



DEPARTMENT OF HEALTH & HUMAN SERVICES
Food and Drug Administration

Public Health Service

Rockville, MD 20857

EOI Services, Inc.
1140 Nineteenth St NW
Washington, DC
20036 5606

10/15/96
In reply refer to:
2004-14339
Your reference:
8234098

Dear Requester:

This is the response to your request for record(s) from the Food and Drug Administration pursuant to the Freedom of Information Act regarding:

2004-1308

Enclosed are the records for this request.

The following charges for this request to date may be included in a monthly invoice:

Reproduction	Search	Review	Fiche	Other	Total
	\$5.00	\$0.00	\$0.00	\$1.00	

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All communications concerning this request should be identified with the reference number above and addressed as follows:

Food and Drug Administration
Division of Freedom of Information, HPI 33
5600 Fishers Lane (Room 6-32)
Rockville, MD 20857

Sincerely yours,

Thelma B. Ghahhari
Freedom of Information Technician
(301)827-6557

Enclosure(s) if indicated

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SUMMARY OF FINDINGS

This was the initial inspection of this clinical investigator.

Current inspection was conducted as an unannounced directed inspection, per 9/27/99 HFM-650 Assignment, and was conducted in accordance with CP7348.811. The purpose of the inspection was to follow-up 5/14/99 clinical hold placed on the [REDACTED] to obtain records for the [REDACTED] patients CBER allowed to be enrolled in the study, and to determine where the sponsor maintained records. (See attached assignment for history of the firm [REDACTED].)

Inspection revealed the reported breakup between the PI and former sponsor, [REDACTED] earlier this summer. The PI expressed no knowledge of some of the individuals listed in the [REDACTED]. He continued to deny doing any investigational studies/alternative treatments—even when asked about specific studies that the IRB has reviewed. One of these is a [REDACTED] study approved in 1997. The second is a recent study--approved by the IRB in Sept., 1999—that the PI claimed no knowledge of until I informed him I was aware of the recent IRB approval. He even asked which IRB before he would provide any study records and tell me if any patients had been entered. He stated [REDACTED] patients have been entered in this study. He only had a copy of the protocol—no roster and no IRB correspondence. The sponsor is reported to be [REDACTED]. He said [REDACTED] of [REDACTED] corresponds with the IRB. He had no records of the [REDACTED] study and no subject roster. He claimed to only have treated the [REDACTED] patients in the [REDACTED] study. He displayed no knowledge of the protocols and Federal regulations. He did not know what a 1572 was even though he has signed them. He did not know of any regulations governing his conduct of the studies. He said he merely participated by seeing the patients and maintaining his usual clinic records. As seen in the [REDACTED] history, subject patients receive various concurrent investigational/alternative treatments while participating in these [REDACTED] studies. Some of the subjects are "participating" in a concurrent [REDACTED] study, with the reported PI to be a physician in Nashville, TN. Consents do not meet CFR requirements. [REDACTED] of the [REDACTED] subjects in the recent study did not sign a consent. No CRF's have been completed. Medical records do not document study activities. FD483 was issued to the PI and discussed with him. He stated he was not aware of any regulations/responsibilities—he was simply seeing the patients. He stated he might be able to do a study "right" if he knew what "right" is. He said, though, that if he has to maintain records, he will have to cease study conduct, as he cannot afford to spend time/money on study documentation.

ADMINISTRATIVE PROCEDURES/PERSONS INTERVIEWED/ INDIVIDUAL RESPONSIBILITIES

The inspection was conducted unannounced. I initially attempted to begin the inspection 12/6/99; however, upon my arrival at the clinic, I found a locked door and no one answered the door. I then observed notices posted on other office doors in the building that reported a power/water outage that day and offices, therefore, were closed.

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I arrived the next morning 12/7/99. I presented my credentials and introduced myself to the [REDACTED] office employees. I asked for Dr. Page. I was told that he was making rounds at local hospitals and would be in later. I then asked to see his study nurse/assistant. They asked what studies. I said "[REDACTED] studies". Ms. Billie C. Sexton, Medical Assistant, then spoke up and said that she is Dr. Page's "right arm". In the meantime, another assistant had paged him. He then asked to speak to me on the phone, as he was phoning from his car. He asked what records I wanted to see. I said the [REDACTED] patients in the [REDACTED] study. He gave his staff permission to retrieve the records for me and stated he would be in the office in an hour.

