CENTER FOR DRUG EVALUATION AND RESEARCH

APPROVAL PACKAGE FOR:

APPLICATION NUMBER

NDA 21-768

Chemistry Review(s)

NDA 21-768

Fludeoxyglucose F 18 Injection

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

Ravindra K. Kasliwal, Ph.D.
DNDC-II, ONDC
Division of Medical Imaging and Radiopharmaceutical Drug Products

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Chemistry Review Data Sheet

1. NDA 21-768
2. REVIEW #: 1
3. REVIEW DATE: 15-Jul-2004, Revised 20-Jul-2004
4. REVIEWER: Ravindra K. Kasliwal, Ph.D.
5. PREVIOUS DOCUMENTS: None
6. SUBMISSION(S) BEING REVIEWED:

Submission(s) Reviewed	Document Date
Original	10-Mar-2002
Amendment (AC)	23-Mar-2003
Amendment (BC)	23-Mar-2003
Amendment (AI)	23-Mar-2004
Amendment (BI)	23-Mar-2004
Amendment (BZ)	25-May-2004
Amendment (BC)	25-May-2004
Amendment (BC)	13-Jul-2004
Amendment (BC)	15-Jul-2004

7. NAME & ADDRESS OF APPLICANT:

Name:	Weill Medical College of Cornell University
Address:	Citigroup Biomedical Imaging Center 516 East 72nd Street New York, NY 10021
Representative:	Barbara L. J. Pifel / Shankar Vallabhajosula
Telephone:	212-746-5883 / 212-746-5694 (SV)

8. DRUG PRODUCT NAME/CODE/TYPE:

a) Proprietary Name: None Proposed
b) Non-Proprietary Name (USAN): Fludeoxyglucose F 18 Injection
c) Code Name/# (ONDC only): None
d) Chem. Type/Submission Priority (ONDC only):

- Chem. Type: 3
- Submission Priority: S

9. LEGAL BASIS FOR SUBMISSION: 505 (b) (2); Listed Drug: NDA 20-306

10. PHARMACOL. CATEGORY: PET Drug (Radiopharmaceutical)

11. DOSAGE FORM: Injection

12. STRENGTH/POTENCY: 10-100 mCi/mL [@EOS]

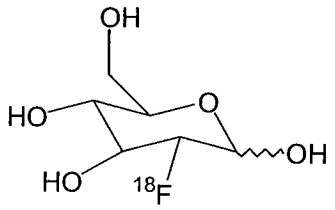
13. ROUTE OF ADMINISTRATION: Intravenous

14. Rx/OTC DISPENSED: _x_Rx ___OTC

15. SPOTS (SPECIAL PRODUCTS ON-LINE TRACKING SYSTEM):
_____SPOTS product – Form Completed

__x___Not a SPOTS product

16. CHEMICAL NAME, STRUCTURAL FORMULA, MOLECULAR FORMULA, MOLECULAR WEIGHT:



$C_6H_{11}{}^{18}FO_5$
Exact Mass: 181.06
Mol. Wt.: 181.15
C, 39.78; H, 6.12; F, 9.94; O, 44.16

2-Deoxy-2-[^{18}F]fluoro-D-glucose

17. RELATED/SUPPORTING DOCUMENTS:

A. DMFs:

DMF #	TYPE	HOLDER	ITEM REFERENCED	CODE[1]	STATUS[2]	DATE REVIEW COMPLETED	COMMENTS
[redacted]	II	[redacted]	[redacted]	1	Adequate	20-Jul-04	n/a
[redacted]	III	[redacted]	[redacted]	4	N/A	N/A	This stopper has been used previously in injectable products.

[1] Action codes for DMF Table:
1 – DMF Reviewed.
Other codes indicate why the DMF was not reviewed, as follows:
2 –Type 1 DMF
3 – Reviewed previously and no revision since last review
4 – Sufficient information in application
5 – Authority to reference not granted

6 – DMF not available
7 – Other (explain under "Comments")
[2] Adequate, Inadequate, or N/A (There is enough data in the application, therefore the DMF did not need to be reviewed)

B. Other Documents:

DOCUMENT	APPLICATION NUMBER	DESCRIPTION
Approved New Drug Application	N 20-306	This is an open application. The NDA applicant has in the past has given permission to the Agency to refer to this application whenever needed.

