to be considered and is that a factor that you consider before the IND?

A The patent status is always part of the

drug development decision; yes. But there's lots of things that are patentable, not just the molecule itself. The drug delivery system delivering that particular drug is a potential patentable product. So drugs that have off patent have been developed. Orphan Drug Product, for instance, gives seven years of exclusivity to that product if developed for that orphan status. So that is as good as a patent.

So if you have an orphan drug status, you get seven years of exclusivity if you develop it for that indication.

Q Okay. Would you please turn to page 228?

MS. CARPENTER: I'm sorry, Mr. Bayly. What was that page number again?

MR. BAYLY: 228.

MS. CARPENTER: Thank you.

BY MR. BAYLY:

Q This is more for reference than anything because I want to ask you this in the context of your general experience, Dr. Martin, but the sentence I'm pointing out to here is the, it's the

first full paragraph, and it starts out "Three points," but then you go down a couple more sentences and it starts "In general."

A Okay.

Q Implies that their development is considered especially risky from a commercial standpoint in that small companies are often willing to assume greater development risk than larger more established firms. In your experience, would that statement be generally true, that there are small companies that would be willing to take more risk than the established older companies?

MS. CARPENTER: Just object here for a moment. The predicate for "their" is unclear when you read that sentence into the record. In general, that implies that their development. And the question is the development of what?

JUDGE BITTNER: Oh, you have to refer to the previous sentence.

MS. CARPENTER: Yes.

JUDGE BITTNER: But I would.

MS. CARPENTER: Okay.

JUDGE BITTNER: Okay.

THE WITNESS: Well, I want to make sure that the witness is aware of what that is.

JUDGE BITTNER: Right. That they're referring specifically to cannabinoids.

THE WITNESS: Right.

MR. BAYLY: Right. It's not necessary to--that's more of a point of reference.

BY MR. BAYLY:

Q So it's just the general question is, Dr. Martin, despite the various hurdles that we've talked about, including the consistency of supply would not the smaller companies be willing to take somewhat more of a risk than your--

A I wouldn't make that broad a generalization.

Q All right. And how would you qualify it then?

A Well, the person whom they're quoting here says often willing. I'm not sure that I would be comfortable saying often. There certainly are small companies who have taken greater risks. It

implies that large companies don't also take great risks because I've seen that as well.

I mean sometimes a Pfizer, for instance, which I think is like $3 billion a year in R&D, for them to invest a couple hundred million dollars on a risky product, that's not a big part of their R&D expenses. For a small company, that would be huge. So risk/benefit risk analysis is a complex thing, and I think this author is taking a little bit too much liberty. I understand what they're implying but I'm not sure I would agree with the word "often."

Q Well, and then of course the risk is there are many, many risks, right, as we've discussed?

A Sure.

Q It's going to be, the risk is relevant to what the particular risk is and how much capital a company has; would that be true?

A I wouldn't--well, the risk is not related to how much capital it may have. What you do with that risk might be, but even then I've seen small companies, you know, take a risk, run out of money

and then go raise more money. I mean that happens all the time, as well. I just think it's too broad a statement and without, you know, specifics, I really wouldn't agree with it.

Q Well, you said you wouldn't agree because of the--

A The often.

Q --the adverb "often." Right?

A Yeah.

Q But it's not totally untrue?

A No, no. There are companies that are often formed. Okay. I won't use the word "often" myself. Companies have been formed to develop a particular compound. And if that compound doesn't work out, the company goes out of business, and then you may have had a couple dozen people, you know, invest a couple of years and that was a risk they were willing to make.

It does happen. Again, it's the "often" part. There are small companies who are as conservative as the big pharma companies. We may be quibbling, but I just think it's too broad a

statement.

Q I think you've already testified a little bit about botanical products as opposed to developing other single entity chemical products; is that correct? Characterize that correctly.

A Well, I testified that the FDA issued a guidance document so therefore they're willing to accept, therefore, the assumption I'm making is they're willing to accept botanicals held to the same standards as drugs and approve them through an NDA process.

Q Okay.

A I have no personal experience in development of botanicals.

Q Okay.

JUDGE BITTNER: And by botanical, you mean?

THE WITNESS: Generally the term is used for plant derived material.

JUDGE BITTNER: Okay. So are, would you consider, for example, hydrocodone produced from opium to be a botanical?

THE WITNESS: No, because it's a purified product that can be controlled.

