CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

21-870

ADMINISTRATIVE and CORRESPONDENCE DOCUMENTS

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
NDA 21-870

NAME OF APPLICANT / NDA HOLDER
North Shore/LIJ Research Institute

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)
Fludeoxyglucose F 18 Injection

ACTIVE INGREDIENT(S)	STRENGTH(S)
2-deoxy-2-[18 F] fluoro-D-glucose	20-200 mCi

DOSAGE FORM
Intravenous 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.

4. GENERAL

a. United States Patent Number	b. Issue Date of Patent	c. Expiration Date of Patent
N/A, CFR March 10, 2000. No Patent Exists.		

d. Name of Patent Owner	Address *(of Patent Owner)*	
N/A This drug was in use for more than 20 years		
	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.)*	
N/A	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

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

PSC Media Arts (301) 443-1090

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.

2. Drug Substance (Active Ingredient)

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 date 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.**

N/A

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

3. Drug Product (Composition/Formulation)

Does the patent claim the drug product, as defined in 21 CFR 314.3, in the pending NDA, amendment, or supplement? ☐ Yes ☐ No

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)*

N/A

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.)*

N/A

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: 1/6/2005

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: Dr.Thomas Chaly

Address: Chief Of Radiochemistry, Cyclotron/Radiochemistry Facility, North Shore/LIJ Research Institute	City/State: Manhasset, New York
ZIP Code: 11030	Telephone Number: 516-562-1042
FAX Number *(if available)*: 516-562-1041	E-Mail Address *(if available)*: tchaly@nshs.edu

The public reporting burden for this collection of information has been estimated to average 9 hours per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing the collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden to:

Food and Drug Administration
CDER (HFD-007)
5600 Fishers Lane
Rockville, MD 20857

An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB control number.

North Shore LIJ Institute for Medical Research
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THOMAS CHALY, Ph.D., FAIC

Chief, Radiochemistry
Cyclotron/Radiochemistry Facility

PATENT CERTIFICATION FOR FLUDEOXYGLUCOSE F 18 INJECTION FOR WHICH NDA APPROVAL IS SOUGHT

DATE: 11-05-2004

TO: Center for Drug Evaluation and Research
Attention: Central Document Room
Food and Drug Administration
5901-B Ammendale Road
Beltsville, MD 20705-1266

FROM: Thomas Chaly, PhD, FAIC
Chief of Radiochemistry
North Shore/LIJ Research Institute
Cyclotron/Radiochemistry Facility
350 Community Drive
Manhasset, New York 11030

In this notice, I am providing a "No Relevant Patents Certification" for the drug Fludeoxyglucose F 18 Injection.

In the opinion and to the best knowledge of Dr. Thomas Chaly, on behalf of North Shore/LIJ Health System, there are no patents that claim the listed drug referred to in this application or that claim a use of the listed drug.

North Shore LIJ Institute for Medical Research
North Shore-Long Island Jewish Health System

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Manhasset, New York 11030
Tel (516) 562-1042
Fax (516) 562-1041
tchaly@nshs.edu

THOMAS CHALY, Ph.D., FAIC

Chief, Radiochemistry
Cyclotron/Radiochemistry Facility

EXCLUSIVITY STATEMENT

DATE: 11-05-2004

TO: Center for Drug Evaluation and Research
Attention: Central Document Room
Food and Drug Administration
5901-B Ammendale Road
Beltsville, MD 20705-1266

FROM: Thomas Chaly, PhD, FAIC
Chief of Radiochemistry
North Shore/LIJ Research Institute
Cyclotron/Radiochemistry Facility
350 Community Drive
Manhasset, New York 11030

Fludeoxyglucose F 18 Injection is an approved PET drug product and currently is not covered by any market exclusivity. Therefore, I, Dr. Thomas Chaly on behalf of North Shore/LIJ Health System, am providing a no exclusivity statement for the drug Fludeoxyglucose F 18 Injection.

According to the publication, Approved Drug Products with Therapeutic Equivalence Evaluations (Orange Book), the reference listed drug Fludeoxyglucose F 18 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).

EXCLUSIVITY SUMMARY FOR: NDA 21-870 HFD-160

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

Applicant Name: North Shore/ LIJ Research Institute

Approval Date If Known: August 19, 2005

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# 21-768: Fludeoxyglucose F 18 Injection

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
Division of Medical Imaging and Hematology Products
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
8/19/2005 11:50:25 AM

North Shore LIJ Institute for Medical Research
North Shore-Long Island Jewish Health System

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tchaly@nshs.edu

THOMAS CHALY, Ph.D., FAIC

Chief, Radiochemistry
Cyclotron/Radiochemistry Facility

DEBARMENT CERTIFICATION

DATE: 11-05-2004

TO: Center for Drug Evaluation and Research
Attention: Central Document Room
Food and Drug Administration
5901-B Ammendale Road
Beltsville, MD 20705-1266

FROM: Thomas Chaly, PhD, FAIC
Chief of Radiochemistry
North Shore/LIJ Research Institute
Cyclotron/Radiochemistry Facility
350 Community Drive
Manhasset, New York 11030

As of June 1, 1992, based on the Federal Act 306(a) or (b) and Act 21 U.S.C. 355a(a) or (b), the applicant submitting a NDA has to provide a Debarment Certification stating that the applicant did not and will not use the service (in any capacity) of any person debarred. Therefore my statement is given below:

I, Dr. Thomas Chaly on behalf of North Shore/LIJ Health System, certify that I did not and will not use the service, in any capacity, of any person debarred under Section 306 of the Federal Food, Drug, and Cosmetic Act in connection with the NDA application for Fludeoxyglucose F 18 Injection.

PEDIATRIC PAGE

(Complete for all filed original applications and efficacy supplements)

NDA# : 21-870 HFD-160

Stamp Date: November 19, 2004 Action Date: August 19, 2005

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

Applicant: North Shore/LIJ Health System

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 19, 2015**

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 Hematology 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)

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/s/

George Mills
8/19/2005 11:46:55 AM

DIVISION OF MEDICAL IMAGING AND HEMATOLOGY PRODUCTS
HFD-160

MEMORANDUM OF TELECONFERENCE

NDA: **21-870**

DRUG NAME: **Fludeoxyglucose F 18 Injection**

DATE: Thursday, August 18, 2005

SPONSOR: North Shore/LIJ Research Institute

TELEPHONE: (516) 562-1042

BETWEEN: Thomas Chaly, Ph.D.

AND: Eldon Leutzinger, Ph.D., Eric Duffy, Ph.D., Milagros Salazar-Driver, Ph.D., Thuy Nguyen, M.P.H .
Division of Medical Imaging and Hematology Products, HFD-160

AGENDA: To discuss the Sponsor's material supply.

Regarding the [redacted] the Sponsor agreed to provide a Letter-of-Commitment from [redacted] that all the materials used from start to finish for the manufacturing of the drug product will be U.S. approved cGMPs of highest quality from a cGMP facility site that has been inspected by the FDA.

ACTION ITEMS
1. The Sponsor will forward to the Division the Letter-of-Commitment from [redacted]

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

DIVISION OF MEDICAL IMAGING AND HEMATOLOGY PRODUCTS
HFD-160

MEMORANDUM OF TELECONFERENCE

NDA: **21-870**

DRUG NAME: **Fludeoxyglucose F 18 Injection**

DATE: Wednesday, August 17, 2005

SPONSOR: ABX (for North Shore/LIJ Research Institute)

TELEPHONE: (888) 390-8568 (temporary)

BETWEEN: Peter Moll, Ph.D., Harald Niegel, Ph.D., Andreas Fintelmann, Ph.D.

AND: Eric Duffy, Ph.D., Eldon Leutzinger, Ph.D., Milagros Salazar-Driver, Ph.D., Compliance - John Dietrick, Jason Chancey, Zi-Qiang Gu, Ph.D. Thuy Nguyen, M.P.H., Division of Medical Imaging and Hematology Products, HFD-160

AGENDA: To discuss the ABX's response to the Compliance 483 Deficiency List issued in April 2005.

