Id : i.m.80e89ad849250d74f598db29c2569e54
CN : SQ1ED01932372
Date : Saturday, June 29, 1996 2:12:00 AM GMT
From : SAHL Mark R.
To : ARVANITIS Lisa A; AUCHARD Judith C.; GRIFFETT Chris R; LAMPERT Steven B.; MANNING Julia W.; MILBAUER Alan J.; MILLER Karen L.; OSHEA W. Jim; RUHL Athena M.
Subject : Seroquel Borison Reserve Press Statement
Attachments : BORIRPS.DOC

From: SAHL Mark R.

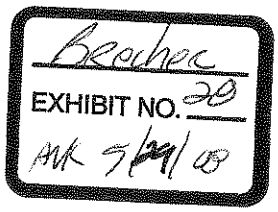
Sent: Friday, June 28, 1996 6:42 PM

To: O'SHEA W. Jim; RUHL Athena M.; LAMPERT Steven B.; MANNING Julia W.;

MILBAUER Alan J.; MILLER Karen L.; AUCHARD Judith C.; ARVANITIS Lisa A;

GRIFFETT Chris R

Subject: Seroquel Borison Reserve Press Statement



Attachments: BORIRPS.DOC

Attached is an approved reserved press statement on the Seroquel Borison issue.

Should we get any media inquiries on this issue, select portions of the RPS will be used on an as-needed basis to respond to any questions we might get from the media.

Any U.S. media inquiries on this issue should be directed to Karen Miller next week and thereafter to me.

cc: Chris Dalton

Bob Black

Ed Seage

SEROQUEL Borison Reserve Press Statement
June 28, 1996

On June 18, 1996, Zeneca Pharmaceuticals was notified by the Medical College of Georgia/ Augusta Veterans Affairs Medical Center (MCG/AVAMC) that allegations of research misconduct had been made against Richard L. Borison, PhD, MD, and Bruce Diamond, PhD. MCG/AVAMC said the allegations were being investigated and they had suspended Drs. Borison and Diamond from enrolling new subjects in any studies and from starting any new study until these allegations are resolved. In addition, they stated Dr. Borison had resigned from MCG on June 5, 1996, and his employment by the AVAMC was terminated on June 7, 1996. Dr. Diamond had resigned from MCG on June 3, 1996.

Dr. Borison serves as principal investigator at AVAMC on a number of key clinical trials for SEROQUEL® (quetiapine), Zeneca Pharmaceuticals' drug in development for the treatment of schizophrenia and other psychotic disorders. Dr. Diamond serves as co-investigator for the phase II placebo-controlled efficacy study and as sub-investigator for all other studies.

Zeneca is now in the process of taking the following actions to address this situation:

-- We are re-auditing clinical data contributed by Dr. Borison's site to these SEROQUEL studies. (Previous regularly scheduled Zeneca audits of this site had found no SEROQUEL clinical data irregularities.)

-- We are undertaking a number of additional activities to determine any impact these circumstances may have on the development of SEROQUEL.

While these activities are in progress, plans are proceeding on schedule for the filing of the SEROQUEL New Drug Application to the FDA in the middle of this year. Until the above actions have been completed, we cannot determine if these developments will have an impact on the NDA.

The SEROQUEL studies that Drs. Borison and Diamond have been involved in and each study's current status are as follows:

204636/0006 (Phase II): placebo controlled efficacy study -- completed
5077IL/0013 (Phase III): U.S. acute efficacy study -- completed, except for open label portion
5077IL/0015 (Phase III): relapse trial -- completed, except for open label portion
5077IL/0031 (Phase III): treatment resistance trial -- ongoing
5077IL/0044: clinical pharmacology -- 1 subject ongoing
5077IL/0045: clinical pharmacology -- 0 subjects ongoing, study not closed out
5077IL/0056 (Phase IIIb): health outcomes trial -- 3 subjects ongoing
5077IL/0061 (Phase IIIb): Abrupt withdrawal trial -- 2 subjects ongoing

became more and more obvious that this isn't right." Dr. Diamond's attorney acknowledges that employees were paid recruiting bonuses, but says, "If the incident with the cocktail napkin occurred, it was obviously a joke."
Paige Horan, who coordinated Borison-Diamond drug trials at the VA hospital, says Dr. Diamond pushed her so hard to recruit and retain subjects for a Sandoz study of a schizophrenia drug that she misled patients -- claiming the experimental medicine may be the "next wonder" drug. The recruiters "were promising them things that we knew were wrong," she says in an interview. "I was very wrong for doing it."

Ms. Hernandez says Dr. Diamond "just wanted us to recruit as many people as possible, and whether we thought they would be eligible or not." Dr. Diamond's attorney says some unqualified patients may have been enrolled but denies his client knew at the time that anybody was ineligible.