18. STATUS:

CONSULTS/ CMC RELATED REVIEWS	RECOMMENDATION	DATE	REVIEWER
Biometrics	Not applicable	n/a	n/a
EES	Acceptable	22-Jun-2004	Office of Compliance
Pharm/Tox	Not applicable	n/a	n/a
Biopharm	Not applicable	n/a	n/a
LNC	Not applicable	n/a	n/a
Methods Validation	Not applicable	n/a	n/a (USP methods used)
ODS	Not applicable – No trademark proposed.	n/a	n/a
EA	Claim for categorical exclusion acceptable	15-Jul-2004	Ravindra K. Kasliwal, Ph.D.
Microbiology	Approval	25-May-2004	Bryan S. Riley, Ph.D.

The Chemistry Review for NDA 21-768

The Executive Summary

I. Recommendations

A. Recommendation and Conclusion on Approvability

The application is recommended for approval action for manufacturing and controls under section 505 of the Act. Manufacturing facilities were inspected on June 15 and June 16, and have been determined to be in acceptable compliance with the currently applicable standards for PET drug products (i.e., USP chapter <823>).

B. Recommendation on Phase 4 (Post-Marketing) Commitments, Agreements, and/or Risk Management Steps, if Approvable

None

II. Summary of Chemistry Assessments

A. Description of the Drug Product(s) and Drug Substance(s)

The drug substance is 2-deoxy-2-[^{18}F] fluoro-D-glucose and is formed in situ during the production of the drug product. The drug product consists of a ready to use isotonic, sterile, pyrogen free, clear, colorless citrate buffered solution. Each mL contains between 0.37 to 3.7 GBq (10.0 – 100 mCi) of 2-deoxy-2-[^{18}F]fluoro-D glucose at the end of synthesis (EOS), 4.5 mg of sodium chloride and 7.2 mg of citrate ions. The pH of the solution is between 5.0 to 7.5. The solution is packaged in a multiple-dose glass vial and does not contain any preservative.

The active ingredient 2-deoxy-2-[^{18}F]fluoro-D-glucose, contains a radioactive atom F-18 which has a short [ ] physical decay half life. Since F-18 related radiation properties are necessary for the effectiveness of this product, the shelf life of the product is limited to 12 hours from the time it is produced.

B. Description of How the Drug Product is Intended to be Used

The finished drug product will be produced in a multiple dose vial, which is common practice for this class of drugs. Each batch consists of the product in a single multiple dose vial. The vial is generally sent to a Radio-pharmacy, where individual doses (5-10 mCi, as prescribed) are aseptically withdrawn from the vial as necessary. Immediately, after withdrawal the dose is assayed in a dose calibrator, the amount is recorded and the dose is administered intravenously to the patient. Subsequently the distribution of radioactive drug (through its emitted gamma radiation from the body) is imaged using a positron imaging

camera. The image information is used in the diagnosis as indicated below. The product is normally used in hospital setting (in this case Cornell Medical Center).

Fludeoxyglucose F 18 Injection is indicated 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. It is also indicated 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. Fludeoxyglucose F 18 Injection is indicated in positron emission tomography (PET) imaging in patients for the identification of regions of abnormal glucose metabolism associated with foci of epileptic seizures.

C. Basis for Approvability or Not-Approval Recommendation

The applicant has submitted data to sufficiently demonstrate control over the quality of the components used, the production process and the identity, strength, purity and quality of the finished drug product. The controls to assure quality of the finished drug product are adequate. The facilities have been inspected and have been found to be in acceptable compliance (EES on 22-Jun-2004) with the currently applicable standards for PET drug products (i.e., USP chapter <823>).

III. Administrative

A. Reviewer's Signature

Ravindra K. Kasliwal, Ph.D., **Signed 20-Jul-04**

B. Endorsement Block

ChemistName/Date: Kasliwal / 20-Jul-04
ChemistryTeamLeaderName/Date: Leutzinger/ see electronic review
ProjectManagerName/Date: Nguyen/see electronic review

C. CC Block

See electronic review.

26 Page(s) Withheld

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

___ § 552(b)(5) Deliberative Process

___ § 552(b)(4) Draft Labeling

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

/s/

Ravi Kasliwal
7/21/04 08:34:29 AM
CHEMIST

Eldon Leutzinger
7/21/04 08:49:23 AM
CHEMIST
I concur with the conclusions and recommendation.