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TITLE: PET Imaging of Estrogen Metabolism in Breast Cancer

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Fort Detrick, Maryland 21702-5012

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13. ABSTRACT (Maximum 200 Words) We propose that estrogen metabolism in breast cancer can be imaged with positron emission tomography (PET). It is well known that many breast tumors associate with estrogen and the presence of catecholestrogens in breast tumors cause changes in the DNA which may lead to uncontrolled cell growth. Catecholestrogens are broken down by an enzyme called catechol-O-methyltransferase (COMT). COMT is known to be elevated in malignant breast tumors, and abnormal COMT genetics have recently been found in individuals with breast cancer. We have developed [¹⁸ F]Ro41-0960, the first radiotracer for visualizing COMT with PET. The hypothesis that [¹⁸ F]Ro41-0960 can map COMT was demonstrated both <i>in vivo</i> and <i>ex vivo</i> in baboon and rodents. We have also adapted our COMT enzyme assay method and performed studies in breast tumor tissue samples from cancer patients undergoing surgery. Preliminary results showed elevated COMT activities in the breast tumor tissues of all patients studied; the difference can be as high as 26 fold increase. We then carried out toxicology tests and submitted an IND application that was finally approved by the FDA on Oct., 1999 to conduct studies in breast cancer patients. After receiving the IND, we have been working on documents that required to get approvals from the HSRRB at US Army Medical Research and local IRBs at BNL and Stony Brook. This novel approach to an extremely important medical problem goes beyond diagnosis in that it seeks to delineate the fundamental biochemical properties and molecular signatures of tumor cells. PET imaging studies on breast cancer patients are underway.				
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INTRODUCTION

The progressive increase in the number of women suffering with breast cancer places a sense of urgency on the development of diagnostic methods. The current method, mammography, is limited by its high degree of false positives which results in unnecessary biopsies. A noninvasive imaging technique to discriminate between benign and malignant breast masses and detect breast cancer metastases to axillary lymph nodes could reduce many breast biopsies and lymph node dissections following mammography prior to the implementation of definitive therapy. We propose to develop a radiotracer to characterize the biochemical profile of breast tumors using positron emission tomography (PET). It has been reported that the activity of catechol-O-methyltransferase (COMT; EC 2.1.1.6), a soluble enzyme that catalyzes the O-methylation of various catechols including catecholestrogens, is elevated in highly malignant human breast tumors (Amin and Ismail, 1983; Assicot, et al., 1977; Hoffman, et al., 1979; Vandewalle, et al., 1985) and abnormal COMT genetics have recently been found in individuals with breast cancer (Lavigne, et al., 1997; Matsui, et al., 2000; Mitrunen, et al. 2001). The feasibility of mapping COMT in vivo with PET is supported by our recent baboon studies using a highly selective and potent fluorine-18 labeled COMT inhibitor, [¹⁸F]Ro41-0960 (Ding, et al., 1996; Ding, et al., 1997, 1998). The goals of this proposal are to: (1) correlate the radiotracer bindings with COMT activities in normal and abnormal tissues from the same patient suffering with breast cancer; (2) initiate PET studies in human subjects (female normal controls and females with grade III and IV breast carcinomas). We predict that the uptake of [¹⁸F]Ro41-0960 in breast tumor will be substantially greater than background and that the uptake of the radiotracer will be quantitatively different between normal controls and grade III and IV breast carcinomas. It is believed that the localization and quantitation of COMT in breast tumors would be important in understanding its role in the metastases of breast tumor. These studies will set the stage for the development of a diagnostic tool to characterize the biochemical profile of breast tumors in human subjects. If successful, the benefit of this new method would lead to a better understanding of the biochemistry of human breast cancer, reduce the need for unnecessary breast biopsies and enhance the staging capabilities of current diagnostic procedures. Furthermore, this novel approach to an extremely important medical problem goes beyond diagnosis in that it seeks to delineate the fundamental biochemical properties and molecular signatures of tumor cells.

Technical Objectives

Specific Aim 1.

In vitro studies in breast tumor tissue samples from cancer patients undergoing surgery: We will determine whether the degree of binding of [^{18}F]Ro41-0960 is sensitive to and reflects the activity of COMT. The correlation between the radiotracer bindings and COMT activities will serve as a model prior to human PET studies.

Specific Aim 2.

Human PET imaging: We will determine feasibility of PET imaging of COMT with [^{18}F]Ro 41-0960 in human breast cancer patients with palpable breast carcinomas. As part of these studies, we will correlate [^{18}F]Ro41-0960 binding with COMT levels obtained by analysis of biopsied tissue. For this specific aim, in order to conduct PET scanning in human breast cancer patients, we have to: (a) carry out toxicology studies and obtain an IND for using [^{18}F]Ro41-0960 in humans; (b) obtain approvals for carrying out studies in human from both the Human Subjects Research Review Board (HSRRB) at the US Army Medical Research and Material Command, and from local IRBs, including our institute (BNL) and collaborating institute (SUNY at Stony Brook). Breast cancer patients will be recruited from Stony Brook Hospital, and PET scans with [^{18}F]Ro41-0960 will be conducted on patients at BNL.

PROGRESS REPORT

Specific Aim (1): Correlate [^{18}F]Ro41-0960 binding with COMT activities in normal and abnormal tissues from the same patient suffering with breast cancer.

We have demonstrated in baboon and mouse that the binding of [^{18}F]Ro41-0960 to COMT sites in periphery is saturable and sensitive to COMT inhibition [Ding, et al.,1996; Ding, et al.,1998; Ding, et al.,1997]. An *ex vivo* approach in which we correlated the radiotracer uptake with COMT activities in rodents further demonstrated the ability of [^{18}F]Ro41-0960 in mapping COMT activity *in vivo* [Ding, et al.,1999]. We have also adapted our COMT enzyme assay method and performed studies in breast tumor tissue samples from cancer patients undergoing surgery. COMT activities in normal and abnormal human breast tissues from the same patient were compared. This will serve as a model prior to human studies.

COMT activities in normal and abnormal human breast tissues from the same patient were compared. Protein assay was used to normalize the amount of protein used in each experiment, and COMT activity was expressed as pmole of radioactive metanephrine formed per 20 min per mg of cytosol protein [Lowry, et al., 1951]. Though COMT activities varied among subjects, preliminary results showed elevated COMT activities in the breast tumor tissues of all patients studied; the difference can be as high as a 26 fold increase. This could be a potential signal to noise ratio for the future PET studies with [^{18}F]Ro41-0960 in breast cancer patients. The most important finding is that these data were consistent with the pathology reports obtained for each patient.

