CENTER FOR DRUG EVALUATION AND RESEARCH

APPROVAL PACKAGE FOR:

APPLICATION NUMBER

NDA 21-768

Administrative/Correspondence

Sections 13 and 14 of NDA

Patent Certification

In the opinion and to the best knowledge of Weill Medical College of Cornell University, Citigroup Biomedical Imaging Center (at 516 East 72nd street, New York), there are no patents that claim the listed drug referred to in this application or that claim a use of the listed drug.

Shankar Vallabhajosula

3/22/04

Shankar Vallabhajosula, Ph.D.
Professor of Radiochemistry and Radiopharmacy
Weill Medical College of Cornell University
Citigroup Biomedical Imaging Center
New York, NY 10021

Date

Department of Health and Human Services
Food and Drug Administration

PATENT INFORMATION SUBMITTED WITH THE FILING OF AN NDA, AMENDMENT, OR SUPPLEMENT

For Each Patent That Claims a Drug Substance (Active Ingredient), Drug Product (Formulation and Composition) and/or Method of Use

Form Approved: OMB No. 0910-0513
Expiration Date: 07/31/06
See OMB Statement on Page 3.

NDA NUMBER
21-768 "FDG"

NAME OF APPLICANT / NDA HOLDER
Weill Medical College of Cornell University
Citigroup Biomedical Imaging Center

The following is provided in accordance with Section 505(b) and (c) of the Federal Food, Drug, and Cosmetic Act.

TRADE NAME (OR PROPOSED TRADE NAME)
None

ACTIVE INGREDIENT(S)	STRENGTH(S)
2-Deoxy-2[18F]fluoro-D-glucose	4 - 90 mCi/mL

DOSAGE FORM
Sterile, Pyrogen Free Injection

This patent declaration form is required to be submitted to the Food and Drug Administration (FDA) with an NDA application, amendment, or supplement as required by 21 CFR 314.53 at the address provided in 21 CFR 314.53(d)(4). Within thirty (30) days after approval of an NDA or supplement, or within thirty (30) days of issuance of a new patent, a new patent declaration must be submitted pursuant to 21 CFR 314.53(c)(2)(ii) with all of the required information based on the approved NDA or supplement. The information submitted in the declaration form submitted upon or after approval will be the only information relied upon by FDA for listing a patent in the Orange Book.

For hand-written or typewriter versions (only) of this report: If additional space is required for any narrative answer (i.e., one that does not require a "Yes" or "No" response), please attach an additional page referencing the question number.

FDA will not list patent information if you file an incomplete patent declaration or the patent declaration indicates the patent is not eligible for listing.

For each patent submitted for the pending NDA, amendment, or supplement referenced above, you must submit all the information described below. If you are not submitting any patents for this pending NDA, amendment, or supplement, complete above section and sections 5 and 6.

1. GENERAL

a. United States Patent Number	b. Issue Date of Patent	c. Expiration Date of Patent

d. Name of Patent Owner	Address *(of Patent Owner)*	
	City/State	
	ZIP Code	FAX Number *(if available)*
	Telephone Number	E-Mail Address *(if available)*

e. Name of agent or representative who resides or maintains a place of business within the United States authorized to receive notice of patent certification under section 505(b)(3) and (j)(2)(B) of the Federal Food, Drug, and Cosmetic Act and 21 CFR 314.52 and 314.95 (if patent owner or NDA applicant/holder does not reside or have a place of business within the United States)	Address *(of agent or representative named in 1.e.)*	
	City/State	
	ZIP Code	FAX Number *(if available)*
	Telephone Number	E-Mail Address *(if available)*

f. Is the patent referenced above a patent that has been submitted previously for the approved NDA or supplement referenced above? ☐ Yes ☐ No

g. If the patent referenced above has been submitted previously for listing, is the expiration date a new expiration date? ☐ Yes ☐ No

For the patent referenced above, provide the following information on the drug substance, drug product and/or method of use that is the subject of the pending NDA, amendment, or supplement.

Drug Substance (Active Ingredient)

2.1	Does the patent claim the drug substance that is the active ingredient in the drug product described in the pending NDA, amendment, or supplement?	☐ Yes	☐ No
2.2	Does the patent claim a drug substance that is a different polymorph of the active ingredient described in the pending NDA, amendment, or supplement?	☐ Yes	☐ No
2.3	If the answer to question **2.2** is "Yes," do you certify that, as of the date of this declaration, you have test data demonstrating that a drug product containing the polymorph will perform the same as the drug product described in the NDA? The type of test data required is described at 21 CFR 314.53(b).	☐ Yes	☐ No
2.4	Specify the polymorphic form(s) claimed by the patent for which you have the test results described in **2.3**.		
2.5	Does the patent claim only a metabolite of the active ingredient pending in the NDA or supplement? (Complete the information in section 4 below if the patent claims a pending method of using the pending drug product to administer the metabolite.)	☐ Yes	☐ No
2.6	Does the patent claim only an intermediate?	☐ Yes	☐ No
2.7	If the patent referenced in **2.1** is a product-by-process patent, is the product claimed in the patent novel? (An answer is required only if the patent is a product-by-process patent.)	☐ Yes	☐ No

Drug Product (Composition/Formulation)

3.1	Does the patent claim the drug product, as defined in 21 CFR 314.3, in the pending NDA, amendment, or supplement?	☐ Yes	☐ No
3.2	Does the patent claim only an intermediate?	☐ Yes	☐ No
3.3	If the patent referenced in **3.1** is a product-by-process patent, is the product claimed in the patent novel? (An answer is required only if the patent is a product-by-process patent.)	☐ Yes	☐ No

4. Method of Use

Sponsors must submit the information in section 4 separately for each patent claim claiming a method of using the pending drug product for which approval is being sought. For each method of use claim referenced, provide the following information:

4.1	Does the patent claim one or more methods of use for which approval is being sought in the pending NDA, amendment, or supplement?	☐ Yes	☐ No
4.2	Patent Claim Number *(as listed in the patent)*	Does the patent claim referenced in **4.2** claim a pending method of use for which approval is being sought in the pending NDA, amendment, or supplement? ☐ Yes ☐ No	
4.2a	If the answer to **4.2** is "Yes," identify with specificity the use with reference to the proposed labeling for the drug product.	Use: *(Submit indication or method of use information as identified specifically in the approved labeling.)*	

5. No Relevant Patents

	For this pending NDA, amendment, or supplement, there are no relevant patents that claim the drug substance (active ingredient), drug product (formulation or composition) or method(s) of use, for which the applicant is seeking approval and with respect to which a claim of patent infringement could reasonably be asserted if a person not licensed by the owner of the patent engaged in the manufacture, use, or sale of the drug product.	☒ Yes

6. Declaration Certification

6.1 ***The undersigned declares that this is an accurate and complete submission of patent information for the NDA, amendment, or supplement pending under section 505 of the Federal Food, Drug, and Cosmetic Act. This time-sensitive patent information is submitted pursuant to 21 CFR 314.53. I attest that I am familiar with 21 CFR 314.53 and this submission complies with the requirements of the regulation. I verify under penalty of perjury that the foregoing is true and correct.***

Warning: A willfully and knowingly false statement is a criminal offense under 18 U.S.C. 1001.

6.2 Authorized Signature of NDA Applicant/Holder or Patent Owner *(Attorney, Agent, Representative or other Authorized Official) (Provide Information below)*	Date Signed
Shankar Vallabhajosula	4/22/2004

NOTE: Only an NDA applicant/holder may submit this declaration directly to the FDA. A patent owner who is not the NDA applicant/holder is authorized to sign the declaration but may not submit it directly to FDA. 21 CFR 314.53(c)(4) and (d)(4).

Check applicable box and provide information below.

☒ NDA Applicant/Holder	☐ NDA Applicant's/Holder's Attorney, Agent (Representative) or other Authorized Official
☐ Patent Owner	☐ Patent Owner's Attorney, Agent (Representative) or Other Authorized Official

Name Shankar Vallabhajosula, Ph.D.	
Address Citigroup Biomedical Imaging Center, WMCCU 516 East 72nd Street	City/State New York, New York
ZIP Code 10021	Telephone Number 212-746-5694
FAX Number *(if available)* 212-746-6681	E-Mail Address *(if available)* svallabh@med.cornell.edu

Exclusivity Statement

According to the publication "*Approved Drug Products with Therapeutic Equivalence Evaluations*" (Orange Book), the reference listed drug (Fludeoxyglucose F18 injection) has not been granted a period of marketing exclusivity under section 505(c)(3)(D) of the Act (21 U.S.C. 355(c)(3)(D)).

Shankar Vallabhajosula

3/22/04

Shankar Vallabhajosula, Ph.D.
Professor of Radiochemistry and Radiopharmacy
Weill Medical College of Cornell University
Citigroup Biomedical Imaging Center
New York, NY 10021

Date

EXCLUSIVITY SUMMARY FOR: NDA 21-768 HFD-160

Trade Name: N\A Generic Name: Fludeoxyglucose F 18 Injection

Applicant Name: Weill Medical College of Cornell University
Citigroup Biomedical Imaging Center

Approval Date If Known: August 5, 2004

PART I IS AN EXCLUSIVITY DETERMINATION NEEDED?

