DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

DISTRICT ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
4040 North Central Expressway, Suite 300 Dallas, TX 75204 (214) 253-5200 Fax:(214) 253-5314 Industry Information: www.fda.gov/oc/industry	01/17/2013 - 03/15/2013* FEI NUMBER 3005553411

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED

TO: Stanislaw R. Burzynski, M.D.,Ph.D, President

FIRM NAME	STREET ADDRESS
Burzynski Research Institute	9432 Katy Fwy Ste 200
CITY, STATE, ZIP CODE, COUNTRY	TYPE ESTABLISHMENT INSPECTED
Houston, TX 77055-6330	Sponsor

This document lists observations made by the FDA representative(s) during the inspection of your facility. They are inspectional observations, and do not represent a final Agency determination regarding your compliance. If you have an objection regarding an observation, or have implemented, or plan to implement, corrective action in response to an observation, you may discuss the objection or action with the FDA representative(s) during the inspection or submit this information to FDA at the address above. If you have any questions, please contact FDA at the phone number and address above.

DURING AN INSPECTION OF YOUR FIRM WE OBSERVED:

OBSERVATION 1

Failure to monitor the progress of an investigation conducted under your IND.

Specifically,

1. The S.R. Burzynski Study Monitoring Plan, MQA-001 Revision A (Monitoring Plan), Section 12.5.1, requires Dynamic Audits as a part of the monitoring plan.

   You failed to conduct Dynamic Audits as required by your Monitoring Plan. There have been no Dynamic Audits performed since 2005.

2. The S. R. Burzynski Study Monitoring Plan, MQA-001 Revision A (Monitoring Plan), Section 7.2.1, requires that a Quality Assurance (QA) Monitor "monitor clinical trials including source document verification, query report generation and final resolution, and drug accountability." Section 7.2.2 requires, in part, that the QA Monitor ensure that investigator obligations are met and in compliance with FDA regulations. Section 7.2.3 requires that the QA Monitor review and analyze case report forms (CRFs) and subject charts for clarity, content, and data integrity.

   You failed to monitor as required by Sections 7.2.1, 7.2.2, and 7.2.3 of your Monitoring Plan.

   a. You did not have a QA Monitor verify that the investigator complied with protocol requirements for assessing the efficacy endpoint of tumor response, and you did not have a QA Monitor properly monitor CRFs and subject charts for data integrity related to these assessments. For 18 of 27 (67%) of subjects, the investigator did not comply with the protocol requirements for assessing the efficacy endpoint of tumor response and recorded inaccurate assessments for tumor response in study records. For example:

      - Study BT-09: Subjects 005297 and 007197 were inaccurately classified as Complete Response (CR). Subjects 004721 and 008765 were inaccurately classified as Partial Response (PR).

      - Study BT-10: Subjects 06389, 11819 and 13660 were inaccurately classified as CR. Subjects 21428 and 23399 were inaccurately classified as PR.

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SEE REVERSE OF THIS PAGE	Joel Martinez, Investigator Hugh M. Mcclure, Investigator Cynthia F. Kleppinger, Investigator	03/15/2013

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Subjects 005974, 011373, 012184, 012206 and 12252 were inaccurately classified as Stable Disease (SD).

- Study BT-21: Subject 009990 was inaccurately classified as CR.
  Subjects 004881 was inaccurately classified as PR.

- Study BT-22: Subject 006239 was inaccurately classified as PR.
  Subject 004240 was inaccurately classified as SD.

b. You did not have a QA Monitor properly monitor CRFs and subject records. The investigator destroyed critical subject case history records (target tumor measurement worksheets) or misplaced case history records (original subject CRFs) for all subjects.

c. You did not have a QA Monitor properly monitor drug accountability. The investigator did not maintain adequate/accurate test article accountability records.

3. The S. R. Burzynski Study Monitoring Plan, MQA-001 Revision A (Monitoring Plan), Section 13.1.1, requires that the Monitoring and Quality Assurance Department (MQA) ensure that all subjects participated in the consenting process and are provided with a consent form describing the study. Section 13.1.2 requires that the MQA verify that a subject's consent is obtained before the subject undergoes any study procedure.

   You failed to monitor as required by Sections 13.1.1 and 13.1.2 of your Monitoring Plan.

   a. Informed consent documents (ICDs) used by the investigator to obtain informed consent in Studies BT-09, BT-10. BT-21 and BT-22 were inadequate in that they did not contain all of the required elements of informed consent. Specifically, the ICDs did not include a statement of any additional costs to the subject that might result from participation in the research.

   b. The investigator never consented BT-22 Subject 5586 (start date 12/13/1997, stop date 3/16/98), but this was not discovered until June 6, 2006. Chart progress notes of August 1999 had corrections made 9/30/12.

   c. The investigator never consented Subject 9896 (b) (4)

4. The S. R. Burzynski Study Monitoring Plan, MQA-001 Revision A (Monitoring Plan), Section 16, Adverse Events, requires Monitoring and Quality Assurance (MQA) staff to "verify that information on all AE are …summarized in the CRFs on monthly basis."

   You failed to monitor as required by Section 16 of your Monitoring Plan. The investigator did not report adverse events (AEs) experienced by study subjects, including 18 cases of hypernatremia. Examples of unreported AEs are as follows:

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Study Number	Subject Number	Date of AE	AE Description
AD-02	010526-05	11/04/2005	Hypernatremia (165 meq/L)
		11/07/2005	Hypernatremia (152 meq/L)
		11/14/2005	Hypernatremia (159 meq/L)
		11/16/2005	Hypernatremia (156 meq/L)
		11/22/2005	Hypernatremia (156 meq/L)
		11/25/2005	Hypernatremia (202 meq/L)

5. The S. R. Burzynski Study Monitoring Plan, MQA-001 Revision A (Monitoring Plan), Section 11, requires the Clinical Research Assistant Regulatory [sic] to ensure that a signed Form FDA 1572 and a Curriculum Vitae (CV) are obtained from each "local physician."

   These documents were missing for approximately 65% of the "local physicians" reviewed during the inspection. Specifically, a random selection of 20 "local physicians" from the sponsor's list revealed that the sponsor does not have a CV on file for 13 of the 20 "local physicians" randomly selected.

By failing to monitor in accordance with your Monitoring Plan, you did not identify the above deficiencies.

OBSERVATION 2

Failure to obtain from an investigator sufficient financial information to allow complete and accurate certification or disclosure statements.

Specifically, you failed to provide upon request financial information for each of the 122 sub-investigators participating in Studies BT-09, BT-10, BT-21 and BT-22 to allow for complete and accurate certification or disclosure statements. There was no financial information for 40 sub-investigators for BT-09, 34 sub-investigators for BT-10, 40 sub-investigators for BT-21 and 8 sub-investigators for BT-22.

*** DATES OF INSPECTION:**
01/17/2013(Thu), 01/18/2013(Fri), 01/22/2013(Tue), 01/23/2013(Wed), 01/24/2013(Thu), 01/25/2013(Fri), 01/28/2013(Mon), 01/29/2013(Tue), 01/30/2013(Wed), 01/31/2013(Thu), 02/01/2013(Fri), 02/19/2013(Tue), 02/20/2013(Wed), 02/21/2013(Thu), 02/22/2013(Fri), 02/26/2013(Tue), 02/27/2013(Wed), 02/28/2013(Thu), 03/01/2013(Fri), 03/12/2013(Tue), 03/15/2013(Fri)

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