LENTZ, MEREDITH RIGDON, M.D.
397 Wallace Rd, Suite 314
Nashville, TN 37211

EI
3/5/01- 5/10/01
PSS

SUMMARY OF FINDINGS

This sponsor/clinical investigator has no inspectional history in New Orleans District; however, he has been inspected in LOS-DO. Last EI was 5/12/92.

HFZ 1/17/01 Assignment requested directed inspection of Dr. Lentz as Sponsor/Monitor and as Principal Investigator. Per compliance program and assignment, the inspection was conducted unannounced, in accordance with CP7348.810 and CP7348.811. (b) (7)(E)

(b) (7)(E)

Per assignment, Dr. Lentz' three IDE studies ((b) (4) metastatic melanoma; (b) (4) metastatic breast cancer; and (b) (4) metastatic colorectal cancer) were reviewed. In addition, per assignment, Dr. Lentz was asked if he had treated any patients with his proposed affinity column (that has no approved IDE). It was determined that since Sept., 2000 he has treated at least eight patients with the column--with multiple procedures. It was also determined that since the opening of his practice in Aug., 1997 he routinely has treated patients (non-study subjects) with the IDE ultrafiltration device (that has no approved use in the U.S.). Per Lentz, these patients' treatments were identical to the subjects' treatments—including a signed consent. The various versions of the consents state that FDA can review the records but do not mention IRB review or a contact for questions regarding subjects' rights.

Inspection revealed that Dr. Lentz is conducting various studies without FDA/IRB knowledge/approval. All observed consents, however, reference FDA review of the records. Serious non-compliance with the regulations and protocols was observed. Case report forms were not completed for two of the three IDE studies and were inadequate/incomplete for the third study (melanoma). The IRB was not informed of 2 of the IDE studies (breast and colorectal cancer). Subject rosters were not maintained. Device accountability records were not maintained. Patients are charged for the investigational apheresis treatments—approximately (b) (4) per procedure and usually 15 treatments per course with multiple courses. Claims are filed with insurance carriers and Medicare. Correspondence was observed in patients' files whereby insurance carriers were provided the (b) (4) classification for the IDE device as Category B Reimbursable—even if the patient was not a subject in one of the three IDE studies.

Dr. Lentz demonstrated little knowledge of the sponsor/monitor regulations. He asked what "monitoring" is. His Regulatory Affairs person asked what an IRB is. She is a nurse that he hired on a part-time basis to do the paperwork/regulatory filings. She has no background/training in this field. She told me that she questioned why Lentz hired her for such a position. Discrepant reports were submitted to FDA as compared to what was submitted to the IRB.

Due to the severe lack of compliance observed in the device studies, Dr. Lentz' three single patient IND's for (b) (4) and his general (b) (4) study (fourth IND) were reviewed. Again, proper test article accountability records were not maintained. "Subjects" were "enrolled" that Lentz never saw and who never came into his clinic. Consents were faxed to patients/their local doctors. Dr. Lentz did not follow the

(b) (4) protocol for follow-up visits/labs. He conducted a "new" (b) (4) study that added two additional drugs- (b) (4) There was no documentation of FDA/IRB/drug manufacturer knowledge of /approval. Proper consents were not signed by the patients.

FD483 was issued to the sponsor/PI at the conclusion of the inspection. Although he admitted that he had treated eight patients with the affinity column, he insisted that he had NOT initiated the protocol, stating he was awaiting FDA approval before he started the study. He said that he could not ethically deny patients a "potential cure", however. For the other studies that were not approved by FDA/an IRB (such as the "Unblocking" study or the "Biomodulation" study or the "new (b) (4) study"), Lentz insisted that the patients simply signed an erroneous consent—that those studies were never "enacted". Lentz promised he would respond in writing to the Center in order to clarify the mis-statements on the 483. He said he never submitted the (b) (4) study to the local IRB, so the local IRB could not have disapproved it.

ADMINISTRATIVE PROCEDURES/PERSONS INTERVIEWED/ INDIVIDUAL RESPONSIBILITIES

As stated above, the inspection was conducted unannounced. Upon my arrival, I initially asked for (b) (7)(C) as she was listed as the contact person for the IDE studies. I met (b) (7)(C) who stated that (b) (7)(C) is now the contact person. (b) (7)(C) serves as the data manager and Regulatory Affairs person for the IDE studies. I was then introduced to (b) (7)(C) She informed me that Dr. Lentz was available. Credentials were displayed and FD482, Notice of Inspection, was issued to Meredith Rigdon Lentz, M.D., Sponsor and Principal Investigator. I informed Dr. Lentz that the purpose of my visit was to review the three IDE studies. He inquired several times throughout the inspection what prompted the inspection. He expressed surprise that I had not pre-announced my visit. I stated that per compliance program, sponsor-monitor inspections are conducted unannounced.

(b) (7)(C) stated that prior to May, 1997 she worked with Dr. Lentz as an oncology nurse at (b) (4) (b) (4). She said she left there on maternity leave. In 1999 Dr. Lentz phoned her at home and asked if she would like to work part-time and could even work from her home. He asked her to complete some regulatory forms and work with (b) (4) (a consulting firm out of (b) (4) According to Lentz, (b) (4) was hired to create case report forms for the melanoma study and to assist him in writing final reports. (b) (7)(C) said that she transcribed data into those CRF's. She said that if she could not locate something in the patient's medical record, the item would remain blank in the CRF. When I asked why the CRF's only covered up to five procedures even though most patients received many more procedures than 5, she did not know the answer. Neither did Dr. Lentz. He asked (b) (7)(C) to phone (b) (4) (During the 483 discussion, Dr. Lentz said that the CRF's only covered 5 procedures because (b) (4) was only trying to show him and (b) (7)(C) how to complete the pages. He said (b) (4) thought he knew to follow through and complete the forms for all of the patients' procedures.)

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(b) (7)(C) told me that in mid-2000 she began working in Lentz' clinic three days a week. She assists Dr. Lentz in preparing annual reports for FDA. For example, he gave her six metastatic breast cancer subjects' names and asked her to pull the patients' information from their medical records. She said she does not assist with treatments.

During the inspection, I asked Dr. Lentz for a company organization chart. He said they do not have one. I then asked that he provide names of employees that assist in the studies and their duties/responsibilities. He said that he is the primary physician. (b) (7)(C) is a partner in his practice and is his backup. He said (b) (7)(C) is a vascular surgeon.

Lentz hired (b) (7)(C) last summer to work on the column. He said (b) (7)(C) has a PhD in microbiology and immunology. (b) (7)(C) is responsible for the lab (within Lentz' office suite) and for science review. For the past 6-9 months, (b) (7)(C) has provided the scientific guidance behind the manufacture of the column.

(b) (7)(C) came here 1 ½ years ago from (b) (7)(C) in (b) (4) He is in charge of the (b) (4) studies. Per patient records, Mr. Fender also assisted in the column treatment procedures.

The nurses that assist with the procedures are as follows: (b) (7)(C) is a dialysis nurse that came here 4-5 years ago. (b) (7)(C) is an oncology nurse that came here 1 ½ years ago. (b) (7)(C) is an oncology nurse who has been here approximately one year.

(b) (7)(C) He has only been here six months. (b) (7)(C) (b) (7)(C) secretary/receptionist, has been employed here 3 years. (b) (7)(C) is at the front desk and has been employed here 2 years. (b) (7)(C) told me that her husband also works in the clinic on a part-time basis.

When the IDE Melanoma study began in 1996 Dr. Lentz was still employed at Tennessee Oncology. Some of the practice partners were also listed as co-investigators- (b) (7)(C) Lentz told me that while he was still at Tennessee Oncology, (b) (7)(C) and another nurse, (b) (7)(C) went to (b) (7)(C) with him in order to be trained by the (b) (4) in the use of the apheresis equipment. Once (b) (7)(C) went on maternity leave in May, 1997, she no longer treated the patients.

FDA correspondence should be directed to Dr. Lentz at the above address.

The most responsible person at (b) (4) is (b) (7)(C)
(b) (7)(C)

The most responsible person over the (b) (7)(C)
(b) (7)(C)

INTERVIEWS

During the initial week of the inspection, I asked Dr. Lentz if he had used the column to treat any patients. He stated that he had not. He did say that he was waiting for word from CDRH regarding pre-IDE approval. He expected to hear something by the end of that week (3/9/01). He asked several times about the purpose of my visit and asked if I thought his pre-IDE would get held up due to my inspection. He said he was ready to go with the column study as soon as he got approval. He said the IRB was "on board" and was ready to review it. I asked if that would be a local Board. He responded that he only uses the (b) (4) oversees all of the system hospitals in the (b) (4) -including the one that (b) (4)

He gave me a tour of the treatment area. He pointed out his new (b) (4) machines. He said that he has (b) (4) of the (b) (4) machines, but has already put some in storage. (b) (7)(C) had told me when I initially arrived that the clinic was "on hold" waiting for column approval. She said they weren't doing apheresis anymore.) Dr. Lentz and (b) (7)(C) also said they weren't doing much apheresis. I asked Lentz if his clinic did other procedures besides the IDE studies. He said they do plasma exchange.

On the initial day of the inspection, I stated I would look at the subjects' records and would need to see their medical records. (b) (7)(C) asked the front desk staff to pull the medical records for her. After the records were brought into the conference room, (b) (7)(C) began counting the charts. She said they brought "too many". She went through the records and sorted them by IDE study. I later asked her if they had a subject roster for each study. She said they did not but she would make one. She did and it is attached as **EXHIBIT #21.**

Dr. Lentz explained the theory behind the device. He discussed some of his "successes". I asked which patients were still alive. He mentioned an 8-year-old girl, (b) (7)(C) (I did not see this name on the roster.) He said she may have been one of the "exceptions". For the colon study, he mentioned a name, (b) (7)(C) who he said was a non-responder. (b) (7)(C) name is not on the roster. He also mentioned a (b) (7)(C) also not on the roster). He said his two "humanitarian exemptions" have died—one was a responder who died from a bleeding ulcer. The second was a non-responder.

