List of Enclosures

A. 483's issued to Burzynski Research Institute, Houston, Texas, on the dates indicated

1. 9/13/2000;
2. 2/15/2002;
3. 12/10/2008;
4. 10/28/2010; and
5. 2/7/2013.

B. 483 issued to Stanislaw R. Burzynski, Houston, Texas, on 8/10/2001.

DEPARTMENT OF HEALTH AND HUMAN SERVICES PUBLIC HEALTH SERVICE FOOD AND DRUG ADMINISTRATION	DISTRICT ADDRESS AND PHONE NUMBER 3310 Live Oak St. 3rd floor Dallas, TX 75204 Telephone: 214 655-5310	
NAME OF INDIVIDUAL TO WHOM REPORT ISSUED TO: Carlton E. ~~Hazelwood~~ Hazlewood Ph. D.	PERIOD OF INSPECTION 09/11-13/2000	C.F. NUMBER 1626573
TITLE OF INDIVIDUAL Burzynski Research Inst. IRB Chairman	TYPE ESTABLISHMENT INSPECTED IRB	
FIRM NAME Burzynski Research Inst. IRB	NAME OF FIRM, BRANCH OR UNIT INSPECTED same	
STREET ADDRESS 9432 Old Katy Rd. Suite 200	STREET ADDRESS OF PREMISES INSPECTED same	
CITY AND STATE (Zip Code) Houston, Texas 77055	CITY AND STATE (Zip Code) same	

DURING AN INSPECTION OF YOUR FIRM I OBSERVED:

1) The IRB does not have documentation in the meeting minutes or other IRB records to show specific study protocols were reviewed annually.

Annotation: Corrections Promised

2) The IRB meeting minutes fail to show the following as required in their policies and procedures:

a) The number of members voting for or against study protocols;

b) The names of all persons in attendance at convened IRB meetings; and

c) The status of each attendee; i.e. voting or non-voting members.

Annotation: Corrections Promised

3) The IRB membership list does not delineate which members are voting or non- voting and which members are alternates.

Annotation: Corrections Promised

SEE REVERSE OF THIS PAGE	EMPLOYEE(S) SIGNATURE	EMPLOYEE(S) NAME AND TITLE (Print or Type)	DATE ISSUED
		Patrick D. Stone Investigator	09/13/2000

DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

T OFFICE ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
North Central Exp. s, TX 75204 53-5200	8/6-10/01 FEI NUMBER

ND TITLE OF INDIVIDUAL TO WHOM REPORT IS ISSUED

Stanislaw R. Burzynski, M.D., Ph.D., sponsor, clinical investigator

AME	STREET ADDRESS
ynski Reasearch Institute	9432 Old Katy Rd.
'ATE AND ZIP CODE ton, TX 77055	TYPE OF ESTABLISHMENT INSPECTED sponsor / clinical investigator

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

Phase II Studies of Antineoplastons A10 and AS2-1 In Children and Adults with Cancer

1. Protocol Violations:
Subjects were started on antineoplaston treatment prior to the protocol-specified interval following prior chemotherapy and/or radiation therapy.

Protocol Patient ID	Prior Therapy	Last Date of Prior Therapy	Date Antineoplastons started	Interval (days)
(b)(4)-BT-11	Etopoxide	(b) (4)	24-Apr-1998	(b) (4)
(b)(4) (b) (4)	Stereotactic radiation		10-Nov-1999	
(b)(4) BT-22 (b)(4)	Etopoxide		30-Apr-1999	
(b)(4) PA-02-(b)(4)	Combined Chemotherapy (b) (4) and Radiation		05-Aug-1999	

2. Not all serious adverse events and adverse events are reported to FDA and IRB. Examples are shown in the following table.

