



**DEPARTMENT OF HEALTH AND HUMAN SERVICES  
FOOD AND DRUG ADMINISTRATION**

DISTRICT OFFICE ADDRESS AND PHONE NUMBER 4040 North Central Expressway, Suite 300 Dallas, TX 75204 214-253-5200	DATE(S) OF INSPECTION 12/16-17/2002
	FEI NUMBER 3003874250

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT IS ISSUED  
**To: Neil N. Dishon, MD/former IRB Chairman**

FIRM NAME North Texas Institutional Review Board	STREET ADDRESS 605 S. West St.
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CITY, STATE AND ZIP CODE Arlington, TX 76019	TYPE OF ESTABLISHMENT INSPECTED Institutional Review Board
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DURING AN INSPECTION OF YOUR FIRM WE OBSERVED:

**OBSERVATION 1:**

The IRB failed to prepare and maintain written procedures for:

- a.) conducting initial and continuing review of research and for reporting its findings and actions to the investigator;
- b.) determining which projects require review more often than annually;
- c.) ensuring prompt reporting to the IRB of changes in research activity;
- d.) ensuring that changes in approved research may not be initiated without IRB approval;
- e.) ensuring prompt reporting to the IRB and the FDA of any unanticipated problems involving risks to human subjects, instances of serious or continuing non-compliance with regulations, or any suspensions or termination of IRB approval.

**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 reviews. For example:

- a.) For Protocol UTA-98001, the IRB Chairman obtained approval of changes to the protocol and informed consent on 1/26/98 by telephoning six IRB members individually to obtain their votes. No group discussion was conducted.
- b.) For Protocol KV-9820, IRB members reviewed changes to the protocol and consent form and then telephoned their votes to the IRB Chairman. The changes were approved on 4/29/99. No group discussion was conducted.
- c.) For Protocol "Doxycycline Cytokine Receptor Stimulation", a telephone vote was conducted on 6/21/00, but only four members, including the IRB Chairman, were listed as voting.

SEE REVERSE OF THIS PAGE	EMPLOYEE(S) SIGNATURE <i>Cynthia A. Harris, CSO</i> <i>Robert T. Harris, CSO</i>	EMPLOYEE(S) NAME AND TITLE (Print or Type) Cynthia A. Harris, Consumer Safety Officer Robert T. Harris, Consumer Safety Officer	DATE ISSUED 12/17/02
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**EXHIBIT**  
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**OBSERVATION 3:**

The IRB failed to conduct continuing review of research. For example:

- a.) Protocol UTA-98001 was originally approved by the IRB on 11/10/97. Changes to the Protocol and Informed Consent were approved by the IRB on 1/26/98, 7/1/98, and 1/20/99. However, there was no documentation to indicate the IRB was notified of the study status, including dates of subject enrollment, number of subjects enrolled, or any adverse events experienced by subjects. There was no renewal of IRB approval.
- b.) Protocol KV-9820 was originally approved by the IRB on 11/10/97. Changes to the Protocol and Informed Consent were approved by the IRB on 9/30/98, 1/20/99, 4/29/99, and 5/5/99. However, there was no documentation to indicate the IRB was notified of the study status, including dates of subject enrollment, number of subjects enrolled, any adverse events experienced by subjects, or whether the study is still ongoing. There was no renewal of IRB approval.

**OBSERVATION 4:**

The IRB files were missing copies of documents related to research proposals reviewed. For example:

- a.) The file for Protocol UTA-98001 was missing copies of revised consent forms approved by the IRB on 1/26/98, 7/1/98, and 1/20/99. The file was missing copies of the revised protocols approved by the IRB on 7/1/98 and 1/20/99. There was no Investigator's Brochure in the file and no progress reports.
- b.) The file for Protocol KV-9820 was missing copies of the original consent forms approved by the IRB on 11/10/97 and copies of the revised consent forms approved by the IRB on 9/30/98 and 4/29/99. The file was missing copies of the original protocol approved by the IRB on 11/10/97 and copies of the revised protocols approved by the IRB on 4/29/99 and 5/5/99. There was no Investigator's Brochure in the file and no progress reports.
- c.) The file for US99-101-TT was missing copies of the revised consent form approved by the IRB on 10/7/99. The file was missing the copies of the revised protocols approved by the IRB on 7/28/99 and 10/7/99. There was no Investigator's Brochure in the file and no progress reports.

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d.) The file for US99-102-TT was missing copies of the revised consent form approved by the IRB on 1/6/00. The file was missing the copies of the revised protocol approved by the IRB on 1/6/00. There was no Investigator's Brochure in the file and no progress reports.

**OBSERVATION 5:**

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

- a.) For Protocol UTA-98001, minutes were present in the IRB files for the initial review and approval of the protocol and consent form on 11/10/97, but there was no record of the vote or of the IRB members in attendance at that meeting. For approval of protocol and consent form revisions on 1/26/98, 7/1/98, and 1/27/99 there was only a record of the names of members approving the changes, but no other minutes. In addition, approval letters for changes to the protocol and consent form were dated 1/20/99, while the record of the IRB vote was dated 1/27/99.
- b.) For Protocol KV-9820, the minutes for the initial review of the protocol and consent form on 9/30/98 were present, but there was no record of the vote. For approval of revisions to the protocol and consent on 1/27/99, there was only a record of the vote and no other minutes. Also, the vote was dated 1/27/99 while the approval letter was dated 1/20/99. For the approval of revisions to the protocol and consent form on 5/5/99, the minutes do not document the vote. In addition, the IRB approval letter was dated 4/29/99 while the meeting did not occur until 5/5/99.
- c.) For Protocol US99-101-TT, there were no minutes present in the files for approval of revisions to the protocol and consent form on 7/28/99 and 10/7/99.
- d.) For Protocol US99-102-TT, there were no minutes present in the files for approval of revisions to the protocol and consent form on 1/6/00.

**OBSERVATION 6:**

The IRB failed to adequately evaluate all relevant information related to research proposals under review. Specifically, all thirteen studies reviewed and approved by the IRB included healthy subjects as the study

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population. However, there was no documentation present in the meeting minutes or in correspondence between the IRB and the clinical investigators to indicate that subject recruitment methods had been evaluated, or that the sources for the study subjects had been considered. Only one example of advertising was found in the IRB records, for Protocol UTA-98001, and there was no documentation to indicate that this ad was evaluated or reviewed by the IRB prior to its use by the clinical investigator.

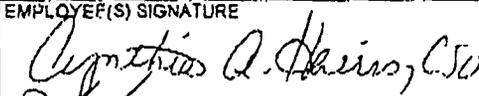
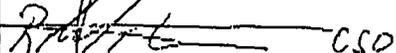
**OBSERVATION 7:**

One of the voting IRB members had a conflicting interest. Specifically, one of the IRB member's CVs stated he was 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 approvals and approval of changes to protocols and consent forms.

**OBSERVATION 8:**

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

- a.) For Protocol UTA-98001:
  - The consent form contains the statement, "the new liquid formulation of the Ty21a vaccine has been shown to be safe".
  - The Confidentiality section of the consent form contains a statement that "Officials of the Food and Drug Administration (FDA) ... may inspect all records from this study due to their interest in and support of this vaccine".
- b.) For Protocol KV-9820:
  - The Confidentiality section of the consent form contains a statement that "Officials of the Food and Drug Administration (FDA) ... may inspect all records from this study due to their interest in and support of this vaccine".

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