The inspection was interrupted due to another assignment. When I departed Lentz' clinic on 3/8/01, I told them I would call before I returned. The firm was informed 4/6/01 that I would be returning April 9. I was asked to bring back the exhibits I had obtained earlier. (b) (7)(C) stated that they wanted to make copies of the exhibits (for themselves). I had been told that Dr. Lentz and (b) (7)(C) would be available the following week. Upon my return, I learned that Dr. Lentz was in Florida for the week. (b) (7)(C) assisted me in retrieving records for my review. As she brought medical charts, she told me that they had realized that they did not know what they were doing when I showed up in March. They had since spoken to (b) (4) who advised them to make a copy of every record copy I obtain. They also told her to pull from the charts any references to money, charging, or finances and anything not directly related to the initial protocol treatment. I advised (b) (7)(C) that I was entitled to the financial records as they apply to the charging for an investigational device/treatment and am entitled to see all medical records—including pre-study to

see a patient's history and to see if the patient meets study inclusion criteria. Since they are reporting on the success of the patients' treatment (s) to date (or to death), I can look at the medical records to present to determine whether there have been adverse events related to the test article. She then brought me everything she said she had earlier pulled from the files.

When I completed review of the reported "subjects", I told (b) (7)(C) that I had other patient names and I wanted to see their files. I said Dr. Lentz had mentioned some patients and I had some other names. She asked if I meant the "off-study patients". I said yes. I asked her if the "off-study patients" had been treated the same as the "subjects". She said yes. She said they signed consents. She said that if I looked at those patients' charts, I would not be able to tell any difference between an "off study patient" and a study subject. I asked how Lentz decided which patients were "subjects" and which were considered to be treated "off-study". She said she did not know. She has often wondered that same thing. She said the device treatment was the same. I asked if there were many off-study patients, and I said I suspected they would comprise his entire practice. She nodded in agreement. I asked if the number would be in the thousands? She said probably in the hundreds.

She said she guessed the apheresis treatment had been his entire practice since he opened his solo practice in August, 1997. She pointed to eight boxes on the floor in the hall and stated that the boxes contained the "dead patient files".

She told me that when he handed her (b) (4) metastatic breast cancer patient names and asked her to prepare the annual report, she searched the medical records and retrieved the information he wanted. She then wrote the report and forwarded it to the Center—with Lentz' review and signature. When the Center wrote back asking why he enrolled (b) (4) when he had only been approved to enroll (b) (4) she said he screamed at her for "messing up". She told me that she did not know that he had only been approved to treat (b) (4) patients. She only retrieved the information he wanted and she got blamed for the "mistake". She said that since (b) (4) had already been reported, they had to stand by that number.

I told (b) (7)(C) that I had not seen any references to complaints in any of the files/charts. I asked whether a patient complaint would be filed in the patient's clinic chart. She said it would not, adding that none of the staff would even see a complaint. She said Dr. Lentz would lock something like that up in his office.

I asked her if Dr. Lentz had used the column. She asked me if I meant "on humans"? I said yes. She said yes, he had treated some patients. She was aware of an older lady and a father of one of the clinic nurses. I said I needed those patients' names and medical charts. She said Dr. Lentz had told her it was "OK" to use the column. When she asked him about it, he told her it was within his practice of medicine.

She said Lentz has been making his own columns since Christmas, 2000. She stated he visited (b) (4) last year and went to the manufacturing site of (b) (4) He wanted to see how much it would cost for a manufacturer to make just a few columns, a prototype. He decided the cost was too high so he decided to make his own. She guesses he has made (b) (4) of the columns, as he asked her to come

up with a prototype label for the pre-IDE device. She thinks she made that many labels ((b) (4)) and he used them all.

After (b) (7)(C) asked the nurses for the names of the column-treated patients, she came back to the conference room to inform me that the nurses got "anxious" about my request and phoned Dr. Lentz in Florida. He told them to tell me that he would return from Florida to the clinic—that he wanted to be the one to tell me about the column patients. I agreed to wait for that information when he and I would both return to his office at a later date.

(b) (7)(C) stated she did not understand why Dr. Lentz had hired her for a position as Regulatory Affairs. She said she has no experience or training in this field. She asked me what an IRB was.

On April 30 I returned to Lentz' clinic to meet with Dr. Lentz and obtain additional information. I began by asking him about his results with the column treatments. He stated he had treated eight patients—one of whom is the patient he treated in (b) (4) He said, though, that he did not make that column. That column was made in (b) (4) In his clinic, he stated he had treated seven patients. He explained that they have been "working with families of antibodies". He said the best antibodies are from rabbits. He said they use a USDA rabbit and veal farm in (b) (4) (Lentz said the farm was a (b) (4) facility.) He bought a number of rabbits. He pays for feed, etc. (b) (7)(C) goes to the farm to inject the rabbits in order to make antibodies. He said they already knew how the column worked—they saw the results in (b) (4) He said they tested the column in vitro to see if the results were reproducible. They worked on the column in their lab after they met with CDRH. They initially tried a (b) (4) column but decided they needed a larger column. He said they tried to emulate "FDA approved equipment" so it would be better for safety, etc.

He said the (b) (4) column that is approved is (b) (4) The matrix for his column is (b) (4) (manufactured by (b) (4) . They bought a column, (b) (4) added their antibodies and put it together in a test column. They tried the column using blood bank plasma. Lentz said they followed the FDA Guideline on how to make columns. He said they did their own QA and developed SOP's. They tested the column and it "was fine".

Dr. Lentz said the only patients that were treated with the column were ones that he knew "very well" from his practice. He said these patients had previously been "responders" to the apheresis (the investigational treatment—treated either as subjects in the IDE studies or treated "off-study") but had a recurrence. He said he had a choice of re-treating them with apheresis (the investigational treatment) and give them blood bank plasma or use the column which is a closed system that requires no additional blood products. He said the column treatment is safer than the old apheresis (investigational treatment) because he does not have to use (b) (4) (b) (4) blood products. He said he continually received recall notices from (b) (4) and he was worried about the safety of the plasma.

He said he did not recruit any patients. The patients were desperately ill and begged for the column treatment. I asked how the patients knew about the column if he had *not* "advertised" it. He said his patients are aware that he is working on other things.

He said the column is comprised of "FDA-approved parts" and as far as he is concerned the column is then equivalent to something that FDA has approved. He said he hopes he was not breaking the rules. He said the seven patients would not meet his protocol inclusion criteria and the column treatment was "justifiable in these circumstances". He said the patients asked for the column treatment because they knew it was even safer than the older apheresis (IDE) method. He said that he would be comfortable having the column used on him. He said that if I were diagnosed with breast cancer, for example, I would want him to do this treatment, knowing that he had a possible cure for me. He said that although he wanted to write up his seven column patients, he has not yet done so. He did offer a manuscript about the Russian patient he treated. See **EXHIBIT #2.**

Dr. Lentz summarized the seven patients as follows:

1. (b) (7)(C) has breast, lung and liver cancer and has refused chemotherapy. She has a relative that is a physician at (b) (4) He said she had 15 procedures (one/day). The cancer is now "completely gone". She experienced no AE's or fever.

2 & 3. (b) (7)(C) and (b) (7)(C) both were subjects in the (b) (4) study (according to the subject rosters provided by (b) (7)(C) during the inspection, **EXHIBIT #21**). Dr. Lentz described (b) (7)(C) as a complete responder following column treatments and (b) (7)(C) as a partial responder in that her tumors shrank by at least (b) (4)

4. (b) (7)(C) is an ex-(b) (7)(C) operative, according to Lentz. Lentz stated he received pressure to treat (b) (7)(C) The patient was sent to Lentz from (b) (7)(C) and had terminal cancer. It is not yet clear if he is a responder, as the mass did not shrink. His tumor markers did go down, per Lentz. Following column treatment, the patient was sent to (b) (4) where he underwent a laparoscopy. Tumor was removed, but per Lentz, greater than 40% of what was removed was dead tissue. The patient is now recovering from that surgery.

5. (b) (7)(C) is an 80-year-old with metastatic lung cancer. Lentz said she is (b) (7)(C) Post treatment she had a (b) (4) decrease in the tumor in her chest and (b) (4) decrease in the tumor markers, according to Dr. Lentz. She received low dose radiation to her brain mets that have resolved. She and her son have "contributed (b) (4) . She is a Medicare patient.

6. (b) (7)(C) is (b) (7)(C) . He is 56 years old and has metastatic lung cancer. He had had extensive radiation and chemotherapy so Lentz treated him "gently". He had 15 treatments but they have seen no effect yet. He said no harm was done. The patient is stable. I asked what "gently" meant. Lentz said they did the treatment every other day instead of every day and ran the column for less time.

7. (b) (7)(C) has metastatic renal cancer. She was treated "off study" three years ago. She was a complete responder. She had a recurrence last summer. She is a very poor single mother. She had no AE's. Her tumor decreased considerably. Medicare was billed for her treatments, according to Lentz.

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Dr. Lentz was asked if the patients were charged. As indicated above, Medicare was billed for some patients. Others like (b) (7)(C) paid (b) (4) or their insurance carriers were charged (b) (7)(C).

