DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administratic
Rockville MD 20857

APR 15 1999

CERTIFIED MAIL
RETURN RECEIPT REQUESTED

NOTICE OF OPPORTUNITY FOR A HEARING

[redacted]

Dear Mr. [redacted]

The Center for Drug Evaluation and Research (the Center) of the United States Food and Drug Administration (FDA) has information indicating that your client, Layne O. Gentry, M.D., repeatedly and/or deliberately violated federal regulations as investigator of record in clinical trials with investigational new drugs. Moreover, Dr. Gentry caused the submission of false information to the sponsor in required reports for studies of investigational new drugs that are subject to Section 505 of the Federal Food, Drug, and Cosmetic Act. These violations provide the basis for withdrawal of his eligibility to receive investigational new drugs as a clinical investigator.

The Center's findings are based on information obtained during FDA's inspection of Dr. Gentry's conduct as the investigator of record for the following studies: Protocols [redacted] and [redacted] of the investigational new drug Elequin (levofloxacin) sponsored by R. W. Johnson Pharmaceutical Research Institute.

Pursuant to Section 312.70 of Title 21, Code of Federal Regulations (CFR), the Center informed Dr. Gentry, by letter titled "Notice of Initiation of Disqualification Proceedings and Opportunity to Explain" (NIDPOE) dated March 23, 1998, of the specific matters complained of and offered him an opportunity to respond to them in writing or at an informal conference. The NIDPOE also offered him the option of entering into a consent agreement with the agency, thereby terminating any administrative proceeding against him.

In response to the NIDPOE, Dr. Gentry initially expressed interest in entering into a consent agreement with FDA. Subsequently, however, he decided not to enter into an agreement with FDA and instead chose to offer his explanations for the matters complained of in the NIDPOE at an informal conference with the Center.

On June 17, 1998, during the informal conference with the Center, you and [ ] as attorneys representing Dr. Gentry, offered explanations to the matters complained of in the NIDPOE. The Center reviewed these explanations and informed Dr. Gentry, by letter dated November 3, 1998, that the Center accepted his explanations only for the following matters:

1. Items II.A.2.a. and II.A.2.b. on pages two and three of the NIDPOE, pertaining to enrollment of subject #2208 in protocol [ ] and lack of follow-up of the elevated SGOT and SGPT for this subject.

2. Item II.B.2.f. on page four of the NIDPOE, pertaining to reporting of concomitant medications on page 13 of the case report form (CRF) for subject #1402 in protocol [ ]

The letter dated November 3, 1998, also informed Dr. Gentry that the Center did not accept his explanations for the remaining matters complained of in the NIDPOE.

Accordingly, Dr. Gentry is being offered an opportunity for a regulatory hearing pursuant to 21 CFR Parts 16 and 312, to determine whether he is entitled to receive investigational new drugs. As you are aware, Dr. Gentry has the right to be advised and represented by counsel at all times. Any regulatory hearing on this matter will be governed by the regulations in 21 CFR Part 16 and the agency's guidelines on electronic media coverage of administrative proceedings, 21 CFR Part 10, Subpart C. A listing of the specific violations follows. Applicable provisions of the CFR are cited for each violation.

I. For studies conducted in San Jose, Costa Rica.

   A. Dr. Gentry failed to prepare and maintain adequate and accurate records of all observations and other data pertinent to the investigation for each subject in clinical studies as required by federal regulations [21 CFR 312.62(b), and 312.62(c)]. For example:

1. Study [ ]

   a. The x-ray films (source documents) were not available for FDA inspection for all 60 subjects who participated in study [ ]

   b. The radiology reports were unsigned and/or undated (e.g., subjects #2609, and #2418).

2. Study [ ]

   a. There were two medication dosing records in the subjects' hospital charts with discrepant information regarding the doses of study drug administered (e.g., subjects #1903 and #1403). One medication dosing record appears to have been generated by the individuals who actually dispensed the study drug to each subject. The second medication dosing record was prepared by Dr. [ ] an individual who was identified during the inspection as a study coordinator although she carried out the responsibilities of a sub-investigator. Dr. [ ] appears to have prepared the medication dosing record for study purposes and reports that study medications were dispensed as specified in the protocol by [ ] (a study nurse).

   b. Subject #1403 - The medication label on page 15 of the CRF reports the subject's study number to be #1413.

   c. Subject #1916 - The medication label on page 15 of the CRF reports the subject's study number to be #1904.

   d. Subject #1403 - Page 7 of the CRF inaccurately reported a post therapy date of September 28, 1992. Records document this subject continued taking study medications until October 5, 1992.

   e. Subject #2117 - Page 14 of the CRF inaccurately reports the last day of this subject's study medication was May 10, 1993, but the subject's hospital medication chart and physician's notes report this subject's

last day of study medication was May 13, 1993.

f. Subject #1920 - Concomitant therapies (Furosemide and Cimetidine) are reported on the subject's hospital chart but are not reported on the CRF.

3. Study [ ]

Dr. Gentry failed to maintain a subject enrollment screening log which would have been the source record to document that approximately 150 subjects were screened as stated in his final report dated March 17, 1993, to [ ] IRB.