- FDA Office of Compliance asked ABX for clarifications regarding ABX's recent compliance responses to the 483 Deficiency List issued April 2005.

- Regarding the protocol, ABX provided clarifications to Observation #1C, 2, 3, 4, and 5, as well as to [redacted] #10. ABX agreed to provide the clarifications as an official submission to the FDA Office of Compliance by the end of August 2005.

- Regarding the DMF, the primary and secondary labels varied among the lots. The Division will forward to [redacted] information table to revise\unify the formatting of the codes for the label lot numbers.

- As for the pharmaceutical and chemical grade, in the new [redacted] #5, page 5 of 24, for "Supplier # - ABX 100", ABX stated it was a typo and should be "Supplier # - ABX 10."

- ABX stated that the [redacted] for the bulk product is performed for both products, the pharmaceutical and chemical grades.

ACTION ITEMS

1. ABX agreed to revised and update the manufacturing protocol accordingly, as discussed, and will submit the clarifications and revisions in an official submission to the FDA Office of Compliance by the end of August 2005.
2. The Division will forward to ABX the information table to revise\unify the codes for the label lot numbers.

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

DIVISION OF MEDICAL IMAGING AND HEMATOLOGY PRODUCTS
HFD-160

INTERNAL TEAM MEETING MINUTES

NDA: **21-870**

DRUG NAME: **Fludeoxyglucose F 18 Injection**

DATE: Monday, August 15, 2005

ATTENDEES: George Mills, M.D., M.B.A., Sally Loewke, M.D., Eldon Leutzinger, Ph.D., Milagros Salazar-Driver, Ph.D., Kaye Kang, Pharm.D., Thuy Nguyen, M.P.H. Division of Medical Imaging and Hematology Products, HFD-160

AGENDA: To discuss the status of the Compliance foreign inspection report.

- As of August 15, 2005, the foreign inspection report is still in DRAFT form and the inspector is recommending a "withhold". During the foreign inspection in April 2005, the facility was issued a 483 deficiency list. A re-inspection is needed after the facility has addressed the deficiencies.
- The foreign inspection report will need to be reviewed by the inspection Team Leader and then forwarded to the Office of Compliance for review and recommendations.
- The Agency may suggest to the Sponsor that he commits to using only pharmaceutical grade materials for manufacturing until the 483 deficiencies are resolved.
- The Division has completed its review and would like to issue an action on the Goal Date of August 17, 2005, however, due to the pending foreign inspection report, the action may be delayed. However, an action will take place by the PDUFA Date of September 19, 2005.

ACTION ITEMS

1. The CMC team will follow up with ONDC II, and the Office Compliance regarding the status of the foreign inspection report.
2. The Team will meet on Wednesday, August 17, 2005, for an update regarding the status of the foreign inspection report.

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

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

FACSIMILE TRANSMITTAL SHEET

DATE: August 9, 2005

TO: DR. THOMAS CHALY Chief, Radiochemistry	**From:** Thuy Nguyen Regulatory Health Project Manager
Company: North Shore\LIJ Research Institute	Division of Division of Medical Imaging and Radiopharmaceutical Drug Products
Fax number: (516) 562-1041	**Fax number:** (301) 480-6036
Phone number: (516) 562-1042	**Phone number:** (301) 827-7510

Subject: NDA 21-870: Fludeoxyglucose F 18 Injection

Total no. of pages including cover: 15

COMMENTS: Please find attached the FDA labeling and labels as of August 9, 2005, for NDA 21-870: [F-18] FDG. Please review and provide a formal concurrence agreement [along with Form FDA 356(h)] to the Division by Thursday, August 11, 2005, at 12:00 pm. If you have any questions, please feel free to contact me. Thank you.

THIS DOCUMENT IS INTENDED ONLY FOR THE USE OF THE PARTY TO WHOM IT IS ADDRESSED AND MAY CONTAIN INFORMATION THAT IS PRIVILEGED, CONFIDENTIAL, AND PROTECTED FROM DISCLOSURE UNDER APPLICABLE LAW.

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_____ Deliberative Process

Withheld Track Number: Administrative- 1

DIVISION OF MEDICAL IMAGING AND HEMATOLOGY PRODUCTS
HFD-160

INTERNAL PM LABELING REVIEW

NDA: **21-870**

DRUG NAME: **Fludeoxyglucose F 18 Injection**

SPONSOR: **North Shore/LIJ Research Institute**

DATE: **Thursday, August 4, 2005**

As of August 4, 2005, the review team along with the Project Manager has completed the review of the the Fludeoxyglucose F 18 Injection labeling and labels dated August 3, 2005, and found it adequate to move forward with a regulatory action.

The PM will forward the labeling and labels to the Sponsor for a concurrence agreement.

PM Labeling Review Completed By: T.Nguyen, HFD-160

DIVISION OF MEDICAL IMAGING AND HEMATOLOGY PRODUCTS
HFD-160

MEMORANDUM OF TELECONFERENCE

NDA: **21-870**

DRUG NAME: **Fludeoxyglucose F 18 Injection**

DATE: Thursday, August 4, 2005

SPONSOR: North Shore/LIJ Research Institute

TELEPHONE: (516) 562-1042

BETWEEN: Thomas Chaly. Ph.D.

AND: Eldon Leutzinger, Ph.D., James McVey, Ph.D., Tiffany Brown, M.P.H., Thuy Nguyen, M.P.H.
Division of Medical Imaging and Hematology Products, HFD-160

AGENDA: To discuss the Sponsor's submission dated July 22, 2005, specifically Page 134 of the SOPs.

The Sponsor agreed to omit Page 134, of the SOPs and the Division will make a note of the omission in the submission of July 22, 2005.

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

DIVISION OF MEDICAL IMAGING AND HEMATOLOGY PRODUCTS
HFD-160

INTERNAL TEAM MEETING MINUTES

NDA: **21-870**

DRUG NAME: **Fludeoxyglucose F 18 Injection**

DATE: Thursday, August 4, 2005

ATTENDEES: Eldon Leutzinger, Ph.D., James McVey, Ph.D., Tiffany Brown, M.P.H., Thuy Nguyen, M.P.H.
Division of Medical Imaging and Hematology Products, HFD-160

AGENDA: To finalize the labeling and labels.

- The draft labeling and labels dated August 3, 2005, was found acceptable by the Team.
- The Division's draft labeling and labels dated August 3, 2005, will be forwarded to the Sponsor for review and concurrence agreement.
- Regarding the Foreign Inspection, the ABX foreign facility site was not ready for inspection in June 2005. As of August 1, 2005, the foreign inspection report has not been completed. Office of Compliance may recommend a contingency approval once the foreign inspection report is completed.
- In the submission dated July 22, 2005, the Sponsor mistakenly included Page 134, in the SOPs. In a teleconference following this Team Meeting, the Division will remind the Sponsor to omit Page 134, from the SOPs.
- The Action Goal Date of August 17, 2005, may change depending on the completion of the Foreign Inspection Report and the Office of Compliance's recommendations.

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

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

FACSIMILE TRANSMITTAL SHEET

DATE: August 3, 2005

TO: DR. THOMAS CHALY Chief, Radiochemistry	**From:** Thuy Nguyen Regulatory Health Project Manager
Company: North Shore\LIJ Research Institute	Division of Division of Medical Imaging and Radiopharmaceutical Drug Products
Fax number: (516) 562-1041	**Fax number:** (301) 480-6036
Phone number: (516) 562-1042	**Phone number:** (301) 827-7510

Subject: NDA 21-870: [F-18] FDG

Total no. of pages including cover: 2

COMMENTS: **Please find attached *MICROBIOLOGY* comments. Thank you.**

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MICROBIOLOGY COMMENTS TO THE SPONSOR

NDA 21-870: [F-18] FDG **August 3, 2005**

1. Please review the FDA "Guidance for Validation of the LAL Test --- ", http://www.fda.gov/cder/guidance/old005fn.pdf . It explains the establishment of the maximum valid dilution which would provide additional flexibility in your endotoxin testing acceptance limits.

