perspective of the law if data was not submitted for three and a half years after a surgery, correct?

A Correct.

Q Were ophthalmologists permitted to advertise their Sullivan Laser System as part of their IDE study?

A No.

Q And would that be under Section 812 of the Federal Regulations?

A Correct.

Q What's the reason for that prohibition?

A The reason is that it's not an approved device. It's an investigational device, and the objective is to make sure that people who are seeking the treatment with the device understand that it's investigational, that it's an experimental device, and to not be misled to thinking that because the FDA has approved the investigation that the FDA has approved the laser.

Q Okay.

So if an advertise reads: "Are your glasses getting in your way? Do your contacts hurt at the end of the day? Are your glasses foggy during your

favorite activities? Do you have problems with sand at the beach or finding your blanket when you come out of the water? Today these problems really can be remedied."

Is that misleading? Is that inappropriate?

A That's advertising. It's -- yeah. Basically.

Q It's illegal?

A Correct. It's prohibited by 812.

Q You okay?

A What's that?

Q You okay?

A I'm fine. As okay as I'm going to get.

Q Did the FDA shut down the Nevyases' Sullivan Laser System, to your knowledge?

A Did they shut down the IDE?

Q Correct.

A Excuse me. Sorry about that. My throat is dry. If I drink any more water, I'm going to float away.

The only evidence that I have, after going over many documents that were given to me since I left the agency related to this trial, I discovered an email from someone in my research monitors whose name escapes me -- he was part of the Office of

Compliance -- that essentially said that the IDE had been put on hold or stopped. I think that was the word used.

Other than that, I wouldn't know because I wasn't at the FDA at that time; and even if I -- with the consequence, I wouldn't have -- be privy to that information.

Q Do you recall if that email cited concerns over research misconduct?

A Correct, as I recall.

Q And concerns that the device was endangering the public?

MR. SILVERMAN: Objection. This is evidence that comes as hearsay.

MS. FITZGERALD: The document will be introduced.

THE COURT: There's been testimony that an application was filed by the Nevyases to use this. There were some complaints from the investigation, but they were never closed down.

MR. SILVERMAN: Correct. They were never closed down.

THE COURT: They were never -- the

word "closed down" is not a good term. They were never prohibited from using the Excimer laser, that in '91 they discontinued it anyway.

BY MS. FITZGERALD:

Q Is that your understanding, Mr. Waxler, of what happened, that the Nevyases voluntarily discontinued using the laser device in 2001?

A There's two things I say in addition to the letter of Mr. Troski (ph) --

THE COURT: Trotsky?

THE WITNESS: That's that email that I have read that says that it was shut down. I don't know -- I have no verification of that. I don't know what -- the other thing is that what we did routinely was that even when there was a withdraw of an IDE, which did happen, one of our objectives was -- because there were 100 some IDEs, believe it or not, that we had under our control of folks that were not complying with the rules, we systemically applied pressure to those that we knew there were in violation, essentially jawboning them to withdraw their application.

So this was a typical -- whether it occurred here in this case, I have no idea.

But --

BY MS. FITZGERALD:

Q Looking at the summary findings and all of the directed inspections --

A Right.

Q -- is that the type of pressure that the FDA applies?

A Correct.

Q And they conduct all those inspections to apply pressure to get the investigator to withdraw the device?

A Correct.

Q Is that what was done in this case?

A Well, certainly the directed inspections are a part of it; the piece about whether there was jawboning with regard to withdraw, I have no way of knowing.

Q Now, the Nevyases submitted their application for an IDE in March of 1997, and the FDA denied it twice before they granted conditional approval in August of 1997.

Were you aware of that?

A I am.

Q Why would the FDA be denying the application on two different occasions?

A Because they had safety concerns, information about the -- there were a whole series of issues. I forgot the exact number. There were 15 or 16 deficiencies having to do with the software violation, verification, having to do with aspects of protocol, having to do with profilometry, that is the evenness of the profile on the surface of the cornea. There were many issues. It's a long, long list.

So until the -- this is typical. Until the agency is satisfied that the laser is -- meets certain minimum safety conditions, that it would not even allow a clinical trial to proceed with the first patients.

Q Okay.

Now, I understand that you're not involved in the complaint resolution process at the FDA, but in your 26 years there, are you aware of whether the FDA typically responds to individuals who submit complaints?

A No.

Q No you are not aware, or no they don't?

A They want complaints, but typically the agency does not respond to complaints. Even when I complained to the agency, they don't respond. The reason for that is it's an institution, and the response has to come from the institution.

