The National Oncologic PET Registry (NOPR):

B. Operations Manual for

NOPR (NaF-PET)

Sponsored by: Academy of Molecular Imaging (now World Molecular Imaging Society)

Managed by: American College of Radiology
American College of Radiology Imaging Network

Endorsed by: American College of Radiology
American Society of Clinical Oncology
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National Oncologic PET Registry (NaF-PET) – Schema

Referring Physician
- Refers Patient to PET Facility
- Completes Pre-PET Form (can use blank form)
- Returns it to PET Facility
- Sends Confirmation E-Mail*

PET FACILITY
- Registers Patient via Web Patient Registration Form
- Confirms Referring MD Received Pre-PET Form
- Sends Pre-PET Form*

PET Registry Database at ACRIN HQ
- Sends Confirmation E-Mail*
- Sends Pre-PET Form*
- Reminder Sent q 7 Days if Pre-PET Form not Received*
- Reminder E-mailed q 7 Days if PET Completion or Report Forms not Received

PET must be done and PET Completion Form must be entered within 14 calendar days of patient registration
- Performs PET
- Notifies Database via PET Completion Form
- Interpreting MD completes Scan Assessment Form

Post-PET Form must be entered within 30 calendar days of PET
- Sends Report to Referring MD
- Sends Report and Records If Patient gave Consent to Database via PET Report Form
- Contacts Referring MD if Post-PET Form not received by Day 14
- Enters Post-PET Form into Database
- Case Complete
- CMS Invoiced
- E-mails Case Completion Notice
- Data Sent to CMS Quarterly
- Research Subset Created

- Pre- and Post-PET forms can be sent to and from the referring physician via FAX, mail, or hand delivery.
- The PET Facility enters all forms into the database. **All forms must be entered within 30 calendar days of the PET scan for the case to be eligible for CMS reimbursement.**

* E-mailed to PET Facility

1 Patient Information Sheet asks patient for oral consent to use data for research purposes. The Patient Information Sheet can be given to the patient at any time prior to the PET scan.

2 Referring physician is asked to provide consent for use of their management data as research.

3 All data sent to CMS. Data included in research dataset only if BOTH patient and referring MD information sheets are given.
Abstract-NOPR (NaF-PET)

As discussed in Section A, the National Oncologic PET Registry (NOPR) (http://www.cancerpetregistry.org/) was developed and began collecting data in 2006 and revised in 2009. The NOPR was created in response to the Centers for Medicare and Medicaid Services (CMS) proposal to expand coverage for positron emission tomography (PET) with F-18 fluorodeoxyglucose (FDG) to include cancers and indications not eligible for Medicare reimbursement at that time. Medicare reimbursement for these cancers became available if the patient's referring physician and the provider submit data to a clinical registry to assess the impact of PET on cancer patient management (“coverage with evidence development” [CED]).

In 2009, CMS opened for reconsideration the evidence supporting the use of positron emission tomography with sodium fluoride F-18 (NaF-PET) to identify bony metastasis of cancer. CMS subsequently released its Decision Memo on February 26, 2010 (CAG-00065R) and concluded that the evidence was not sufficient to determine that the results of NaF-PET to identify bone metastases improved health outcomes. The decision memo also concluded that the available evidence was sufficient to allow for NaF-PET coverage under coverage with evidence development.

In response to this decision memo and in consultation with CMS, the NOPR investigators have initiated a new (second) registry within NOPR that builds upon current experience, infrastructure, and staffing for the ongoing FDG-PET evaluations to begin prospective data collection, evaluation, and reporting of NaF-PET. While the overall design and concept of the new registry [hereinafter called NOPR (NaF-PET)] are similar to those of the FDG-PET registry, this manual lays out the revisions in design, endpoints, and statistical plans of the new registry. The NOPR (NaF-PET) registry will again only use the dataset from consented patients and physicians (both referring and interpreting physicians).

Changes in intended patient management as a result of upstaging or downstaging, and changes to more appropriate palliative or curative care are of specific interest.

This section of the NOPR manual addresses the structure, goals, and analysis plan for NOPR (NaF-PET).
B.1.0 Objectives

B.1.1 Primary objective

To assess the effect of NaF-PET on referring physicians’ plans of intended management of patients with known or suspected bone metastases participating in NOPR (NaF-PET).

B.1.2 Secondary objectives

B.1.2.1 To prospectively collect Medicare claims data on NOPR (NaF-PET) participants to allow comparisons between physicians’ intended patient management and actual management (inferred from their claims).

B.1.2.2 To assess the effect of NaF-PET on referring physicians’ plans of intended patient management in relation to:

   B.1.2.2.1 Specific type of cancer (including, but not limited to, prostate, lung, female breast, metastatic cancer of unknown primary origin)

   B.1.2.2.2 Specific symptoms or signs: Bone pain vs. none vs. all other abnormal signs or imaging

   B.1.2.2.3 Indication: Initial staging vs. suspected first recurrence vs. suspected development of bone involvement in patients with known metastatic disease.

   B.1.2.2.4 Working summary stage before NaF-PET

Specifically, attention will focus on:

   a) Detection of unsuspected osseous metastases with otherwise local/regional disease (by cancer type)

   b) Down-staging patients with suspected osseous metastases found to have skeletal changes consistent with non-cancer origins of bone pain (e.g., degenerative disk disease).

B.1.2.3 To assess the impact on the therapeutic plan of NaF-PET when done for treatment monitoring.

Specific attention will focus on timing in the course of intended therapy, duration between monitoring assessments, and cancer type being monitored.

B.2.0 Introduction

B.2.1 Background, Context and Rationale

NaF refers to sodium fluoride F-18. PET refers to positron emission tomography that is usually integrated with computed tomography (PET/CT) and is included in the term PET. NaF-PET refers to PET (or PET/CT) imaging utilizing sodium fluoride F-18 as the radioactive tracer.

Following initial FDA approval in 1972, under New Drug Application (NDA) 17-042 for clinical imaging, sodium fluoride F-18 has been an approved radiopharmaceutical for imaging areas of altered osteogenic activity in bone, but has been rarely used for several decades because of widespread use of conventional bone scintigraphy with Tc-99m phosphate and phosphonate radiopharmaceuticals. Over the last several years, however, there has been increasing interest in the use of NaF-PET (or PET/CT) as an alternative to conventional bone scintigraphy, because of evidence indicating superior sensitivity and specificity. Additionally, recent worldwide shortages of Tc-99m have led to heightened interest in NaF-PET.

In 2009, the Cancer Imaging Program of the Division of Cancer Treatment and Detection of the National Cancer Institute reviewed the literature from 1972 to 2009 about NaF-PET and cancer metastases, as a component of its submission to FDA of a new drug application for sodium fluoride F-18. This review was a major component of the background to the 2010 CMS Decision Memo (CAG-00065R).
The key conclusions of the CMS Decision Memo were that 1) there is inconsistent evidence that the results of NaF-PET scans are used to alter recommended treatment strategy and 2) while current clinical trials are assessing the question, to date there is no evidence on positive benefits of NaF-PET on impacting patient-centered outcomes. However, CMS also concluded that the available evidence is sufficient to determine that NaF-PET to identify bone metastasis of cancer to inform the initial antitumor treatment strategy or to guide subsequent antitumor treatment strategy after the completion of initial treatment is reasonable and necessary under Coverage with Evidence Development (CED) under the following circumstances: (a) when the beneficiary’s treating physician determines that the NaF-PET is needed to inform the initial antitumor treatment strategy or to guide subsequent antitumor treatment strategy after the completion of initial treatment; and (b) when the beneficiary is enrolled in, and the NaF-PET provider is participating in a suitable prospective clinical study. The CMS Decision Memo further indicates that a suitable prospective clinical study must answer one or more of the following questions:

Does NaF-PET imaging used in Medicare beneficiaries inform treating physicians to guide antitumor strategies that lead to:

1) A change in patient management to more appropriate palliative care; or
2) A change in patient management to more appropriate curative care; or
3) Improved quality of life; or
4) Improved survival?

Changes in discrete events that can be readily identified in a prospective trial or registry-claims linkage include surgical procedures, biopsies, anti-cancer chemotherapy and hormonal therapy, short course vs. multi-fraction radiation, and hospitalizations.

Other CMS requirements were a carryover from those requested from earlier versions of the ‘coverage with evidence development’ policy.

In response to the CMS decision memo, the NOPR investigators have developed this registry for NaF-PET. This manual of operations outlines the mechanics and clinical specifics of the data that will be collected and subsequently analyzed by the registry.

The Registry is sponsored by the Academy of Molecular Imaging (AMI) and managed by the American College of Radiology (ACR) through the American College of Radiology Imaging Network (ACRIN). The Registry is endorsed by the ACR, the American Society of Clinical Oncology and the Society of Nuclear Medicine. CMS is an advisor to the Registry.

B.3.0 PET Facility Eligibility and Registration

Table B.1 lists the eligibility criterion, fees, and initial registration information required from each participating PET Facility. A facility that is already registered to participate in NOPR 2009 will also be considered registered to participate in NOPR (NaF-PET). Each participating PET facility is required to keep its PET Facility Information up to date, and will be reminded annually by the NOPR database to confirm that the information is correct.
Table B.1: PET Facility Eligibility and Registration Requirements

| Eligibility                                                                 | PET facility in good standing approved to bill Medicare. The entity applying as a PET facility should be the entity that bills Medicare for either the technical charges or the global charges for PET studies. Mobile PET providers must submit a separate application for each location of service. The PET facility must submit an executed business associate agreement (BAA) to the NOPR before patient registration can begin. The required BAA is available on the NOPR Web site. |
| Fees                                                                       | $50 initial facility registration fee $50 per case registered (prepaid) |
| PET Facility Information                                                   | Name of Imaging Center and entity responsible for payment Address, Telephone number, FAX number Fixed or Mobile Scanner; Hospital or Free Standing |
| PET Facility Administrator                                                 | Name and e-mail address of individual who will serve as official point of contact for correspondence |
| Physicians interpreting PET scans                                          | Names, UPINs or NPIs |
| Staff eligible to register patients and enter data                         | Names, e-mail addresses |
| Equipment description                                                      | Scanner Designation (if facility has more than one scanner) Manufacturer and Model |

B.4.0 Patient Eligibility

All Medicare beneficiaries who are referred for NaF-PET for suspected primary or metastatic cancer are eligible to be included in the NOPR (NaF-PET). In contrast to NOPR 2009, there are no restrictions to specific cancer types.

B.4.1 Exclusions

NaF-PET performed as part of a clinical trial approved by CMS.

B.5.0 Registry Workflow

The schema (page B3 NaF-PET only manual) for NOPR (NaF-PET) is nearly identical to that used in NOPR 2009. The only important change is that in NOPR (NaF-PET), the interpreting physician at the participating PET facility is now required to complete a form summarizing the interpretation of the NaF-PET scan. Appendix B.I contains an expanded narrative description of the NOPR (NaF-PET) workflow and Appendix B.II contains the NOPR (NaF-PET) case report forms.

B.5.1 Patient Registration

The patient registration process is identical to that used in NOPR 2009. When a referring physician contacts a PET facility to schedule a patient for an NaF-PET scan that is eligible for inclusion in the Registry, the PET facility will register the case in the database via a secure Web-based application by providing identifying
information about the patient and referring physician on the *Patient Registration Form*. The database will issue a unique registry case number for that patient and send confirmation e-mail to the PET facility.

At some time before the NaF-PET study, or when the patient arrives for the NaF-PET scan, the PET facility will provide the patient with the ACR IRB-approved standard NOPR Patient Information Sheet that is posted on the NOPR Web site. The patient will be able to contact the NOPR directly for more information, if necessary. The patient will indicate his or her consent verbally to staff at the PET facility, either on the day of the NaF-PET study or by telephone within two working days after the NaF-PET study is completed. Written consent is not required. The PET facility will note in the database, on the F-18 Fluoride PET Report Submission Form, if the patient gave or withheld consent for use of his or her data in future NOPR research.

B.5.2. Pre-PET Form

The process of submitting the Pre-PET form is identical to that used in NOPR 2009.

In addition to the confirmation e-mail sent to the PET facility, if the PET facility indicates on the Case Registration Form that the F-18 Fluoride Pre-PET Form has not yet been received, the NOPR will also send the PET facility a case-specific fax cover sheet and F-18 Fluoride Pre-PET Form. These materials can be used to notify the referring physician that the PET scan will be done under the conditions of the Registry, and that he/she will be required to complete both an *F-18 Fluoride Pre-PET Form* and an *F-18 Fluoride Post-PET Form* in order for the procedure to be covered by CMS. The referring physician must complete and sign the F-18 Fluoride Pre-PET Form and deliver it to the PET facility for **entry into the database by the PET facility by midnight on the day the scan is performed or the case will be declared ineligible.** The referring physician may also download a blank *F-18 Fluoride Pre-PET Form* from the NOPR Web site and send the completed and signed form with the initial patient referral to the PET facility. For all cases, the paper *F-18 Fluoride Pre-PET Form* that is completed and signed by the referring physician must be retained by the PET facility as a source document (and as a document that a Medicare administrative contractor may require in the event of an audit). The data to be collected in the F-18 Fluoride Pre-PET Form, the F-18 Fluoride PET Interpreting Physician Scan Assessment Form, and the F-18 Fluoride Post-PET form are compared in Table B.2.

B.5.2.1 Pre-PET Form Details

The F-18 Fluoride Pre-PET Case Report Form includes clinical questions that have been modestly changed from those collected in the NOPR 2009 registry. The specifics are further described below and in Table B.2. Additional changes made in the form revision dated January 30, 2012 query whether conventional bone scintigraphy was performed in the month before the NaF-PET request and focus on the specific type of additional imaging that would be performed if “Additional Imaging” is selected as the planned patient management.

The F-18 Fluoride Pre-PET form will collect the following information: 1) the clinical indication for imaging, 2) symptoms (bone pain) or signs, or other findings prompting NaF-PET, 3) cancer type with the four most common types provided as checkboxes—lung, female breast, prostate, and metastatic cancer to bone of unknown primary origin, 4) working summary stage, and 5) intended management plan if NaF-PET were not available.

Of particular interest are measuring the frequency of abnormal NaF-PET scans in patients without skeletal pain and the subsequent frequency of initiating bone-directed therapy.

For the indication of treatment monitoring, there are three additional questions.
The classification of the intended management plan options is more complex for the NaF-PET registry. First, the referring physician must indicate whether conventional bone scintigraphy was performed in the month prior to the request for the NaF-PET scan and whether conventional bone scintigraphy would be performed now if PET were not available. He or she then must select one of five options of intended management (observation, other imaging including the type of imaging study, tissue biopsy, supportive care only, or treatment). Second, if treatment is chosen, then the physician is asked to provide information about (1) treatment goal, 2) whether the treatment is targeted at bone or is a systemic therapy, and 3) the type of treatment or treatments to be used (among eight different categories).

As required in NOPR 2009, the referring physician must sign attesting to the data accuracy described above. The research team believes this requirement will markedly reduce the frequency of illogical data entered.

Clinical examples have been prepared to assist the referring physician in completing the F-18 Fluoride Pre-PET Form.

### Table B.2: Timing, Type and Number of Questions in NOPR (NaF-PET) Case Report Forms

<table>
<thead>
<tr>
<th>Pre-PET Form Questions</th>
<th>Number of Questions</th>
<th>Scan Assessment Form Questions</th>
<th>Number of Questions</th>
<th>Post-PET Form Questions</th>
<th>Number of Questions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinical indications (initial staging, restaging/suspected recurrence, treatment monitoring)</td>
<td>1</td>
<td>Overall assessment</td>
<td>1</td>
<td>Compared to pre-PET, impression of extent of patient’s cancer?</td>
<td>1</td>
</tr>
<tr>
<td>Symptoms, signs or other findings prompting imaging</td>
<td>1</td>
<td>Comparisons to other imaging studies</td>
<td>2</td>
<td>Did the PET scan avoid more tests or procedures?</td>
<td>1</td>
</tr>
<tr>
<td>Cancer type</td>
<td>1</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pathologically proven cancer?</td>
<td>1</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Summary stage</td>
<td>1</td>
<td></td>
<td>Summary Stage</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Intended management (see Table B.5)</td>
<td>1 or 2</td>
<td></td>
<td>Intended management (Table B.5)</td>
<td>1 or 2</td>
<td></td>
</tr>
<tr>
<td>For Treatment monitoring only, 3 specific questions</td>
<td>3</td>
<td></td>
<td>For Treatment monitoring, prognosis and potential modifications of therapy plan.</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Physician consent for research use of data</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Total Questions</td>
<td>6 or 9</td>
<td>4</td>
<td></td>
<td>5-7</td>
<td></td>
</tr>
</tbody>
</table>

Note: For patients having NaF-PET done before a tissue diagnosis of cancer has been made, the referring physician will not be asked about intended management on either the Pre-PET or Post-PET Form. Instead, information will be collected regarding the referring physician’s assessment of the likelihood of osseous metastatic disease and whether a tissue biopsy was performed.