Dr. Lentz stated that he was not sure that he even needs an IDE for the column. He said his colleagues told him that he would not need one since all of the parts are FDA approved. He said the empty column is approved for hema-perfusion as is (b) (4) (b) (4) He said the (b) (4) s the safest for humans. He said they make their antibody just like what is already approved. He said he thinks his treatment is OK if he is only trying to help patients. He said the (b) (4) machine is approved. He uses (b) (4) tubing sets. He uses (b) (4) filter that is approved. The (b) (4) beads are approved; and the (b) (4) (b) (4) is made "under GMP's and GLP's". He said there is nothing new or experimental. He said there is no problem with safety, as they made the column just like they would in an operating room. He says they only made enough columns for these patients.

He said that CDRH has asked what is the shelf life of these columns. He said they hope to use theirs within (b) (4) –that is what they plan to do for the (b) (4) patient pilot study. He said they have a waiting list o(b) (4) atients who want column treatment.

I asked Dr. Lentz if he could use a column for more than one treatment. He said yes, they have regenerated a column in his lab for up to (b) (4) treatments. Ideally, he plans to use one column for up to (b) (4) procedures. I asked if the columns were sent off for sterilization? He said they were not—the columns are put together "totally sterile" under a hood and do not need further sterilization.

I then asked Dr. Lentz about his "off-study patients" (as he had referred to them). He said that when he initially proposed the apheresis study (the initial IDE study), he made it clear that if a patient responded, he wanted to be able to re-treat, as it would not be ethical to turn that patient away. He said (b) (7)(C) told him that he could continue to treat the patient as long as the patient wishes to be treated. I asked him how he decided which patients would be reported as "subjects" and which patients would be his "off-study" treatments. He said he determined ahead of time who was a subject, as that would be "bad science" if he did not and the "data would be suspect". He said the off-study patients were "exceptions" (to the protocol) and that he wasn't looking for them (recruiting them). He said he did not treat "many". If the treatment did not help, he stopped it. The off-study patients signed "essentially the same consent" as if they were subjects.

I asked about complaints—if Dr. Lentz had ever received any complaints or had lawsuits filed against him. He said he could not remember any complaints. He said he has only been sued once in his life and that was by (b) (7)(C) (b) (7)(C). He said he "thinks he got permission from FDA" to treat (b) (7)(C) as an exception. (b) (7)(C) had a rare cancer and had received a lot of experimental therapy in (b) (4) After apheresis, the tumor initially suggested a response (nothing works in this tumor, according to Lentz). Lentz said he wrote a letter to (b) (7)(C) referring physician saying that he was encouraged but to wait a month and do a CAT scan. He claims the Weddles went back to their church

and announced a miracle. One month later the tumor was larger and the disease had progressed. Lentz said he did not give (b) (7)(C) a second cycle. He lived another 9 months. (See patient records, **EXHIBIT #26**.) One and ½ years later (b) (7)(C) filed a lawsuit saying that Lentz gave her husband hope for that month. Lentz said the suit just got dismissed. He asked if that is what triggered the inspection. I asked again if he had received any other complaints. He responded, "No other complaints that I can think of". He added that he receives more complaints because he doesn't treat the patients.

I asked about patents, saying I had seen a reference in one of his reprints. He said he has a patent for the column and a patent for "ultrapheresis". He trademarked the technique/process for ultrapheresis (a process patent). He said the IDE for the devices creates a dilemma, as he already knows the device is safe and effective. He said some would argue that it is a **treatment.**

Lentz said his nurses have already attended training in the use of the (b) (4) machines. He said this manufacturer was much more receptive to the nurses than the (b) (4) manufacturer had been. I asked if the (b) (4) machines could be used for standard plasma exchange? He said they'll probably exchange (b) (4) patients per year and are looking into doing (b) (4) testing with the machines. He said they have purchased (b) (4) machines at approximately (b) (4) each. He said the (b) (4) equipment can only do the one thing with it--apheresis.

I asked about his supplier of the (b) (4) equipment. He said the only U.S. distributor is (b) (4) He said the only way to get the filters, etc, is through (b) (7)(C) at (b) (4) who is connected to (b) (4) He said (b) (7)(C) (b) (7)(C) is one of the principals in the design of the equipment. I asked again if the (b) (4) equipment were the only equipment he used for the IDE patients and for the off-study patients. He said it was. All patients were treated with the same machines/tubing sets/filters—whether they were in a study or not.

I asked about Immutherapeutics. He told me that is an old company that no longer exists. He said he put the company together with friends to do cancer research. He said the plan did not work; they could not raise money. Lentz said that he was the Medical Director for the company. He said the company was not really affiliated with the IDE. He said they could not afford product liability. Lentz was the sponsor and the sole proprietorship.

I asked if he had any contracts with outside firms to do study activities. He said he had no contracts or written agreements. He said again that he hired (b) (4) to review regulatory affairs, create CRF's. He said he's used them the past 3-4 years. They've taught (b) (7)(C) about regulatory affairs. In his upcoming column study, he'd like (b) (4) to provide the monitor and he would let them (b) (4) do regulatory affairs. He says he now sees that he cannot be the physician/clinical investigator and do regulatory affairs. He added that he realizes that he must keep data better organized.

I asked about the (b) (4) studies. Lentz stated that he did not think that he was the sponsor of the study. (See, however, related IRB EIR for the three IND studies submitted to that Board. He submitted the 1571's to CDER for these three studies

naming himself as the sponsor. He also submitted a 1571 for a third single-patient IND, naming himself as the sponsor. See **EXHIBIT #75.**) He said (b) (7)(C) has the primary responsibility for the (b) (4) study. (b) (7)(C) acquired the study in-progress. Another nurse had overseen the project until she left Lentz' employment. Dr. Lentz said that for (b) (4) (b) (4) s a great drug. It is promising for prostate cancer and melanoma. He sees no effect at a dose below (b) (4)

I asked Dr. Lentz for (b) (7)(C) chart. He stated that since she was never treated, her chart would not have come to his clinic from (b) (4) And given that she died that long ago, it would have been archived off site by now.

I asked for (b) (7)(C) chart. Lentz said he did not remember that name. I said he had a patient by that name. (b) (7)(C) said she did not recognize it. She looked on the shelf and found the chart, but told me later when I again asked for it that Dr. Lentz was reviewing it in his office. Some time later he brought the chart to me. He said he could not know how I would know this name when he could not remember it. I said that we "get reports from all over". Some of the patient's records are attached as **EXHIBIT #22**. This patient received chemotherapy and (b) (4) as well as two courses of apheresis. (b) (7)(E)

Dr. Lentz saw a few patients during my visit 4/30-5/1/01. He informed me that one of the patients (a female) was one of the (b) (4) who he had treated with the column. He kept insisting that I meet the patient and see how well she is doing. I told him that it would be inappropriate for me to meet her. He offered to introduce me as his friend and not as FDA. I told him it would be inappropriate.

OBJECTIONABLE CONDITIONS

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

DEVICE STUDIES

1. The PI (who is also the sponsor) conducted investigational "studies" (using investigational devices) that did not have FDA/IRB knowledge of/approval. Patients signed "consents" to participate in these unapproved studies. The consents referenced that the patients' medical records "may be reviewed by the U.S. Food and Drug Administration and other government regulatory agencies". Examples of the unapproved studies/consents include:

- (b) (4)

This consent can be seen in **EXHIBIT #8**. According to Dr. Lentz, he treated (b) (4) patients with the column. During my review of the (b) (4) study records, I observed another patient, (b) (7)(C) who had received column treatment. I asked for her file. Her clinic chart entries ended prior to the column treatment in Sept., 2000. When I asked (b) (7)(C) about this, she said that was all that was on the shelf. She

checked with Dr. Lentz who later brought me a paper file that contained records of the column treatment. He stated he had forgotten about this patient. See her records, **EXHIBIT #10**. She signed the consent 10/12/00 and 11/30/00. The column consent was not observed in Patient PDP's file; however the staff contacted the patient during the inspection and asked that she fax her copy. She did. It was signed 1/22/01. Patient (b) (7)(C) signed the consent 11/27/00 **(EXHIBIT #4)**. Patient (b) (7)(C) signed the consent 10/16/00; 12/4/00; and 1/9/01 **(EXHIBIT #7).** Patient signed the consent 9/25/00; 10/9/00; and 2/5/01? **(EXHIBIT #9)**. Patient signed the consent 10/10/00 and 1/9/01 **(EXHIBIT #3)**.

- (b) (4)

Patients were observed to have signed this consent. For example, Patient (b) (7)(C) signed it 1/20/98 and 3/9/98 **(EXHIBIT #71).** Patient (b) (7)(C) signed it 7/7/99. Patient (b) (7)(C) signed it 1/6/98 **(EXHIBIT #72)**. Patient (b) (7)(C) signed it 3/16/99. Patient (b) (7)(C) signed it 11/1/99; Patient (b) (7)(C) signed it 5/22/00 **(EXHIBIT #65).** Patient (b) (7)(C) signed it 10/27/99.

- (b) (4)

Examples of patients that signed this consent include Patient (b) (7)(C) who signed it 10/11/99 **(EXHIBIT #54).** Patient (b) (7)(C) signed it 10/18/99 and 1/17/00 **(EXHIBIT #56).** Patient (b) (7)(C) signed it 3/16/99, 7/6/99, and 10/4/99 **(EXHIBIT #70).** Patient (b) (7)(C) signed it 5/4/99 **(EXHIBIT #69)**. Patient (b) (7)(C) signed it 3/20/00 **(EXHIBIT #65)** as did Patient (b) (7)(C) **(EXHIBIT #8).** "Biomodulation Orders" were observed throughout the patients' records.

