





May 11, 2005

Via Facsimile 301 927 6830

Lyle Jaffe  
Food and Drug Administration  
Department of Health and Human Services  
Division of Dockets Management Branch  
Room 1061  
5630 Fishers Lane  
Rockville, MD 20852

Re: Citizen Petition of Terry Fredeking and Antibody Systems, Inc.

Dear Mr. Jaffe:

This will confirm our telephone conversation earlier today to the effect that we do not object to two of the exhibits attached to our Citizen's Petition, Exhibit Numbers 6 and 8, from being disclosed.

The Exhibit Numbers contain the term, "confidential", but for this Citizen Petition they are not.

Please call me if you have any further questions.

Sincerely,

A handwritten signature in black ink, appearing to read "Bob McConachie".

Charles R. McConachie

CRM/qlc  
cc: Antibody Systems, Inc.

CONFIDENTIAL

Response to FEI No 30038742450 483 Issued to North Texas Institution Review Board on 17-DEC-02

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CONFIDENTIAL

Mr. Michael Chappell  
Dallas District Director  
4040 N. Central Expressway  
Suite 300  
Dallas, TX 75204

Re FEI No 30038742450 483 Issued to North Texas Institution Review Board on 17-DEC-02

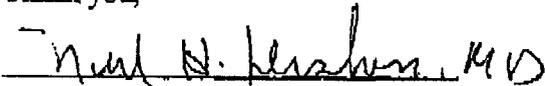
Dear Mr. Chappell:

Please note that the following the response of the North Texas IRB (NTIRB) to the FDA 483 form received on December 17, 2002. The inspection, completed by FDA investigator Ms. Cynthia A. Harris and Mr. Robert Harris was issued to Dr Neil N, Dishon, the former IRB Chairman. It provided observations regarding NTIRB operation in connection with clinical studies conducted under its supervision from 1997 to June, 2000. In the attached letter we have attempted to respond to the observations noted in the 483, however given that essentially all of the research was completed more than three years before the inspection many of the records are no longer available.

According to our records, we believe that the only study conducted after December 1999 was a one-day, IND exempt study (Doxycycline Cytokine Receptor Stimulation) in which a few healthy subjects were administered a subtherapeutic dose of doxycycline solely to obtain blood samples needed for some non-clinical research. Another study was approved, but was terminated by the sponsor without having been implemented.

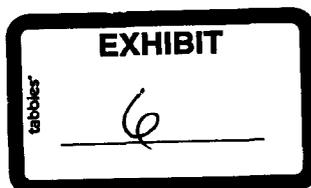
In any event, the IRB has not acted on or had any responsibility for any research since June 20, 2000, nor will it undertake any such responsibility. The IRB is being disbanded except for maintenance of the remaining record until the end of the required retention period. Nevertheless, if an IRB were to be reconstituted, substantial and definitive action would be taken to comprehensively address each of the observations to ensure that the IRB operates in full compliance with all applicable obligations. The attached memo provides our comments to each observation noted on the 483 based on our further examination of the records we could locate. For your convenience, I have attached a copy of the 483 we received. Please let me know if there are any questions or problems with the receipt of this information. I can be reached at 817.272.2771, or via fax at 817.272.2715.

Thank you,



Dr. Neil H. Dishon  
Chief of Staff

The University of Texas at Arlington Health Services



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Response to FEI No 30038742450 483 Issued to North Texas Institution Review Board on 17-DEC-02

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Cc: Ms. Cynthia A. Harris Mr. Robert Harris

**Observation 1: The IRB failed to prepare and maintain written procedures**  
**Comment:** As noted many of the records could not be located as essentially of the research was completed before December 1999. During its existence the IRB had responsibility for relatively few studies (approximately 2 per year). According to our records, we believe that the only study conducted after December 1999 was a one-day, IND exempt study (Doxycycline Cytokine Receptor Stimulation) in which a few healthy subjects were administered a subtherapeutic dose of doxycycline solely to obtain blood samples needed for some non-clinical research. Another study was approved, but was terminated by the sponsor on July 10, 2000 without ever having been implemented.

Due to the long period since the IRB ceased activity, we have not located all of the procedures used by the IRB. We believe, however that it used procedures discussed in the FDA IRB Information Sheets and provide as a handbook to each IRB member as the basis for the procedures it followed. We agree that because the study noted above was approved and conducted between December 16 1999 and July 10 2000 that copies of specific written procedures used should have been available for review by the investigators during their inspection.

**Corrective Actions:** We will attempt to locate all missing records for activities between December 16, 1999 and July 10, 2000 and maintain them on file for inspection until the end of the applicable retention period. No studies are now under IRB review and none will be undertaken.

**Observation 2: The IRB Failed to review proposed and continuing research at convened meetings at which a majority of IRB members were present. Specifically, members were frequently polled by telephone as to their votes on amendments and changes to ongoing research. The IRB had no procedures or policies regarding expedited review**

**Comment:** The studies identified under items "a.)" and "b.)" of this observation were completed more than three years before the inspection and thus most of the records are no longer available. With respect to observation "c.)", we believe that this study met all requirements for approval on an expedited basis as set forth in 21 CFR §56.110. The study involved the one time administration of a subtherapeutic dose of a legally marketed antibiotic, doxycycline, and collection of a blood sample by venipuncture. The sole purpose was to obtain blood samples from healthy subjects to carry out in vitro and animal basic research into the effect of doxycycline on certain cytokines. Accordingly, the IRB should be considered justified in deeming that the study was one that involved no more than minimal risk to the subjects and did not require IND approval under 21 CFR Part 312 or any procedure that would make ineligible for expedited review and approval by the IRB chairman. The IRB Chairman obtained the further input and approval of the IRB members through the telephonic meeting indicated in the observation.