Specific Aim (2): Initiate studies in human subjects (females with positive needle biopsy and palpable breast tumor). This specific aim has three major goals: (a) carry out toxicology studies and obtain an IND for using [^{18}F]Ro41-0960 in humans; (b) obtain

approvals for carrying out studies in human from both the Human Subjects Research Review Board (HSRRB) at the US Army Medical Research and Material Command, and from local IRBs, including our institute (BNL) and collaborating institute (SUNY at Stony Brook); (c) PET scanning in human breast cancer patients.

(a) carry out toxicology studies and obtain an IND for using [¹⁸F]Ro41-0960 in humans:

On February 1998, we submitted an IND to apply for permission to carry out human PET studies with [¹⁸F]Ro41-0960 and have been in communication with the FDA since then. Though the amount of [¹⁸F]Ro41-0960 which we will use in humans is very small (a total dose of 5 µg required for a PET study is on the order of 1x10⁶ below its lethal dose), the FDA requires a toxicology study be performed by a GLP laboratory before they can approve the use of the tracer in PET studies. We purchased an acute toxicity study from Covance Laboratory (Princeton, NJ) in the rat. The acute toxicity of Ro41-0960 was evaluated in female rats when the test material was administered as a single intravenous injection. All animals appeared normal throughout the study. There were no significant differences in body weights or body weight gains between the control and test groups. Administration of the test material had no related effects on clinical pathology test results. Administration of the control or test materials did not result in any macroscopic or microscopic lesions or findings at necropsy that were directly related to the test or control materials. The No Observance Effect Level (NOEL) for Ro41-0960 given as a single intravenous injection to female rats was 0.6 mg/kg.

Our IND application to carry out human PET studies was finally approved by the FDA on October 1, 1999

(b) obtain approvals for carrying out studies in human from both the Human Subjects Research Review Board (HSRRB) at the US Army Medical Research and Material Command, and from local IRBs, including our institute (BNL) and collaborating institute (SUNY at Stony Brook):

After received the IND from the FDA, we submitted a human study protocol and obtained approvals from the IRB of Brookhaven National Laboratory (BNL) on May 30, 2000, and from our collaborating institute (Stony Brook University, Hospital & Medical Center) on Jan. 20, 2000. We then submitted a package of documents to the HSRRB at the US Army Medical Research and Material Command on July 31, 2000 (see Appendix A). The first review by the HERRB was conducted on Sept. 13, 2000 and the second review was on Dec. 19, 2000. After all the revisions, the revised protocol and consent forms for both BNL and Stony Brook were finally pre-approved by the US Army Medical Research and Material Command on Jan. 16, 2001.

A final approval won't be given until re-approvals from two IRBs on the revised protocol and consent forms are received by the HSRRB. The revised protocol and consent forms were re-approved by the IRB at BNL on April 17, 2001. Currently, we are waiting for the re-approval from Stony Brook.

(c) PET scanning in human breast cancer patients:

Once we receive the final approval from the HSRRB at the US Army Medical Research and Material Command, we'll recruit breast cancer patients from Stony Brook Hospital and carry out PET scans with [¹⁸F]Ro41-0960 at BNL.

KEY RESEARCH ACCOMPLISHMENTS

(1). COMT activities in normal and abnormal human breast tissues from the same patient were compared. Preliminary results showed elevated COMT activities in the breast tumor tissues of all patients studied; the difference can be as high as a 26 fold increase. This will serve as a model prior to human studies.

(2). Our IND application to carry out human PET studies was approved by the FDA on October 1, 1999.

(3). The revised protocol and consent forms have been pre-approved by the HSRRB at the US Army Medical Research and Material Command, and re-approved by the IRB at BNL to carry out PET studies using [^{18}F]Ro41-0960 on breast cancer patients.

REPORTABLE OUTCOMES

Manuscripts:

Ding, Y-S. Fluorine-18 Labeled Biomolecules for PET Studies in the Neurosciences. *J. Fluorine Chem.* 101, 291-295 (2000).

Oral presentations (Invited lectures):

The Cancer Institute of Long Island at Stony Brook, School of Medicine, State University of New York at Stony Brook, New York, June 14, 2000. (*Novel Approach to Image Estrogen Metabolism in Breast Cancer Using PET*)

Scientific Committee, representative of Life Science, presenting one of the three labwide scientific talks to the Department of Energy Office of Science, Institutional Plan On-Site Review, July 24, 2000. (*PET Imaging of Chemistry in Living Systems*)

MRC Cyclotron Unit, Imperial College School of Medicine, Hammersmith Hospital, United Kingdom, October 16, 2000. (*Highlights of PET Studies at Brookhaven*)

Wolfson Brain Imaging Centre, University of Cambridge Clinical School, United Kingdom, October 18, 2000. (*Highlights of PET Studies at Brookhaven*).

DOE Biological and Environmental Research Nuclear Medicine Workshop, Williamsburg, VA, October 17-20, 2000. (*Radiotracer Chemistry and Technology Development and Applications*).

CONCLUSIONS

Our ability to assay COMT activities in human breast tissues sets the stage for us to examine the role of COMT in breast cancer, and will allow us to correlate between the radiotracer bindings and tissue COMT activities in the future PET imaging studies with [^{18}F]Ro41-0960. Preliminary results showing elevated COMT activities in the breast tumor tissues of all patients studied support our hypothesis that elevated uptake of [^{18}F]Ro41-0960 would be observed in breast cancer patients.

This novel approach to an extremely important medical problem goes beyond diagnosis in that it seeks to delineate the fundamental biochemical properties and molecular signatures of tumor cells. The benefit of this new knowledge would lead to a better understanding of the biochemistry of human breast cancer, suggest new therapies based on the tumor's molecular profile, and enhance the detecting and staging capabilities

of current diagnostic procedures. Unfortunately, obtaining all the approvals that are required to initiate the PET imaging studies in human has been far from straightforward. With all the effort and time we have invested on this project, and considering the seriousness of breast cancer and the need for reliable diagnostic procedures, we intend to see the scientific outcome of this project in spite of what hurdles are in front of us.

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Appendices:

**A. Initial submission to the HSRRB at US Army Medical Research and
Material Command.**

Appendix A

Dear HSRRB members,

Thank you very much for your time and effort to review once again our protocol for breast cancer studies. I'm writing to request that you reconsider giving us your final approval to our protocol. We understand it would probably be more clear if the two groups involved in the study have their own informed consent; however, this would cost so much time to restart this cycle all over again. That is, this new revised version would again go through our BNL's IRB and Stony Brook's IRB review again. The paper work will go back and forth, waiting around for two IRB meeting reviews and the signatures of all investigators, and then finally go back to your HSRRB for another review. This would require at least another half year! That is, we will have spent a total of about three years revising the protocol over and over again and shuffling it from one IRB to another IRB to get re-approved since receiving its initial approval in Nov. 1999 from our IRB. Sadly, so far no study has ever happened! Frankly speaking, this additional recommendation (two new consent forms) does not add any strength to the scientific outcome of this project, neither does it provide additional protection for patients. I would appreciate it very much if you would reconsider your decision and give your final approval to this protocol without the revision requested.

