Commercial Manufacturing

To: REP-49438

From: Kristie Taber

Date: February 12, 2024

Subject: Document Clinical Operations Approval of REP-49438

1. PURPOSE

The purpose of this document Clinical Operations approval of REP-49438 routed in GVault for approval.

•

Doc. Status Approved Document No. MEMO-16025
Approved Date 12 Feb 2024 GVault Ver. No. 1.0
Date Printed 29 Sep 2025 Legacy Doc. No.

External Quality Operations

GILEAD Creating Possible	TITLE	DOCUMENT NUMBER	VERSION	PAGE
	Risk Assessment to Mitigate the Introduction of Intrinsic, Extrinsic, and the Formation of Inherent Particulate Matter in Magrolimab at the Clinical Site	REP-49438	1.0	1 of 29

Table of Contents

Clinical Operations Approval

Name	Signature	Date
Tyler Prater	DocuSigned by Tyler Prater Tyler Prater I approve this document February 12, 2024 | 3:19:57 PM PST 198B3D4C50A64F12B068D3CBFD0ABBBD	February 12, 2024 | 3:21:03 PM PS

1. Executive Summary

The risk assessments to mitigate the risks associated with the introduction of intrinsic, extrinsic and the formation of inherent particulate matter in magrolimab were performed for the following clinical studies:

Pharmacy Manual for:	Revision #	Approval Date
GS-US-546-5920	6.0	22-Aug-2023
GS-US-558-5915	6.0	22-Aug-2023
GS-US-590-6154	6.1	02-Nov-2023
GS-US-586-6144	8.0	24-Jul-2023

As requested in IE-00229, a risk assessment was required for administration of magrolimab for the presence of visible particulate matter found in drug product vials and IV bag.

Magrolimab drug product is a sterile, clear, preservative-free solution for intravenous (IV) administration. The drug product is supplied at a concentration of approximately 20 mg/mL in single-use 10R Type I clear glass vials, stoppered with an elastomeric stopper and sealed with an aluminum flip-off overseal. Each 10R vial contains sufficient volume to allow withdrawal of 10 mL sterile solution containing 200 mg of magrolimab (20 mg/mL). Magrolimab is formulated in 6.5 mM sodium acetate trihydrate, 3.5 mM glacial acetic acid, 5% (w/v) sorbitol, and 0.01% (w/v) polysorbate 20 at pH 5.0. The route of magrolimab administration is intravenous through an administration line which contains a polyethersulfone (PES) in-line filter at the point of delivery to the patient that may reduce the risk of adverse events. The use of an in-line filter started being implemented in January 2023.

This report documents the approach that the Gilead Sciences Inc. (GSI) cross-functional team representatives (Foster City, Oceanside and New Jersey) employed to identify and prioritize risk areas and implement subsequent actions. The outcome of the risk assessment concluded that clinical site administration controls had no high-risk processes and nineteen (19) medium risk were identified which could potentially contribute to the introduction of particulates (introduction of extrinsic and formation of inherent). Actions identified in Section 6 – Mitigation Plan will reduce the potential introduction / formation.

2. Revision History

Revision	Description of Change	Justification
1.0	New document	New document

3. Scope

The risk assessment focused on magrolimab, which includes – but not limited to:

- Drug product (DP) at clinic and DP introduced to the IV bag at the clinical site
- Receiving and storage of drug product at the clinical site
- Drug product preparation, IV bag preparation by pharmacist, formulation (magrolimab) in diluted IV bag
- Dosage concentration in IV Bag

Out of scope:

- Manufacturing Processes (DS, DP, Clinical Labeling, Storage prior to arriving at clinical site and Distribution)
- Analytical testing, stability testing
- Accuracy of the dosage calculation in IV Bag

4. Methodology

A cross functional team utilized the Failure Modes and Effects Analysis (FMEA) per SOP-05362, *Quality and Compliance Risk Management*, to assess the risk factors which potentially contribute to the introduction of intrinsic and extrinsic particulate matter in magrolimab and the risks associated with the formation of inherent particulate matter in magrolimab at the clinical facility. The following questions were asked related to the process steps to determine the ranking:

Questions:

- What are the risks associated with the introduction of intrinsic and extrinsic particulate matter to magrolimab at the Clinical Site that may impact product quality and/or patient safety?

- What are the risks associated with the formation of inherent particulate matter to magrolimab at the Clinical Site that may impact product quality and/or patient safety?

Major Process Steps:

- Receipt and Storage of magrolimab DP at the Clinical Site
  - Receipt of Clinical Material at the Clinical Site
  - Storage at the Clinical Site
- Preparation of Drug-Infusion Solution
- Transport of Drug Product Vial Between Clinical Facilities
- Transportation of Prepared Magrolimab Infusion Bags

Risk Assessment Team Members		
Area	**Name**	**Title**
Team Lead/Facilitator	Kristie Taber	Sr Director, Quality
Facilitator	Joseph Rogers	Sr Manager, Quality Systems
Quality Assurance Representative	Jeff Hoinowski	Sr Director, External QA Biologics Development
	Maria del Rocio Bende	Sr Manager, External QA Biologics Dev
	Alma Kelley	Manager, Quality Assurance
R&D Quality	Tracy Tucker	Assoc Director, R&D Quality
Clinical Operations	Kyla Ramey	Clinical Program Manager
Technical Representative	Yajie Zhang	Sr Research Scientist I, FPD
	Marco Rodriquez	Sr Supply Chain Specialist
	Brandy Searcy	Sr Associate Scientist, FPD

Risk Analysis

The cross functional team discussed the potential failure modes, the cause of failures, and the effect of the failures within each of the process steps for magrolimab. The cross functional team then discussed the contamination control mechanisms for each of the identified failure modes.

