[^{18}F]FLUOROMISONIDAZOLE, [^{18}F]FMISO

FREQUENTLY ASKED QUESTIONS

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

We have an established IND (9/2006) for FMISO 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 FMISO 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 FMISO?

FMISO 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 FMISO for purposes of conducting clinical investigations of that drug. IND information can be found here: **http://www.fda.gov/cder/regulatory/applications/ind_page_1.htm**. PET drug information can be found here: **FDA PET Page.**

How can I use FMISO in my clinical trial?

In order to use FMISO, 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 FMISO?

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

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

Some commercial firms do provide FMISO 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, one company has a DMF on file with the FDA for this agent, which will permit use of this material in your IND-approved trial if the company provides you with an appropriate authorization letter or if you have a letter of authorization to our IND, which contains appropriate authorizations.

How can NCI help?

NCI can assist in two ways. NCI holds an IND for FMISO that is based on a specific automated synthesis performed on a nucleophilic substitution box. Documents necessary to prepare and test FMISO 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's Drug Brochure, all of which have been accepted by the FDA as part of the NCI IND. Some full toxicology reports are also available at this site. The synthesis procedure follows that reported by Lim and Berridge (1993), An efficient radiosynthesis of [18F]fluoromisonidazole. *Appl. Radiat. Isot.* 44, 1085-1091. 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 FMISO 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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