		is provided in attachment _____, page_____.
6.	Is the target material recycled?	_____ Yes _____ No. If yes, its reprocessing procedures are described in attachment _____, page_____. Does the reprocessed material meet the acceptance criteria for the target material? ____ Yes _____No. [Note: If the recycled material does not meet the acceptance criteria for the target material, its use may not be acceptable]

We intend to use additional suppliers for this target material: _____Yes _____No.

If yes, for each additional supplier, the target material information specifically identified in items 1, 2, and 5 above is provided in attachment _____, page_____.

(ii) We will use the radioactive fluoride reagent, obtained from other sources, for the production of 2-deoxy-2[^{18}F]fluoro-D-glucose: _____Yes _____No.

If yes, provide the following information for each supplier of radioactive fluoride reagent:

1.	Name and composition of the fluoride reagent solution	
2.	Name and address of manufacturer	
3.	Method of preparation	☐ 1. The fluoride reagent is prepared using a ____MeV particle accelerator using $^{18}O(p, n)^{18}F$ reaction on $H_2{}^{18}O$. ☐ 2. The fluoride reagent is reactor produced. If fluoride is produced by methods described in 2, provide a description of the method of preparation, purification, and acceptance criteria that are appropriate for such production method. Information is provided in attachment _____, page_____.
4.	Test and acceptance criteria	TEST — PROCEDURE — ACCEPTANCE CRITERION Identity _____ _____ Purity _____ _____ Radioconcentration _____ _____ (if applicable) _____ _____ _____ Attachment _____, page _____.
5.	Provide procedure(s) used to	

	release each lot of the reagent for use in production	Attachment _____, page_____.
6.	Certificate of analysis	Copy of representative certificate of analysis is provided in attachment _____, page _____.

We intend to use additional suppliers for this fluoride reagent: _____Yes _____No.

If yes, for each additional supplier, the fluoride reagent information is provided in attachment _____, page_____.

C. OTHER INGREDIENTS

The following other ingredient(s) are used in the formulation of finished fludeoxyglucose F 18 injection.

Name	Purpose	Name and address of manufacturer	Specifications, representative COA and acceptance criteria for each lot
			Attachment ___, page ____.
			Attachment ___, page ____.

Note: COA need not be provided if ingredient is an approved drug product. If additional ingredients are used, they should be listed and information provided in attachment _____, page _____.

D. REAGENTS, SOLVENTS, GASES, PURIFICATION COLUMNS, AND OTHER AUXILIARY MATERIALS

Provide following information for each reagent, solvent, gas, purification column, and other auxiliary material that is used in the production of fludeoxyglucose F 18 injection:

	Name	Name and address of the supplier	Quality grade (e.g., ACS, USP, etc.) or specifications, representative COA and acceptance criteria for each lot
1			Attachment _____, page ____.
2			Attachment _____, page ____.
3			Attachment _____, page ____.

4			Attachment _____, page ____.
5			Attachment _____, page ____.
6			Attachment _____, page ____.
7			Attachment _____, page ____.

Note: Information on additional other ingredients is provided in attachment _____, page _____.

3. REFERENCE STANDARDS

The following reference standards are used in the quality control methods of fludeoxyglucose F18 injection:

[Note: Following are presented as an example. Reference standards appropriate for the synthesis should be included here. If a reference standard is obtained from USP, it should be so stated. If a reference standard is not obtained from USP, data to support that the reference standard lot has the desired structure must be submitted in the indicated attachment. Purity of the reference standard lot should be provided.]

	Name of reference standard	Name and address of the supplier	Specifications, representative COA and acceptance criteria for each lot
1	2-Fluoro-2-deoxy-D-glucose		Attachment __, page____
2	2-Chloro-2-deoxy-D-glucose		Attachment___, page____
3	Kryptofix, 222 (4,7,13,16,21,24-hexaoxa-1,10diazabicyclo[8.8.8]hexacosane)		Attachment___, page____

4. MANUFACTURING AND TESTING FACILITIES

Name of PET drug production facility: _____

Address: _____

Name of contact person: _____
Phone number of contact person: _____

Additional manufacturing and/or testing facilities (if any), including their function, are listed in attachment _____, page ____.

