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DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NOTICE OF INITIATION OF DISQUALIFICATION PROCEEDINGS AND OPPORTUNITY TO EXPLAIN (NIDPOE)

CERTIFIED MAIL
RETURN RECEIPT REQUESTED

Arthur Ericsson, M.D.
6560 Fannin St., Suite 720
Houston, TX 77030

Dear Dr. Ericsson:

Between March 22 and April 18, 2007, Ms. Andrea Branche, representing the U.S. Food and Drug Administration (FDA), conducted an investigation and met with you to review your conduct of a clinical investigation (protocol [ ] entitled "Evaluation of [ ] for the therapy of autoimmune/inflammatory conditions involving the nervous system") of the investigational drug [ ] performed for [ ]

This inspection is a part of FDA's Bioresearch Monitoring Program, which includes inspections designed to evaluate the conduct of research and to ensure that the rights, safety, and welfare of the human subjects of those studies have been protected. At the conclusion of the inspection, Ms. Branche presented and discussed with you the items listed on Form FDA 483, Inspectional Observations. We have reviewed the inspection report and the documents submitted with that report.

Based on our evaluation of information obtained by the Agency, we believe that you have repeatedly or deliberately violated regulations governing the proper conduct of clinical studies involving investigational products as published under Title 21, Code of Federal Regulations (CFR), Part 312 (copy enclosed). We also note that in a Warning Letter dated November 17, 1993, FDA informed you that you violated a clinical hold for another investigational product, you failed to maintain adequate records of the disposition of the drug, and you failed to maintain adequate and accurate case histories of individuals treated with the test article [ ] It appears that you committed the same violations in your clinical investigation of [ ]

This letter provides you with written notice of the matters under complaint and initiates an administrative proceeding, described below, to determine whether you should be disqualified from receiving investigational products as set forth under 21 CFR 312.70.

A listing of the violations follows. The applicable provisions of the CFR are cited for each violation.

1. **You failed to comply with the requirements for use of an investigational new drug in a clinical investigation by administering the investigational new drug [ ] to subjects without an IND in effect. [21 CFR 312.40]**

   FDA regulations (21 CFR Part 312) contain procedures and requirements governing the use of investigational new drugs. 21 CFR 312.3(b) defines a clinical investigation as "any experiment in which a drug is administered or dispensed to, or used involving, one or more human subjects. For the purposes of this part, an experiment is any use of a drug except for the use of a marketed drug in the course of medical practice." [ ] is not approved for marketing in the U.S.A; therefore, any clinical investigation involving the use of [ ] must meet the general requirements for use of an investigational new drug in a clinical investigation. An investigational new drug may be used in a clinical investigation if the following conditions are met: the sponsor submits an IND for the drug to FDA, the IND is in effect under FDA regulations, and the sponsor complies with all applicable requirements of 21 CFR Parts 50, 56, and 312; and each participating investigator conducts his investigation in compliance with the requirements of 21 CFR Parts 50, 56, and 312. [21 CFR 312.40(a)]

   According to 21 CFR 312.40(b), an IND goes into effect thirty days after FDA receives the IND, unless FDA notifies the sponsor that the investigations described in the IND are subject to a clinical hold, or on earlier notification by FDA that the clinical investigations in the IND may begin. On December 19, 2006, [ ] submitted an IND for this product. Within thirty days of the IND submission and without receiving any notification from FDA that the clinical investigation might begin, you administered the investigational new drug to at least six subjects [ ] 1909 (January 3, 2007); [ ] 1906 (January 4, 2007); [ ] 1907 and [ ] 1912 (January 8, 2007); [ ] 1908 (January 10, 2007); and [ ] 1916 (January 15, 2007)]. Therefore, you violated 21 CFR 312.40(a) by administering the investigational new drug [ ] to subjects without an IND in effect.