I then issued the Notice of Inspection, FD482, to Ms. Sexton. I provided her the [REDACTED] names and asked to see their records. She said I could wait for him in his office. I waited over an hour and still was not provided any records. I asked Ms. Sexton about the records and she said that she had pulled them, but wanted Dr. Page to review them before she handed them to me. At that time, she informed me that she was relatively new—began here August 20, 1999, and that Dr. Page had broken from [REDACTED] before Ms. Sexton began employment here. Ms. Sexton said that she did not replace anyone—that they needed a [REDACTED] person since his other assistant was going to nursing school part-time. Ms. Sexton expressed her admiration of Dr. Page and pointed to his certificates on his office wall. She said he is a nice, Christian elderly doctor ([REDACTED] years old) and rarely says anything bad about anyone. She has heard him speak negatively of [REDACTED] and her company, however. She says he does surgery and has privileges at [REDACTED] local hospitals. With or without surgery, he does a combination of [REDACTED] and [REDACTED]. A patient told her that she saw in a book a list of the roughly [REDACTED] sites in the country that do [REDACTED]. I asked if they have a website. She said they hope to have it up and running in two weeks.

Ms. Sexton explained all of the good treatment Dr. Page was doing and mentioned [REDACTED]. I asked her what that is and she said it is [REDACTED]. She said the patients sometimes sweat during the treatments. She said that their patients come from out of town since so few doctors do this treatment in conjunction with [REDACTED]. Some of their patients go to Atlanta [REDACTED] for the [REDACTED] treatment. One patient flew from Memphis to Atlanta that morning for the treatment. She said they do NOT draw blood for the treatment here. They only draw routine labs.

Dr. Page arrived some time later. His patients were already waiting for him, so his schedule was tight trying to fit in those that he could not see the previous day due to the power/water outage. I informed him that I was there to follow up the [REDACTED]

He stated that [REDACTED] was the one who promoted the program that was a combination of emotional support, exercise, and spiritual support along with the [REDACTED] treatment. He said [REDACTED] in Cincinnati made the [REDACTED] that has been discontinued. He said that he (Page) has no financial involvement in the company. He said that when FDA wanted certain studies done, he and [REDACTED] were willing to do them, but that [REDACTED] wanted to be the sponsor and she is not a scientist. She wanted things done that could not be done. Page said that [REDACTED] was the scientist and should have been the sponsor, not [REDACTED]. He said that in June

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or July, 1999 they stopped producing the [REDACTED]. He said they only treated the patients permitted by CBER.

Page said that he does not do chemotherapy. He said that the people he works with are interested in improving the care of cancer patients. He said that by the time he sees most of his patients, the patients have gone through standard treatments and have had recurrences.

When asked about payment for treatments, he stated that [REDACTED] collected the money for the treatments. He said they never collected any. He has been in practice here for [REDACTED] years and it is primarily by "word-of-mouth". He sees the "toughest" patients with the majority from outside of Memphis. He gets referrals from non-local doctors who know of his work.

He said that when the [REDACTED] was active, they would have seminars roughly every 6 weeks. They would see [REDACTED] patients per session in Memphis. The patients would stay in a hotel for 4-5 days, undergo gentle exercises, attend lectures and hear discussions of immunology, nutrition, and pharmacy. He said one of their pharmacists could make different varieties of preparations than would be on the market. The patients would be taught how to self-inject the [REDACTED]. By the time of the seminar, the patient would have been screened, signed a consent, and had blood drawn.

I asked about [REDACTED] and [REDACTED]. He said they make their own [REDACTED] and that FDA is looking at them. He said they have quite a few patients. They can't ship [REDACTED], so the patients have to get their [REDACTED] at [REDACTED] office. Some of [REDACTED] patients come to Page's clinic for treatment, as Dr. Page performs [REDACTED]. He said the device is approved for [REDACTED] and he uses it for [REDACTED]. Dr. Page is the only one in Memphis doing the procedure. He said the liver is the best tissue for it. He does it as an outpatient procedure. He provided some literature on the procedure. See **EXHIBIT #1**. He added, though, that he currently has to do the [REDACTED] procedure in an outpatient surgical clinic since [REDACTED] radiologists do not want him doing it in the hospital. He said they are concerned about liability. They [REDACTED] asked him to get IRB approval. When he attempted to do that, he said the IRB told him that the IRB does not need to review it since it is an approved device. He said the [REDACTED] takes 2 1/2 hours and the radiologists were probably concerned [REDACTED] took too much time from ultrasounds, etc. At the outpatient clinic, he can keep a patient overnight one night, but he would prefer to do the procedure in a hospital should he need an ICU.

Dr. Page said that for the [REDACTED] patients the [REDACTED] was shipped directly to their homes. He said the manufacturer planned to eventually package it in [REDACTED] increments, but never got around to it. It went out in [REDACTED] units. He claimed his clinic sent the [REDACTED] patients monthly questionnaires. He said the patients got labs checked monthly. If the patient could travel to Memphis, the patient would be seen by him. Otherwise, he relied on the patients' local physicians.