5. MANUFACTURE OF DRUG SUBSTANCE

A. BATCH FORMULA: The following components and their quantities are used in the production of each batch of 2-deoxy-2[^{18}F]fluoro-D-glucose:

Provide below the name of each component used in the production of 2-deoxy-2[^{18}F]fluoro-D-glucose, whether or not it appears in the final product; its function; and the amount (mass or volume) used in each batch (include all reactants, solutions, solvents, and reagents used in the chemical synthesis and purification operation).

Name of component	Component's function	Amount used
[Example: 1,3,4,6-Tetra-O-acetyl-2-O-trifluoro methanesulfonyl-□-D-mannopyranose]		_____ mg ± __mg
[^{18}F]Fluoride reagent		_____mCi to _____mCi

NOTE: Upon scale-up, only the mCi amount of radioactive [^{18}F]fluoride reagent is changed. The other components and their amounts remain as stated in the batch formula.

B. PRODUCTION OF RADIONUCLIDE

We will produce radioactive fluoride reagent only on site at the PET drug production facility?____Yes___No.

NOTE: If the radioactive fluoride reagent is obtained from outside sources, the following information (i, ii, & iii), and information for the recycling of the target material should be provided on the supplier's signed and dated letterhead.

(i) Particle Accelerator (e.g., cyclotron) Used

The following particle accelerator is used for the production of [^{18}F]fluoride radionuclide:

MAKE : _____
MODEL: _____

Information concerning additional particle accelerators is provided in attachment _____, page _____.

(ii) Operating Parameters

- During irradiation a beam current of _____ □A ± _____ □A is used.
- Irradiation times of _____ minutes to _____ minutes are used.
- We *use/do not use* high-pressure targets. When high-pressure targets are used, irradiations are performed under _____ *psi* pressure.

(iii) Specifications for Target Body

- Volume of the target _____ □l or ml.
- The target body used in our production operation is composed of _____.
- The target windows used in our targets are _____ (state thickness) and are composed of _____
- The schedule for the replacement of target windows is _____.
- The acceptance criteria for the target body and the target windows (that come in contact with target material) are provided in attachment _____, page _____.

If multiple target bodies of different types are used, the above information concerning each is provided in attachment _____, page _____.

C. SYNTHESIS AND PURIFICATION OF THE DRUG SUBSTANCE

(i) Description of Radiochemical Synthesis and Purification Equipment

Descriptions of the radiochemical synthesis and purification equipment, including components, their acceptance criteria, and a schematic flow diagram are provided in attachment _____, page _____.

We use the following synthesis and purification unit(s):

Make _____
Model _____

If more than one unit is used, and if units are different, provide information for each in attachment _____, page _____.

(ii) Description of Radiochemical Synthesis and Purification Operation

A step-wise description of the synthesis and purification procedure, including the amount of each reactant, reagent, solvent used, and acceptable radiochemical yields obtained, is provided in attachment _____, page _____.

(iii) In-Process Controls

All controls that are necessary to assure reproducible production of the stated drug should be

described. The following are examples of the in-process parameters that should be controlled in the synthesis and purification procedure:

- Drying of radioactive fluoride ions during the azeotropic evaporations.
  Number of azeotropic evaporations performed: _____.
  For evaporation, the vessel is heated between: _____°C to _____°C for _____minutes.

- Temperature and duration of reaction between radioactive fluoride ions and mannose triflate.

  The reaction vessel is heated between _____°C to _____°C for _____minutes.

- Temperature and duration of the hydrolysis reaction.
  The reaction vessel is heated between _____°C to _____°C for _____minutes.

- The amount of reactants, reagents, solvents, and solutions during each phase of synthesis and purification is controlled as described in master production and control records. _____ Yes.