Eligibility requirements for drug studies are designed to make sure that drugs are tested on patients they are most likely to help. The studies' rules usually specify the type and stage of disease the test subjects must have, and they exclude people with other health or substance-abuse problems. The results could be skewed if researchers enroll ineligible patients, and patients could suffer because they pass up opportunities to try other therapies that might be more helpful.

When Nancy Sisk brought her husband, Leroy, to BioTech Park in June 1995, intrigued by an experimental Sandoz drug for Alzheimer's, the retired minister couldn't even remember what state he lived in. At Dr. Borison's clinic, Mrs. Sisk says a staff member, whom she can't identify, took her husband into a back room and administered a mental-acuity test with a scale from zero to 30. "She came and told us, `He made an eight, but we'll give him a 12,' " Mrs. Sisk says. A score of 10 was needed to enroll in the study, which was aimed at people who still retained much of their cognitive ability.
Three months into the study, Mrs. Sisk, concerned that her husband wasn't improving, took him to Edward Zamrini at the VA hospital. Dr. Zamrini gave him the same acuity test. Mr. Sisk's score was two. "There was no way he could have legitimately been admitted or enrolled in the Sandoz study," Dr. Zamrini later testified to the VA investigative board. Because Mrs. Sisk had said her husband hadn't deteriorated significantly since the first test, Dr. Zamrini added, "In my opinion, their initial score of 12 is suspect." Mr. Sisk ultimately quit the study. Dr. Diamond, his attorney says, didn't perform the test on Mr. Sisk or order any employee to put him in the study.

As activity at Suite 7 picked up, rumors began circulating around the college that Drs. Borison and Diamond were making a killing by running drug studies on the side. Dr. Borison amassed a collection of antiques, including suits of armor, and made plans to build a full-scale castle outside Augusta. Dr. Diamond bought a Mercedes. Dr. Borison, who earned $154,000 at the college, reported gross income of $1.2 million on his 1995 federal tax return. Dr. Diamond, who earned $65,000 at the school, reported $1.1 million. (The tax returns were attached to the indictments.) In both cases, most of the money came from PharmEd Inc., their research company.

The drug companies complied when Dr. Borison asked that money be sent directly to PharmEd or his home rather than to the college. A Warner-Lambert spokesman says one company unit sent a $10,000 check to PharmEd at Dr. Borison's request because it trusted him and the request came on medical-college stationery. The U.S. unit of Japan's Otsuka Pharmaceutical Co. also sent payments this way. "We were relying on his representations as a prestigious person," Scott Willoughby, Otsuka's U.S. general counsel, explains. The company has adopted controls to prevent a recurrence, he says.

In January 1996, Drs. Borison and Diamond opened a new research site to prospect for subjects in Charlotte, North Carolina. John Stokes, an inspector from Quintiles Transnational Corp., visited it a few months later. Sandoz had hired Quintiles, a medical-research contractor in Research Triangle Park, North Carolina, to help oversee its Alzheimer's studies, and Mr. Stokes questioned how Dr. Borison could sign records for patients seen in Charlotte on a day when he was nearly 320 kilometers away in Augusta. "The more questions he asked, the more nervous Dr. Diamond got," says a former study coordinator.

A person familiar with the matter says Dr. Diamond complained to Mr. Stokes's superiors at Quintiles. The next business day, Mr. Stokes was off the case. "Poor guy, he got in trouble," says Sharad Mogul, who managed the Charlotte office for Drs. Borison and Diamond at the time and had formerly worked at Quintiles. The drug- testing inspection system, he says, "is a joke, and what happened to John Stokes is a classic example." He says drug companies treat researchers like "kings" and are reluctant to antagonize them because they supply the study data. Mr. Stokes and Quintiles decline to comment.

Things began to unravel for the two researchers when Ms. Touey left her job in Suite 7 to go to graduate school. A few months later, in the autumn of 1995, she took a part-time job with David Hess, a neurologist and researcher at the VA hospital. Dr. Hess told the VA investigative board that Ms. Touey asked him, on her first day on the job, how she should obtain a patient's consent to participate in a stroke study. He testified that when he explained that as the principal investigator, only he was supposed to obtain consent, she said it didn't work that way at her previous job.
Alarmed by this and other accounts from Ms. Touey, Dr. Hess spoke to other former employees and alerted officials at the medical college and the VA hospital, he testified. Days later, in June 1996, Drs. Borison and Diamond resigned their medical-school positions and are no longer testing any drugs; drug companies either stopped the trials or transferred them to other researchers. In February, the two men were indicted on state criminal charges. No trial date has been set.