Protocol Patient ID	Date	Serious Adverse Events or Adverse Events
(b)(4) BT-07 (b)(4)	31-Oct-2000	Subject became lethargic, with diarrhea and blood in the urine, and was hospitalized during which significant hematuria persisted.
	04-Dec-2000	Cystoscopy showed severe hemorrhagic cystitis and necrotic bladder mucosa.
(b)(4) BT-08 (b)(4)	17-Jun-2000	Left subclavian vein thrombosis.
	14-Aug-2000	Subject experienced shortness of breath, and his chest X-ray showed suspicious consolidations in right lung base.
	20-Aug-2000	Hospitalized; bronchoscopy and lavage revealed *Pneumocystic carinii*.
(b)(4)-BT-11 (b)(4)	02-Feb-1997	Pancreatitis; antineoplastons were discontinued for one week and restarted on 28-Feb-1997. Patient developed pancreatitis again and required antineoplastons to be discontinued permanently on 10-Mar-1997
(b)(4) BT-11 (b)(4)	18-May-2000	Central line sepsis (blood culture positive for Staphylococcus aureus) requiring hospitalization.
	20-May-2000	Broviac catheter had to be removed.

EE ERSE THIS GE	EMPLOYEE(S) SIGNATURE	EMPLOYEE(S) NAME AND TITLE (Print or Type)	DATE ISSUED
		Kevin Mahnke, M, MD, Medical Officer Patrick D Hanson	08/10/01

DA 483 (8/00) PREVIOUS EDITION OBSOLETE **INSPECTIONAL OBSERVATIONS** PAGE 1 OF 5 PAGES

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DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

DISTRICT OFFICE ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
4040 North Central Exp. Dallas, TX 75204 214 253-5200	8/6-10/01 FEI NUMBER

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT IS ISSUED

TO: Stanislaw R. Burzynski, M.D., Ph.D., sponsor, clinical investigator

FIRM NAME	STREET ADDRESS
Burzynski Reasearch Institute	9432 Old Katy Rd.
CITY, STATE AND ZIP CODE Houston, TX 77055	TYPE OF ESTABLISHMENT INSPECTED sponsor / clinical investigator

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

(b)(6)(c) BT-15 (b)(4)	30-Sep-1999	Hospitalized with fever for pneumonia and sepsis, deteriorated, requiring transfer to ICU. Subject expired on 17-Oct-1999.
(b)(6)(c) BT-21 (b)(7)(c)	08-Mar-1998	Hospitalized for fever, hypotension, central line sepsis; subject also developed an aspiration pneumonia in hospital.
(b)(6)(c) BT-22 (b)(4)	29-Jun-1999	Cushingoid features, steroid myopathy
	13-Sep-1999	Renal acidosis requiring daily treatment with sodium bicarbonate.
	04-Oct-1999	Hypertension, requiring medication, e.g., Vasotec
	07-Oct-1999	Venous thrombosis in left arm confirmed by venogram.
	29-Oct-1999	Central line sepsis, blood culture grew coagulase negative Staphylococcus that required treatment with Vancomycin
	21-22-Nov-1999	Diarrhea with stool cultures positive for Clostridium difficile for which the subject was treated with Vancomycin
LY-06 (b)(4)	19-Sep-1999	Shortness of breath
	22-Sep-1999	Lung biopsy revealed fibrosis of lung for which the subject was hospitalized and required Oxygen. The subject died on 01-Oct-1999.
(b)(6)(c) (b)(4)	11-Aug-1997	Occlusion of both subclavian veins.
(b)(6)(c) UP-02 (b)(4)	03-Jul-1998	Hospitalized for septic shock (fever, hypotension), was intubated and placed on ventilator the next morning, and died at noon on 04-Jul-1998.

3. Special exception treatment request (b)(4) dated 7-31-97 for (b)(6)(c) PR-04-(b)(6)(c) was approved based on the incorporation of certain statements into the consent form. The consent form signed by (b)(6)(c) did not incorporate these statements. The statements included:

   a) (b)(4) patients with renal cell carcinoma who received antineoplastons had a response.
   b) (b)(4) patients with prostate cancer receiving antineoplaston infusions had a response.

