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1.0 Purpose

This procedure describes how to study the effects of short-term storage or incubation of products at ambient temperature and 2 – 8°C, so as to mimic short-term storage conditions upon usage in the clinic. The product will be analyzed for stability by size exclusion chromatography (SEC-HPLC) over a period of time determined by the Project Scientist and Biopharmaceutical Quality Assurance (BQA). The modeling of extended (> 6 hours) clinical administration procedures and I.V. infusions will require a dedicated product administration stability and compatibility study protocol as determined by the Project Scientist and Quality Assurance (BQA).

2.0 Scope

This procedure applies to Process Analytics/Quality Control (PA/QC) personnel who perform this procedure.

3.0 Authority and Responsibility

3.1 The Director, PA/QC has the authority to define this procedure.

3.2 PA/QC is responsible for training laboratory personnel and documenting this training to BQA.

3.3 PA/QC personnel are responsible for the implementation of this procedure.

3.4 PA/QC is responsible for reviewing the data and documentation of the results of this procedure.

3.5 BQA is responsible for quality oversight of this procedure.

4.0 Materials and Equipment

4.1 Analytical HPLC system and peripherals (as described in ***SOP 22178 – Operation of the Agilent Technologies 1100 HPLC/1200 RRHPLC Using OpenLAB Chromatographic Data System (CDS) ChemStation Edition***).

4.2 Two (2) vials/containers of the product to be tested (container and volume requirements will be dependent upon the particular product and the length of the study, as determined by PA/QC personnel and/or the Project Scientist).

5.0 Procedure

5.1 Short-Term Stability at 2 - 8°C.

5.1.1 Prior to analysis, rapidly thaw one (1) of the two (2) vials of the product to be tested in an ambient temperature water bath with gentle agitation, then store at 2 - 8°C until analysis is started.

5.1.2 Remove a sample and analyze by HPLC (as per ***SOP 22178 – Operation of the Agilent Technologies 1100 HPLC/1200 RRHPLC Using OpenLAB Chromatographic Data System (CDS) ChemStation Edition***) and **SOP 22720 - *HPLC Technical Information Form*** (for product-specific method information). The first analysis will be identified as “Time=0 @ 2 - 8°C.” This is the control sample that all subsequent analyses will be compared to for determination of the product stability.

5.1.3 Place the remainder of the material at 2 - 8°C.

5.1.4 Repeat Steps 5.1.2 and 5.1.3 at one (1) to two (2) hour intervals for a minimum of six (6) hours during one (1) workday. Identify samples/analysis by time.

5.1.5 Repeat HPLC analysis daily until results fail specification or until the Project Scientist terminates the study.

5.2 Short-Term Stability at Ambient Temperature

5.2.1 Prior to analysis, rapidly thaw the second of the two (2) vials of the product to be tested in an ambient temperature water bath with gentle agitation, then store at 2° - 8°C until analysis is started.

5.2.2 Remove a sample and analyze by HPLC (as per ***SOP 22178 – Operation of the Agilent Technologies 1100 HPLC/1200 RRHPLC Using OpenLAB Chromatographic Data System (CDS) ChemStation Edition*** and **SOP 22720 - *HPLC Technical Information Form*** (for product-specific method information).

The first analysis will be identified as “Time=0 @ RT.” This is the control sample that all subsequent analyses will be compared to for determination of the product stability.

NOTE: “RT” = room temperature.

5.2.3 Place the remainder of the material at ambient temperature.

5.2.4 Repeat Steps 5.2.2 and 5.2.3 at one (1) to two (2) hour intervals for a minimum of six (6) hours during one (1) workday. Identify sample/analysis by time.

5.2.5 Repeat HPLC analysis daily until results fail specification or until the Project Scientist terminates the study.

NOTE: Some products manufactured at the Biopharmaceutical Development Program (BDP) are permanently stored at 2 - 8°C and need only be tested for short-term stability at ambient temperature; stability at 2 - 8°C will be determined by the testing performed as part of the long-term stability protocol for that particular product.

6.0 Interpretation of Results

6.1 Purity is reported as % Area (i.e., $\frac{\text{Product Peak Area}}{\text{Total Peak Area}} \times 100$) as printed on the Waters Chromatogram Report. The purity specification for each analysis will be the same as the release specification for that product, as specified on the approved Certificate of Analysis.

6.2 Product recovery is determined by comparing the product peak area at each time point with the control peak area (Time =0). This is obtained by dividing the product peak area in each analysis by the product peak area from the “Time = 0 @ x” analysis. Decreasing recovery is an indication of product aggregating to the point of precipitation.

6.3 Some products manufactured at the BDP are sensitive to both aggregation and degradation. Some observations of factors that attribute to this include:

6.3.1 Loss of peak height and/or area (e.g., loss of monomeric product, which could include an increase of dimer).

6.3.2 Loss of peak symmetry.

6.3.3 Presence of lower molecular weight peaks.

6.3.4 Increase in column back pressure (an indication of aggregation on the guard column or resin bed).

6.3.5 Increase in peak tailing (an indication of protein interaction with the resin; be aware that increased tailing can cause increased peak area).

7.0 Documentation

7.1 Document the results on the QC Test Request (Form 22001-01, if applicable) or in an issued laboratory notebook, and electronically on the designated computer.

7.2 Because of the large amount of data gathered from the study, a summary of the results of the study can be generated in a memorandum or spreadsheet format and attached to the QC form or lab notebook.

8.0 References and Related Documents

SOP *22178* **Operation of the Agilent Technologies 1100 HPLC/1200 RRHPLC Using OpenLAB Chromatographic Data System (CDS) ChemStation Edition**

SOP 22720 **HPLC Technical Information Form** (for product-specific method information)

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