The consents lacked a contact person/phone number to call for questions regarding subjects' rights. Moreover, for the "column study", the column was "put together" on site by the sponsor. At least (b) (4) patients have received multiple procedures/treatment courses with the column. These patients/records are as follows:

1) Patient (b) (7)(C) According to progress notes, this patient received six of a planned 15 procedures with the affinity column beginning 10/11/00. She had problems with extreme fatigue, weakness, dyspnea and a nonproductive cough. There were "wide gaps" between her procedures because she was unable to tolerate treatment. She was admitted to the hospital because of pleural fluid volume and significant anemia that required transfusions. She also developed severe left chest pain. It was determined that she had developed an intra-pleural bleed. She returned in Jan., 2001 for additional treatments; and in Feb-March for her 8th cycle of apheresis (second cycle of selective (b) (4) removal) for 14 additional procedures from 2/20/01-3/9/01. (Note her latest procedures took place during the initial week of the inspection.) See records, **EXHIBIT #3**.

2) Patient (b) (7)(C) received 17 "selective apheresis" treatments in Nov.-Dec., 2000. He signed the column consent 11/27/00. He returned 1/8/01 for 32 additional treatments through 2/21/01. See records, **EXHIBIT #4**.

3) Patient (b) (7)(C) His first cycle consisted of 18 treatments from 1/24/01-2/16/01. He returned for four additional treatments 3/23/01-4/4/01. See records, **EXHIBIT #5**.

4) Patient (b) (7)(C) completed 15 treatments 1/22/01-2/16/01. She was scheduled for additional treatments in April, 2001. See records, **EXHIBIT #6**.

5) Patient (b) (7)(C) an 80-year-old woman, received no prior treatment for her lung mass before arriving at Lentz' clinic in Oct., 2000. She completed 15 column treatments from 10/16/00-11/8/00. At the end of that cycle she "developed an infiltrate consistent with pneumonia" and was hospitalized. She then began Lentz' (b) (4) protocol and received no other cancer treatments. MRI of 11/27/00 revealed brain metastases. She completed 9 column treatments between 12/5-15/00. She completed 16 additional treatments between 1/10/01 and 2/9/01. She returned for 8 additional treatments 3/15/01-4/3/01 (after initiation of the inspection). See records, **EXHIBIT #7**. Although Dr. Lentz had told me that he only used the column on patients he had previously treated with apheresis and had responded, this was not the case for this patient. She had received NO prior cancer treatment before her arrival at Lentz' clinic, according to the progress notes.

6) Patient (b) (7)(C) received 14 of the planned 15 treatments from 2/6-23/01. See records, **EXHIBIT #8**.

7) Patient (b) (7)(C) received 18 column procedures beginning 10/9/00-11/2/00. He received 17 procedures 2/6/01-3/1/01 along with concurrent radiation treatment. See records, **EXHIBIT #9**.

8) Patient (b) (7)(C) received 15 treatments from 10/12/00 - 11/1/00; fourteen of the planned 15 treatments from 12/1-21/00. As of 12/21/00 the patient was considering an NIH vaccine program. See records, **EXHIBIT #10**. This is the patient that Dr. Lentz forgot he had treated with the column. Her treatment was discovered while I was reviewing (b) (4) study records. She participated in that study as well.

2. The sponsor failed to assure that the trials were conducted per the protocols as submitted to FDA and per the regulations for the three IDE studies (IDE #'s (b) (4). The sponsor failed to report to FDA non-compliance with the regulations/protocols.

According to Dr. Lentz, none of the subjects enrolled in the three IDE studies were registered at the (b) (4) as per protocol.

3. No monitoring of the three IDE trials was conducted.

4. The PI failed to report all deaths/adverse events that occurred during the studies. For example, one of the (b) (4) subjects that was reported to FDA as participating in the colorectal cancer trial (b) (4) arrested immediately following her apheresis procedure on 10/26/99. The death was not reported to FDA. As this

study had not been submitted to an IRB for review, the death was not reported to an IRB. See records for Patient (b)(7)(C), **EXHIBIT #69**.

5. The sponsor has no written procedures for study monitoring or data handling for any of the studies.

6. The PI failed to maintain all submissions to/correspondence with the IRB. For example, there was no documentation of receipt of two complaints and subsequent follow-up correspondence with the IRB. See related EIR of the IRB.

7. Patients that were reported to FDA as subjects in the three IDE trials also participated in other concurrent studies (as in #1 above). Their participation was not reported to FDA. See Item #1 above that lists the other consents signed by the IDE subjects. In addition, many of the IDE subjects also participated in Lentz' (b) (4) studies.

8. At least two studies were submitted to the IRB for review/approval 1/22/96 prior to FDA approval for the study to proceed. One study, (b) (4) (b) (4) was disapproved by FDA, per 1/17/96 letter; yet this study was submitted to the IRB 1/22/96 without an approved IDE. There is no documentation that the Board was informed of FDA's disapproval to conduct the study/lack of IDE or that the PI had withdrawn the protocol 2/16/96 from his IDE submission. The 4/13/00 Metastatic Cancer study progress report/request for renewal submitted to the IRB states (b) (4) subjects were enrolled in this study. See related EIR for the IRB.

   The protocol, (b) (4) (b) (4) was submitted to the Board 1/22/96-- prior to receiving FDA's conditional approval 3/1/96 to proceed with the study. No documentation was observed that the Board was informed of this conditional approval to proceed. See related EIR for the IRB.

9. Two IDE studies were conducted without IRB review/approval. These are: (b) (4) (b) (4) (b) (4) See related EIR of the IRB.

10. No case report forms or study subject rosters were completed for the colorectal cancer study (b) (4)) or breast cancer study (b) (4) above. A subject roster was not maintained for the melanoma study. During the inspection, subject rosters for the three IDE studies were generated per FDA request **(EXHIBIT #21)**. Only limited case report forms were filled out for the melanoma study (covered up to 5 procedures even though several additional procedures were performed on the study subjects). These forms were not filled out concurrent with study activities—they were filled out after the fact in 1999 even though the study began in 1996. No case report form was observed for one of the subjects as reported to FDA—Patient (b)(7)(C) on the generated roster). A case report form was observed for patient (b)(7)(C) **(EXHIBIT #24)**; yet this

patient is not listed on that study roster **(EXHIBIT #21)**. See case report forms, **EXHIBITS #27, 31, 33, 35, 37, 39, 41, 43, 45, 47, 49, 51, 53, 55, 58** for the melanoma study "subjects".

11. Numbers of treated/enrolled subjects and their names do not match what was reported to FDA as compared to what was reported to the IRB. FDA approved two "humanitarian exemptions" for the melanoma study (b) (4) —patients (b) (7)(C), and (b) (7)(C). The PI reported to the IRB, however, that patients (b) (7)(C) **(EXHIBITS #26, 27)** and (b) (7)(C) **(EXHIBITS #30, 31)** were the FDA-approved exemptions-- but for the Metastatic Cancer study (the study that never received FDA approval/approved IDE). See related EIR for the IRB. The patient, (b) (7)(C) signed a consent 6/12/96—before the exemption was granted per 6/13/96 FDA letter. Moreover, the PI signed this consent 6/11/96-- prior to the patient's signature **(EXHIBIT #30)**. Per PI's 7/26/96 letter to FDA, he reports only one of the two exemptions was enrolled ((b) (7)(C)). Patient (b) (7)(C) was reported as "never enrolled", as her disease progressed beyond the restrictions as stated in the protocol. Per Dr. Lentz, her chart is not in his clinic. He insisted she had not been treated with apheresis and said her chart had remained at (b) (4) when he departed that practice. He said that since she had expired before he left that practice, her chart would now be archived.

In addition, numbers of patients treated exceeded the FDA-approved enrollment. For example, only (b) (4) patients could be enrolled in the breast cancer trial (b) (4) (b) (4) ; yet the site reported data for (b) (4) subjects **(EXHIBITS #60-65)**. And, as indicated earlier, patient (b) (7)(C) signed a consent to participate in the melanoma study; a limited case report form was completed for this patient—but his name is not on the generated list of subjects for this study **(EXHIBITS #23, 24)**. Per PI, he treated patients "off-study" with the investigational device. Several (b) (4) study patients were observed to have received apheresis treatments—these patients are not IDE study subjects. Examples include:

-Patient (b) (7)(C) **EXHIBIT #92**
-Patient **EXHIBIT #95**
-Patient **EXHIBIT #97**
-Patient **EXHIBIT #98**
-Patient **EXHIBIT #102**

12. None of the consents observed met FDA specific IDE provisions for the specific study/IDE as applicable. The consents for the unapproved studies lack a contact person for subjects to call regarding subjects' rights. None of the consents are specific for the costs incurred by the patients. For the "column study", patients signed a (b) (4) **(EXHIBIT # 7)** and were asked to, (b) (4) (b) (4)

Only 2 (NOTE: it should be 3) of the reported (b) (4) subjects enrolled in the breast cancer study (b) (4) signed a consent for "metastatic breast cancer". These are subjects (b) (7)(C) This consent does not mention IRB review or list a contact for questions regarding subjects' rights. In addition, it promises confidentiality and that the subject "will never be identified by name in

any report". The PI failed to make FDA-required corrections to the consent and add, for example, "potential adverse event" such as "iatrogenic anemia" to the consent, per 6/3/99 and 8/17/99 letters. No documentation of this change was observed, as none of the breast cancer subjects signed the consent as per the IDE. An example of this consent can be seen in **EXHIBIT #64**.

None of the (b) (4) reported subjects for the colorectal cancer study signed the consent as per (b) (4) Per 12/30/97 FDA letter, Dr. Lentz was informed of the required changes to be made to the informed consent. No documentation of changes was observed, as again, the subjects in this study (colorectal cancer) did not sign such a consent. Patient (b) (7)(C) signed a (b) (4) consent **(EXHIBIT #70)**. Note: this study was not submitted to the IRB for review; yet the IRB Chairman is listed in this consent as a contact person regarding subjects' rights. Subject (b) (7)(C) also signed "Unblocking" consent and the "Biomodulation" consent and the "Metastatic Cancer" study consent.