As you are probably aware, this protocol, which received our IRB initial approval in Nov. 1999 and Stony Brook's (our collaborating hospital) approval in early 2000, was subjected to the first HSRRB review in Sept. 2000 and the revised version was given conditional approval by the HSRRB in Jan. 2001. When the revised version was sent back to our BNL's IRB and Stony Brook's IRB to get re-reviewed, Dr. Kemeny, our collaborator for this breast cancer study, left Stony Brook. In order to get the re-approval for the consent form from Stony Brook, I talked to many surgeons, received many suggestions, and finally a new investigator, Dr. Brain O'Hea, agreed to be the collaborating PI at Stony Brook. Now, based on the HSRRB review meeting on Mar. 13, 2002, we have to re-revise the protocol again and restart this "time consuming cycle" once again.

The funding for this project is supposed to end in September of this year. I have been trying so hard to overcome all the administrative hurdles and hoping to start the studies as soon as I can get the final approvals from all the IRBs. I hope you can understand all the time and effort I have devoted to this project and all the frustration that I have experienced, only hoping that someday soon I'll see the scientific outcome of this study.

As we all know, this is a pilot study. It would be tremendously important to carry out the study to show whether or not this novel idea can provide vital information to allow us to better understand breast cancer, and whether or not this study can provide a new diagnostic tool to detect breast cancer. However, as of now, we are still struggling to get approvals, even though the FDA had issued the IND in Oct. 1999. We need the financial support of the USAMRMC in order to carry out this study. Most likely, we won't be able to initiate the study soon and we

would like to request continued funding for the next two years in order to accomplish the goal of this research. Please let me know how I should proceed in this matter. Thanks so much.

Sincerely,

XXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXX

Yu-Shin Ding, Ph.D.

Senior Scientist

Head of Radiotracer Development

Neuroscience and Imaging Group

Chemistry Department

Brookhaven National Laboratory

Upton, NY 11973-5000

E-mail: ding@bnl.gov

Phone: (631) 344-4388

FAX: (631) 344-7902

Yu-Shin Ding

Pierson, Jerry F LTC USAMRMC, 4/18/01 11:19 AM -0400, RE: FW: HSRRB

From: "Pierson, Jerry F LTC USAMRMC" <Jerry.Pierson@DET.AMEDD.ARMY.MIL>
To: "Dr. Yu-Shin Ding" <ding@bnl.gov>
Subject: RE: FW: HSRRB minutes
Date: Wed, 18 Apr 2001 11:19:58 -0400

Thanks - I will be looking for them in the mail - if received early enough, I may be able to get the protocol to COL Zadinsky before the end of the week for approval - jp

-----Original Message-----

From: Dr. Yu-Shin Ding [<mailto:ding@bnl.gov>]
Sent: Wednesday, April 18, 2001 11:24 AM
To: Pierson, Jerry F LTC USAMRMC
Subject: RE: FW: HSRRB minutes

Dr. Pierson,

I just sent the two approvals and two consent forms to the following address:

Commander, USAMRMC

ATTN: MCMR-RCQ (LTC Pierson)

504 Scott Street

Fort Detrick, MD 21702-5012

The package should arrive tomorrow. Please look for it. Please also let me know when they will be reviewed and when they will be given the final approval. Thanks.

Yu-Shin Ding

Dr. Ding,

Thank you for the update. There is nothing else that I am waiting on at this time. Regards.

Jerry Pierson

-----Original Message-----

From: Dr. Yu-Shin Ding [<mailto:ding@bnl.gov>]
Sent: Monday, April 09, 2001 5:32 PM
To: Pierson, Jerry F LTC USAMRMC
Subject: RE: FW: HSRRB minutes

Dear Dr. Pierson,

I should be able to get approvals from both Stony Brook IRB and BNL IRB soon and I'll send them to you as soon as I get them. I have made minor changes (only for clarification purpose) on the consent form (see attachment). I'll mail you a copy of this final revised consent form. Please let me know if there is anything else you need me to include in the mail, besides the two approvals and two consent forms.

Look forward to hearing from you soon.

Yu-Shin Ding

XXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXX

Yu-Shin Ding, Ph.D.,

Senior Scientist

Head of Radiotracer Development

Neuroscience and Imaging Group

Chemistry Department

Brookhaven National Laboratory

Upton, NY 11973-5000

E-mail: ding@bnl.gov

Phone: (631) 344-4388

FAX: (631) 344-7902

Dr. Ding,

I reviewed the documents and found that they met the Board's recommendations. Please obtain local IRB approvals. Thank you.

Jerry Pierson, R.Ph., Ph.D.

Lieutenant Colonel, U.S. Army Medical Service Corps

Chief, Regulatory Affairs

Office of Regulatory Compliance and Quality

U.S. Army Medical Research and Materiel Command

504 Scott Street

Fort Detrick, MD 21702-5012

301-619-2602 (fax 7803)

pager 1-800-946-4646 (pin 1500792)

-----Original Message-----

From: Dr. Yu-Shin Ding [<mailto:ding@bnl.gov>]

Sent: Friday, January 12, 2001 2:20 PM

To: Pierson, Jerry F LTC USAMRMC

Subject: RE: FW: HSRRB minutes

I'm faxing the documents to you now. Total is 30 pages (I have to fax them in several batches). Please let me know if they look OK to you. I look forward to hearing from you soon.

Yu-Shin

Go ahead and fax me the documents as "clean" versions so I can see the form in the same way that the subjects will see the form. Thanks. jp

fax 301-619-7803 or fax 301-619-6694

From: "Pierson, Jerry F LTC USAMRMC" <Jerry.Pierson@DET.AMEDD.ARMY.MIL>
To: "Ding, Yu-Shin" <ding@bnl.gov>
Subject: RE: FW: HSRRB minutes
Date: Mon, 18 Jun 2001 12:19:23 -0400

Yes, I agree, thanks for keeping me informed.

Jerry Pierson

-----Original Message-----

From: Ding, Yu-Shin [<mailto:ding@bnl.gov>]
Sent: Monday, June 18, 2001 12:17 PM
To: Pierson, Jerry F LTC USAMRMC
Cc: Fowler, Joanna; Volkow, Nora D
Subject: RE: FW: HSRRB minutes

Dr. Pierson,

Sadly I was finally informed that Dr. Kemeny, our collaborator for this breast cancer study, just left Stony Brook. In order to get the re-approval for the consent form from Stony Brook, a new investigator has to take the responsibility for this study. Currently, two investigators expressed their interests and we've arranged a meeting to discuss the details about the study with them. I'll keep you informed on this matter. As you know, it hasn't been smooth to get to this stage; after all the effort and time we have investigated on this project, we would like to see the scientific outcome of this project no matter what hurdles are in front of us. I hope you agree with me. Thanks for your concern.