So when a letter comes in to the commissioner or the president or the Office of Criminal Investigations -- except for the latter one -- the complaint will trickle down to the appropriate division or branch; and then the branch has to figure out -- assign it to somebody to figure out is this something we want to respond to, or we just want to sort of ignore it.

If they decide that they want to respond, if it's an important enough issue to respond, then it will -- someone will draft a response and it will trickle back up to whomever the letter was assigned. And sometimes there's a response.

Typically, there's not a response because the agency doesn't want to engage in a public dialogue by letters on each of these complaints. Essentially what it will do is to keep copies of them; and except in a rare instances, it will not

respond.

Q But they do want to hear these complaints?

A Absolutely.

Q Particularly if they address matters of public concern other safety of medical devices.

A Absolutely.

Q Going back to the protocol in the case of the Nevyases, the FDA granted conditional approval with limited parameters as to how that device could be used, right?

A Correct.

Q If the Nevyases went outside those parameters, for instance, if they operated on patients who had criteria that put them out, that would be a violation?

A Correct.

Q And that would be the case even though they had technically an IDE approval in place?

A Correct.

Q Did the FDA become aware of a number of those instance where the Nevyases were operating outside of the parameters after conditional approval of the IDE had been given?

A From my reading of the -- one of these

documents of the inspector, yes.

Q Now, as part of the IDE process, do clinical investigators use an institutional review board?

A Yes.

Q Is it essential that the investigator submit accurate and timely data to the intuitional review board as well?

A Absolutely.

Q So it wouldn't be sufficient for a clinical investigator so say, "That's not my responsibility; it was the IRB's responsibility"?

A Correct.

Q Mr. Waxler, do you know the Nevyases personally?

A Yes. I do.

Q How do you know them?

A Well, I'm -- I -- I did a little work for Dr. Anita Nevyas-Wallace. I have a consultancy that I help manufactures get their products on the market. She had a surgical of tool of some sort; I helped her out with that.

Her husband, Dr. Ira Wallace, has a very interested device I helped him out with a couple years ago -- not related to Lasik -- we worked on.

Fun and interesting and profitable.

Q So they sought your advise out in terms of getting their devices in order in terms of regulatory matters?

A I'm sorry. I didn't understand the question.

Q They sought your advise out to help them for purposes of regulatory issues?

A Correct. Correct.

Q Okay.

MS. FITZGERALD: Those are all the questions I have at this time.

THE COURT: Mr. Silverman.

MR. SILVERMAN: Yes.

- - - - -

CROSS-EXAMINATION

- - - - -

BY MR. SILVERMAN:

Q Dr. Waxler, when you heard the terms of the advertisement that Ms. Fitzgerald read to you, could that treatment be done by radial cartonomy (ph)?

A It could be.

Q So if that's what they were advertising, they wouldn't be in violation of the FDA regulations;

would they?

A But my -- yes.

Except that -- if I may continue -- my recollection of reading that advertisement had to do with Lasik, as I recall.

Q What she read to you didn't mention Lasik.

A What she read to me, that's correct.

Q And that's what I'm asking you about.

A Okay.

Q If that was an advertisement for radial cartonomy, it wouldn't be in violation of the FDA regulations, would it?

A Correct.

Q Okay.

Are you aware that during the term that the Nevyases' IDE was in place that the scope of what they were permitted to do kept being enlarged?

A Correct.

Q Isn't it true, Doctor, that once an IDE is applied for and the Food and Drug Administration gets the plans, makes an inspection of the laser, that it's no longer a black box laser?

Is that correct? You've had an opportunity to look inside of it.

A Not completely correct.

Q What's incorrect?

A What's incorrect is the fact that we look at the particulars. There were a long list of technical issues that the Nevyases, as far as I can tell, never answered.

Q Never what?

A Never answered.

There were issues related to profilometry issues related to quality, issues related to verification and validation.

So it is not exactly correct to say that the agency looked at the laser and now it is no longer a black box because typically what happens in a usual sort of manufacturing scheme is that the -- when the -- when we receive the documentations, the -- it will be a quality system manual that was prepared that shows all of the issues that are required, and that eventually was developed later on in the process.

I believe Dr. Fant must have developed that quality system, so it wasn't until fairly late. You could say, well, it was sort of a semi-black box with more information coming forward, but it's

not ipso facto that once the IDE is been approved, we, the agency, say it's no longer a black box. It's a black box under an IDE.

Q Okay.

A In fact, if I had my records with me, it was a -- unfortunately, I don't have -- I think it would be clear that we -- the agency continued to refer to all those IDEs that were originally black boxes and gray boxes, they remained black boxes and gray boxes after they remained in their IDEs because we still didn't know until a later point -- understand fully what their parameters of use were.

Q The FDA had every opportunity to -- that they asked to examine the Nevyases' laser; isn't that correct?