During risk identification of processing steps, the table below was used to help score the **Severity** level of the failure modes:

Score	Category	Severity Description per SOP-05362	Severity Description to consider during magrolimab administration at the Clinical Site
1	Low	Failure has no impact on patient health, system, product quality or regulatory compliance.	Minor compliance deviations with no quality impact
3		Failure unlikely to impact patient health or product quality. Failure could result in minor system problems and disruptions, potential nonconformance with internal quality standards and procedures.	Results in minor loss of effect or requires minor medical attention; results in customer nuisance/ dissatisfaction; minor GMP deviations with no or marginal quality impact. Impacted product may require rework
5	Medium	Failure could result in minor injury to patient. Failure could result in moderate	Major loss of effect or otherwise results in customer complaint. Potential for a percentage of product (<50%) to be

Score	Category	Severity Description per SOP-05362	Severity Description to consider during magrolimab administration at the Clinical Site
		system disruptions, may impact product quality; may result in major deviations from internal GMP procedures or failure to meet regulatory requirements.	scrapped
7		Failure could result in moderate injury to patient. Loss of product efficacy or product quality leading to adverse events Failure could result in drug shortage or stock out. Failure could result in major system/process and disruptions with impact to critical parameters; and/or requiring notification of the event to health authorities or a product recall. Failure may lead to high levels of variability in the quality of the material supplied leading to loss of efficacy or material being unusable	A temporary or medically-reversible event or major loss of effect with a high degree of customer dissatisfaction; potential to destroy product; leads to stability failures, render distributed product nonconforming or adulterated or unavailable; may endanger operator but warnings in place; stock out of product or risk to patient supply but alternative drug available.
10	High	Failure could result in serious adverse events. Significant loss of efficacy or product quality. Failure could result in total system/process breakdown or extensive system disruptions; potentially leading to regulatory action by health authorities. Failure may lead to complete supply disruption with no alternate suppliers creating medicinal shortages / lack of availability	Death or major/permanent injury or disability to customer; complete loss of effect /system or process failure leading to shut down of manufacturing; may endanger operator without warning; revoked marketing authorization; stock out or risk to patient supply with no alternative drug available.

Occurrence and **Detectability** scoring was based on the risk assessment SOP, SOP-05362. In addition, occurrence will take into account Gilead's experience from similar clinical studies and sites and the potential for those issues to occur at these facilities. Based on the risk scoring criteria established per SOP-05362, the team analyzed each of the scores (Severity, Occurrence, Detectability) and calculated the Risk Priority Number (RPN) for each failure mode.

Risk Analysis

The team then computed the risk scores for each of the quality risks and based on the outcome of those risks, the team gave their suggestion, when possible, to control the medium and high risks.

Risk Priority Number (RPN)	RPN scale	Risk Priority Level Description
0-49	Low Risk	The potential failure has a low risk of particulate matter that would result in harm to patients The risk is at an acceptable level where no further mitigation or analysis is needed
50-300	Medium Risk	The potential failure could possibly have an adverse effect of particulate matter that would result in harm to patients. The risk needs to be evaluated and prioritized whether a mitigation plan is needed to further reduce the risk to as low as reasonably practical (ALARP) and/or increase detection/controls.
301-1000	High Risk	The potential failure poses an immediate threat to the continuity of the process and adversely affects the quality of the product and could result in harm to the patients. The risk is considered an intolerable level which would require mitigations and a CAPA plan. These risks are to be transferred into the Risk Registry.

Risk Identification and Assessment

The number of risks with the magrolimab drug product/dose preparation at the clinical site can be summarized in the table below:

	Number of Risks Identified for each RA session[1]					
Risk Type	Receipt and Storage of Magrolimab at the Clinical Facility	Transport of Drug Product Vial Between Clinical Facilities	Preparation of Drug-Infusion Solution	Transportation of Prepared Magrolimab Infusion Bags	Sub-Totals	TOTAL
High: Requires Risk Control Action	0	0	0	0	0	58
Medium	15	6	34	2	57	
Low: Acceptable	1	0	0	0	1	

[1]The number and type of risks identified are the same for all four (4) clinical study risk assessments: GS-US-546-5920, GS-US-558-5915, GS-US-590-6154, and GS-US-586-6144.

Details of the risk assessments, along with the initial risk ratings, assigned score weights and final risk rankings for the identified materials are listed in Appendix 1. All four (4) clinical studies (GS-US-546-5920, GS-US-558-5915, GS-US-590-6154, and GS-US-586-6144) have the same instructions in the pharmacy manual and therefore only one risk assessment was executed on clinical study GS-US-586-6144 to represent the process for all studies.

4.1. Risk Assessment Conclusion

The final evaluation concluded that there is no high risk of potential introduction of intrinsic, extrinsic, or formation of inherent particulate matter in magrolimab drug product, dose preparation and transportation.

Of the fifty-seven (57) contributing areas of potential impact to the potential introduction of intrinsic, extrinsic, and the formation of inherent particulate matter in Magrolimab that were rated as medium, nineteen (19) had an RPN of 100 to 300. Refer to Section 6 for the mitigation plans for these nineteen (19) medium areas of potential impact.

