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# PURPOSE

The purpose of this document is to describe the drug substance (DS) and drug product (DP) clinical manufacturing process – including unit operations with process inputs and outputs[PRODUCT NAME].

The manufacturing process outlined in this document has been designed to control the safety, identity, quality, purity, and strength of the [PRODUCT NAME] drug product.

# SCOPE

The manufacturing process as defined in this process description and control strategy document includes all unit operations from receipt of [starting material] at the manufacturing site to packaging and shipment of the formulated drug product. A summary of the raw materials and consumables used in the [PRODUCT NAME] process will not be included in this document. Refer to Attachment 1 for the complete Bill of Materials of the [PRODUCT NAME] manufacturing process.

Thaw and administration of the drug product at the clinical site are out of scope of this document. Additionally, analytical methods are referenced but method details and qualification are out of scope.

The [PRODUCT NAME] vector manufacturing process and control strategy is out of scope.

# DEFINITIONS/ACRONYMS

| TERMS | DEFINITIONS |
| --- | --- |
| APH | Leukapheresis |
| BSC | Biosafety Cabinet |
| CDP | Cryopreserved Drug Product |
| CS10 | CryoStor® CS10 |
| CRF | Controlled Rate Freezer |
| FDP | Formulated Drug Product |
| HMI | Human Machine Interface |
| IPC | In Process Control, confirms process performance within experience |
| NOR | Normal Operating Range |
| nCPP | Non-Critical Process Parameter. Parameter controlled in the process, but with none or unknown impact to critical quality attributes of the drug product |
| PBS | Phosphate-Buffered Saline |
| PCP | Process Control Point |
| pCPP | Preliminary Critical Process Parameter. Parameter known to have impact on one or more critical quality attributes of the drug product |
| PLT | Platelet |
| PM | Process Measurement, generates continued process understanding, may be part of characterization / monitoring |
| Production Duration | Hold Time (defined storage condition), Processing Time (between two production steps, limits to ensure consistent process performance), Unit Operation Time (duration of end-to-end unit operation) |
| TVC | Total Viable Cell Count |
| VCC | Viable Cell Concentration |
| WBC | White Blood Cells |

# PROCESS DESCRIPTION

# Introduction

The manufacturing process is outlined in Figure 1.

Process introduction—starting material collection/shipment, transport to facility, high-level overview of process and key critical reagents/consumables/formulations.

Refer to Process Development History Report for process development history and data supporting the process design and ranges presented in this document.

**Table 1: [PRODUCT NAME] Dosing and Scale**

| **Dose Level** | **# of Expansion Vessels** | **In-Process Control** |
| --- | --- | --- |
|  |  | (per vessel) |

# Critical Parameter Summary

The preliminary CPPs, In Process Controls (IPCs), and Critical Durations for the process are summarized below in Table 2.

**Table 2: Summary of pCPPs, IPCs, and Key Process Durations**

| **Parameter** | **Classification** | **Target** | **Range** |
| --- | --- | --- | --- |
|  | pCPP |  |  |
| **In-Process Control** | | **Target** | |
|  | |  | |
| **Critical Durations/Hold Times** | | **Target** | **Range** |
|  | |  |  |

a Footnotes for clarifications/supporting documents for lot specific ranges

# Process Flow Diagram

Refer to **Figure 1** for an overview of the manufacturing process.

**Figure 1: Process Flow Diagram with Unit Operation Descriptions**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Day |  | Description | |  | Testing |
|  |  |  |  |  |  |
| Intermediate |  | **Unit Operation**  Key operations, temperatures, hold times, formulations/ volumes, process equipment | |  | * In-process samples/FIO |
|  |  |  |  |  |  |
| Day |  | **Description** | |  | **Testing** |
|  |  |  |  |  |  |
| Drug Substance |  | **Unit Operation**  Key operations, temperatures, hold times, formulations/ volumes, process equipment | |  | In-Process testing:   * Samples/FIO   Release testing:   * Safety testing |
|  |  |  |  |  |  |
| Drug Product |  | **Unit Operation**  Key operations, temperatures, hold times, formulations/ volumes, process equipment | |  | Release testing (container format):   * Safety testing * Potency * Purity * Identity * Characterization |

# Process Day (X of X)

…Description of unit operation…

…Process parameters for unit op are included in Table 5, process outputs are included in Table 6, and buffer and solution compositions are outlined in Table 7.