A Every? I don't think so.

Q Were you ever denied access to look at their laser? Was the FDA ever denied that access?

A The FDA was denied information related to the deficiencies that were specific.

The agency doesn't actually look at the laser and say was this connected to this capacitor. It's the manufacturer -- in this case the manufacturer

of record was the Nevyases -- to provide the agency with the details requested in the IDE.

If you look back at the deficiency list, that deficiency list continued to grow related to multi-focal issues, safety, quality. So it is not correct to say that we had every opportunity to inspect the laser.

Q Do you have any record that shows that you were denied access to the laser and denied the opportunity to inspect it?

A Not denied access to the laser, but denied the information that was requested.

Q What information were you denied?

A Profilometry software validation verification, and I can read the deficiency list. That deficiency list remained, at least from my reading of the IDE protocol, remained for up until '99, 2000. I don't know. There were deficiencies that remained forever as far as I can tell from the record.

Q And the FDA allowed the laser to be used even knowing of these deficiencies?

A Correct.

Q Who is Ralph Rosenthal?

A The Director of the Ophthalmic division.
Q Okay.
And --
A Unfortunately deceased.
Q When he -- is he the person that would confirm that an IDE was closed?
A I would make the recommendation or somebody in my stead would make the recommendation. The process is as follows:
My staff would review -- in this case Dr. Beers, I believe was the lead reviewer in the investigation device exemption -- and he would make his recommendations to me. When I left he would make recommendations to himself because he was the chief. But he would make recommendations, and then I would make recommendations to Dr. Rosenthal. That's the process.
Q Would you look at Plaintiff's Exhibit No. 66. It's in that first large book that's sitting there in front of you.
A This book here?
Q Yes.
Can you look at that, please, Doctor.
A Yes.

Q Does that indicate to you that the Food and Drug Administration acknowledged the completion of Dr. Nevyases' investigation?

A That's what it says.

Q Do you have any reason to disagree with that?

A No.

Q And do you have any reason to disagree that this was closed voluntarily by the Nevyases?

A The only disagreement I would have is to whether jawboning occurred because of the other evidence and the other issue, the email from Mr. Trotsky. There was issues to that day, so I'd have look to other documents.

Q Do you have any personal knowledge of any action by the FDA to close the Nevyases' IDE?

A I was not in the agency then, so I can't speak to that.

Q Do you know when the last investigation of -- or use of the IDE was made by the Nevyases?

A No. I don't recall.

Q Would it surprise to you to know it was November 30, 2001?

A No. Not necessarily.

Q And would it surprise you to know that it was

closed because the Nevyases purchased a laser that had more functionality than theirs?

A No.

Q Because theirs was a broad beam laser, and on the market came Flying Spot Lasers.

A Uh-huh.

Q You are not a medical doctor; are you?

A That is correct.

Q If a medical doctor examines a prospective Lasik patient and finds that that patient had retinopathy of prematurity, but that the retinas were stable, that...

- - - - -

(Pause.)

- - - - -

BY MR. SILVERMAN:

Q That there were no disorders regarding that patient's retinas which would contraindicate Lasik surgery, is it your testimony that that person is not a candidate for Lasik surgery even after a retinal specialist clears him for that?

A Correct.

And the reason, if I may add, is that the protocol is clear with regard to exclusion and

inclusion criteria; so the fact that someone says that this retinal problem is not a problem for inclusion of that patient is irrelevant from the regulatory point of view. I'm not speaking of an ophthalmologist's point of view, since I'm not --

Q Are you saying, Dr. Waxler, that there was a part of the protocol that said, "Don't operate on ROP patients"?

A Not specifying ROP, but there's a broad exclusion for retinal issues, for retinal problems.

Q And if a medical doctor examines the patient's retinas, a retinal specialist, and says, "You're fine to undergo this procedure, there's no reason that you can't," you're saying that that violates the protocol?

A In this case, if I understand it, the patient had ROP. That no one disagrees. So the fact that the retinal surgeon or retinal specialist said that despite this history of ROP it's fine or stable is irrelevant from a regulatory point of view.

Q Patient had no vascular problems, no retinal strands, no vitreous strands, and you are still saying he's not a proper candidate?

A Did he have ROP?

Q Yes.

A Yes.

Q But there's nothing in the protocol that says an ROP patient can't have Lasik surgery; is there? You admitted that ROP is not mentioned in the protocol.

A But the objective of that -- if they -- I can't get into the minds of the principal investigators, but I helped design these protocols; even though it's a long time ago, I'm quite familiar. It's etched in my brain.

We really did not want patients who had any retinal risk factors included in the clinical trials, and it was there in the protocol. So we made a particular point. In fact, it was there in the original guidance document.