JUDGE BITTNER: Okay. That's kind of where I was trying to go.

THE WITNESS: Yeah.

JUDGE BITTNER: So a botanical is something that stays botanical all the way through?

THE WITNESS: In my mind, it's the ability--yeah, you grind up those leaves, you know, and there may be some extraction, but not a whole lot more than a simple extraction.

JUDGE BITTNER: So if tobacco were a drug, it would be a botanical?

THE WITNESS: Tobacco would never be a drug.

JUDGE BITTNER: And I was just--because I couldn't think of anything else, but if it were, it would be--you would classify it.

THE WITNESS: DEA should do something about tobacco, but that's a whole another story.

JUDGE BITTNER: Right, right. No, I realize that and I realize that was a poor choice.

I just couldn't think of something better off the top of my head without going into marijuana, which I didn't want to do.

THE WITNESS: You know the St. John's Wort and that kind of stuff that basically is ground-up plant material that is now sold as food supplements and the like. Those are botanicals.

JUDGE BITTNER: Okay. So it's that it's not purified down to it's sort of chemical composition.

THE WITNESS: Yeah, because if you do that, generally people can either use that very pure extracted compound or make it themselves synthetically. That's in my mind the difference. I haven't read that guidance carefully enough to see if the FDA has another definition for what they consider a botanical is.

JUDGE BITTNER: Okay. Thank you.

BY MR. BAYLY:

Q Dr. Martin, I think you also talked a little bit about orphan drug status. That is allowed for how long? Did you say seven years?

A Well, once a drug is developed as--an orphan drug status designation--you apply for the orphan drug status designation.

Q Right.

A And if you receive that designation, then you proceed to develop the drug as an orphan drug. Once that drug reaches the market, it is given seven years exclusivity, in essence, a FDA patent, if you will.

Q Is there any time limit on developing this orphan drug? In other words, you apply for it and then you're hoping to--

A Yeah.

Q --get it and get that seven year--

A Does it expire, you mean?

Q Right.

A Does the status--I'm not sure. I frankly don't know. I've never been in that situation. I've developed orphan drugs, but I don't know whether there is, you know, a statute of limitation on that designation.

Q Dr. Martin, are you familiar with what a

Schedule I substance is?

A I'm familiar with the nomenclature, yeah.

Q And would the fact that a pharmaceutical product being developed from a Schedule I have to be, the company would also have to petition to lower it another schedule--

A Right.

Q --would that be another hurdle that the company would consider?

A As I mentioned earlier, yes. Those things would all be part of the consideration of whether to proceed with drug development.

MR. BAYLY: Nothing further. Thank you, Dr. Martin.

THE WITNESS: Thank you.

JUDGE BITTNER: Redirect?

MS. CARPENTER: I do, Your Honor. Give me just one minute.

REDIRECT EXAMINATION

BY MS. CARPENTER:

Q Dr. Martin, you were asked some questions about the amount of money it would take to deliver

a new drug, and I think you had indicated the latest number was 800 million, and that that was derived from including lost opportunity costs as well as direct development, as well as losses from other things it didn't develop; do you recall that?

A Right.

Q Okay. Maybe you could go into--could you explain a little bit more what you meant by that? What kinds of costs go into that $800 million number?

A Well, it's basically the cost of all of R&D absorbed by those few products that actually make it on to the market, so the thousands of chemicals that were synthesized and screened that led to the five to ten INDs that led to the one approved drug, well, that one approved drug then absorbs, if you will, the cost of all that research and all that development.

So it's really how much a hugh pharmaceutical company spends on all their R&D divided by how many NDAs they get at the end of the year.

Q Okay. So it's not the actual cost of developing a particular drug; is that right?

A No. It's how much it costs for that company to remain in business, but certainly a smaller company with a very directed R&D on an orphan drug, for instance, is not going to spend anywhere near $800 million.

Q Okay. And that was my next question. Are there differences in development costs for different drugs?

A Oh, absolutely, sure.

Q Okay. And those could range quite a bit with it?

A There are clinical studies that cost a couple hundred thousand dollars, and there's clinical studies that cost $100 million.

Q Okay.

A I don't know. Well, hundreds of, tens of millions of dollars. How's that?

Q Okay.

A So, yes, the prices are all over the board. The costs are all over the board.

