National Cancer Institute

Cancer Imaging Program

Protocol Template Components and General Requirements for Studies that will use [F-18]FES

Under the NCI CIP-held IND # 79,005

VERSION: 4.0

EFFECTIVE: Nov. 1st, 2011

This Document Contains

General requirements for protocols & consents for studies using the radiopharmaceutical [F-18]FES in qualifying studies

and

[F-18]FES related prompts, suggestions, and sample content that may be used for guidance, IN ADDITION TO EXISTING NCI/CTEP PROTOCOL DEVELOPMENT TEMPLATES AND TOOLS, to develop a new protocol for an NCI study that will use [F-18]FES.

General Protocol & Consent Requirements:

1. The IND holder [e.g. NCI], and the specific IND number under which this investigational radiopharmaceutical PET agent will be provided, must be explicitly stated in an appropriate and prominent place in the opening sections of the protocol.

2. [F-18]FES must be clearly identified as an investigational agent, per se, in the protocol and consent, and [F-18]FES must appear in the 'investigational agent' section, or equivalent, of the protocol.

3. The distinction between the following must remain clear throughout the protocol and consent:

   - standard of care imaging [e.g. FDG-PET scans that are non-study specific].
   - study specific [research] use of standard imaging [e.g. FDG-PET scans added solely for the study].
   - inherently investigational imaging [e.g. any FES-PET scans].

   Referring to FES-PET scans as 'study specific' procedures [i.e., like an additional standard CT or MRI might be described] is NOT, by itself, adequate, as FES-PET is currently investigational.

4. [F-18]FES risks must be consistent with the current applicable Investigator's Brochure, which may be obtained by forwarding a request to NCICIPINDAGENTS@mail.nih.gov.

Template Text Conventions & Comments:

- Sample/Suggested template text and placeholders appear as normal/**bold** text.
- Prompts for possible insertion or substitution of study specific information appear in _____underline highlight_____ or [brackets with yellow highlight].

THE TEMPLATE BEGINS ON THE NEXT PAGE

[Document Identification]

TABLE OF CONTENTS

SCHEMA [Please indicate, in schema, when FES-PET will be performed in the study]

STUDY AIMS/RATIONALE/OBJECTIVES

Primary Objective [Please Specify FES Primary Objective if applicable]

Secondary/Exploratory Objective [Please Specify FES Secondary/Exploratory Objective if applicable]

SAMPLE SIZE [Please add information regarding FES-PET as appropriate]

ABSTRACT [Please add information regarding FES-PET as appropriate]

BACKGROUND [Please add information regarding FES-PET as appropriate]

IMAGING AGENT INFORMATION

For complete information, please refer to the current Investigator's Brochure: [Insert title, version and date of NCI IB] [NOTE: to obtain the most current IB contact NCICIPINDAGENTS@mail.nih.gov .]

Pharmacology and Toxicology: [Insert appropriate text from the current Investigator's Brochure]

Toxicity of FES in Humans: [Insert appropriate text from the current Investigator's Brochure]

Dosimetry: [Insert appropriate text from the current Investigator's Brochure]

Previous Human [F-18]FES Imaging Studies: [Insert appropriate text from the current Investigator's Brochure]

[F-18]FES Administered Dose:

[F-18]FES will be administered to subjects over 1 minute by intravenous bolus injection. Doses will be pre-calibrated to [___ mCi or ___ mCi/kg], with a dose range of [_____]. The dose will not exceed _____ mCi total.

Quality Assurance, Quality Control and Storage:

In accordance with regulations, the radioisotope vendor conducts several quality control tests on the [F-18] FES product prior to release for human administration. Once delivered to the participating institution, doses will be stored in the appropriate storage area in the nuclear medicine facility until they are administered to the patient on the same day.

Supplier of [F-18]FES:

Drug Ordering:

[F-18] FES will be purchased from [specify by name and telephone number the NCI IND AUTHORIZED commercial vendor (e.g. PetNet, Cardinal, IBA) of radioisotopes to be used] under

the NCI IND. The vendor must be specifically authorized within the NCI IND. The investigator or appropriate investigator-designee will order subject doses of [F-18] FES for this specific trial. The investigational radiopharmaceutical [F-18]FES solution will be shipped to the site the same day the participant is to be injected.

The [investigational pharmacist or qualified nuclear medicine technologist] at the participating institution will be the responsible party designated by the investigator.