1. An exclusivity determination will be made for all original applications, and all efficacy supplements. Complete PARTS II and III of this Exclusivity Summary only if you answer "yes" to one or more of the following question about the submission.

a) Is it a 505(b)(1), 505(b)(2) or efficacy supplement?
YES /X/ NO /___/

If yes, what type? Specify 505(b)(1), 505(b)(2), SE1, SE2, SE3,SE4, SE5, SE6, SE7, SE8

505(b)(2)

c) Did it require the review of clinical data other than to support a safety claim or change in labeling related to safety? (If it required review only of bioavailability or bioequivalence data, answer "no.")

YES /___/ **NO /X/**

If your answer is "no" because you believe the study is a bioavailability study and, therefore, not eligible for exclusivity, EXPLAIN why it is a bioavailability study, including your reasons for disagreeing with any arguments made by the applicant that the study was not simply a bioavailability study.

***See FR Notice - March 10, 2000.**

If it is a supplement requiring the review of clinical data but it is not an effectiveness supplement, describe the change or claim that is supported by the clinical data:

_____

_____

d) Did the applicant request exclusivity?

YES /___/ **NO /X/**

If the answer to (d) is "yes," how many years of exclusivity did the applicant request?

_____

e) Has pediatric exclusivity been granted for this Active Moiety? **N\A**

If the answer to the above question is YES, is this approval a result of the studies submitted in response to the Pediatric Writen Request?_____

IF YOU HAVE ANSWERED "NO" TO ALL OF THE ABOVE QUESTIONS, GO DIRECTLY TO THE SIGNATURE BLOCKS AT THE END OF THIS DOCUMENT.

2. Is this drug product or indication a DESI upgrade?

YES /___/ **NO /X/**

IF THE ANSWER TO QUESTION 2 IS "YES," GO DIRECTLY TO THE SIGNATURE BLOCKS ON PAGE 8 (even if a study was required for the upgrade).

PART II FIVE-YEAR EXCLUSIVITY FOR NEW CHEMICAL ENTITIES

(Answer either #1 or #2 as appropriate)

1. Single active ingredient product.

Has FDA previously approved under section 505 of the Act any drug product containing the same active moiety as the drug under consideration? Answer "yes" if the active moiety (including other esterified forms, salts, complexes, chelates or clathrates) has been previously approved, but this particular form of the active moiety, e.g., this particular ester or salt (including salts with hydrogen or coordination bonding) or other non-covalent derivative (such as a complex, chelate, or clathrate) has not been approved. Answer "no" if the compound requires metabolic conversion (other than deesterification of an esterified form of the drug) to produce an already approved active moiety.

YES /X/ NO /___/

If "yes," identify the approved drug product(s) containing the active moiety, and, if known, the NDA #(s).

NDA# 20-306: Fludeoxyglucose F 18 Injection

NDA# _____ _____

NDA# _____ _____

2. Combination product.

If the product contains more than one active moiety(as defined in Part II, #1), has FDA previously approved an application under section 505 containing any one of the active moieties in the drug product? If, for example, the combination contains one never-before-approved active moiety and one previously approved active moiety, answer "yes." (An active moiety that is marketed under an OTC monograph, but that was never approved under an NDA, is considered not previously approved.)

YES /___/ NO /___/

If "yes," identify the approved drug product(s) containing the active moiety, and, if known, the NDA #(s).

NDA# _____ _____

NDA# _____ _____

NDA# _____ _____

IF THE ANSWER TO QUESTION 1 OR 2 UNDER PART II IS "NO," GO DIRECTLY TO THE SIGNATURE BLOCKS ON PAGE 8. (Caution: The questions in part II of the summary should only be answered "NO" for original approvals of new molecular entities.) IF "YES" GO TO PART III.

PART III THREE-YEAR EXCLUSIVITY FOR NDA'S AND SUPPLEMENTS

To qualify for three years of exclusivity, an application or supplement must contain "reports of new clinical investigations (other than bioavailability studies) essential to the approval of the application and conducted or sponsored by the applicant." This section should be completed only if the answer to PART II, Question 1 or 2 was "yes."

1. Does the application contain reports of clinical investigations? (The Agency interprets "clinical investigations" to mean investigations conducted on humans other than bioavailability studies.) If the application contains clinical investigations only by virtue of a right of reference to clinical investigations in another application, answer "yes," then skip to question 3(a). If the answer to 3(a) is "yes" for any investigation referred to in another application, do not complete remainder of summary for that investigation.

YES /___/ **NO /X/**

IF "NO," GO DIRECTLY TO THE SIGNATURE BLOCKS ON PAGE 8.

2. A clinical investigation is "essential to the approval" if the Agency could not have approved the application or supplement without relying on that investigation. Thus, the investigation is not essential to the approval if 1) no clinical investigation is necessary to support the supplement or application in light of previously approved applications (i.e., information other than clinical trials, such as bioavailability data, would be sufficient to provide a basis for approval as an ANDA or 505(b)(2) application because of what is already known about a previously approved product), or 2) there are published reports of studies (other than those conducted or sponsored by the applicant) or other publicly available data that independently would have been sufficient to support approval of the application, without reference to the clinical investigation submitted in the application.

(a) In light of previously approved applications, is a clinical investigation (either conducted by the applicant or available from some other source, including the published literature) necessary to support approval of the application or supplement?

YES /___/ NO /___/

If "no," state the basis for your conclusion that a clinical trial is not necessary for approval AND GO DIRECTLY TO SIGNATURE BLOCK ON PAGE 8:

_____

(b) Did the applicant submit a list of published studies relevant to the safety and effectiveness of this drug product and a statement that the publicly available data would not independently support approval of the application?

YES /___/ NO /___/

(1) If the answer to 2(b) is "yes," do you personally know of any reason to disagree with the applicant's conclusion? If not applicable, answer NO.

YES /___/ NO /___/

If yes, explain:

(2) If the answer to 2(b) is "no," are you aware of published studies not conducted or sponsored by the applicant or other publicly available data that could independently demonstrate the safety and effectiveness of this drug product?

YES /___/ NO /___/

If yes, explain:

(c) If the answers to (b)(1) and (b)(2) were both "no," identify the clinical investigations submitted in the application that are essential to the approval:

Studies comparing two products with the same ingredient(s) are considered to be bioavailability studies for the purpose of this section.

3. In addition to being essential, investigations must be "new" to support exclusivity. The agency interprets "new clinical investigation" to mean an investigation that 1) has not been relied on by the agency to demonstrate the effectiveness of a previously approved drug for any indication and 2) does not duplicate the results of another investigation that was relied on by the agency to demonstrate the effectiveness of a previously approved drug product, i.e., does not redemonstrate something the agency considers to have been demonstrated in an already approved application.

a) For each investigation identified as "essential to the approval," has the investigation been relied on by the agency to demonstrate the effectiveness of a previously approved drug product? (If the investigation was relied on only to support the safety of a previously approved drug, answer "no.")

Investigation #1 YES /___/ NO /___/

Investigation #2 YES /___/ NO /___/

If you have answered "yes" for one or more investigations, identify each such investigation and the NDA in which each was relied upon:

_____ _____

_____ _____

b) For each investigation identified as "essential to the approval", does the investigation duplicate the results of another investigation that was relied on by the agency to support the effectiveness of a previously approved drug product?

Investigation #1 YES /___/ NO /___/

Investigation #2 YES /___/ NO /___/

If you have answered "yes" for one or more investigation, identify the NDA in which a similar investigation was relied on:

_____ _____

c) If the answers to 3(a) and 3(b) are no, identify each "new" investigation in the application or supplement that is essential to the approval (i.e., the investigations listed in #2(c), less any that are not "new"):

_____ _____

_____ _____

4. To be eligible for exclusivity, a new investigation that is essential to approval must also have been conducted or sponsored by the applicant. An investigation was "conducted or sponsored by" the applicant if, before or during the conduct of the investigation, 1) the applicant was the sponsor of the IND named in the form FDA 1571 filed with the Agency, or 2) the applicant (or its predecessor in interest) provided substantial support for the study. Ordinarily, substantial support will mean providing 50 percent or more of the cost of the study.

a) For each investigation identified in response to question

3(c): if the investigation was carried out under an IND, was the applicant identified on the FDA 1571 as the sponsor?

Investigation #1

IND # _____ YES /___/ ! NO /___/ Explain: _____

Investigation #2

IND # _____ YES /___/ ! NO /___/ Explain: _____

(b) For each investigation not carried out under an IND or for which the applicant was not identified as the sponsor, did the applicant certify that it or the applicant's predecessor in interest provided substantial support for the study?