SEE REVERSE OF THIS PAGE	EMPLOYEE(S) SIGNATURE	EMPLOYEE(S) NAME AND TITLE (Print or Type)	DATE ISSUED
		Medical Officer	08/10/01

FORM FDA 483 (5/00) PREVIOUS EDITION OBSOLETE INSPECTIONAL OBSERVATIONS PAGE 2 OF 5 PAGES

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DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

DISTRICT OFFICE ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
[redacted] North Central Exp. Dallas, TX 75204 214 253-5200	8/6-10/01 FEI NUMBER

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT IS ISSUED

TO: Stanislaw R. Burzynski, M.D., Ph.D., sponsor, clinical investigator

FIRM NAME	STREET ADDRESS
Burzynski Reasearch Institute	9432 Old Katy Rd.
CITY, STATE AND ZIP CODE Houston, TX 77055	TYPE OF ESTABLISHMENT INSPECTED sponsor / clinical investigator

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

4. Exception treatment request (SN (b) (4) dated 8-28-97 for (b) (7) (C) (b) (4) was approved based on the incorporation of certain statements into the consent form. The consent form that Pt. (b) (7) (C) signed did not incorporate these statements that included:

   a) An awareness to the patient that protocol (b) (4) is intended to measure response
   b) To date there have been (b) (4) from [redacted] patients on this protocol
   c) (b) (4) in [redacted] patients on Special Exception

5. Failure to keep adequate drug accountability records. For example:

   a) A random selection of Lot 258C (A10 capsules) revealed that (b) (4) capsules were received at BRI. One accountability record accounts for (b) (4) capsules while a second accountability record accounts for (b) (4) capsules.
   b) Random selection of Lot 058B (AS2-1) revealed that (b) (4) capsules were received at BRI. Drug accountability records account for (b) (4) on one database and (b) (4) in a second accountability record.
   c) Random selection of Lot 823-1 (AS2-1 500 ml bags) show that BRI received (b) (4) bags. Accountability records account for only (b) (4)
   d) Lot 809 (A10 IV bags) show that (b) (4) bags were received. Accountability records can account for (b) (4) bags.
   e) Receipt records for Lot 199 (AS2-1) show that (b) (4) bags were received. Accountability records can only account for (b) (4)

6. Failure to address and resolve reported patient overdoses in BRI query reports to determine the reason for the possible overdose and to take corrective actions to prevent recurrence. For example:

   a) (b) (7) (C) BT-07 (b) (7) (C) query dated 11-8-00
   b) (b) (7) (C) BT-11-(b) (7) query dated 4-3-01
   c) (b) (7) (C) BT-11-(b) (7) query dated 8-7-01

SEE REVERSE OF THIS PAGE	EMPLOYEE(S) SIGNATURE	EMPLOYEE(S) NAME AND TITLE (Print or Type)	DATE ISSUED
	[signature]	[illegible], MD Medical Officer Patricia DeStefano	08/10/01

FORM FDA 483 (8/00) PREVIOUS EDITION OBSOLETE INSPECTIONAL OBSERVATIONS

DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

DISTRICT OFFICE ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
4040 North Central Exp. Dallas, TX 75204 214 253-5200	8/6-10/01 FEI NUMBER

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT IS ISSUED

TO: Stanislaw R. Burzynski, M.D., Ph.D., sponsor, clinical investigator

FIRM NAME	STREET ADDRESS
Burzynski Reasearch Institute	9432 Old Katy Rd.
CITY, STATE AND ZIP CODE Houston, TX 77055	TYPE OF ESTABLISHMENT INSPECTED sponsor / clinical investigator

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

7. Patient (b)(4)-BT-07-(b)(4) was observed to be receiving (b)(4) while on study.

8. Inadequate / Inaccurate Record Keeping:

(a) There are discrepancies between the case report forms and the source documents for the following subjects:

Protocol Patient ID	Information on CRF	Information on Source Document
(b)(4)-BT-17-(b)(4)	Withdrawn on 27-Nov-1996; Reason = Patient's request	Patient was withdrawn with MRI findings (18-Jun-1996 vs 30-Sep-1996) suggestive of recurrent tumor
	Withdrawn 09-Oct-19/99	Patient continued on study until 09-Nov-1999.
(b)(4)-BT-13-(b)(4) (b)(4)-BT-20-	Withdrawn on 30-Jul-1996; Reason = Patient's request	Patient was hospitalized on 30-Jul-1996 with grand mal seizures and antineoplaston dose was reduced. Then, the patient decided to stop antineoplastons permanently.
(b)(4)-BT-22-(b)(4)	Withdrawn on 27-Nov-1999; Reason = Worsening of clinical condition	Patient died the morning of 27-Nov-1999
(b)(4)-LY-06-(b)(4)	Withdrawn on 29-Dec-1999; Reason = Patient's request	On 28-Dec-1999, patient's abdominal CT of 23-Nov-1999 was reported with splenomegaly and patient was recommended on 29-Dec-1999 to undergo splenectomy and stop antineoplaston treatment.
(b)(4)-(b)(4)	Patient died on 27-Nov-1997.	Patient died on 27-Dec-1997
(b)(4)-UP-02-(b)(4)	Withdrawn on 04-Jul-1998; Reason = Worsening of clinical condition	Patient was hospitalized in ICU on 03-Jul-1998 for bacterial sepsis, and died on 04-Jul-1998.

(b) Cross-outs and additions were made in source documents For example, in progress notes of Subject (b)(4)-BT-07-(b)(4) dated 03-Nov-2000 is the statement "The patient will remain off antineoplastons at this time." This was crossed out and replaced with the sentence "The patient will discontinue antineoplastons permanently." This alteration was made despite many subsequent progress notes that contain the sentence, "The patient will continue to be off antineoplastons at this time."

SEE REVERSE OF THIS PAGE	EMPLOYEE(S) SIGNATURE	EMPLOYEE(S) NAME AND TITLE (Print or Type)	DATE ISSUED
		[illegible] Medical Officer Patrick Strong CSO	08/10/01

FORM FDA 483 (8/00) PREVIOUS EDITION OBSOLETE INSPECTIONAL OBSERVATIONS PAGE 4 OF 5 PAGES

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DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

DISTRICT OFFICE ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
4040 North Central Exp. Dallas, TX 75204 214 253-5200	8/6-10/01 FEI NUMBER

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT IS ISSUED

TO: Stanislaw R. Burzynski, M.D., Ph.D., sponsor, clinical investigator

FIRM NAME	STREET ADDRESS
Burzynski Reasearch Institute	9432 Old Katy Rd.
CITY, STATE AND ZIP CODE	TYPE OF ESTABLISHMENT INSPECTED
Houston, TX 77055	sponsor / clinical investigator

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

9. The subject case report forms do not always contain complete and concurrent patient information such as:
   a) (b)(4) tumor measurements for patients (b)(7)(C) BT-11-(b)(4) or (b)(7)(C) BT-11-(b)(4) do not contain the tumor measurments that were done by the consultants.
   b) The case report forms for patients (b)(7)(C) BT-23-(b)(4) (b)(7)(C) BT-23-(b)(4) and (b)(7)(C) BT-09-(b)(4) do not contain inclusion/exclusion criteria entries.

10. Failure to address and resolve reported patient overdoses in BRI query reports to determine the reason for the possible overdose and to take corrective actions to prevent recurrence. For example:

JM -
   d) (b)(7)(C) BT-07-(b)(4) query dated 11-8-00
   e) (b)(7)(C) BT-11-(b)(4) query dated 4-3-01
   f) (b)(7)(C) BT-11-(b)(4) query dated 8-7-01

11. The subject case report forms do not always contain complete and concurrent patient information such as:

JM -
   c) (b)(4) tumor measurements for patients (b)(7)(C) BT-11-(b)(4) or (b)(7)(C) BT-11-(b)(4) do not contain the tumor measurments that were done by the consultants.

- Written response will be submitted

SEE REVERSE OF THIS PAGE	EMPLOYEE(S) SIGNATURE	EMPLOYEE(S) NAME AND TITLE (Print or Type)	DATE ISSUED
	[signature]	Kenneth Hamilton, MD Medical Officer Patricia D. Stanciso	08/10/01

FORM FDA 483 (8/00) PREVIOUS EDITION OBSOLETE INSPECTIONAL OBSERVATIONS PAGE 5 OF 5 PAGES

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DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

DISTRICT OFFICE ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
4040 N. Centeral Expwy., Suite 300 Dallas, TX. 75204 (214) 253-5200	2/12-15/02
	FEI NUMBER 1000220451

