Standard Operating Procedure

Form-Q112
Radionuclidic Identity of Zr-89 by Half-Life Determination

1. Purpose: To describe the quality control procedure for radionuclidic identity of radiopharmaceuticals by half-life determination.

2. Scope: Half-life determination is utilized for verifying the radionuclidic identity of the final product. This procedure will be performed at all of the contract sites manufacturing radiopharmaceuticals under [Insert your institution name here] IND. This quality control procedure is one of the lot release tests performed on the final product and it must be completed prior to releasing the lot for human administration.

3. Responsibilities
3.1. Sites: To follow this procedure as written and to ensure that all results, control information, and raw data are documented as specified in dedicated Quality Control Laboratory Notebooks and recorded on the appropriate testing forms.

4. References
4.1 USP 28 ‹821› Radioactivity
4.2 USP 28 ‹823› Radiopharmaceuticals For Positron EmissionTomography—Compounding
4.3 Form-Q015, "Investigating Out of Specification QC TestResults"
4.4 FDA Draft Guidance PET Drug Products—Current Good Manufacturing Practice (CGMP)—September 2005 (CDER)

5. Forms

- **Form FQC-###**, Corresponding "Final Product QC Test Results" Form

- **Form IOS-001**, "Investigating Out of Specification (OOS) QC Test Results Form"

6. Policies

6.1. Ensure that the radiation detector, used in this quality control procedure is in compliance with the local radioactive materials license regulations as specified for each laboratory.

6.2. Follow all safety precautions for handling radiolabeled samples.

6.3. Half-life of 89-Zr is 78.4 hours.

7. Materials and Equipment

7.1. Gamma Well Counter or Dose Calibrator

7.2. Timer (may be integral to the well counter)

8. Procedures

8.1. **Obtaining Measurements for the Gamma Counter**

8.1.1. Record the equipment number for the gamma counter used.

8.1.2. Prepare the sample by making a solution of 1 µL of the final product in 5 mL of water. Pipet 1 mL of the diluted final product solution into a counting tube.

8.1.3. Place the test sample in the gamma counter. Add an empty tube for counting background.

8.1.4. Count the test sample so that there are at least 10,000 counts in each count. Record the counts and the time the sample was counted using a 0.1 minute or better timing resolution.

8.1.5. Count the background tube for at least one minute.

8.1.6. Repeat step 8.1.4 approximately every four hours until at least three data points have been collected.

8.2 **Obtaining Measurements for the Dose Calibrator**

8.2.1. Record the equipment number for the dose calibrator.

8.2.2. Obtain the 2 mL sample prepared for the sterility test as specified in SOP Form -Q114 or Form-Q114A.

8.2.3. Zero adjust the dose calibrator according to the manufacturer's manual.

8.2.4. Place the sterility test sample in the dose calibrator.

8.2.5. Record the activity and the time the sample was counted.

8.2.6. Remove the sample for determination of background activity. Record the background activity.

8.2.7. Repeat steps 8.2.4 through 8.2.6 approximately every four hours, until at least three data points have been collected.

8.3. **Calculations**

8.3.1. Determine the half-life of the product at each activity measurement by doing an exponential fit to the data to determine the half-life. If software to do an exponential fit is not available, use the following equation to determine the half-life. Calculate these values for each measurement obtained:

$$T_{½} = \frac{\ln 2\,(t_x - t_{x-1})}{}$$

$$\mathbf{lnA_{(x-1)} - lnA_x}$$

Where $\mathbf{A_x}$ is the activity at a given time-point (other than time zero).
$\mathbf{A_{x-1}}$ is the activity (background subtracted) measured at the time count just previous to time x.
$\mathbf{t_x}$ is the time in hours at time x and
$\mathbf{t_{x-1}}$ is the time in hours at time x-1 and
$\mathbf{T_{½}}$ is the calculated half-life in units of hours

8.3.2. Average the calculated values determined for the half-lives. The value obtained should be between 75 – 80 hours

8.3.3. Record the final calculated half-life result on the Form **FQC-###**, corresponding "Final Product QC Test Results," Form.

8.3.4. If the product fails to meet the half-life criteria, do not release the product. Due to the possibility of normal statistical error or contamination causing the failure, re-run the half-life determination with a different aliquot of the same counting sample and count the sample three times over a period of at least 12 hours. If the second determination passes the half-life test, the batch may be released pending the results of the other quality control tests. If the second half-life determination fails, you must fail the product. In either case, you must conduct an investigation as per Form**-Q015**, "Investigating Out of Specification QC Test Results," and record the observations on **Form IOS-001**, "Investigating Out of Specification (OOS) QC Test Results Form."

DRAFT