Subject (b) (7)(C) signed the "Unblocking" consent 1/6/98 **(EXHIBIT #72)**. Subject (b) (7)(C) signed the "Unblocking" consent; "Biomodulation" consent; and the "Metastatic Cancer" study consent **(EXHIBIT #69)**.

Subject (b) (7)(C) signed the "Unblocking" consent **(EXHIBIT #71)**.

13. Consents to participate in the studies were often obtained after the vascular catheter had been surgically placed in preparation for the apheresis procedures. Examples include: Subject (b) (7)(C) who signed the consent 9/16/97; yet the port placement was 9/15/97 and Dr. Lentz signed the consent 9/15/97 **(EXHIBIT #48)**. Subject (b) (7)(C) signed the "Unblocking" consent 3/16/99; yet her catheter was placed 3/15/99 **(EXHIBIT #69)**.

14. Records show a discrepancy as to the identity of the sponsor of the investigational device studies. Per submissions to FDA, Dr. Meredith Rigdon Lentz is identified as the sponsor and as the Principal Investigator. Some records submitted to the IRB report the sponsor to be "Immutherapeutics", a company described by Lentz as the U.S. and foreign patent holder of the filtration device (manufactured by (b) (4) Lentz is identified as the "inventor and a stockholder in Immutherapeutics, Inc."—"the sponsor of the research in the US". He reports in his CV **(EXHIBIT #1)**, however, that from Jan. 1993 to present he holds the positions of Chairman Board of Directors and Medical Research Director of Immutherapeutics, Nashville, TN. (Also see related EIR of the IRB.)

15. The PI failed to maintain adequate test article accountability records. No records were observed of the PI's purchase/receipt of the apheresis machines. Moreover, invoices covering shipment of the filters/blood tubing sets were dated Dec., 1998 through 2000. No earlier invoices were observed covering the period from study initiation in mid-1996 to late 1998. In addition, per invoices, the filters received by Dr. Lentz were 4A. No documentation was observed of FDA notification/approval of the filter change. See records, **EXHIBIT #14.**

16. No documentation was observed of IRB review/approval of any "educational material" that was provided to the patients/prospective subjects or Dr. Lentz' web site that described his research activities. It was observed in patient records that Dr. Lentz and his staff provided the patients and their family members information about the studies/treatment.

II. MELANOMA STUDY (b) (4)

A. Protocol Deviations

1. Subjects received concurrent chemotherapy and/or radiation. These therapies were not reported in the CRF's. For example, Subject (b) (7)(C) was being apheresed from 6/18/97 through 8/15/97; yet received "a course of palliative irradiation" from 8/6-20/97. Subject (b) (7)(C) also participated in the "Biomodulation" study 1/26/99. (He received 14 treatments from Jan. 26 through Feb. 12, 1999.) He again signed the "Biomodulation" consent 6/8/99. He received 10 treatments from June 8-21, 1999. This subject also received radiation treatments 6/21/99 - 7/9/99. See records, **EXHIBIT #36**, and case report form, **EXHIBIT #37.**

-Subject (b) (7)(C) was initially apheresed 10/16/97-11/7/97 (17 procedures). He was receiving concurrent chemotherapy. He received 19 additional procedures 4/7/98 through 5/1/98. (See records, **EXHIBIT #46** and case report form, **EXHIBIT #47.**)

-Subject (b) (7)(C) was initially apheresed 8/25/98- 9/15/98 (15 procedures). She also received concurrent chemotherapy during the apheresis procedures. This is true for the nine procedures she received 12/1-14/98; the 8 procedures of 2/9-18/99, and the nine procedures of 10/19-29/99. She signed the "Biomodulation" study consent 10/18/99 and 1/18/00. **(EXHIBIT #56)**

-Subject (b) (7)(C) received (b) (4) during his initial procedures of 10/21/97 - 11/7/97. He participated in the "Biomodulation" study, and he signed that consent 10/11/99. **(EXHIBITS #54, 55)**

2. Subject (b) (7)(C) began apheresis less than 21 days post Interferon **(EXHIBITS #34, 35)**, as did Subjects (b) (7)(C) **(EXHIBITS #32, 33)** and (b) (7)(C) **(EXHIBITS #38, 39)**.

3. Subject (b) (7)(C) was enrolled with a WBC of (b) (4) per protocol should be greater than (b) (4), **EXHIBITS #32, 33**.

4. Subject (b) (7)(C) was enrolled with a lesion in a site that had previously received radiation (pelvis), **EXHIBITS #50, 51**. This was also seen for Subject (b) (7)(C) who had new lesions in the axilla where he had previously received radiation therapy, **EXHIBITS #52, 53**.

5. Subject (b) (7)(C) only received 4 apheresis treatments, **EXHIBITS #40, 41**.

6. Subject (b) (7)(C) who was from outside of the U.S., did not have any documentation of scans done here (PI's site) pre or post treatment. The patient arrived with

records. His file contained no additional scans. See patient records, **EXHIBIT #57**, and case report form, **EXHIBIT #58.**

7. Subject (b)(7)(C) was enrolled without having failed any previous therapies such as (b)(4) **EXHIBITS #42, 43)**. This was seen for Subject (b)(7)(C) also **(EXHIBITS #57, 58).**

B. Consent Deviations

1. On 6/13/96 FDA approved the inclusion of two subjects that failed to meet study inclusion provided that the PI amend the consent and obtain IRB approval of the amended consent. No documentation was observed of IRB review/approval of an amended consent. Moreover, the consent submitted to FDA and signed by Subject "JMS" and dated 6/12/96 entitled (b)(4) (b)(4) with a revision date of 5/15/96 was not observed in the subject's file. The signed consent in the subject's medical file was the "Metastatic Melanoma" consent with the words "Metastatic Melanoma (b)(4) marked through and "Adenocarcinoma" written in above. This consent signature page does not bear the revision date of 5/15/96. See **EXHIBIT #30**.

2. No signed informed consent was observed in the files for Subject (b)(7)(C) who began treatment 12/18/96; and Subject (b)(7)(C) (who flew in from (b)(7)(C). His initial procedure was 12/2/97.

   -No signed informed consents were observed for Subject (b)(7)(C) who received apheresis treatments 10/21/97 -11/7/97; and fifteen procedures beginning 4/6/98. He did not sign the melanoma study consent until 6/5/98 for procedures that began at that time.

3. The PI signed the informed consent 9/15/97—a day prior to the date the subject (b)(7)(C) signed on 9/16/97 **(EXHIBIT #48)**. Moreover, the port placement was on 9/15/97—prior to the subject's consent.

C. Reporting Discrepancies

1. According to the final report submitted to the IRB dated 12/9/98, this site enrolled a total of (b)(4) subjects—(b)(4) Per roster generated during the inspection, however, (b)(4) females were enrolled ((b)(7)(C) and (b)(7)(C)), **EXHIBIT #21**. It appears that patient (b)(7)(C) was included in this "final report"; yet Subject (b)(7)(C) was not. In addition, there is no mention in this report of the two "humanitarian exemptions".

2. As noted earlier, not all adverse events were reported to FDA/the IRB. Subject (b)(7)(C) was noted to have experienced a seizure while being apheresed; however no documentation was observed that this event was reported to the IRB **(EXHIBITS #46, 47)**.

3. No documentation was observed of the PI's notification to FDA or the IRB of his elimination of co-investigators. When the study was initially submitted to and

reviewed by the IRB in 1996, three co-investigators were identified. Lentz at that time was employed in the same group practice as the three co-investigators. When the PI formed his own practice 8/1/97, the three co-investigators were no longer a part of the study. His submission to the IRB dated 8/8/97 includes a revised protocol that still lists the three co-investigators. His 8/29/97 progress report to the IRB identifies two "Associate Investigators". See related EIR of the IRB.

4. Subjects received multiple treatments/longer courses that were not reported to FDA and/or IRB. For example, Subject (b)(7)(C) initial aphersis course of 12 treatments was from 1/27/97 - 2/21/97. The subject returned for an additional "course" from 6/18/97 through 8/15/97—31 procedures. From his study entry to 8/15/97 he was treated 43 times. He again signed the melanoma study consent 11/17/98 (treated 20 times from 11/18/98 - 12/18/98) and signed a longer consent version 6/8/99. See **EXHIBITS #36, 37**. It was discovered later in the inspection that the patient was also treated with the column **(EXHIBIT #9)**.

   -Subject (b)(7)(C) received 12 apheresis procedures 3/7/97 - 4/7/97 and an additional 23 from 6/19/97- 8/1/97 **(EXHIBITS #38, 39)**.

5. No documentation was observed of the submission to the IRB or the IRB's review/approval of enrollment of the two patients that did not meet protocol inclusion.

6. The PI failed to submit to the IRB progress reports at the required intervals, thus allowing IRB approval to expire. For example, the study was initially approved 2/6/96 for six months. Progress report/request for renewal was not submitted until 8/26/96. Re-approval for another year was not granted until 10/2/96. The next progress report was not submitted until 8/29/97, with re-approval for another year granted 11/4/97. Final report was submitted to the Board 12/9/98. See related EIR of the IRB.