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT IS ISSUED

TO: Carlton F. Hazlewood, Ph.D., IRB Chairman

FIRM NAME	STREET ADDRESS
Burzynski Research Institute IRB	9432 Old Katy Rd. Suite 370
CITY, STATE AND ZIP CODE Houston, TX. 77055	TYPE OF ESTABLISHMENT INSPECTED Institutional Review Board

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

1. Protocol [redacted] received tentative IRB approval on 9-16-99 and then received final IRB approval on 10-28-99. The IRB has failed to keep a copy of the [redacted] protocol and informed consent form

2. While the [redacted] study received final IRB approval on 10-28-99, it has not (to date) received any progress reports from the principal investigator.

3. While the [redacted] study protocol was removed from the IRB's list of active studies, there is no final report from the principal investigator to show that the [redacted] study was terminated and to assure that all reports of injuries/SAE's were reported during the conduct of the [redacted] study.

4. The IRB issued a provisional approval for the special exception (compassionate exception) request of [redacted] however, it failed to assure that FDA approval was obtained by the principal investigator prior to commencement of treatment.

5. The IRB accepted 2 special exception requests, one that is unsigned [redacted] and one signed by a research associate ([redacted]) instead of being signed by the principal investigator or co-investigator.

6. There is no record that the IRB reviewed and approved the following protocols: [redacted] and [redacted]

7. Special Exceptions receive provisional approval via expedited review exercised by the chairperson or co-chair. The BRI's IRB SOP 3, (3.4 Expedited Review) does not provide a provision for such provisional approvals.

8. A letter dated 3-30-01 states that the IRB reviewed the new pump, [redacted] Pump Model [redacted] and full board approval was granted on 3-29-01. The meeting minutes dated 3-29-01 do not document full board review and final voting results of approval.

9. Expedited review approval was given to a change in protocol and informed consent form for study [redacted] The revised protocol and informed consent form are not on file.

SEE REVERSE OF THIS PAGE	EMPLOYEE(S) SIGNATURE	EMPLOYEE(S) NAME AND TITLE (Print or Type)	DATE ISSUED
		Joel Martinez, Investigator Patrick D. Stone, Investigator	2-15-02

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	12/03/2008 - 12/10/2008
	FEI NUMBER 1000220451

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED

TO: Carlton F. Hazlewood, Ph.D., IRB Chairman

FIRM NAME	STREET ADDRESS
Burzynski Research Institute / IRB	9432 Katy Freeway # 370
CITY, STATE, ZIP CODE, COUNTRY	TYPE ESTABLISHMENT INSPECTED
Houston, TX 77055-6349	IRB

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 I OBSERVED:

OBSERVATION 1

A clinical investigation requiring prior submission to the FDA was initiated without IRB approval.

Specifically, On February 01, 2008 The BRI IRB was presented with study protocol #(b) (4) entitled (b) (4) (b) (4) by (b) (4) M.D., Principal Investigator (P.I.) and Carlton F. Hazelwood, Ph.D., Co-P.I. Fifteen human subjects' were entered into protocol #(b) (4) under pilot case reports between January and February 2007 without an effective FDA Investigational New Drug number. On February 15, 2008 the BRI IRB approved the protocol to begin human accrual.

OBSERVATION 2

The IRB does not conduct continuing review of research at intervals of not less than once per year.

Specifically;

A) Clinical protocol entitled (b) (4) (b) (4) was not reviewed & approved by the IRB annually from 2006 through 2008. In addition there are no continuing review reports on file from the P.I. to the IRB.

B) Clinical Device Protocol #(b) (4) entitled (b) (4) (b) (4) (b) (4) conducted by Carlton F. Hazelwood, Ph.D., Co-P.I. was not reviewed & approved by the IRB annually from 2005 through 2008. In addition there are no continuing review reports on file from the P.I. to the IRB.