### B.5.3 PET Scan Completion and Interpreting Physician Scan Assessment Form
The NaF-PET scan must be completed within two weeks of entering the Patient Registration Form. If the PET scan is delayed for more than two weeks from the time of initial registration, the registration will be cancelled, the PET facility will be notified that this has occurred, and the $50 registration fee will be refunded. If the NaF-PET scan is still to be performed at a later date, it will be necessary for the patient to be registered again, with the expectation that the information on the pre-PET form will be updated, as necessary. These expectations are unchanged from NOPR 2009.

When the NaF-PET scan has been completed, the PET facility documents this by submitting the F-18 Fluoride PET Completion Form via the Web site and uploads the PET report to the database by completing the F-18 Fluoride PET Report Submission Form on the Web site.

New to the NOPR (NaF-PET) registry, the interpreting physician will complete a brief F-18 Fluoride PET Interpreting Physician Scan Assessment Form that will ask for the following information: 1) the overall assessment of the NaF-PET study using a categorical scale, 2) whether the NaF-PET was compared with prior conventional bone scintigraphy or NaF-PET, and whether there was a change in the scan appearance. The interpreting physician is also asked on this form to give consent for use of the data for NOPR research.

The F-18 Fluoride PET Interpreting Physician Scan Assessment Form will be submitted at the same time as the F-18 Fluoride PET Report Submission Form, which contains the NaF-PET report as text inserted on the form.

The PET facility will note on the F-18 Fluoride PET Report Submission Form if the patient gave or withheld consent for use of his or her data in future NOPR research.

B.5.4 Post-PET Form Submission

The process for handling the Post-PET forms is identical to that used in NOPR 2009. The specific questions on the post-PET forms for the different indications for NaF-PET differ slightly and are generally shorter than those used for NOPR 2009.

After the NaF-PET scan has been performed, the PET facility will be e-mailed a case-specific F-18 Fluoride Post-PET Form and fax cover sheet for delivery to the referring physician.

The Post-PET form for NaF-PET scans done for diagnosis of suspected osseous metastasis (without a confirmed primary site) does not ask questions about intended management. Four questions are asked addressing the confirmation of osseous metastases and the avoidance of other procedures.

The Post-PET forms for initial staging and for restaging/suspected recurrence each ask four questions: 1) the impression of the extent of patient’s osseous cancer, 2) working overall summary stage, 3) whether any tests or procedures were avoided, and 4) the next step of patient management in light of the NaF-PET findings.

The Post-PET form for treatment monitoring asks five questions: 1) assessment of response to therapy, 2) assessment of prognosis, 3) potential modifications of the Pre-PET therapeutic plan, 4) the next step of patient management in light of the NaF-PET findings, and 5) whether any tests or procedures were avoided.

As is the case for the F-18 Fluoride Pre-PET Form, the referring physician must complete and sign the F-18 Fluoride Post-PET Form and send it to the PET facility for data entry into the Registry. This form will also include an ACR IRB-approved Referring Physician Information Sheet for the physician. Additionally, the physician will indicate on the Post-PET Form whether consent for use of the response data in future NOPR research has been given or withheld. A reminder notice to the facility will be sent every 7 days if the registry does not receive the Post-PET form.
B.5.5 Case Completion and Reimbursement

The data collection timelines are summarized in Table B.3. After all the required Registry forms have been entered into the database, the Registry will notify the PET facility that it can submit its claim to CMS for the PET study (global or separate professional and technical claims). **Note: All data must be entered into the Registry database within 30 days of the PET scan or the case will not be eligible for CMS reimbursement.**

The NOPR will submit all collected data to CMS. The dataset compiled for use by NOPR investigators will only contain the data for those PET scans where the patient’s and both the referring and interpreting physicians’ consent have been obtained.

**Table B.3: Data Collection Timeline**

<table>
<thead>
<tr>
<th>Form</th>
<th>Completed by</th>
<th>Submitted to</th>
<th>Due Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>Case Registration Form</td>
<td>PET Facility</td>
<td>Database</td>
<td>No more than 2 weeks prior to the PET scan</td>
</tr>
<tr>
<td>F-18 Fluoride Pre-PET Form</td>
<td>Referring Physician</td>
<td>PET Facility for entry into Database</td>
<td>Before Midnight on date of NaF-PET scan</td>
</tr>
<tr>
<td>F-18 Fluoride PET Completion Form*</td>
<td>PET Facility</td>
<td>Database</td>
<td>Within 14 days of registration</td>
</tr>
<tr>
<td>F-18 Fluoride PET Report Submission*</td>
<td>PET Facility</td>
<td>Database</td>
<td>Within 30 days after NaF-PET scan performed</td>
</tr>
<tr>
<td>F-18 Fluoride PET Interpreting Physician Scan Assessment Form*</td>
<td>Interpreting Physician</td>
<td>PET Facility for entry into Database</td>
<td>Within 30 days after NaF-PET scan performed</td>
</tr>
<tr>
<td>F-18 Fluoride Post-PET Form*</td>
<td>Referring Physician</td>
<td>PET Facility for entry into Database</td>
<td>Within 30 days after NaF-PET scan performed</td>
</tr>
</tbody>
</table>

*The F-18 Fluoride PET Completion form must be entered within 14 days of registration and the F-18 Fluoride PET Report Submission, the F-18 Fluoride PET Interpreting Physician Scan Assessment Form and the F-18 Fluoride Post-PET Form must be entered within 30 days after the NaF-PET scan is completed or the NaF-PET scan will not be eligible for CMS reimbursement.*

B.5.6 Institutional Review Board (IRB) Approval for Registry Participation

The NaF-PET registry has been created as an amendment to the existing NOPR 2009 registry.

As such, the only entity engaged in research is the registry itself (i.e., NOPR); the NOPR intends to use the data it is collecting for research purposes when the patient, the interpreting physician, and the referring physician have consented to the use of the information for this purpose.

The American College of Radiology institutional review board has approved the NaF-PET registry as an amendment of the current NOPR. A copy of this approval letter is included in Appendix B-III).

Individual PET facilities, interpreting physicians and referring physicians and their respective staffs are not engaged in research and, therefore, are not required to have IRB approval for their participation in the activities.
of the NOPR. Submission of the information for the registry (pre-PET and post-PET case report forms, NaF-PET scan assessment form, and the PET scan report) is required by CMS for payment for PET studies for all Medicare-insured patients included in the registry. Additionally, CMS is not conducting research.

Any participating PET facility may nevertheless elect to have its local IRB review its participation in the NOPR (NaF-PET) registry. Some IRBs require, as a matter of institutional policy, that they review all research conducted in the institution, even if only to determine that the facility is not engaged in the research. Materials are provided in Appendix B-III to assist in this process. The Office of Human Research Protections (OHRP) has reviewed the NOPR procedures for protection of human research subjects and finds them to be in compliance with the applicable DHHS regulations. Any individual IRB with questions can contact OHRP.

B.5.7 Prospective Collection of Medicare Claims Data for NOPR (NaF-PET) Participants

Since the initiation of NOPR in 2006, a planned research goal has been to evaluate the concordance between the referring physician’s intended management after PET and the inferred actual management based on an analysis of the cohort member’s Medicare claims. An assessment of this concordance for NOPR FDG-PET studies is one of the major goals of a NIH Grand Opportunity Grant awarded in 2009 to develop the Center for Comparative Effectiveness Research (CER) in Cancer Imaging that provides a national infrastructure for CER initiatives for advanced imaging in cancer. It brings together the resources of the Dartmouth Medical School, including the Dartmouth Institute for Health Policy and Clinical Practice (TDI) and the Norris Cotton Cancer Center (NCCC); the American College of Radiology Imaging Network (ACRIN), and the Tufts Evidence-based Practice Center (EPC). This multi-institutional research center promotes and conducts comparative effectiveness research on advanced imaging in clinical cancer care.

As of June 2010, the NOPR cohort identifier file has been sent to the Research Data Assistance Center (ResDAC), the Center for Medicare Services contractor that maintains the Medicare claims files and assists research in using their claims. The first analysis is expected to begin in September 2010, but will be able to use claims data only through 2007. The long delay in data analysis and time lag can be avoided if participants in NOPR (NaF-PET) are identified prospectively.

When the NaF-PET registry opens, the NOPR investigators have requested that a prospective Medicare claims database be created to facilitate more timely evaluation of the impact of NaF-PET. The data requested are outlined below.

1) Every three months, the NOPR data center will send a participant data file with specific identifiers (social security number, gender, date of birth, date of NaF-PET) to ResDAC. ResDAC will create an internal CMS database that will ‘flag’ NaF-PET participants’ and will include their claims from 90 days before the scan and will include their subsequent claims for the next year. The data files returned to the NOPR investigators will be de-identified.

2) The CMS claims database for NOPR (NaF-PET) enrollees would include all the standard administrative claim elements of Medicare beneficiaries in fee-for-service Medicare. These include:
   a. MedPAR (inpatient hospitalizations, skilled nursing and rehab facilities)
   b. Hospital outpatient
   c. Physician bills and free standing ambulatory care centers (the carrier files)
   d. Hospice

3) This database will be maintained by ResDAC and will be provided annually to the NOPR data center for analysis, primarily looking for concordance between NOPR intended vs. actual management. The analysis plans are discussed in the Statistical Section B.9.0.

4) This plan was approved by the CMS Coverage and Analysis Group. (conference call August 5, 2010).
B.6.0 NaF-PET Registry and CMS-Suggested Design Specifications

As noted earlier, in its decision memo (CAG-00065R) to include coverage of NaF-PET under CED, CMS indicated that NaF-PET needed to inform the initial anti-tumor treatment strategy or guide subsequent treatment after the completion of initial treatment. For Medicare beneficiaries undergoing NaF-PET as part of a prospective clinical trial, the scans will be covered services and are not subsequently further discussed herein. In addition, CMS suggested specific elements be included in any planned assessment. These are listed in Table B.4 and include comments on how the NaF-PET registry will address it.

The primary endpoint of interest to CMS is that clinical studies including registries under the coverage with evidence development program must answer one or more of the following questions associated with NaF-PET use:

- A change in patient management to more appropriate palliative care; or
- A change in patient management to more appropriate curative care; or
- Improved quality of life; or
- Improved survival.

**Table B.4: CMS National Coverage Standards of Scientific Integrity and Relevance to Medicare Beneficiaries for Coverage with Evidence Development Assessments**

<table>
<thead>
<tr>
<th>Suggested Elements</th>
<th>NOPR (NaF-PET)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hospitals and Providers are qualified to provide the PET scan and interpret the results</td>
<td>Yes. Same standards as for FDG-PET.</td>
</tr>
<tr>
<td>Accurately report data on all enrolled patients</td>
<td>Yes. Reporting practices established in the FDG-PET registry will continue.</td>
</tr>
<tr>
<td>Patient confidentiality, privacy and other Federal laws are followed</td>
<td>Yes. All data will be entered through the secure NOPR Web site. Each PET facility is assigned a unique identifier and each registered user has a unique user ID# and password.</td>
</tr>
</tbody>
</table>

**Specific Research Elements**

- The principal purpose of the research study is to test whether a particular intervention potentially improves the participants’ health outcomes. Yes. See objectives (section 1) and statistical plan (section 9).
- The research study is well-supported by available scientific and medical information or it is intended to clarify or establish the health outcomes of interventions already in common clinical use. Yes. Evidence suggests that NaF-PET offers advantages by comparison with conventional bone scintigraphy, but only limited data exist regarding its impact on health outcomes.
- The research study does not unjustifiably duplicate existing studies. Yes.
- The research study design is appropriate to answer the research question being asked in the study. Yes.
- The research study is sponsored by an organization or individual capable of executing the proposed study successfully. Yes. See past participation rates, subject accrual, and peer-reviewed reports of NOPR 2006.
- The research study is in compliance with all applicable Federal regulations concerning the protection of human subjects. Yes. The registry has IRB approval.
- All aspects of the research study are conducted according to the Yes.
<table>
<thead>
<tr>
<th><strong>appropriate standards of scientific integrity.</strong></th>
<th>Yes. This document and its appendices.</th>
</tr>
</thead>
<tbody>
<tr>
<td>The research study has a written protocol that clearly addresses, or incorporates by reference, the Medicare standards.</td>
<td></td>
</tr>
<tr>
<td>The clinical research study is not designed to exclusively test toxicity or disease pathophysiology in healthy individuals. Trials of all medical technologies measuring therapeutic outcomes as one of the objectives meet this standard only if the disease or condition being studied is life-threatening as defined in 21 CFR §312.81(a) and the patient has no other viable treatment options.</td>
<td>Not applicable</td>
</tr>
<tr>
<td>The clinical research study is registered on the <a href="http://www.ClinicalTrials.gov">www.ClinicalTrials.gov</a> Web site by the principal sponsor/investigator prior to the enrollment of the first study participant.</td>
<td>Yes. NaF-PET registry represents an amendment to the current NOPR, which is registered at Clinical Trials.gov (NCT00868582).</td>
</tr>
<tr>
<td>The research study protocol specifies the method and timing of public release of all pre-specified outcomes to be measured including release of outcomes if outcomes are negative or study is terminated early. The results must be made public within 24 months of the end of data collection. If a report is planned to be published in a peer-reviewed journal, then that initial release may be an abstract. However, a full report must be made public no later than 3 years after the end of data collection.</td>
<td>Yes. These reporting standards were all achieved in our prior work with the FDG-PET registry.</td>
</tr>
<tr>
<td>The research study protocol must explicitly discuss subpopulations affected by the treatment under investigation, particularly traditionally underrepresented groups in clinical studies, how the inclusion and exclusion criteria affect enrollment of these populations, and a plan for the retention and reporting of said populations on the trial. If the inclusion and exclusion criteria are expected to have a negative effect on the recruitment or retention of underrepresented populations, the protocol must discuss why these criteria are necessary.</td>
<td>Yes. Subpopulations include a) different cancer types, b) different extent of pre-PET metastatic disease, and c) age (&lt; 65 vs. &gt;65 yrs). There are no specific exclusions associated with the NaF-PET registry.</td>
</tr>
<tr>
<td>The research study protocol explicitly discusses how the results are or are not expected to be generalizable to the Medicare population to infer whether Medicare patients may benefit from the intervention. Separate discussions in the protocol may be necessary for populations eligible for Medicare due to age, disability or Medicaid eligibility.</td>
<td>Yes. The study is open to all cancer types. Assessment of impact stratified by age &lt;65 (disabled) vs. &gt; 65 are planned. The study will not address the potential impact or associations with concurrent Medicaid eligibility.</td>
</tr>
</tbody>
</table>

**Other Desirable Characteristics for Registries**

<table>
<thead>
<tr>
<th>Baseline patient characteristics</th>
<th>Included</th>
</tr>
</thead>
<tbody>
<tr>
<td>Scan results</td>
<td>Included as free text and in summary case report from completed by interpreting physician.</td>
</tr>
<tr>
<td>Results of all other imaging studies</td>
<td>Interpreting physician is asked about comparison to other radionuclide bone imaging. Impractical to collect results of other imaging studies, but whether other imaging studies were performed before or after PET will</td>
</tr>
</tbody>
</table>

ClinicalTrials.gov Identifier NCT00868582 Version: January 18, 2012 (Page last revised January 11, 2011)
be assessed by subsequent linkage to CMS claims.