B. Dr. Gentry failed to obtain institutional review board (IRB) approval prior to enrolling twenty-five subjects at the Hospital Calderon Guardia into study protocols [ ] and [ ] thereby violating federal regulations pertaining to the protection of human research subjects [21 CFR 50.27, 56.103(a), 312.53(c)(1)(vii), 312.60, and 312.66]. The IRB of record, identified as the [ ] IRB in [ ] approved the conduct of studies at the Hospital Calderon Guardia on November 25, 1992. Prior to the [ ] IRB approval Dr. Gentry enrolled the following 25 study subjects:

Protocol Subject #	Enrollment date
1315	9-15-92
1403	9-24-92
1404	9-15-92
1405	10-7-92
1406	10-7-92
1407	10-8-92
1411	10-20-92
1413	10-30-92
1415	11-6-92
1417	11-17-92

Protocol Subject #	Enrollment date
1605	9-4-92
1607	9-14-92
1608	9-16-92
1611	10-1-92
1613	10-6-92
1615	10-14-92
1618	10-23-92
2202	11-6-92
2203	11-6-92
2204	11-8-92
2205	11-9-92
2209	11-16-92
2211	11-17-92
2212	11-18-92
2213	11-23-92

C. Dr. Gentry failed to maintain adequate records of the disposition of study drugs, including dates, quantity, and use by subjects [21 CFR 312.62(a), 312.62(c)]. For example:

1. Dr. Gentry did not maintain adequate records to document the shipment of study medications used in protocols [ ] and [ ] from his study site in St. Luke's Episcopal Hospital, Houston, Texas to the study sites in San Jose, Costa Rica.

2. Medication Lot #5146 (Augmentin), which was designated for subjects #1101 to #1120 (in Protocol [ ] was shipped to Dr. Gentry by the sponsor (R.W. Johnson Pharmaceuticals) on July 6, 1992. He did not enroll subjects #1101 to #1120 in Protocol [ ] at his study sites and has not provided any records to document how he used and/or disposed of medication from Lot #5146 for subjects #1101 to #1120.

D. Dr. Gentry failed to conduct study [ ] in accordance with the approved protocol [21 CFR 312.53(c)(1)(vi)(a), and 312.60]. Subject #1403 did not have the protocol required pre-study blood samples collected prior to the initiation of study treatment on September 24, 1992.

E. Dr. Gentry failed to list on the Form FDA 1572 the names of all the subinvestigators (e.g., Dr. [ ] Dr. [ ] Dr. [ ] who assisted him in the conduct of the clinical investigations [21 CFR 312.53(c)(1)(viii), and 312.60].

F. Dr. Gentry failed to personally conduct or supervise his clinical studies, which he committed to when he signed the Form FDA 1572 [21 CFR 312.53(c)(1)(vi)(c), and 312.60]. This failure caused the submission of false information in required reports to sponsors [21 CFR 312.70].

II. For protocol [ ] which Dr. Gentry conducted at St. Luke's Hospital in Houston, he failed to: (1) prepare and maintain adequate and accurate records of all observations and other data pertinent to the investigation for each subject in the clinical study [21 CFR 312.62(b), and 312.62(c)]; and (2) conduct the clinical study in accordance

with the approved protocol [21 CFR 312.53(c)(1)(vi)(a) and 312.60]. For example, Protocol [ ] Section V.F.2., required that the clinical outcome for subjects who received "non-study antimicrobials" be classified as "unable to evaluate." Dr. Gentry reclassified the clinical outcome for study subject #801, one of three subjects enrolled at the Houston site, from "unable to evaluate" to "improved."

Dr. Gentry's request for a hearing must be made, in writing, within ten (10) business days of receipt of this letter and should be directed to Dr. James F. McCormack, Coordinator, Bioresearch Monitoring Program, Office of Enforcement, Division of Compliance Policy (HFC-230), 5600 Fishers Lane, Rockville, Maryland, 20857, Telephone (301)827-0425, FAX (301)827-0482. If no response to this letter is received by that time, Dr. Gentry will be deemed to have waived any right to a regulatory hearing, and a decision in this matter will be made based on the facts available to the agency without a hearing.

A request for a hearing may not rest upon mere allegations or denials but must present specific facts showing that there is a genuine and substantial issue of fact that warrants a hearing. Pursuant to 21 CFR 16.26, a request for a hearing may be denied, in whole or in part, if the Commissioner or his delegate determines that no genuine and substantial issue of fact had been raised by the material submitted. A hearing will not be granted on issues of policy or law. Written notice of a determination of summary judgment will be provided, explaining the reasons for denial of the hearing.

If Dr. Gentry wishes to respond but does not desire a hearing, he should contact Dr. McCormack within the time period specified above and send a written response containing his reply. The letter should state that Dr. Gentry waives his right to a hearing and that he wants a decision on the matter to be based on his written response and other information available to the agency.

The agency's offer to enter into a consent agreement, attached to the NIDPOE dated March 23, 1998, remains available. Entering into a consent agreement would terminate the administrative procedures, but would not preclude the possibility of a corollary judicial proceeding.

No final decision by FDA has been made at this time on Dr. Gentry's eligibility to continue to use investigational drugs. Moreover, there will be no prejudgment of this matter if Dr. Gentry declines to enter into a consent agreement and decides instead to either request a regulatory hearing or to request that

the decision be based on information currently available to the agency.

Please inform Dr. McCormack within ten (10) days of whether Dr. Gentry wishes to request a hearing or to have this matter resolved by consent agreement or information available to the agency.

Sincerely,

Dennis E. Baker
Associate Commissioner
for Regulatory Affairs

Enclosures:
21 CFR Part 10, Subpart C
21 CFR Part 16
21 CFR Part 312.70