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As for the [REDACTED], Dr. Page said they [REDACTED] and [REDACTED]. He said few doctors do it because there is no money in it. Insurance only pays for [REDACTED]. He's been doing that treatment for [REDACTED] years.

He said he wants to get into [REDACTED]. He said there is a doctor in Nashville ([REDACTED]) that is doing it. He said the drawback to it is the cost of the filter [REDACTED]. The patients are [REDACTED] daily for 3 weeks. The filter removes blocking antibodies. (Ms. Sexton had also told me about visiting a Nashville doctor who was doing this procedure and having wonderful results. Ms. Sexton said she was anxious to learn more about the procedure.)

I asked about [REDACTED]. Page said that [REDACTED] is not a Medical Doctor. Page met him recently. He said [REDACTED] is associated with [REDACTED]. He thinks [REDACTED] does plastic surgery in Atlanta ([REDACTED]) and [REDACTED] in Mexico.

He said that without the [REDACTED] there is not much attraction for the patients. [REDACTED] needed the [REDACTED] to attract/treat the patients. I asked where she is located. He gave me her phone numbers: HOME, [REDACTED], and OFFICE, [REDACTED]. He said [REDACTED] is working with a German who produces [REDACTED]. The German, [REDACTED], has sessions in Atlanta. He makes the [REDACTED] in Germany. Page does not know how the [REDACTED] gets into the U.S.

I asked him about various people named in the assignment. I asked about Dr. [REDACTED]. Page said that [REDACTED] was the "brains" behind the [REDACTED]. Page said that [REDACTED] is not currently doing anything—he thinks [REDACTED] is in Florida taking care of [REDACTED]. [REDACTED] died unexpectedly a few years ago and [REDACTED] then began taking care of his [REDACTED].

I asked about the [REDACTED] study. He could not recall the term, but said it seems like he had heard of it before. I then showed him the IRB letter (and assignment attachment) and he said he now remembered the term. He said that was [REDACTED] term. [REDACTED] made the [REDACTED] in Germany and somehow got the [REDACTED] into the U.S. He said Customs frequently detained the [REDACTED] though, and the refrigerated [REDACTED] would go out of temperature. He did not have a copy of the [REDACTED] protocol. The only study record he could find was the 4-page study description (EXHIBIT #2) which also had been attached to the assignment. He said his previous assistant, [REDACTED], now works for [REDACTED] and that [REDACTED] would know where the records are. He did not have a study roster. It appeared, however, that one of the patients listed in the assignment as a [REDACTED] patient ([REDACTED]) could have been in the [REDACTED] study based on what was noted on the patient's clinic chart (EXHIBIT #13). See "Objectionable Conditions".

He said in the [REDACTED] study the [REDACTED] would initially be sent to [REDACTED] who would then use it for patient instruction at the seminar. She would show the patient how to inject it. After the initial injection, the [REDACTED] would be shipped directly to the patients' homes for self-injection. He said the trial stopped since they could no longer import [REDACTED]. He said he has no study files, no patient roster, that [REDACTED] must have all of that. See "Objectionable Conditions". I asked whether [REDACTED] had ever

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had an office in his suite. He stated she did not. He said, though, that a patient offered [REDACTED] use of a home when [REDACTED] was in town.

Ms. Sexton then provided the [REDACTED] patient files. I reviewed them and photocopied all records within the files. These records are attached as **EXHIBITS #3-7**.

Ms. Sexton informed me during the second day of the inspection that [REDACTED], who had worked there [REDACTED] years, left and went to work for [REDACTED]. She said Dr. Page found out that [REDACTED] had been receiving money both from Page and [REDACTED] for her work on the studies. [REDACTED] left in late August, 1999. Ms. Sexton checked her address book and found a newer address for [REDACTED]. She said the most recent office phone number is: [REDACTED]. She gave me [REDACTED] home phone: [REDACTED]. Dr. Page offered to have the new bookkeeper call [REDACTED] to ask her to fax him a copy of the [REDACTED] protocol. I stated that would not be necessary.

I continued to ask Dr. Page if he were conducting any other studies or had submitted any other studies to the IRB for review. He continued to deny any participation. I then wrote on a piece of paper the title of the most recent study that the Board approved in Sept., 1999 and handed the paper to him. I asked for his file on this study. He just stared at the paper. I asked again for the one he had just submitted to the Board. He then asked me, "Which Board?" I responded, [REDACTED]. He said that [REDACTED] did all of that and that [REDACTED] should have the paperwork. I said that as PI he is required to maintain the paperwork. He said he only saw the patients. I asked if he had entered/treated any patients in this study. He said he could not remember-- that he is not good with names. He then asked his bookkeeper who identified [REDACTED] patients-- [REDACTED] who was just seen the previous day in the clinic and treated (during the inspection, unbeknownst to me). He then relayed how that patient was doing so well. I asked for the [REDACTED] patient files that I then photocopied. They are attached as **EXHIBITS #8-9**. [REDACTED] (**EXHIBIT #9**), is the patient that had been seen in the clinic the previous day that he "could not remember".