<table>
<thead>
<tr>
<th>Facility type and provider characteristics</th>
<th>Facility demographics and provider UPIN or NPI will be collected during the registration process.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Discuss subpopulations affected by the condition under investigation</td>
<td>Unlikely since ethnicity was inconsistently collected in NOPR 2006.</td>
</tr>
</tbody>
</table>

**B.7.0 NOPR Web Site and Data Collection**

The NOPR Web site ([www.cancerPETregistry.org](http://www.cancerPETregistry.org)) is the portal for all facility registrations, case registrations and data entry of the CRFs. The manual of operations, blank CRFs, as well as instructional and informational material are available for downloading from the Web site by participating facilities and other interested parties.

**B.8.0 Endpoint Definitions**

The primary objective of the Registry is to assess the effect of NaF-PET on intended patient management in patients performed to assist or guide:

1) Initial treatment strategy in a patient with known cancer; or
2) Subsequent treatment strategy for suspected recurrence or progression in a patient with known cancer; or
3) Subsequent treatment strategy in a patient with known cancer undergoing monitoring to assess the effectiveness of ongoing treatment. Additionally, in instances of treatment monitoring, the impact on adjusting ongoing treatment will also be an endpoint.

The key management questions that will be asked before the NaF-PET study are shown below (Figure B.1):
If neither the F-18 fluoride PET bone scan nor a conventional bone scan were available, which ONE of the following would be the next step in your current management strategy? [Note: For purposes of this question, you should assume that neither an F-18 fluoride PET bone scan nor a conventional bone scan would be available as the next step.](check only one)

- **Observation** (with close follow-up)
- **Additional Imaging** (other than conventional bone scan or F-18 fluoride PET bone scan)

  [Note: Do not check this option if you would order a conventional bone scan if the F-18 fluoride PET bone scan were not available.]

  If additional imaging is selected, please indicate which specific type of imaging you would order next. (check one)

  - Plain radiographs
  - Body CT (neck, chest, and/or abdomen/pelvis)
  - Extremity CT
  - Body MRI (spine, neck, chest, and/or abdomen/pelvis)
  - Extremity MRI
  - FDG-PET
  - Other, specify: __________________________

- **Tissue Biopsy** (surgical, percutaneous, or endoscopic).

  Note: If concurrent biopsy and a surgical procedure are planned, then mark “treatment” below.

- **Supportive care only** (e.g., pain management, hospice care)

- **Treatment for the cancer**

  If treatment is selected, please also answer the following (a, b and c):

  a. **Treatment Goal:**

     (check one)

     - Curative
     - Palliative

  b. **Treatment will be directed to:** (check all that apply)

     - Primary tumor and/or locoregional disease
     - Non-osseous distant metastatic disease
     - Osseous distant metastatic disease

  c. **Type(s):** (check all that apply)

     - Surgery
     - Radiation
     - Chemotherapy (including biologic modifiers)
     - Hormonal therapy
     - Bisphosphonate therapy
     - Immunotherapy (e.g., sipuleucel T (Provenge®) for prostate cancer)
     - Radiopharmaceutical therapy (strontium-89, samarium-153, etc.)
     - Other

     Specify type:
On the post-PET form, the following stem question is asked:

“In light of the PET findings, which one of the following are you planning or have you already done as the next step in your current management strategy?”

The response choices are the same as above.

As previously done in analyzing the results from NOPR 2006, changes associated with PET can be measured using a variety of approaches. The approaches compare the Pre-PET to the Post-PET plans using different indicators of change:

1. **Dichotomizing management changes**, and measure changes from treatment to non-treatment (observation, additional imaging, tissue biopsy, supportive care) and vice-versa.

2. **For changes within treatments**, define major changes as changes in the *mode of therapy* (change from surgery to radiation) that may or may not correlate with a change in treatment goal. Changes in mode of therapy will also include changes in type of systemic therapy, such as from hormonal to chemotherapy in breast and prostate cancer.

3. **Changes in the treatment goal** (usually reflecting a marked change in extent of cancer burden). Such a change in goal will usually reflect a change in clinical stage or extent of disease. A change is more likely to be “upstaging” (e.g., new or more extensive osseous metastatic disease) and occasionally “down-staging” (e.g., symptoms suspected to be due to osseous metastasis are found to be due to degenerative joint disease).

4. **Actions to prevent skeletal complications** (pathologic fracture, cord compression) that are independent of continuing systemic therapies directed at the cancer.

5. **Co-variants or factors for multivariate analyses** are listed in Table B.5. For example, prognosis as well as response to osseous metastasis varies by cancer type and extent of prior systemic treatments. In contrast to NOPR 2009, the Pre-PET forms collect information about selected symptoms and signs (bone pain, neurologic signs) and the potential importance of bone-only metastatic disease vs. bone and other organ site metastatic disease.

Note: For patients having NaF-PET done before a tissue diagnosis of cancer has been made, the referring physician will not be asked about intended management on either the Pre-PET or Post-PET Form. Instead, information will be collected regarding the referring physician’s assessment of the likelihood of osseous metastatic disease and whether a tissue biopsy was performed.

<table>
<thead>
<tr>
<th>Table B.5: Secondary Endpoints or Factors for Multivariate Analyses</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>By Cancer type</strong></td>
</tr>
<tr>
<td><strong>By Cancer indication</strong></td>
</tr>
<tr>
<td><strong>Bone pain</strong></td>
</tr>
<tr>
<td><strong>Evidence of new (or progressive) metastasis in non-osseous sites</strong></td>
</tr>
<tr>
<td><strong>Pre-PET working stage</strong></td>
</tr>
<tr>
<td><strong>For treatment monitoring</strong></td>
</tr>
</tbody>
</table>
B.9.0 Statistical Considerations

The relative value or impact of bone imaging in the initial staging of patients with breast and prostate cancer depends upon the extent of known disease. In asymptomatic patients with stage I or II breast cancer (based on the extent of breast and axillary node involvement), numerous studies from single centers and the National Surgical Adjuvant Breast and Bowel Project (NSABP) have shown that conventional bone scintigraphy rarely detects occult bone metastases and is, thus, generally not indicated.\(^3\)-\(^6\) For initial staging of patients with prostate cancer, the relative value of conventional bone scintigraphy is limited to a relatively small number of men with high PSA levels (minimum cut-off of 20 to 40 ng/mL), locally advanced disease at surgery, or Gleason scores of 8 or 9.\(^7\),\(^8\)

For patients with known or suspected osseous metastases, the relative change in management after conventional bone scintigraphy compared to other bone imaging (conventional radiographs, CT, MRI and FDG-PET) is difficult to estimate and will likely vary with the type of cancer and the clinical context (bone pain and site of pain). The sensitivity of conventional bone scintigraphy has been estimated at 60-90% in detecting osseous metastases, depending on the cancer and symptoms.\(^9\),\(^10\) Radiographs are specific but insensitive, whereas scintigraphy is sensitive but relatively non-specific.\(^11\) Between 30% and 50% of bone mineral must be lost before a lesion is identifiable on conventional radiographs.\(^16\) Up to 80% of patients with a single symptomatic osseous site will have new, asymptomatic osseous sites identified on conventional bone scintigraphy. The potential incremental value of CT and MRI also vary by symptomatic site and are usually used after bone scintigraphy to better characterize specific sites.

The role of serial bone scintigraphy to monitor systemic therapies in metastatic breast and prostate cancer patients is controversial.\(^10\)-\(^12\) Imaging changes in bone associated with treatment, if they do occur, do so very slowly and do not necessarily concur with the extent or duration of pain. Yet, serial bone scintigraphy is commonly performed.

B.9.1 Current Volume of Bone Scintigraphy and Projected NaF-PET Participation

To estimate the potential annual number of NaF-PET patients, we have used the following sources and estimations that are summarized in Table B7.

1. From the AMA/Specialty Society Relative Value Scale Update Committee (RUC), we obtained the number of Medicare patients having whole-body bone scintigraphy (CPT 78306) in 2008.\(^13\)
2. From the RUC, we also obtained the five leading indications for whole-body bone scintigraphy. Prostate (26%) and breast cancer (12%) were the two most common indications.
3. We estimated that all other cancer types accounted for an additional 12% of the whole-body bone scans performed each year (and, thus, that a cancer indication accounts for half of requests for whole-body bone scintigraphy).
4. As a conservative estimate, we project that 5% of Medicare beneficiaries, age 65 or more, will undergo NaF-PET each year instead of conventional bone scintigraphy.
5. We anticipate that patients, interpreting physicians and referring physicians will consent to allow their data to be used for purposes of NOPR research with frequency similar to that observed in the NOPR population to date. Accordingly, we expect that the fraction of cases where the patient, the referring physician and the interpreting physician all give their consent to be at least 85% (95% for each group). In NOPR-2006, 97% of physicians and 92% of patients consented to using their data.

The dataset used by the NOPR investigators will contain only the data of patients and physicians when all have consented to have the data included. The NOPR investigators will track the fraction of NaF-
PET scans for which consent to use the data for research is withheld by the patient, the interpreting physician, the referring physician, or combinations of these individuals.

6. The primary scientific objective of this registry is to assess the effect of NaF-PET on referring physicians’ plans of intended patient management when used for:
   a. initial treatment strategies (initial staging);
   b. subsequent treatment strategies for restaging or suspected recurrence of known cancer; and
   c. therapy monitoring during a planned course of therapy.
Changes in intended management may or may not align with the presence, absence or number of sites of osseous metastatic disease, since the impact is likely to vary by cancer type and timing in the natural history/indication.

7. The primary or default definition of a change in intended management will be a change in treatment/no (active) treatment as was used in FDG-PET NOPR analyses. [This analysis specifically excludes NaF-PET performed for treatment monitoring.]

8. The anticipated rate of change in intended management is projected to be lower with NaF-PET than with FDG-PET since the imaging assesses only one potential site of disease.
   a. The estimated rate of change in management with NaF-PET will be 15%.
   b. The estimated rate of change in management for initial treatment strategies (initial staging) and subsequent treatment strategies (restaging) will be similar (15%).
   c. The change in intended management will be similar in all cancer types. Therefore, the baseline analysis will consider all cancers together.

9. The above data were used to estimate 95% confidence intervals (Table B.6, far right column) around the 15% change in intended management of all cancer types and then broken down by cancer type (prostate, breast, or other).

10. The sample size calculations used an arbitrary one-year time frame.
Table B.6: Precision of Estimates Based on Expected Sample Size

<table>
<thead>
<tr>
<th>Bone scans by cancer type (%)</th>
<th>Scans per year (N)</th>
<th>Projected Participation in NOPR registry (%)</th>
<th>NOPR NaF-PET Scans per year</th>
<th>Change in Management Associated with NaF-PET (%)</th>
<th>Change in Management (N)</th>
<th>Overall Rate of consent (%)</th>
<th>95% C.I. around 15%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Whole-body bone scans (CPT 78306) in 2008 in Medicare beneficiaries</td>
<td>521,587&lt;sup&gt;17&lt;/sup&gt;</td>
<td>5</td>
<td>13,040</td>
<td>15</td>
<td>1,956</td>
<td>85</td>
<td>13.3-16.8</td>
</tr>
<tr>
<td>All cancers</td>
<td>50</td>
<td>260,794</td>
<td>5</td>
<td>13,040</td>
<td>15</td>
<td>1,956</td>
<td>85</td>
</tr>
<tr>
<td>Prostate Cancer</td>
<td>26&lt;sup&gt;17&lt;/sup&gt;</td>
<td>135,613</td>
<td>5</td>
<td>6,781</td>
<td>15</td>
<td>1,017</td>
<td>85</td>
</tr>
<tr>
<td>Breast Cancer</td>
<td>12&lt;sup&gt;17&lt;/sup&gt;</td>
<td>62,590</td>
<td>5</td>
<td>3,130</td>
<td>15</td>
<td>469</td>
<td>85</td>
</tr>
<tr>
<td>All other cancers</td>
<td>12</td>
<td>62,590</td>
<td>5</td>
<td>3,130</td>
<td>15</td>
<td>469</td>
<td>85%</td>
</tr>
</tbody>
</table>

The analysis plan will include:

1. Estimation of the frequency of change in management from pre- to post-PET for all cancers combined, by cancer type, and by initial vs. subsequent treatment strategies.

For initial treatment strategies, we anticipate that management changes associated with NaF-PET will be predominantly “upstaging”. For example, men with prostate cancer and high PSA levels but no bone pain would be staged as having local disease and treated with surgical or radiation therapy if no osseous metastases are identified; however, if osseous metastases are detected (and confirmed), such patients would be upstaged accordingly and typically treated with hormonal therapy with a change in treatment intent (curative to palliative). A similar scenario is likely for women with stage II breast cancer with involvement of multiple axillary nodes, some of whom will have osseous metastases (without bone pain), and for patients with lung cancer thought to be limited to the thorax, such that either surgical or chemoradiation therapy with curative intent is planned—in both circumstances, the detection of osseous metastatic disease would lead to a change in summary stage, prognosis and treatment plan.

Rarely, patients may be down-staged by NaF-PET. One likely scenario is a patient with breast, prostate or lung cancer with skeletal symptoms, but NaF-PET suggesting changes of degenerative disk disease or spinal stenosis.<sup>14,15</sup>

2. Estimation of the impact of NaF-PET in enabling avoidance of other testing will be further evaluated with respect to non-invasive vs. invasive procedures.

3. Estimation of the effect of various factors (refer to Table B.5) on the frequency of change in intended management after PET.

Our previous work showed only small differences in the impact of PET as a function of specific cancer type. However, FDG-PET scans performed in patients with non-small cell lung cancer and breast cancer were not included in the NOPR 2006 cohort (except for treatment monitoring in lung cancer). We are less certain,
that the relative impact of NaF-PET will be similar across cancer types.

Association of pre-PET summary stage with change in management and the association of change in management with changes in summary stage before and after NaF-PET will be explored.

4. In contrast to the pre-PET data collection for FDG-PET in NOPR 2006 and NOPR 2009, the F-18 Fluoride Pre-PET Form asks about a specific symptom (bone pain) and a variety of other diagnostic or imaging indicators of metastatic bone disease. The relative impacts on intended management associated with these factors are likely to be greater when changes in therapeutic types, goals, and bone-associated complications define intended management.

We intend to assess, using logistic regression models, the impact of NaF-PET on intended management by controlling for a number of covariates in secondary analyses, such as those listed above and in Table B.5. The dependent variable is whether the referring physicians reported a change of intended management after NaF-PET.

B.9.1 Evaluation of Intended vs. Actual Management Concordance

The intended management care options will need to be classified by time frame and clinical action. We anticipate using a 30-day window after the NaF-PET for defining relevant clinical actions that may be related to the information provided by NaF-PET. We anticipate using a pre-PET window for defining pre-PET actions that may potentially influence concordance. We will explore using 30- and 90-day windows of pre-PET claims. The clinical action categorization will be specified by cancer type.

The cross-talk definitions will vary in complexity across treatment types and specific cancers. We anticipate that >80% of NaF-PET scans will be done for one of four cancer types: prostate, female breast, lung, and cancer of unknown primary origin. For each cancer, relevant treatment categories will be created using broad CPT and/or HCPCPS code categories (e.g., surgery, chemotherapy, radiation) and potentially specific actions (e.g., types of chemotherapy).

For hospice and palliative care, the hospice and home health files will be evaluated.

To date, only limited studies in selected cancers have prospectively compared physician intended vs. actual management. Therefore, a priori judgments about the quality of the levels of agreement as assessed by kappa statistics and intra-class coefficients will be deferred and these evaluations will be judged as exploratory and hypothesis generating. Analyses will include the following:

a. Assess the concordance by type of intended management (treatment vs. non-treatment);

b. Assess when treatment is intended, if the same type of treatment is actually delivered;

c. Assess whether the level of agreement between intended and actual management differs if the referring physician is or is not the treating provider;

d. Assess if the level of concordance differs by treatment goal; and

e. Assess if the above levels of agreement differ among indications for NaF-PET.