**Table 5: Process Parameters**

| **Parameter** | **Classification** | **Target/Set Point** | **Range** |
| --- | --- | --- | --- |
|  | pCPP/nCPP |  |  |
| **In-Process Controls** | | **Target/Set Point** | **Range** |
|  | |  |  |
| **Critical Duration/Hold Times** | | **Target/Set Point** | **Range** |
| Stability/Exposure times | |  |  |

**Table 6: Process Outputs**

| **Process Durations** | **Target** | **Range** |
| --- | --- | --- |
| Volumes/total cells |  |  |
| **Process Measurements** | **Expected Range** | |
| Yields/viability |  | |

**Table 7: Buffers and Solutions**

| **Solution Name** | **Composition** | | **Purpose** |
| --- | --- | --- | --- |
| **Component** | **Quantity** |
| Buffer | A | mL | Buffer exchange, concentration, and dilution |
| B | mL |

# DP Specification

The DP specification for [PRODUCT NAME] inclusive of product information and release testing requirements are outlined in…

An example sample plan for [PRODUCT NAME] is attached…

# DP Batch Formula

The DP Batch Formula is outlined in Table 28.

**Table 28: [PRODUCT NAME] Drug Product Batch Formula Table**

|  |  |  |
| --- | --- | --- |
| **Component** | **Amount per DP Batch** | |
| **Dose Level 1**  **(# of expansion vessels)** | **Dose Level 2 and 3**  **(# of expansion vessels)** |
|  | **# of DP containers** | **# of DP containers \*** |
| A | List NOR | List NOR |

\*specify fill volume(s), capacity and any constraints

# DP Composition

The composition of [PRODUCT NAME] DP is shown in Table 29 and outlines the composition of each bag produced per batch.

**Table 29: Composition of [PRODUCT NAME] Drug Product**

| **Component** | **Amount in Final Container** | **Function** | **Grade** |
| --- | --- | --- | --- |
| A | Up to X total viable cells; specify minimum threshold |  | cGMP/USP |

# DP Excipients

The [PRODUCT NAME] DP excipients are listed in Table 30. These excipients are commonly used in... The excipients have been evaluated as part of process development...

**Table 30:** **[PRODUCT NAME] Drug Product Excipients**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Excipient** | **Composition** | **Function** | **Grade/Reference** | **Certificate of Analysis** |
| A | % |  | cGMP/USP | Attachment # |

# EQUIPMENT

# Process Equipment

A summary of the primary equipment used to manufacture [PRODUCT NAME] drug product is listed in Table 31 with suitable models based on process requirements.

Process specific programs are listed, where applicable, in the descriptions below.

**Table 31: [PRODUCT NAME] Equipment List**

| **Equipment Name** | **Manufacturer / Model** |
| --- | --- |
|  |  |

# Equipment Programs

The equipment programs used for the manufacture of [PRODUCT NAME] are listed in Table 33 below.

**Table 33: Equipment Programs**

| **Equipment Description** | **Program Name** | **Description** |
| --- | --- | --- |
| CRF | [PRODUCT NAME] Freeze Profile | Controlled freeze profile for bags and vials |

# ATTACHMENTS

| ATTACHMENT # | TITLE |
| --- | --- |
| Attachment 1 | Bill of Materials |
| Attachment 2 | [PRODUCT NAME] Sampling Plan |
| Attachment 3 | Certificate of Analysis of Drug Product Excipients |

# REFERENCES

| DOCUMENT ID | TITLE |
| --- | --- |
| 1 | [PRODUCT NAME] Change requests |
| 2 | [PRODUCT NAME] MOI Memo |
| 3 | [PRODUCT NAME] Intermediate Stability Report |
| 4 | [PRODUCT NAME] Method Development Report |
| 5 | [PRODUCT NAME] Non-Clinical Material Generation Report |
| 6 | [PRODUCT NAME] Process Development History Report |
| 7 | [PRODUCT NAME] Drug Product Specification |

# PROCESS VERSION

| **Change Classification** | **Changes Included** | **Versioning** | **Version #** |
| --- | --- | --- | --- |
| Minor | * Extending intermediate expiry * Batch record clarifications/updates * Process change with no major impact on process flow, product composition, critical consumable or reagent impact (i.e. updating number of DS filters | None | 1.0 |
| Major – no new platform element | * Updating wash program to remove additional impurities * Adding DS filter * Adding media exchange step * Updating parameter targets/ranges | Minor | 1.1 |
| Major – new platform element | * New process equipment * New expansion platform (static vs. dynamic) * New cell culture media * Sequential vs. combined processing of product intermediates * Adding in-process cryopreservation step * Changing DP container | Major | 2.0 |

# VERSION HISTORY

| VERSION NO. | DESCRIPTION OF CHANGES |
| --- | --- |
| 1 | Initial version |