Dr. Page asked me repeatedly during the inspection about the reason for my visit. I continued to respond that I was following up the clinical hold.

Of interest and concern is the fact that Dr. Page apparently allows non-medically trained/licensed individuals to perform/oversee "medical" activities. During the inspection, patients were undergoing [REDACTED] when Dr. Page was out of the clinic/building (doing rounds or surgery at other local hospitals). One afternoon the bookkeeper was overseeing a patient's [REDACTED] treatment while Dr. Page and Ms. Sexton were out running errands. When the bookkeeper had to meet Ms. Sexton outside to retrieve supplies, I was the only one in the clinic besides the patients—one who was finishing his [REDACTED] treatment. The bookkeeper told me that she even had to pitch in and draw blood earlier that morning—something that she had not done in a while. Ms. Sexton injects the [REDACTED], according to the file for patient [REDACTED], **EXHIBIT #8, PAGE 3**. Ms. Sexton told me her title was "medical

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assistant". She does not appear to be a nurse. She said she had previously worked as a technician in a lab.

OBJECTIONABLE CONDITIONS

The following objectionable conditions/practices were observed and so noted on the FD483:

An attempt was made to review the following three studies that list Dr. Page as Principal Investigator:

- 1- [REDACTED]
- 2- [REDACTED]
- 3- [REDACTED]

A total of [REDACTED] patient files were reviewed. [REDACTED] of the patients reviewed were the ones approved by CBER for study enrollment/treatment. [REDACTED] patients were reviewed (per assignment request) who were treated pre-issuance of [REDACTED]. [REDACTED] names had been listed in the assignment; however, [REDACTED] was not in the patient database and none of Page's office assistants had ever heard of him. I later saw his name on the cover of the latest protocol and he is listed as a Trial Site Director in Knoxville, TN (**EXHIBIT #10**). Files were reviewed for the [REDACTED] patients identified as being enrolled in the [REDACTED] study. There is no documentation of an [REDACTED] for the [REDACTED] study or for the [REDACTED] study.

I. LACK OF KNOWLEDGE

Although Dr. Page signed the 1572's, he displayed no knowledge/recognition of federal regulations governing conduct of human trials. He failed to conduct the studies in accordance with the regulations or the protocols. He stated his sole responsibility in the studies was to see the patients and to maintain the usual clinic records for them. During the inspection, he provided a copy of his consultant agreement (**EXHIBIT #11**), stating that he was only to see the patients.

II. FAILURE TO MAINTAIN RECORDS

1. No study regulatory files were maintained. No IRB correspondence has been maintained. It cannot be ascertained, therefore, what was submitted to an IRB for review (if anything) and what was approved and when. Patients reportedly paid for the study treatments; however, there is no documentation of IRB approval of payment. FDA has not approved cost recovery. [REDACTED] IRB reportedly approved study #3 above. [REDACTED] 9/25/99. At least one patient received the study treatment/[REDACTED] prior to IRB approval to even conduct the study. Patient [REDACTED] was injected 9/13/99. (**EXHIBIT #8, Page 3, medical records**)

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2. No study rosters have been maintained. It cannot be ascertained who was screened/enrolled/treated/dropped/completed and who may have experienced adverse events.
3. There is no documentation of study status. With the clinical hold on Study #1 ([REDACTED]), Dr. Page considers this study to be closed even though the patients should continue to be followed. He stated the [REDACTED] study (#2) was halted because the test article was constantly detained by Customs and the test article was not held at the proper temperature. Dr. Page does not have a copy of the [REDACTED] protocol. No progress or termination reports were observed.
4. No case report forms were observed for any of the patients—[REDACTED] of the [REDACTED] reviewed are in the newly approved [REDACTED] study (#3). Dr. Page informed me at the beginning of the inspection that ALL patient records—including study records—are within the patient clinic charts. I photocopied ALL records within these [REDACTED] charts. NO CRF's were observed. See patient records, **EXHIBITS #3-9 AND #12-14.**
5. Test article accountability records were not maintained. Patient files do NOT document test article administration. Patient files do not specify what trial the patient is in. There is no record of patient return of empty vials as per protocol. Drug was reportedly shipped from the manufacturer to the sponsor who then instructed the patient on the initial self-injection. Subsequent doses were then shipped directly to the patients' homes from the manufacturer. Number of treatments and doses cannot be determined. For the [REDACTED] study, the manufacturer shipped the test article to Page's office. The patients were instructed on self-injection in the office. Subsequent doses are shipped to patients' homes.