III. BREAST CANCER STUDY (b) (4)

A. Protocol Deviations

1. Files for (b) (4) enrolled subjects lacked documentation of biopsy-proven diagnosis of "infiltrating ductal breast cancer" as per protocol inclusion eligibility criteria. These are Subjects (b)(7)(C) **(EXHIBIT #65)**; (b)(7)(C) **(EXHIBIT #61)**; (b)(7)(C) **(EXHIBIT #60)**; (b)(7)(C) **(EXHIBIT #62)**;

2. At least (b)(4) Subjects, (b)(7)(C) **EXHIBIT #61**; (b)(7)(C) **-EXHIBIT #62**; (b)(7)(C) **-EXHIBIT #65**; (b)(7)(C) **EXHIBIT #60**; and (b)(7)(C) **EXHIBIT #63**, of the (b)(4) reported subjects enrolled also received chemotherapy and/or other therapies (such as (b) (4) concurrent with the apheresis procedures. These other therapies were not reported to FDA.

   Subject (b)(7)(C) signed the "Unblocking" consent 11/1/99. Her initial procedure was 11/2/99. She received (b) (4) during her first procedure ("Biomodulation Orders").

Subject (b)(7)(C) was participating in a concurrent Thalidomide study of Lentz'.

Subject (b)(7)(C) received biomodulation/chemotherapy during apheresis that included (b)(4) She was receiving (b)(4) at study entry and during apheresis.

Subject (b)(7)(C) signed the "Unblocking" consent 10/27/99. During her first apheresis she receive (b)(4)

Subject (b)(7)(C) received (b)(4) during her apheresis treatments.

3. Subject (b)(7)(C) was enrolled even though she was ineligible as per protocol (b)(4) (b)(4) in sites of previous radiation therapy, **EXHIBIT #62**). Subject (b)(7)(C) was ineligible as per protocol (b)(4), **EXHIBIT #63**.

B. Consent Deviations

1. As stated earlier, none of the (b)(4) enrolled subjects signed the consent as per the IDE. Subject (b)(7)(C) signed the "Unblocking" consent 11/1/99 and a different (unapproved) metastatic breast cancer consent 1/24/00, **EXHIBIT #61**. Subject (b)(7)(C) signed this same unapproved consent 2/17/98, **EXHIBIT #64**. Subject (b)(7)(C) signed that consent 2/9/98, **EXHIBIT #62**; as did "Subject (b)(7)(C) on 4/20/98, **EXHIBIT #63**.

   -Subject (b)(7)(C) signed the "Unblocking" consent 11/1/99 and 5/22/00; and the "Biomodulation" consent 3/20/00, **EXHIBIT #65**.

   -Subject (b)(7)(C) signed the "Unblocking" consent 10/27/99, **EXHIBIT #60**.

C. Reporting Discrepancies

1. Subjects received multiple procedures/courses that were not reported to FDA. For example, Subject (b)(7)(C) received 15 treatments during her first cycle beginning 11/2/99. She received a second cycle consisting of 15 procedures from 1/25/00 – 2/15/00, **EXHIBIT #61**.

   -Subject (b)(7)(C) completed 17 procedures during cycle #1 (2/17/98-3/11/98) and 9 procedures during cycle #2 (4/22/98 - 5/4/98), **EXHIBIT #64**.

   -Subject (b)(7)(C) received thirteen procedures during her first cycle 2/10-26/98; eight during her second cycle 3/24/98- 4/3/98; and one procedure during her third cycle beginning 5/5/98. Ten minutes into the procedure on 5/5/98, the patient was unresponsive and "appeared to be seizing". CPR was started but the patient arrested. Report to FDA did not indicate the patient arrested during the procedure. Since this study was not reviewed by an IRB, the death was not reported to an IRB. See patient records, **EXHIBIT #62**.

   -Subject (b)(7)(C) received 15 treatments during cycle #1 (11/2-22/99); 5 treatments in March, 2000; 5 treatments in May, 2000, **EXHIBIT #65**.

-Subject (b)(7)(C) received 15 procedures 4/21/98 - 5/15/98; and 10 procedures beginning 6/30/98, **EXHIBIT #63.**

III. COLORECTAL CANCER STUDY (b) (4)

A. Protocol Deviations

1. All (b) (4) subjects received concurrent chemotherapy with their apheresis procedures. The concurrent therapies were not reported to FDA. See patient records, **EXHIBITS #69-72.**

2. Of the (b) (4) reported subjects enrolled in this study, Subject (b)(7)(C) began apheresis 1/20/98; yet had received radiation through 1/7/98—not a minimum of 21 days as per protocol, **EXHIBIT #71.**

B. Consent Deviations

1. As stated earlier, none of the (b) (4) enrolled subjects signed a consent to participate in the IDE study entitled, (b) (4) (b) (4)

-When subject (b)(7)(C), was enrolled in this study, he signed a consent 1/20/98 to participate in the "Immune Unblocking" study. His "vas cath" was placed 1/19/98--prior to the consent. He signed a second "Unblocking" consent 3/9/98 for his second cycle of apheresis, **EXHIBIT #71.**

-Subject (b)(7)(C) signed a consent for a (b) (4) study 2/2/99 and completed 15 procedures. He completed an additional 9 procedures in March, 1999 after signing the "Biomodulation" study consent and the "Metastatic Cancer" study consent 3/16/99. He signed the "Unblocking" study consent 7/7/99 and completed 15 additional procedures. On 10/4/99 he signed the "Biomodulation" study consent and completed 18 additional apheresis procedures, **EXHIBIT #70.**

-Subject (b)(7)(C) signed the "Unblocking" study consent 1/6/98. He completed 15 procedures, **EXHIBIT #72.**

-Subject (b)(7)(C) signed the "Unblocking" study consent 3/16/99; although her vas cath was placed 3/15/99—prior to her consent. She completed 15 procedures by 4/99. She signed the "Biomodulation" study consent 5/4/99. She completed 13 procedures. She signed the "Metastatic Cancer" study consent 7/19/99 and completed 10 procedures. She again signed the "Metastatic Cancer" consent 10/11/99. As her ninth procedure on 10/26/99 was finishing, she became unresponsive and expired in the emergency room. As stated earlier, this death was not reported to FDA nor was it reported to an IRB, as the study had not been submitted to an IRB for review. See patient records, **EXHIBIT #69.**

The multiple courses of treatments were not reported to FDA.

DRUG STUDIES

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EI
3/5/01- 5/10/01
PSS

1. The PI conducted investigational drug studies without documentation of FDA and/or IRB approval. Examples include:

(b) (4)

(b) (4) There is no documentation that the drug manufacturer (b) (4) who provided the drug for another (b) (4) "Investigator IND study" that Lentz was conducting) was aware of this "new protocol" and approved the use of the test article in the new study. Per (b) (4) 4/13/98 Investigator IND Letter of Agreement, the PI signed and agreed "to use any drug provided by (b) (4) under this Investigator IND exclusively as proposed in the Investigator IND protocol" submitted to (b) (4) and FDA. Study drug, therefore, was to be used for the IND protocol only. See **EXHIBIT #86** for a copy of the "new protocol". **EXHIBIT #79** is a list of patients receiving (b) (4) It is supposed to be for IND#55, 418; yet several patients were noted to be in the "new protocol". **EXHIBIT #87** is a dosing record for the "new protocol" for year 2000 and records for the "old" protocol, (b) (4) **EXHIBITS #80, 88** are examples of "accountability records". See related EIR of the IRB for a copy of Lentz' agreement with (b) (4) the manufacturer/supplier of (b) (4)

-Treatment (b) (4) No documentation was observed of IRB approval of Dr. Lentz as sponsor and Principal Investigator. (b) (4) approved (b) (7)(C) (b) (7)(C) to be PI and Dr. Lentz to be sponsor. FDA, however, stated that it was not appropriate for the patient's family member to be the PI/treating physician. Dr. Lentz then agreed to be the PI; however, no Board approval of this change was observed. Dr. Lentz was not the treating physician - (b) (7)(C) was. The test article was shipped directly from (b) (4) to (b) (7)(C) yet no signed 1572 identifying (b) (7)(C) as subinvestigator was observed nor was documentation of (b) (7)(C) approval by an IRB to be a sub-investigator for Dr. Lentz as PI. See **EXHIBIT #75.**

2. Dr. Lentz failed to assure that the trials were conducted per the protocols as submitted to FDA and per the regulations. The studies include: (b) (4)

(b) (4) (b) (4) (under (b) (4) and the above Treatment (b) (4) (b) (4) as indicated below, Dr. Lentz "enrolled" patients that he never saw. He faxed a copy of the consent to a patient or the patient's referring physician. Study drug was then shipped directly to the patient. The patient was never examined/followed by Dr. Lentz or his staff. Phone calls were made to the patient or the referring physician. See **EXHIBIT #77** for Lentz' copy of the "protocol". Also see related EIR of the (b) (4) (b) (7)(E) for Lentz' protocol submission to that Board. The Board tabled the review in April, 1998 pending further revisions and disapproved the project in Oct., 1998. Dr. Lentz submitted it to (b) (4) who approved the project in June, 1998.

3. No monitoring of the (b) (4) studies has been conducted. Inadequate recordkeeping was observed of test article accountability. No documentation was observed of disposition of test article that was returned by patients/patients' families. See **EXHIBIT #125** for examples of notations regarding returned drug due to patient death, and **EXHIBIT #118** that noted five bottles had been

returned for Patient (b) (7)(C) after her death. Twenty-one full bottles were returned for Patient (b) (7)(C), **EXHIBIT #91**. Further, no study case report forms were observed.

4. No documentation was observed that Dr. Lentz informed (b) (4) in his initial submission to (b) (4) that the study under (b) (4) had been disapproved by his local IRB. (b) (7)(E) for the local Board's disapproval of the project.

5. Dr. Lentz failed to maintain all submissions to and correspondence with (b) (4) It could not be determined what Dr. Lentz submitted to the Board for initial review.