Investigation #1

YES /___/ Explain _____ ! NO /___/ Explain _____

_____ ! _____

_____ ! _____

Investigation #2

YES /___/ Explain _____ ! NO /___/ Explain _____

_____ ! _____

_____ ! _____

(c) Notwithstanding an answer of "yes" to (a) or (b), are there other reasons to believe that the applicant should not be credited with having "conducted or sponsored" the study? (Purchased studies may not be used as the basis for exclusivity. However, if all rights to the drug are purchased (not just studies on the drug), the applicant may be considered to have sponsored or conducted the studies sponsored or conducted by its predecessor in interest.)

YES /___/ NO /___/

If yes, explain: _____

_____

NAME: Thuy M. Nguyen, M.P.H.
TITLE: Regulatory Health Project Manager, HFD-160
Signature\Date: *See DFS

NAME: George Q. Mills, M.D., M.B.A.
TITLE: Division Director, HFD-160
Signature\Date: *See DFS

Form OGD-011347 Revised 05/10/2004

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

George Mills
8/5/04 02:10:09 PM

PEDIATRIC PAGE

(Complete for all filed original applications and efficacy supplements)

NDA# : 21-768 **HFD-160**

Stamp Date: March 24, 2004 **Action Date:** August 5, 2004

Generic Name/Dosage Form: Fludeoxyglucose F 18 Injection **Therapeutic Class:** 3S

Applicant: Weill Medical College of Cornell University - Citigroup Biomedical Imaging Center

Indication(s) previously approved: See FR Notice – March 10, 2000

Each approved indication must have pediatric studies: Completed, Deferred, and/or Waived.

Number of indications for this application(s): 3

Indications #1& 2: **As stated in the FR Notice – March 10, 2000.**

1) **In positron emission tomography (PET) imaging for assessment of abnormal glucose metabolism to assist in the evaluation of malignancy in patients with known or suspected abnormalities found by other testing modalities, or in patients with an existing diagnosis of cancer.**
2) **In positron emission tomography (PET) imaging in patients with coronary artery disease and left ventricular dysfunction, when used together with myocardial perfusion imaging, for the identification of left ventricular myocardium with residual glucose metabolism and reversible loss of systolic function.**

Is there a full waiver for this indication (check one)? NO

Please check all that apply: ____Partial Waiver __X__Deferred ____Completed
NOTE: More than one may apply
Please proceed to Section B, Section C, and/or Section D and complete as necessary.

Section A: Fully Waived Studies

Reason(s) for full waiver:

- ☐ **Products in this class for this indication have been studied/labeled for pediatric population**
- ☐ **Disease/condition does not exist in children**
- ☐ **Too few children with disease to study**
- ☐ **There are safety concerns**
- ☐ **Other:**_____

If studies are fully waived, then pediatric information is complete for this indication. If there is another indication, please see Attachment A. Otherwise, this Pediatric Page is complete and should be entered into DFS.

Section B: Partially Waived Studies

Age/weight range being partially waived:

Min_____ kg_____ mo._____ yr._____ Tanner Stage_____
Max_____ kg_____ mo._____ yr._____ Tanner Stage_____

Reason(s) for partial waiver:

- ☐ **Products in this class for this indication have been studied/labeled for pediatric population**
- ☐ **Disease/condition does not exist in children**
- ☐ **Too few children with disease to study**
- ☐ **There are safety concerns**
- ☐ **Adult studies ready for approval**
- ☐ **Formulation needed**
- ☐ **Other:**_____

If studies are deferred, proceed to Section C. If studies are completed, proceed to Section D. Otherwise, this Pediatric Page is complete and should be entered into DFS.

Section C: Deferred Studies

Age/weight range being deferred:

Min : ≥ 1 yr kg: ~9.5 mo._____ yr._____ Tanner Stage: Not known
Max: 16 yrs kg: ~50 mo._____ yr._____ Tanner Stage: Not known

Reason(s) for deferral:

- ☐ **Products in this class for this indication have been studied/labeled for pediatric population**
- ☐ **Disease/condition does not exist in children**
- X **Too few children with disease to study**
- ☐ **There are safety concerns**
- ☐ **Adult studies ready for approval**
- ☐ **Formulation needed**

Other:_____

Date studies are due (mm/dd/yy): August 5, 2014

If studies are completed, proceed to Section D. Otherwise, this Pediatric Page is complete and should be entered into DFS.

Section D: Completed Studies

Age/weight range of completed studies:

Min _____ kg_____ mo._____ yr._____ Tanner Stage_____
Max_____ kg_____ mo._____ yr._____ Tanner Stage_____

Comments:

If there are additional indications, please proceed to Attachment A. Otherwise, this Pediatric Page is complete and should be entered into DFS.

Attachment A

(This attachment is to be completed for those applications with multiple indications only.)

Indication #3: As stated in the FR Notice –March 10, 2000.
In positron emission tomography (PET) imaging in patients for the identification of regions of abnormal glucose metabolism associated with foci of epileptic seizures.

Is there a full waiver for this indication (check one)? NO

Please check all that apply: ____Partial Waiver ____Deferred _X__Completed
NOTE: More than one may apply
Please proceed to Section B, Section C, and/or Section D and complete as necessary.

Section A: Fully Waived Studies

Reason(s) for full waiver:

- ☐ **Products in this class for this indication have been studied/labeled for pediatric population**
- ☐ **Disease/condition does not exist in children**
- ☐ **Too few children with disease to study**
- ☐ **There are safety concerns**
- ☐ **Other:**_____

If studies are fully waived, then pediatric information is complete for this indication. If there is another indication, please see Attachment A. Otherwise, this Pediatric Page is complete and should be entered into DFS.

Section B: Partially Waived Studies

Age/weight range being partially waived:

Min _____	**kg**_____	**mo.**_____	**yr.**_____	**Tanner Stage**_____
Max_____	**kg**_____	**mo.**_____	**yr.**_____	**Tanner Stage**_____

Reason(s) for partial waiver:

- ☐ **Products in this class for this indication have been studied/labeled for pediatric population**
- ☐ **Disease/condition does not exist in children**
- ☐ **Too few children with disease to study**
- ☐ **There are safety concerns**
- ☐ **Adult studies ready for approval**
- ☐ **Formulation needed**
- ☐ **Other:**_____

If studies are deferred, proceed to Section C. If studies are completed, proceed to Section D. Otherwise, this Pediatric Page is complete and should be entered into DFS.

Section C: Deferred Studies

Age/weight range being deferred:

Min _____ kg_____ mo._____ yr._____ Tanner Stage_____
Max_____ kg_____ mo._____ yr._____ Tanner Stage_____

Reason(s) for deferral:

- ☐ **Products in this class for this indication have been studied/labeled for pediatric population**
- ☐ **Disease/condition does not exist in children**
- ☐ **Too few children with disease to study**
- ☐ **There are safety concerns**
- ☐ **Adult studies ready for approval**
- ☐ **Formulation needed**
- ☐ **Other:**_____

Date studies are due (mm/dd/yy): _____

If studies are completed, proceed to Section D. Otherwise, this Pediatric Page is complete and should be entered into DFS.

Section D: Completed Studies

Age/weight range of completed studies:

Min: 4 mos. kg: Not known **mo.**_____ **yr.**_____ **Tanner Stage:** Not known
Max: 58 yrs kg: Not known **mo.**_____ **yr.**_____ **Tanner Stage:** Not known

Comments:

If there are additional indications, please copy the fields above and complete pediatric information as directed. If there are no other indications, this Pediatric Page is complete and should be entered into DFS.

{See appended electronic signature page}

Thuy M. Nguyen, M.P.H.
Regulatory Health Project Manager, HFD-160

{See appended electronic signature page}

George Q. Mills, M.D., M.B.A.
Division Director
Division of Medical Imaging and Radiopharmaceutical Drug Products, HFD-160

cc: **NDA 21-768**
HFD-960/ Grace Carmouze

FOR QUESTIONS ON COMPLETING THIS FORM CONTACT THE DIVISION OF PEDIATRIC DRUG DEVELOPMENT, HFD-960, 301-594-7337.

(revised 10-14-03)

Appears This Way
On Original

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/s/

George Mills
8/5/04 02:07:40 PM

Section 16 of NDA

Debarment certification

I or we at Weill Medical College of Cornell University, Citigroup Biomedical Imaging Center (at 516 East 72nd street, New York), certify that I, or we, did not and will not use the services, in any capacity, of any person debarred under section 306 of the Federal Food, Drug, and Cosmetic Act in connection with this application.