The remaining thirty-eight (38) areas of potential impact that were rated as medium were discussed with the team members and identified from the risk assessments to have sufficient clinical site administration controls in place to be deemed as risks that are currently as low as reasonably practicable (ALARP).

The one (1) remaining area of potential impact was low and the risk is at an acceptable level where no further mitigation or analysis is needed.

5. Mitigation Plan

Based on the conclusion of the risk assessment, mitigating action is not required. However, as a precaution, mitigating actions to medium-risk areas were identified to further lower the risk of potential introduction of intrinsic, extrinsic, and the formation of inherent particulate matter in magrolimab.

The nineteen (19) medium risks and their corresponding mitigating plans are listed below:

#	PID[1]	Cause of Failure	Mitigation Plan	Target Implementation	CAPA Number	Anticipated Risk Rating Post-Implementation
1	23	Low concentration of surfactant in drug-infusion solution.	**Action Item:** Allowance of 100 mL infusion bag for the preparation of low concentration drug infusion solution.	28Feb 2024	QE-183389	Low
2	24	Low concentration of surfactant in drug-infusion solution.	**Action Item:** Allowance of 100 mL infusion bag for the preparation of low concentration drug infusion solution.	28Feb 2024	QE-183389	Low
3	27	Multiple vials required resulting in multiple instances of septum being punctured by needle.	**Action Item:** Update to *Pharmacy Manual*[2] to instruct to use new needle on each drug product vial.	28Feb 2024	QE-183389	Low
4	28	Multiple introductions of drug product into the same infusion bag required.	**Action Item:** Update to *Pharmacy Manual*[2] to instruct to use new needle on each drug product vial.	28Feb 2024	QE-183389	Low
5	29	Dulling of syringe needle as a result of multiple septum puncture instances.	**Action Item:** Update to *Pharmacy Manual*[2] to instruct to use new needle on each drug product vial.	28Feb 2024	QE-183389	Low
6	34	Pharmacy adds lowest volume of drug product to infusion bag first during multiple vial addition preparation for high dose preparation	**Action Item:** Update to *Pharmacy Manual*[2] to instruct the large volume additions.	30May2024	QE-183695	Low
7	35	Pharmacy adds lowest volume of drug product to infusion bag first during multiple vial addition preparation for high dose preparation	**Action Item:** Update to *Pharmacy Manual*[2] to instruct the large volume additions.	30May2024	QE-183695	Low

External Quality Operations

#	PID[1]	Cause of Failure	Mitigation Plan	Target Implementation	CAPA Number	Anticipated Risk Rating Post-Implementation
8	40	Vial is not allowed to equilibrate to room temperature prior to preparation of drug-infusion solution.	**Action Item:** Update to *Pharmacy Manual*[2] to instruct on drug product vial equilibration to room temperature before preparation of drug infusion solution.	28Feb 2024	QE-183389	Low
9	41	Vial is not allowed to equilibrate to room temperature prior to preparation of drug-infusion solution.	**Action Item:** Update to *Pharmacy Manual*[2] to instruct on drug product vial equilibration to room temperature before preparation of drug infusion solution.	28Feb 2024	QE-183389	Low
10	43	Particulate Matter present in the empty bag prior to dose preparation.	**Action Item:** Update to *Pharmacy Manual*[2] for the preparation and instruct on inspection of empty bag prior to preparation of drug infusion solution.	28Feb 2024	QE-183389	Low
11	44	Alcohol swab debris present on drug product septum introduced to drug infusion solution.	**Action Item:** Update to *Pharmacy Manual*[2] to instruct on ensuring no debris present on septum after cleaning with an alcohol wipe.	28Feb 2024	QE-183389	Low
12	45	Alcohol present on stopper from cleaning septum introduced into drug product vial.	**Action Item:** Update to *Pharmacy Manual*[2] to ensure alcohol is dried prior to puncturing the vial septum with the needle.	28Feb 2024	QE-183389	Low
13	46	Alcohol present on stopper from cleaning septum introduced into drug product vial.	**Action Item:** Update to *Pharmacy Manual*[2] to ensure alcohol is dried prior to puncturing the vial septum with the needle.	28Feb 2024	QE-183389	Low
14	53	Drug infusion mixture stored beyond allowable timeframe beyond recommended storage condition.	**Action Item:** Update to *Pharmacy Manual*[2] to perform visual inspection on drug infusion solution immediately prior to administration to patient.	28Feb 2024	QE-183389	Low
15	54	Drug infusion mixture stored beyond allowable timeframe beyond recommended storage condition.	**Action Item:** Update to *Pharmacy Manual*[2] to perform visual inspection on drug infusion solution immediately prior to administration to patient.	28Feb 2024	QE-183389	Low
16	55	Drug infusion mixture was not allowed to equilibrate for long enough.	**Action Item:** Update to *Pharmacy Manual*[2] to perform visual inspection on drug infusion solution immediately prior to administration to patient. **Action Item:** Update to *Pharmacy Manual*[2] to ensure time out of temperature range is documented.	28Feb 2024	QE-183389	Low