Meanwhile, a court-appointed receiver is overseeing assets of the testing operations -- including equipment, files, money and bank accounts -- which, if the two are convicted, are subject to state forfeiture.

George Schuster, chairman of the medical school's institutional review board, says he is still disturbed by the drug companies' response to the scandal. He notified about two dozen companies in June 1996 that Drs. Borison and Diamond had resigned their positions after allegations of research misconduct and wrote that the school was "very concerned" about patients' welfare. But many of the companies "didn't seem particularly concerned" about patients, Dr. Schuster says, adding that most were interested only in whether data had been faked. Told there was no immediate evidence of that, "most of them seemed to lose interest," he says.

Ms. Brown recalls a time when Sandoz did show some concern. Two years ago, it sent a representative to Augusta after discovering that she was dispensing medication at a time of day before most doctors' offices had opened -- suggesting that Dr. Borison wasn't around. Sandoz says its representative told the clinic to stop dispensing medication without a physician present. But employees say the practice continued anyway. Ms. Brown says the Sandoz representative never asked her any questions and left Augusta saying that if she "had a mother with Alzheimer's disease, [she] would want her to come to our clinic."

~~~~~~~~~~~~

Reprinted on Eli Lilly Drugs by Karl Loren http://www.oralchelation.net/data/Lilly/data6.htm#p9

http://www.mhsource.com/pt/p970401b.html
Ex-Profs Charged in Psych Department Research Scam
by Michael Jonathan Grinfeld
Psychiatric Times April 1997 Vol. XIV Issue 4

A scandal-rocked Medical College of Georgia (MCG) has announced tightened compliance controls for clinical studies in the wake of a 172-count indictment that charged two former professors with diverting more than $10 million in research funds. Richard L. Borison, M.D., the former chair of MCG's department of psychiatry and health behavior, and Bruce I. Diamond, Ph.D., once a professor in the department, were jailed in February pending the posting of a $1 million bond each. Borison posted bond on March 5 after spending 10 days behind bars; Diamond remained incarcerated at the time this article was filed.

The charges stem from claims that the pair spent the last eight years conducting over 100 research projects for more than 20 pharmaceutical companies using MCG resources, but then pocketing the proceeds. The alleged scheme began to unravel during the last week of May 1996, according to MCG officials, after a whistleblower complained about irregularities in the medical management of research subjects. The study coordinator who raised the red flag, however, didn't even know they were working for research enterprises that weren't a part of MCG.

Within three days after MCG officials began asking questions about Borison and Diamond's operations, both researchers resigned their positions and refused to cooperate with an internal investigation, according to Malcolm Kling, Ph.D., a pharmacologist and MCG's interim vice-president of research. The Augusta-based medical school, one of the oldest in the country, then notified the attorney general's office, the U.S. Food and Drug Administration, other federal regulators and the pharmaceutical companies about the irregularities.

In a prepared statement, school officials said that they were initially "appalled by the conduct of these two former faculty members." But as the internal investigation proceeded "the initial reaction changed to frank anger as the extent of the allegations of misconduct became more apparent."

The 3-inch thick indictment chronicles a history of alleged misconduct dating back to 1988. The grand jurors charged that Borison and Diamond "developed and executed a scheme through which they systematically stole in excess of $10 million from the Medical College of Georgia," and that they "routinely lied to conceal their crimes and endangered the safety of the patients and study participants they were employed to serve, protect and heal."

Borison and Diamond conducted research into a broad spectrum of mental illnesses including Alzheimer's disease, schizophrenia, anxiety and depression, and they contracted with pharmaceutical companies throughout the United States and abroad. Their research included clinical trials for drugs such as olanzapine, Eli Lilly's new schizophrenia treatment, and Janssen Pharmaceutica's risperidone. A Medline search revealed that Borison and Diamond published more than 20 articles since 1988.

But the indictment, coming after months of painstaking investigation, charges that Borison and Diamond's national reputations were built upon a foundation of theft, false statements and representations, prescription forgeries, violations
~~~~~~~~~~~~

of controlled substances laws, income tax evasion, reckless conduct in the providing of medical care, bribery and racketeering. In addition to the criminal indictment, the Georgia attorney general has also brought a civil forfeiture suit against Borison and Diamond, claiming that millions of dollars in assets located in three states and London, England, are in actuality the fruits of their alleged illegal activities. A receiver appointed in the case has taken control of assets that include bank accounts, real estate, antiques and art work.

Michael Hobbs, counsel to Attorney General Michael Bowers, told Psychiatric Times that it could be a year before the criminal trial begins. Although he declined to comment on the merits of the case, other than to refer to allegations in the indictment, Hobbs said that the state will seek to prove that this is not just a case about financial misfeasance, but also one that involves patient safety.