6. Dr. Lentz failed to report to FDA all adverse events. See CDER records for Dr. Lentz' annual report. Examples of AE's observed in the patients' records include:

   - Patient (b) (7)(C) was "wired" and unable to fall asleep **(EXHIBIT #92)**

   - Patient (b) (7)(C) fell down, had been dizzy and feeling unsteady, memory seemed worse **(EXHIBIT #94)**

   - Patient (b) (7)(C) developed shortness of breath after she "re-attempted" (b) (4) and was unable to tolerate it **(EXHIBIT #95)**

   - Patient (b) (7)(C) had extreme anxiety and abdominal distress, intolerable lethargy and depression. All symptoms "abated" when he stopped taking Thalidomide **(EXHIBIT #102)**

   - Patient (b) (7)(C) complained of upset stomach, swelling in legs and spleen area. She was advised to stop (b) (4) for one week until she could be evaluated. **(EXHIBIT #109)**

   - Patient (b) (7)(C) complained of peripheral neuropathy and of feeling mentally foggy **(EXHIBIT #113)**

   - Patient (b) (7)(C) experienced early daytime somnolence and lethargy and shakiness all day **(EXHIBIT #124)**

7. "Subjects" that Dr. Lentz never saw were enrolled in the (b) (4) studies. Consents were faxed to the patients' physicians. The patients signed the consents that were then faxed back to Dr. Lentz. These patients were never seen in Lentz' clinic. The patients' local physicians were never identified/approved as subinvestigators. Examples include:

   -Patient (b) (7)(C) **EXHIBIT #91**

   -Patient (b) (7)(C) was enrolled without being seen by Dr. Lentz. Five months after start of the study, the patient came in for an apheresis consult. **(EXHIBIT #99)**

   -Patient (b) (7)(C) **EXHIBIT #101**

-**EXHIBIT #103** reports the drug was shipped to a patient out of the country

-Patient (b) (7)(C) was in Moscow and drug was shipped to him, **EXHIBIT #104**

-Patient (b) (7)(C) was faxed the consent 4/15/99 and shipped the drug. She was not seen in Lentz' clinic until 5 months later, **EXHIBIT #105**.

-Patient (b) (7)(C), **EXHIBIT #109**

-Patient (b) (7)(C) **EXHIBIT #120**

8. "Subjects" signed consents for the (b) (4) study that were not the IRB-approved version. At least four subjects signed consents that referenced (b) (4) (b) (4) (b) (7)(C) and his phone number. His Board disapproved this study. Patient (b) (7)(C) (who has prostate cancer) signed a consent 6/21/00. His consent references (b) (7)(C) **EXHIBIT #124**. Two patients signed consents with the title, (b) (4). Patient (b) (7)(C) signed it 10/9/98 **(EXHIBIT #121)**; and Patient (b) (7)(C) signed it 8/3/98 **(EXHIBIT #122)**. The consent references (b) (7)(C) as the contact regarding subjects' rights or questions about the research.

One patient, (b) (7)(C), signed a consent 6/17/98 with the title (b) (4) (b) (4). The consent also references (b) (7)(C) **(EXHIBIT #123)**.

The above four consents state that (b) (4) s approved in the U.S. It did not receive FDA approval (for one use, leprosy) until 7/98. The (b) (4) consents were submitted to the two Boards prior to July, 1998 when the drug received FDA approval. The local Board approved two single-patient IND studies (b) (4) for Patient (b) (7)(C), and (b) (4) for Patient (b) (7)(C). Western IRB approved the study/consent 6/11/98 for (b) (4) (the study the local Board disapproved).

I. Failure to Follow the Protocol

1. Per protocol and informed consent for the (b) (4) study under (b) (4) the subjects were to be "seen by the study doctor every two weeks for twelve months". As stated earlier, some patients were never seen in Lentz' clinic or by Dr. Lentz. The other patients were not seen on a biweekly basis as per protocol. Examples of patients that were not seen biweekly include:

-Patient (b) (7)(C) began dosing 3/8/00. There was no further contact with the patient. Was considered lost to follow-up as of 5/9/00. **(EXHIBIT #117)**

-Patient (b) (7)(C) was dispensed study drug 2/11/00. The patient was not seen again. She died 8/8/00. **(EXHIBIT #116)**

-Patient (b) (7)(C) was dispensed study drug 11/9/00. He has not been seen since. **(EXHIBIT #112)**

-Patient (b) (7)(C) was dispensed study drug 7/2/99. He was not seen after completing apheresis on 7/17/99 **(EXHIBIT #108)**

-Patient (b) (7)(C) was dispensed study drug 9/13/00 and was to "call monthly". Patient has not been seen since. **(EXHIBIT #102)**

-Patient (b) (7)(C) was dispensed study drug 8/10/00 and was not seen after that date. The patient died 10/3/00. **(EXHIBIT #98)**

-Patient (b) (7)(C) was dispensed study drug 3/23/99. She was not seen for study follow-up—only phone calls. There was no patient contact since 1/14/00. The patient died in May, 2000. **(EXHIBIT #97)**

-Patient (b) (7)(C) was dispensed study drug 12/1/00. She was not seen after that time. Per phone call on 2/15/01, (b) (7)(C) learned of her AE's and inability to tolerate Thalidomide. He discontinued her from the study. **(EXHIBIT #95)**

-Patient (b) (7)(C) was not seen from 9/21/99 through mid-January, 2000, and was not seen after 2/11/00. The patient died 11/6/00. **(EXHIBIT #94)**

-Patient (b) (7)(C) was dispensed study drug 11/9/00. She has not been seen since. **(EXHIBIT # 89)**.

2. Documentation was not observed that all female subjects of childbearing potential had pregnancy tests performed at the protocol stated intervals—pre (b) (4) initiation, 9 to 10 days after receiving the initial dose, and once a month (if menstrual cycle is regular—more frequently if menstrual cycle is irregular).

Although not listed on the FD483, other consent deviations were observed. Examples include:

-Dr. Lentz signed the consent 6/30/99—BEFORE Patien (b) (7)(C) signed it 7/1/99, **EXHIBIT #96.**

-No physician/investigator signed the consent of Patient (b) (7)(C), **EXHIBIT #120**; or the one for Patient (b) (7)(C) **EXHIBIT #121**; or the one for Patient (b) (7)(C), **EXHIBIT #114**. Dr. Lentz did not sign the consent for Patient (b) (7)(C)—no investigator signed it. This consent was faxed to the patient's physician. **EXHIBIT #99.**

-Dr. Lentz did not sign Patient (b) (7)(C) consent. (b) (7)(C) signed for him, **EXHIBIT #100**. This is true for Patien (b) (7)(C) **EXHIBIT #106**; and Patient (b) (7)(C) **EXHIBIT #107**; Patient (b) (7)(C) **EXHIBIT #110**; Patient (b) (7)(C) **EXHIBIT #124**; Patient (b) (7)(C) **EXHIBIT #112**; Patien (b) (7)(C) **EXHIBIT #102**; Patient (b) (7)(C), **EXHIBIT #95**; and Patient (b) (7)(C), **EXHIBIT #89**.

-Dr. Lentz signed the consent day/days after the patient/witness had signed. Examples include: Patient (b) (7)(C) **EXHIBIT #117**; and Patient (b) (7)(C) **EXHIBIT #115**.

LENTZ, MEREDITH RIGDON, M.D.
397 Wallace Rd, Suite 314
Nashville, TN 37211

EI
3/5/01- 5/10/01
PSS

DISCUSSION WITH MANAGEMENT

At the conclusion of the inspection, FD483, Inspectional Observations, was issued to Meredith Rigdon Lentz, M.D., Sponsor and Principal Investigator. Also present during this discussion was (b) (7)(C) who was provided a photocopy of the 483 to read and follow along. I stated that the items were my opinion and were not meant to be all-inclusive. I said that my report and the exhibits (photocopies of records) would be submitted to the Centers for review and evaluation. I told Dr. Lentz that it was not required that I read each item. It was his choice if we discussed the items. He said he would like to look over them and discuss as needed.

To Item #1, Dr. Lentz stated that he has NOT initiated the column study. He said he is waiting for FDA approval to start the study. Dr. Lentz said that I needed to understand that the (b) (4) column treated patients are NOT a part of a study—this was done OFF-STUDY. For the second study listed (the unblocking one), Dr. Lentz said that this study is under the three IDE studies—with a basic consent and the addition of the words: breast, colon, or melanoma. The third study (Biomodulation) Dr. Lentz insists that he never did. He said he wrote the protocol but then never submitted it. He asked how I found it. I said that signed consents were observed in patient files. He said the study was never instituted. The patients must have signed the wrong consents.

As far as the column treatments, Dr. Lentz insisted that he only treated eight subjects.

To Item #2, Dr. Lentz stated that he originally submitted the "Metastatic Cancer" study to the IRB. The study was later amended, per FDA, to be a colorectal cancer study and a breast cancer study. Dr. Lentz and (b) (7)(C) both said that some of the initial subjects went through the (b) (4) I reminded Dr. Lentz that I had asked him this question at the beginning of the inspection and he told me that NONE of the subjects had been registered with (b) (4)

To Item #3, Dr. Lentz asked me what monitoring was. I explained. He said that he would have "monitored the data", as he was the one that generated it.

To Item #4, (b) (7)(C) stated that she remembers sending FDA the autopsy report for this subject. I said I saw the autopsy report for the breast cancer subject but did not see that the report was submitted for the colon cancer subject. I said I saw nothing in the file. She said she might have filed her fax elsewhere. She will check. Dr. Lentz added that the patient's death was related to pulmonary embolism—NOT related to the protocol.

To Item #6, Lentz said that they have "had things that the IRB did not receive that we did send".