- Flow rate of gas used for movement of materials within the synthesis and purification equipment.
  The flow rate used is _____.

- Total synthesis and purification time.
  The synthesis and purification operation takes a total of _____ minutes.

- Other parameters (provide any additional parameters that are controlled in your individual operation):
  Attachment _____, page _____.

  All in-process controls are monitored and documented in the master production and controls records:
  ___ Yes.

(iv) Post-Synthesis Procedures

Descriptions of procedures used to prepare the production equipment, including any cleaning and purging procedures, for a subsequent batch are provided in attachment _____, page _____.

6. MANUFACTURE OF DRUG PRODUCT

A. PRODUCTION OPERATION

The drug substance 2-deoxy-2[^{18}F]fluoro-D-glucose is not isolated. The synthesized, purified drug substance obtained from the synthesis and purification procedure is collected in the drug product vial. The specific procedures used in the formulation and preparation of our finished drug product are provided in attachment _____, page _____.

The master production and control records which provide the exact procedures used in the controlled production of and ensure full traceability of all components, materials, and equipment used for each batch of fludeoxyglucose F 18 injection, are provided in attachment _____, page _____.

B. REPROCESSING OF PET DRUG PRODUCT

☐ A manufactured PET drug product batch or lot will not be reprocessed.

☐ A manufactured PET drug product batch or lot may be reprocessed under the conditions (circumstances) specifically described in attachment _____, page _____.

The validated procedures (include SOP) used in reprocessing are described in attachment _____, page _____.

C. PACKAGING AND LABELING

The components used in the packaging of the drug product vial and the method of labeling are described in master production and control records on page _____ (attachment _____). The specifications and the acceptance criteria for the packaging component are provided in attachment _____, page _____.

7. CONTAINER/CLOSURE

- We use a presterilized, presealed, pyrogen-free container/closure, consisting of USP Type I glass, gray butyl rubber stopper, and aluminum crimp seal, from an established commercial supplier. _____Yes _____ No.

- If no, full information on the container/closure along with its sterilization procedures and sterility assurance is provided in attachment _____, page _____.

- If yes, the _____ ml container/closure, consisting of USP Type I glass, gray butyl stopper, and aluminum crimp seal, is obtained from the following manufacturer. The specifications and acceptance criteria for each lot of the container/closure are provided in attachment _____, page _____.

Container/Closure catalog # _____.
Name and address of supplier _____
_____
_____
Drug master file number _____

A letter of authorization from the DMF holder, authorizing FDA to refer to the DMF in connection with our application, is provided in attachment _____, page _____.

8. CONTROLS FOR THE FINISHED DOSAGE FORM

A. SAMPLING PROCEDURES

Each batch of fludeoxyglucose F 18 injection will be produced for distribution:
- In a single multidose vial _____.
- In multiple vials (single or multiple dose) _____.

(i) If each batch is produced in a single vial, a description of the amount of volume that is withdrawn from the finished drug product container and how it is distributed among individual tests is provided in attachment _____, page _____.

(ii) If each batch is produced in multiple vials, a description of sampling techniques that assure that the test sample is representative of the entire batch is provided in attachment _____, page _____.

B. REGULATORY SPECIFICATIONS, PROCEDURES, AND TESTING SCHEDULES

Each batch of the fludeoxyglucose F 18 injection will meet the following specifications during its entire shelf life when tested according to the standard test procedures (STPs) described in this application.

[Note: The following tests are related to a commonly used production method. In the event that the production method does not use a component listed below or uses an alternate method of production or produces additional impurities, appropriate tests, acceptance criteria, procedures, and a testing schedule that is more appropriate for such production should be proposed.]