SEE REVERSE OF THIS PAGE	EMPLOYEE(S) SIGNATURE Patrick D Stone, Investigator PDS	DATE ISSUED 12/10/2008

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	12/03/2008 - 12/10/2008 FEI NUMBER 1000220451

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED
TO: Carlton F. Hazlewood, Ph.D., IRB Chairman

FIRM NAME	STREET ADDRESS
Burzynski Research Institute / IRB	9432 Katy Freeway # 370
CITY, STATE, ZIP CODE, COUNTRY	TYPE ESTABLISHMENT INSPECTED
Houston, TX 77055-6349	IRB

OBSERVATION 3

Copies have not been maintained of all research proposals reviewed.

Specifically, ;

A) The Investigators Brochure for study protocol # (b) (4) was not found in the BRI IRB study records.

B) The device description or detailed information regarding the (b) (4) device (Protocol # (b) (4) was not found in the BRI IRB study records.

OBSERVATION 4

Documentation has not been maintained of written procedures for the IRB, as required by 21 CFR 56.108(a) and (b).

Specifically, The BRI IRB written procedures section 4.2.2.1 states that "These policies and Procedures (SOPs) will be reviewed annually". The SOPs were not reviewed from 2003 through 2008.

SEE REVERSE OF THIS PAGE	EMPLOYEE(S) SIGNATURE Patrick D Stone, Investigator	DATE ISSUED 12/10/2008

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	10/12/2010 - 10/28/2010* FEI NUMBER 1000220451

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED

TO: Carlton F. Hazlewood, Ph.D., Chairman

FIRM NAME	STREET ADDRESS
Burzynski Research Institute / IRB	9432 Katy Freeway #105
CITY, STATE, ZIP CODE, COUNTRY	TYPE ESTABLISHMENT INSPECTED
Houston, TX 77055-6349	Institutional Review Board

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 I OBSERVED:

OBSERVATION 1

The IRB has no written procedure for conducting its initial and continuing review of research.

Specifically,

A). The Continuing review for studies under IND (b) (4) #(b) (4) was approved for continuation during the March 26, 2010 meeting. The IRB did not have, nor request any copies of the current Informed Consent in use from the Investigator. The Investigator provided the date of approval of the current cosent form in use. The approval date of the IC provided by the Investigator for Protocols #(b) (4) and (b) (4) is 12/05/02. There was no available consent form approved for this date for thes two studies. The consent forms found in the IRB records for studies (b) (4) and (b) (4) were dated 12/11/2001 and 10/22/2002 respectively.

B). the BRI IRB Standard Operating Procedures (Both Approved Version - Rev H, and Draft) do not include any procedures for conducting reviews of device studies to determine whether they involve a significant risk device per 21 CFR 812.66.

OBSERVATION 2

The IRB has no written procedure for determining which projects require review more often than annually .

Specifically, your SOPs do not provide any evaluation of studies based on risk/harm to the subject for continuing review.

OBSERVATION 3

Copies have not been maintained of all approved sample consent documents and progress reports submitted by investigators.

Specifically, The IRB has accepted [redacted] study closure notices during the 01/22/2010 meeting for Protocols #(b) (4) and [redacted] from the Investigator. There is no final study report available for these studies. Additionally, the IRB records for Study Protocol (b) (4) do not indicate when the last version of the IC was approved, and what is the actual date of this Infomed Consent.

SEE REVERSE OF THIS PAGE	EMPLOYEE(S) SIGNATURE	DATE ISSUED
	Andrea A. Branche, Investigator	10/28/2010

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	10/12/2010 - 10/28/2010* FEI NUMBER 1000220451

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED

TO: Carlton F. Hazlewood, Ph.D., Chairman

FIRM NAME	STREET ADDRESS
Burzynski Research Institute / IRB	9432 Katy Freeway #105
CITY, STATE, ZIP CODE, COUNTRY	TYPE ESTABLISHMENT INSPECTED
Houston, TX 77055-6349	Institutional Review Board

OBSERVATION 4

The IRB did not determine at the time of initial review and at the time of continuing review for an on-going study which was started on/before April 30, 2001 that a study was in compliance with 21 CFR Part 50 Subpart D, "Additional Safeguards for Children in Clinical Investigations."

