DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Silver Spring, MD 20993

TRANSMITTED BY FACSIMILE

Fabio Almeida, MD
Phoenix Molecular Imaging Center
4540 East Cotton Gin Loop Ste 150
Phoenix, AZ 85040

RE: (b) (4)
Sodium Acetate C-11
MA 1

Dear Dr. Almeida:

The Office of Prescription Drug Promotion (OPDP) of the U.S. Food and Drug Administration (FDA) has reviewed a webpage[1] entitled "Overview of PET/CT Imaging in Recurrent Prostate Cancer-Current and Emerging Techniques" (webpage) that discusses the investigational new drug Sodium Acetate C-11 (11C-Acetate), which is the subject of the above-referenced IND. You are receiving this letter as the sponsor and principal investigator for that IND. The webpage suggests in a promotional context that 11C-Acetate, an investigational new drug, is safe and effective for the purpose for which it is being investigated or otherwise promotes the drug. As a result, 11C-Acetate is misbranded under section 502(f)(1) of the Federal Food, Drug, and Cosmetic Act (FD&C Act) and in violation of section 301(k) of the FD&C Act. The claims and presentations made on the webpage are concerning from a public health perspective because they make conclusory representations in a promotional context regarding the safety and efficacy of an investigational new drug that has not been approved by the FDA and whose safety and efficacy have not yet been established.

Background

11C-Acetate is an investigational new drug for which there is no marketing authorization in the United States. (b) (4)

Misbranding of an Investigational Drug

Under section 502(f)(1) of the FD&C Act, a drug shall be deemed to be misbranded unless its labeling bears adequate directions for use. Under FDA regulations, adequate directions for use means directions under which the layman can use a drug safely and for the purposes for

[1] Found at http://www.drfabio.com/imagingblog/2018/1/9/overview-of-petct-imaging-in-recurrent-prostate-cancer-current-and-emerging-techniques. Last accessed February 15, 2019.

which it is intended. 21 CFR 201.5. Your webpage describes 11C-Acetate as a useful PET scan agent for detecting recurrent prostate cancer. This use is one for which a prescription would be needed because it requires the supervision of a physician and, thus, adequate directions for lay use cannot be written.

Although 21 CFR 201.115(b) provides an exemption from the adequate directions for use requirement in section 502(f)(1) of the FD&C Act if a new drug "complies with section 505(i) . . . and regulations thereunder," your investigational drug fails to do so.[2] Among the requirements for the exemption for investigational drugs, 21 CFR 312.7 provides that "[a] sponsor or investigator, or any person acting on behalf of a sponsor or investigator, shall not represent in a promotional context that an investigational new drug is safe or effective for the purposes for which it is under investigation or otherwise promote the drug. This provision is not intended to restrict the full exchange of scientific information concerning the drug, including dissemination of scientific findings in scientific or lay media. Rather, its intent is to restrict promotional claims of safety or effectiveness of the drug for a use for which it is under investigation and to preclude commercialization of the drug before it is approved for commercial distribution."

The webpage contains claims and presentations that promote 11C-Acetate as safe and effective for the purpose for which it is being investigated or otherwise promote the drug, including the examples that follow (emphasis added). We note that 11C-choline and fluciclovine F 18 are approved products for PET imaging.

- "11C-choline and 11C-acetate are lipid metabolism PET agents. **Both of these agents are useful for detecting recurrent disease after a PSA** [prostate-specific antigen] **relapse**."

- "Small direct comparison studies of 11C-acetate and 11C-choline have revealed no clear clinical differences between these agents, although a few studies have **suggested a slightly higher detection rate** of local recurrences and small pelvic lymph node metastases **with 11C-acetate**."

- "In some patients, the muscle uptake of Axumin [(fluciclovine F 18)] may be so high as to render the study non-diagnostic, despite having properly abstained from physical activity prior to the scan. Additionally, in a small but significant number of patients, interfering urinary excretion is seen. **These factors likely help explain the apparent lower performance of this agent compared to 11C-Acetate and Choline**."

- "The lack of urinary tracer excretion of **11C-Acetate allows visualization** of small and subtle lesions in this region, not typically possible with PSMA [prostate-specific membrane antigen] based agents."