TEST	ACCEPTANCE CRITERIA	PROCEDURES	TESTING SCHEDULE
Appearance	Colorless and free from particulate matter when observed visually behind leaded glass	Visual observation under adequate light STP#_____	Test completed prior to release of drug product
Radionuclidic identity	The measured half-life is between 105.0 – 115.0 minutes	Measurement of radioactivity decay of the sample over a 10 minutes STP#_____	Test completed prior to release of drug product
Radiochemical identity	The Rf of 2-deoxy-2[^{18}F]fluoro-D-glucose corresponds (+/-10%) to the Rf (about 0.4) of 2-deoxy-2-fluoro-D-glucose reference standard, when both are chromatographed together side by side on the same TLC	TLC, activated silica gel plate developed in 95:5 / acetonitrile : water (TLC scanned in a radio-chromatographic scanner) STP#_____	Test completed prior to release of drug product
Radionuclidic purity	State limit	Gamma spectroscopy of decayed sample STP#_____	State schedule
Radiochemical purity	NLT[1] 90.0% 2-deoxy-2[^{18}F]fluoro-D-glucose	TLC, activated silica gel plate developed in 95:5/ acetonitrile : water STP#_____	Test completed prior to release of drug product
Radiochemical	NMT[2] 4.0 % fluoride F 18	Provide procedure	Test completed

impurities	(free)	STP#	prior to release of drug product
Assay (radioactivity concentration)	____mCi to ____ mCi / mL @ EOS (This should be same as stated strength of drug product)	USP STP#_____	Test completed prior to release of drug product
Specific activity	No carrier added 2-deoxy-2[^{18}F]fluoro-D-glucose	None - prepared by no carrier method of synthesis	No testing performed
PH	Specify limits	pH paper with pH reference standards STP#_____	Test completed prior to release of drug product
Kryptofix 222 (if used in synthesis)	The size and intensity of the spot in test sample, that corresponds to the 50□g/ml kryptofix 222 reference standard spot, does not exceed that of the standard solution	TLC, comparison of drug product with 50□g / mL reference standard solution STP#_____	Test completed prior to release of drug product
Residual solvents[4] 1. Acetonitrile 2. Diethyl Ether 3. Ethanol	1. NMT[2] 0.04% (w/v) 2. NMT[2] 0.5% (w/v) 3. NMT[2] 0.5% (w/v)	Gas chromatography, flame ionization detection STP#_____	Test completed prior to release of drug product
2-Chloro-2-deoxy-D-glucose (if it is a possibility in synthesis)	NMT[2] 1.0 mg / V[3]	HPLC STP#_____	Validation and on annual batch thereafter
Membrane Filter Integrity	Specify limit for the filter being used	Bubble point measurement STP#_____	Test completed prior to release of drug product
Bacterial endotoxins (LAL)	NMT 175/V USP EU mL of the injection, in which V is the maximum recommended total dose in mL, at the expiration time	STP#_____	State schedule
Sterility testing	Sterile	STP#_____	Test initiated within 24 hours of preparation
Osmolality	Isotonic (specify range)	STP#_____	Validate /

			calculate
Glucose	NMT ___ mg/V[3]	No test performed	Calculated based on the amount of mannose triflate used

1. NLT = No Less Than
2. NMT = No More Than
3. *V* = Total volume of the batch of fludeoxyglucose F 18 injection produced
4. Acceptance criteria should assure that the amount of each residual solvent impurity administered to a human subject is within the limits provided in the ICH Guidance on Impurities: residual solvents (Federal Register dated December 24, 1997, Vol. 62, No. 247, Pages 67377 – 67388).

[Note: If a stabilizer is added, test for the assay of stabilizer should be included in the specifications]

9. DESCRIPTION OF ANALYTICAL TEST PROCEDURES

The relevant validated test procedures (STPs) for each test are provided as described below.

Note: Each procedure, at a minimum, should include the following: (1) the analytical supplies and their quality used; (2) all the equipment and the settings used during the performance of the procedure; (3) the preparation of test, standard, and analytical solutions; (4) detailed description of the test procedure; (5) exact calculations performed in quantitative procedures; (6) the recording of the results; and (7) the system suitability test performed (including schedule, the system suitability standards used, and the acceptance criteria to ensure proper performance of the equipment).