Agreement between the post-PET intended management and the actual management as reported in Medicare
claims data will be assessed using kappa statistics and intra-class correlation coefficients. Additional analyses will focus on ranking the differences between intended and actual management on an ordinal scale (none – actual management and intended management are identical; minor – actual management varies from the intended management plan, but only by the addition or deletion of one component; major – the actual management differed in its primary components or its intended purpose; complete – no aspect of the intended management plan was implemented), and evaluating the effect of various covariates on this ordinal scale. Patient co-morbidity and performance status will be obvious, important co-variants.

B.9.2 Evaluation of Treatment Monitoring

For cases where NaF-PET is performed for treatment monitoring, the changes in the overall management may be too insensitive as a primary endpoint. Instead, we will explore using the frequency with which the therapeutic plan is modified as a better indicator and as the primary endpoint.

Cases of treatment monitoring are anticipated to be predominantly patients with breast and prostate cancer having bone-only or bone-dominant metastatic disease. The relative frequency of change in management will likely vary with type of systemic therapy (hormonal vs. chemotherapy) and extent of prior treatments for metastatic disease. The registry will not be able to address the impact of number or type of prior treatments since these data will not be available or asked of the treating physician.

Switching to another therapy or mode of therapy, including supportive care, are endpoints in common for all NaF-PET cases. Unique to treatment monitoring will be modifications in dose or schedule reflecting a subtle but meaningful change that will be recorded on the post-PET form.

B.9.3 Interpreting Physician Assessment

The interpreting physician overall assessment and comparison to prior bone imaging, if performed, will be used in logistic regression models only for predicting changes in intended management.
B.10.0 References


Appendix B-I:
National Oncologic PET Registry (NOPR)
NOPR (NaF-PET)
Workflow and Web Site Applications

1. PET Facility Registration

a. PET Facilities will register for the NOPR via [http://www.cancerpetregistry.org/](http://www.cancerpetregistry.org/) by completing the PET Facility Pre-Registration and Registration Forms, submitting an executed Business Associates Agreement (BAA) and paying the $50 registration fee.

b. The Pre-Registration Form requires the basic information needed to create a new site account in the database and assign a unique user password:
   - Name of the Imaging Center
   - Facility E-mail Address. This user will be the PET Facility Administrative User. The Administrative User will receive all e-mail correspondence and notices from the database and be able to modify facility account information including adding and deleting registered physicians and staff.
   - Name of Person Registering the PET facility

c. A confirmation e-mail is generated containing the assigned facility ID and a second e-mail is generated that contains the password. The facility Administrative User can then log in to the facility’s account and complete the PET Facility Registration Form. The PET Facility Registration Form requires:
   - Facility mailing address and telephone number
   - Facility Medicare Provider Number or National Provider Identification (NPI) Number
   - The name of the business entity responsible for escrow payments
   - Name and e-mail address of the Facility’s NOPR contact person (Administrative User)
   - The physical address of the PET facility
   - Name and UPIN or NPI number for each participating physician who will interpret PET scans
   - Name and e-mail address for each staff person (in addition to the Administrative User) who will be allowed to register patients and enter data into the database. This will trigger an e-mail with their usernames and passwords to be sent by the database.
   - Description of each PET scanner
   - Calculation of the initial escrow deposit
   - Setting the amount to trigger a low escrow balance e-mail

d. When the PET Facility Registration Form is submitted, an e-mail is generated that confirms completion of the form. A second e-mail is generated that contains an invoice for the $50 application fee and the amount the facility wishes to deposit into its escrow account.
   - Facility can pay the invoice with a check or via a credit card payment on the NOPR Web site. Checks should be made payable to the ACR-NOPR and mailed to the American College of Radiology, 1818 Market Street, Suite 1600, Philadelphia PA 19103. The facility ID# must be written on the check.
   - Facility will be sent an email when its escrow account dips below their pre-specified amount and subsequent payments to the escrow account can be made by check or credit card.
   - Facility will be notified by e-mail when its deposit is received.
• Registered PET facility staff who are allowed to register patients and enter data will also receive e-mails containing their facility number, usernames and passwords.
e. Facility can begin entering patients on the NOPR when its BAA, facility registration fee, and escrow deposit are submitted to NOPR headquarters. The facility must also submit the HITECH amendment to the BAA. Please allow 48 hours for processing of these materials before scheduling the first patient entry for your facility.

2. Clinician Refers a Patient to the PET Facility

When the PET Facility determines that a referral qualifies for the registry (is eligible for Medicare and the scan is for an eligible indication) it must then verify that the referring physician will complete the F-18 Fluoride Pre- and Post PET Forms within 30 calendar days of the PET scan. The referring physician can also complete the F-18 Fluoride Pre-PET Form in advance (blank forms are available for downloading on the NOPR Web site) and send it to the Facility with the referral.

3. Patient is Entered into the NOPR

a. The PET Facility enters the patient into the NOPR by completing the F-18 Fluoride Case Registration Form on the Web site by entering the following information:
   • Patient’s first and last name
   • Patient’s date of birth
   • Patient’s Social Security Number
   • Patient’s gender, ethnicity, race, and zip code
   • Referring physician’s name, UPIN or NPI number, telephone #, and Fax #
   • Date patient is scheduled for the PET scan (must be within 2 weeks of case registration)

b. When the F-18 Fluoride Case Registration Form is completed, the database will:
   • Assign a case number
   • Deduct $50 from the PET Facility’s escrow account
   • A confirmation e-mail is sent to the PET Facility containing:
     o Case ID number
     o Directions and timeline for data submission
     o Fax cover sheet for delivery of the F-18 Fluoride Pre-PET Form to the referring physician with (if not already submitted with the referral)
     o F-18 Fluoride Pre-PET Form (if not submitted with the referral)

c. At some time before the PET study, or when the patient arrives for the PET scan, the PET facility will provide the patient with the ACR IRB approved standard NOPR Patient Information Sheet that is posted on the NOPR Web site. The patient will be able to contact the NOPR directly for more information, if necessary. The patient will indicate his or her consent verbally to staff at the PET facility, either on the day of the PET study or by telephone within two working days after the PET study is completed. Written consent is not required. The PET facility will note in the database, on the F-18 Fluoride PET Report Form, if the patient gave or withheld consent for use of his or her data in future NOPR research. The PET facility will note on the F-18 Fluoride PET Report Form if the patient gave or withheld consent for use of his or her data in future NOPR research.
4. Pre-PET Form Submission
   a. The referring physician completes the *F-18 Fluoride Pre-PET Form* (if not already submitted with the referral) and sends it to the PET Facility by fax, hand or postal delivery.
   b. The PET Facility enters the data on the *F-18 Fluoride Pre-PET Form* into the database via the Web site by midnight the day of the scan.
   c. It is the PET Facility’s responsibility to ensure that the *F-18 Fluoride Pre-PET Form* is entered into the database by midnight of the date of the scan. Entries after that deadline will be deemed ineligible.
   d. The PET Facility will receive a confirmation e-mail that the form has been entered.

5. Patient Undergoes PET Scan
   Note that the *F-18 Fluoride Pre-PET Form* must be entered into the database by midnight of the day of the scan or the case will be marked ineligible. If the PET scan is not performed within 14 calendar days of case registration the case is cancelled, the $50 registration fee is returned to the escrow account, and PET Facility is notified by e-mail.

6. PET Facility Sends PET Report to Referring Physician and the Database
   a. The PET Facility transmits the PET report to the referring physician.
   b. The PET Facility uploads the PET report to the database by completing the *F-18 Fluoride PET Report Submission Form* on the Web site and submitting the report as free text only on that form.
   c. The PET facility notes on the *F-18 Fluoride PET Report Form* if the patient gave or withheld consent for use of his or her data in future NOPR research.
   d. The *F-18 Fluoride PET Completion Form* must be entered prior to the *F-18 Fluoride PET Report Submission Form*. If the *F-18 Fluoride PET Report Submission Form* is not entered within 7 calendar days of the PET scan date, an e-mail reminder is sent every 7 days until 30 calendar days after the PET scan at which time the case is declared ineligible.
   e. The interpreting physician completes the *F-18 Fluoride PET Interpreting Physician Scan Assessment Form*, which must be entered into the database within 30 days after the PET scan. The physician will indicate on the *F-18 Fluoride Interpreting Physician Scan Assessment Form* whether consent has been given or withheld for use of his or her response data in future NOPR research.

7. Referring Physician Completes Post-PET Form
   a. After the PET scan is completed, the appropriate *F-18 Fluoride Post-PET Form* (as determined by information supplied on *F-18 Fluoride Pre-PET Form*) is e-mailed to the PET facility for delivery to the referring physician.
   b. This form will also include a fax cover sheet and an ACR IRB-approved Referring Physician Information Sheet for the physician. The physician will indicate on the *F-18 Fluoride Post-PET Form* whether consent has been given or withheld for use of his or her response data in future NOPR research.
   c. The referring physician completes the appropriate *F-18 Fluoride Post-PET Form* and returns it to the PET Facility by Fax or Hand or Postal Delivery.
   d. If the *F-18 Fluoride Post-PET Form* is not entered into the database an e-mail reminder is sent every 7 calendar days to the PET Facility until 30 calendar days after the PET scan at which time the case is declared ineligible.
e. It is the responsibility of the PET Facility to ensure that the *F-18 Fluoride Post-PET Form* is entered into the database within 30 calendar days of the PET scan. If the PET Facility receives a second reminder (day 14) that the *F-18 Fluoride Post-PET Form* has not been entered into the database, the PET Facility should confirm that the referring physician has received it and fax or hand deliver a second copy to the referring physician.

8. **The PET Facility is Notified by the Database that the Case is Complete**

A confirmation e-mail is sent by the database to the PET Facility when all data items are received.

9. **The PET Facility Bills CMS for Reimbursement.** (If applicable, the interpreting physician also bills CMS.)

10. **General Considerations**

    a. Data entered into the database can only be changed via an email to NOPR Headquarters.

    b. If the database is down or otherwise unavailable, and failure to enter a form will cause the case to become ineligible, the PET Facility will Fax a paper copy of the completed form to NOPR Headquarters and then enter it into the database as soon as the database is operational. **This is the only instance in which a form may be entered after a due date.**

    c. If all of the required CRFs are not entered into the database within 30 calendar days of the PET scan, the case is declared incomplete and is ineligible. The registration fee is not refundable.

    d. All data will be sent to CMS. Data for a particular patient will be used for NOPR research and included in the research dataset only if the patient, the referring physician, and the interpreting physician consent to use of the data for this purpose.

    e. The PET Facility can use the NOPR Web site to:

        - Check on its escrow account balance
        - Change its password
        - Add to or update its list of Facility Scanners (database will prompt facility to update this information annually)
        - Add to or update its list of Facility Radiologists (database will prompt facility to update this information annually)
        - Add to or update its list of staff members who can register patients and enter data into the database (database will prompt facility to update this information annually)
        - Review the status of all cases; review the list of received/outstanding forms

    f. All interested parties may obtain the following information from the NOPR Web site:

        - A description of the NOPR
        - The manual of operations
        - A copy of all case report forms
        - Instructional/tutorial documents
        - Contact information
Appendix B-II

National Oncologic PET Registry (NOPR)

F-18 Fluoride PET Case Report Forms

<table>
<thead>
<tr>
<th>Form</th>
<th>Version Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient Information Sheet</td>
<td>06/17/10</td>
</tr>
<tr>
<td>(Spanish translation available at: <a href="http://www.cancerpetregistry.org/pdf/patient_info_spanish.pdf">http://www.cancerpetregistry.org/pdf/patient_info_spanish.pdf</a>)</td>
<td></td>
</tr>
<tr>
<td>Interpreting Physician Information Sheet</td>
<td>06/17/10</td>
</tr>
<tr>
<td>Referring Physician Information Sheet</td>
<td>06/17/10</td>
</tr>
<tr>
<td>PET Facility Registration Form</td>
<td>06/17/10</td>
</tr>
<tr>
<td>Case Registration Form</td>
<td>06/17/10</td>
</tr>
<tr>
<td>F-18 Fluoride Pre-PET Form</td>
<td>01/11/11</td>
</tr>
<tr>
<td>F-18 Fluoride PET Completion Form</td>
<td>01/11/11</td>
</tr>
<tr>
<td>F-18 Fluoride PET Report Submission Form</td>
<td>01/11/11</td>
</tr>
<tr>
<td>F-18 Fluoride PET Interpreting Physician Scan Assessment Form</td>
<td>01/11/11</td>
</tr>
<tr>
<td>F-18 Fluoride Post-PET Forms (complete one based on initial indication):</td>
<td></td>
</tr>
<tr>
<td>F-18 Fluoride Post-PET Diagnosis/Suspected Osseous Metastasis Form</td>
<td>01/11/11</td>
</tr>
<tr>
<td>F-18 Fluoride Post-PET Initial Staging Form</td>
<td>01/11/11</td>
</tr>
<tr>
<td>F-18 Fluoride Post-PET Treatment Monitoring Form</td>
<td>01/11/11</td>
</tr>
<tr>
<td>F-18 Fluoride Post-PET Restaging Form</td>
<td>01/11/11</td>
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</table>

PRA Disclosure Statement

According to the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it displays a valid OMB control number. The valid OMB control number for this information collection is 0938-0968. The time required to complete this information collection is estimated to average five (5) minutes per response, including the time to review instructions, search existing data resources, gather the data needed, and complete and review the information collection. If you have comments concerning the accuracy of the time estimate(s) or suggestions for improving this form, please write to: CMS, 7500 Security Boulevard, Attn: PRA Reports Clearance Officer, Mail Stop C4-26-05, Baltimore, Maryland 21244-1850.
The National Oncologic PET Registry (NOPR)

Patient Information Sheet for PET Bone Scan

You are being invited to take part in a research study conducted by the National Oncologic PET Registry (NOPR). Before you decide whether or not to participate, it is important for you to understand why the research is being done and what it will involve. Please take time to read the following information carefully. Talk to your family or friends about the study to help you decide whether or not you wish to take part. If you have any questions or if you would like more information after reading the information sheet, please go to the NOPR website, http://www.cancerpetregistry.org/, or contact the NOPR staff by telephone toll free at 800-227-5463, ext. 4859. Your doctor who ordered the PET bone scan and the staff at the PET facility where your scan will be performed will not be able to answer your questions concerning this research study. The NOPR staff will be able to assist you and answer any questions you may have.

You are being asked to participate in this research study because you are a Medicare patient and your doctor has ordered a PET or a PET/CT bone scan for you that is currently not covered (paid for) by Medicare. The PET bone scan has been ordered to evaluate for spread of cancer to bone. Having the PET scan is not the research in this study. PET bone scans are part of routine clinical care. For the research, the NOPR will study how the information obtained from the PET bone scan is used by your doctor.

WHY IS THIS STUDY BEING DONE?

The Centers for Medicare and Medicaid Services (CMS), a Federal agency that manages the Medicare program, currently does not pay for PET bone scans. However, CMS has a policy called “coverage with evidence development” (CED) to pay for PET bone scans ordered for evaluation of patients with known or suspected cancer. This means Medicare will pay for PET or PET/CT bone scans in the same way that it pays for other testing.

CMS wants to determine if they should pay for PET bone scans for evaluating spread of cancer to bone. In order to collect the information needed to make this decision, CMS will provide payment for the PET bone scans of patients who are properly registered with the National Oncologic PET Registry (NOPR). In addition, if you and your doctor agree to participate in the research, your information will be entered into the registry and will then be analyzed to determine how PET bone scans effect the way doctors plan treatment for their patients.

In order for Medicare to pay for your PET bone scan, Medicare is requiring that your doctor provide certain information about the reason for your scan and how the scan results may influence your treatment. This information, along with information about the results of your scan, will be sent by the PET facility to Medicare as a requirement for payment for your PET bone scan. In addition, the NOPR is requesting your consent to use this information for research. Specifically, the NOPR plans to study how PET scans affect the treatment plans of the doctors who order PET bone scans. Eventually, the results of this research may help to obtain coverage by Medicare and other insurers for PET bone scans.

