Template

"Insert Your Institution Information Here"

[^{18}F]DCFBC: Master Batch Record

Batch No.: MBR-[^{18}F]DCFBC-_____ Manufacturing Date: _____(Expires 06 hr EOS)

Equipment Description	Internal Tracking Number/ Identification	Manufacturer	Verified By (Initials)
Microwave reactor		Biotage	
Prep HPLC system (Injector, Column, UV detector etc.)		Eckert & Ziegler	
Dose Calibrator (calibrated ion chamber)		Capintec Inc.	

GENERAL (Non-Inventoried per Batch) SUPPLIES	Verified By (Initials)
Appropriate Safety Wear including radiation badges, lab coat, safety glasses, shielding, gloves	
2 beakers. One for filter integrity test, one for clean up.	
Container for Solvent Waste, 500mL bottle	

Reagents / Compounded Solutions	Internal Tracking Number/ Identification	Quantity	Verified By (Initials)
DCFBC supplies kit	**Form-S-DCFBC___**	1	
[^{18}F]fluorobenzaldehyde Precursor	**SS-PRE_____**	10.0 mg	
Targeting ligand precursor	**SS-PEP_____**	0.6-1.0 mg	
Freshly prepared $NaBH_4$ solution	**SS-NABH-L_____**	~0.5 mL	
1.0 M TBAH solution	**SS-TBAH-L_____**	~ 0.2 mL	
48% HBr solution	**SS-HBr_____**	~2.0 mL	
Prep. HPLC mobile phase	**SS-PHOS30-L_____**	≥ 300 mL	

[^{18}F]DCFBC: DCFBC Injection Master Batch Record Version: **V1**
Effective Date:_____12/11/2013__ Supersedes:

Author:_____Date:__12/11/2013_____
Signature

Regulatory Approval:_____Date: _____ .
Signature

Procedure becomes effective on latest date of the two approval signatures above.
Procedure applies to [18F]DCFBC IND.

Setting up of preparative HPLC system

a) HPLC system power on. Computer on and Windows software initialized.
b) Add ≥ 300 mL of mobile phase (**PHOS30-L-)** to eluent bottle 1

Mobile Phase: volume added: _____ mL (≥ 300 mL)

c) Make certain that the Atlantis T3 prep C-18 HPLC column (**SS-Atlan**) is installed.
d) Run the method previously set for this purification. Check that the flow is steady.
e) Make sure the column is clean and there is no unusual UV absorption until 30 min.
f) Go to the software menu bar and select manual stop. Reset the program.

_____ initials.

Production area clearance and setup

a) Inspect the production area. Assure all extraneous materials and labels have been removed.
b) Verify materials, supplies and equipment required for synthesis are in place and properly organized.
c) Set the oil-bath temp. to 120 °C and turn on the stirring system.
d) Turn on the biotage microwave reactor.

_____initials

RADIOSYNTHESIS

1. Elute [^{18}F]fluoride from QMA cartridge to a microwave glass vial (Biotage) using K_2CO_3 (0.15 mL, **KCO2-L-**) and K222 (0.9 mL, **KRY-L-**) mixture.

_____ initials

2. Azeotropically dry the eluted solution at 120 °C on under vacuum and gentle flow of N_2 for 8 min.

3. Then transfer ~1 mL of acetonitrile 2 times to the reaction vial at 6 min of interval and continue the drying process until all solvent is evaporated.