"There are a number of allegations in the indictment concerning the use of untrained, undertrained, inadequately trained, or improperly trained clerical personnel to perform some of the procedures that were necessary in conducting the studies, such as drawing blood," Hobbs said. "There is some indication in the indictment of inattentiveness on the part of Dr. Borison and Dr. Diamond to subjects in the studies who had suffered from a serious, adverse event and were not seen or followed up with by Borison or Diamond."

A bribery count in the indictment alleges that Borison and Diamond paid an undisclosed sum to an MCG employee in exchange for her not filing a complaint regarding a patient suicide that occurred during a clinical study of olanzapine. A spokesperson for Eli Lilly and Co., the drug's manufacturer, said that despite the allegations of financial misfeasance against Borison and Diamond, they are confident that none of the data provided was compromised in any way. Following the pair's resignation from MCG, Lilly arranged for new principal investigators to take over ongoing trials.

According to Hobbs, he has no evidence, "one way or the other," that data provided to any of the pharmaceutical firms was falsified, fabricated or plagiarized, although an FDA investigation is underway. A spokesperson for the agency refused to comment on the status of their inquiry while it is pending.

Meanwhile, Jay Sawilowsky, an Augusta attorney representing Borison and Diamond in connection with the civil forfeiture suit and the FDA audit, and who is consulting with respect to their criminal defense, denies that his clients were involved in any improper conduct. Rather he says the case is a dispute over money and who is entitled to the wealth generated by Borison and Diamond's research. He lashed out at MCG's leadership, calling it "maladministration," and charged that school officials will have some explaining of their own to do when the business arrangements involving the research are "finally hashed out in court."

"They are not accused of any plagiarism; they're not accused of faking data...," Sawilowsky said. "When you get down to what is the dispute between them, the doctors and the medical college, it is about a dispute over money, money, money. That's what it's about."

Sawilowsky accused the attorney general's office of turning the situation into a media circus, and filed a motion in the civil suit to prevent further disclosures of the identities of psychiatric patients involved in research programs. The indictment named the psychiatric patients in conjunction with forged prescription allegations, individuals who were then deluged by media requests for interviews after the charges became public. The motion to restrain further disclosures was denied, though Sawilowsky claimed that the attorney general's office promised the judge there would be no further disclosures unless absolutely necessary.

"The torment to these psychiatric patients who have been publicly exposed is terrible," Sawilowsky said. "I accuse the staff of the attorney general's office of being completely indifferent to the welfare of the patients. Of being completely unconcerned about harm to the patients."

Jill P. Hauenstein, M.D., president of the Georgia Psychiatric Physicians Association (GPPA), and an associate clinical professor at MCG, agreed that the disclosure of confidential patient identities by the attorney general's office was inappropriate and could have been handled more sensitively. "Confidentiality is the cornerstone of the psychiatric doctor-patient relationship, and to violate that is [to violate] one of the most basic trusts that a patient has. This was not done by Dr. Borison or Dr. Diamond or their attorneys, it was done by the attorney general's office."

Efforts by the GPPA's legislative consultant to sensitize the attorney general's office to confidentiality issues has thus far not resulted in any assurances that any changes will take place. In a letter from Attorney General Michael Bowers, the GPPA was told that while he is concerned about confidentiality, the disclosures were necessary in order to ensure the indictment passed legal muster.

Meanwhile, MCG's Kling said that the school is instituting changes to assure better controls over research contracts and the investigators who enter into them. "We will be doing things after the barn door was left open and the horse is long gone, but we'll keep the next horse from getting out," he said.

Already, a new Office of Clinical Trials Compliance will monitor all research contracts, and manage their compliance with

"federal, state and local regulations and policies to protect the research subjects and the interests of the university," according to an MCG announcement.

In addition Kling said that audit controls would be tightened so that issues like the ones that arose in connection with Borison and Diamond's research project would be discovered sooner. For instance, no one noticed when research projects by the two former faculty members dropped off precipitously. Some of the research was performed literally across the street from MCG's campus using the medical school's employees, but no one caught on for years, Kling said.

"The way we manage our studies and we manage the flow of money and we manage contracts, they're handled through different offices," Kling said. "...We didn't know where they were working. Why didn't we know where they were working? We're going to take a look at that process. Why didn't someone hold up some red flags, and say 'look at this?'"

Finding answers to these questions will occupy the medical school for some time, Kling added. Thus far, there are no indications that irregularities in the management of research contracts will surface in other departments, though efforts are underway to ascertain whether problems exist elsewhere in the medical school.

webmaster@mhsource.com
~~~~~~~~~~~~~~~~~~~~~
~~~~~~~~~~~~~~~~~~~~~