Shankar Vallabhajosula

3/22/04

Shankar Vallabhajosula, Ph.D.
Professor of Radiochemistry and Radiopharmacy
Weill Medical College of Cornell University
Citigroup Biomedical Imaging Center
New York, NY 10021

Date

NDA ACTION PACKAGE CHECKLIST

Application Information

NDA: 21-768		
DRUG NAME: Fludeoxglucose F 18 Injection	**APPLICANT: Weill Medical College of Cornell University Citigroup Biomedical Imaging Center**	
RPM: Thuy M. Nguyen, M.P.H.	**HFD-160**	**Phone #: (301) 827-7510**

Application Type: 505(b)(2) (This can be determined by consulting page 1 of the NDA Regulatory Filing Review for this application or Appendix A to this Action Package Checklist.) **If this is a 505(b)(2) application, please review and confirm the information previously provided in Appendix B to the NDA Regulatory Filing Review. Please update any information (including patent certification information) that is no longer correct.** **Confirmed.**	**Listed drug(s) referred to in 505(b)(2) application (NDA #(s), Drug name(s)): NDA #20-306\FDG**

❖ **Application Classifications:**	
• **Review priority**	**Standard**
• **Chem class (NDAs only)**	**3S**
❖ **User Fee Goal Date**	**January 24, 2005**
❖ **Special programs (indicate all that apply)**	**(X) None** Subpart H ( ) 21 CFR 314.510 (accelerated approval) ( ) 21 CFR 314.520 (restricted distribution) ( ) Fast Track ( ) Rolling Review ( ) CMA Pilot 1 ( ) CMA Pilot 2
❖ **User Fee Information**	
• **User Fee**	**X**
• **User Fee Waiver**	( ) Small business ( ) Public health ( ) Barrier-to-Innovation **(X) Other (specify)** **FR Notice – March 10, 2000**
• **User Fee Exception**	( ) Orphan designation **(X)** No-fee 505(b)(2) (see NDA Regulatory Filing Review for instructions) ( ) Other (specify)
Application Integrity Policy (AIP)	
• **Applicant is on the AIP**	**NO**

• **This application is on the AIP**	**NO**
• **Exception for review (Center Director's memo)**	
• **OC clearance for approval**	
❖ **Debarment certification**: verified that qualifying language (e.g., willingly, knowingly) was not used in certification & certifications from foreign applicants are cosigned by US agent.	**(X) Verified**
❖ **Patent**	
• **Information:** Verify that form FDA-3542a was submitted for patents that claim the drug for which approval is sought.	**(X) Verified**
• **Patent certification [505(b)(2) applications]:** Verify that a certification was submitted for each patent for the listed drug(s) in the Orange Book and identify the type of certification submitted for each patent.	**X**
• [505(b)(2) applications] If the application includes a paragraph III certification, it cannot be approved until the date that the patent to which the certification pertains expires (but may be tentatively approved if it is otherwise ready for approval).	**N\A**
• [505(b)(2) applications] For each paragraph IV certification, verify that the applicant notified the NDA holder and patent owner(s) of its certification that the patent(s) is invalid, unenforceable, or will not be infringed (review documentation of notification by applicant and documentation of receipt of notice by patent owner and NDA holder). ***(If the application does not include any paragraph IV certifications, mark "N/A" and skip to the next box below (Exclusivity)).***	**N/A (no paragraph IV certification)**
• [505(b)(2) applications] For each paragraph IV certification, based on the questions below, determine whether a 30-month stay of approval is in effect due to patent infringement litigation. Answer the following questions for each paragraph IV certification: (1) Have 45 days passed since the patent owner's receipt of the applicant's notice of certification? (Note: The date that the patent owner received the applicant's notice of certification can be determined by checking the application. The applicant is required to amend its 505(b)(2) application to include documentation of this date (e.g., copy of return receipt or letter from recipient acknowledging its receipt of the notice) (see 21 CFR 314.52(e))). *If "**Yes**," skip to question (4) below. If "**No**," continue with question (2).* (2) Has the patent owner (or NDA holder, if it is an exclusive patent licensee) submitted a written waiver of its right to file a legal action for patent infringement after receiving the applicant's notice of certification, as provided for by 21 CFR 314.107(f)(3)? *If "**Yes**," there is no stay of approval based on this certification. Analyze the next paragraph IV certification in the application, if any. If there are no other paragraph IV certifications, skip to the next box below (Exclusivity).* *If "**No**," continue with question (3).* (3) Has the patent owner, its representative, or the exclusive patent licensee filed a lawsuit for patent infringement against the applicant?	

(Note: This can be determined by confirming whether the Division has received a written notice from the applicant (or the patent owner or its representative) stating that a legal action was filed within 45 days of receipt of its notice of certification. The applicant is required to notify the Division in writing whenever an action has been filed within this 45-day period (see 21 CFR 314.107(f)(2))).	
*If "**No**," the patent owner (or NDA holder, if it is an exclusive patent licensee) has until the expiration of the 45-day period described in question (1) to waive its right to bring a patent infringement action or to bring such an action. After the 45-day period expires, continue with question (4) below.*	( ) Yes ( ) No
(4) Did the patent owner (or NDA holder, if it is an exclusive patent licensee) submit a written waiver of its right to file a legal action for patent infringement within the 45-day period described in question (1), as provided for by 21 CFR 314.107(f)(3)?	
*If "**Yes**," there is no stay of approval based on this certification. Analyze the next paragraph IV certification in the application, if any. If there are no other paragraph IV certifications, skip to the next box below (Exclusivity).*	( ) Yes ( ) No
*If "**No**," continue with question (5).*	
(5) Did the patent owner, its representative, or the exclusive patent licensee bring suit against the applicant for patent infringement within 45 days of the patent owner's receipt of the applicant's notice of certification?	
(Note: This can be determined by confirming whether the Division has received a written notice from the applicant (or the patent owner or its representative) stating that a legal action was filed within 45 days of receipt of its notice of certification. The applicant is required to notify the Division in writing whenever an action has been filed within this 45-day period (see 21 CFR 314.107(f)(2)). If no written notice appears in the NDA file, confirm with the applicant whether a lawsuit was commenced within the 45-day period).	
*If "**No**," there is no stay of approval based on this certification. Analyze the next paragraph IV certification in the application, if any. If there are no other paragraph IV certifications, skip to the next box below (Exclusivity).*	
*If "**Yes**," a stay of approval may be in effect. To determine if a 30-month stay is in effect, consult with the Director, Division of Regulatory Policy II, Office of Regulatory Policy (HFD-007) and attach a summary of the response.*	

❖ **Exclusivity (approvals only)**	
• Exclusivity summary • Is there remaining 3-year exclusivity that would bar effective approval of a 505(b)(2) application? (Note that, even if exclusivity remains, the application may be tentatively approved if it is otherwise ready for approval.)	**X**
• Is there existing orphan drug exclusivity protection for the "same drug" for the proposed indication(s)? *Refer to 21 CFR 316.3(b)(13) for the definition of "same drug" for an orphan drug (i.e., active moiety). This definition is NOT the same as that used for NDA chemical classification.*	( ) Yes, Application #_____ **(X) NO**
❖ **Administrative Reviews** (Project Manager, ADRA) *(indicate date of each review)*	**July 30, 2004**

General Information	
Actions	
• **Proposed action**	**(X) AP - APPROVAL**
• **Previous actions (specify type and date for each action taken)**	**N\A**
• **Status of advertising (approvals only)**	**(X) Materials requested in AP letter** ( ) Reviewed for Subpart H
❖ **Public communications**	
• **Press Office notified of action (approval only)**	**(X) YES**
• **Indicate what types (if any) of information dissemination are anticipated**	**(X) Report Update** ( ) Press Release ( ) Talk Paper ( ) Dear Health Care Professional Letter
❖ **Labeling** (package insert, patient package insert (if applicable), MedGuide (if applicable))	
• **Division's proposed labeling** (only if generated after latest applicant submission of labeling)	**X**
• Most recent applicant-proposed labeling	
• Original applicant-proposed labeling	**X**
• Labeling reviews (including DDMAC, DMETS, DSRCS) and minutes of labeling meetings *(indicate dates of reviews and meetings)*	
• Other relevant labeling (e.g., most recent 3 in class, class labeling)	
❖ **Labels** (immediate container & carton labels)	
• **Division proposed** (only if generated after latest applicant submission)	**X**
• Applicant proposed	**X**
• Reviews	
❖ **Post-marketing commitments**	
• Agency request for post-marketing commitments	**X – See Action Letter**
• Documentation of discussions and/or agreements relating to post-marketing commitments	**X**
❖ **Outgoing correspondence (i.e., letters, E-mails, faxes)**	**X**
❖ **Memoranda and Telecons**	**X**
❖ **Minutes of Meetings**	
• EOP2 meeting (indicate date)	**N\A**
• Pre-NDA meeting (indicate date)	**N\A**
• Pre-Approval Safety Conference (indicate date; approvals only)	**N\A**
• Other	**X**
❖ **Advisory Committee Meeting**	
• Date of Meeting	**N\A**
• 48-hour alert	**N\A**
❖ **Federal Register Notices, DESI documents, NAS/NRC reports (if applicable)**	***March 10, 2000**