#	PID[1]	Cause of Failure	Mitigation Plan	Target Implementation	CAPA Number	Anticipated Risk Rating Post-Implementation
17	56	Drug infusion mixture was not allowed to equilibrate for long enough.	**Action Item:** Update to *Pharmacy Manual*[2] to perform visual inspection on drug infusion solution immediately prior to administration to patient. **Action Item:** Update to *Pharmacy Manual*[2] to ensure time out of temperature range is documented.	28Feb 2024	QE-183389	Low
18	57	Drug infusion solution not stored at recommended temperature of 2–8 °C during transport between clinical facilities.	**Action Item:** Update to *Pharmacy Manual*[2] to perform visual inspection on drug infusion solution immediately prior to administration to patient.	28Feb 2024	QE-183389	Low
19	58	Drug infusion solution not stored at recommended temperature of 2–8 °C during transport between clinical facilities.	**Action Item:** Update to *Pharmacy Manual*[2] to perform visual inspection on drug infusion solution immediately prior to administration to patient.	28Feb 2024	QE-183389	Low

[1]Process ID

[2]Update to the *Pharmacy Manual* applies to all four (4) clinical studies, respectively: GS-US-546-5920, GS-US-558-5915, GS-US-590-6154, and GS-US-586-6144.

6. Risk Review/Maintenance Plan

Consistent with FDA recommendation listed in the guidance of the Risk Management Plans (RMP), GSI will conduct a risk review of the potential of the introduction of intrinsic, extrinsic, and the formation of inherent particulate matter in Magrolimab biennially (every two years). A revision to this document will be performed upon completion of the biennial review. The revision will include the latest update and progress of mitigating actions, changes to the ratings of risk factors, and any new identified risks.

7. Appendix 1 – FMEA Risk Assessment for GS-US-586-6144

PID	Process Step	Failure Mode	Effect of Failure	Rationale for S	Severity (S)	Cause of Failure	Controls	Rationale for O	Occurrence (O)	Monitoring Plan	Rationale for D	Detectability (D)	RPN	Comments / Action Items
Ref # 1.0	**Receipt and Storage of Magrolimab at the Clinical Facility**													
Ref # 1.1	**Receipt of Clinical Material at Clinical Facility**													
1	Drug product arrives at the clinical facility and is sent to pharmacy.	Drug product subjected to elevated temperatures above recommended storage conditions of 2–8 °C	Formation of particulate matter (protein) in drug product. Particulate matter introduced to patient intravenously resulting in serious adverse event.	Per SOP-05362 *Quality and Compliance Risk Management* (v 5.0) Table 1: Severity Rating Scale: Introduction of particulate matter to patient intravenously may result in serious adverse events resulting in severity rating	**10**	Drug product left at receiving area for extended duration and storage temperature not maintained.	Drug product is packaged in a pre-qualified shipping container to maintain storage conditions. Drug product secondary packaging labeling states the required storage condition. Per GS-US-586-6144 *Pharmacy Manual* (v 8.0) Section 4.3, Drug Product is to be stored at 2–8 °C.	Per SOP-05362 *Quality and Compliance Risk Management* (v 5.0) Table 2: Probability of Occurrence Rating Scale: Effective routine manual process interventions and/or preventative controls are in place through procedural and labeling controls.	**3**	Per GS-US-586-6144 *Pharmacy Manual* (v 8.0) the drug product is packaged and shipped with temperature monitoring devices (Temptales). Temperature monitoring device data is reviewed by the Clinical site and excursions are reported to Gilead Sciences upon discovery.	Per SOP-05362 *Quality and Compliance Risk Management* (v 5.0) Table 3: Probability of Detection Rating Scale: There is a manual inspection of the failure and there is a high probability that the failure will be detected within the step.	**3**	**90**	Risk is acceptable as is and no additional actions will be taken. There are currently effective controls and detection mechanisms in place to reduce the risk at the clinical facility.
2			Formation of particulate matter (protein) in drug product. Reduction of drug efficacy.	Per SOP-05362 *Quality and Compliance Risk Management* (v 5.0) Table 1: Severity Rating Scale: Loss of product efficacy or product quality leading to adverse events.	**7**	Drug product left at receiving area for extended duration and storage temperature not maintained.	Drug product is packaged in a pre-qualified shipping container to maintain storage conditions. Drug product secondary packaging labeling states the required storage condition. Per GS-US-586-6144 *Pharmacy Manual* (v 8.0) Section 4.3, Drug Product is to be stored at 2–8 °C.	Per SOP-05362 *Quality and Compliance Risk Management* (v 5.0) Table 2: Probability of Occurrence Rating Scale: Effective routine manual process interventions and/or preventative controls are in place through procedural and labeling controls.	**3**	Per S-US-586-6144 *Pharmacy Manual* (v 8.0) the drug product is packaged and shipped with temperature monitoring devices (Temptales). Temperature monitoring device data is reviewed by the Clinical site and excursions are reported to Gilead Sciences upon discovery.	Per SOP-05362 *Quality and Compliance Risk Management* (v 5.0) Table 3: Probability of Detection Rating Scale: There is a manual inspection of the failure and there is a high probability that the failure will be detected within the step.	**3**	**63**	Risk is acceptable as is and no additional actions will be taken. There are currently effective controls and detection mechanisms in place to reduce the risk at the clinical facility.
3		Drug product subjected to decreased temperatures below recommended storage conditions of 2–8 °C	Formation of particulate matter (protein) in drug product. Particulate matter introduced to patient intravenously resulting in serious adverse event.	Per SOP-05362 *Quality and Compliance Risk Management* (v 5.0) Table 1: Severity Rating Scale: Introduction of particulate matter to patient intravenously may result in serious adverse events resulting in severity rating	**10**	Drug product left at receiving area for extended duration and storage temperature not maintained.	Drug product is packaged in a pre-qualified shipping container to maintain storage conditions. Drug product secondary packaging labeling states the required storage condition. Per GS-US-586-6144 *Pharmacy Manual* (v 8.0) Section 4.3, Drug Product is to be stored at 2–8 °C.	Per SOP-05362 *Quality and Compliance Risk Management* (v 5.0) Table 2: Probability of Occurrence Rating Scale: Effective routine manual process interventions and/or preventative controls are in place through procedural and labeling controls.	**3**	Per GS-US-586-6144 *Pharmacy Manual* (v 8.0) the drug product is packaged and shipped with temperature monitoring devices (Temptales). Temperature monitoring device data is reviewed by the Clinical site and excursions are reported to Gilead Sciences upon discovery.	Per SOP-05362 *Quality and Compliance Risk Management* (v 5.0) Table 3: Probability of Detection Rating Scale: There is a manual inspection of the failure and there is a high probability that the failure will be detected within the step.	**3**	**90**	Risk is acceptable as is and no additional actions will be taken. There are currently effective controls and detection mechanisms in place to reduce the risk at the clinical facility.
4			Formation of particulate matter (protein) in drug product. Reduction of drug efficacy.	Per SOP-05362 *Quality and Compliance Risk Management* (v 5.0) Table 1: Severity Rating Scale: Loss of product efficacy or product quality leading to adverse events.	**7**	Drug product left at receiving area for extended duration and storage temperature not maintained.	Drug product is packaged in a pre-qualified shipping container to maintain storage conditions. Drug product secondary packaging labeling states the required storage condition. Per GS-US-586-6144 *Pharmacy Manual* (v 8.0) Section 4.3, Drug Product is to be stored at 2–8 °C.	Per SOP-05362 *Quality and Compliance Risk Management* (v 5.0) Table 2: Probability of Occurrence Rating Scale: Effective routine manual process interventions and/or preventative controls are in place through procedural and labeling controls.	**3**	Per GS-US-586-6144 *Pharmacy Manual* (v 8.0) the drug product is packaged and shipped with temperature monitoring devices (Temptales). Temperature monitoring device data is reviewed by the Clinical site and excursions are reported to Gilead Sciences upon discovery.	Per SOP-05362 *Quality and Compliance Risk Management* (v 5.0) Table 3: Probability of Detection Rating Scale: There is a manual inspection of the failure and there is a high probability that the failure will be detected within the step.	**3**	**63**	Risk is acceptable as is and no additional actions will be taken. There are currently effective controls and detection mechanisms in place to reduce the risk at the clinical facility.