2. Please be aware that any open bottle methods should not be employed without initial verification of the process capabilities (both equipment and methods of manufacture) with a

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

FACSIMILE TRANSMITTAL SHEET

DATE: July 21, 2005

TO: DR. THOMAS CHALY Chief, Radiochemistry	**From:** Thuy Nguyen Regulatory Health Project Manager
Company: North Shore \ LIJ Health System	Division of Division of Medical Imaging and Radiopharmaceutical Drug Products
Fax number: (516) 562-1041	**Fax number:** (301) 480-6036
Phone number: (516) 562-1042	**Phone number:** (301) 827-7510

Subject: NDA 21-870: [F-18] FDG

Total no. of pages including cover: 2

COMMENTS: Please find attached the Division's *CHEMISTRY* comments. Please provide an official response to the NDA): FDG (in triplicate) along with Form FDA 356(h) as soon as possible or by July 22, 2005. Thank you.

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Withheld Track Number: Administrative- 2

DIVISION OF MEDICAL IMAGING AND HEMATOLOGY PRODUCTS
HFD-160

INTERNAL TEAM MEETING MINTUES

NDA: **21-870**

DRUG NAME: **Fludeoxyglucose F 18 Injection**

DATE: Wednesday, July 20, 2005

ATTENDEES: Eldon Leutzinger, Ph.D., Milagros James McVey, Ph.D.,
Thuy Nguyen, M.P.H.
Division of Medical Imaging and Hematology Products, HFD-160

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

Chemistry

- The Domestic Inspection report has been completed and found the facility site acceptable as of June 10, 2005.
- The Foreign Inspection report is still pending as of July 20, 2005.
- The CMC Team will follow up with Dr. Eric Duffy regarding the status of the foreign inspection. Only parts of the DMFs were received.
- The Sponsor's EDR labeling dated June 29, 2005, is still inadequate. The chemist will forward to the Project Manager (PM) by July 22, 2005, the CMC labeling comments to be faxed to the Sponsor.

Microbiology

The microbiologist forward to the PM the micro comments to be faxed to the Sponsor.
Micro response to the micro fax of June 15, 2005, is still pending. The PM will follow up with the Sponsor regarding the response status.

TimeLine

The updated TimeLine dated July 20, 2005, is acceptable to the Team, pending the Sponsor's micro responses.

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

DIVISION OF MEDICAL IMAGING AND RADIOPHARMACEUTICAL DRUG PRODUCTS HFD-160

INTERNAL TEAM MEETING MINUTES

NDA: **21-870**

DRUG NAME: **Fludeoxyglucose F 18 Injection**

DATE: Wednesday, June 15, 2005

ATTENDEES: Eldon Leutzinger, Ph.D., Milagros James McVey, Ph.D., Thuy Nguyen, M.P.H.
Division of Medical Imaging and Radiopharmaceutical Drug Products, HFD-160

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

Chemistry: The chemist will forward to the Project Manager (PM), by 06\16\05, the CMC labeling and label comments to be faxed to the Sponsor.

Microbiology: The microbiologist faxed to the Sponsor micro comments which he will cc: the PM in DFS. Responses are expected from the Sponsor by mid-July 2005.

TimeLine: The updated TimeLine dated June 13, 2005, is acceptable to the Team, with primary review expected to be completed by July 22, and secondary review completed by July 29, 2005. TimeLine may changed depending on when the responses are received from the Sponsor.

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

DIVISION OF MEDICAL IMAGING AND RADIOPHARMACEUTICAL DRUG PRODUCTS HFD-160

INTERNAL TEAM MEETING MINUTES

NDA: **21-870**

DRUG NAME: **Fludeoxyglucose F 18 Injection**

DATE: Wednesday, June 8, 2005

PM NOTE: Today's team meeting was cancelled because there were no review or labeling issues per the Team.

Drafted By: T.Nguyen, HFD-160

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

FACSIMILE TRANSMITTAL SHEET

DATE: June 3, 2005

To: Thomas Chaly, MD	**From:** Renee Tyson for Thuy Nguyen
Company: North Shore/ LIJ Health System	Division of Medical Imaging and Radiopharmaceutical Drug Products
Fax number: (516) 562-1041	**Fax number:** (301) 480-6036
Phone number: (516) 562-1041	**Phone number:** (301) 827-7510

Subject: NDA 21-870 CMC Comments

Total no. of pages including cover: 4

Comments: Please call the above number to confirm receipt of this fax. Thank you.

Document to be mailed: ☑ YES ☐ NO

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DIVISION OF MEDICAL IMAGING AND RADIOPHARMACEUTICAL DRUG PRODUCTS HFD-160

INTERNAL TEAM MEETING MINUTES

NDA: **21-870**

DRUG NAME: **Fludeoxyglucose F 18 Injection**

DATE: Thursday, June 2, 2005

ATTENDEES: Milagros Salazar-Driver, Ph.D., James McVey, Ph.D., Thuy Nguyen, M.P.H.
Division of Medical Imaging and Radiopharmaceutical Drug Products, HFD-160

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

CHEMISTRY

- The CMC review is ongoing with no issues at this time.
  The labeling dated May 26, 2005, is adequate, however, the labels will need additional edits. The label comments will be forwarded to the Sponsor.
- The Sponsor will have to specify the location of Appendix #2: results of the stability data.
- Foreign Inspection report is still pending. Deficiency List 493, was issued to the foreign facility site. The Sponsor needs to update the DMF.

MICROBIOLOGY

- The micro review is ongoing and the labeling dated May 26, 2005, is adequate.

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

DIVISION OF MEDICAL IMAGING AND RADIOPHARMACEUTICAL DRUG PRODUCTS HFD-160

INTERNAL TEAM MEETING MINUTES

NDA: **21-870**

DRUG NAME: **Fludeoxyglucose F 18 Injection**

DATE: Tuesday, May 10, 2005

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

AGENDA: To discuss the NDA review status and timeline.

Chemistry: The CMC review is ongoing.

Microbiology: The micro review is ongoing and the microbiologist will contact the Sponsor with micro issues.

TimeLine: The TimeLine dated May 4, 2005, is acceptable to the Team, with the primary review expected to be completed by mid-June, and secondary review completed by June 23, 2005.

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

DIVISION OF MEDICAL IMAGING AND RADIOPHARMACEUTICAL DRUG PRODUCTS HFD-160

MEMORANDUM OF TELECONFERENCE

NDA: **21-870**

DRUG NAME: **Fludeoxyglucose F 18 Injection**

DATE: May 5, 2005, AT 3:30 pm

SPONSOR: North Shore/LIJ Research Institute

TELEPHONE: (516) 562-1042

BETWEEN: Thomas Chaly. Ph.D.

AND: Ramesh Raman, M.D., Thuy Nguyen, M.P.H.
Division of Medical Imaging and Radiopharmaceutical Drug Products, HFD-160

AGENDA: An update to today's earlier teleconference to discuss the Sponsor's pediatric studies.

- The Division provided an updated request asking for the pediatric protocol to be submitted within six years from the time of approval (not four years), and complete and submit the pediatric study data within ten years.
- The Sponsor stated that they mostly see pediatric epilepsy cases more so than cardiac or oncology pediatric patients.
- The Sponsor agreed to submit a Letter-of-Commitment to the pediatric study timeline just discussed.