2. **You violated a clinical hold by giving subjects [ ] after FDA issued an order to delay the proposed clinical investigation. [21 CFR 312.42].**

   A clinical hold is an order issued by FDA to the sponsor to delay a proposed clinical investigation or to suspend an ongoing investigation. The clinical hold order may apply to one or more of the investigations covered by an IND. When a proposed study is placed on clinical hold, subjects may not be given the investigational drug. When an ongoing study is placed on clinical hold, no new subjects may be recruited to the study and placed on the investigational drug; patients already in the study should be taken off therapy involving the investigational drug unless specifically permitted by FDA in the interest of patient safety. [21 CFR 312.42(a)]

The IND submission for the[ ]clinical investigation was placed on full clinical hold because insufficient information was submitted to allow FDA to assess risks to human subjects in the proposed study [see 21 CFR 312.42(b)(2)(i), specifically 312.42(b)(1)(iv)]. [ ]was notified of the clinical hold via telephone on January 25, 2007, and was sent a clinical hold letter on March 15, 2007. You were aware of the full clinical hold status for this investigation and the reason for the hold, as you provided the FDA investigator with a copy of the full clinical hold letter and you told the FDA investigator that[ ]notified you of the clinical hold in late January, 2007.

You violated the clinical hold order by administering[ ]to at least five subjects on multiple occasions [1907 (February 5 and 23, 2007), 1912 (January 29, 2007 and February 12, 2007), 1921 (February 27 and 28, 2007), 1924 (March 13 and 14, 2007), and 1928 (January 30, 2007, February 6, 13, and 20, 2007, and March 1 and 14, 2007)] after you were informed that the IND submission for this product was placed on clinical hold.

3. You failed to obtain informed consent in accordance with the provisions of 21 CFR Parts 50 and 56, as required by 21 CFR 312.60 and 312.66.

Informed consent must be documented by the use of a written consent form approved by an Institutional Review Board (IRB) and signed and dated by the subject or the subject's legally authorized representative at the time of consent [21 CFR 50.27, see 21 CFR 312.60]. As an investigator, it is your responsibility to obtain informed consent approved by an IRB in compliance with the requirements of 21 CFR Part 56 [see 21 CFR 312.66]. Except as provided in 21 CFR 50.23 and 50.24, no investigator may involve a human being as a subject in research unless the investigator has obtained the legally effective informed consent of the subject or the subject's legally authorized representative [21 CFR 50.20]. In seeking informed consent, the FDA regulations require that the following information must be provided to each subject [21 CFR 50.25]:

a. A statement that the study involves research, an explanation of the purposes of the research and the expected duration of the subject's participation, a description of the procedures to be followed, and identification of any procedures which are experimental.
b. A description of any reasonably foreseeable risks or discomforts to the subject.
c. A description of any benefits to the subject or to others which may reasonably be expected from the research.
d. A disclosure of appropriate alternative procedures or courses of treatment, if any, that might be advantageous to the subject.
e. A statement describing the extent, if any, to which confidentiality of records identifying the subject will be maintained and that notes the possibility that the Food and Drug Administration may inspect the records.
f. For research involving more than minimal risk, an explanation as to whether any compensation and an explanation as to whether any medical treatments are available if injury occurs and, if so, what they consist of, or where further

information may be obtained.

g. An explanation of whom to contact for answers to pertinent questions about the research and research subjects' rights, and whom to contact in the event of a research-related injury to the subject.

h. A statement that participation is voluntary, that refusal to participate will involve no penalty or loss of benefits to which the subject is otherwise entitled, and that the subject may discontinue participation at any time without penalty or loss of benefits to which the subject is otherwise entitled.

You failed to obtain legally effective informed consent from subjects to whom you administered the investigational new drug, [ ]. You told the FDA investigator that you obtained informed consent from 22 subjects to whom you administered [ ]; however, the documents that you provided as proof of informed consent to the FDA investigator merely stated "I hereby authorize any and all treatment with FDA regulated device(s) for the treatment of my medical condition(s) and I hereby authorize payment to be made directly to the treating Health Practitioner". Those documents are inadequate in that they do not contain the required elements described above and do not seem specific to the investigational drug product administered. In addition, FDA regulations at 21 CFR 312.66 require that the investigator comply with the requirements in 21 CFR Part 56 by using an informed consent document approved by an IRB that contains the information delineated in 21 CFR 50.25. You did not comply with this requirement, nor the protocol for this trial which required that informed consent be approved in writing by the IRB. We note that the informed consent documents you provided to subjects were not approved by an IRB.

