

**Summary of Changes for
[F-18]FMISO (IND 76,042) Investigator's Brochure
Edition 4 (November 9, 2009) to Edition 5 (February 5, 2013)**

SECTION	DESCRIPTION OF CHANGE	RATIONALE
GLOBAL THROUGHOUT DOCUMENT	Formatting changes and other minor edits, including changes to references for consistency/correction, throughout the IB, without change to meaning or substance.	Improve document consistency, accuracy, readability, and adherence to necessary style.
TITLE PAGE	Edition and Approval Date change.	This is Edition 5, February 5, 2013
TABLE OF CONTENTS	Modified to match revised contents and pagination.	To properly reflect content changes throughout document.
II, 3. FINAL PRODUCT SPECIFICATIONS	Removed first paragraph and modified text to reflect the latest final product specifications.	To clarify/remove redundant statement/correct statement as to the basis for specific activity calculation.
V, 4 HUMAN TOXICITY STUDIES: MISO	In the second paragraph, last sentence, minor changes in language.	No change to meaning – improved readability.
V, 9. [F-18] FMISO HUMAN SAFETY STUDIES	In the second paragraph, minor changes in languages.	No change to meaning – improved readability.
V, 12. SAFETY AND TOXICITY OF THE OTHER COMPONENTS OF THE FINAL [¹⁸ F]FMISO DRUG PRODUCT	Minor changes to make clear that the routine use of ethanol in injectates do not pose any danger of toxicity when used in imaging studies.	To explain the basis for the safety profile of the other components.
VI, BIODISTRIBUTION AND RADIATION DOSIMETRY OF FMISO	Last paragraph, statement clarifying the radiation exposure and standardization has been added.	To explain why additional radiation exposure may occur with any PET study.
VII, [¹⁸ F]FMISO PREVIOUS HUMAN EXPERIENCE AND ASSESSMENT OF CLINICAL POTENTIAL Table 8: Summary of Published Manuscripts.	Updated to reflect recent literature. Rearranged to organize papers by anatomic site where possible. Additional text changes to more clearly describe the data in the table, particularly to homogenize the specific data, and overall safety profile development.	To maintain a current list of references. To ensure IB is user friendly and accurate. To update human exposure numbers. Unique human exposures now total: ~ 1,021. Rationale for not counting likely duplicate subjects is provided. Organized by anatomic site for ease of reviewing.
VIII, REFERENCES	New articles added and minor corrections made to existing references.	To maintain a current list of references. To ensure user friendly and accurate.