WHAT WILL HAPPEN IF I TAKE PART IN THIS STUDY?

CMS will collect information about you from your doctor as a requirement of paying for your PET scan. Your personal information such as your name, date of birth, social security number, and your doctor’s information will be entered into NOPR database through a secure web site. All this information will be stored at the
American College of Radiology Imaging Network (ACRIN). ACRIN is a national leader in clinical research involving cancer patients. This database is secure and meets the requirements for the protection of patient confidentiality as required by the U.S. Privacy Rule (HIPAA).

As part of Medicare requirement for payment, your doctor will be asked to complete a brief questionnaire regarding his/her request for PET or PET/CT bone scan and what the doctor would do if PET or PET/CT bone scan were not available. After the PET bone scan is performed, the doctor who reads the scan will be asked to complete a brief questionnaire about the scan results and your doctor will be asked to complete a second questionnaire about how the results of the scan affected your care. These forms, along with information about the results of your scan, must be completed and submitted to the NOPR within a specified period in order for the scan to be eligible for payment. NOPR will send your information to CMS so that your PET bone scan will be paid for by Medicare, like any other covered benefit.

If you agree to participate in the research part of the NOPR, you are giving permission to use your health information for research. However, your information will only be used by the NOPR for research if you and your doctor as well as the doctor who read your scan give permission to use it for research purposes.

WHAT OTHER OPTIONS ARE THERE?

You may choose not to participate in this study. You can choose to have a PET or PET/CT bone scan without participating in the registry study. If you choose not to participate in the NOPR research study, the PET bone scan payment will not be affected.

ARE THERE POTENTIAL BENEFITS TO TAKING PART IN THE STUDY?

There is no immediate direct benefit to you for your participation in this research study. Whether or not you (or your doctor) agree to have your information used for the NOPR research study, Medicare will pay for the PET bone scan so long as your doctor provides the information Medicare requires for payment. If the research study leads to routine coverage by Medicare of PET bone scans, you may benefit in the future if you need another PET bone scan. Other patients with cancer in the future may also be helped if the research leads to routine coverage of PET bone scans by Medicare or other health insurance providers.

WHAT ARE THE RISKS OF THE STUDY?

There are no physical risks associated with this study. There is, however, the potential risk of loss of confidentiality. Every effort will be made to keep your information confidential; however, this cannot be guaranteed.

WHAT ARE THE COSTS?

There are no additional costs to you associated with participating in the NOPR research study. Medicare will pay for the PET or PET/CT bone scan if your information is submitted within a specified timeframe by your doctor. You or your Medicare supplemental (Medigap) insurance will be responsible for any co-payment costs or deductible payments, just as occurs with any other medical service covered by Medicare.

WHAT ABOUT CONFIDENTIALITY?

Your information will be kept permanently in a secure electronic database at the ACRIN and may be used for future research. CMS, the NOPR working group and project staff, and the Center for Statistical Sciences at Brown University will have access to your information. They are responsible for making a recommendation to
CMS on whether PET bone scans should be paid for by Medicare. Your records may be reviewed in order to meet federal regulations. Your name will never be made public.

WHAT ARE MY RIGHTS?

Your participation in the NOPR research study is voluntary. You may choose not to be in the study. If you agree to be in the study, you may withdraw from the study at any time. If you withdraw from the study, no new data about you will be collected for research purposes.

Your decision not to participate or to withdraw from the study will not involve any penalty or loss of benefits. You will continue to receive your usual medical care whether or not you decide to participate in this study. If you decide to withdraw from the study, you will need to let your doctor know in writing.

After you have had a chance to read this information sheet and have made a decision whether you want to participate, please let the staff at the PET facility know what you have decided. You are not required to sign a consent form to participate in this research, but you must let the PET facility staff know whether or not you wish to participate either before you leave the PET facility or at a later date but no more than two (2) working days after you have your PET bone scan. If you have any questions regarding the NOPR research study or the information sheet, please go to the NOPR website, http://www.cancerpetregistry.org/ and click on “Info for Patients”, or contact NOPR at (800) 227-5463, ext. 4859 or pet_registry@phila.acr.org. If you have any questions or concerns about your rights as a research subject or about harms related to this research, you can contact Maria Oh, the American College of Radiology (ACR) IRB coordinator, at (800) 227-5463, ext. 4160. You will be given a copy of this information sheet to take home with you.

Review and Approval by the American College of Radiology Institutional Review Board.

**Interpreting Physician Information Sheet for F-18 Fluoride PET Bone Scan**

The purpose of the National Oncologic PET Registry (NOPR) is to prospectively examine how the use of PET scans impacts the management of patients with suspected or known cancer. This information will be used to develop guidelines for the effective use of PET in a variety of clinical situations and for future requests to the Centers for Medicare and Medicaid Services (CMS) to seek coverage for PET scans that are not covered outside of this registry.

Currently, CMS is providing coverage for PET bone scans in patients with known or suspected cancer under a program known as “coverage with evidence development” (CED). As a condition of payment, CMS requires that you complete a brief form that summarizes your interpretation of the PET bone scan. Information is also collected from the physician who requested the PET bone scan about his or her planned management of the patient before and after the PET bone scan. The information is entered into a secure database maintained by the NOPR and forwarded to CMS for payment purposes.

Your participation in the research component is voluntary. You may choose not to participate. If you agree to participate, you may discontinue participation at anytime. If you withdraw from the study, no new data will be collected about you for research purposes. Your decision not to participate or to withdraw from the study will not involve any penalty or loss of benefits to which you are otherwise entitled. If you agree to participate, the NOPR investigators will also use the information you provide for research purposes. The patient and the physician who requested the PET bone scan will also be asked to allow their information to be used for the same research purposes. The patient’s data and PET bone scan information in the registry will be used for research only if you, the requesting physician and the patient provide consent. However, you, the requesting physician or the patient may choose not to allow this information to be used for the research component of the NOPR. If you choose not to participate, your ability to interpret future PET bone scans will not be affected.

Whether or not you choose to participate, you will need to complete an Interpreting Physician Scan Assessment Form which is necessary for payment by CMS. If you choose to participate in the research study, the same information, as well as the actual report of the PET scan, will become part of the research data. The Interpreting Physician Scan Assessment Form asks questions related to your assessment of the scan findings and the likelihood of metastatic disease. This form should be completed at the time you interpret the PET bone scan and must be completed within 30 days after completion of the PET study.

You and the patient will not directly benefit from participating in the research component at this time. Your participation will help to identify the most effective applications of PET bone scans in oncology patients. The information will be used by CMS and other health insurance providers to decide whether to pay for PET bone scans for cancer-related indications in the future. We hope that the decision may help patients with cancer in the future.

There are no direct risks or discomfort associated with your participation. However, the completion of the Interpreting Physician Scan Assessment Form is a requirement for CMS reimbursement. Completion of the form should take approximately 5 minutes. Participation in the research component will not require additional time for you and your staff. The patient will not know your answers and of your participation in the research.

The NOPR has implemented the necessary infrastructure to ensure security of all data submitted on the Interpreting Physician Scan Assessment Form and in the actual PET scan report. However, we cannot guarantee total privacy. The information will be stored permanently at the American College of Radiology Imaging Network (ACRIN). NOPR investigators will only have access to this information for research purposes, if you consent. All data collected through the NOPR will be made available to CMS for payment purposes regardless of whether consent is given for the research component. The staff at the PET facility where the scan will be performed will not be able to answer any questions concerning this research study. If you have any questions or require any assistance, you can contact the NOPR project manager toll free at 800-227-5463, ext.4859, or pet_registry@phila.acr.org. If you have any questions or concerns about your rights as a research subject or about harms related to this research, you can contact Maria Oh, the American College of Radiology (ACR) IRB coordinator, at (800) 227-5463, ext. 4160.

If you choose to participate and allow the information collected on the Interpreting Physician Scan Assessment Form to be used for the research component of the NOPR, please check the appropriate check box to indicate your participation in the NOPR research study on the Interpreting Physician Scan Assessment Form.

Review and approval by the American College of Radiology Institutional Review Board
Referring Physician Information Sheet for F-18 Fluoride PET Bone Scan

The purpose of the National Oncologic PET Registry (NOPR) is to prospectively examine how the use of PET scans impacts the management of patients with suspected or known cancer. This information will be used to develop guidelines for the effective use of PET in a variety of clinical situations and for future requests to the Centers for Medicare and Medicaid Services (CMS) to seek coverage for PET scans that are not covered outside of this registry.

Currently, CMS is providing coverage for PET bone scans in patients with known or suspected cancer under a program known as “coverage with evidence development” (CED). As a condition of payment, CMS requires that you provide specific patient information before the PET bone scan and within 30 days after the PET bone scan. The information is entered into a secure database maintained by the NOPR and forwarded to CMS for payment purposes.

Your participation in the research component is voluntary. You may choose not to participate. If you agree to participate, you may discontinue participation at anytime. If you withdraw from the study, no new data will be collected about you for research purposes. Your decision not to participate or to withdraw from the study will not involve any penalty or loss of benefits to which you are otherwise entitled. If you agree to participate, the NOPR investigators will also use the information you provide for research purposes. Your patient and the interpreting physician will also be asked to allow their information to be used for the same research purposes. Your patient’s data and PET bone scan information in the registry will be used for research only if you, the interpreting physician and your patient provide consent. However, you, the interpreting physician or your patient may choose not to allow this information to be used for the research component of the NOPR. If you choose not to participate, your ability to request future PET bone scans will not be affected.

Whether or not you choose to participate, you will need to complete pre- and post-PET forms which are necessary for payment by CMS. If you choose to participate in the research study, the same information will become part of the research data. The Pre-PET Form, which must be completed before or on the day of the PET bone scan, will ask you questions related to the reason for requesting the scan, the patient’s cancer type and extent, and the intended management plan if PET were not available. The Post-PET Form, which must be completed and returned to the PET facility within 30 days after the PET bone scan, will ask you questions about the impact of the PET findings on your assessment of the patient’s disease status and your current management plan for the patient.

You and your patient will not directly benefit from participating in the research component at this time. Your participation will help to identify the most effective applications of PET bone scans in oncology patients. The information will be used by CMS and other health insurance providers to decide whether to pay for PET bone scans for cancer-related indications in the future. We hope that the decision may help patients with cancer in the future.

There are no direct risks or discomfort associated with your participation. However, the completion of the pre- and post-PET forms is a requirement for CMS reimbursement. Completion of the forms should take approximately 5 minutes for each form. Participation in the research component will not require additional time for you and your staff. Your patient will not know your answers and of your participation in the research.

The NOPR has implemented the necessary infrastructure to ensure security of all data submitted on the pre- and post-PET forms. However, we cannot guarantee total privacy. The information will be stored permanently at the American College of Radiology Imaging Network (ACRIN). NOPR investigators will only have access to this information for research purposes, if you consent. All data collected through the NOPR will be made available to CMS for payment purposes regardless of whether consent is given for the research component. The staff at the PET facility where the scan will be performed will not be able to answer any questions concerning this research study. If you have any questions or require any assistance, you can contact the NOPR project manager toll free at 800-227-5463, ext.4859, or pet_registry@phila.acr.org. If you have any questions or concerns about your rights as a research subject or about harms related to this research, you can contact Maria Oh, the American College of Radiology (ACR) IRB coordinator, at (800) 227-5463, ext. 4160.

If you choose to participate and allow the information collected on the pre- and post-PET forms be used for the research component of the NOPR, please check the appropriate check box to indicate your participation in the NOPR research study on the Post-PET Form.

Review and approval by the American College of Radiology Institutional Review Board
PET Facility Registration Form
National Oncologic PET Registry

Please complete this form to finalize the NOPR registration process.

Once this completed form is submitted, a confirmation e-mail will be sent with an invoice for the escrow account start-up funds and the $50 application fee.

When the start-up funds are received at NOPR Headquarters an escrow account will be established for the PET Facility. $50 will be debited from this account each time the facility registers a case on the NOPR. E-mail reminders will be sent to the PET Facility Administrator when the account balance dips below a minimum level as defined by the Facility on this Registration Form.

The PET Facility can pay the $50 registration fee and initial escrow deposit either by:
- Mailing a check made payable to ACR-NOPR together with a copy of the e-mailed invoice to the American College of Radiology, 1818 Market Street, Suite 1600, Philadelphia, PA 19103. The facility ID# must be written on the check; or
- Paying by credit card using the information in the e-mailed invoice and confirmation to log into the facility’s account on the NOPR Web site.

Once the ACR receives the facility registration fee and the executed Business Associates Agreement (BAA), the PET Facility will be sent an e-mail approval notice and the facility will be eligible to participate in the National Oncologic PET Registry via the secure Web site.

Only cases that meet the criteria listed in the Coverage Decision will be eligible for registration and CMS reimbursement.

Facility ID #: _________

1. PET FACILITY INFORMATION
   Name of Imaging Center (will be supplied by the system from pre-registration information) _______________________
   Mailing Address (street 1)_________________________ (street 2)__________________________________________
   (city)_________________________________________(state)_______(zip)_________
   Telephone_____________ x _______ FAX: ____________________________
   Business entity responsible for payment _______________________________
   Medicare Provider Number or National Provider Identifier Number: ________________

PHYSICAL ADDRESS OF THE PET FACILITY
   Address (street 1)_________________________ (street 2)__________________________________________
   (city)_________________________________________(state)_______(zip)_________
   Telephone_____________ x ___________

2. PET FACILITY ADMINISTRATOR
   Official facility contact person for the National Oncologic PET Registry (will be supplied by the system from pre-registration information)
   E-mail address (will be supplied by the system from pre-registration information)
3. PARTICIPATING PHYSICIANS - who will interpret PET scans. (Web form will accept as many as needed)
   First Name ________________  Last Name ______________  NPI _________________
   First Name ________________  Last Name ______________  NPI _________________

4. STAFF - People who are allowed to register patients and enter data into the database. A username and password will be emailed to the staff person.
   First Name ________________  Last Name ______________  E-mail ________________
   First Name ________________  Last Name ______________  E-mail ________________

5. EQUIPMENT DESCRIPTIONS – Provide complete information for each PET scanner. (Web Form will allow for entry of multiple scanners)
   Facility’s Scanner Identifier (facility’s name for scanner) ________________
   Manufacturer __________________________  Model __________________________
   ☐ Fixed   ☐ Mobile
   ☐ Hospital-Based   ☐ Not hospital-based (independent diagnostic testing facility)

6. CALCULATION OF ESCROW ACCOUNT
   Payment to the National Oncologic PET Registry for each case entered into the database for CMS reimbursement is required in advance. It is recommended that each facility schedule monthly payments based on the expected number of cases registered for one month. You may stop participating in the Registry at any time. Upon letter to the Program Manager any unexpended credit balance will be refunded.

   Invoice will be E-mailed to registering facility in the amount calculated below.
   
   Initial Facility registration fee:    $50
   Number of cases to prepay @ $50
each:    x $50 =
   Total:

7. FUND BALANCE REMINDER
   PET Facilities can monitor the balance remaining in their NOPR Account via the secure Website. New cases can be registered as long as there is a positive balance remaining. It is recommended that each facility maintain a credit balance at all times commensurate with the facility’s caseload. An E-mail reminder will be sent from the Registry when your fund balance reaches the minimum threshold established by the PET Facility.