Drug Returns:

If for any reason the study imaging is unable to be completed, sites will allow the radioactivity of the [F-18]FES solution to decay and then discard it appropriately per site's policies and procedures, making a record of the event as required. A copy of the policy should be available upon request.

Drug Accountability:

The investigator or the investigator-designee must maintain a detailed record of receipt, disposition, and destruction dates of [F-18]FES solution, using the _____ form appended hereto or available on the web at _____.

STUDY OVERVIEW

PARTICIPANT SELECTION/ELIGIBILTY CRITERIA

STUDY PROCEDURES & STUDY CALENDAR [Please include [F-18]FES PET events in the study calendar]

DATA MANAGEMENT/REGISTRATION [Please discuss local or centralized image review]

IMAGING PROTOCOL

[F-18]FES Administration:

[F-18]FES will be provided by a vendor authorized within the NCI IND. [F-18]FES will be administered according to the guidance provided in the most current Investigators Brochure for this IND.

[F-18]FES-PET Imaging:

[Image Acquisition Details]

[Image Analysis Details]

[Image Interpretation Details]

[Imaging Related Procedures]

ADVERSE EVENTS REPORTING

[Please use the AdEERS Adverse Event reporting table below in addition to the required content per the CTEP AE Reporting Guidelines document]

Phase 1 and Early Phase 2 Studies: Expedited Reporting Requirements for Adverse Events that Occur on Studies under an IND/IDE within 30 Days of the Last Administration of the Investigational Agent/Intervention [1, 2]

FDA REPORTING REQUIREMENTS FOR SERIOUS ADVERSE EVENTS (21 CFR Part 312)

NOTE: Investigators **MUST** immediately report to the sponsor (NCI) **ANY** Serious Adverse Events, whether or not they are considered related to the investigational agent(s)/intervention (21 CFR 312.64)

An adverse event is considered serious if it results in **ANY** of the following outcomes:

1) Death
2) A life-threatening adverse event
3) An adverse event that results in inpatient hospitalization or prolongation of existing hospitalization for ≥ 24 hours
4) A persistent or significant incapacity or substantial disruption of the ability to conduct normal life functions
5) A congenital anomaly/birth defect.
6) Important Medical Events (IME) that may not result in death, be life threatening, or require hospitalization may be considered serious when, based upon medical judgment, they may jeopardize the patient or subject and may require medical or surgical intervention to prevent one of the outcomes listed in this definition. (FDA, 21 CFR 312.32; ICH E2A and ICH E6).

ALL SERIOUS adverse events that meet the above criteria MUST be immediately reported to the NCI via AdEERS within the timeframes detailed in the table below.

Hospitalization	Grade 1 and Grade 2 Timeframes	Grade 3-5 Timeframes
Resulting in Hospitalization ≥ 24 hrs	10 Calendar Days	24-Hour 5 Calendar Days
Not resulting in Hospitalization ≥ 24 hrs	Not required	

NOTE: Protocol-specific exceptions to expedited reporting of serious adverse events are found in the Specific Protocol Exceptions to Expedited Reporting (SPEER) portion of the CAEPR.

Expedited AE reporting timelines are defined as:

- "24-Hour; 5 Calendar Days" - The AE must initially be reported via AdEERS within 24 hours of learning of the AE, followed by a complete expedited report within 5 calendar days of the initial 24-hour report.
- "10 Calendar Days" - A complete expedited report on the AE must be submitted within 10 calendar days of learning of the AE.

[1]Serious adverse events that occur more than 30 days after the last administration of investigational agent/intervention and have an attribution of possible, probable, or definite require reporting as follows:

Expedited 24-hour notification followed by complete report within 5 calendar days for:

All Grade 3, 4, and Grade 5 AEs

Expedited 10 calendar day reports for:

Grade 2 AEs resulting in hospitalization or prolongation of hospitalization

[2] For studies using PET or SPECT IND agents, the AE reporting period is limited to 10 radioactive half-lives, rounded UP to the nearest whole day, after the agent/intervention was last administered. Footnote "1" above applies after this reporting period.

Effective Date: May 5, 2011

STATISTICAL CONSIDERATIONS

Reporting and Exclusions:

Evaluation of toxicity

All subjects will be evaluable for toxicity from the time of injection of [F-18]FES until 24 hours after injection. [See Adverse Event Reporting Section].

Reporting Guidelines

[Please Specify ALL requirements, timing, mechanisms, systems, and backups to be used for recording data to CRFs and reporting data to NCI]

APPENDIX I
[Current [F-18]FES IDB for the NCI held IND]