4. **You failed to assure that an IRB complying with requirements set forth in 21 CFR Part 56 was responsible for the initial and continuing review and approval of a clinical study [21 CFR 56.103, 312.60, and 312.66].**

FDA regulations require that clinical investigations conducted under an IND (i.e. those subject to 21 CFR Part 312) not be initiated unless that investigation has been reviewed and approved by an IRB meeting the requirements of 21 CFR Part 56 [see 21 CFR 56.103]). Clinical investigators are responsible for assuring that an IRB conducts initial and continuing reviews of clinical investigations [21 CFR 312.66]. You violated these requirements by administering the investigational new drug, [ ] to subjects without obtaining IRB approval. You admitted to the FDA investigator that an IRB had not approved the study. However, without IRB approval you initiated the investigation and proceeded to administer the investigational new drug [ ] to subjects.

5. **You failed to maintain adequate and accurate case histories that record all observations and other data pertinent to the investigation on each individual [21 CFR 312.62(b)].**

FDA regulations require you to prepare and maintain adequate and accurate case histories that record all observations and other data pertinent to the investigation on each individual administered the investigational drug [21 CFR 312.62(b)]. In addition, the protocol for the clinical investigation, in its Investigator Obligations section, specified that the investigator is expected to comply with applicable governmental regulations, and particularly emphasized maintaining independent case histories, supply accountability, and record retention. Under the protocol, the investigator is responsible for accurate and complete recording of all therapeutic data on the electronic case report forms. The protocol also states that separate and independent records of the patient's data must be maintained at all times. The Clinical Monitoring section of the protocol specified that during the course of the study the investigator will maintain source documents, such as product infusion records, laboratory reports, radiograms, consultation reports, history and physical examination reports, etc., for possible correlation and review.

You failed to maintain adequate and accurate case histories, including source documents and case report forms for subjects to whom you administered the investigational new drug, [ ] You told the FDA investigator that you did not maintain any true case histories, just some dictated notes for subjects to whom you administered [ ] You provided the FDA investigator with notes for only 10 out of 22 subjects. The notes you provided to the FDA investigator fail to meet the requirements of 21 CFR 312.62(b) and indicate that the study was not performed according to the investigational plan. In addition, the dates when the notes were prepared cannot be determined. Examples include, but are not limited, to the following:

a. For subject 1907 [ ] the notes have a date of January 8, 2007, but contain information to indicate that the subject received the second injection on January 19, 2007, the third injection on February 5, 2007, and the fourth injection on February 23, 2007.
b. For subject 1912 [ ] the notes have a date of January 8, 2007, but contain information to indicate that the subject received the second injection on January 22, 2007, the third injection on January 29, 2007, and the fourth injection on February 12, 2007.
c. For subject 1916, the notes have a date of January 15, 2007, but contain information to indicate that the subject received the second injection on January 16, 2007 and the third injection on January 18, 2007.
d. For subject 1921 [ ] the notes have a date of February 26, 2007, but contain information to indicate that the subject received the second injection on February 27, 2007 and third injection on February 28, 2007.
e. For subject 1924 [ ] the notes have a date of March 12, 2007, but contain information to indicate that the subject received the second injection on March 13, 2007 and the third injection on March 14, 2007.
f. For subject 1928 [ ] the notes have a date of January 24, 2007, but contain information to indicate that the subject received the second injection on January 30, 2007, the third injection on February 06, 2007, the fourth injection on

February 13, 2007, the fifth injection on February 20, 2007, the sixth injection on March 1, 2007, and the seventh injection on March 14, 2007.

6. **You failed to maintain adequate records of the disposition of the drug, including dates, quantity, and use by subjects [21 CFR 312.62(a)].**

   FDA regulations require that an investigator maintain adequate records of the disposition of the investigational drug, including dates, quantity, and use by subjects [21 CFR 312.62(a)]. In addition, the protocol for the clinical investigation specified that the investigator is expected to comply with applicable governmental regulations, and contained particular emphasis on maintaining drug supply accountability. FDA's inspection found inadequate documentation for the receipt, dispensing, and reconciling of the investigational drug. The drug accountability records were inadequate to reconcile the dates of administration and quantity of drug administered to each subject. Examples include, but are not limited to, the following:

   a. For subjects 1901[ ]1906[ ]1907[ ]1908[ ]1909[ ]1912[ ]1916, 1921[ ]1924[ ]and 1928[ ]the notes do not indicate the quantity of the investigational drug that was administered.
   b. For subjects 1901[ ]1906[ ]1908[ ]and 1909[ ]the notes do not indicate the dates or quantity of the investigational drug administered.