Summary Application Review	
Summary Reviews (e.g., Office Director, Division Director, Medical Team Leader) *(indicate date for each review)*	**X – August 5, 2004**
Clinical Information	
❖ **Clinical review(s)** *(indicate date for each review)*	**N\A**
❖ **Microbiology (efficacy) review(s)** *(indicate date for each review)*	**N\A**
❖ **Safety Update review(s)** *(indicate date or location if incorporated in another review)*	
❖ **Risk Management Plan review(s)** *(indicate date/location if incorporated in another rev)*	**N\A**
❖ **Pediatric Page**(separate page for each indication addressing status of all age groups)	**X**
❖ **Demographic Worksheet** *(NME approvals only)*	**N\A**
❖ **Statistical review(s)** *(indicate date for each review)*	**N\A**
❖ **Biopharmaceutical review(s)** *(indicate date for each review)*	**N\A**
❖ **Controlled Substance Staff review(s)** and recommendation for scheduling *(indicate date for each review)*	**N\A**
❖ **Clinical Inspection Review Summary (DSI)**	
• **Clinical studies**	**N\A**
• **Bioequivalence studies**	**N\A**
CMC Information	
❖ **CMC review(s)** *(indicate date for each review)*	**X - July 21, 2004**
❖ Environmental Assessment	
• Categorical Exclusion *(indicate review date)*	**N\A**
• Review & FONSI *(indicate date of review)*	**N\A**
• Review & Environmental Impact Statement *(indicate date of each review)*	**N\A**
❖ **Microbiology (validation of sterilization & product sterility) review(s)** *(indicate date for each review)*	**X - June 30, 2004**
❖ **Facilities inspection (provide EER report)**	**Date completed:** June 22, 2004 **(X) Acceptable**
❖ **Methods validation**	**N\A**
Nonclinical Pharm/Tox Information	
❖ **Pharm/tox review(s)**, including referenced IND reviews *(indicate date for each review)*	**N\A**
❖ **Nonclinical inspection review summary**	**N\A**
❖ **Statistical review(s) of carcinogenicity studies** *(indicate date for each review)*	**N\A**
❖ **CAC/ECAC report**	**N\A**

Food and Drug Administration
Center for Drug Evaluation and Research
Office of Drug Evaluation III

FACSIMILE TRANSMITTAL SHEET

DATE: July 30, 2004

TO: Dr. Shankar Vallabhajosula	**From:** Thuy Nguyen Regulatory Health Project Manager
Company: Weill Medical College of Cornell University	Division of Division of Medical Imaging and Radiopharmaceutical Drug Products
Fax number: (212) 746-6681	**Fax number:** (301) 480-6036
Phone number: (212) 746-5694	**Phone number:** (301) 827-7510

Subject: NDA 21-768: Fludeoxyglucose [F-18] Injection

Total no. of pages including cover: 15

COMMENTS: The Division has reviewed your proposed labeling and container label (Submission Dated – 07\13\04) for your NDA 21-768: Fludeoxyglucose [F-18] Injection. Please review the attached proposed labeling and label as of July 30, 2004, and let us know if agree to the proposed changes. If so, please provide by 10:00 am, Monday, August 2, 2004, in an official submission [along with Form FDA 356(h)] to the NDA, your agreement of the proposed labeling and container label dated 07\30\04. If you have any questions, please feel to contact me. Thank you.

14 Page(s) Withheld

___ § 552(b)(4) Trade Secret / Confidential

___ § 552(b)(5) Deliberative Process

✓ § 552(b)(4) Draft Labeling

DIVISION OF MEDICAL IMAGING AND RADIOPHARMACEUTICAL DRUG PRODUCTS HFD-160

INTERNAL LABELING MEETING MINTUES

NDA: **21-768**

DRUG NAME: **Fludeoxyglucose F 18 Injection**

DATE: Thursday, July 29, 2004

ATTENDEES: Ramesh Raman, M.D., Eldon Leutzinger, Ph.D., Ravi Kasliwal, Ph.D., Eric Duffy, Ph.D., Alfredo Sancho, Ph.D., Vyomika Jairam, Thuy Nguyen, M.P.H.
Division of Medical Imaging and Radiopharmaceutical Drug Products, HFD-160

AGENDA: To discuss the Sponsor's proposed labeling and container label (dated 07\13\04).

The Project Manager incorporated the Division's edits to the Sponsor's proposed labeling and container label (dated 07\13\04) as discussed at the labeling meeting, 07\22\04.

The PM will fax to the Sponsor the Division's proposed labeling and container label. If the Sponsor agrees to the changes then he will submit a letter of agreement.

INTERNAL Meeting Minutes Recorded By: T.Nguyen, HFD-160

DIVISION OF MEDICAL IMAGING AND RADIOPHARMACEUTICAL DRUG PRODUCTS HFD-160

INTERNAL LABELING MEETING MINTUES

NDA: **21-768**

DRUG NAME: **Fludeoxyglucose F 18 Injection**

DATE: Thursday, July 22, 2004

ATTENDEES: Ramesh Raman, M.D., Eldon Leutzinger, Ph.D., Ravi Kasliwal, Ph.D., Eric Duffy, Ph.D., Young-Moon Choi, Ph.D., Alfredo Sancho, Ph.D., Vyomika Jairam, Thuy Nguyen, M.P.H.
Division of Medical Imaging and Radiopharmaceutical Drug Products, HFD-160

AGENDA: To discuss the Sponsor's proposed labeling and container label (dated 07\13\04).

The Division conducted a review of the Sponsor's proposed labeling and container label (dated – 07\13\04) and there were changes through out the labeling.

The Project Manager will incorporate the Division's edits for the next labeling meeting.

INTERNAL Meeting Minutes Recorded By: T.Nguyen, HFD-160

DIVISION OF MEDICAL IMAGING AND RADIOPHARMACEUTICAL DRUG PRODUCTS HFD-160

INTERNAL MEETING MINTUES

NDA: **21-768**

DRUG NAME: **Fludeoxyglucose [F-18] Injection**

DATE: Wednesday, June 9, 2004

ATTENDEES: Sally Loewke, M.D., Eldon Leutzinger, Ph.D., Ravi Kasliwal, Ph.D., Thuy Nguyen, M.P.H.
Division of Medical Imaging and Radiopharmaceutical Drug Products, HFD-160

AGENDA: To discuss the review status of the NDA.

- The chemistry review is on-going.
- The microbiology team did not attend today's meeting.
- At next week's site inspection, the Division will ask if the container closure is a 510K.
- The Project Manager (PM) will ask the Sponsor to submit a safety update.

INTERNAL Meeting Minutes Recorded By: T.Nguyen, HFD-160

DIVISION OF MEDICAL IMAGING AND RADIOPHARMACEUTICAL DRUG PRODUCTS HFD-160

INTERNAL MEETING MINTUES

NDA: **21-768**

DRUG NAME: **Fludeoxyglucose [F-18] Injection**

DATE: Thursday, May 20, 2004

ATTENDEES: George Mills, M.D., Eldon Leutzinger, Ph.D., Ravi Kasliwal, Ph.D., Eric Duffy, Ph.D., Thuy Nguyen, M.P.H.
Division of Medical Imaging and Radiopharmaceutical Drug Products, HFD-160

AGENDA: To discuss the review timeline and the NDA review status.

- The current review timeline as of May 20, 2004, is acceptable.
- Chemistry and microbiology reviews are on-going.
- Manufacturing site inspection scheduled for June 14 and 15, 2004.
- The Project Manager (PM) informed the team that the Sponsor will submit by May 24, 2004, a CMC amendment, pediatric plan, and an electronic copy of the labeling.

INTERNAL Meeting Minutes Recorded By: T.Nguyen, HFD-160

DEPARTMENT OF HEALTH & HUMAN SERVICES
Public Health Service
Food and Drug Administration
Rockville, MD 20857

NDA 21-768

FILING COMMUNICATION

5-11-04

Weill Medical College of Cornell University
Citigroup Biomedical Imaging Center
Attention: Shankar Vallabhajosula, Ph.D.
516 East 72nd Street
New York, NY 10021

Dear Dr. Vallabhajosula:

Please refer to your new drug application (NDA) of March 10, 2004, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for [F-18] Fludeoxyglucose Injection.

We also refer to your submissions dated April 22 and 23, 2004.

We have completed our filing review and have determined that your application is sufficiently complete to permit a substantive review. Therefore, this application will be filed under section 505(b) of the Act on May 21, 2004, in accordance with 21 CFR 314.101(a).

In our filing review, we have identified the following potential chemistry issues:

1. Stability data - Provide stability data on a minimum of two additional batches produced at near upper limit of the proposed concentration of 90 mCi/mL.

2. The company, [ ] does not appear to be a qualified supplier of [ ] currently. We recommend that it be deleted from the application. Provide amended section of the application with the recommended amendment.

3. The acceptance criteria for [ ] should be changed to a range instead of the originally proposed criteria of [ ]

4. The acceptance criteria for [ ] should be changed to [ ] to be consistent with the acceptance criteria specified in the supplier's COA.

5. Specifications - Provide specifications for the [ ] reference standard obtained from [ ]

We are providing the above comments to give you preliminary notice of potential review issues. Our filing review is only a preliminary evaluation of the application and is not indicative of deficiencies that may be identified during our review. Issues may be added, deleted, expanded upon, or modified as we review the application.

We acknowledge that you have provided responses for Item # 2-5. Please provide a response to Item #1.

While we anticipate that any response submitted in a timely manner will be reviewed during this review cycle, such review decisions will be made on a case-by-case basis at the time of receipt of the submission.