Q Okay. Mr. Bayly also asked you a series of questions about a lot of different factors that the drug companies or drug developers have to balance in terms of making a decision about whether to bring a drug to market--size of the market, sources, et cetera, like that.

Who is the one who makes that decision? Who makes, who weighs all that and decides whether or move forward or not?

A Well, clearly it varies in every company. But most companies have a senior management team that or a senior management team within the R&D division, and some CEOs have a little bit more control than others, but most of the time it's the head of R&D and his direct reports, his or her hopefully some day direct reports that make that decision.

Q Okay.

JUDGE BITTNER: The direct reports being the person who report to that head of R&D?

THE WITNESS: To the head of R&D, yes.

JUDGE BITTNER: Okay.

BY MS. CARPENTER:

Q And do you think it's possible that some drug companies would disagree with another drug company's decision about how to balance and weigh those factors?

A That's why there's a very active in licensing and out-licensing department in every pharmaceutical company. Different companies make different decisions, and whereas a company like Pfizer may say if it doesn't, you know, if we're not going to make $500 million a year it's not worth our effort, whereas a smaller company may say, my goodness, that's going to make $50 million a year, and that's huge for us. So absolutely, different decisions by different companies.

Q Okay. And does the FDA have any role in deciding whether or not a drug should be brought to market because of those factors, that is the economics of the decision?

A No.

Q Okay. In your experience, has the FDA ever denied an application because they said

there's no way you're going to get this through the process? As a financial matter?

A Oh, no.

Q Sorry.

A No, you know, they may offhanded say you guys must be crazy, but I'll review whatever you want.

Q Okay.

A But no, clearly from a formal review standpoint, that is outside their responsibility.

MS. CARPENTER: Okay.

JUDGE BITTNER: So, Doctor, then, what would happen, for example, if Company A says this drug isn't going to work for us, but we'll sell it?

THE WITNESS: Right.

JUDGE BITTNER: We'll say the NDA to or the IND to Company X?

THE WITNESS: Yeah, they would sell the rights to that compound to another company.

MS. CARPENTER: I think that's all I had, Your Honor.

JUDGE BITTNER: Any recross?

RECROSS EXAMINATION

BY MR. BAYLY:

Q Dr. Martin, the questions you were just asked, one of the questions by Mrs. Carpenter, I believe, was that the FDA doesn't assess the market potential of the drug; they'll go ahead and approve an IND as long as it meets the IND criteria; would that be correct?

A Yeah, the only market analysis they would do is to grant a orphan drug application, but for an IND, the FDA does not conduct a market analysis.

Q But would it be a fair statement to say that a pharmaceutical company looking for a profit is not going to file an IND where they don't see a potential profit?

A People do--

Q Almost a truism?

A Well, one would think that would be a truism, but I've seen lots of people do lots of silly things. You like to think that you're not going to submit an IND that's not going to lead to a profit, but sometimes INDs are submitted--maybe I

just shut up and answer the question.

[Laughter.]

THE WITNESS: Okay. I've answered your question.

MR. BAYLY: That's fine. That's all I have.

THE WITNESS: Okay.

JUDGE BITTNER: Are INDs ever submitted by nonprofit organizations?

THE WITNESS: Sure.

JUDGE BITTNER: So there could be another motive in there somewhere?

THE WITNESS: There are controversial products that companies did not want to have their names associated with and, yeah, and nonprofits have stepped up and submitted. You know, RU-486, for instance, very few large companies were going to put up with, you know, picketers outside their research offices. So sure, that does happen and has happened successfully.

JUDGE BITTNER: Okay. Anything else, Mr. Bayly?

MR. BAYLY: No, Your Honor.

JUDGE BITTNER: Ms. Carpenter?

MS. CARPENTER: I'm finished, Your Honor.

JUDGE BITTNER: Okay. Dr. Martin.

THE WITNESS: Thank you.

JUDGE BITTNER: Are you flying on Northwest?

THE WITNESS: Yes, and there has been no implication--knock on wood--as far as I can tell.

JUDGE BITTNER: Good luck.

THE WITNESS: Thank you.

JUDGE BITTNER: Thank you. Off the record.

[Discussion held off the record.]

JUDGE BITTNER: Back on the record. We will recess for the day and resume at nine o'clock tomorrow morning. Off the record.

[Whereupon, at 12:20 p.m., the hearing recessed, to reconvene at 9:00 a.m., Tuesday, August 23, 2005.]