PID	Process Step	Failure Mode	Effect of Failure	Rationale for S	Severity (S)	Cause of Failure	Controls	Rationale for O	Occurrence (O)	Monitoring Plan	Rationale for D	Detectability (D)	RPN	Comments / Action Items
5	Drug product arrives at the clinical facility and is sent to pharmacy.	Drug product is subjected to shaking/vibration.	Formation of particulate matter (protein) in drug product. Particulate matter introduced to patient intravenously resulting in serious adverse event.	Per SOP-05362 *Quality and Compliance Risk Management* (v 5.0) Table 1: Severity Rating Scale: Introduction of particulate matter to patient intravenously may result in serious adverse events resulting in severity rating	**10**	Drug product is mishandled upon receipt at the clinical facility.	Per GS-US-586-6144 *Pharmacy Manual* (v 8.0) Section 4.3, states "Do not shake" the drug product.	Per SOP-05362 *Quality and Compliance Risk Management* (v 5.0) Table 2: Probability of Occurrence Rating Scale: Effective routine manual process interventions and/or preventative controls are in place through procedural controls.	**3**	Per GS-US-586-6144 *Pharmacy Manual* (v 8.0) section 4.3, mishandled product is to be quarantine until sponsor disposition for use or destruction. Site submits FRM-11946 *Investigational Medicinal Products (IMPs) Event Reporting for Clinical Sites, Distributors, and other Contract Organizations.* *Per GS-US-586-6144 Pharmacy Manual (v 8.0)* section 4.6.2 step 5, vials are inspected for discoloration or foreign particulate prior to use. Discovery of discoloration or foreign particulate are reported via FRM-06432 *Investigational Medicinal Product (IMP) Complaint Form*	Per SOP-05362 *Quality and Compliance Risk Management* (v 5.0) Table 3: Probability of Detection Rating Scale: There is a manual inspection of the failure and there is a high probability that the failure will be detected within the step.	**3**	**90**	Risk is acceptable as is and no additional actions will be taken. There are currently effective controls and detection mechanisms in place to reduce the risk at the clinical facility.
6			Formation of particulate matter (protein) in drug product. Reduction of drug efficacy.	Per SOP-05362 *Quality and Compliance Risk Management* (v 5.0) Table 1: Severity Rating Scale: Loss of product efficacy or product quality leading to adverse events.	**7**	Drug product is mishandled upon receipt at the clinical facility.	Per GS-US-586-6144 *Pharmacy Manual* (v 8.0) Section 4.3, states "Do not shake" the drug product.	Per SOP-05362 *Quality and Compliance Risk Management* (v 5.0) Table 2: Probability of Occurrence Rating Scale: Effective routine manual process interventions and/or preventative controls are in place through procedural controls.	**3**	Per GS-US-586-6144 *Pharmacy Manual* (v 8.0) section 4.3, mishandled product is to be quarantine until sponsor disposition for use or destruction. Site submits FRM-11946 *Investigational Medicinal Products (IMPs) Event Reporting for Clinical Sites, Distributors, and other Contract Organizations.* *Per GS-US-586-6144 Pharmacy Manual (v 8.0)* section 4.6.2 step 5, vials are inspected for discoloration or foreign particulate prior to use. Discovery of discoloration or foreign particulate are reported via FRM-06432 *Investigational Medicinal Product (IMP) Complaint Form*	Per SOP-05362 *Quality and Compliance Risk Management* (v 5.0) Table 3: Probability of Detection Rating Scale: There is a manual inspection of the failure and there is a high probability that the failure will be detected within the step.	**3**	**63**	Risk is acceptable as is and no additional actions will be taken. There are currently effective controls and detection mechanisms in place to reduce the risk at the clinical facility.
7	Pharmacy cross-checks packing list and performs initial visual inspection of vials for damage.	Vials are damaged/broken	Introduction of particulate matter (glass) to the drug product. Particulate matter introduced to patient intravenously resulting in serious adverse event.	Per SOP-05362 *Quality and Compliance Risk Management* (v 5.0) Table 1: Severity Rating Scale: Introduction of particulate matter to patient intravenously may result in serious adverse events resulting in severity rating	**10**	Drug product is mishandled upon receipt at the clinical facility.	Historical review of complaints related to damaged vials for Magrolimab upon receipt at the clinical facility from 01Apr2020 to 08Dec2023 found 1 complaint related to damaged vials, therefore failure is not expected to occur often.	Per SOP-05362 *Quality and Compliance Risk Management* (v 5.0) Table 2: Probability of Occurrence Rating Scale: Failure not expected to occur often.	**3**	Per GS-US-586-6144 *Pharmacy Manual* (v 8.0) section 4.3, mishandled product is to be quarantine until sponsor disposition for use or destruction. Site submits FRM-11946 *Investigational Medicinal Products (IMPs) Event Reporting for Clinical Sites, Distributors, and other Contract Organizations.* *Per GS-US-586-6144 Pharmacy Manual (v 8.0)* section 4.6.2 step 5, vials are inspected for discoloration or foreign particulate prior to use. Discovery of discoloration or foreign particulate are reported via FRM-06432 *Investigational Medicinal Product (IMP) Complaint Form*	Per SOP-05362 *Quality and Compliance Risk Management* (v 5.0) Table 3: Probability of Detection Rating Scale: There is a manual inspection of the failure and there is a high probability that the failure will be detected within the step.	**3**	**90**	Risk is acceptable as is and no additional actions will be taken. There are currently effective controls and detection mechanisms in place to reduce the risk at the clinical facility.