If you have any questions, call Thuy M. Nguyen, M.P.H., Regulatory Health Project Manager, at (301) 827-7510.

Sincerely,

{See appended electronic signature page}

George Q. Mills, M.D.
Division Director
Division of Medical Imaging and
Radiopharmaceutical Drug Products, HFD-160
Office of Drug Evaluation III
Center for Drug Evaluation and Research

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/s/

George Mills
5/11/04 03:29:44 PM

DIVISION OF MEDICAL IMAGING AND RADIOPHARMACEUTICAL DRUG PRODUCTS HFD-160

INTERNAL FILING MEETING MINTUES

NDA: **21-768**

DRUG NAME: Fludeoxyglucose [F-18] Injection

DATE: Tuesday, April 27, 2004

ATTENDEES: Sally Loewke, M.D., Eldon Leutzinger, Ph.D., Ravi Kasliwal, Ph.D., Kaye Kang, Pharm.D., Thuy Nguyen, M.P.H.
Division of Medical Imaging and Radiopharmaceutical Drug Products, HFD-160

AGENDA: To discuss the filing status of the NDA.

- The same approved dosage will be used for the three approved indications as noted in the FR Notice, March 10, 2000, but this NDA has a new formulation.
- This NDA is considered a 3S - new formulation with a standard 10-month review clock involving the chemistry and microbiology disciplines.
- The NDA is considered fileable from a chemistry and microbiology perspective.
- The PDUFA due date is January 24, 2005. However, the Division most likely will complete its review before the due date and take an action prior to that date.
- The chemistry comments will be addressed in a 74-day filing review letter which will be issued to the Sponsor by June 4, 2004.
- The NDA Regulatory Filing Review Checklist has been completed – See DFS.

ACTION ITEMS

1. The Division will issue the Sponsor a 74-day filing review letter by June 4, 2004.

INTERNAL Meeting Minutes Recorded By: T.Nguyen, HFD-160

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 21-768

4-26-04

Weill Medical College of Cornell University
Citigroup Biomedical Imaging Center
Attention: Shankar Vallabhajosula, Ph.D.
516 East 72nd Street
New York, NY 10021

Dear Dr. Vallabhajosula:

Please refer to your new drug application (NDA) for Fludeoxyglucose [F-18] Injection.

We also refer to your submission dated March 10, 2004.

As discussed in the meeting on April 8, 2004, under the current law [section 121(c)(2) of the Food and Drug Administration Modernization Act (FDAMA) and section 501(a)(2)(C) of the Federal Food, Drug, and Cosmetic Act], PET producers may continue to produce compounded PET drug products without FDA approval until two years after the date that the FDA completes its new approval procedures and current good manufacturing practice regulations for PET products, as long as the activities are within the meaning of the term "compounded positron emission tomography drug" and are in compliance with the USP General Chapter <823> titled *"Radiopharmaceuticals for Positron Emission Tomography - Compounding"* and any applicable USP monographs. We do, however, welcome your submission of a New Drug Application (NDA) for Fludeoxyglucose [F-18] Injection. In fact, the PET provisions of FDAMA encourage the voluntary submission of such applications, and we commend you for taking the initiative of seeking approval at this time. We intend to review your application expeditiously and we will work with you to correct any deficiencies that might inhibit its approval.

If you have any questions, call Thuy M. Nguyen, M.P.H., Regulatory Health Project Manager, at (301) 827-7510.

Sincerely,

{See appended electronic signature page}
George Q. Mills
Division Director
Division of Medical Imaging and
Radiopharmaceutical Drug Products, HFD-160
Office of Drug Evaluation III
Center for Drug Evaluation and Research

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/s/

George Mills
4/26/04 01:49:03 PM

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

4-19-04

NDA 21-768

Weill Medical College of Cornell University
Citigroup Biomedical Imaging Center
Attention: Shankar Vallabhajosula, Ph.D.
516 East 72nd Street
New York, NY 10021

Dear Dr. Vallabhajosula:

We have received your new drug application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for the following:

Name of Drug Product: [F-18] Fludeoxyglucose Injection

Review Priority Classification: Standard (S)

Date of Application: March 10, 2004

Date of Receipt: March 24, 2004

NDA Reference Number: NDA 21-768

Unless we notify you within 60 days of the receipt date that the application is not sufficiently complete to permit a substantive review, we will file the application on May 21, 2004, in accordance with 21 CFR 314.101(a). If the application is filed, the user fee goal date will be January 24, 2005.

All applications for new active ingredients, new dosage forms, new indications, new routes of administration, and new dosing regimens are required to contain an assessment of the safety and effectiveness of the product in pediatric patients unless this requirement is waived or deferred. We note that you have not fulfilled the requirement. Pediatric studies are needed for the oncology and cardiac indications in pediatric patients below the age of 16 years. We are prepared to issue a deferral, but request that you propose a date for when you can meet the requirements. However, in the interim, please submit your pediatric drug development plans within 120 days from the date of this letter.

Pediatric studies conducted under the terms of section 505A of the Federal Food, Drug, and Cosmetic Act may result in additional marketing exclusivity for certain products (pediatric exclusivity). You should refer to the Guidance for Industry on Qualifying for Pediatric

Exclusivity (available on our web site at www.fda.gov/cder/pediatric) for details. If you wish to qualify for pediatric exclusivity you should submit a "Proposed Pediatric Study Request" in addition to your plans for pediatric drug development described above. Please note that satisfaction of the requirements in section 2 of PREA alone may not qualify you for pediatric exclusivity.

Please forward all future communications concerning this NDA in ***triplicate***, identified by the above NDA number along with ***Form FDA 356(h)***, to the following address:

U.S. Postal Service\Courier\Overnight Mail:
Center for Drug Evaluation and Research
Division of Medical Imaging and Radiopharmaceuticals Drug Products
Attention: FDA Document Room, 8B-45
5600 Fishers Lane, HFD-160
Rockville, Maryland 20857

If you have any questions, call Thuy M. Nguyen, M.P.H., Regulatory Health Project Manager, at (301) 827-7510.

Sincerely,

{See appended electronic signature page}

Kyong Kang, Pharm.D.
Chief, Project Management Staff
Division of Division of Medical Imaging and
Radiopharmaceuticals Drug Products, HFD-160
Office of Drug Evaluation III
Center for Drug Evaluation and Research

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/s/

Kyong Kang
4/19/04 03:45:07 PM

DIVISION OF MEDICAL IMAGING AND RADIOPHARMACEUTICAL DRUG PRODUCTS HFD-160

INDUSTRY MEETING MEETING MINUTES

NDA: **21-768**

DRUG NAME: **[F-18] FDG**

DATE: April 8, 2004

SPONSOR
Shankar Vallabhajosula, Ph.D.
Weill Medical College of Cornell University

FDA PARTICIPANTS
George Mills, M.D., Division Director, HFD-160
Sally Loewke, M.D., Deputy Division Director
Florence Houn, M.D., Office Director, Office of Drug Evaluation III
Jane Axelrad, Associate Director, Regulatory Policy
Ravi Kasliwal, Ph.D., Chemistry Reviewer
Kaye Kang, Pharm.D., Chief, Project Management Staff
Thuy Nguyen, M.P.H., Regulatory Health Project Manager

AGENDA: To discuss the Sponsor's NDA.

- The Sponsor asked what was needed to fulfill the pediatric study requirements to which the Division reiterated the TCON discussion of April 7, 2004, and that the Division would assist the Sponsor with developing the pediatric protocols. The Sponsor may be able to ask for a pediatric waiver for the cardiac indication.
- The Sponsor requested and the Division agreed to issue a letter stating that he is allowed to compound FDG at Cornell for his patients, as allowed in section 121 of FDAMA.
- The Sponsor stated that he will use the highest chemical grade raw materials from [ ] but he does not want to be responsible for using only cGMP materials. The Division stated that two manufacturers will need to be evaluated as [ ] raw material) is classified as an intermediate.
- The Sponsor stated that he is using the [ ] like the other PET centers and asked if he could use a different source of precursor to which the Division stated that the Division will need to review the specifications and will get back to the Sponsor on that issue.

- The Division stated that the starting material does not need to meet cGMP, but the intermediate material needs to comply with cGMP. The Sponsor stated he has made both the starting and intermediate materials and the entire kit will be made in cGMP compliance.
- The Sponsor will obtain the cold reference standard FDG from [ ] and will provide the Division with the [ ] specifications for the cold FDG and will make sure that it meets the Sponsor's in-house specifications.
- The Sponsor is using the highest grade USP sodium citrate and [ ] water. The Division asked how the Sponsor can be sure that [ ]) is not [ ] to which the Sponsor explained that he has a statement from [ ] that [ ] for use.
- The Division stated that if the Sponsor decides to buy the raw materials from another supplier (besides [ ] then the Sponsor should run a batch from that supplier. Also, the Division told the Sponsor that in the future the raw material sources should not be changed without FDA approval or notification.
- In regards to trade name, the Division stated that the Sponsor can submit a request for trade name, but it is not required. The Sponsor stated that he does not wish to submit a trade name request.