Test	STP document #	Attachment	Page number
Appearance			
Radionuclidic identity			
Radiochemical identity and purity			
Radinuclidic purity			
Assay (radioactivity concentration)			
PH			
Test for kryptofix 222			
Test for residual solvents			
2-Chloro-2-Deoxy-D-glucose			
Membrane filter integrity test			
Bacterial endotoxins (LAL)			
Sterility test			

Osmolality			

For chromatographic, spectroscopic (e.g., gamma), and microbiologic procedures, validation data to show suitability of the test procedure for the intended purpose are included in attachment _____, page _____.

10. MICROBIOLOGICAL VALIDATION

This part of the application describes the information you should include in Section 10 (microbiological validation) of your application for PET drug products. At the end of this section, there is a table of contents that you can use to list the information included in your application.

The microbiological validation section of the application should be used to describe the procedures that ensure sterility of injectable PET radiopharmaceuticals. Information common to other sections should be provided directly, and not by reference, to other sections because the microbiological validation attachment is reviewed separately from the chemistry section by microbiology reviewers. The introduction to this section should describe the product's container and closure system (size, shape, and composition), and the time and maximum volume of product solution that may be administered to a patient. Additionally, each of the following issues should be addressed in the microbiology section:

- Manufacturing Site. The manufacturing site (name and complete address) should be identified and accompanied by a description of the manufacturing area. The description should include the presence of environmental controls (e.g., laminar air flow hoods, biosafety cabinets, isolators) that protect product components from microbiological sources of contamination.

- Processing Equipment and Components. The methods for preparing equipment and components should be summarized in the submission. When sterile vials, syringes, transfer sets, and filters are obtained from commercial sources and used in the product's manufacture, a Certificate of Analysis from the suppliers may be substituted where appropriate. Reusable equipment that contacts the PET drug solution during its manufacture should be prepared to eliminate endotoxins and sanitized (or sterilized) to control bioburden. If components are sterilized at the PET facility, their sterilization processes and the components' aseptic assembly should be verified experimentally and summarized in application file. For sterilization done on-site, the performance of a sterilizer should be verified periodically and should be described, including a summary of the method and results from the last study. Drug products for parenteral administration must be sterile. PET solutions are usually filtered and aseptically transferred to a sterile, pyrogen-free container (for example, a multiple dose vial). Certain PET products may not use a vial for the finished dosage form, and these require special consideration. Some PET facilities may use a long fluid line to deliver multiple batches of the product solution to a remote area for further processing. These delivery lines should be described in the application, including their preparation and the validation of the duration of use. When special procedures and components are used, their impact on sterility assurance should be described.

- Facility Environmental Controls. A summary of the manufacturing process should address control systems in the work area used for preparing the finished dosage form. The work area should be clean, and the synthesis unit should be in a location that permits materials to be transferred to the aseptic area without adulteration. It is recommended that batch records indicate that sterile components, materials, and equipment are in protective wrapping or containers when transferred into the aseptic area. Also, it is recommended that final containers, filter assembly, sterile fluid lines, vent filters, and needles are sterile, disposable, and for single use only.

- The Aseptic Area. Many facilities have an aseptic area for the transfer of the sterile solution into a

sterile container for the finished product. As appropriate, the application should include descriptions of the aseptic hood, isolator, or other suitable environmental system area used when preparing the finished product. The air classification in the aseptic environment should be specified using standard nomenclature (e.g., ISO or US Fed. Std 209E). Microbiological testing of the aseptic environment should be done periodically, and the microbiological methods (sampling methods and frequency, culture media, incubation time and temperature) described. These methods may include swabs or contact plates for surfaces, and settle plates or dynamic air samplers. Airborne, non-viable particle counting should be summarized as part of the testing program, although these tests may be done less frequently than microbiological testing.