   Please notify our PET Facility when our account balance with the ACR reaches the level selected below:
   ☐ $250 – 5 cases remaining
   ☐ $500 – 10 cases remaining
   ☐ $1,000 – 20 cases remaining
   ☐ $2,000 – 40 cases remaining
PET Facility Registration Form

National Oncologic PET Registry  F-18 Fluoride PET Scan

8. HAS THE BUSINESS ASSOCIATE AGREEMENT (BAA) BEEN EXECUTED?

☐ Yes ☐ No

(Please mail or fax (215-928-0153) the BAA to NOPR Headquarters. Note: patients cannot be entered on the Registry until the BAA is received at Headquarters)

9. NAME OF PERSON SUBMITTING THIS FORM

First Name: ___________________ Last Name: ___________________

Additional information on the National Oncologic PET Registry can be found on the web site, http://www.cancerPETregistry.org/ or by contacting the project manager at 215-717-0859.
PET Facility log-in information (facility ID, password): ______________________________________________________

1. PATIENT INFORMATION

Date: _____/_____/______ Social Security #: _______ _______ _______ _______ _______ 

Last name: _______________________________ First name: _______________________________

Date of Birth: _____/_____/______ Patient’s Zip Code: _____________

Gender: □ Male □ Female 
Ethnicity: □ Hispanic □ Not Hispanic □ Unknown 
Race: □ Asian □ Black or African American □ White or Caucasian □ Other □ Unknown 

2. REFERRING PHYSICIAN INFORMATION

UPIN #: ________________________________ or NPI #: ________________________________

Last name: _______________________________ First name: _______________________________

Office Telephone: [____] ____________________ Office Fax: [____] ____________________

3. HAS THE PRE-PET FORM BEEN COMPLETED? □ Yes □ No
   (if Yes is checked the PET facility will not be E-mailed a Pre-PET form to complete)

4. DATE PATIENT SCHEDULED FOR PET SCAN? _____/_____/______
   (Must be within 14 days of registration.)

5. NAME OF PERSON SUBMITTING THIS FORM

Last name: _______________________________ First name: _______________________________ Date: _____/_____/______
Comment to Clinician:

- You have requested an F-18 Fluoride PET scan, a test for which the Centers for Medicare and Medicaid Services (CMS) requires pre- and post-PET information from the referring physician as a condition for reimbursement. In order for the imaging center to be reimbursed this form must be completed and returned to the PET facility before the PET scan is performed.
- You will be required to complete a follow-up form in a timely fashion after the PET scan is done. Thank you for your assistance completing the brief pre- and post-PET forms. The required follow-up questionnaire will be sent to you by the PET facility. By requesting that this patient be entered on the NOPR you agree to also complete the post-PET follow-up form and return it to the PET scan facility within 30 days of the PET scan.

**PATIENT INFORMATION**

Date: ______/_____/______  Social Security #: ____ ____ ____ — ____ ____ — ____ ____ ____

Last name: ___________________________  First name: ___________________________

Date of Birth: ______/_____/______  Patient's Zip Code: ______ ______ ______

**REFERRING PHYSICIAN INFORMATION**

UPIN #: ___________________________  or  NPI #: ___________________________

Last name: ___________________________  First name: ___________________________

Office Telephone: [____] ________________  Office Fax: [____] ________________

1. **SPECIFIC REASON FOR F-18 FLUORIDE PET STUDY**

   See page 6 of this form for definitions / instructions to assist you in completing Question 1.

a. Check the single best match for the reason for the PET (you must check only one of the following)
   - Diagnosis of suspected osseous metastatic disease in a patient without a pathologically proven diagnosis of cancer
     [If this option is selected, answer only questions 1.b, 2, 3, and 6. Also, note that guidance to help you answer parts a, b, and c of question 2 is provided on page 7 of this form.]
   - Initial staging of newly diagnosed cancer
   - Suspected new osseous metastasis as a site of recurrence or progression
   - Suspected progression of known osseous metastasis
   - Monitoring Treatment Response during systemic therapy (including chemotherapy, biologic modifiers, hormonal therapy, and immunotherapy)
   - Monitoring Treatment Response during radiation therapy
   - Monitoring Treatment Response during combined systemic therapy and radiation therapy
b. Symptoms, signs, or other findings prompting F-18 fluoride PET bone imaging

☐ NONE
[If selected, go directly to Question 2; otherwise select all of the following that apply]

☐ Skeletal pain
☐ New focal neurologic signs or symptoms
☐ Findings on other imaging studies suggesting osseous metastatic disease
☐ Hypercalcemia
☐ Elevated or increasing tumor marker(s) (including alkaline phophatase)

☐ Evidence of new metastases in non-osseous sites
[Do not select this option if reason for study is “Diagnosis of suspected osseous metastatic disease in a patient without a pathologically proven diagnosis of cancer”.

☐ Evidence of progression of known metastatic disease in non-osseous sites
[Do not select this option if reason for study is “Diagnosis of suspected osseous metastatic disease in a patient without a pathologically proven diagnosis of cancer”.

See page 7 of this form for guidance in the completion of Question 2 when the PET bone scan is requested for “Diagnosis of suspected osseous metastatic disease in a patient without a pathologically proven diagnosis of cancer”.

ClinicalTrials.gov Identifier NCT00868582  Version: January 18, 2012  (Page last revised January 18, 2012)
2. CANCER TYPE

- Please mark the corresponding box of the pathologically proven or strongly suspected primary cancer type in section 2a and answer question 2b.
- If your patient’s cancer is not listed, check the “Other” box and enter as text the cancer type.
- For a patient with pathologically proven or strongly suspected metastatic cancer of unknown primary origin, please also mark the corresponding box of the site of metastatic disease in section 2c.

a. Cancer Type - check the one pathologically proven or strongly suspected cancer type that most closely relates to the specific reason for the PET study indicated in response to Question 1. (Check only one)
   - [ ] Lung
   - [ ] Female breast
   - [ ] Prostate
   - [ ] Metastatic cancer of unknown primary origin (also answer question 2c below)
   - [ ] Other

   If other, please describe cancer type: ____________________________________________
   and give the first 3 digits of the ICD-9 code. [ ] [ ] .XX

b. Has this cancer diagnosis been pathologically proven?  
   - [ ] Yes  [ ] No

c. Unknown primary: dominant site of pathologically proven or strongly suspected metastatic disease
   - [ ] Lymph node(s)
   - [ ] Lung
   - [ ] Liver
   - [ ] Brain
   - [ ] Bone/bone marrow
   - [ ] Other

   If other, please indicate dominant site: ____________________________________________
   and give the first 3 digits of the ICD-9 code. [ ] [ ] .XX  [Acceptable responses are 196-199]

3. YOUR WORKING SUMMARY STAGE FOR THE PATIENT BEFORE THE PET SCAN IS:

   (you must check only one)
   - [ ] No evidence of disease / In remission
   - [ ] Localized only
   - [ ] Regional by direct extension or lymph node involvement or both
   - [ ] Metastatic (distant) with a single suspected site
   - [ ] Metastatic (distant) with multiple suspected sites
   - [ ] Unknown or uncertain
4. ADDITIONAL RESPONSES REQUIRED ONLY IF THE SPECIFIC REASON FOR THE PET STUDY IS MONITORING TREATMENT RESPONSE

a. Which of the following types of treatment is this patient now receiving?
   (check one)
   - Systemic therapy (including chemotherapy, biologic modifiers, hormonal therapy, and immunotherapy)
   - Radiation therapy
   - Combined systemic therapy and radiation therapy

b. What is your impression (before PET) of your patient’s response to currently ongoing therapy?
   (check one)
   - Probable complete response
   - Possible partial response, but uncertain about degree of response
   - Suspect no response (stable disease)
   - Suspect progressive disease

c. If you were to continue your patient’s management without doing any other testing first (e.g., PET, CT, MRI, biopsy), what would be your treatment plan today?
   (check one)
   - Continue and complete currently ongoing therapy
   - Modify dose or schedule of currently ongoing therapy
   - Switch to another therapy or add another mode of therapy
   - Stop therapy and switch to supportive care
5. MANAGEMENT PLAN

a. Has the patient had a conventional bone scan within the last month?
   - Yes
   - No

b. If the F-18 fluoride PET bone scan were not available, would you order a conventional bone scan instead?
   - Yes
   - No

c. If neither the F-18 fluoride PET bone scan nor a conventional bone scan were available, which ONE of the following would be the NEXT step in your current management strategy? [Note: For purposes of this question, you should assume that NEITHER a F-18 fluoride PET bone scan NOR a conventional bone scan would be available as the next step.]

<table>
<thead>
<tr>
<th>Check only one</th>
</tr>
</thead>
<tbody>
<tr>
<td>Observation (with close follow-up)</td>
</tr>
<tr>
<td>Additional Imaging (CT, MRI, FDG-PET)</td>
</tr>
</tbody>
</table>

[Note: Do not check this option if you would order a conventional bone scan if the F-18 fluoride PET bone scan were not available.]

If additional imaging is selected, please indicate which specific type of imaging you would order next. (check one)

<table>
<thead>
<tr>
<th>Check</th>
</tr>
</thead>
<tbody>
<tr>
<td>Plain radiographs</td>
</tr>
<tr>
<td>Body CT (neck, chest, and/or abdomen/pelvis)</td>
</tr>
<tr>
<td>Extremity CT</td>
</tr>
<tr>
<td>Body MRI (spine, neck, chest, and/or abdomen/pelvis)</td>
</tr>
<tr>
<td>Extremity MRI</td>
</tr>
<tr>
<td>FDG-PET</td>
</tr>
<tr>
<td>Other, specify: ____________________________</td>
</tr>
</tbody>
</table>

- Tissue Biopsy (surgical, percutaneous, or endoscopic).
  Note: If concurrent biopsy and a surgical procedure are planned, then mark "treatment" below.

- Supportive care only (e.g., pain management, hospice care)
- Treatment for the cancer

If treatment is selected, please also answer the following (a, b and c):
a. Treatment Goal:

(check one)

☐ Curative
☐ Palliative

b. Treatment will be directed to: (check all that apply)

☐ Primary tumor and/or locoregional disease
☐ Non-osseous distant metastatic disease
☐ Osseous distant metastatic disease

c. Type(s): (check all that apply)

☐ Surgery
☐ Radiation
☐ Chemotherapy (including biologic modifiers)
☐ Hormonal therapy
☐ Bisphosphonate therapy
☐ Immunotherapy (e.g., sipuleucel T (Provenge®) for prostate cancer)
☐ Radiopharmaceutical therapy (strontium-89, samarium-153, etc.)
☐ Other

Specify type: _______________________________________________________________

6. NAME OF PERSON WHO COMPLETED THE PAPER FORM

First Name: __________________ Last Name: __________________ Date: ___/___/___

7. PHYSICIAN ATTESTATION OF DATA ACCURACY

By signing below I verify that, to the best of my knowledge, the information on this form is accurate.

Physician Signature: __________________________________________ Date: ___/___/___

Printed Name of Physician: __________________________________________

Thank you for your assistance.

PRA Disclosure Statement

According to the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it displays a valid OMB control number. The valid OMB control number for this information collection is 0938-0968. The time required to complete this information collection is estimated to average five (5) minutes per response, including the time to review instructions, search existing data resources, gather the data needed, and complete and review the information collection. If you have comments concerning the accuracy of the time estimate(s) or suggestions for improving this form, please write to: CMS, 7500 Security Boulevard, Attn: PRA Reports Clearance Officer, Mail Stop C4-26-05, Baltimore, Maryland 21244-1850.
ADDITONAL INSTRUCTIONS FOR COMPLETING PRE-PET FORM QUESTION 1

The following definitions/instructions are provided to assist you in the completion of Question 1 (“SPECIFIC REASON FOR PET STUDY”) on the next page of this form. This information is derived from the 2009 Medicare National Coverage Determination for F-18 Fluoride PET.


Indications for F-18 Fluoride PET Scans and Limitations/Requirements for Usage

Initial Treatment Strategy

F-18 Fluoride PET performed as part of an evaluation for determination of an initial treatment strategy is covered by CMS only with participation in this registry. F-18 fluoride PET may be used both for diagnosis of strongly suspected bone metastases in a patient without a pathologically proven diagnosis of cancer and as part of initial staging in a patient with a pathologically proven cancer.

Note: F-18 fluoride PET is covered only in clinical situations in which (1) the PET results may assist in avoiding an invasive diagnostic procedure, or in which (2) the PET results may assist in determining the optimal anatomical location to perform an invasive diagnostic procedure. In general, for most solid tumors, a tissue diagnosis is made prior to doing a PET bone scan and therefore the scan is performed for staging rather than diagnosis.

PET is not covered as a screening test (i.e., testing patients without specific signs and symptoms of disease).

Subsequent Treatment Strategy

F-18 fluoride PET is also covered by CMS only with participation in this registry when used in subsequent treatment strategy to identify bone metastases in a patient with a pathologically proven cancer.

F-18 fluoride PET is covered for restaging and detection of suspected recurrences:

(1) after completion of treatment for the purpose of detecting residual disease; or
(2) for detecting suspected recurrence or metastasis; or
(3) to determine the extent of a known recurrence:
(4) if it could potentially replace one or more conventional imaging studies when it is expected that conventional study information is insufficient for the clinical management of the patient.
(5) Restaging applies to testing after a course of treatment is completed, and is covered subject to the conditions above.

Comment: As noted above, F-18 fluoride PET is not covered as a screening test (i.e., testing patients without specific signs and symptoms of disease) and thus is not covered for surveillance of patients treated for cancer in whom there is no clinical reason to suspect recurrent disease.

Treatment Monitoring

Treatment monitoring refers to use of PET to monitor tumor response to treatment during the planned course of therapy (i.e., when a change in therapy is anticipated).

Comment: As an example, F-18 fluoride PET performed under NOPR may be covered for monitoring after 2 or 3 of a planned 6 cycles of chemotherapy in a patient considered not to be responding as expected.
ADDITIONAL INSTRUCTIONS FOR COMPLETING 
PRE-PET FORM QUESTION 2 

The following guidance is provided to assist you in answering Questions 2a, b, and c when the PET bone scan is requested for “Diagnosis of suspected osseous metastatic disease in a patient without a pathologically proven diagnosis of cancer”.

Below are several common clinical scenarios that serve as illustrations.

- A man with back pain, a markedly elevated PSA and sclerotic lesions in several vertebrae on a recent chest radiograph. Answer “Prostate” to question 2a and “No” to question 2b. Do not answer question 2c.
- A woman with a long smoking history, now with a left upper lobe mass, mediastinal adenopathy, and an adrenal nodule on CT. Answer “Lung” to question 2a and “No” to question 2b. Do not answer question 2c.
- A man with multifocal bone pain and several ill-defined lytic osseous lesions on a recent chest, abdomen and pelvis CT (with no evidence of a primary tumor on the CT study). Answer “Metastatic cancer of unknown primary origin” to question 2a, “No” to question 2c, and “Bone/bone marrow” to question 2c.
- A woman with severe headache and multiple enhancing lesions on brain MRI. Answer “Metastatic cancer of unknown primary origin” to question 2a, “No” to question 2c, and “Brain” to question 2c.
This form is completed by the PET Facility via Web-based data entry within 14 days of case registration.

The PET scan must be completed within 14 days of case registration. If the case was registered more than 14 days prior to the PET scan the patient must be re-registered. The original case registration will be cancelled and the $50 will be refunded.

PET FACILITY ID #: __________________________________________

REGISTRY CASE #: _________________________________________

1. DATE SCAN COMPLETED: _____/_____/_____

   (must be within 14 days of registration)

2. SCAN TYPE (you must check one)
   - PET
   - PET-CT

3. REGION(S) SCANNED (you must check only one)
   - Limited Body Region
     (Study will be billed using CPT Codes: 78811 or 78814.)
   - Skull base to proximal thighs
     (Study will be billed using CPT Codes: 78812 or 78815.)
   - Whole-body (vertex to toes)
     (Study will be billed using CPT Codes: 78813 or 78816.)

4. SCANNER INFORMATION
   Facility’s Scanner Identifier (facility’s name for scanner) - [Pull Down Menu of Facility’s Scanner Info]

5. NAME OF PERSON SUBMITTING THIS FORM
   First Name: __________________ Last Name: __________________ Date: _____/_____/_____

ClinicalTrials.gov Identifier NCT00868582   Version: January 18, 2012   (Page last revised January 11, 2011)
This form is used to transmit the PET Report. It is completed by the PET facility via Web-based data entry within 30 days of completing the PET scan.

PET FACILITY ID #: __________________________________________

REGISTRY CASE #: __________________________________________

6. DATE SCAN COMPLETED: ___/___/___

7. DATE PET REPORT COMPLETED: ___/___/___

8. INTERPRETING PHYSICIAN INFORMATION

Pull Down Menu of Interpreting Physicians

9. PET REPORT (You must enter the report as free text. No other entry method is accepted.)

Free text

Cut and paste from Microsoft Word document or other text document. You must enter the complete text of the PET report, pasting or typing all pages.

