



[¹⁸F]FLUOROESTRADIOL, [¹⁸F]FES

FREQUENTLY ASKED QUESTIONS

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What is the status of FES at the Cancer Imaging Program?

We have an established IND (8/2007) for FES that we actively encourage investigators to cross-file on

- We freely provide manufacturing and quality control documentation to assist this effort <http://imaging.cancer.gov/programsandresources/Cancer-Tracer-Synthesis-Resources>,
- We encourage academic and pharmaceutical investigators to evaluate FES for therapeutic drug evaluation/development
- We anticipate that the data resulting from wider availability of this agent will support an eventual New Drug Application (NDA) by a commercial entity

What is the Regulatory Status of FES?

FES is an investigational PET agent. Several individuals and organizations hold an Investigational New Drug (IND) Exemption from the FDA under which they are permitted to make and use FES. IND information can be found here:

http://www.fda.gov/cder/regulatory/applications/ind_page_1.htm

How can I use FES in my clinical trial?

In order to use FES, you must hold an IND or have your basic science trial approved by your Institution's RDRC (Radioactive Drug Research Committee). In either case, you must have your trial approved by an Institutional Review Board (IRB).

Can I make my own FES?

If you have appropriate facilities (cyclotron, radiochemistry lab and personnel, capacity to manufacture PET agents for human use), you can make FES. Your chemistry procedures must be acceptable to FDA for your IND or to the RDRC, and to the IRB.

Can I buy FES from someone to use in my trial?

Some commercial firms may provide FES for research use. That material can be used in your clinical trial only if you are allowed to submit the full chemistry information to FDA in your IND or provided with a letter of authorization to a Drug Master File (DMF). At this time, to the best of our knowledge, no company has a DMF on file with the FDA for this agent, which would permit use of this material in your IND-approved trial if the company provides you with an appropriate authorization letter.

How can NCI help?

NCI can assist in two ways. NCI holds an IND for FES that is based on a specific automated synthesis performed on a nucleophilic substitution box. Documents necessary to prepare and test FES for use in clinical trials are available on the Cancer Imaging Program (CIP) website.

<http://imaging.cancer.gov/programsandresources/Cancer-Tracer-Synthesis-Resources>

The documents include a full set of manufacturing and QC documents ("SOPs") and an Investigator Drug Brochure, all of which have been accepted by the FDA as part of the NCI IND. The synthesis follows that reported by Lim (Lim, JL, Zheng, L, et al: The use of 3-methoxymethyl-16 beta, 17 beta-epiestriol-O-cyclic sulfone as the precursor in the synthesis of F-18 16 alpha-fluoroestradiol. Nucl Med Biol 23:911-5, 1996). Investigators at each site can implement this synthesis and testing in their radiochemistry laboratory. There is a CMC template that may need to be modified to match the local procedures (e.g. specific brands of equipment). Investigators can then write and file their own IND with the FDA by modifying the CMC section to fit local conditions and adding the Investigator's proposed Clinical protocol.

Additionally, CIP will provide a Letter of Authorization (cross-file letter) to the FDA in conjunction with your IND that can simplify your IND application. This letter may substitute for the Pharmacology, Toxicology, Radiation Dosimetry and Previous Human Experience sections of the IND.

If you do purchase FES from a company that holds a DMF, their Letter of Authorization will substitute for the Chemistry, Manufacturing, and Control section of your IND.

For additional information

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