_____ initials

4. Dissolve 10 mg of precursor with ~ 0.7 mL of ACN and transfer to the dried reaction vial.

_____ initials

5. Microwave the reaction mixture at 100 °C for 4 min.

_____initials

6. Transfer ~0.2 mL of $NaBH_4$ solution (**NABH-L-**) and stir the mixture for 5 min.
_____mL, _____ initials

7. Transfer ~ 2 mL of HBr (**SS-HBR**) to the vented reaction vial.
_____mL, _____ initials

8. Microwave the reaction mixture at 100 °C for 3 min.

9. Dilute the reaction mixture with 4-5 mL of water.

_____mL, _____ initials

10. Remotely pass the diluted reaction mixture through an activated C-18 Plus Sep-Pak (SS-PSP).

11. Wash the Sep-Pak with 5-10 mL of water (**SS-HGW**)..

    _____mL, _____ initials

12. Dry the Sep-Pak by gentle flow of N_2 for 3 min.

13. In a new reaction vial transfer ~ 0.6 mg of targeting ligand (**SS-PEP**) in ~ 0.2 mL of water.

    _____mg, _____ initials

14. Transfer ~ 0.15 mL of 1.0 M TBAH solution (**TBAH-L-**) to the new reaction vial.

    _____mL, _____ initials

15. Elute the trapped activity of C-18 Plus Sep-Pak to the new reaction vial using ~ 1.5 mL of acetonitrile.

    _____mL, _____ initials

16. Microwave the reaction mixture at 80 °C for 3 min.

17. Dilute the reaction mixture with 3-4 mL of water (**SS-HGW**).

    _____mL, _____ initials

PURIFICATION

18. Remotely transfer the diluted reaction mixture on to the prep HPLC column (**SS-Atlan**).

19. Elute the HPLC column at a flow rate of 4 mL/min. Observe the elution and collect fraction containing [18F]DCFBC based on the retention time (~ 11min) of the observed radiation peak.
    Collection time start_____min;
    Collection time end_____ min. _____initials

20. Dilute the collected product with 20 mL of water (**SS-HGW**).

21. Remotely pass the diluted product through a C-18 Light Sep-Pak (**SS-LSP**).

22. Wash the Sep-Pak with 5 mL of sterile water for injection (**SS-WFI**).

23. Dry the Light Sep-Pak with 5 mL of air.

STERILE FILTRATION AND FORMULATION

24. Connect the Light Sep-Pak cartridge with a 30 mL vented (**SS-VFN**) sterile vial (**SS-SBV**) through a 0.2 micron sterile filter (**SS-SPF**).

25. Elute the [^{18}F]DCFBC product from Light Sep-Pak to sterile vial using 1.0 mL of absolute ethanol (USP) followed by 14 mL of 0.9% saline (**SS-NSI**).

26. Detach the product vial from sterile filter and assay the product. Record the assay results with time.

    Activity_____mCi; Time_____am/pm; _____initials

27. Record the specific concentration of the product _____mCi/mL

28. Perform bubble point test of the sterile filter following standard procedure (**SAIC-Frederick-Q110**). Filter test result:_____psi _____initials

29. Aseptically draw ~ 400 µL of the product for QC tests

POST-SYNTHESIS CLEAN UP OF PREP HPLC SYSTEM

a) Replace the mobile phase bottle of the HPLC system by 70% absolute ethanol in water (≥ 300 mL) (**ETH70-L**).
b) Transfer ~ 4 mL 70% ethanol mobile phase to the injection vial of HPLC.
c) Run the HPLC system for 30 min at 4 mL/min flow rate.
d) Keep the HPLC system (injector and column) under 70% ethanol solution until next production day.

_____initials

Operator signature _____ Date

Performed By: _____ Date: _____ Checked By: _____Date:_____
Signature *Signature*

We certify that [^{18}F]DCFBC Production Batch **MBR-[18F]DCFBC-_____** was prepared according to the Manufacturing Instructions in the Manufacturing Production Record **MPR-[18F]DCFBC**. Any additional manufacturing modifications have been captured along with the appropriate control information as outlined in **SAIC-Frederick-M120**, "Documentation of Manufacturing Variances, and attached as appropriate.

_____ The QC release tests are complete and this batch of product has been preliminarily released according

to **Leidos-R011**, "QC Testing, Review, and Final Release for [^{18}F]DCFBC" for administration to human subjects. Final approval will be complete once the results of the Final product Sterility Testing have been met and reviewed as per **SAIC-Frederick-Q117A**.

_____ The QC release tests are complete and this batch of product will not be released, as it has failed to meet at least one or more of the specifications outlined in **Leidos-R011**, "QC Testing, Review, and Final Release for [18F]DCFBC," and the OOS investigation as per **SAIC-Frederick-Q015** could not rule out the possibility of product quality issues.

Date of Batch Completion: _____

Manufacturing Operator: _____ Date: _____
Signature

Manufacturing Manager: _____ Date: _____
Signature

Date Final Sterility Results Received: _____

Final Sterility Results: _____ Pass _____ Fail

Final Status of [18F]DCFBC Production Batch **MBR-[18F]DCFBC-_____:**

_____ Final approval and release has been granted.

_____ After careful review and consideration of the QC release testing and OOS investigation, this batch of product *cannot* be granted final approval and release; and therefore cannot be used for any further testing, if it passed all but the sterility tests previously. Notify all doctors of previously treated patients within 24 hours if the sterility test does not pass specification.

Manufacturing Manager: _____ Date: _____
Signature

QA/Regulatory Affairs: _____ Date:_____
Signature