PID	Process Step	Failure Mode	Effect of Failure	Rationale for S	Severity (S)	Cause of Failure	Controls	Rationale for O	Occurrence (O)	Monitoring Plan	Rationale for D	Detectability (D)	RPN	Comments / Action Items
8	Maintain accountability of drug lots from receipt to destruction. - Date received - Qty of study drug - Kits or vials - Date/Patient Number/Study number dispensed - Date, Qty Used, and Unused study drug returned. Initial/Date of individual	Drug product subjected to elevated temperatures above recommended storage conditions of 2–8 °C	Formation of particulate matter (protein) in drug product. Particulate matter introduced to patient intravenously resulting in serious adverse event.	Per SOP-05362 *Quality and Compliance Risk Management* (v 5.0) Table 1: Severity Rating Scale: Introduction of particulate matter to patient intravenously may result in serious adverse events resulting in severity rating	**10**	Drug product not stored at recommended temperature of 2–8 °C or removed from recommended temperature for longer than allowed per storage conditions.	Per GS-US-586-6144 *Pharmacy Manual* (v 8.0) Section 4.3, Drug Product is to be stored at 2–8 °C. Drug vials are labeled with temperature storage requirements.	Per SOP-05362 *Quality and Compliance Risk Management* (v 5.0) Table 2: Probability of Occurrence Rating Scale: Effective routine manual process interventions and/or preventative controls are in place through procedural and labeling controls.	**3**	Per GS-US-586-6144 *Pharmacy Manual* (v 8.0) section 4.3, mishandled product is to be quarantine until sponsor disposition for use or destruction. Site submits FRM-11946 Investigational Medicinal Products (IMPs) Event Reporting for Clinical Sites, Distributors, and other Contract Organizations. Per GS-US-586-6144 *Pharmacy Manual* Section 4.3 storage temperature should be monitored and documented on a temperature log. Per GS-US-586-6144 *Pharmacy Manual* (v 8.0) section 4.6.2 step 5, vials are inspected for discoloration or foreign particulate prior to use. Discovery of discoloration or foreign particulate are reported via FRM-06432 Investigational Medicinal Product (IMP) Complaint Form	Per SOP-05362 *Quality and Compliance Risk Management* (v 5.0) Table 3: Probability of Detection Rating Scale: There is a manual inspection of the failure and there is a high probability that the failure will be detected within the step.	**3**	**90**	Risk is acceptable as is and no additional actions will be taken. There are currently effective controls and detection mechanisms in place to reduce the risk at the clinical facility.
9			Formation of particulate matter (protein) in drug product. Reduction of drug efficacy.	Per SOP-05362 *Quality and Compliance Risk Management* (v 5.0) Table 1: Severity Rating Scale: Loss of product efficacy or product quality leading to adverse events.	**7**	Drug product not stored at recommended temperature of 2–8 °C or removed from recommended temperature for longer than allowed per storage conditions.	Per GS-US-586-6144 *Pharmacy Manual* (v 8.0) Section 4.3, Drug Product is to be stored at 2–8 °C. Drug vials are labeled with temperature storage requirements.	Per SOP-05362 *Quality and Compliance Risk Management* (v 5.0) Table 2: Probability of Occurrence Rating Scale: Effective routine manual process interventions and/or preventative controls are in place through procedural and labeling controls.	**3**	Per GS-US-586-6144 *Pharmacy Manual* (v 8.0) section 4.3, mishandled product is to be quarantine until sponsor disposition for use or destruction. Site submits FRM-11946 Investigational Medicinal Products (IMPs) Event Reporting for Clinical Sites, Distributors, and other Contract Organizations. Per GS-US-586-6144 *Pharmacy Manual* Section 4.3 storage temperature should be monitored and documented on a temperature log. Per GS-US-586-6144 *Pharmacy Manual* (v 8.0) section 4.6.2 step 5, vials are inspected for discoloration or foreign particulate prior to use. Discovery of discoloration or foreign particulate are reported via FRM-06432 Investigational Medicinal Product (IMP) Complaint Form	Per SOP-05362 *Quality and Compliance Risk Management* (v 5.0) Table 3: Probability of Detection Rating Scale: There is a manual inspection of the failure and there is a high probability that the failure will be detected within the step.	**3**	**63**	Risk is acceptable as is and no additional actions will be taken. There are currently effective controls and detection mechanisms in place to reduce the risk at the clinical facility.