Yu-Shin Ding

> Dr. Ding - any word on the changes to the consent form from Stonybrook?
> Thanks. jp

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-----Original Message-----

> From: Dr. Yu-Shin Ding [<mailto:ding@bnl.gov>]
> Sent: Wednesday, May 09, 2001 1:45 PM
> To: Pierson, Jerry F LTC USAMRMC
> Subject: RE: FW: HSRRB minutes

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> Would you please update me regarding the status of our protocol?

> Thanks.

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> Yu-Shin Ding

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> Yu-Shin Ding

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> Jerry Pierson

> -----Original Message-----

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> Sent: Friday, January 12, 2001 2:20 PM
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> To: Pierson, Jerry F LTC USAMRMC
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> Subject: RE: FW: HSRRB minutes
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> I'm faxing the documents to you now. Total is 30 pages (I have to
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> look forward to hearing from you soon.
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> Yu-Shin
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> Go ahead and fax me the documents as "clean" versions so I can see
> the form in the same way that the subjects will see the form. Thanks. jp
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> fax 301-619-7803 or fax 301-619-6694
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From: "Swatson, Mercy P Ms AMDEX" <Mercy.Swatson@DET.AMEDD.ARMY.MIL>
To: "ding@bnl.gov" <ding@bnl.gov>
Cc: "Christian, Carole B Dr CDMRP" <Carole.Christian@DET.AMEDD.ARMY.MIL>,
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"Pascal, Louise M Ms AMDEX" <Louise.Pascal@DET.AMEDD.ARMY.MIL>,
"Bennett, Jodi Ms USAMRMC" <Jodi.Bennett@DET.AMEDD.ARMY.MIL>,
"Bourne, Juanita M Ms USAMRAA" <Juanita.Bourne@DET.AMEDD.ARMY.MIL>,
"Swatson, Mercy P Ms AMDEX" <Mercy.Swatson@DET.AMEDD.ARMY.MIL>
Subject: Re: Proposal No. BC980045, HSRRB Log No. A-8956,
Date: Mon, 1 Oct 2001 16:47:31 -0400

RE: Protocol Entitled, "PET Studies of Catechol-o-Methyltransferase (COMT) with [18F]Ro41-0960," Submitted by Yu-Shin Ding, Ph.D., Brookhaven National Laboratory,

To Yu Shin Ding, Ph.D.

I am a Human Subject Protection Specialist in the Office of Regulatory Compliance and Quality at USAMRMC, Fort Detrick, Maryland. Your protocol was assigned to me on 18 September 2001 from Col Jerry Pierson. This initial e-mail is to get a sense of where you are in the document submission process of your protocol. From a correspondence dated 14 September 2001, the above protocol was conditionally approved by the HSRRB in December 2000 and is waiting for submission of revisions that would have allowed full approval. If I can be of any assistance to you in your efforts to meet all submission requirements, do not hesitate to let me know.

Additional information on Protocol Submission Guidelines is available on our website at <http://mrmc-www.army.mil>. I look forward to working with you and I hope to hear from you soon.

Mercy P. Swatson, RN, MSN
Human Subjects Protection Specialist (AMDEX Corporation)
U.S. Army Medical Research and Materiel Command
Office of Regulatory Compliance and Quality
Telephone #: 301-619-6237 or DSN 343-2607
FAX #: 301-619-7803 or DSN 343-7803
Electronic Mail: mercy.swatson@det.amedd.army.mil
Mailing Address:
Commanding General
U.S. Army Medical Research and Materiel Command
ATTN: MCMR-RCQ-HR/Mercy P. Swatson, RN, MSN
504 Scott Street
Fort Detrick, Maryland 21702-5012

From: "Swatson, Mercy P Ms AMDEX" <Mercy.Swatson@DET.AMEDD.ARMY.MIL>
 To: "Ding, Yu-Shin" <ding@bnl.gov>
 Cc: "Zadinsky, Julie K COL USAMRMC" <Julie.Zadinsky@DET.AMEDD.ARMY.MIL>,
 "Pascal, Louise M Ms AMDEX" <Louise.Pascal@DET.AMEDD.ARMY.MIL>,
 "Swatson, Mercy P Ms AMDEX" <Mercy.Swatson@DET.AMEDD.ARMY.MIL>
 Subject: RE: Proposal No. BC980045, HSRRB Log No. A-8956
 Date: Tue, 2 Oct 2001 10:26:03 -0400

To Dr. Ding, Yu-Shin.

Thank you for your immediate response to my e-mail . I look forward to receiving the final documents from you soon. Best of luck to you.

Sincerely,

Mercy P. Swatson, RN, MSN
 Human Subject Protection Specialist
AMDEX Corporation

-----Original Message-----

From: Ding, Yu-Shin [mailto:ding@bnl.gov]
Sent: Tuesday, October 02, 2001 9:49 AM
To: mercy.swatson@det.amedd.army.mil
Subject: Re: Proposal No. BC980045, HSRRB Log No. A-8956

Dear Mercy P. Swatson, RN, MSN

Thanks very much for your e-mail. I have been corresponding with Dr. Pierson for quite a while; a few recent correspondences are attached below. As you can see there have been quite a few administrative hurdles that we have experienced. Dr. Kemeny, our collaborator for this breast cancer study, just left Stony Brook. In order to get the re-approval for the consent form from Stony Brook, a new investigator has to take the responsibility for this study. Currently, Dr. Brain O'Hea is willing to be the collaborating PI at Stony Brook and their IRB is going to review the revised protocol and consent forms (they were revised based on USAAMRMC HSRRB's suggestions). I certainly hope that I'll get their approval soon so that I can send to you the final copies of the documents along with the two new approvals from both IRBs at BNL and Stony Brook. Please let me know if you have any questions. Thanks again.

Best regards,

Yu-Shin Ding

XX

Yu-Shin Ding, Ph.D.
 Senior Scientist
 Head of Radiotracer Development
 Neuroscience and Imaging Group
 Chemistry Department
Brookhaven National Laboratory
Upton, NY 11973-5000
 E-mail: ding@bnl.gov
 Phone: (631) 344-4388
 FAX: (631) 344-7902

From: "Swatson, Mercy P Ms AMDEX" <Mercy.Swatson@DET.AMEDD.ARMY.MIL>
To: "Dr. Yu-Shin Ding" <ding@bnl.gov>
Subject: RE: changes made to the protocol and consent of BC980045
Date: Tue, 12 Feb 2002 08:18:05 -0500

To Dr. Yu Shin Ding:

Thank you for submitting these documents. I will reweiw them as soon as I can and I will give you feed back.