Our point was here's a procedure which is designed as essentially as a cosmetic procedure, and we did not want to be party to having patients at risk of having a retinal problem.

Q Do you know whether Lasik surgery is presently being performed on patients who have ROP?

A I have no idea, and it would be irrelevant from the point of this protocol.

Q Dr. Waxler, I want you to look at...

- - - - -

(Pause.)

- - - - -

BY MR. SILVERMAN:

Q Dr. Waxler, are you familiar with a letter that was written in July of 1997 that made the same type of statement that the previous letter that you were shown -- actually, may be better -- can you look at 133? I think it's in the different book.

MS. FITZGERALD: It's right here.

BY MR. SILVERMAN:

Q Do you have that letter in front of you, Doctor?

A I have a July 29, 1997, letter.

Q That's a letter from the Department of Health and Human Services, FDA to Dr. Nevyas; is that correct?

A Correct.

MR. SILVERMAN: And may I approach the witness, Your Honor?

THE COURT: Yes.

BY MR. SILVERMAN:

Q You look at the second page of the letter

starting with the word "however." You see where I'm indicating?

A Yes.

Q Could you read that?

A "However, the agency in an exercise of its enforceable discretion does not intend to consider your previous use, if any, of such a device to be grounds for disapproval of your IDE. Nevertheless, the FDA does intend to consider any use of your lasers to treat patients after the close of business July 28, 1997, unless and until the agency approves an IDE for your device to be grounds for disapproval of your IDE."

Q So let me stop you there.

As long as the Nevyases applied for the IDE, got approval for the IDE, and then after that started to use the laser, all previous transgressions were forgiven; is that correct?

A No.

Q Is it correct that their previous alleged transgressions would not be a barrier to have them get IDE approval?

A Correct.

Q And what's what happened; isn't it? They got

IDE approval?

A Correct.

- - - - -

(Pause.)

- - - - -

BY MR. SILVERMAN:

Q Dr. Waxler, how many inspection visits did the FDA make of the Nevyas laser after IDE approval?

A I would have to recollect from this document. I think it looks like one or two. I'm not sure.

Q No more than two; is that correct?

A It appears, yes.

Q Can you turn to Page 9 of that document?

A Of this inspection report?

Q Yes.

A Page 9.

MR. SILVERMAN: May I approach the witness, please?

THE COURT: Yes.

BY MR. SILVERMAN:

Q Could you read No. 1?

A "Subjects records: The clinical investigator's raw data file were easy to follow; they were in good condition, organized, complete

and legible."

Q Okay.

And they were made completely available to the investigator; weren't they?

A Correct.

I mean, I don't know. This -- it says that they -- it says that -- what it says.

Q Nothing was hidden?

A At the time, I don't know.

Q Is there anything in that report that says that something was hidden?

A No.

Q The Nevyases cooperated with the clinical -- with the investigator?

A It says that data files were easy to follow, in good condition, organizer, complete and legible.

Q Complete, right? That's what he says?

A Organized and complete and legible.

Q Okay.

Dr. Waxler, I would like you to turn to Plaintiff's Exhibit No. 14. It's in a different book.

A I admire your ability to identify which book it's in.

Q We don't make this easy.

Can you see that? I also have a big blow up.

A I can read this easier than that.

Q Okay. Then use whatever's easier.

A Oh, yes. This is the Vermillion letter.

Q You're familiar with that letter.

A Yes. I've read it. I don't remember every part of it.

Q How did you become familiar with it?

A I think originally Dominic sent me the letter some time ago, and I read it a long time ago; but I've read it again in preparation to refresh my memory of things that happened.

Q Did you get it from anybody else besides Mr. Morgan?

A Yes. I think that counsel, Maureen Fitzgerald, sent me a copy.

Q Anybody else?

A No.

Q Mr. Friedman ever send you a copy?

A No.

Q What did Mr. Morgan tell you about this letter?

A I don't recall he told me anything

specifically about this letter. He asked me to review a bunch of documents.

Q Do you know who Mr. Vermillion is?

A I do.

Q Was he there when you were there?

A Probably.

Q Okay.

And this letter is written to him as the Director of the Office of Criminal Investigation; isn't that right?

A Right.

Q And the request is that there be an urgent investigation because there's outright criminal activity --

MS. FITZGERALD: Objection.

THE COURT: Possible outright criminal activity.

MR. SILVERMAN: Excuse me. Possible outright criminal activity.

BY MR. SILVERMAN:

Q Were you aware of any outright criminal activity engaged in by the Nevyases?

A I wouldn't use that phrasing. I would say that there were -- from my previous testimony,