

DEPARTMENT OF HEALTH AND HUMAN SERVICES PUBLIC HEALTH SERVICE FOOD AND DRUG ADMINISTRATION		DISTRICT ADDRESS AND PHONE NUMBER 60 8th Street N.E. Atlanta, GA 30309 (404) 347-3218	
NAME OF INDIVIDUAL TO WHOM REPORT ISSUED	PERIOD OF INSPECTION	C. F. NUMBER	
TO: Richard L. Borison, M.D., Ph.D.	11/6/96-4/22/97		
TITLE OF INDIVIDUAL	TYPE ESTABLISHMENT INSPECTED		
Clinical Investigator	Clinical Investigator		
FIRM NAME	NAME OF FIRM, BRANCH OR UNIT INSPECTED		
Richard L. Borison, M.D., Ph.D.	Same		
STREET ADDRESS	STREET ADDRESS OF PREMISES INSPECTED		
1021 15th Street, Ste. 7	Same		
CITY AND STATE (Zip Code)	CITY AND STATE (Zip Code)		
Augusta, GA 30901	Same		

DURING AN INSPECTION OF YOUR FIRM (I (WE) OBSERVED:

1. Dr. Ananda Pathiraja's signatures on study documents at the Biotech Park office and the Veteran's Administration Medical Center (VAMC), were not his, i.e. made by him. Study documents he purportedly signed included, but are not limited to: Human Assurance Committee (HAC) applications, personnel identification and signature forms, laboratory reports, CT scans, ECG tracings, subject chart notes, and case report forms.
2. Dr. Pathiraja was identified, without his knowledge or consent, as the subinvestigator responsible for medical oversight in the absence of Dr. Borison at the Biotech Park office for several studies. Dr. Pathiraja did not participate in the studies conducted at the Biotech Park office.
3. Bruce Diamond, Ph.D., routinely signed Dr. Richard Borison's name on study documents. Both Dr. Diamond and Dr. Borison state that Dr. Borison authorized this practice. This practice, however, was not disclosed to the sponsors or monitors. Study records signed by Dr. Diamond with Dr. Borison's signature include, but are not limited to: personnel identification and signature forms, consent forms, laboratory results, ECG tracings, CT scans, medication authorizations, subject chart notes, adverse event reports, case report forms, sponsor agreements, sponsor reports, IRB applications and reports, and a FDA-1572.
4. Dr. Scott Balogh's signature on a HAC application submitted for Risperidone was found not to be his, i.e. made by him.
5. Bruce Diamond, Ph.D., is not medically qualified and not an expert in the evaluation of investigational new drugs within the meaning of the Food, Drug and Cosmetic Act. He nevertheless performed duties such as: evaluating laboratory reports, CT scans, and ECG results; completing diagnostic evaluations and psychiatric assessments; determining study eligibility; evaluating adverse events; prescribing medications; and determining dosing changes.

SEE REVERSE OF THIS PAGE	EMPLOYEE(S) SIGNATURE	EMPLOYEE(S) NAME AND TITLE (Print or	DATE ISSUED
	<i>Stephanie E. Hubbard</i> <i>Sandra L. Calhoun</i> <i>Robert S.K. Young</i>	Stephanie E. Hubbard, CSO Sandra L. Calhoun, CSO Robert S.K. Young, Medical Officer	04/22/97
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NAME OF INDIVIDUAL TO WHOM REPORT ISSUED TO: Richard L. Borison, M.D., Ph.D.		PERIOD OF INSPECTION 11/6/96-4/22/97	C. F. NUMBER
TITLE OF INDIVIDUAL Clinical Investigator		TYPE ESTABLISHMENT INSPECTED Clinical Investigator	
FIRM NAME Richard L. Borison, M.D., Ph.D.		NAME OF FIRM, BRANCH OR UNIT INSPECTED Same	
STREET ADDRESS 1021 15th Street, Ste. 7		STREET ADDRESS OF PREMISES INSPECTED Same	
CITY AND STATE (Zip Code) Augusta, GA 30901		CITY AND STATE (Zip Code) Same	