- Aseptic Technique. The qualification program for aseptic area operators should be summarized in the application. The aseptic techniques used to make a sterile product should be evaluated by process simulation studies. Simulations should be done 3 times to qualify a new operator. Each operator should repeat one simulation annually, or anytime changes occur in the procedures. Microbiological methods, acceptance criteria and results of these simulations (initial studies, or the last annual study) should be provided.

- Filtration Process Qualification. Sterilizing filtration is a critical procedure for removing microorganisms from solutions of injectable PET radiopharmaceuticals. When the filters are made and sterilized by a commercial filter manufacturer, the filtration conditions of pressure and flow rate are generally provided by the filter manufacturer. A certificate from the manufacturer is acceptable, but the filtration conditions such as pressure or volume should be identified in the batch record and not exceeded. Filter integrity tests to demonstrate that the membrane and housing have not lost the ability to retain microorganisms may be done according to the manufacturer's recommended method. An alternative filter integrity test method may be used if it is demonstrated to be acceptable. The batch record should indicate that after filtering the PET radiopharmaceutical, the sterilizing membrane filter is tested for integrity before the product is released. Filter integrity test methods and acceptance criteria should be described in the application.

- Finished Product Microbiological Testing. All products for parenteral administration, including PET radiopharmaceuticals, must be sterile and free of endotoxins (USP <1>, Injections). Sterility and endotoxin tests should be initiated promptly after preparing the product (21 CFR 211.167(a)). Test methods should be described (or provided by a reference) in the application. Details of the methods should include sampling method, sample sizes, microbiological methods, acceptance criteria and actions following a failure. The acceptance limit for endotoxins test results should also include the calculations that relate the patient dose to the endotoxins limit.

You can use the following as a table of contents for the information you include in Section 10 on microbiological validation.

Test or Criterion	Document(s)	Page Number(s)
Product Summary		
Container and Closure System		
Maximum Volume of Patient Dose		
Facility Description		
Sterile Equipment and Components		
Single Use	Certificate of Analysis	
Reusable	Sterilization Validation	
Environmental Controls		
Aseptic Area Environmental Monitoring		
Aseptic Process Simulation Methods and Results		
Sterile Filtration Process		
Microbial Retention Test or Certificate		
Pressure and Flow Rate Limits		
Filter Integrity Test Method		
Post-Use Integrity Test Limits		
Sterility Test Methods, Limits and Controls		
Actions if Test Fails		
Endotoxins Test Methods, Limits and Controls		
Determination of Endotoxins Limit		
Actions if Test Fails		

11. STABILITY AND BATCH DATA

A. EXPIRATION DATING PERIOD

We propose an expiration-dating period of _____ hours from the EOS calibration time when fludeoxyglucose F 18 injection is stored at _____°C +/- ____°C (or controlled room temperature). (Note: Refer to USP for controlled room temperature definition)

B. STABILITY DATA/BATCH DATA

If the submission is an NDA (under section 505 (b)(2) of the act), complete release and stability data on three batches of fludeoxyglucose F 18 injection prepared at the upper range of proposed radioconcentration and stored at _____°C +/- ____°C, are provided in attachment _____, page _____.

If the submission is an ANDA (under section 505(j) of the act), complete release data on three batches prepared at the upper range of proposed radioconcentration along with the stability data on one of the three batches of fludeoxyglucose F 18 injection prepared at the upper range of proposed radioconcentration and stored at _____°C +/- ____°C, are provided in attachment _____, page _____.

Additionally for each stability batch,

- The entire batch was stored in the same container/closure as it was produced._____Yes.
- The vial was stored in an inverted position._____Yes.
- All tests indicated in the specification section were performed at release._____Yes.
- The appearance, radiochemical purity, radionuclidic purity, and pH (and stabilizer concentration when present) were also evaluated at the end of proposed expiration dating period._____Yes.

[Note: If the application incorporates multiple manufacturing sites, please discuss with the reviewing division in advance of submitting the application concerning the stability and batch data that should be submitted. The phone number for the Division of Medical Imaging and Radiopharmaceutical Drug Products is (301) 827-7510.]