III. FAILURE TO FOLLOW THE PROTOCOL

1. Patients (especially in the [REDACTED] study #1) were rarely seen by Dr. Page or followed by him after the initial screening/treatment visits. The patients do not come in for monthly follow-ups. There is no record of the questionnaire for quality of life being sent monthly to the patients. Few questionnaires were observed in the patient charts.
2. Subjects received concomitant therapies/treatments while being treated or in the follow-up phase of the studies. These therapies include [REDACTED] and [REDACTED] of the [REDACTED] subjects who were granted CBER approval for [REDACTED] also received [REDACTED] (patients: [REDACTED]). Patients [REDACTED] and [REDACTED] even signed consents to participate in a [REDACTED] trial—**EXHIBITS #3,6.** (The P.I. is listed as [REDACTED] in Nashville). Dr. Page signed as "witness" on one of the consents (**EXHIBIT #3, page 10**). Neither consent had an investigator signature.

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3. Patient files do not contain documentation that the subjects met all inclusion criteria prior to study entry.
4. Per [REDACTED] protocol (#3), test article preparation involved the use of [REDACTED]. Dr. Page, however, [REDACTED] and shipped it to the sponsor/manufacture. See patient records, **EXHIBIT #8, page 3**, which report that [REDACTED] for [REDACTED] on 9/2/99 and [REDACTED] done on 9/3/99 and sent to [REDACTED]

IV. INFORMED CONSENTS

1. For the [REDACTED] study (#3), no consent was observed for [REDACTED] of the [REDACTED] identified subjects (S.S., **EXHIBIT #8**). The consent signed by the [REDACTED] subject (**EXHIBIT #9**) is a copy of the model consent from the protocol which bears blanks to be filled in. The blanks were not filled in. The consent is not in lay language. The consent should list a contact other than the PI for the subjects regarding subjects' rights. Per consent, the subject is to initial each page. This was not done.
2. The consent for the [REDACTED] study (#1) is not in lay language. The consent lacks a contact for research-related injuries, and a contact for research information and research subjects' rights. This same consent was used for [REDACTED] study as well, according to what patient [REDACTED] signed (**EXHIBIT #13 RECORDS**). Neither consent is specific for patient costs.

NOTE: Per assignment, [REDACTED] patient names were listed to track. These patients reportedly were administered the test article prior to issuance of the clinical hold. I asked for the [REDACTED] patient files. No one had heard of the patient, [REDACTED]. His name was not listed in the computer database of patients. When Dr. Page provided me a copy of the newest protocol for the [REDACTED] study (protocol, **EXHIBIT #10**, I was surprised to see that [REDACTED] was listed as a "Trial Site Director". His address is reported as [REDACTED].

DISCUSSION WITH MANAGEMENT

At the conclusion of the inspection, a discussion was held with Dr. Page prior to issuance of the FD483. I again asked him about payments for study treatments. He said that he doesn't accept money for the seminars. He only gave lectures on the [REDACTED] system. For the [REDACTED] study, he charged for labs, office visits, and surgery. He said they've learned that [REDACTED] therapy is not successful unless the [REDACTED] is reduced. He said he tries to reduce the [REDACTED] by [REDACTED] combined with [REDACTED] treatments—with the additional possibility of surgery. For the new [REDACTED] study he [REDACTED] and collects a [REDACTED] sample that is then sent to [REDACTED] for [REDACTED] production. He said that [REDACTED] sends the [REDACTED] in [REDACTED] vials, but has plans to change that to [REDACTED] vials.

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I asked who is [REDACTED] as I had seen her name on the top of faxed consent forms. He stated she is a [REDACTED] who has since moved to [REDACTED]. She helped them with writing/format of consents/protocols. He said she may have a loose relationship with [REDACTED] and has probably helped [REDACTED].

I asked where the "seminars" took place. He said usually in Memphis. He said none have been held in Memphis since early summer (1999). I asked if they were now held in Mexico. He stated that he had heard [REDACTED] was planning a seminar in Mexico, but did not think that the seminar actually took place.

I asked if [REDACTED] has ever come to his site. Dr. Page said that [REDACTED] might have come two times. Page has never heard of [REDACTED]. He said [REDACTED] is a Ph.D. that Page only met once, and Page understands that [REDACTED] did [REDACTED] in Mexico. Page thinks that [REDACTED] and [REDACTED] may have discussed "things". He said [REDACTED] is a forensic pathologist with expertise in immunology. [REDACTED] developed several protocols along with [REDACTED]. He said [REDACTED] would be available to talk, as [REDACTED] lives somewhere in Florida, maybe an island. [REDACTED] is [REDACTED] and Page attended a lot of meetings together and [REDACTED] presented interesting papers. Page stated he does not know why [REDACTED] was asked to do an audit here, but he guesses that they were attempting to bring things (data) together. Page said that it is easier to remember the successes and failures, but those patients in the middle are easier to forget. One could get the impression that one is doing better than they really are.