7. **You failed to conduct the clinical investigation according to the signed investigator statement and investigational plan, and to fulfill other responsibilities of an investigator, including to protect the rights, safety, and welfare of subjects under your care, as required by 21 CFR 312.40(a)(2), 312.60, and 312.66.**

When you signed the investigator statement (Form FDA 1572) for the above referenced clinical investigation, you agreed to take on the responsibilities of a clinical investigator. Each investigator using an investigational new drug in a clinical investigation must conduct his investigation in compliance with the requirements of Parts 50 and 56 [21 CFR 312.60, 312.40(a)(2), and 312.66]. Your general responsibilities as a clinical investigator (21 CFR 312.60) include ensuring that the investigation is conducted according to the signed investigator statement, the investigational plan, and applicable regulations; for protecting the rights, safety and welfare of subjects under your care; and for the control of drugs under investigation. Our investigation indicates that you have failed to meet all of these responsibilities as outlined in items 1-6 above. These violations resulted in a failure to protect the rights, safety, and welfare of the subjects under your care.

This letter is not intended to be an all-inclusive list of deficiencies with your clinical studies of investigational products. It is your responsibility to ensure adherence to each requirement of the law and relevant regulations.

On the basis of the above listed violations, FDA asserts that you have failed to protect the rights, safety and welfare of subjects under your care, repeatedly or deliberately failed to

comply with the cited regulations, which placed unnecessary risks to human subjects, and FDA proposes that you be disqualified as a clinical investigator. You may reply to the above stated issues, including an explanation of why you should remain eligible to receive investigational products and not be disqualified as a clinical investigator, in a written response or at an informal conference in my office. This procedure is provided for by regulation 21 CFR 312.70.

Within fifteen (15) days of receipt of this letter, write or call me at 301-796-3150 to arrange a conference time or to indicate your intent to respond in writing.

Should you choose to respond in writing, your written response must be forwarded within thirty (30) days of receipt of this letter.

Your reply should be sent to:

Leslie K. Ball, M.D.
Director
Division of Scientific Investigations
Office of Compliance
Center for Drug Evaluation and Research
Food and Drug Administration
Bldg. 51, Rm. 5342
10903 New Hampshire Avenue
Silver Spring, MD 20993

Should you request an informal conference, we ask that you provide us with a full and complete explanation of the above listed violations. You should bring with you all pertinent documents, and a representative of your choice may accompany you. Although the conference is informal, a transcript of the conference will be prepared. If you choose to proceed in this manner, we plan to hold such a conference within 30 days of your request.

At any time during this administrative process, you may enter into a consent agreement with FDA regarding your future use of investigational products. Such an agreement would terminate this disqualification proceeding. Enclosed you will find a proposed agreement between you and FDA.

FDA's Center for Drug Evaluation and Research (the Center) will carefully consider any oral or written response. If your explanation is accepted by the Center, the disqualification process will be terminated. If your written or oral responses to our allegations are unsatisfactory, or we cannot come to terms on a consent agreement, or you do not respond to this notice, you will be offered a regulatory hearing before FDA, pursuant to 21 CFR 16 (enclosed) and 21 CFR 312.70. Before such a hearing, FDA will provide you notice of the matters to be considered, including a comprehensive statement of the basis for the decision or action taken or proposed, and a general summary of the information that will be presented by FDA in support of the decision or action. A presiding officer free from bias or prejudice and who has not participated in this matter

will conduct the hearing. Such a hearing will determine whether or not you will remain entitled to receive investigational products.

You should be aware that neither entry into a consent agreement nor pursuit of a hearing precludes the possibility of a corollary judicial proceeding or administrative remedy concerning these violations.

Sincerely yours,

{See appended electronic signature page}

Leslie K. Ball, M.D.
Director
Division of Scientific Investigations
Office of Compliance
Center for Drug Evaluation and Research
Food and Drug Administration

Enclosures:
#1 - Consent Agreement
#2 - 21 CFR 16
#3 - 21 CFR 312.60
#4 - 21 CFR 312.70
#5 - 21 CFR 50
#6 - 21 CFR 56

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

LESLIE K BALL
03/31/2008