C. POSTAPPROVAL COMMITMENTS

We commit that; annually post-approval a minimum of one batch of fludeoxyglucose F 18 injection will be tested according to the protocol described below. The entire content of the batch vial will be stored inverted at _____ °C for _____ hours (from EOS), and tested according to the specifications and procedures described in this application for finished product testing. The results of such testing will be provided to the FDA in the annual report.

Test	Test performed at Release	Test performed at the end of expiry
Appearance	YES	YES
Radionuclidic Identity	YES	NO
Radiochemical identity and purity	YES	YES
Radiochemical impurities	YES	YES
Radionuclidic purity	YES	YES
Assay (radioconcentration)	YES	NO
PH	YES	YES
Test for kryptofix 222 (or other catalyst)	YES	NO
Test for residual solvents	YES	NO

2-Chloro-2-deoxy-D-glucose	YES	NO
Membrane filter integrity test	YES	NO
Bacterial endotoxins (LAL)	YES	NO
Sterility test	YES	NO
Osmolality	YES	NO

(Note: Include stabilizer at both time intervals, if present)

Additionally, we commit that any batch of fludeoxyglucose F 18 injection that fails to meet the acceptance criteria will not be released or, if already distributed, will be withdrawn from the market.

We also commit that FDA will be notified of any changes to the approved application, beyond the variations already provided for in the application, and that any such change will be implemented according to the requirements under section 506A of the Food and Drug Modernization Act and/or 21CFR 314.70 and 21 CFR 314.71 (for NDA) or under 21CFR 314.97 (for ANDA), as applicable.

12. VIAL AND OUTER PACKAGING LABELS

Draft copies of proposed vial and outer packaging labels are provided in attachment _____, page _____.

13. ENVIRONMENTAL ASSESSMENT

In accordance with 21 CFR 25.31(b), the (insert name of sponsor) claims a categorical exclusion from the environmental assessment requirements of 21 CFR 25.20 for approval of fludeoxyglucose F 18 injection on the basis that the estimated concentration of 2-deoxy-2[^{18}F]fluoro-D-glucose at the point of entry into the aquatic environment will be below 1 part per billion. Additionally, to (name of the sponsor)'s knowledge no extraordinary circumstances exist.

資料 6-3

[^{13}N]アンモニア注射液

化学、製造および管理の章

[^{13}N]アンモニア注射液

1. 薬剤の成分と定量的組成

成分	量/mL(濃度)	量/バッチ
薬剤成分 [^{13}N]アンモニア	_____ から_____mCi @EOS[1] (_____から_____MBq @EOS)	_____から_____mCi @EOS[1] (_____から_____MBq @EOS)
他の含有物[2] 1._____ (例 塩化ナトリウム注射液、USP)	_____ (例 1 mL)	_____mL

1. EOS = 合成終了時での測定値
2. 薬剤合成に使用する他のすべての原料を記述する。例として、希釈剤、緩衝剤、安定剤、防腐剤など。

2. 成分/原料の管理

A. ターゲット液(出発原料)

[^{13}N]アンモニアの製造のために、以下のターゲット液が使用される。

[注: ターゲットに複数の成分が使用される場合は、薬剤合成するために核反応を経たものすべてを含める。]

1	ターゲット液の名称	
2	ターゲット液の製造者の名称および住所	
3	試験および合格基準 [同定、純度、関連品質を管理する試験項目、方法および合格基準を設定しなければならない。	試験 合格基準 付録____、 ページ____
4	製造用の各ロットに実施される同定試験	試験 方法 合格基準 _____ _____ _____ STP(または SOP)は添付資料_____、ページ____に記述する。
5	分析証明書(COA) Certificate of Analysis	代表的供給者の COA のコピーを添付資料_____、ページ____に記述する。
6	ターゲット液を再利用するか。	____イエス____ノー。