Mercy P. Swatson
Human Subjects Protection Scientist
AMDEX Corporation

-----Original Message-----

From: Dr. Yu-Shin Ding [<mailto:ding@bnl.gov>]
Sent: Wednesday, February 06, 2002 3:26 PM
To: Swatson, Mercy P Ms AMDEX
Subject: changes made to the protocol and consent of BC980045

Dear Mercy,

Attached are the documents that you requested. Please let me know if you have any questions. As you can see, it hasn't been smooth to get to this stage; after all the effort and time we have investigated on this project, we would like to see the scientific outcome of this project. I hope you agree with me and help us to achieve the goal of this important research. Thanks very much. I look forward to hearing from you soon.

Best regards,

Yu-Shin Ding

XXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXX
Yu-Shin Ding, Ph.D.
Senior Scientist
Head of Radiotracer Development
Neuroscience and Imaging Group
Chemistry Department
Brookhaven National Laboratory
Upton, NY 11973-5000
E-mail: ding@bnl.gov
Phone: (631) 344-4388
FAX: (631) 344-7902

From: "Swatson, Mercy P Ms AMDEX" <Mercy.Swatson@DET.AMEDD.ARMY.MIL>
To: "ding@bnl.gov" <ding@bnl.gov>
Cc: "Zadinsky, Julie K COL USAMRMC" <Julie.Zadinsky@DET.AMEDD.ARMY.MIL>, "Bennett, Jodi Ms USAMRMC" <Jodi.Bennett@DET.AMEDD.ARMY.MIL>
Subject: FW: Protocol A-8956
Date: Tue, 26 Feb 2002 09:42:42 -0500

This e-mail is to correct the Protocol Number for the e-mail below. The correct protocol number is A- 8956. I apologize for the error.

[Swatson, Mercy P Ms AMDEX]
-----Original Message-----

From: Swatson, Mercy P Ms AMDEX
Sent: Tuesday, February 26, 2002 9:29 AM
To: 'Dr. Yu-Shin Ding'
Cc: Zadinsky, Julie K COL USAMRMC; Bennett, Jodi Ms USAMRMC
Subject: RE: Protocol 10428

To Dr. Ding:

Thank you for responding to my call. I wanted to let you know that I am preparing your protocol to be reviewed by the HSRRB on 13 March 2002. The HSRRB policy is that if a protocol receives conditional approval and does not follow through to receive a full approval within six months, it should received a full Board review. This is because policies and guidelines may have changed, and the protocol and the consent form may have been modified which is true in the case of your protocol.

In preparation to submit your protocol to the Board for review, there are a few documents that I need from you, and a few clarifications that need to be made.

Please submit copies of the following documents or let me know the status of them.

1. A revised FDA 1572 document.
2. A continuing review approval notice from BNL IRB that was due 2 November 2001.
3. Please provide an official IRB approval notice for the latest version of the revised protocol and consent form. The approval document that you submitted was unofficial electronic copy which does not have the signature of the chairman of the IRB or the signature of the designated official.
4. If the data collection forms or the case report forms have changed, please provide updated copies.
5. Please clarify if the consent form that was provided was a combined consent form for BNL and Stony Brook, and if both facilities will use the same consent form.
6. Please clarify if Dr. Nora Volkow of BNL is still on the study team.

Thank you for your immediate attention to these matters. You may fax the documents to me at fax # (301) 619- 7803.

Sincerely,

Mercy P. Swatson, RN, MSN
Human Subjects Protection Specialist (AMDEX Corporation)
U.S. Army Medical Research and Materiel Command
Office of Regulatory Compliance and Quality
Telephone #: 301-619-6237 or DSN 343-2607
FAX #: 301-619-7803 or DSN 343-7803
Electronic Mail: mercy.swatson@det.amedd.army.mil

Mailing Address:
Commanding General
U.S. Army Medical Research and Materiel Command

ATTN: MCMR-RCQ-HR/Mercy P. Swatson, RN, MSN
504 Scott StreetFort Detrick, Maryland 21702-5012

-----Original Message-----

From: Dr. Yu-Shin Ding [<mailto:ding@bnl.gov>]
Sent: Monday, February 25, 2002 12:01 PM
To: Swatson, Mercy P Ms AMDEX
Subject: Re: E- Mail Adress

Dear Mercy,

Sorry I missed your call. Perhaps the sound resolution was pretty bad in our phone system, your message was not clear at all and I could not hear your complete requests. Would you please e-mail me ASAP the list of all the documents that required for your HSRRB review? Thanks very much.

Best regards,

Yu-Shin Ding

XX

Yu-Shin Ding, Ph.D.
Senior Scientist
Head of Radiotracer Development
Neuroscience and Imaging Group
Chemistry Department
Brookhaven National Laboratory

Upton, NY 11973-5000

E-mail: ding@bnl.gov

Phone: (631) 344-4388

FAX: (631) 344-7902

From: "Swatson, Mercy P Ms AMDEX" <Mercy.Swatson@DET.AMEDD.ARMY.MIL>
To: "Dr. Yu-Shin Ding" <ding@bnl.gov>
Cc: "Zadinsky, Julie K COL USAMRMC" <Julie.Zadinsky@DET.AMEDD.ARMY.MIL>
Subject: RE: PET study
Date: Thu, 28 Feb 2002 17:06:39 -0500

To Dr. Ding,

Here are the documents that I received earlier and have included in the packet. The BNL IRB approval letter, the revised FDA 1571 and the letter regarding recruitment of subjects referred from surgeons in the outpatient clinics. I have revised the Read Ahead packet including the above mentioned documents.

Thank you.

Sincerely, Mercy P. Swatson
Human Subjects Protection Scientist
AMDEX Corporation.

-----Original Message-----

From: Dr. Yu-Shin Ding [mailto:ding@bnl.gov]
Sent: Thursday, February 28, 2002 3:13 PM
To: Swatson, Mercy P Ms AMDEX
Subject: Fwd: PET study

Dear Mercy,

I'm back from the meeting. I wonder if you have received everything I sent, and are ready to submit the package to your HSRRB. Please let me know if there is anything that I can do to facilitate the "getting approval" process. Thanks.

Yu-Shin

Dear Mercy,

Attached is one of the e-mails I received from Dr. O'Hea which indicated his willingness to collaborate with us on this breast cancer study. I'll try to get his CV soon.

I also attached the revised CRF form.

Regarding the change on the "age range" for inclusion criteria on the revised protocol, in fact, this age range was originally stated in our IND. For some reasons, it got changed, and now we changed it back in order to be consistent with our IND.

Please let me know if you have further questions. Thanks so much!

Yu-Shin Ding

p.s. I have a meeting 1-3pm this afternoon. Please e-mail me or leave a message if you need to contact me again.