10. AFTER BEING GIVEN THE NOPR PATIENT INFORMATION STATEMENT, DID THE PATIENT CONSENT TO HAVE HIS OR HER DATA USED FOR NOPR RESEARCH?

☐ Yes

☐ No

11. NAME OF PERSON SUBMITTING THIS FORM

First Name: ___________________ Last Name: __________________________ Date: ___/___/___
• This form is used to summarize the findings of the PET bone scan. It should be completed by the interpreting physician at the time the PET scan is interpreted.
• It must be submitted by the PET facility via Web-based data entry within 30 days of completing the PET scan.

1. OVERALL ASSESSMENT
   □ Normal study
   □ Benign skeletal abnormalities only
   □ Osseous metastatic disease or primary malignant bone tumor
     □ Unifocal
     □ Multifocal
     □ Diffuse skeletal involvement

   If osseous metastatic disease or primary malignant bone tumor selected, indicate level of confidence
   □ Definitely present
   □ Probably present
   □ Equivocal

2. WAS COMPARISON MADE WITH PRIOR RADIONUCLIDE BONE IMAGING?
   □ Yes
   □ No

   a. If yes, indicate type of study:
      □ Conventional bone scintigraphy
      □ F-18 fluoride bone PET

   b. Date of prior study   _____/_____/____
c. Based on the comparison, there has been:

- No change; there is no evidence of metastatic disease on either the prior study or current study
- Resolution of previously seen metastatic disease
- Improvement of previously seen metastatic disease
- No change in previously seen metastatic disease
- Worsening of previously seen metastatic disease
- Development of new metastatic disease on the current study (no metastatic disease was seen on the prior study)

3. I HAVE READ THE INTERPRETING PHYSICIAN INFORMATION STATEMENT AND:

- I DO give my consent for the inclusion of data collected for this patient in NOPR research.
- I DO NOT give my consent for the inclusion of data collected for this patient in NOPR research.

4. NAME OF PERSON SUBMITTING THIS FORM

First Name: __________________  Last Name: ______________________  Date: ____ / ____ / ____

5. PHYSICIAN ATTESTATION OF DATA ACCURACY

By signing below I verify that, to the best of my knowledge, the information on this form is accurate.

Physician Signature: _____________________________________________  Date: ____ / ____ / ____

Printed Name of Physician: _________________________________________

Thank you for your assistance.

PRA Disclosure Statement

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Your patient had a PET scan on: mm/dd/yyyy.

You previously indicated that the PET scan was done for diagnosis of suspected osseous metastatic disease in a patient without a pathologic diagnosis of cancer.

- After reviewing the PET report, please complete the following questions and return the form to the PET Facility.
- This form must be entered into the database within 30 days of the PET scan.

1. IN LIGHT OF THE PET FINDINGS, WHAT IS YOUR CURRENT ASSESSMENT OF THE LIKELIHOOD OF OSSEOUS METASTATIC DISEASE?
   - Definitely present
   - Probably present
   - Uncertain
   - Probably not present
   - Definitely not present

2. SINCE OBTAINING THE SCAN, HAS A TISSUE BIOPSY BEEN PERFORMED OF A SUSPICIOUS OSSEOUS SITE?
   - Yes
   - No

   If yes, indicate whether the bone biopsy results are:
   - Negative
   - Positive
   - Pending

3. HAS A PATHOLOGIC DIAGNOSIS OF CANCER BEEN CONFIRMED FROM ANY SITE?
   - Yes
   - No

4. DID THE PET SCAN ENABLE YOUR PATIENT TO AVOID ANY
   a. noninvasive diagnostic tests?
      - Yes
      - No
   b. any invasive procedures?
      - Yes
      - No
5. I HAVE READ THE REFERRING PHYSICIAN INFORMATION STATEMENT AND:
   ☐ I DO give my consent for the inclusion of data collected for this patient in NOPR research.
   ☐ I DO NOT give my consent for the inclusion of data collected for this patient in NOPR research.

6. NAME OF PERSON SUBMITTING THIS FORM
   First Name: __________________  Last Name: ______________________  Date: _____/_____/_____

7. PHYSICIAN ATTESTATION OF DATA ACCURACY
   By signing below I verify that, to the best of my knowledge, the information on this form is accurate.
   Physician Signature: ____________________________________________  Date: _____/_____/_____
   Printed Name of Physician: ________________________________________

Thank you for your assistance.

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Your patient had a PET scan on mm/dd/yyyy. [Date will automatically be filled.]

You previously indicated that the PET scan was done for initial staging of cancer type [Cancer type will automatically be filled in from data supplied on Pre-PET form.]

- After reviewing the PET report, please complete the following questions and return the form to the PET Facility.
- This form must be entered into the database within 30 days of the PET scan.

1. COMPARED TO YOUR PRE-PET ASSESSMENT, WHAT IS YOUR IMPRESSION OF THE EXTENT OF THE PATIENT’S CANCER?
   - More extensive
   - No change
   - Less extensive

2. DID THE PET SCAN ENABLE YOUR PATIENT TO AVOID ANY
a. noninvasive diagnostic tests?
   □ Yes
   □ No

b. any invasive procedures?
   □ Yes
   □ No

3. YOUR POST-PET WORKING CLINICAL SUMMARY STAGING IS? (You must check only one)
   □ No evidence of disease / In remission
   □ Localized only
   □ Regional by direct extension
   □ Metastatic (distant) with a single suspected site
   □ Metastatic (distant) with multiple suspected sites
   □ Unknown or uncertain

4. IN LIGHT OF THE PET FINDINGS, WHICH ONE OF THE FOLLOWING ARE YOU PLANNING OR HAVE
   YOU ALREADY DONE AS THE NEXT STEP IN YOUR CURRENT MANAGEMENT STRATEGY? (check
   only one)
   □ Observation (with close follow-up)
   □ Additional Imaging
      ○ If additional imaging is selected, please indicate which specific type of imaging you
        would order next. (check one)
        ○ Plain radiographs
        ○ Body CT (neck, chest, and/or abdomen/pelvis)
        ○ Extremity CT
        ○ Body MRI (spine, neck, chest, and/or abdomen/pelvis)
        ○ Extremity MRI
        ○ FDG-PET
        ○ Other, specify: ____________________________
Initial Staging Form
National Oncologic PET Registry

Post-Scan
F-18 Fluoride PET Scan

☐ Tissue Biopsy (surgical, percutaneous, or endoscopic).
   [Note: If concurrent biopsy and a surgical procedure are planned, then mark “treatment” below. ]

☐ Supportive care only (e.g., pain management, hospice care)

☐ Treatment for the Cancer
   If treatment was selected, answer the questions below:

   a. Treatment Goal: (check one)
      ☐ Curative
      ☐ Palliative

   b. Treatment will be directed to: (check all that apply)
      ☐ Primary tumor and/or locoregional disease
      ☐ Non-osseous distant metastatic disease
      ☐ Osseous distant metastatic disease

   c. Type(s): (check all that apply)
      ☐ Surgery
      ☐ Radiation
      ☐ Chemotherapy (including biologic modifiers)
      ☐ Hormonal therapy
      ☐ Bisphosphonate therapy
      ☐ Immunotherapy (e.g., sipuleucel T (Provenge®) for prostate cancer)
      ☐ Radiopharmaceutical therapy (strontium-89, samarium-153, etc.)
      ☐ Other
         Specify other treatment type: ____________________________________________

5. I HAVE READ THE REFERRING PHYSICIAN INFORMATION STATEMENT AND:
   ☐ I DO give my consent for the inclusion of data collected for this patient in NOPR research.
   ☐ I DO NOT give my consent for the inclusion of data collected for this patient in NOPR research.

6. NAME OF PERSON SUBMITTING THIS FORM
   First Name: __________________  Last Name: ______________________  Date: _____/_____/____

7. PHYSICIAN ATTESTATION OF DATA ACCURACY
By signing below I verify that, to the best of my knowledge, the information on this form is accurate.

Physician Signature: ___________________________________________________ Date: _____/_____/____

Printed Name of Physician: ____________________________________________

Thank you for your assistance.

PRA Disclosure Statement

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Your patient had a PET scan on mm/dd/yyyy. [Date will automatically be filled.]

You previously indicated that the PET scan was done for treatment response monitoring of cancer type [Will automatically be filled in from data supplied on Pre-PET form.] to chemo / radiation / or other therapy.

• After reviewing the PET report, please complete the following questions and return the form to the PET Facility.
• This form must be entered into the database within 30 days of the PET scan.

1. WHAT IS YOUR CURRENT IMPRESSION (IN LIGHT OF THE PET FINDINGS) OF YOUR PATIENT’S RESPONSE TO CURRENTLY ONGOING THERAPY? (CHECK ONE)?
   □ Complete response
   □ Partial response
   □ No response (stable disease)
   □ Progressive disease

2. IN LIGHT OF THE PET RESULTS, HOW HAS THE PROGNOSIS FOR YOUR PATIENT CHANGED? (CHECK ONE)
   □ Better
   □ No change
   □ Worse

3. PLEASE INDICATE IF AND HOW YOU WILL MODIFY YOUR THERAPEUTIC PLAN IN LIGHT OF THE PET FINDINGS. (You must check only the one response that best characterizes your therapeutic plan)
   □ Continue and complete currently ongoing therapy
   □ Modify dose or schedule of currently ongoing therapy
   □ Switch to another therapy or add another mode of therapy
   □ Stop therapy and switch to supportive care
4. IN LIGHT OF THE PET FINDINGS, WHICH ONE OF THE FOLLOWING ARE YOU PLANNING OR HAVE YOU ALREADY DONE AS THE NEXT STEP IN YOUR CURRENT MANAGEMENT STRATEGY?

(check only one)

☐ Observation (with close follow-up)

☐ Additional Imaging
   o If additional imaging is selected, please indicate which specific type of imaging you would order next. (check one)
     o ☐ Plain radiographs
     o ☐ Body CT (neck, chest, and/or abdomen/pelvis)
     o ☐ Extremity CT
     o ☐ Body MRI (spine, neck, chest, and/or abdomen/pelvis)
     o ☐ Extremity MRI
     o ☐ FDG-PET
     o ☐ Other, specify: ____________________________

☐ Tissue Biopsy (surgical, percutaneous, or endoscopic).
   [Note: If concurrent biopsy and a surgical procedure are planned, then mark “treatment” below. ]

☐ Supportive care only (e.g., pain management, hospice care)

☐ Treatment for the Cancer

If treatment was selected, answer the questions below:

a. Treatment Goal: (check one)
   ☐ Curative
   ☐ Palliative

b. Treatment will be directed to: (check all that apply)
   ☐ Primary tumor and/or locoregional disease
   ☐ Non-osseous distant metastatic disease
   ☐ Osseous distant metastatic disease

c. Type(s): (check all that apply)
   ☐ Surgery
   ☐ Radiation
   ☐ Chemotherapy (including biologic modifiers)
☐ Hormonal therapy
☐ Bisphosphonate therapy
☐ Immunotherapy (e.g., sipuleucel T (Provenge®) for prostate cancer)
☐ Radiopharmaceutical therapy (strontium-89, samarium-153, etc.)
☐ Other

Specify other treatment type: _________________________________________

5. DID THE PET SCAN ENABLE YOUR PATIENT TO AVOID ANY

a. noninvasive diagnostic tests?  
   ☐ Yes  ☐ No

b. any invasive procedures?  
   ☐ Yes  ☐ No

6. I HAVE READ THE REFERRING PHYSICIAN INFORMATION STATEMENT AND:
   ☐ I DO give my consent for the inclusion of data collected for this patient in NOPR research.
   ☐ I DO NOT give my consent for the inclusion of data collected for this patient in NOPR research.

7. NAME OF PERSON SUBMITTING THIS FORM
   First Name: _______________  Last Name: _______________  Date: ______/_____/____

8. PHYSICIAN ATTESTATION OF DATA ACCURACY
   By signing below I verify that, to the best of my knowledge, the information on this form is accurate.

   Physician Signature: ____________________________________________  Date: ______/_____/____

   Printed Name of Physician: __________________________________________

Thank you for your assistance.

PRA Disclosure Statement
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Your patient had a PET scan on _mm/dd/yyyy_. [Date will automatically be filled.]

You previously indicated that the PET scan was done for _restaging of cancer type_ [Will automatically be filled in from data supplied on Pre-PET form] to assess for

- new osseous metastatic disease as a site of recurrence or
- progression of known osseous metastatic disease.

[Reason will automatically be filled in from data supplied on Pre-PET form.]

- After reviewing the PET report, please complete the following questions and return the form to the PET Facility.
- This form must be entered into the database within 30 days of the PET scan.

1. **COMPARED TO YOUR PRE-PET ASSESSMENT, WHAT IS YOUR IMPRESSION OF THE EXTENT OF THE PATIENT'S CANCER?**
   - More extensive
   - No change
   - Less extensive

2. **YOUR POST-PET WORKING CLINICAL STAGING IS: (SELECT ONLY ONE)**
   - No evidence of disease / In remission
   - Low probability of local recurrence or metastases
   - Local recurrence
   - Metastatic (distant) with a single suspected site
   - Metastatic (distant) with a multiple suspected sites

3. **DID THE PET SCAN ENABLE YOUR PATIENT TO AVOID ANY**
   a. noninvasive diagnostic tests?
      - Yes
      - No
   b. any invasive procedures?
      - Yes
      - No
4. IN LIGHT OF THE PET FINDINGS, WHICH ONE OF THE FOLLOWING ARE YOU PLANNING OR HAVE YOU ALREADY DONE AS THE NEXT STEP IN YOUR CURRENT MANAGEMENT STRATEGY? (check only one)

- Observation (with close follow-up)

- Additional Imaging
  - If additional imaging is selected, please indicate which specific type of imaging you would order next. (check one)
    - Plain radiographs
    - Body CT (neck, chest, and/or abdomen/pelvis)
    - Extremity CT
    - Body MRI (spine, neck, chest, and/or abdomen/pelvis)
    - Extremity MRI
    - FDG-PET
    - Other, specify: __________________________

- Tissue Biopsy (surgical, percutaneous, or endoscopic).
  [Note: If concurrent biopsy and a surgical procedure are planned, then mark “treatment” below.]

- Supportive care only (e.g., pain management, hospice care)

- Treatment for the Cancer

  If treatment was selected, answer the questions below:

  a. Treatment Goal: (check one)
     - Curative
     - Palliative

  b. Treatment will be directed to: (check all that apply)
     - Primary tumor and/or locoregional disease
     - Non-osseous distant metastatic disease
     - Osseous distant metastatic disease

  c. Type(s): (check all that apply)
     - Surgery
     - Radiation
     - Chemotherapy (including biologic modifiers)
     - Hormonal therapy
     - Bisphosphonate therapy
     - Immunotherapy (e.g., sipuleucel T (Provenge®) for prostate cancer)
     - Radiopharmaceutical therapy (strontium-89, samarium-153, etc.)
☐ Other
Specify other treatment type: ________________________________________________

5. I HAVE READ THE REFERRING PHYSICIAN INFORMATION STATEMENT AND:
   ☐ I DO give my consent for the inclusion of data collected for this patient in NOPR research.
   ☐ I DO NOT give my consent for the inclusion of data collected for this patient in NOPR research.

6. NAME OF PERSON SUBMITTING THIS FORM
   First Name: ________________  Last Name: ___________________  Date: ___/___/____

7. PHYSICIAN ATTESTATION OF DATA ACCURACY
   By signing below I verify that, to the best of my knowledge, the information on this form is accurate.
   Physician Signature: _________________________________________  Date: ___/___/____
   Printed Name of Physician: ____________________________________

   Thank you for your assistance.