To Item #7, Lentz said that the IDE subjects did NOT participate in other studies. They must have signed the wrong consents.

To Item #8, Dr. Lentz emphasized that he did not start the study (Melanoma) until FDA approved it. I said he should not submit studies to the Board that have not

received FDA approval. He said they could treat "other patients" under the Metastatic cancer protocol since the IRB had approved that protocol.

To Item #9, Dr. Lentz said that he informed the Board that FDA wanted the Metastatic Cancer study split into two studies: breast and colorectal—and that the Board had no problem with that—that is was "not an issue". He said that breast and colorectal cancers are both metastatic cancers and are applicable under the Metastatic Cancer protocol.

To Item #10, Dr. Lentz stated that (b) (4) had "kicked" them for that too. He said they never suggested doing CRF's for the other two studies (breast and colon). He said that he did not want to spend the money for CRF's for the other two studies since they were going to close out the studies. He said the Center never told him he had to have CRF's. He said he did not have them for his studies in (b) (4) and he was not written up for it when he was inspected. In fact, he said he was commended for his work by that FDA Investigator. Lentz said that he did not think CRF's were necessary. Now, he's been educated. Lentz said that (b) (4) was only doing a spot check- (b) (4) was getting them started. "They figured we would carry on", according to Lentz.

To Item #11, Lentz said that they "screwed up" and enrolled too many breast patients.

As far as consents, Lentz stated that patients signed the wrong ones. He said that he has had this discussion with his staff before. He said he did make the consent changes as the Center requested. I said that he might have but the patients never signed the correct consents. And, there is no documentation that the IRB ever approved the consents.

To Item #16, Dr. Lentz said that the only information given the patients were copies of consents, protocols, and published articles. I said they still should have asked their IRB if the Board needed to review the articles. He said his Web site only went up a month ago—and it is a general information site for doctors. He said he did not have a Web site prior to this one. The site is designed to be an authoritarian source for doctors—and is NOT for patient recruitment.

Dr. Lentz emphasized that not all apheresis treatments are protocol treatments. If someone has been treated in the past and comes back and receives radiation and apheresis, for example, that is not a protocol deviation. He said he could continue to treat the patient later off-study.

Dr. Lentz said that he thinks their record keeping has improved dramatically since (b) (7)(C) returned to help out. That is why she is here; why Lentz hired her. He said his record keeping was not this detailed in the 80's.

For the drug studies, (b) (7)(C) asked if those studies were to be conducted like IDE studies. I stated yes. She asked Dr. Lentz if she should be keeping those records instead of (b) (7)(C) To Item #4 under "Drug Studies", Dr. Lentz stated that he never received a disapproval from the local IRB as he never submitted a general (b) (4) study to the local IRB.

Lentz stated that Accureg looked over his IRB correspondence and told him that the local IRB is "not helping" and recommended "a professional one like (b) (4). Again, he said that patients signed the wrong consents. (b) (7)(C) asked if the (b) (4) study (s) were closed? Dr. Lentz responded that they "are going to close it after this—too much liability". He looked at the 483 and stated, "That pretty well ends it". He said that if he were (b) (7)(C) at the (b) (4) he (Lentz) would not approve him (Lentz) to do another study. Dr. Lentz asked about FDA's options following the inspection. I explained the Centers would review my report. I explained the options. Dr. Lentz said that he would like to respond in writing to the 483 in order to clarify some things. He did not think it was correct to state he had initiated studies such as the column study when he has not. Those treatments were not done in a study, but were done off-study. The protocol was not "enacted".

Lentz said that he cannot ethically turn down a patient when he has a potential cure. He said he is not looking for patients; they come to him. He said that he cannot ethically continue doing apheresis (the investigational treatment as in the IDE and used for his "off-study patients") when the column treatment is so much safer—it's a closed system and does not require (b) (7)(C) blood products that carry the risk of HIV, etc. He asked me what is he supposed to do? I told him that was between him and the Center. He asked me if I thought the deviations were serious. I said yes—especially the fact that the patients were not being properly informed.

EXHIBITS

Device Studies:

1. C.V. Of Dr. Lentz
2. Case Report Manuscript (of column)
3. Patient (b) (7)(C) (column treatments)
4. Patient (column treatments)
5. Patient column treatments)
6. Patient column treatments)
7. Patient (column treatments)
8. Patient column treatments)
9. Patient column treatments)
10. Patient (column treatments)
11. Abstract, (b) (4)
12. Abstract, (b) (4)

LENTZ, MEREDITH RIGDON, M.D.
397 Wallace Rd, Suite 314
Nashville, TN 37211

EI
3/5/01- 5/10/01
PSS

13. Abstract, (b) (4)

14. Device shipping/receiving records

15. (b) (4) protocol dated Nov, 1997

16. "Draft copy" of Protocol, (b) (4) (b) (4) dated Nov., 1997 (found in Patient (b) (7)(C) file)

17. 2/6/96 approval notice from IRB of study, (b) (4) (b) (4)

18. 11/4/97 IRB notice of re-approval of MISC 16 study, NHN-96-005

19. Pre-signed blank apheresis flow sheet

20. 5/3/99 letter to CDRH from (b) (4) stating Dr. Lentz has not been affiliated with th (b) (4) ince 8/1/97

21. "Protocol Patients" (subject rosters generated during the inspection for the 3 IDE studies)

22. Records for Patient (b) (7)(C) (not on roster) who has parotid cancer & signed (b) (4) consent

23. Records for Patient (b) (7)(C) (not on roster)

24. Case Report Form for Patient (b) (7)(C)

25. Records for Patient (b) (7)(C) (not on roster)

26. Records for Patient (b) (7)(C)

27. CRF for (b) (7)(C)

28. Earlier version of melanoma protocol, 5/15/96 version

29. 7/26/96 letter to CDRH (update of 2 exemptions, (b) (7)(C)

30. Patient (b) (7)(C) records

31. CRF for (b) (7)(C)

32. Patient (b) (7)(C) records

33. CRF for (b) (7)(C)

34. Patient (b) (7)(C) records

LENTZ, MEREDITH RIGDON, M.D.
397 Wallace Rd, Suite 314
Nashville, TN 37211

EI
3/5/01- 5/10/01
PSS

35. CRF for (b) (7)(C)
36. Patient (b) (7)(C) records
37. CRF for (b) (7)(C)
38. Records for (b) (7)(C)
39. CRF for (b) (7)(C)
40. Records for (b) (7)(C)
41. CRF for (b) (7)(C)
42. Records for (b) (7)(C)
43. CRF for (b) (7)(C)
44. Records for (b) (7)(C)
45. CRF for (b) (7)(C)
46. Records for (b) (7)(C)
47. CRF for (b) (7)(C)
48. Records for (b) (7)(C)
49. CRF for (b) (7)(C)
50. Records for (b) (7)(C)
51. CRF for (b) (7)(C)
52. Records for (b) (7)(C)
53. CRF for (b) (7)(C)
54. Records for (b) (7)(C)
55. CRF for (b) (7)(C)
56. Records for (b) (7)(C)
57. Records for (b) (7)(C)
58. CRF for (b) (7)(C)
59. 11/8/99 response to CDRH & revised consent for IDE study--metastatic breast cancer

LENTZ, MEREDITH RIGDON, M.D.
397 Wallace Rd, Suite 314
Nashville, TN 37211

EI
3/5/01- 5/10/01
PSS

60. Subject (b) (7)(C) records
61. Subject records
62. Subject records
63. Subject records
64. Subject records
65. Subject records
66. Metastatic Colorectal Cancer protocol dated Aug, 1997
67. 3/1/98 response to CDRH & consent version March, 1998
68. 1/23/01 notice to IRB that G970290 is closed (Metastatic Colorectal Cancer study)
69. Subject (b) (7)(C) records
70. Subject records
71. Subject records
72. Subject records

Drug Studies:

73. Single Patient (b) (7)(C) (b) (7)(C) records
74. Single Patient (b) (7)(C) records
75. Single Patient (b) (7)(C) records
76. (b) (4) 6/11/98 approval of Thalidomide study, (b) (4) approved consent
77. (b) (4) protocol
78. (b) (4) patient list
79. (b) (4) usage (b) (4)
80. (b) (4) Medication Log
81. 6/7/99 IRB notice
82. 5/22/00 Continuing Review Report

83. 11/14/00 AE reports

84. 2/16/01 Continuing Review Report

85. 4/11/01 Continuing Review Report w/note re. current FDA inspection

86. (b) (4) ." protocol & informed consent

87. (b) (4) patient log, accountability records

88. Drug accountability records

89. Patient (b) (7)(C) records

90. Patient " record

91. Patient ' records

92. Patient ' record

93. Patient 1" record

94. Patient records

95. Patient ' records

96. Patient ' records

97. Patient ' records

98. Patient ' records

99. Patient records

100. Patient (b) (7)(C) records

101. Patient records

102. Patient records

103. 5/99 faxed records

104. Patient (b) (7)(C) records

105. Patient records

106. Patient consent

107. Patient consent

LENTZ, MEREDITH RIGDON, M.D.
397 Wallace Rd, Suite 314
Nashville, TN 37211

EI
3/5/01- 5/10/01
PSS

108. Patient (b)(7)(C) records
109. Patient records
110. Patient records
111. Patient records
112. Patient records
113. Patient record
114. Patient records
115. Patient records including "new Thalidomide study" consent
116. Patient records
117. Patient records
118. Patient records
119. Patient record ("new" protocol)
120. Patient records (new" protocol)
121. Patient (b)(7)(C), records
122. Patient consent
123. Patient consent for treatment of renal cell carcinoma
124. Patient records
125. Accountability records/returns/deaths

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