>From: "Brian Ohea" <ohea@surg.som.sunysb.edu>
>Organization: Surgery, SOM SUNY Stony Brook
>To: ding@bnl.gov

>Date: Fri, 7 Sep 2001 12:48:07 -0400
>Subject: PET study
>CC: ctornos@path.som.sunysb.edu (Carmen Tornos)
>Priority: normal
>
>Dr. Ding,
>
>I spoke to Dr. Carmen Tornos, who is our Breast pathologist. I think
>we can get small pieces of cancer and small pieces of normal breast
>on most patients with big tumors. Sometimes, it won't be possible.
>Lymph nodes will be more difficult unless grossly involved. For
>now, we should focus on assays from healthy breast as well as the
>tumor.
>
>Please contact Dr. Tornos 444-2222 or by
>E-mail (ctornos@path.som.sunysb.edu) when we are ready to start.
>
>it was nice meeting with you last week
>
>Dr. O'Hea

From: "Swatson, Mercy P Ms AMDEX" <Mercy.Swatson@DET.AMEDD.ARMY.MIL>
 To: "Dr. Yu-Shin Ding" <ding@bnl.gov>
 Cc: "Zadinsky, Julie K COL USAMRMC" <Julie.Zadinsky@DET.AMEDD.ARMY.MIL>,
 "Bennett, Jodi Ms USAMRMC" <Jodi.Bennett@DET.AMEDD.ARMY.MIL>
 Subject: RE: PET study
 Date: Thu, 7 Mar 2002 09:41:11 -0500

To Dr. Ding.

Thank you for that information. The packet for the Board members had already gone out when your message was delivered. Besides, there was not enough time to prepare the updated protocol for North Shore Hospital for this Board meeting. You should please submit a complete packet for amendment to add North Shore Hospital as an additional patient recruitment site. Please submit a letter of amendment, the updated protocol and consent form that was approved by the North Shore IRB, the IRB approval letter, a letter of collaboration from the collaborator at Northshore and his/her CV.

Thank you for your cooperation.

Mercy P. Swatson, RN, MSN.
 Human Subjects Protection Specialist
AMDEX Corporation

-----Original Message-----

From: Dr. Yu-Shin Ding [<mailto:ding@bnl.gov>]
Sent: Friday, March 01, 2002 2:35 PM
To: Swatson, Mercy P Ms AMDEX
Subject: RE: PET study

Thank you. I just found out that our addendum to add North Shore Hospital as a collaborator got approved yesterday. Do you want me to send you the updated protocol and approval once I receive it? Please let me know.

Thanks again.

Yu-Shin Ding

Yes, the revised CRFs were included.

Thank you.

Mercy Swatson

-----Original Message-----

From: Dr. Yu-Shin Ding [<mailto:ding@bnl.gov>]
Sent: Thursday, February 28, 2002 5:29 PM
To: Swatson, Mercy P Ms AMDEX
Subject: RE: PET study

Did you include the CRF form? Thanks very much!

Yu-Shin

To Dr. Ding,

Here are the documents that I received earlier and have included in the packet. The BNL IRB approval letter, the revised FDA 1571 and the letter regarding recruitment of subjects referred from surgeons in the outpatient clinics. I have revised the Read Ahead packet including the above mentioned documents.

Thank you.

Sincerely, Mercy P. Swatson
Human Subjects Protection Scientist
AMDEX Corporation.

From: "Swatson, Mercy P Ms AMDEX" <Mercy.Swatson@DET.AMEDD.ARMY.MIL>
To: "ding@bnl.gov" <ding@bnl.gov>
Cc: "Zadinsky, Julie K COL USAMRMC" <Julie.Zadinsky@DET.AMEDD.ARMY.MIL>
Subject: Re Protocol A- 8956
Date: Mon, 11 Mar 2002 14:13:41 -0500

To Dr. Ding,

On page 10/14 of the protocol, the Medical Monitor section indicates that the Medical Monitor has the authority "to suspend the entire study for review by the WRAMC (Walter Reed Army Medical Center) Human Use Committee (HUC) at any time; 4) notification ... the Department of Clinical Investigation..."

Since the protocol is not being executed at WRAMC, it would seem that these references to WRAMC-specific entities (e.g., the HUC and DCI) need to be changed to reflect the Brookhaven National Laboratory IRB.

It is noted in the latest version of the protocol that you have changed the medical monitor from Dr. John L Coulehan to Dr. Helene Benveniste. We do not have Dr. Benveniste's CV on file. Could you please fax her CV/biosketch to me today/as soon as possible in order to make it available to the Board members to review.

Thank you for your cooperation.

Mercy P. Swatson, RN, MSN
Human Subjects Protection Scientist
AMDEX Corporation

From: "Swatson, Mercy P Ms AMDEX" <Mercy.Swatson@DET.AMEDD.ARMY.MIL>
To: "Dr. Yu-Shin Ding" <ding@bnl.gov>
Subject: RE: Re Protocol A- 8956
Date: Tue, 12 Mar 2002 14:35:51 -0500

To Dr. Ding

Thanks for sending the CV for Dr. Helene Benveniste.

Mercy P. Swatson, RN, MSN.

-----Original Message-----

From: Dr. Yu-Shin Ding [mailto:ding@bnl.gov]
Sent: Tuesday, March 12, 2002 10:49 AM
To: Zadinsky, Julie K COL USAMRMC; Swatson, Mercy P Ms AMDEX
Subject: Fwd: Re Protocol A- 8956

Dear Dr. Zadinsky and Mercy,

Attached please find the medical monitor's CV (Dr. Helene Benveniste) for our breast cancer study. I also attached the updated recap sheet from our IRB to indicate that all the addendum we submitted have been approved by our IRB. I hope it would be useful for you and for your HSRRB review. If there are any questions, please do not hesitate to ask me. Thanks.

Yu-Shin Ding

p. s. I'll also fax you a copy of those documents.

XX

Yu-Shin Ding, Ph.D.
Senior Scientist
Head of Radiotracer Development
Neuroscience and Imaging Group
Chemistry Department
Brookhaven National Laboratory
Upton, NY 11973-5000
E-mail: ding@bnl.gov
Phone: (631) 344-4388
FAX: (631) 344-7902

Dear Mercy,

I just got back from a business trip to DC. I'm trying to get the medical monitor's CV you requested. I'll fax it to you as soon as I receive it. Please let me know if there is any questions.

Thanks.

Yu-Shin Ding

outpatient clinics where patients would be referred from. The Board made additional recommendations to the protocol and the consent form documents. Complete Board recommendations will be sent to you soon so that you can incorporate the recommendations in the revised protocol and the consent form.

3. You are reminded not to initiate this study until you have resolved all human subjects protection issues and you have received HSRRB approval.

4. Please contact Ms. Mercy Swatson at mercy.swatson@det.amedd.army.mil or at (301) 619-6237 for questions about the HSRRB review of the subject protocol.