- "So far Axumin [(fluciclovine F 18)] (detection rate 68%, 38% false positive) . . . does not appear to perform nearly as well as Acetate or Choline (88-90% detection rate and

[2] 21 CFR 201.100 offers another exemption from the requirement for adequate directions for use for prescription drugs provided certain requirements are met; however, 11C-Acetate does not fall within that exemption because it is an investigational new drug for which there is no marketing authorization in the United States.

<10% false positive rate) . . . **Acetate or Choline remain overall much better choices for imaging**."

The above claims and presentations make numerous conclusory statements about the safety and effectiveness of 11C-Acetate. Furthermore, the webpage states that 11C-Acetate "has [been] shown…to be a valuable and accurate tool, providing a better understanding of the location and extent of local recurrences and distant disease," an efficacy claim of clinical benefit that has not been established. These claims and presentations suggest in a promotional context that 11C-Acetate, an investigational new drug, has been shown to be different from or superior to approved therapies for PET imaging, specifically 11-C choline and fluciclovine F 18, and is safe or effective for such uses.

The benefit and risk profile associated with 11C-Acetate, an investigational therapy, is currently under development and not fully known. The conclusions made in these claims and presentations, especially considering the serious nature of disease recurrence and the need for early detection, create a misleading impression regarding the usefulness and regulatory status of this product.

While there is one sentence on the webpage stating that 11C-Acetate "is available under expanded access clinical trials at multiple institutions," this does not convey that the product is investigational, in light of the repeated suggestions the drug is interchangeable with, or even superior to the approved product 11C-choline. This statement neither adequately conveys that the product is unapproved, nor sufficiently mitigates impressions conveyed by other presentations, such as those noted above, that 11C-Acetate is safe and effective for any use.

In summary, the above cited claims and presentations on the webpage represent the drug as having an established role in the PET imaging of prostate cancer, when 11C-Acetate has not been proven to be safe and effective within the meaning of the FD&C Act and has not been approved as a drug under that authority for any use.

Conclusion and Requested Action

For the reasons discussed above, 11C-Acetate is misbranded under section 502(f)(1) of the FD&C Act and in violation of section 301(k) of the FD&C Act. The claims and presentations on the webpage are concerning from a public health perspective because they make representations in a promotional context regarding the safety and efficacy of an investigational new drug that has not been approved by the FDA.

OPDP requests that Fabio Almeida, MD immediately cease violating the FD&C Act, as discussed above. Please submit a written response to this letter on or before March 1, 2019, stating whether you intend to comply with this request, listing all promotional materials for 11C-Acetate that contain statements such as those described above, and explaining your plan for discontinuing use of such violative materials. If you believe that your products are not in violation of the FD&C Act, include your reasoning and any supporting information for our consideration.

Please direct your response to the undersigned at the **Food and Drug Administration, Center for Drug Evaluation and Research, Office of Prescription Drug Promotion, 5901-B Ammendale Road, Beltsville, Maryland 20705-1266**. A courtesy copy can be sent by facsimile to (301) 847-8444. To ensure timely delivery of your submissions, please use the full address above and include a prominent directional notation (e.g. a sticker) to indicate that the submission is intended for OPDP. Please refer to MA 1 in addition to the IND number in all future correspondence relating to this particular matter. All correspondence should include a subject line that clearly identifies the submission as a Response to Untitled Letter. OPDP reminds you that only written communications are considered official.

The violations discussed in this letter do not necessarily constitute an exhaustive list. It is your responsibility to ensure that your promotional materials for 11C-Acetate comply with each applicable requirement of the FD&C Act and FDA implementing regulations.

Sincerely,

{See appended electronic signature page}

David Foss, PharmD, MPH, BCPS
Regulatory Review Officer
Division of Advertising & Promotion Review 2
Office of Prescription Drug Promotion

{See appended electronic signature page}

James Dvorsky, PharmD, RAC, CPH
Team Leader
Division of Advertising & Promotion Review 2
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This is a representation of an electronic record that was signed electronically. Following this are manifestations of any and all electronic signatures for this electronic record.

/s/

DAVID F FOSS
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JAMES S DVORSKY
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