PID	Process Step	Failure Mode	Effect of Failure	Rationale for S	Severity (S)	Cause of Failure	Controls	Rationale for O	Occurrence (O)	Monitoring Plan	Rationale for D	Detectability (D)	RPN	Comments / Action Items
Ref # 1.2 Storage at the Clinical Facility														
10	Store in a secure and controlled environment with limited access.	Drug product subjected to elevated temperatures above recommended storage conditions of 2–8 °C.	Formation of particulate matter (protein) in drug product. Particulate matter introduced to patient intravenously resulting in serious adverse event.	Per SOP-05362 *Quality and Compliance Risk Management* (v 5.0) Table 1: Severity Rating Scale: Introduction of particulate matter to patient intravenously may result in serious adverse events resulting in severity rating	**10**	Drug product not stored at recommended temperature of 2–8 °C or removed from recommended temperature for longer than allowed per storage conditions.	Per GS-US-586-6144 *Pharmacy Manual* (v 8.0) Section 4.3, Drug Product is to be stored at 2–8 °C. Drug vials are labeled with temperature storage requirements.	Per SOP-05362 *Quality and Compliance Risk Management* (v 5.0) Table 2: Probability of Occurrence Rating Scale: Effective routine manual process interventions and/or preventative controls are in place through procedural and labeling controls.	**3**	Per GS-US-586-6144 *Pharmacy Manual* (v 8.0) section 4.3, mishandled product is to be quarantine until sponsor disposition for use or destruction. Site submits FRM-11946 Investigational Medicinal Products (IMPs) Event Reporting for Clinical Sites, Distributors, and other Contract Organizations. Per GS-US-586-6144 *Pharmacy Manual* Section 4.3 storage temperature should be monitored and documented on a temperature log. Per GS-US-586-6144 *Pharmacy Manual* (v 8.0) section 4.6.2 step 5, vials are inspected for discoloration or foreign particulate prior to use. Discovery of discoloration or foreign particulate are reported via FRM-06432 Investigational Medicinal Product (IMP) Complaint Form	Per SOP-05362 *Quality and Compliance Risk Management* (v 5.0) Table 3: Probability of Detection Rating Scale: There is a manual inspection of the failure and there is a high probability that the failure will be detected within the step.	**3**	**90**	Risk is acceptable as is and no additional actions will be taken. There are currently effective controls and detection mechanisms in place to reduce the risk at the clinical facility.
11	Store in a secure and controlled environment with limited access.	Drug product subjected to elevated temperatures above recommended storage conditions of 2–8 °C.	Formation of particulate matter (protein) in drug product. Reduction of drug efficacy.	Per SOP-05362 *Quality and Compliance Risk Management* (v 5.0) Table 1: Severity Rating Scale: Loss of product efficacy or product quality leading to adverse events.	**7**	Drug product not stored at recommended temperature of 2–8 °C or removed from recommended temperature for longer than allowed per storage conditions.	Per GS-US-586-6144 *Pharmacy Manual* (v 8.0) Section 4.3, Drug Product is to be stored at 2–8 °C. Drug vials are labeled with temperature storage requirements.	Per SOP-05362 *Quality and Compliance Risk Management* (v 5.0) Table 2: Probability of Occurrence Rating Scale: Effective routine manual process interventions and/or preventative controls are in place through procedural and labeling controls.	**3**	Per GS-US-586-6144 *Pharmacy Manual* (v 8.0) section 4.3, mishandled product is to be quarantine until sponsor disposition for use or destruction. Site submits FRM-11946 Investigational Medicinal Products (IMPs) Event Reporting for Clinical Sites, Distributors, and other Contract Organizations. Per GS-US-586-6144 *Pharmacy Manual* Section 4.3 storage temperature should be monitored and documented on a temperature log. Per GS-US-586-6144 *Pharmacy Manual* (v 8.0) section 4.6.2 step 5, vials are inspected for discoloration or foreign particulate prior to use. Discovery of discoloration or foreign particulate are reported via FRM-06432 Investigational Medicinal Product (IMP) Complaint Form	Per SOP-05362 *Quality and Compliance Risk Management* (v 5.0) Table 3: Probability of Detection Rating Scale: There is a manual inspection of the failure and there is a high probability that the failure will be detected within the step.	**3**	**63**	Risk is acceptable as is and no additional actions will be taken. There are currently effective controls and detection mechanisms in place to reduce the risk at the clinical facility.