DURING AN INSPECTION OF YOUR FIRM (X) (WE) OBSERVED:

6. Assurances given to Western Institutional Review Board (WIRB) as to the division of responsibility between Dr. Diamond and Dr. Borison for Sandoz study B351 were not carried out as promised.
7. The study coordinators were not qualified by training or experience to perform many of the duties assigned to them. These duties include, but are not limited to, the following: obtaining medical histories, performing ECGs and phlebotomies, reviewing laboratory and ECG results, completing diagnostic evaluations and psychiatric assessments, determining study eligibility, evaluating adverse events, and determining dosing changes.
8. Statements were placed in patient charts indicating that Dr. Borison or Dr. Pathiraja had personally seen or reviewed a patient or patient report, when in fact neither had.
9. Not all studies requiring HAC approval were submitted to the HAC for approval. For example, studies in which MCG or VAMC resources (employees and/or equipment) were used to conduct the studies, or the investigator's association with these institutions was advertised to promote the recruitment of subjects, should have been submitted to the HAC for clearance.
10. For those studies approved by the HAC, not all participating subinvestigators were named in the applications submitted to the HAC.
11. The HAC restricts the obtaining of consent to investigators and co-investigators identified on the HAC application. Consents in innumerable instances were obtained by study coordinators.

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12. The Medical College of Georgia (MCG) was never reported as a study site on the FDA-1572 for Sandoz trial B351, yet the study was approved and reviewed by the HAC from 11/28/94 to 4/4/96. The HAC Request for Continuation dated 8/22/95 was answered to the effect that no subjects had been enrolled due to difficulty recruiting subjects who met the study criteria, when in fact 48 subjects had been randomized at the Biotech Park office.
13. Sandoz trial B353 was submitted to and approved by the HAC on 9/2/95, yet MCG was not reported as a study site on the FDA-1572 until 1/10/96. The HAC was removed as an IRB from the FDA-1572 on 5/14/96 although MCG continued to be listed as a study site. MCG was removed from the FDA-1572 on 7/26/96 and the HAC was not notified or provided a final report.
14. The MCG study site reported on the FDA-1572 for Seroquel, 1021 15th Street, Augusta, GA, was not approved by the HAC.
15. The severity of adverse events experienced by the subjects involved in the Physostigmine study were under-reported to WIRB.
16. The person who performed the physical examinations, neurological examinations, and Modified Hachinski evaluations on the majority of the Physostigmine source notes cannot be identified.
17. Several protocol violations were identified in the studies audited. For example: Seroquel vital signs records document that the measurements were taken in the sitting position, not the required supine position; Seroquel subject #120 did not meet eligibility criteria due to a history of alcohol abuse yet was enrolled; Physostigmine subject #92 did not meet eligibility criteria due to the MMSE yet was enrolled; Physostigmine subject #87 was enrolled with a CT scan which was exclusionary.

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PUBLIC HEALTH SERVICE
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18. The investigator failed to promptly report several serious adverse events (SAE) to the sponsor and/or HAC. The 9/93 SAE of Olanzapine subject #344 was not reported to the HAC until 3/94. The 9/23-30/93 SAE of Olanzapine subject #341 was not reported to the HAC until 5/95. The 5/95 SAE of Sandoz B351 subject #422 was not reported to the sponsor until 6/21/95.
19. Several consent form deficiencies were noted in the Seroquel trial. Duplicate copies were found for subjects #114, #117, #122, #123, and #124 which bore no investigator's signature, i.e. one copy did contain the investigator's signature. The consent forms for subjects #103 and #122 did not bear the HAC approval stamp. No consent form was found for subject #121.
20. The study coordinators routinely dated the subject's signature when obtaining consent.

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