Specifically, this IRB approved Protocol (b) (4) and (b) (4) These protocols were approved to include children from (b)(6) months to (b)(6) year of age. This IRB has no procedures for safeguarding children, the assent of children in clinical trials, and determining the need for both parents to sign the informed consent as required by the state.

* DATES OF INSPECTION:
10/12/2010(Tue), 10/13/2010(Wed), 10/14/2010(Thu), 10/15/2010(Fri), 10/18/2010(Mon), 10/19/2010(Tue), 10/20/2010(Wed), 10/28/2010(Thu)

SEE REVERSE OF THIS PAGE	EMPLOYEE(S) SIGNATURE	DATE ISSUED
	Andrea A. Branche, Investigator	10/28/2010

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	01/22/2013 - 02/07/2013* FEI NUMBER 1000220451

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED

TO: Carlton F. Hazelwood, Ph.D., Chairman

FIRM NAME	STREET ADDRESS
BRI-IRB	9432 Katy Freeway # 370
CITY, STATE, ZIP CODE, COUNTRY	TYPE ESTABLISHMENT INSPECTED
Houston, TX 77055-6349	Institutional Review Board

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

The IRB used an expedited review procedure for research which did not appear in an FDA list of categories eligible for expedited review, and which had not previously been approved by the IRB.

Specifically, your IRB routinely provided expedited approvals for new subjects to enroll under Single Patient Protocols. For Example:

(A) Subject (b) (4) (pediatric) was given IRB Approval via Expedited Review to enroll in a Single Patient Protocol on March 28, 2012 and was approved by the full IRB meeting on August 3, 2012.

(B) Subject (b) (4) (pediatric) was given IRB Approval via Expedited Review to enroll in a Single Patient Protocol on May 2, 2012 and was approved by the full IRB meeting on August 3, 2012.

(C) Subject (b) (4) (pediatric) was given IRB Approval via Expedited Review to enroll in a Single Patient Protocol on May 3, 2012 and was approved by the full IRB meeting on August 3, 2012.

(D) Subject (b) (4) (adult) was given IRB Approval via Expedited Review to enroll in a Single Patient Protocol on June 21, 2012 and was re-approved via an expedited mechanism after FDA requested changes to the informed consent document on July 19, 2012.

(E) Subject (b) (4) (adult) was given IRB Approval via Expedited Review to enroll in a Single Patient Protocol on two separate occasions; On June 21, 2012 and again on July 20th, 2012 after FDA requested changes to the informed consent. The Single Patient Protocol was approved by the full IRB meeting on October 19, 2012.

SEE REVERSE OF THIS PAGE	EMPLOYEE(S) SIGNATURE Andrea A. Branche, Investigator Patrick J. Mcneilly, Investigator	DATE ISSUED 02/07/2013

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	01/22/2013 - 02/07/2013* FEI NUMBER 1000220451

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED

TO: Carlton F. Hazelwood, Ph.D., Chairman

FIRM NAME	STREET ADDRESS
BRI-IRB	9432 Katy Freeway # 370
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OBSERVATION 2

The IRB approved the conduct of research, but did not determine that the risks to subjects were reasonable in relation to the anticipated benefits (if any) to subjects, and to the importance of the knowledge that might be expected to result.

Specifically, Your IRB gave Expedited Approval for several Single Patient Protocols (SPP) without all the clinical information necessary to determine that the risk to subjects are minimized. For Example:

(A) Subject #(b) (4) was given IRB Approval via Expedited Review on June 21, 2012, by the IRB Vice-Chairman. The information provided by the Investigator only included the Informed Consent document. No additional clinical and/or health history information was provided prior to provisional and subsequent full board approval.

(B) Subject #(b) (4) was given IRB Approval via Expedited Review on June 21, 2012, by the IRB Vice-Chairman. The information provided by the Investigator only included the Informed Consent document. No additional clinical and/or health history information was provided prior to provisional and subsequent full board approval.

(C) Subject #(b) (4) was given IRB Approval via Expedited Review on June 21, 2012, by the IRB Vice-Chairman. The information provided by the Investigator only included the Informed Consent document. No additional clinical and/or health history information was provided prior to provisional and subsequent full board approval.