I asked why he does not use a local, free IRB such as [REDACTED] that is next door to his office building. He responded that since these are not hospital studies, he did not submit the studies to them. He said the IRB Director is difficult to get approvals from. That Director told Page that he could not collect the [REDACTED] for the study. Page said there is too much politics/problems in using a local IRB.

He again brought up the [REDACTED] procedure. He said he has done [REDACTED] cases and the [REDACTED] is FDA approved. The radiology group at [REDACTED] did not approve of his use of the [REDACTED]; as a [REDACTED] procedure takes 2 1/2 hours per procedure. The radiologists can do several ultrasounds in that time, so they asked him to get IRB approval before he can continue at [REDACTED]. He said he submitted the project to [REDACTED] IRB, but was told by them that since the [REDACTED] is approved, they do not have to review it. The radiologists do not agree and are worried about liability. As a result, he performs the procedure at a local outpatient surgical center; however, he would prefer to do the procedure in a hospital in the event there are complications and the patient would need an ICU. At the outpatient center, a patient can only remain overnight. He said to date he has only kept [REDACTED] patients overnight—and one of those was a [REDACTED] patient.

I then presented the 483 to him. I stated that the 483 was not meant to be all inclusive. Each item was read and discussed. I explained that FDA holds the Principal Investigator to be responsible for the conduct of the study/studies at his site. I stated that Dr. Page was identified as Principal Investigator for the [REDACTED] studies I attempted to review. I further stated that he signed the 1572's as Principal

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Investigator and as such agreed to conduct the studies in accordance with the protocol and regulations.

He then asked me what a 1572 was. I showed him one of the assignment attachments, a 1572, that he had signed. I pointed out the back page listing his commitments/responsibilities. He then asked what are the regulations. I said that when I got back to BIR-RP I would send him a copy from the CFR. I added that his questions regarding 1572's and regulations further demonstrate his lack of knowledge. I said that the sponsor has the obligation to select an experienced investigator or assume the responsibility of training an investigator in the requirements/laws governing study conduct. I stated the sponsors [REDACTED] or [REDACTED] did not meet their obligations. He again said that his only responsibility in the studies was to see the patients.

I again explained what the regulatory files should be. He said that he has never communicated with the IRB-- that he thought that is what the sponsor is supposed to do. Even the recently approved (9/25/99) study submitted to [REDACTED] IRB was handled by [REDACTED]. Dr. Page said that he supposed [REDACTED] submitted the project to the IRB and maintained any kind of paperwork. I said that it is the PI's responsibility to communicate with the IRB, not the sponsor's. At Page's site, it cannot be ascertained what if anything has ever been submitted to an IRB. Dr. Page was disturbed about the mention of patients' payment. He reiterated that he NEVER collected any money from any patients for study treatment, [REDACTED]. He said [REDACTED] did all of that. I asked if he charged the [REDACTED] identified patients that he has recently entered in the new [REDACTED] study. He said that he only charges for labs, office visits, and surgery. Billing records as provided by the bookkeeper are attached as exhibits.

Dr. Page said that they regularly sent out the questionnaires, that [REDACTED] would know about that. I said I only saw [REDACTED] in roughly [REDACTED] patient files.

As far as concomitant therapies, I said that you cannot enter subjects in more than one trial and expect to be able to evaluate/separate the effects of each test article. I added that I had observed [REDACTED] consents in [REDACTED] patient files. I asked if those patients were in a [REDACTED] study. He said yes. I asked who was the PI. He said [REDACTED] in Nashville. I stated no PI signed the consents and that he signed [REDACTED] as a witness. He has no test article accountability for that study as well. He said [REDACTED] nurse is following those [REDACTED] patients.

He asked about the [REDACTED] (FD483 item #III.4.). I said that is how the protocol [REDACTED] study) described the [REDACTED]. He stated that they are not yet doing that--that procedure will be something in the future. I said that the protocol should not have been written that way then--the protocol is supposed to describe the procedures to follow. He should perhaps assist in the writing of the protocol in order to assure that the protocol can describe what he does.

He said that study status should be clear--with the hold on the [REDACTED] study, we should be able to ascertain that study has closed. I said that they still have to follow the subjects and maintain study records. He asked what are case report forms. I

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explained that studies have specific forms for recording raw data (clinical data) which is then in a form to be analyzed by the sponsor for submission to FDA.