ACTION ITEMS

1. The Sponsor will submit a Letter-of-Commitment regarding the pediatric study timeline discussed.

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

DIVISION OF MEDICAL IMAGING AND RADIOPHARMACEUTICAL DRUG PRODUCTS HFD-160

MEMORANDUM OF TELECONFERENCE

NDA:	**21-870**
DRUG NAME:	**Fludeoxyglucose F 18 Injection**
DATE:	May 5, 2005, AT 2:00 pm
SPONSOR:	North Shore/LIJ Research Institute
TELEPHONE:	(516) 562-1042
BETWEEN:	Thomas Chaly. Ph.D. Vijay Dhawan, Ph.D., (physicist, investigator for pediatric studies)
AND:	Ramesh Raman, M.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 Division requested that the Sponsor submit a pediatric clinical protocol within four years from time of the NDA approval and complete the studies and submit the data for review within ten years.
- The Sponsor agreed to submit the data for the epilepsy cases and stated that within the last ten years there were no adverse events (AEs). The Sponsor stated that the epilepsy protocol has not been reviewed by the FDA, however, the Sponsor's IRB has reviewed it since the study began before FDG was approved.
- The Division requested the Sponsor to submit a prospectively designed epilepsy protocol for review. The Division explained that the Sponsor's current epilepsy pediatric data can be considered as supportive information along with a new, prospectively designed protocol.
- The Division stated that currently FDG is approved for three indications: cardiac, oncology, and epilepsy, and understood that there are limitations for the pediatric patient enrollment. The Sponsor stated the pediatric cases for cardiac and oncology are less than five per year. The Sponsor asked if there is a minimum number of pediatric patients required to which the Division explained that it would depend on the indication and the Sponsor's statistician would be able to help power the number of cases needed.

- The Sponsor stated that from 1989 – 2005, the patient enrollment was 260 patients; 15 patients a year; one patient a month. The Division explained that the data captured should be of merit which can be considered as supportive information for the new protocol. The aim is for a safe and an effective pediatrics protocol.

- The Sponsor asked for the content of the pediatric protocol to which the Division explained briefly that it should contain the target population, blinded-reads, methodology, statistical plan, patient monitoring, AEs, images, case report forms (CRFs), etc. The Division referred the Sponsor to the Medical Imaging guidance document, Part 3, which can be found on the FDA website.

ACTION ITEMS

1. The Sponsor will submit the pediatric protocol and data accordingly as discussed.

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

DIVISION OF MEDICAL IMAGING AND RADIOPHARMACEUTICAL DRUG PRODUCTS HFD-160

INTERNAL TEAM MEETING MINTUES

NDA: **21-870**

DRUG NAME: **Fludeoxyglucose F 18 Injection**

DATE: Monday, May 2, 2005

ATTENDEES: Ramesh Raman, M.D., Thuy Nguyen, M.P.H.
Division of Medical Imaging and Radiopharmaceutical Drug Products, HFD-160

AGENDA: To prepare for the teleconference on May 5, 2005, regarding the pediatric studies.

The Division will ask the Sponsor of NDA 21-870, to commit to a pediatric study timeline similar to the approved NDA 21-768: FDG, of August 4, 2004.

The Division will request that the Sponsor submit from the time of approval, a pediatric clinical protocol four years before completion and complete the pediatric study and submit the results for review in less than ten years.

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 21-870 **FILING COMMUNICATION**

North Shore\LIJ Research Institute
Cyclotron\Radiochemistry Facility
Attention: Thomas Chaly, Ph.D.
350 Community Drive
Manhasset, NY 11030

Dear Dr. Chaly:

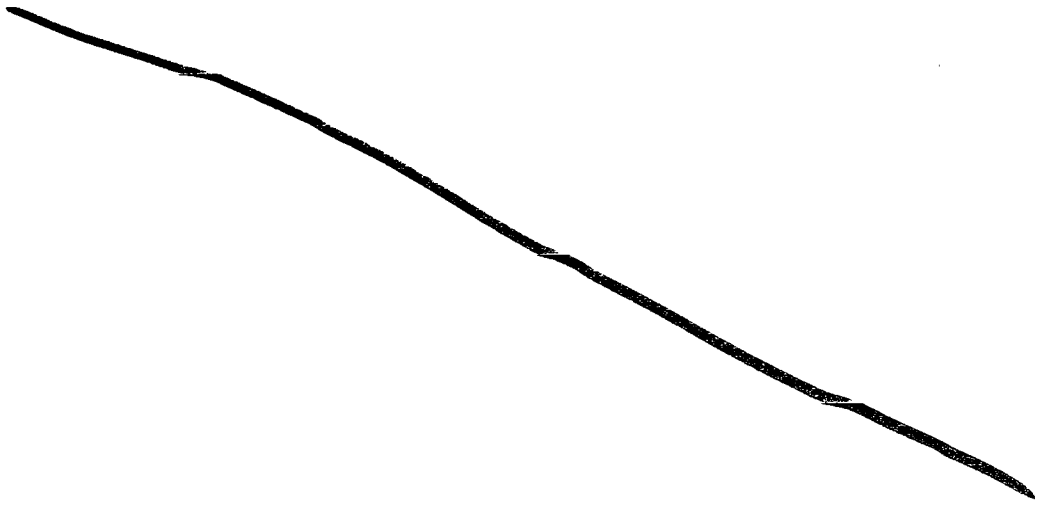
Please refer to your new drug application (NDA) of November 5, 2004, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for [F-18] Fludeoxyglucose Injection.

We also refer to your submissions dated January 6, 10, and 12, 2005.

We have completed our filing review and have determined that your application is sufficiently complete to permit a substantive review. Therefore, this application has been filed under section 505(b) of the Act on January 17, 2005, in accordance with 21 CFR 314.101(a).

In our filing review, we have identified the following chemistry issues that need to be addressed.

1. [redacted]



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Withheld Track Number: Administrative- 4

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/

Sally Loewke
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Signing for G. Mills

NDA REGULATORY FILING REVIEW
(Including Memo of Filing Meeting)

NDA # 21-870 Supplement # Efficacy Supplement Type SE-

Trade Name: N\A
Established Name: [F-18] Fludeoxyglucose Injection
Strengths: 20.0 - 200.0 mCi\mL

Applicant: North Shore\LIJ Health System
Agent for Applicant: Thomas Chaly, Ph.D.

Date of Application: November 5, 2004
Date of Receipt: November 19, 2004
Date clock started after UN: November 19, 2004
Date of Filing Meeting: January 5, 2005
Filing Date: January 18, 2005
Action Goal Date (optional): User Fee Goal Date: September 19, 2005

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

Type of Original NDA: (b)(1) ☐ (b)(2) ☒
OR
Type of Supplement: (b)(1) ☐ (b)(2) ☐

NOTE:

(1) If you have questions about whether the application is a 505(b)(1) or 505(b)(2) application, see Appendix A. 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), complete Appendix B.

(2) If the application is a supplement to an NDA, please indicate whether the NDA is a (b)(1) or a (b)(2) application:

☐ NDA is a (b)(1) application OR ☐ NDA is a (b)(2) application

Therapeutic Classification: S ☒ P ☐
Resubmission after withdrawal? ☐ Resubmission after refuse to file? ☐
Chemical Classification: (1,2,3 etc.) 5
Other (orphan, OTC, etc.)

Form 3397 (User Fee Cover Sheet) submitted: YES ☒ NO ☐

User Fee Status: Paid ☐ Exempt (orphan, government) ☐
Waived (e.g., small business, public health) ☒

NOTE: *If the NDA is a 505(b)(2) application, and the applicant did not pay a fee in reliance on the 505(b)(2) exemption (see box 7 on the User Fee Cover Sheet), confirm that a user fee is not required. The applicant is required to pay a user fee if: (1) the product described in the 505(b)(2) application is a new molecular entity or (2) the applicant claims a new indication for a use that that has not been approved under section 505(b). Examples of a new indication for a use include a new indication, a new dosing regime, a new patient population, and an Rx-to-OTC switch. The best way to determine if the applicant is claiming a new indication for a use is to compare the applicant's proposed labeling to labeling that has already been approved for the product described in the application. Highlight the differences between the proposed and approved labeling.*

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If you need assistance in determining if the applicant is claiming a new indication for a use, please contact the user fee staff.