		イエスならば、その再生方法を添付資料_____、ページ____に説明する。 再生水はターゲット液に対する合格基準を満たすか。____イエス、____ノー [注: 再生水がターゲット液に対する合格基準を満たさない場合、その使用は認められない。]

このターゲットは別のサプライアーも使用する予定である:_____イエス _____ノー

イエスならば、それぞれのサプライアーに関して、上記 1,2 および 5 項に示されるターゲット液の情報を添付資料_____、ページ_____ に記述する

B. その他の原料

[^{13}N]アンモニア注射液の製造には以下に示す原料が使用される

名称	目的	製造業者の名称と住所	各ロットに対する仕様、代表的分析証明書および合格基準
			添付資料____、ページ____
			添付資料____、ページ____

[注: 原料が承認済みの医薬製品である場合は分析証明書を提出する必要はない。他の原料を使用する場合は、それらをリストにし、その情報を添付資料_____、ページ____に記述しなければならない。]

C. 試薬、溶媒、ガス、精製カラム、およびその他の原料

[^{13}N]アンモニア注射液の製造に使用される各試薬、溶媒、ガス、精製カラムおよびその他の原料に関する情報を以下に記す。

名称		購入先の名称と住所	各ロットに関する品質等級(例: ACS, USP など)または仕様書、代表的分析証明書、および合格基準
1			添付資料____、ページ____

2			添付資料____、ページ____
3			添付資料____、ページ____
4			添付資料____、ページ____
5			添付資料____、ページ____

[注: 他の原料に関する情報を添付資料_____、ページ____に記述する。

3. 標準物質

[^{13}N]アンモニア注射液の品質管理方法には以下の標準物質が使用される。

[注: USP の標準物質を利用する場合、その旨を記載する。USP の標準物質を利用しない場合は、標準物質が正当な数値であることを裏付けるデータを指定の添付書類として提出しなければならない。 標準物質のロットの純度を記述しなければならない。]

標準物質の名称		供給先の名称と住所	各ロットに対する仕様、代表的分析証明書および合格基準
1	塩化アンモニウム		添付資料____、ページ____

4. 製造およびテスト設備

PET 薬剤製造設備名称: _____

住所: _____

_____

_____

連絡担当者氏名: _____

連絡担当者電話番号: _____

他の製造および試験設備とそれらの機能(該当する場合)を添付資料_____、____ページに記述する。

5. 医薬品物質の製造

A. バッチ処方

[^{13}N]アンモニアの各バッチの製造には、以下の原料とそれぞれの量が使用される。

[^{13}N]アンモニアの製造に使用される各原料の名称の下に、それが最終製品に存在するかどうか、その機能、および、各バッチに使用される量(質量または容量)(化学合成と精製過程

で使用されるすべての反応物質、溶液、溶媒、および試薬を含む)を記述する。

原料の名称	原料の機能	使用量

B. 放射性核種の生産

(i) 使用する加速器(たとえばサイクロトロン)

[^{13}N]アンモニアの生産には以下の加速器が使用される。

製造元: _____

型式 : _____

他の加速器に関する情報を添付資料_____、ページ____に記述する。

(ii) 運転パラメータ

- o __μA ±__μAのビーム電流で照射する。
- o ____分から____分間、照射する。(該当する場合、バッチまたはサブポーション用を識別する)。
- o 高圧ターゲットを使用する/使用しない。高圧ターゲットを使用する場合、____psiの圧力下で照射する。

(iii) ターゲット容器の仕様

- o ターゲットの容量は____μLまたはmL。
- o 生産運転に使用されるターゲット容器は、_____(材質)で構成されている。
- o ターゲットフォイルは_____(厚さを記入する)で、_____(材質)で構成されている。
- o ターゲットフォイルの交換頻度は_____。
- o ターゲット容器とターゲットフォイルの検査基準を添付資料_____、ページ____に記述する。

タイプの異なる複数のターゲット容器が使用される場合、各々に関する上記の情報を添付資料_____、ページ____に記述する。

C. 薬剤の合成および精製