Meeting Minutes Recorded By: T. Nguyen, HFD-160

DIVISION OF MEDICAL IMAGING AND RADIOPHARMACEUTICAL DRUG PRODUCTS HFD-160

MEMORANDUM OF TELECONFERENCE

NDA: **21-768**

DRUG NAME: **[F-18] FDG**

DATE: April 7, 2004

SPONSOR: Shankar Vallabhajosula, Ph.D.
Weill Medical College of Cornell University

TELEPHONE: (212) 746-5694

BETWEEN: Shankar Vallabhajosula, Ph.D.

AND: George Mills, M.D., Sally Loewke, M.D., Kaye Kang, Pharm.D., Thuy Nguyen, M.P.H.
Division of Medical Imaging and Radiopharmaceutical Drug Products, HFD-160

AGENDA: To discuss the Sponsor's pediatric studies.

- The Sponsor will submit a pediatric plan within 120 days from the date of the NDA Acknowledgment letter for the oncology and cardiac indications in pediatric patients. The Sponsor agreed to propose a deferral date and the Division will issue a deferral for the pediatric studies.
- The Sponsor agreed to submit a pediatric clinical protocol 4 years before completion and will complete the pediatric studies and submit data in less than 10 years.
- The Sponsor stated they have currently enrolled a few pediatric patients from time to time in their on-going studies for the oncology indication.

ACTION ITEMS

1. The Sponsor will propose a deferral date.
2. The Sponsor will submit a pediatric plan with specific goal dates as well as clinical pediatric protocols as discussed.

TCON Meeting Minutes Recorded By: T. Nguyen, HFD-160

RECORD OF TELEPHONE CONVERSATION/MEETING	Date: 18-Mar-04
I called Dr. Shankar Vallabhjosula to discuss the number of batches he needs to submit in support of the proposed strength of 4-90mCi/mL in the NDA. I told him that since the [ ] batches in the submitted NDA are not at or near the upper strength of 90mCi/mL he would need to submit a minimum two batches at or near the upper strength of 90mCi/mL, along with the stability data to demonstrate the stability of the product at higher radio-concentration. He indicated that he would submit the results and the stability data in an amendment soon. I said that would be fine. Ravindra K. Kasliwal, Ph.D. --- **Name:** **HFD-160**	**NDA 21-768** Telecon/Meeting **initiated by:** **O** Applicant/Sponsor **X** FDA **By:** Ravindra K. Kasliwal, Ph.D **Product Name:** **Fludeoxyglucose F 18 Injection** **Firm Name:** Weill Medical College of Cornell University **Name and Title of Person with whom conversation was held:** Shankar Vallabhajosula, Ph.D. **Phone:** (212) 746-5694

cc : Orig.21-768
HFD-160/Division File/Nguyen
R/D Init. by: Leutzinger

4-29-03

NDA REGULATORY FILING REVIEW
(Including Memo of Filing Meeting)

NDA #: 21-768

Trade Name: N\A
Generic Name: [F-18] Fludeoxyglucose Injection
Strengths: 4-90 mCi\mL

Applicant: Weill Medical College of Cornell University (Dr. Shankar Vallabhajosula)

Date of Application: March 10, 2004
Date of Receipt: March 24, 2004
Date of Filing Meeting: April 27, 2004
Filing Date: May 21, 2004
User Fee Goal Date: January 24, 2005

Indication(s) requested:
See FR Notice - March 10, 2000

Type of Original NDA: (b)(2)
NOTE: A supplement can be either a (b)(1) or a (b)(2) regardless of whether the original NDA was a (b)(1) or a (b)(2). If the application is a (b)(2) application, complete the (b)(2) section at the end of this review.

Therapeutic Classification: (S) Standard
Resubmission after withdrawal? NO **Resubmission after refuse to file?** NO
Chemical Classification: (1,2,3 etc.) 3

User Fee Status: Waived - See FR Notice March 10, 2000

Form 3397 (User Fee Cover Sheet) submitted: YES
Clinical data? NO, Referenced to FR Notice March 10, 2000

Is there any 5-year or 3-year exclusivity on this active moiety in either a (b)(1) or a (b)(2) application? **NO**

Does another drug have orphan drug exclusivity for the same indication? **NO**

If yes, is the drug considered to be the same drug according to the orphan drug definition of sameness [21 CFR 316.3(b)(13)]? **N\A**

Is the application affected by the Application Integrity Policy (AIP)? **NO**
If yes, explain.

If yes, has OC/DMPQ been notified of the submission? **N\A**

- Does the submission contain an accurate comprehensive index? **YES**

- Was form 356h included with an authorized signature? **YES**
  If foreign applicant, both the applicant and the U.S. agent must sign.

- Submission complete as required under 21 CFR 314.50? **YES**
  If no, explain:

- If an electronic NDA, does it follow the Guidance? **N\A**
  If an electronic NDA, all certifications must be in paper and require a signature.
  Which parts of the application were submitted in electronic format?

  Additional comments:

- If in Common Technical Document format, does it follow the guidance? **NO**

- Is it an electronic CTD? **NO**
  If an electronic CTD, all certifications must be in paper and require a signature.
  Which parts of the application were submitted in electronic format?

  Additional comments:

- Patent information submitted on form FDA 3542a? **YES**

- Exclusivity requested? **NO**
  Note: An applicant can receive exclusivity without requesting it; therefore, requesting exclusivity is not required.

- Correctly worded Debarment Certification included with authorized signature? **YES**
  If foreign applicant, both the applicant and the U.S. Agent must sign the certification.

  NOTE: Debarment Certification should use wording in FD&C Act section 306(k)(1) i.e., *"[Name of applicant] hereby certifies that it did not and will not use in any capacity the services of any person debarred under section 306 of the Federal Food, Drug, and Cosmetic Act in connection with this application."* Applicant may not use wording such as "To the best of my knowledge . . . ."

- Financial Disclosure forms included with authorized signature? **YES**
  (Forms 3454 and 3455 must be used and must be signed by the APPLICANT.)

- Field Copy Certification (that it is a true copy of the CMC technical section)? **YES**

Refer to 21 CFR 314.101(d) for Filing Requirements

- PDUFA and Action Goal dates correct in COMIS? **YES**
  If not, have the document room staff correct them immediately. These are the dates EES uses for calculating inspection dates.

- Drug name/Applicant name correct in COMIS? **YES**

- List referenced IND numbers: **N\A**

- End-of-Phase 2 Meeting(s)? **NO**
  If yes, distribute minutes before filing meeting.

- Pre-NDA Meeting(s)? **NO**
  If yes, distribute minutes before filing meeting.

Project Management

- All labeling (PI, PPI, MedGuide, carton and immediate container labels) consulted to DDMAC?
  NO. See FR Notice – March 10, 2000 and *Guidance to Industry: PET Drug Applications – Content and Format For NDAs and ANDAs* (March 2000).

- Trade name (plus PI and all labels and labeling) consulted to ODS/DMETS?
  NO. Sponsor did not make a trade name request.

- MedGuide and/or PPI (plus PI) consulted to ODS/DSRCS? **NO**

- If a drug with abuse potential, was an Abuse Liability Assessment, including a proposal for scheduling, submitted?
  N/A

If Rx-to-OTC Switch application:

- OTC label comprehension studies, all OTC labeling, and current approved PI consulted to ODS/DSRCS?
  N/A

- Has DOTCDP been notified of the OTC switch application? **N\A**

Clinical

- If a controlled substance, has a consult been sent to the Controlled Substance Staff?
  N\A

Chemistry

- Did applicant request categorical exclusion for environmental assessment? **YES**
  If no, did applicant submit a complete environmental assessment? **YES**
  If EA submitted, consulted to Nancy Sager (HFD-357)? **YES**

- Establishment Evaluation Request (EER) submitted to DMPQ? **YES**

- If a parenteral product, consulted to Microbiology Team (HFD-805)? **YES**

If 505(b)(2) application, complete the following section:

- Name of listed drug(s) and NDA#: Fludeoxyglucose [F-18] Injection, NDA 20-306

- Describe the change from the listed drug(s) provided for in this (b)(2) application (for example, "This application provides for a new indication, otitis media" or "This application provides for a change in dosage form, from capsules to solution").

  NEW FORMULATION. Same dosage and indications.

- Is the application for a duplicate of a listed drug and eligible for approval under section 505(j) as an ANDA? (Normally, FDA will refuse-to-file such NDAs.) **NO**

- Is the extent to which the active ingredient(s) is absorbed or otherwise made available to the site of action less than that of the reference listed drug (RLD)? (See 314.54(b)(1)). If yes, the application should be refused for filing under 314.101(d)(9). **N\A**

- Is the rate at which the product's active ingredient(s) is absorbed or otherwise made available to the site of action unintentionally less than that of the RLD? (See 314.54(b)(2)). If yes, the application should be refused for filing under 314.101(d)(9). **N\A**

- Which of the following patent certifications does the application contain? Note that a patent certification must contain an authorized signature.