I stated that I was sure he was aware that it is a felony to provide false information to the government. I explained that FDA has various options to assure patient protection/PI compliance. I listed Warning Letter, disqualification so that he cannot participate in clinical trials, and prosecution. He then laughed and said it sounded serious. I said it was very serious and that he surely is aware of the emphasis placed on subject protection/rights. He responded that he certainly does not neglect the patients. He said the [REDACTED] study and the [REDACTED] study are past. He said he only had a "passive involvement" in that he helped get patients treated. He said he knew what FDA's interest is but that he has to spend his time trying to help the patients get well. He added that he has to now decide whether he wants to continue in studies. He said that he does not have the money to continue if it means keeping up with paperwork. He said he needs to know what the regulations are. He added that he did not know he was putting himself in jeopardy with FDA. He "figured the IRB and sponsor would deal with FDA". He is "in the trenches doing the work". He said he wants "to do the right thing", but he needs to know what that is. He said he has nothing to hide. During our conversation, the phone rang and Dr. Page accepted a call from [REDACTED]. Dr. Page told him that "things are not as good as we'd like", but would call him back shortly.

Dr. Page was advised that CBER would communicate with him regarding the inspection/studies. He was told that should he like to respond to the 483 he could send his response to me to forward both to NSV-BR and CBER. He then asked if he should respond. I stated that was his choice/decision. I added that the sponsors may have a desire one way or the other.

Dr. Page was thanked for his time and his staff's time and assistance during the inspection.

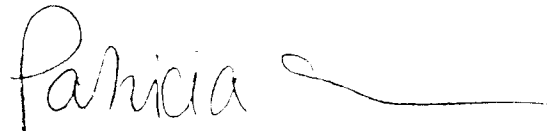
EXHIBITS

1. [REDACTED] literature
2. [REDACTED] "protocol"
3. [REDACTED] patient [REDACTED]
4. [REDACTED] patient [REDACTED]
5. [REDACTED] patient [REDACTED]
6. [REDACTED] patient [REDACTED]
7. [REDACTED] patient [REDACTED]
8. [REDACTED] study patient [REDACTED]

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9. [REDACTED] study patient [REDACTED]
10. [REDACTED] study protocol
11. 10/21/97 consultant/researcher agreement w/ [REDACTED]
12. [REDACTED] patient [REDACTED]
13. Patient [REDACTED]
14. [REDACTED] patient [REDACTED]
15. Billing records for patient [REDACTED]
16. Billing records for patient [REDACTED]
17. Billing records for patient [REDACTED]
18. Billing records for patient [REDACTED]
19. Billing records for patient [REDACTED]
20. Billing records for patient [REDACTED]
21. Billing records for patient [REDACTED]



Patricia S. Smith, Investigator
Birmingham RP/Nashville Branch
New Orleans District

FORM FDA 483 (12-78) PREVIOUS EDITION MAY BE USED. INSPECTIONAL OBSERVATIONS PAGE 10 OF 11

PAGE CLINIC

MID-SOUTH SURGICAL ONCOLOGY CENTER
ROY C. PAGE, M.D., F.A.C.S., F.S.S.O.
SURGERY-ONCOLOGY

rec'd
5/11/00
11/3/00

December 22, 1999

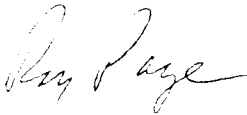
Patricia Smith
Food and Drug Administration
600 Beacon Parkway West, #120
Birmingham, AL 35209

Dear Ms. Smith:

I appreciated your visit on December 7 - 9, 1999. Your comments are most helpful and provocative. Much thought has been given to this subject, and I have responded in this letter to the concerns you expressed in the report left with us on December 9th. I hope this information will help clarify my position as a clinical investigator and not a sponsor of the studies.

Your patience is appreciated. Have a very merry Christmas and a safe holiday.

Sincerely,



Roy C. Page

Response to FDA Report of Inspection, filed 12-9-99 by Patricia Smith, New Orleans District

The review included three studies that list Roy C. Page as Principal Investigator.

1) [REDACTED]
[REDACTED] - Trial Sponsor
IRB approval, 1998
IND application, April 1999
Clinical Hold for duration of IND application review

2) [REDACTED] Trial Sponsor: [REDACTED]
IRB approval, 1997
Study halted, 1998, due to concerns about product shipment (see Section II:3 below)

3) [REDACTED]
[REDACTED] Trial Sponsor: [REDACTED]
IRB approval, 1999

Complete IRB documentation for each study is available for FDA review. All Clinical Sponsor files for Study #1 and Study #2 were removed when the studies were discontinued and the sponsor, [REDACTED], moved its office from the Clinical Study Site. All questions about that material should be forwarded to [REDACTED].

Your examination of the studies took place December 7 - 9, 1999, and consisted of a review of [REDACTED] patient files. The [REDACTED] patients whose files you initially requested were subjects in Study #1. Their blood had been drawn before the clinical hold was placed in April 1999. The [REDACTED] for these five patients was released by the FDA in July 1999. I volunteered three additional patient files from Study #3, the [REDACTED] study that is currently in the process of being developed as a product. [REDACTED] was deceased, and you informed my staff that it was not important to review that particular file. This letter will address the concerns you expressed in your report.