- Is there any 5-year or 3-year exclusivity on this active moiety in an approved (b)(1) or (b)(2) application? YES ☐ NO ☒
  If yes, explain:

- Does another drug have orphan drug exclusivity for the same indication? YES ☐ 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)]? YES ☐ NO ☒

  If yes, consult the Director, Division of Regulatory Policy II, Office of Regulatory Policy (HFD-007).

- Is the application affected by the Application Integrity Policy (AIP)? YES ☐ NO ☒
  If yes, explain:

- If yes, has OC/DMPQ been notified of the submission? YES ☐ NO ☐

- Does the submission contain an accurate comprehensive index? YES ☒ NO ☐

- Was form 356h included with an authorized signature? YES ☒ NO ☐
  If foreign applicant, both the applicant and the U.S. agent must sign.

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

- If an electronic NDA, does it follow the Guidance? N/A ☒ YES ☐ NO ☐
  If an electronic NDA, all forms and certifications must be in paper and require a signature.
  Which parts of the application were submitted in electronic format?

  Additional comments:

- If an electronic NDA in Common Technical Document format, does it follow the CTD guidance? N/A ☒ YES ☐ NO ☐

- Is it an electronic CTD (eCTD)? N/A ☒ YES ☐ NO ☐
  If an electronic CTD, all forms and certifications must either be in paper and signed or be electronically signed.

  Additional comments:

- Patent information submitted on form FDA 3542a? YES ☒ NO ☐

- Exclusivity requested? YES, _____ Years 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 ☒ NO ☐
  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 ☒ NO ☐
  (Forms 3454 and 3455 must be included and must be signed by the APPLICANT, not an agent.)
  NOTE: *Financial disclosure is required for bioequivalence studies that are the basis for approval.*

- Field Copy Certification (that it is a true copy of the CMC technical section)? Y ☒ NO ☐

- PDUFA and Action Goal dates correct in COMIS? YES ☒ NO ☐
  If not, have the document room staff correct them immediately. These are the dates EES uses for calculating inspection dates.

- Drug name and applicant name correct in COMIS? If not, have the Document Room make the corrections. Ask the Doc Rm to add the established name to COMIS for the supporting IND if it is not already entered.

- List referenced IND numbers: N\A

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

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

Project Management

- Was electronic "Content of Labeling" submitted? YES ☐ NO ☒
  If no, request in 74-day letter.

- All labeling (PI, PPI, MedGuide, carton and immediate container labels) consulted to DDMAC?
  YES ☐ NO ☒

- Risk Management Plan consulted to ODS/IO? N/A ☒ YES ☐ NO ☐

- Trade name (plus PI and all labels and labeling) consulted to ODS/DMETS? Y ☐ NO ☒

- MedGuide and/or PPI (plus PI) consulted to ODS/DSRCS? N/A ☒ YES ☐ NO ☐

- If a drug with abuse potential, was an Abuse Liability Assessment, including a proposal for scheduling, submitted?
  N/A ☒ YES ☐ NO ☐

If Rx-to-OTC Switch application:

- OTC label comprehension studies, all OTC labeling, and current approved PI consulted to ODS/DSRCS? N/A ☐ YES ☐ NO ☐

- Has DOTCDP been notified of the OTC switch application? YES ☐ NO ☐

Clinical

- If a controlled substance, has a consult been sent to the Controlled Substance Staff? YES ☐ NO ☐

Chemistry

- Did applicant request categorical exclusion for environmental assessment? YES ☒ NO ☐
  If no, did applicant submit a complete environmental assessment? YES ☐ NO ☐
  If EA submitted, consulted to Florian Zielinski (HFD-357)? YES ☐ NO ☐
- Establishment Evaluation Request (EER) submitted to DMPQ? YES ☒ NO ☐
- If a parenteral product, consulted to Microbiology Team (HFD-805)? YES ☒ NO ☐

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ATTACHMENT

MEMO OF FILING MEETING

DATE: January 5, 2005

BACKGROUND: See FR Notice - March 10, 2000
(Provide a brief background of the drug, e.g., it is already approved and this NDA is for an extended-release formulation; whether another Division is involved; foreign marketing history; etc.)

ATTENDEES: Sally Loewke, M.D, Eldon Leutzinger, Ph.D., Eric Duffy, Ph.D., Milagros Salazar-Driver, Ph.D., James McVey, Ph.D., Patricia Stewart, Thuy Nguyen, M.P.H.

ASSIGNED REVIEWERS (including those not present at filing meeting) :

Discipline	**Reviewer**
Medical:	George Mills, M.D.\Ramesh Raman, M.D.
Secondary Medical:	N\A
Statistical:	N\A
Pharmacology:	N\A
Statistical Pharmacology:	N\A
Chemistry:	Milagros Salazar-Driver, Ph.D.
Environmental Assessment (if needed):	Milagros Salazar-Driver, Ph.D.
Biopharmaceutical:	N\A
Microbiology, sterility:	James McVey, 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 ☒ NO ☐
If no, explain:

CLINICAL FILE ☒ REFUSE TO FILE ☐

- Clinical site inspection needed? YES ☐ NO ☒
- Advisory Committee Meeting needed? YES, date if known _____ NO ☒
- 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 ☐ YES ☐ NO ☐

CLINICAL MICROBIOLOGY N/A ☒ FILE ☐ REFUSE TO FILE ☐

STATISTICS N/A ☒ FILE ☐ REFUSE TO FILE ☐

BIOPHARMACEUTICS FILE ☒ REFUSE TO FILE ☐

- Biopharm. inspection needed? YES ☐ NO ☐

PHARMACOLOGY	N/A ☒	FILE ☐	REFUSE TO FILE ☐
• GLP inspection needed?			YES ☐ NO ☐
CHEMISTRY		FILE ☒	REFUSE TO FILE ☐
• Establishment(s) ready for inspection?			YES ☒ NO ☐
• Microbiology			YES ☒ NO ☐

ELECTRONIC SUBMISSION:
Any comments: N\A for Clinical, Stat, P\T, and PK - See FR Notice - March 10, 2000.

REGULATORY CONCLUSIONS/DEFICIENCIES:
(Refer to 21 CFR 314.101(d) for filing requirements.)

☐ The application is unsuitable for filing. Explain why:

☒ 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.
- ☒ Filing issues to be communicated by Day 74. List (optional):

ACTION ITEMS:

1. ☐ If RTF, notify everybody who already received a consult request of 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. ☒ Convey document filing issues/no filing issues to applicant by Day 74.

See 74-Day Letter for filing issues conveyed to Sponsor.

Thuy Nguyen, M.P.H.
Regulatory Project Manager, HFD-160
January 5, 2005

Appendix A to NDA Regulatory Filing Review

An application is likely to be a 505(b)(2) application if:

(1) it relies on literature to meet any of the approval requirements (unless the applicant has a written right of reference to the underlying data)
(2) it relies on the Agency's previous approval of another sponsor's drug product (which may be evidenced by reference to publicly available FDA reviews, or labeling of another drug sponsor's drug product) to meet any of the approval requirements (unless the application includes a written right of reference to data in the other sponsor's NDA)
(3) it relies on what is "generally known" or "scientifically accepted" about a class of products to support the safety or effectiveness of the particular drug for which the applicant is seeking approval. (Note, however, that this does not mean *any* reference to general information or knowledge (e.g., about disease etiology, support for particular endpoints, methods of analysis) causes the application to be a 505(b)(2) application.)
(4) it seeks approval for a change from a product described in an OTC monograph and relies on the monograph to establish the safety or effectiveness of one or more aspects of the drug product for which approval is sought (see 21 CFR 330.11).

Products that may be likely to be described in a 505(b)(2) application include combination drug products (e.g., heart drug and diuretic (hydrochlorothiazide) combinations), OTC monograph deviations, new dosage forms, new indications, and new salts.