  ____ 21 CFR 314.50(i)(1)(i)(A)(1): The patent information has not been submitted to FDA.

  ____ 21 CFR 314.50(i)(1)(i)(A)(2): The patent has expired.

  ____ 21 CFR 314.50(i)(1)(i)(A)(3): The date on which the patent will expire.

  ____ 21 CFR 314.50(i)(1)(i)(A)(4): The patent is invalid, unenforceable, or will not be infringed by the manufacture, use, or sale of the drug product for which the application is submitted.

  IF FILED, and if the applicant made a "Paragraph IV" certification [21 CFR 314.50(i)(1)(i)(A)(4)], the applicant must submit a signed certification that the patent holder was notified the NDA was filed [21 CFR 314.52(b)]. Subsequently, the applicant must submit documentation that the patent holder(s) received the notification ([21 CFR 314.52(e)].

  _X__ 21 CFR 314.50(i)(1)(ii): No relevant patents.

  ____ 21 CFR 314.50(i)(1)(iii): The patent on the listed drug is a method of use patent and the labeling for the drug product for which the applicant is seeking approval does not include any indications that are covered by the use patent. Applicant must provide a statement that the method of use patent does not claim any of the proposed indications.

  ____ 21 CFR 314.50(i)(3): Statement that applicant has a licensing agreement with the patent owner (must also submit certification under 21 CFR 314.50(i)(1)(i)(A)(4) above.)
  ____ Written statement from patent owner that it consents to an immediate effective date upon approval of the application.

- Did the applicant:

  - Identify which parts of the application rely on information the applicant does not own or to which the applicant does not have a right of reference?

    YES

  - Submit a statement as to whether the listed drug(s) identified has received a period of marketing exclusivity?

    YES

  - Submit a bioavailability/bioequivalence (BA/BE) study comparing the proposed product to the listed drug?

    N\A

  - Certify that it is seeking approval only for a new indication and not for the indications approved for the listed drug if the listed drug has patent protection for the approved indications and the applicant is requesting only the new indication (21 CFR 314.54(a)(1)(iv).?
    NO. See FR Notice – March 10, 2000.

- If the (b)(2) applicant is requesting exclusivity, did the applicant submit the following information required by 21 CFR 314.50(j)(4): **NO.** The Sponsor did not request exclusivity.

  - Certification that each of the investigations included meets the definition of "new clinical investigation" as set forth at 314.108(a).

    N\A

  - A list of all published studies or publicly available reports that are relevant to the conditions for which the applicant is seeking approval.

    N\A

  - EITHER
    The number of the applicant's IND under which the studies essential to approval were conducted.

    N\A

    OR

    A certification that it provided substantial support of the clinical investigation(s) essential to approval if it was not the sponsor of the IND under which those clinical studies were conducted?

    N/A

- Has the Director, Div. of Regulatory Policy II, HFD-007, been notified of the existence of the (b)(2) application?

  YES

ATTACHMENT

MEMO OF FILING MEETING

DATE: April 27, 2004

ATTENDEES: S.Loewke, E.Leutzinger, R.Kasliwal, K.Kang, T.Nguyen

ASSIGNED REVIEWERS:

Discipline	Reviewer
Medical:	Ramesh Raman, M.D. (for pediatric plan)
Statistical:	N\A
Pharmacology:	N\A
Statistical Pharmacology:	N\A
Chemistry:	Ravi Kasliwal, Ph.D.
Environmental Assessment:	Ravi Kasliwal, Ph.D.
Biopharmaceutical:	N\A
Microbiology, sterility:	Bryan Riley, Ph.D.
Microbiology, clinical (for antimicrobial products only):	N\A
DSI:	N\A
Regulatory Project Management:	Thuy Nguyen, M.P.H.
Other Consults:	N\A

Per reviewers, are all parts in English or English translation? YES

CLINICAL: **N\A – See FR Notice March 10, 2000**

- Clinical site inspection needed: **N\A**
- Advisory Committee Meeting needed? **N\A**
- If the application is affected by the AIP, has the division made a recommendation regarding whether or not an exception to the AIP should be granted to permit review based on medical necessity or public health significance? **N/A**

CLINICAL MICROBIOLOGY: **N\A – See FR Notice March 10, 2000**

STATISTICS: **N\A – See FR Notice March 10, 2000**

BIOPHARMACEUTICS: **N\A – See FR Notice March 10, 2000**

- Biopharm. inspection needed: **N\A**

PHARMACOLOGY: **N\A – See FR Notice March 10, 2000**

- GLP inspection needed: **N\A**

CHEMISTRY: **FILE**

- Establishment(s) ready for inspection? **YES**
- Microbiology **YES**

ELECTRONIC SUBMISSION: **NO**

REGULATORY CONCLUSIONS/DEFICIENCIES:

_____ The application is unsuitable for filing. Explain why:

__X___ The application, on its face, appears to be well organized and indexed. The application appears to be suitable for filing.

_____ No filing issues have been identified.

___X___ Filing and\or Review issues to be communicated by Day 74.

ACTION ITEMS:

1. If RTF, notify everybody who already received a consult request of the RTF action. Cancel the EER.
2. If filed and the application is under the AIP, prepare a letter either granting (for signature by Center Director) or denying (for signature by ODE Director) an exception for review.
3. Document filing issues/no filing issues conveyed to applicant by Day 74.

*See DFS Signatory
Thuy Nguyen
Regulatory Health Project Manager, HFD-160
April 27, 2004

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

Thuy Nguyen
4/29/04 03:46:29 PM
CSO

DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION

Form Approved: OMB No. [illegible]
Expiration Date: February 2[illegible]

USER FEE COVER SHEET

See Instructions on Reverse Side Before Completing This Form

A completed form must be signed and accompany each new drug or biologic product application and each new supplement. See exceptions on the reverse side. If payment is sent by U.S. mail or courier, please include a copy of this completed form with payment. Payment instructions and fee rates can be found on CDER's website: http://www.fda.gov/cder/pdufa/default.htm

1 APPLICANT'S NAME AND ADDRESS

Weill Medical College of Cornell University
Citigroup Biomedical Imaging Center
516 East 72nd Street
New York, NY 10021

4 BLA SUBMISSION TRACKING NUMBER (STN) / NDA NUMBER

5 DOES THIS APPLICATION REQUIRE CLINICAL DATA FOR APPROVAL?

☒ YES ☐ NO

IF YOUR RESPONSE IS "NO" AND THIS IS FOR A SUPPLEMENT, STOP HERE AND SIGN THIS FORM

IF RESPONSE IS "YES," CHECK THE APPROPRIATE RESPONSE BELOW:

☐ THE REQUIRED CLINICAL DATA ARE CONTAINED IN THE APPLICATION

☒ THE REQUIRED CLINICAL DATA ARE SUBMITTED BY REFERENCE TO

Federal Register Notice of March 2000, V 65.
(APPLICATION NO. CONTAINING THE DATA)

2 TELEPHONE NUMBER *(Include Area Code)*

(212) 746-5694

3 PRODUCT NAME

Fludeoxyglucose F18 injection

6 USER FEE I.D. NUMBER

7 IS THIS APPLICATION COVERED BY ANY OF THE FOLLOWING USER FEE EXCLUSIONS? IF SO, CHECK THE APPLICABLE EXCLUSION.

☐ A LARGE VOLUME PARENTERAL DRUG PRODUCT APPROVED UNDER SECTION 505 OF THE FEDERAL FOOD, DRUG, AND COSMETIC ACT BEFORE 9/1/92
(Self Explanatory.)

☐ A 505(b)(2) APPLICATION THAT DOES NOT REQUIRE A FEE
(See item 7, reverse side before checking box.)

☐ THE APPLICATION QUALIFIES FOR THE ORPHAN EXCEPTION UNDER SECTION 736(a)(1)(E) of the Federal Food, Drug, and Cosmetic Act
(See item 7, reverse side before checking box.)

☐ THE APPLICATION IS A PEDIATRIC SUPPLEMENT THAT QUALIFIES FOR THE EXCEPTION UNDER SECTION 736(a)(1)(F) of the Federal Food, Drug, and Cosmetic Act
(See item 7, reverse side before checking box.)

☐ THE APPLICATION IS SUBMITTED BY A STATE OR FEDERAL GOVERNMENT ENTITY FOR A DRUG THAT IS NOT DISTRIBUTED COMMERCIALLY
(Self Explanatory.)

8 HAS A WAIVER OF AN APPLICATION FEE BEEN GRANTED FOR THIS APPLICATION?

☒ YES ☐ NO

(See item 8, reverse side if answered YES.)

Shankar Vallabhajosula — 3/22/04

SIGNATURE OF AUTHORIZED COMPANY REPRESENTATIVE	TITLE	DATE
[signature]	Grants & Contracts, Senior Director	11/21/03

FORM FDA 3397 (4/01)

PLEASE REFER TO **FEDERAL REGISTER** VOLUME 65
(PAGES 12999-13010), No. 48, MARCH 10, 2000