(D) Subject #(b) (4) was given IRB Approval via Expedited Review on July 28th, 2011 by the IRB Chairman. The Expedited Review approval included a request stating, "Please clarify history and physical for assigning (b) (4) - not evident at present." This information was needed to ensure risks were reasonable in relation to benefits.

OBSERVATION 3

The IRB did not determine at the time of initial review that a study was in compliance with 21 CFR Part 50 Subpart D, "Additional Safeguards for Children in Clinical Investigations."

Specifically, An IRB that reviews and approves research involving children is required to make a

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finding at the time of approval that the study is in compliance with 21 CFR 50, Subpart D" Additional Safeguards for Children in Clinical Investigations." Your IRB approved research involving children without documentation of the IRBs finding that the clinical investigation satisfied the criteria under Subpart D. For Example:

(A) The IRB approved a Single Patient Protocol (SPP) for pediatric subject #(b) (4) on May 2, 2012. There is no documentation of the IRBs determination under 21 CFR 50 Subpart D for this subject.
(B) The IRB approved SPP for pediatric subject #(b) (4) on May 3, 2012. There is no documentation of the IRBs determination under 21 CFR 50 Subpart D for this subject.
(C) The IRB approved SPP for pediatric subject #(b) (4) on March 29, 2012. There is no documentation of the IRBs determination under 21 CFR 50 Subpart D for this subject.

This is a repeat observation from the 10/2010 FDA Inspection.

OBSERVATION 4

The IRB did not follow its written procedure for conducting its initial review of research.

Specifically, The IRB is required to follow its written procedures for conducting initial and continuing review. Your IRB did not follow your procedures for conducting initial and continuing review because these subjects received IRB initial approval via an expedited review procedure not described in your Standard Operating Procedures. If your IRB would have followed your own SOP for initial and continuing review, the following subjects would have received review and approval from the full board rather than through expedited review. For Example:

(A) Subject (b) (4) (pediatric) was given Expedited Review approval for a Single Patient Protocol (SPP) on March 28, 2012 and was approved by the full IRB on August 3, 2012.

(B) Subject (b) (4) (pediatric) was given Expedited Review approval for a SPP on May 2, 2012 and was approved by the full IRB meeting on August 3, 2012.

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(C) Subject (b) (4) (pediatric) was given Expedited Review approval for a SPP on May 3, 2012 and was approved by the full IRB meeting on August 3, 2012.

(D) Subject (b) (4) (adult) was given Expedited Review approval on two occasions for a SPE on June 21, 2012 and after FDA requested changes to the informed consent document on July 19, 2012. The SPP was approved by the full IRB meeting on October 19, 2012.

(E) Subject (b) (4) (adult) was given Expedited Review approval on two occasions for an SPP on June 21, 2012 and after FDA requested changes to the informed consent document on July 20, 2012. The SPP was approved by the full IRB meeting on October 19, 2012 .

OBSERVATION 5

The IRB has no written procedures for ensuring prompt reporting to the IRB, appropriate institutional officials, and the FDA of any unanticipated problems involving risks to human subjects or others.

Specifically, Your current SOP -2012 v2-draft doc does not describe the requirements of Investigators on how unanticipated problems are reported to the IRB, Institutional Official, and the FDA, such as time intervals and the mode of reporting, or otherwise address how the prompt reporting of such instances will be ensured.

OBSERVATION 6

The IRB has no written procedures for ensuring prompt reporting to the IRB, appropriate institutional officials, and the FDA of any instance of serious or continuing noncompliance with theses regulations or the requirements or determinations of the IRB.

Specifically, Your current SOP - 2012 v2-draft doc does not address how the IRB will report issues of serious or continuing noncompliance to [appropriate institutional officials and/or FDA], or otherwise address how the prompt reporting of such instances will be ensured.

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DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

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OBSERVATION 7

A list of IRB members has not been prepared and maintained, identifying members by name, earned degrees, representative capacity, and any employment or other relationship between each member and the institution.

Specifically, The IRB Roster does not include the member employment or other affiliation between the member and the IRB.

*** DATES OF INSPECTION:**
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), 02/05/2013(Tue), 02/06/2013(Wed), 02/07/2013(Thu)

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