I. Principal Investigator's role in the conducting of human trials

On file in my office are

- Signed Investigator Agreement forms (#1572) for each clinical study
- Complete FDA guidelines for the administration of human trials
- Complete protocols for Studies 1 and 3, including IRB and FDA correspondence; questions about the [REDACTED] protocol should be referred to the Trial Sponsor.

The primary responsibility of the Principal Investigator is to ensure the welfare of each patient. In the [REDACTED] studies under review, treatment plans were constructed on an individual basis to balance patient needs with criteria of protocol procedure. Final study results presented to the FDA at the conclusion of the trial will include only those subjects whose treatment follows protocol guidelines.

II. Clinical Trial Records

1. IRB correspondence and documentation is on file in my office as Principal Investigator and is available for review.

No payment for study treatment has been accepted by the Principal Investigator, [REDACTED]. Clinical Trial sponsor for Study #1 and Study #2, has handled all financial arrangements with patients and the laboratory acting as [REDACTED]. Full financial records are available for

review. Subjects for Study #3 are not charged for Theracine.

[REDACTED] IRB approved Study #3 verbally on September 10, 1999. Written documentation of approval was received on September 25, 1999. Patient [REDACTED] was injected with a first dosage on September 13, 1999, in the office of the Principal Investigator.

2. Study rosters are available for each clinical trial. Individual patient files include clinical study screening results and treatment plans. No adverse effects have been reported to date.
3. Study Status - Study #1 has been placed on clinical hold until the Trial Sponsor, [REDACTED], responds to questions posed by the FDA. Subjects are no longer administered study treatment, but they continue to receive follow-up care, and their progress is recorded in patient files. Data on patient response is collected but will not be analyzed until the Trial Sponsor agrees to continue the study.
Study #2 was discontinued because of my concerns as Principal Investigator about maintaining proper temperatures during product shipment. Patient records are maintained in my office, but questions about the [REDACTED] protocol should be addressed to the [REDACTED].
4. Case Report Forms are available for all patients.
5. Test Article accountability records are maintained by the Trial Sponsor and the laboratory that produced the [REDACTED] and/or [REDACTED]. Empty vials are returned per protocol directly to the manufacturing laboratory. Complete records of shipment and return are kept by the laboratory and are available for FDA review. Number of treatments and doses for each patient are available in study records.

III. Following Protocol Procedure

1. I have been directly involved as Principal Investigator with the screening, treatment, and follow-up care of each patient. Patients in Study #1 and Study #2 were not informed by the Trial Sponsor of the need for monthly examinations, a problem addressed by the FDA in its review of the study's IND application. Quality of Life Questionnaires were completed by subjects in these trials on a monthly basis and kept on file. Patients in Study #3, currently being developed, receive monthly follow-ups.
2. Subjects received concomitant therapies or treatments in Study #3 when the protocol was initially designed to include such treatments. Current patients are screened according to the preclusions directed by subsequent protocol revisions.
3. Study records include documentation of patients who meet inclusion criteria.
4. Initial drafts of Study #3 protocol allowed [REDACTED] Clinical Investigator and shipped directly to the production site. Subsequent [REDACTED] will be obtained through [REDACTED].

IV. Informed Consent

1. All patients have signed consent forms approved for the study in which they are subjects. Consent Forms for Study #3, because of their brevity, do not require patients to initial each page. No patient has expressed problems understanding the language either of the consent form or of the patient information section of the protocol. It has been made clear to each patient that the Principal Investigator and his staff are available to answer any questions that may arise during or after treatment. In addition to normal contact with patients, two or three phone calls are made to each patient's home from the Principal Investigator's office during the first month of treatment to answer questions and to ensure that any adverse effect can be documented and treated.
2. Problems with informed consent forms used in Study #1 and Study #2 have been addressed in communication between the FDA and [REDACTED] Trial Sponsor of the two studies. Since both studies have been halted and no new patients enrolled since April 1999, no changes have been made to the form.

In summary, Ms. Smith, your concerns with Study #1 and Study #2 are shared by myself as Principal Investigator and investigators of other branches of the FDA. With the exception of follow-up care for patients previously enrolled, no further investigation is taking place in either study. Questions about product safety led me to place a permanent halt on Study #2 in 1998. Study #1 will proceed only if the Trial Sponsor agrees to address questions put in writing by the FDA. I anticipate no more activity in the two studies.

Study #3, [REDACTED] is in the process of being developed as a product, but its protocol rests on the collaborative effort of researchers over several years. On file in my office are the complete protocol, Investigator's Brochure, Patient Information, and Patient Consent Form. All have been approved by the IRB of the [REDACTED]
[REDACTED]