Appendix VI Finished Drug Product Controls and Acceptance Standards

1. Medical institutions must establish the quality specifications and test methods for each PET drug product which are included in the Chinese Pharmacopoeia, the U.S. Pharmacopoeia or the European Pharmacopoeia, they should be subject to these compendial test procedures; And the quality control tests are given below:

1.1 For PET drug products with a half-life of greater than or equal to 25 minutes radionuclides, the following quality control tests should be performed on each batch of products in addition to the sterility test before release for administration:

1.1.1 The pH value.

1.1.2 Visual inspection for color and clarity.

1.1.3 The radiochemical identity and purity.

1.1.4 The radionuclidic identity and purity.

1.1.5 The specific activity.

1.1.6 Other toxic substances, residual solvents, radioactivity, bacterial endotoxins used or produced in the synthesis or purification processes.

1.1.7 Preservative or stabilizer, if present.

1.2 For PET drug products with a half-life of less than 25 minutes radionuclides, the following quality control tests should be performed on the first sub-batch of products in addition to the sterility test:

1.2.1 The pH value.

1.2.2 Visual inspection for color and clarity.

1.2.3 The radiochemical identity and purity.

1.2.4 The radionuclidic identity and purity.

1.2.5 The specific activity.

1.2.6 Other toxic substances, residual solvents, radioactivity,

bacterial endotoxins used or produced in the synthesis or purification processes.

1.2.7 Preservative or stabilizer, if present.

1.3 The PET drug products that are sterile filtered for injection should pass the bubble point test and other methods for each batch, and release after checking the integrity of the membrane filter; And the oxygen-15 water for injection can be released for human administration before completion of the filter integrity test, but the test should be completed as soon as possible.

2. The PET drug products for injection with a half-life of greater than or equal to 25 minutes radionuclides should be performed the sterility test on each batch, and that with a half-life of less than 25 minutes radionuclides should be performed the sterility test on the first sub-batch; And the provisions of sterility tests are as follow:

2.1 Sterility tests need not be completed before final release but must be started within 30 hours after completion of production. If the sample for sterility tests is held longer than 30 hours, medical institutions must demonstrate that the longer period does not adversely affect the sample and the test results obtained will be equivalent to test results that would have been obtained if the test had been started within the 30-hour time period.

2.2 Tested samples must be from individual batches and not pooled.

2.3 If the product fails to meet a criterion for sterility, medical institutions must immediately notify all facilities that received the product of the test results and provide any appropriate recommendations. The notification must be documented. Upon completion of an investigation into the failure to meet a criterion for sterility, medical institutions must notify all facilities that received the product of the findings from the

investigation.

3. For the test method that is an established compendial test procedure in paragraph 1. of this appendix, medical institutions must first verify its actual feasibility; And for other compendial test procedures, medical institutions must confirm, document and store the accuracy, sensitivity, specificity, and reproducibility of the procedure.

4. The provisions of the final release procedure are as follows:

4.1 General final release: medical institutions must establish and follow written procedures to ensure that each batch of a PET drug product is not given final release until the following are done:

4.1.1 Review associated laboratory data and documentation, and demonstrate that the PET drug product meets specifications, except for sterility to make appropriate judgments based on the test results.

4.1.2 A designated qualified individual authorizes final release by dated signature.

4.2 Conditional final release:

4.2.1 If medical institutions cannot complete one of the required finished-product tests for a PET drug product because of a malfunction involving analytical equipment, it may approve the conditional final release of the product if meeting the following conditions except for radiochemical identification, purity test or product specific activity examination:

4.2.1.1 Data document that preceding consecutive batches, produced using the same methods used for the conditionally released batch, and demonstrated that the conditionally released batch will likely meet the

established specifications.

4.2.1.2 All other acceptance criteria are met.

4.2.1.3 Retain a reserve sample of the conditionally released batch of drug product.

4.2.1.4 Promptly correct the malfunction of analytical equipment, complete the omitted test using the reserve sample after the malfunction is corrected, and document that reasonable efforts have been made to prevent recurrence of the malfunction.

4.2.1.5 When obtaining an out-of-specification result based on test results of the reserve sample, medical institutions should immediately notify the receiving facility.

4.2.1.6 Medical institutions should document all actions regarding the conditional final release of the drug product, including the justification for the release, all follow-up actions, results of completed testing, all notifications, and corrective actions to prevent recurrence of the malfunction involving analytical equipment.

4.2.2 Conditional final release is limited to one batch. Medical institutions may not release another batch of the PET drug product until correcting the problem concerning the malfunction of analytical equipment and completed the omitted finished-product test.

5. Nonconforming products must be rejected and proceeded in accordance with the following provisions:

5.1 Medical institutions must establish and follow written procedures to identify and segregate the PET drug product that does not conform to specifications to avoid mix-ups.

5.2 Medical institutions must establish and follow written procedures to investigate the causes of the nonconforming product, including examination of processes, operations, records, complaints, and any other relevant sources of information concerning the nonconforming product.

6. Medical institutions must document the investigation of a PET drug product that does not meet specifications, including the results of the investigation and what happened to the rejected PET drug product; And take action to correct any identified problems to prevent recurrence of any other quality problem.

7. If appropriate, medical institutions may reprocess a batch of a PET drug product that does not conform to specifications; And the reprocessing procedures must be established. The release procedures for reprocessed products are the same as those for non-reprocessed products.