Sincerely,

Mercy P. Swatson, RN, MSN

Human Subjects Protection Scientist

AMDEX Corporation

From: "Swatson, Mercy P Ms AMDEX" <Mercy.Swatson@DET.AMEDD.ARMY.MIL>
To: "Dr. Yu-Shin Ding" <ding@bnl.gov>
Subject: RE: Re Protocol A-8956
Date: Wed, 17 Apr 2002 09:07:29 -0400

That will be fine.

Mercy

-----Original Message-----

From: Dr. Yu-Shin Ding [<mailto:ding@bnl.gov>]
Sent: Wednesday, April 17, 2002 9:04 AM
To: Swatson, Mercy P Ms AMDEX
Subject: RE: Re Protocol A-8956

Another question, whom I should address to on my response letter? Is this correct?
JULIE K. ZADINSKY, COL,
Acting Chair, Human Subjects
Research Review Board

To Dr. Ding,

You should mail all materials to:

Commanding General

U.S. Army Medical Research and Materiel Command

ATTN: MCMR-RCQ-HR/Mercy P. Swatson, RN, MSN,

504 Scott Street

Fort Detrick, Maryland 21702-5012

The fax number is (301) 619-7803

Mercy Swatson

HSP Scientist

AMDEX Corporation

-----Original Message-----

From: Dr. Yu-Shin Ding [<mailto:ding@bnl.gov>]
Sent: Tuesday, April 16, 2002 3:40 PM
To: Swatson, Mercy P Ms AMDEX
Subject: Re: Re Protocol A-8956

Mercy,

Please advise me the address that all the documents that are supposed to mail to. Thanks.

XXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXX

Yu-Shin Ding, Ph.D.
Senior Scientist
Head of Radiotracer Development
Neuroscience and Imaging Group
Chemistry Department
Brookhaven National Laboratory
Upton, NY 11973-5000
E-mail: ding@bnl.gov
Phone: (631) 344-4388
FAX: (631) 344-7902 or 344-5815

SUBJECT: Protocol Entitled "PET Studies of Catechol-O- Methyltransferase (COMT) with [18F]Ro41-0960," Submitted by Yu-Shin Ding, Ph.D., Brookhaven National Laboratory, HSRRB Log No. A-8956, CDMRP Proposal BC980045 (IND-55,193 - Sponsor, Dr. Yu-Shin Ding, Brookhaven National Laboratory)

To Dr. Ding,

1. I am sending this e-mail on behalf of the Acting Chair of the HSRRB who is still conducting the Board meeting.
2. The Surgeon General's Human Subjects Research Review Board (HSRRB) reviewed the subject protocol and the supporting documents on 13 March 2002 for compliance with applicable Human Subjects Protection regulations and guidelines. The Board has withheld approval of your protocol and has requested that you clarify the two study groups in the protocol and consent form. The Board recommended that the two groups involved in the study should be clearly defined in the protocol and each group should have its own informed consent. The Board also requested clarification regarding which Institutional Review Board (IRB) oversees the outpatient clinics where patients would be referred from. The Board made additional recommendations to the protocol and the consent form documents. Complete Board recommendations will be sent to you soon so that you can incorporate the recommendations in the revised protocol and the consent form.
3. You are reminded not to initiate this study until you have resolved all human subjects protection issues and you have received HSRRB approval.
4. Please contact Ms. Mercy Swatson at mercy.swatson@det.amedd.army.mil or at (301) 619-6237 for questions about the HSRRB review of the subject protocol.

Sincerely,

Mercy P. Swatson, RN, MSN
Human Subjects Protection Scientist
AMDEX Corporation

From: "Swatson, Mercy P Ms AMDEX" <Mercy.Swatson@DET.AMEDD.ARMY.MIL>
To: "Dr. Yu-Shin Ding" <ding@bnl.gov>
Subject: RE: Protocol A-8956 : responses to the HSRRB Review (3/13/02)
Date: Wed, 17 Apr 2002 12:05:57 -0400

To Ding:

Thank you for sending the revised protocol, consent form and the responses to the Board recommendations that were sent electronically. The CV for Dr. O'Hea and letters from Italo, Zanzi, M.D., and Brian O'Hea that were faxed have been received.

Mercy P. Swatson, RN, MSN

-----Original Message-----

From: Dr. Yu-Shin Ding [<mailto:ding@bnl.gov>]
Sent: Wednesday, April 17, 2002 11:14 AM
To: Swatson, Mercy P Ms AMDEX
Subject: Protocol A-8956 : responses to the HSRRB Review (3/13/02)

Here are the responses to the HSRRB Review (3/13/02), These include:

1. response letter;
2. revised protocol with changes marked;
3. revised consent with changes marked;
4. CVs:
 - Responsible physician (Associate Investigator)--Dr. Gene-Jack Wang;
 - Collaborators: Stony Brook--Dr. Brian O'Hea *
 - North Shore Hospital--Dr. Italo Zanzi
5. letters of collaboration from Drs. Brian O'Hea and Italo Zanzi *

* Items will be faxed, and the original will be mailed by express mail today.

The rest of the documents are attached to this e-mail. Please let me know if you receive all the e-mail items and the faxed items today. Thanks very much.

Yu-Shin Ding

XXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXX
Yu-Shin Ding, Ph.D.
Senior Scientist
Head of Radiotracer Development
Neuroscience and Imaging Group
Chemistry Department
Brookhaven National Laboratory
Upton, NY 11973-5000
E-mail: ding@bnl.gov
Phone: (631) 344-4388
FAX: (631) 344-7902 or 344-5815

From: "Swatson, Mercy P Ms AMDEX" <Mercy.Swatson@DET.AMEDD.ARMY.MIL>
To: "Dr. Yu-Shin Ding" <ding@bnl.gov>
Subject: RE: Protocol A-8956 : responses to the HSRRB Review (3/13/02)
Date: Wed, 17 Apr 2002 15:21:56 -0400

Yes, I did receive the electronic copies of the CVs for Dr. Gene-Jack Wang and Dr. Italo Zanzi. Sorry I did not make that clear.

Thank you.

Mercy P. Swatson

-----Original Message-----

From: Dr. Yu-Shin Ding [mailto:ding@bnl.gov]
Sent: Wednesday, April 17, 2002 1:54 PM
To: Swatson, Mercy P Ms AMDEX
Subject: RE: Protocol A-8956 : responses to the HSRRB Review (3/13/02)

I'm going to mail you the original letters and documents that I don't have electronic versions. Please let me know ASAP if there is anything else that is required for the next review.

By the way, it was unclear from your previous e-mail whether or not you have also received CVs of Dr. Gene-Jack Wang and Dr. Italo Zanzi in the e-mail I sent you? Please let me know ASAP. Thanks again.