PRA Disclosure Statement
According to the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it displays a valid OMB control number. The valid OMB control number for this information collection is 0938-0968. The time required to complete this information collection is estimated to average five (5) minutes per response, including the time to review instructions, search existing data resources, gather the data needed, and complete and review the information collection. If you have comments concerning the accuracy of the time estimate(s) or suggestions for improving this form, please write to: CMS, 7500 Security Boulevard, Attn: PRA Reports Clearance Officer, Mail Stop C4-26-05, Baltimore, Maryland 21244-1850.
Appendix B-III

HIPAA Compliance and IRB Approval for the NOPR (NaF-PET)

HIPAA Compliance and Participation in the NOPR
The Health Insurance Portability and Accountability Act of 1996 (HIPAA) requires that providers (Covered Entities as that term is defined under HIPAA) have in place an agreement with any Business Associate if the parties in their business dealings exchange Protected Health Information (PHI), as that term is defined in the HIPAA regulations. Under the regulations, submission of claims data by a PET facility (Covered Entity) to the American College of Radiology (ACR) (Business Associate) requires execution of a business associate agreement.

The American Recovery and Reinvestment Act of 2009 (ARRA) contained provisions called the Health Information Technology and Economic and Clinical Health Act (HITECH) that extend the original requirements related to administrative, physical and technical safeguards that applied to covered entities under HIPAA to the business associates of those covered entities.

The business associate agreement (BAA) serves the purpose of obtaining satisfactory assurance that the Business Associate will appropriately safeguard any PHI received from the Covered Entity. The HITECH amendment serves as an amendment to our current BAA that extends to the NOPR. With these agreements in place, the exchange of information between the Covered Entity and the Business Associate will meet HIPAA requirements without disruption of the business arrangement.

In order to facilitate the submission of your claims data to the NOPR, the ACR has developed a business associates agreement (BAA) and a HITECH amendment to the HIPAA BAA for your use. (The BAA and HITECH amendment to the BAA are available on the NOPR web site at http://www.cancerpetregistry.org/under NOPR Forms.) These agreements fully comply with the requirements of HIPAA and the new requirements under the law.

Institutional Review Board (IRB) Approval for Registry
The only entity engaged in research is the registry itself (i.e., NOPR) because the NOPR intends to use the data it is collecting for research purposes when both the patient and the referring physician have consented to the use of the information for this purpose. The ACR IRB has granted approval for the NOPR to engage in research using these data as described in the original NOPR research plan and this revised research plan (ACR IRB approval letters are posted on the NOPR website).

Individual PET facilities, interpreting physicians, referring physicians and their staffs are not engaged in research and therefore are not required to have IRB approval for their participation in the activities of the NOPR. Submission of the information for the registry (pre-PET and post-PET case report forms, the PET scan report and the interpreting physician scan assessment form) is required by CMS for payment for PET studies for all Medicare-insured patients with cancer indications included in the registry. Additionally, CMS is not conducting research.

Any participating PET facility may nevertheless elect to have its local IRB review its participation in the NOPR. Some IRBs require, as a matter of institutional policy, that they review all research conducted in the institution, even if only to determine that the facility is not engaged in the research. Materials are provided below to assist in this process (See below, Submission Materials for Institutional IRB Review). The Office of Human Research Protections (OHRP) has reviewed the NOPR procedures for protection of human research subjects and finds them to be in compliance with the applicable DHHS regulations. Any individual IRBs with questions can contact the NOPR Working Group co-chairs or OHRP.
Appendix B-IV:

National Oncologic PET Registry (NOPR)

ACR Clinical Research Center

The ACR Clinical Research Center is the research arm of the American College of Radiology, a professional medical organization composed of diagnostic radiologists, radiation oncologists, interventional radiologists, nuclear medicine physicians, and medical physicists, with headquarters in Reston, VA. The ACR Clinical Research Center, located in Philadelphia, PA, has been involved in pioneering clinical research for over 40 years. The center houses the four research entities: American College of Radiology Imaging Network (ACRIN), Radiation Therapy Oncology Group (RTOG), Quality Research in Radiation Oncology (QRRO), and ACR Image Metrix. Over 175 clinical trial specialists are dedicated to supporting high-quality research conducted at over 300 facilities nationwide, which includes:

- Medical imaging clinical trials
- Radiation oncology clinical trials
- Patterns of care
- Patient outcomes
- Cost effectiveness
- Translational research

ACR research enterprises have published landmark papers on critical health care issues such as breast cancer screening with digital mammography, the effectiveness of CT colonography, post-operative treatment outcomes of patients with head and neck cancer, magnetic resonance imaging of patients with breast cancer, treatment advances for patients with pancreatic cancer, and the practice of brachytherapy for patients with cervical cancer. These and other patient care altering publications produced throughout the center’s history are the result of a sophisticated clinical research infrastructure made up of:

- A full GCP-compliant diagnostic imaging and radiation oncology core laboratory that carries out:
  - Reader studies
  - Quality assurance programs that includes image and dose review and site qualification of scanners and images
  - The development of new imaging and treatment planning techniques in support of clinical trial aims
  - Investigator training on new imaging techniques and applications

- Innovative statistical techniques that allow for rapid assessment of phase II study data reducing the time to the start of phase III testing.

- State-of-the-art information technology resources that can expedite data collection and provide data auditing to insure compliance with FDA clinical practice standards.

- A novel image acquisition and management system that allows for easy transfer of images from participating sites to an image archive.

- Independent data monitoring committees for study monitoring and interim data analyses.

The network of investigators that design and carry out the center’s clinical trials include radiologists, medical oncologists, physicists, biologists, epidemiologists, and biostatisticians who are located in a variety of practice settings. In addition, the center has conducted clinical trial research on behalf of over 20 pharmaceutical and biological agent manufacturers including Bristol-Myers Squibb, Eli Lilly, Genentech, and Schering Plough. These corporations rely upon our national network of contracted facilities and our ability to rapidly collect, review and analyze study data.
The ACR Clinical Research Center has the expertise and resources to partner with industry leaders in radiology and radiation oncology, pharmaceutical communities and devise manufacturers to conduct clinical trials testing new technologies and applications.

**Radiation Therapy Oncology Group (RTOG®)**
[www.rtog.org](http://www.rtog.org)

The RTOG, established in 1968, is a major international radiation oncology research organization with over 300 member institutions in the US and abroad. Since its inception, RTOG has conducted over 460 protocols and accrued over 75,000 patients. In 2008, the research enterprise was awarded 60.5 million dollars by the National Cancer Institute to carry out its research agenda for the next six years. Approximately 40 actively accruing studies are currently being managed along with an additional 115 studies (representing 27,000 patients) that are in follow up phase. RTOG investigators publish and present internationally well over 100 manuscripts and abstracts annually.

**American College of Radiology Imaging Network (ACRIN®)**
[www.ACRIN.org](http://www.ACRIN.org)

First funded in 1999 to perform multicenter clinical trials of medical imaging, ACRIN has become a major participant in the cancer research community during its relatively short history. ACRIN has conducted three landmark screening trials: the Digital Mammographic Imaging Screening Trial enrolled over 50,000 women and reported that digital mammography was superior to standard film for the majority of women; the National CT Colonography (CTC) Trial confirmed that this technology is ready for adoption as a front line colorectal cancer screening tool; and the results of the National Lung Cancer Screening Trial that accrued 53,000 participants at high risk for lung cancer demonstrated a 20 percent mortality benefit for those patients screened with low dose CT. Having received full funding from the National Cancer Center for grant years 2008-2012, ACRIN is focused on establishing imaging as an important tool in the development and monitoring of targeted interventions for cancer treatment and prevention. For example, the trial “FDG-PET/CT as a Predictive Marker of Tumor Response and Patient Outcome: Prospective Validation in Non-small Cell Lung Cancer”, currently enrolling patients, is at the forefront of establishing PET imaging as a biomarker for monitoring cancer patients’ treatment.

**Quality Research in Radiation Oncology (QRRO®)**
[www.qrro.org](http://www.qrro.org)

Funded in 1973 as the Patterns of Care Study (PCS) to compare recommended management guidelines to actual practice of radiation therapy throughout all types of facilities in the U.S., the PCS made possible the identification of new approaches to radiation oncology leading to improved patient outcome and/or reduced complications. The PCS program built on prior findings of six national process and outcome surveys in radiation oncology to further enhance cancer patient management.

In 2005 the PCS program was reorganized and renamed Quality Research in Radiation Oncology (Q-RRO). Emphasis shifted from measurements of processes to quality of care to better fit into the National Cancer Institute priorities. Pooled survey data collected at 45 institutions nationwide provides a rich resource for investigating if improved radiation oncology practices reported are actually making their way into clinical practice.
ACR Image Metrix®
www.acr-imagemetrix.net

In February 2007, the ACR Image Metrix contract research organization (CRO) was formed to pursue commercial research opportunities in the pharmaceutical, device manufacturing, and biomedical industries. The business operations leverage the ACR Clinical Research Center’s extensive research infrastructure and the CRO has been successful in attracting business from startup companies to major corporations.

Resources for Project Management, Data Security, and Quality Assurance

Project Management
As detailed above, ACR has extensive experience in the management of clinical trials. As is its custom, ACR will assign a Project Manager for the National Oncologic PET Registry (NOPR). Working with the NOPR Working Group the Project Manager will be responsible for coordinating all aspects of the registry development, implementation, monitoring and reporting. The Project Manager will be a resource for the PET Facilities in need of information or help with the Web-based applications.

Informatics
The Management Information Systems (MIS) Department of the American College of Radiology provides computer and informatics services. The department has a long history of outstanding support to practitioners and large national cooperative groups and is completely familiar with their unique needs of clinical trial management. MIS staff are located in the Philadelphia, PA and Reston, VA locations, and utilize staff from the other office as necessary.

The MIS Department operates the National Oncologic PET Registry (NOPR), which is a collaboration of the American College of Radiology Imaging Network (ACRIN), the American College of Radiology (ACR), and the Academy of Molecular Imaging (AMI), since May 2006. This system was developed by the ACR in response to the Centers for Medicare and Medicaid Services (CMS) proposal to expand coverage for positron emission tomography (PET) with F-18 fluorodeoxyglucose (FDG) to include cancers and indications not presently eligible for Medicare reimbursement. It is a comprehensive system, providing a modern informatics infrastructure that enables the participating facilities to submit PET study and PET scan data to the registry using sophisticated electronic collection techniques via the World Wide Web. It also provides a wide array of management tools that are invaluable in supporting the needs of both the HQ and the facilities. Since 2006, multiple enhancements have been added to the system to assure that it remains up-to-date and provides the latest in informatics capabilities. The system has particularly strong capabilities in interfacing with participating facilities via the World Wide Web. Details of both the hardware and software components of the ACR system are covered in the Resources section.

ACR has also developed a range of leading edge Web based registries under the National Radiology Data Registry (NRDR. https://nrdr.acr.org). The NRDR is used to provide regional and national benchmarks on practice performance. The NRDR is an important tool for improving the quality of patient care.

Security
The NOPR collects certain patient information (name, date of birth, social security number, gender, race, and ethnicity). The ACR is committed to protecting patient information and implements procedures and policies to ensure the information remain confidential. The NOPR provides secure services that will enable participating facilities to access information, communicate, and engage in transactions with confidence.
Security at the ACR Reston computer facilities entails both physical and software restraints limiting access to patient data. The computer facilities are located within the office space of the ACR Reston offices. Access to the ACR Reston offices and the ACR data centers are restricted by cardkey access. The security capabilities in Windows 2003/2008 Servers are built on standard protocols and supported by the Active Directory. System Administrators manage user accounts and access rights by granting or denying access rights, and delegating security administration. System accounts for both current employees and registered institutions are maintained by system administration personnel and are continuously updated based upon changing user environments.

The NOPR patient data will be encrypted using the Triple DES algorithm. The NOPR only allows authorized users to enter the site. The NOPR users must enter a valid username and password to gain access to the system. The user accounts are created and managed by the participating facility administrator within the NOPR application. Facilities can only manage their own user accounts. Once authenticated, a user can access only the data that belongs to his/her facility. The NOPR application does not share patient information across facilities.

Passwords are stored as hash values. No one except the user has access to his/her password. The NOPR application provides a password reset function that allows the facility administrators and/or the NOPR administrator (ACRIN staff) to reset the user passwords. Once reset, the application sends an e-mail notification with a randomly generated password to the specified user, and forces him/her to change the password upon the next log in.

Password must be at least eight characters long and must contain characters from at least three of the following sets:

- Lower case: a b c d e f g h i j k l m n o p q r s t u v w x y z
- Number: 0 1 2 3 4 5 6 7 8 9
- Special character: ! @ # $ % ^ & * ()

All data transmissions are encrypted using the VeriSign Class 3 Extended Validation certificate.

The NOPR application automatically terminates sessions that are idled for twenty minutes.

The NOPR site uses a clustered pair of Cisco Adaptive Security Appliances (ASA 5540) firewalls with built-in intrusion detection modules (SSM-20). The firewall limits access to the site via HTTPS traffic to the web server only. The database server (Microsoft SQL server) is not directly accessible to the internet. Remote Desktop Access to the Web and SQL servers are restricted to the internal ACR network only, and enforce user and password identification for access.

System security is further enhanced by 24x7 monitoring. The ACR has contracted with SecureWorks (www.secureworks.com) to provide a 24x7 solution which aggregates all of the logs from the firewall and the IDS module to form an overall picture of threats to the system protected by the firewall. SecureWorks then performs an analysis of the threat and alerts the ACR of any corrective actions required.

Database administration access is restricted to DBA and System Administration personnel only. Access to the NOPR data is restricted to DBAs, Administrators, and the NOPR Application account.

The Web and SQL machines are built on the Microsoft Windows 2003/2008 x 64 platforms. Administrative level accounts utilize password complexity, enforce a password of 8 or more characters in length, and are changed on a regular basis. Administrative level account passwords are known only to the DBA and System Administration personnel.
Servers are patched and rebooted monthly on the third Saturday of every month as part of our normal maintenance process. Machines are patched to the latest Microsoft patch levels, unless there is an application conflict. In an event of a conflict, all dependencies are researched and resolved and the patch is applied as soon as possible.

The ACR performs a weekly full backup of the web and SQL machines every Friday night. On Monday through Thursday, a differential backup is performed. Backup tapes are removed from the tape library Monday through Friday and are stored in a different building. Once a week, tapes are sent off site to a secure tape facility. In addition to our tape backups, a nightly full SQL backup is also performed.

**Quality Assurance**
The NOPR manual of operations gives a detailed description of the data requirements and the timeline for data submission. The statistical section provides the framework in which the Working Group will make decisions concerning coverage recommendations.

The quality assurance program for the NOPR will revolve around the validation checks that are built into the Web-based data entry applications. PET Facilities will not be able to complete the data form entry process if there are missing data elements or if the data elements are outside specified range values. In addition, patient identifiers will be collected so that CMS will have the option of including Registry compliance in its standard auditing procedures. PET Facilities are instructed to keep all paper copies and e-mails received from referring physicians as source data.

**Resources**
The ACR Reston Offices are housed in 2 separate buildings, one in 1891 Preston White Drive and the second in 1892 Preston White Drive. Each building has its own datacenter and the datacenters are connected via dark fiber. Available computer hardware and software includes:

**Software**

**Major Equipment**
Dell PowerEdge 1950, 2950, R710,and R900 Servers. EMC CX700 SAN, NS-40 NAS, and EMC NS4-80 SAN/NAS. Cisco ASA5540 Firewalls-This will be upgraded to Layer 7 Fortinet Firewalls, Cisco 3750, 4510, and 6513 Switches, Dell ML6020 Tape Libraries.

**Automated Backup Tape Libraries**
Tape libraries deliver fast file access and high capacity for automated backup and storage for distributed networks and servers. They provide up to 115 Terabyte of storage and up to 2 TB per hour per-drive sustained throughput. Multiple tape drives in these auto libraries provide higher performance, redundancy, and allow scalability-drives to be added to increase performance or to upgrade to newer technology.

**Internet Links**
Dedicated 10 MB Ethernet connection that is capable of bursting to 50 MB during peak loads. This will be upgraded to a dedicated 100 MB connection in 2011. 10 MB Ethernet Provivate Line (EPL) connecting the Philadelphia and Virginia data centers. This will be upgraded to a 20 MB MPLS network.