If you have questions about whether an application is a 505(b)(1) or 505(b)(2) application, please consult with the Director, Division of Regulatory Policy II, Office of Regulatory Policy (HFD-007).

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Appendix B to NDA Regulatory Filing Review
Questions for 505(b)(2) Applications

1. Does the application reference a listed drug (approved drug)? YES ☒ NO ☐

*If "**No**," skip to question 3.*

2. Name of listed drug(s) referenced by the applicant (if any) and NDA/ANDA #(s): [F-18] Fludeoxyglucose Injection; NDA 20-306 and NDA 21-768

3. The purpose of this and the questions below (questions 3 to 5) is to determine if there is an approved drug product that is equivalent or very similar to the product proposed for approval and that should be referenced as a listed drug in the pending application.

(a) Is there a pharmaceutical equivalent(s) to the product proposed in the 505(b)(2) application that is already approved?

YES ☐ NO ☒

(***Pharmaceutical equivalents*** are drug products in identical dosage forms that: **(1)** contain identical amounts of the identical active drug ingredient, i.e., the same salt or ester of the same therapeutic moiety, or, in the case of modified release dosage forms that require a reservoir or overage or such forms as prefilled syringes where residual volume may vary, that deliver identical amounts of the active drug ingredient over the identical dosing period; **(2)** do not necessarily contain the same inactive ingredients; **and** **(3)** meet the identical compendial or other applicable standard of identity, strength, quality, and purity, including potency and, where applicable, content uniformity, disintegration times, and/or dissolution rates. (21 CFR 320.1(c))

*If "**No**," skip to question 4. Otherwise, answer part (b).*

(b) Is the approved pharmaceutical equivalent(s) cited as the listed drug(s)? YES ☐ NO ☐
(The approved pharmaceutical equivalent(s) should be cited as the listed drug(s).)

*If "**Yes**," skip to question 6. Otherwise, answer part (c).*

(c) Have you conferred with the Director, Division of Regulatory Policy II, Office of Regulatory Policy (ORP) (HFD-007)? YES ☐ NO ☐

*If "**No**," please contact the Director, Division of Regulatory Policy II, ORP. Proceed to question 6.*

4. (a) Is there a pharmaceutical alternative(s) already approved? YES ☒ NO ☐

(***Pharmaceutical alternatives*** are drug products that contain the identical therapeutic moiety, or its precursor, but not necessarily in the same amount or dosage form or as the same salt or ester. Each such drug product individually meets either the identical or its own respective compendial or other applicable standard of identity, strength, quality, and purity, including potency and, where applicable, content uniformity, disintegration times and/or dissolution rates. (21 CFR 320.1(d)) Different dosage forms and strengths within a product line by a single manufacturer are thus pharmaceutical alternatives, as are extended-release products when compared with immediate- or standard-release formulations of the same active ingredient.)

*If "**No**," skip to question 5. Otherwise, answer part (b).*

(b) Is the approved pharmaceutical alternative(s) cited as the listed drug(s)? YES ☒ NO ☐
(The approved pharmaceutical alternative(s) should be cited as the listed drug(s).)

NOTE: *If there is more than one pharmaceutical alternative approved, consult the Director, Division of Regulatory Policy II, Office of Regulatory Policy (ORP) (HFD-007) to determine if the appropriate pharmaceutical alternatives are referenced.*

*If "**Yes**," skip to question 6. Otherwise, answer part (c).*

(c) Have you conferred with the Director, Division of Regulatory Policy II, ORP? YES ☐ NO ☐

*If "**No**," please contact the Director, Division of Regulatory Policy II, ORP. Proceed to question 6.*

5. (a) Is there an approved drug product that does not meet the definition of "pharmaceutical equivalent" or "pharmaceutical alternative," as provided in questions 3(a) and 4(a), above, but that is otherwise very similar to the proposed product?

YES ☐ NO ☐

*If "**No**," skip to question 6.*

*If "**Yes**," please describe how the approved drug product is similar to the proposed one and answer part (b) of this question. Please also contact the Director, Division of Regulatory Policy II, Office of Regulatory Policy (HFD-007), to further discuss.*

(b) Is the approved drug product cited as the listed drug? YES ☐ NO ☐

6. 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 and Strength. Same dosage and indications.

7. 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 (see 21 CFR 314.101(d)(9)). YES ☐ NO ☒

8. 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 21 CFR 314.101(d)(9)). YES ☐ NO ☒

9. 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 21 CFR 314.54(b)(2))? If yes, the application should be refused for filing under 21 CFR 314.101(d)(9). YES ☐ NO ☒

10. Are there certifications for each of the patents listed for the listed drug(s)? YES ☒ NO ☐

11. Which of the following patent certifications does the application contain? (Check all that apply and identify the patents to which each type of certification was made, as appropriate.)

☐ 21 CFR 314.50(i)(1)(i)(A)(1): The patent information has not been submitted to FDA. (Paragraph I certification)
Patent number(s):

☐ 21 CFR 314.50(i)(1)(i)(A)(2): The patent has expired. (Paragraph II certification)

Patent number(s):

☐ 21 CFR 314.50(i)(1)(i)(A)(3): The date on which the patent will expire. (Paragraph III certification)
Patent number(s):

☐ 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. (Paragraph IV certification)
Patent number(s):

NOTE: *IF FILED, and if the applicant made a "Paragraph IV" certification [21 CFR 314.50(i)(1)(i)(A)(4)], the applicant must* ***subsequently*** *submit a signed certification stating that the NDA holder and patent owner(s) were notified the NDA was filed [21 CFR 314.52(b)]. The applicant must also submit documentation showing that the NDA holder and patent owner(s) received the notification [21 CFR 314.52(e)].*

☒ 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 as described in the corresponding use code in the Orange Book. Applicant must provide a statement that the method of use patent does not claim any of the proposed indications. (Section viii statement)
Patent number(s):

☐ 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).
Patent number(s):

☐ Written statement from patent owner that it consents to an immediate effective date upon approval of the application.
Patent number(s):

12. Did the applicant:

- Identify which parts of the application rely on information (e.g. literature, prior approval of another sponsor's application) that the applicant does not own or to which the applicant does not have a right of reference?

  YES ☒ NO ☐

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

  YES ☒ NO ☐

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

  N/A ☒ YES ☐ NO ☐

- 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).?

  N/A ☒ YES ☐ NO ☐

13. If the (b)(2) applicant is requesting 3-year exclusivity, did the applicant submit the following information required by 21 CFR 314.50(j)(4):

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

  YES ☐ NO ☐

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

  YES ☐ NO ☐

- EITHER

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

  IND# _____ NO ☐

  OR

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

  YES ☐ NO ☐

14. Has the Associate Director for Regulatory Affairs, OND, been notified of the existence of the (b)(2) application?

YES ☒ NO ☐

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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
1/12/05 02:44:40 PM
CSO

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

FACSIMILE TRANSMITTAL SHEET

DATE: January 6, 2005

TO: DR. THOMAS CHALY Chief, Radiochemistry	**From:** Thuy Nguyen Regulatory Health Project Manager
Company: North Shore\LIJ Health System	Division of Division of Medical Imaging and Radiopharmaceutical Drug Products
Fax number: (516) 562-1041	**Fax number:** (301) 480-6036
Phone number: (516) 562-1042	**Phone number:** (301) 827-7510

Subject: NDA 21-870: [F-18] FDG

Total no. of pages including cover: 2

COMMENTS: **Please find attached general comments. Please provide an official response to the NDA (in triplicate) along with Form FDA 356(h) as soon as possible or by Monday, January 10, 2005 at 12:00 pm. Additional comments may be forthcoming. Thank you.**

THIS DOCUMENT IS INTENDED ONLY FOR THE USE OF THE PARTY TO WHOM IT IS ADDRESSED AND MAY CONTAIN INFORMATION THAT IS PRIVILEGED, CONFIDENTIAL, AND PROTECTED FROM DISCLOSURE UNDER APPLICABLE LAW.