**Corrective Actions:** We will attempt to locate any other records for the Doxycycline Cytokine Receptor Stimulation study and maintain them on file for inspection until the end of the applicable retention period. No studies are now under IRB review and none will be undertaken,

but if they were then all activities would be carried out under appropriate written procedures and record keeping.

**Observation 3:** The IRB failed to conduct continuing review of research. For example  
**Comment:** We agree that collecting and maintaining the documents described in this observation are appropriate. However, because the research activities for both cited studies were completed more than three years before the inspection, the records necessary to address the observations are no longer available, nor required to have been retained for such a period.

**Corrective Action:** Because these studies are past the required record retention period, it is not possible to obtain the documents indicated as not available. No studies are now under IRB review and none will be undertaken, but if they were then all activities would be carried out under appropriate written procedures and record keeping.

**Observation 4:** The IRB files were missing copies of documents related to research proposal reviewed. For Example

**Comment:** We agree that collecting and maintaining the documents described in this observation are appropriate. However with respect to items "a.)", "b.)" and "c.)", because the research activities for the cited studies were completed more than three years before the inspection, the records necessary to fully address the observation are no longer available, nor required to have been retained for such a period.

With respect to item "d.)" (Protocol US99 102-TT), we believe that the approval on 06-Jan-00 was for extension for the study to enroll additional patients. Despite IRB approval of study extension, our records indicate that no research under that protocol was performed after the last subject was enrolled in October 1999 and the notice of termination received on July 10, 2000. Thus, there would be no progress reports. We have located the consent form and study documents reviewed at that meeting, and can provide them if so requested.

**Corrective Action:** Except for item "d.)" these studies are past the required record retention period, it is not possible to obtain the documents indicated as not available. We have located the pertinent records for item "d.)" and will provide them on request. No studies are now under IRB review and none will be undertaken, but if they were then all activities would be carried out under appropriate written procedures and record keeping.

**Observation 5:** Minutes of the IRB meeting lacked sufficient detail to show meeting attendance, actions taken by the IRB, votes on actions and written summaries of the discussions at the meeting. For example

**Comment:** We agree that collecting and maintaining the documents described in this observation are appropriate. However with respect to items "a.)", "b.)" and "c.)", because the research activities for the cited studies were completed more than three years before the inspection, the records necessary to fully address the observation are no longer available, nor required to have been retained for such a period.

With respect to item "d.)" (Protocol US99 102-TT), we are making every effort to locate all of the minutes for that meeting and will provide them when found. As indicated in the response to

Observation 4, we have located the consent form and protocol reviewed at that meeting. Also, no research was in fact conducted under the approval that meeting.

**Corrective Action:** Except for item "d.)" these studies are past the required record retention period, it is not possible to obtain the documents indicated as not available. We have located the pertinent records for item "d.)" and will provide them on request. No studies are now under IRB review and none will be undertaken, but if they were then all activities would be carried out under appropriate written procedures and record keeping.

**Observation 6:** **The IRB failed to adequately evaluate all relevant information related to the research proposal under review. Specifically thirteen studies reviewed and approved by the IRB included healthy subjects as the study population. ...**

**Comment:** We agree that collecting and maintaining the documents described in this observation are appropriate. However, because the research activities for both cited studies were completed more than three years before the inspection, the records necessary to fully address the observation are no longer available, nor required to have been retained for such a period. With respect to the two protocols reviewed after 16-Dec-1999, recruitment review was not deemed necessary nor was there any recruitment advertising. One was an extension of a previously reviewed protocol and no changes in recruitment were requested, and in fact no new subjects were recruited or enrolled prior to its termination. The other study was a minimal risk study, properly conducted under expedited review, that required a very few {NUMBER} subjects and who were recruited without advertising.

**Corrective Action:** Except for one study and one study extension, the studies are past the required record retention period. Thus, it is not possible to obtain the documents needed to address this observation. No studies are now under IRB review and none will be undertaken, but if they were then all activities would be carried out under appropriate written procedures and record keeping.

**Observation 7:** **One of the voting IRB Members had a conflicting interest. Specifically, one of the IRB member's CVs state he was an employed as the Director of Research and Development for Antibody Systems Inc from 1990 to the present. All thirteen projects reviewed and approved by the IRB were sponsored and/or conducted by Antibody Systems Inc. This member voted on all thirteen projects, including initial approval s and approval of changes to the protocols and consent forms**

**Comment:** Dr. Stewart was not an employee of Antibody Systems. He was a full-time employee of the University of Texas, who also was a consultant to Antibody Systems. In his consulting role he directed and carried out non-clinical research activities as his lab at the university for Antibody Systems that was entirely unrelated to the products involved in the clinical protocols (his research involved parasitology, while the clinical studies involved third party vaccines for bacterial infections). He never had any role in the conduct or supervision of the clinical studies or a financial interest in their performance or outcome. Accordingly, the IRB

did not believe that he had a disqualifying conflict of interest. In any event, to the best of records and recollection, his vote did not change the outcome of any decision taken by the IRB.

**Corrective Action:** We agree that members with conflicting interest should not participate in IRB decisions except to provide requested information. No studies are now under IRB review and none will be undertaken, but if they were then only members without conflicting interested would be permitted to vote.

**Observation 8:** Consent forms reviewed and approved by the IRB were lacking required elements for Informed Consent and used misleading language. For example.

**Comment:** Each of the cited studies was conducted more than three years ago and, consequently, we do not have the records to respond fully. However, we agree that consent forms should not contain representations that investigational products are safe, effective, or endorsed by FDA.

**Corrective Action:** No studies are now under IRB review and none will be undertaken, but if they were then all consent forms will strictly follow applicable requirements and not contain in appropriate statements.