Yu-Shin

To Ding:

Thank you for sending the revised protocol, consent form and the responses to the Board recommendations that were sent electronically. The CV for Dr. O'Hea and letters from Italo, Zanzi, M.D., and Brian O'Hea that were faxed have been received.

Mercy P. Swatson, RN, MSN

-----Original Message-----

From: Dr. Yu-Shin Ding [mailto:ding@bnl.gov]
Sent: Wednesday, April 17, 2002 11:14 AM
To: Swatson, Mercy P Ms AMDEX
Subject: Protocol A-8956 : responses to the HSRRB Review (3/13/02)

Here are the responses to the HSRRB Review (3/13/02), These include:

1. response letter;
2. revised protocol with changes marked;
3. revised consent with changes marked;

4. CVs:

Responsible physician (Associate Investigator)--Dr. Gene-Jack Wang;

Collaborators: Stony Brook--Dr. Brian O'Hea *

North Shore Hospital--Dr. Italo Zanzi

5. letters of collaboration from Drs. Brian O'Hea and Italo Zanzi *

* Items will be faxed, and the original will be mailed by express mail today.

The rest of the documents are attached to this e-mail. Please let me know if you receive all the e-mail items and the faxed items today. Thanks very much.

Yu-Shin Ding

XXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXX

Yu-Shin Ding, Ph.D.

Senior Scientist

Head of Radiotracer Development

Neuroscience and Imaging Group

Chemistry Department

Brookhaven National Laboratory

Upton, NY 11973-5000

E-mail: ding@bnl.gov

Phone: (631) 344-4388

FAX: (631) 344-7902 or 344-5815

From: "Swatson, Mercy P Ms AMDEX" <Mercy.Swatson@DET.AMEDD.ARMY.MIL>
To: "ding@bnl.gov" <ding@bnl.gov>
Cc: "Zadinsky, Julie K COL USAMRMC" <Julie.Zadinsky@DET.AMEDD.ARMY.MIL>,
"Bennett, Jodi Ms USAMRMC" <Jodi.Bennett@DET.AMEDD.ARMY.MIL>,
"Christian, Carole B Dr CDMRP" <Carole.Christian@DET.AMEDD.ARMY.MIL>,
"Pascal, Louise M Ms AMDEX" <Louise.Pascal@DET.AMEDD.ARMY.MIL>,
"Bourne, Juanita M Ms USAMRAA" <Juanita.Bourne@DET.AMEDD.ARMY.MIL>
Subject: Re: A-8956- Follow-Up MFR
Date: Thu, 25 Apr 2002 15:29:34 -0400

SUBJECT: Protocol Entitled, "PET Studies of Catechol-O-Methyltransferase (COMT) With [18F]Ro41-0960," Submitted by Yu-Shin Ding, Ph.D., Brookhaven National Laboratory, Upton, New York, Proposal Log Number BC980045, Award Number DAMD17-99-1-9089, HSRRB Log Number A-8956

To Dr. Ding,

1. Thank you for submitting the revised protocol, consent form and the supporting documents. The Acting Chair of the Human Research Review Board (HSRRB), along with the Area Research Manager of your protocol, a Senior Human Subjects Protection Scientist and I have reviewed your revised human research protocol, and the revised consent form based on the Board recommendations.
2. We have made a few observations regarding the content of your protocol and consent form. At this time, we would like to schedule a conference call with the Acting Chair of HSRRB to discuss the best way to assist you to improve on the organization of the information provided in your protocol.
3. Current recommendations are included in item number 17 of the attached Memorandum For Record (MFR). Please review so that any topics that require clarification may be raised during the conference call.
4. Please contact Ms. Swatson at mercy.swatson@det.amedd.army.mil or at (301) 619-6237 to discuss your availability for the conference call. Appendix J as attached should provide additional guide specific to required elements of a protocol.

<<A-8956.mfr5.doc>> <<Human Subjects Appendix (19 Feb 02).doc>>
Sincerely,

Mercy P. Swatson, RN, MSN
Human Subjects Protection Specialist (AMDEX Corporation)
Telephone #: 301-619-6237 or DSN 343-2607
FAX #: 301-619-7803 or DSN 343-7803
Electronic Mail: mercy.swatson@det.amedd.army.mil

Attachment converted: YSD_System1:A-8956.mfr5.doc (WDBN/MSWD) (00044C2C)
Attachment converted: YSD_System1:Human Subjects Appendix (19 Feb (WDBN/MSWD) (00044C2D)

From: "Swatson, Mercy P Ms AMDEX" <Mercy.Swatson@DET.AMEDD.ARMY.MIL>
To: "Dr. Yu-Shin Ding" <ding@bnl.gov>
Subject: RE: Re Protocol A-8956
Date: Fri, 3 May 2002 11:27:24 -0400

To Dr. Ding;

Thank you for your message. Your revised protocol that was e-mail on 30 April 2002 is currently under review. You should be hearing from us within the next week.

Mercy P. Swatson, RN, MSN
Human Subjects Protection Scientist
AMDEX Corporation

-----Original Message-----

From: Dr. Yu-Shin Ding [<mailto:ding@bnl.gov>]
Sent: Friday, May 03, 2002 9:20 AM
To: Swatson, Mercy P Ms AMDEX
Subject: RE: Re Protocol A-8956

Mercy,

I mailed the brochure, video, and the protocol recertification yesterday, and you should be able to receive it today. Please let me know when you receive it. Thanks.

I also requested our IRB to send you the format that was required by our IRB when this breast cancer study protocol was originally generated. Please let me know if you receive it OK. Thanks.

If you have further questions, please do not hesitate to contact me.

Yu-Shin Ding

XXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXX
Yu-Shin Ding, Ph.D.
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Head of Radiotracer Development
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Brookhaven National Laboratory
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E-mail: ding@bnl.gov
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FAX: (631) 344-7902 or 344-5815

From: "Swatson, Mercy P Ms AMDEX" <Mercy.Swatson@DET.AMEDD.ARMY.MIL>
To: "Dr. Yu-Shin Ding" <ding@bnl.gov>
Subject: RE: Re Protocol A-8956
Date: Tue, 7 May 2002 14:42:23 -0400

To Dr. Ding,

A brochure, a video and a copy of IRB protocol recertification for BNL was received by this office via Federal Express on 3 May 2002. The documents will be reviewed as soon as possible and you will be contacted if there are any human subjects protection issues to be resolved.

Thank you.

Mercy P. Swatson, RN, MSN
Human Subjects Protection Scientist
AMDEX Corporation

-----Original Message-----

From: Dr. Yu-Shin Ding [<mailto:ding@bnl.gov>]
Sent: Friday, May 03, 2002 9:20 AM
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Subject: RE: Re Protocol A-8956

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Yu-Shin Ding

XXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXX

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