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GENERAL COMMENTS TO THE SPONSOR

NDA 21-870: [F-18] FDG **January 6, 2005**

1. Please submit on diskette, in MS Word format:

   A) Your proposed, annotated labeling and labels for [F-18] Fludeoxyglucose Injection
   B) A clean version of your proposed labeling and labels for [F-18] Fludeoxyglucose Injection

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

FACSIMILE TRANSMITTAL SHEET

DATE: January 5, 2005

TO: DR. THOMAS CHALY Chief, Radiochemistry	**From:** Thuy Nguyen Regulatory Health Project Manager
Company: North Shore\LIJ Health System	Division of Division of Medical Imaging and Radiopharmaceutical Drug Products
Fax number: (516) 562-1041	**Fax number:** (301) 480-6036
Phone number: (516) 562-1042	**Phone number:** (301) 827-7510

Subject: NDA 21-870: [F-18] FDG

Total no. of pages including cover: 2

COMMENTS: Please find attached general comments. Please provide an official response to NDA 21-870 (in triplicate) along with Form FDA 356(h) as soon as possible or by Friday, January 7, 2005, at 10:00 am. Additional comments may be forthcoming. If you have any questions, please feel free to contact me. Thank you.

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GENERAL COMMENTS TO THE SPONSOR

NDA 21-870: [F-18] FDG **January 5, 2005**

1. Please confirm who is the NDA\Sponsor\Applicant holder of NDA 21-870: FDG – North Shore\LIJ Health System or yourself (T.Chaly, Ph.D.). If it is not yourself, then a **new** Form FDA 356(h) along with other statements will need to be submitted to reflect the correct NDA holder.

2. Please complete and submit the patent information – Form FDA 3542(a). [The form is available on-line at the FDA web site.]

3. Please complete and submit the financial disclosure information – Forms FDA 3454 & 3455. [The forms are available on-line at the FDA web site.]

4. Please complete and submit a **new** Form FDA 356 (h). Sign and date it as the original: 11\05\04. However, on the new Form FDA 356(h) in the **Cross References section,** please also reference the FR Notice – March 10, 2000, and the FDG approved NDA 20-306 and NDA 21-768.

5. Please complete and submit a **new** Prescription Drug User Fee Cover Sheet to reflect the correct reference made to the FR Notice – March 10, 2000, for Item #5, along with any written correspondences (such as a waiver letter) you may have received from the CDER User Fee Office.

6. In addition to your current Pediatric Assessment statement, please update and submit to include the following:

   The Safety and Effectiveness of Fludeoxyglucose F 18 Injection has not been established in the cardiac and oncology pediatric population. However, cardiac and oncology studies will be conducted in the pediatric population.

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

FACSIMILE TRANSMITTAL SHEET

DATE: December 21, 2004

TO: DR. THOMAS CHALY Chief, Radiochemistry	**From:** Thuy Nguyen Regulatory Health Project Manager
Company: North Shore University Hospital	Division of Division of Medical Imaging and Radiopharmaceutical Drug Products
Fax number: (516) 562-1041	**Fax number:** (301) 480-6036
Phone number: (516) 562-1042	**Phone number:** (301) 827-7510

Subject: NDA 21-870: [F-18] FDG

Total no. of pages including cover: 2

COMMENTS: Please find attached *CHEMISTRY* comments. Please provide an official response to the NDA (in triplicate) along with Form FDA 356(h) as soon as possible or by December 30, 2004. Thank you.

THIS DOCUMENT IS INTENDED ONLY FOR THE USE OF THE PARTY TO WHOM IT IS ADDRESSED AND MAY CONTAIN INFORMATION THAT IS PRIVILEGED, CONFIDENTIAL, AND PROTECTED FROM DISCLOSURE UNDER APPLICABLE LAW.

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CHEMISTRY COMMENTS TO THE SPONSOR

NDA 21-870: [F-18] FDG **December 21, 2004**

1. Please provide the manufacturing registration number. If you do not have one yet, please request one immediately from the FDA New York O.R. District Office and notify the Division of the registration number A.S.A.P.

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
1/4/05 12:27:00 PM
CSO

DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

PRESCRIPTION DRUG USER FEE COVER SHEET

Form Approved: OMB No. 0910-0297
Expiration Date: December 31, 2006.

See Instructions on Reverse Side Before Completing This Form

ompleted form must be signed and accompany each new drug or biologic product application and each new supplement. See exceptions on the rse 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 ...l be found on CDER's website: http://www.fda.gov/cder/pdufa/default.htm

1. APPLICANT'S NAME AND ADDRESS
North Shore/LIJ Research Institute
ATTN: Dr.Thomas Chaly
Cyclotron/Radiochemistry Facility
350 Community Drive
Manhasset, New York 11030

2. TELEPHONE NUMBER *(Include Area Code)*
(516) 562-1042

3. PRODUCT NAME
Fludeoxyglucose F 18 Injection

4. BLA SUBMISSION TRACKING NUMBER (STN) / NDA NUMBER
NDA 21-870

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:

See FR Notice March 10, 2000
(APPLICATION NO. CONTAINING THE DATA).

6. USER FEE I.D. NUMBER
N/A as per FD&C Section 505(b)(2)

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 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 FORTHIS APPLICATION?
N/A SEE FR NOTICE MARCH 10, 2000 ☒ YES ☐ NO
(See Item 8, reverse side if answered YES)

Public reporting burden for this collection of information is estimated to average 30 minutes per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing the collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden to:

Department of Health and Human Services
Food and Drug Administration
CBER, HFM-99
1401 Rockville Pike
Rockville, MD 20852-1448

and

Food and Drug Administration
CDER, HFD-94
12420 Parklawn Drive, Room 3046
Rockville, MD 20852

An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB control number.

...TURE OF AUTHORIZED COMPANY REPRESENTATIVE	TITLE	DATE
[signature]	Chief, Radiochemistry	11/5/2004

FORM FDA 3397 (12/03)

PSC Media Arts (301) 443-1090 EF

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

REQUEST FOR CONSULTATION

TO *(Division/Office)*:	FROM
,r. David Hussong, HFD-805 (via Pat Tuegel)	Thuy Nguyen, Project Manager, HFD-160

DATE:	IND NO.:	NDA NO.:	TYPE OF DOCUMENT:	DATE OF DOCUMENT:
Nov 24, 2004		21-870	New NDA	11\05\04

NAME OF DRUG:	PRIORITY CONSIDERATION:	CLASSIFICATION OF DRUG:	DESIRED COMPLETION DATE:
[F-18] FDG	Standard	5020600 (PET)	08\19\05

NAME OF SPONSOR: Thomas Chaly, Ph.D., North Shore\LIJ Health System

REASON FOR REQUEST

I. GENERAL

- NEW PROTOCOL
- PROGRESS REPORT
- NEW CORRESPONDENCE
- DRUG ADVERTISING
- ADVERSE REACTION REPORT
- MANUFACTURING CHANGE/ADDITION
- MEETING PLANNED BY
- PRE--NDA MEETING
- END OF PHASE II MEETING
- RESUBMISSION
- SAFETY/EFFICACY
- **PAPER NDA = X**
- CONTROL SUPPLEMENT
- RESPONSE TO DEFICIENCY LETTE
- FINAL PRINTED LABELING
- LABELING REVISION
- ORIGINAL NEW CORRESPONDENC
- FORMULATIVE REVIEW
- OTHER *(SPECIFY BELOW)*:

II. BIOMETRICS

STATISTICAL EVALUATION BRANCH	STATISTICAL APPLICATION BRANCH
• TYPE A OR B NDA REVIEW • END OF PHASE II MEETING • CONTROLLED STUDIES • PROTOCOL REVIEW OTHER:	• CHEMISTRY REVIEW • PHARMACOLOGY • BIOPHARMACEUTICS • OTHER:

III. BIOPHARMACEUTICS

- DISSOLUTION
- BIOAVAILABILTY STUDIES
- PHASE IV STUDIES
- DEFICIENCY LETTER RESPONSE
- PROTOCOL-BIOPHARMACEUTICS
- IN-VIVO WAIVER REQUEST

IV. DRUG EXPERIENCE

- PHASE IV SURVEILLANCE/EPIDEMIOLOGY PROTOCOL
- DRUG USE e.g. POPULATION EXPOSURE, ASSOCIATED DIAGNOSES
- CASE REPORTS OF SPECIFIC REACTIONS (List below)
- COMPARATIVE RISK ASSESSMENT ON GENERIC DRUG GROUP
- REVIEW OF MARKETING EXPERIENCE, DR AND SAFETY
- SUMMARY OF ADVERSE EXPERIENCE
- POISON RISK ANALYSIS

V. SCIENTIFIC INVESTIGATIONS

• CLINICAL	• PRECLINICAL

COMMENTS/SPECIAL INSTRUCTIONS:

- **Please check your email and Outlook calendar for upcoming meetings.**

SIGNATURE OF REQUESTER: T. Nguyen, 11/24/04	METHOD OF DELIVERY (Check one): HAND (1 vol total) & DFS
SIGNATURE OF RECEIVER:	SIGNATURE OF DELIVERER:

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
11/24/04 02:49:23 PM

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

FACSIMILE TRANSMITTAL SHEET

DATE: November 3, 2004

TO: DR. THOMAS CHALY Chief, Radiochemistry	**From:** Thuy Nguyen Regulatory Health Project Manager
Company: North Shore University Hospital	Division of Division of Medical Imaging and Radiopharmaceutical Drug Products
Fax number: (516) 562-1041	**Fax number:** (301) 480-6036
Phone number: (516) 562-1042	**Phone number:** (301) 827-7510

Subject: NDA 21-870: FDG F-18 Injection

Total no. of pages including cover: 2

COMMENTS: Please find attached the responses to your voice mail inquiry, 11\02\04, and to your facsimile of 11\03\04, regarding submission of an NDA. Thank you.

THIS DOCUMENT IS INTENDED ONLY FOR THE USE OF THE PARTY TO WHOM IT IS ADDRESSED AND MAY CONTAIN INFORMATION THAT IS PRIVILEGED, CONFIDENTIAL, AND PROTECTED FROM DISCLOSURE UNDER APPLICABLE LAW.

If you are not the addressee, or a person authorized to deliver this document to the addressee, you are hereby notified that any review, disclosure, dissemination, copying, or other action based on the content of this communication is not authorized. If you have received this document in error, please notify us immediately by telephone at (301) 827-7510. Thank you.

GENERAL COMMENTS TO THE SPONSOR

FDG **November 3, 2004**

1. If you wish to submit an NDA to the CDER - Division of Medical Imaging and Radiopharmaceutical Drug Products, HFD-160, please address the cover letter and submit 12 copies (1 original and 11 desk copies) of the initial NDA as follow to the following address:

   Dr. George Mills, M.D., M.B.A.
   FDA – Center for Drug Evaluation and Research
   Division of Medical Imaging and Radiopharmaceutical Drug Products, HFD-160
   ATTN: FDA - Central Document Room
   5901-B Ammendale Road
   Beltsville, MD 20705-1266

2. Once the NDA is received and processed by the FDA- Central Document Room (CDR), the Division will contact you with the assigned NDA #. Once you have been assigned an NDA #, all future correspondences should be addressed as follow and mailed to the following address:

   Dr. George Mills, M.D., M.B.A.
   FDA – Center for Drug Evaluation and Research
   Division of Medical Imaging and Radiopharmaceutical Drug Product
   ATTN: FDA - Document Room #8B-45
   5600 Fishers Lane, HFD-160
   Rockville, MD 20857

3. Regarding User Fee questions, please contact the User Fee Office: (301) 594-2041.

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
8/10/05 02:29:16 PM
CSO

DIVISION OF MEDICAL IMAGING AND RADIOPHARMACEUTICAL DRUG PRODUCT HFD-160

MEMORANDUM OF TELECONFERENCE

NDA #:	**21-870**
DRUG NAME:	**Fludeoxyglucose F 18 Injection**
DATE:	Thursday, September 30, 2004
SPONSOR:	Thomas Chaly, Ph.D., North Shore-Long Island Jewish Research Institute
TELEPHONE:	(561) 562-1042
BETWEEN:	Thomas Chaly, Ph.D.
AND:	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 Sponsor's correspondences of September 22 and 29, 2004, regarding a possible submission of a drug application.

- The Sponsor would like to submit a drug application with the same formulation, strength, dosage, and indications as the recently approved application for [F-18] Fludeoxyglucose Injection (FDG) of August 5, 2004. The Division suggested that the Sponsor review the recently approved FDG labeling to determine if the proposed drug product would be the same as the approved FDG. If so, the Sponsor should contact FDA – Office of Generic Drugs in regards to submitting an Abbreviated New Drug Application (ANDA) as well as reviewing the guidance document for an ANDA submission.

- The Division informed the Sponsor that if the proposed drug product has a different formulation, strength, dosage, or indications from the approved FDG then a New Drug Application (NDA) may need to be submitted. However, at this time it is best to confirm with OGD since the Sponsor's proposed drug product appears to be the same as the approved FDG. Should it be determined after the Sponsor has consulted with OGD that an NDA should be submitted (instead of an ANDA) then the Division will assist the Sponsor with the NDA process.

- In regards to the Sponsor's correspondence of September 29, 2004, Question #1, if the Sponsor submits an NDA, on the Form FDA 356(h), the Sponsor will only need to list the manufacturer's name and address, and include the actual establishment information in the NDA itself. Regarding Question #2, the original field copy certification should be sent to the field office and a copy should be included in the NDA submission. In regards to Questions # 3& 4, the number of copies of the NDA and mailing address will be determined later should the Sponsor decides to submit an NDA (instead of an ANDA).

ACTION ITEMS

1. The Division gave the Sponsor the contact information for OGD and the Sponsor will consult with OGD on whether or not to submit an ANDA, as appropriate.

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

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 21-870

Thomas Chaly, Ph.D.
North Shore/LIJ Health System
350 Community Drive
Manhasset, NY 11030

Dear Dr. Chaly:

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:	November 5, 2004
Date of Receipt:	November 19, 2004
NDA Reference Number:	NDA 21-870

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 January 19, 2005, in accordance with 21 CFR 314.101(a). If the application is filed, the user fee goal date will be September 19, 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:
Food and Drug Administration
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

NDA ACTION PACKAGE CHECKLIST

Application Information		
NDA: 21-870		
DRUG NAME: Fludeoxglucose F 18 Injection	**APPLICANT:** North Shore/LIJ Research Institute	
RPM: Thuy Nguyen, M.P.H.	**Division of Medical Imaging and Hematology Products**	**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 drugs referred to in 505(b)(2) application:** **NDA 20-306: FDG** **NDA 21-768: FDG**

❖ **Application Classifications:**	
• **Review priority**	**Standard**
• **Chem class (NDAs only)**	**5**
User Fee Goal Date	**September 19, 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**	**N\A**
• **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)*	**August 11, 2005**

General Information	
❖ **Actions**	
• **Proposed action**	**APPROVAL**
• **Previous actions (specify type and date for each action taken)**	**N\A**
• **Status of advertising (approvals only)**	**X - Materials requested in AP letter**
❖ **Public communications**	
• **Press Office notified of action (approval only)**	**N\A**
• **Indicate what types (if any) of information dissemination are anticipated**	() 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)*	**August 4, 2005**
• 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	**X - See CMC Review**
❖ **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 19, 2005**
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)*	**August 11, 2005**
❖ **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 – August 18, 2005**
❖ 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 – August 2, 2005**
❖ **Facilities inspection (provide EER report)**	**X - Acceptable** **Domestic: June 10, 2005** **Foreign: August 17, 2005**
❖ **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**