PID	Process Step	Failure Mode	Effect of Failure	Rationale for S	Severity (S)	Cause of Failure	Controls	Rationale for O	Occurrence (O)	Monitoring Plan	Rationale for D	Detectability (D)	RPN	Comments / Action Items
12	Store in a secure and controlled environment with limited access.	Drug product subjected to decreased temperatures below recommended storage conditions of 2–8 °C.	Formation of particulate matter (protein) in drug product. Particulate matter introduced to patient intravenously resulting in serious adverse event.	Per SOP-05362 *Quality and Compliance Risk Management* (v 5.0) Table 1: Severity Rating Scale: Introduction of particulate matter to patient intravenously may result in serious adverse events resulting in severity rating	**10**	Drug product not stored at recommended temperature of 2–8 °C or removed from recommended temperature for longer than allowed per storage conditions.	Per GS-US-586-6144 *Pharmacy Manual* (v 8.0) Section 4.3, Drug Product is to be stored at 2–8 °C. Drug vials are labeled with temperature storage requirements.	Per SOP-05362 *Quality and Compliance Risk Management* (v 5.0) Table 2: Probability of Occurrence Rating Scale: Effective routine manual process interventions and/or preventative controls are in place through procedural and labeling controls.	**3**	Per GS-US-586-6144 *Pharmacy Manual* (v 8.0) section 4.3, mishandled product is to be quarantine until sponsor disposition for use or destruction. Site submits FRM-11946 Investigational Medicinal Products (IMPs) Event Reporting for Clinical Sites, Distributors, and other Contract Organizations. Per GS-US-586-6144 *Pharmacy Manual* Section 4.3 storage temperature should be monitored and documented on a temperature log. Per GS-US-586-6144 *Pharmacy Manual* (v 8.0) section 4.6.2 step 5, vials are inspected for discoloration or foreign particulate prior to use. Discovery of discoloration or foreign particulate are reported via FRM-06432 Investigational Medicinal Product (IMP) Complaint Form	Per SOP-05362 *Quality and Compliance Risk Management* (v 5.0) Table 3: Probability of Detection Rating Scale: There is a manual inspection of the failure and there is a high probability that the failure will be detected within the step.	**3**	**90**	Risk is acceptable as is and no additional actions will be taken. There are currently effective controls and detection mechanisms in place to reduce the risk at the clinical facility.
13			Formation of particulate matter (protein) in drug product. Reduction of drug efficacy.	Per SOP-05362 *Quality and Compliance Risk Management* (v 5.0) Table 1: Severity Rating Scale: Loss of product efficacy or product quality leading to adverse events.	**7**	Drug product not stored at recommended temperature of 2–8 °C or removed from recommended temperature for longer than allowed per storage conditions.	Per GS-US-586-6144 *Pharmacy Manual* (v 8.0) Section 4.3, Drug Product is to be stored at 2–8 °C. Drug vials are labeled with temperature storage requirements.	Per SOP-05362 *Quality and Compliance Risk Management* (v 5.0) Table 2: Probability of Occurrence Rating Scale: Effective routine manual process interventions and/or preventative controls are in place through procedural and labeling controls.	**3**	Per GS-US-586-6144 *Pharmacy Manual* (v 8.0) section 4.3, mishandled product is to be quarantine until sponsor disposition for use or destruction. Site submits FRM-11946 Investigational Medicinal Products (IMPs) Event Reporting for Clinical Sites, Distributors, and other Contract Organizations. Per GS-US-586-6144 *Pharmacy Manual* Section 4.3 storage temperature should be monitored and documented on a temperature log. Per GS-US-586-6144 *Pharmacy Manual* (v 8.0) section 4.6.2 step 5, vials are inspected for discoloration or foreign particulate prior to use. Discovery of discoloration or foreign particulate are reported via FRM-06432 Investigational Medicinal Product (IMP) Complaint Form	Per SOP-05362 *Quality and Compliance Risk Management* (v 5.0) Table 3: Probability of Detection Rating Scale: There is a manual inspection of the failure and there is a high probability that the failure will be detected within the step.	**3**	**63**	Risk is acceptable as is and no additional actions will be taken. There are currently effective controls and detection mechanisms in place to reduce the risk at the clinical facility.

PID	Process Step	Failure Mode	Effect of Failure	Rationale for S	Severity (S)	Cause of Failure	Controls	Rationale for O	Occurrence (O)	Monitoring Plan	Rationale for D	Detectability (D)	RPN	Comments / Action Items
14	Store in a secure and controlled environment with limited access.	Drug product is subjected to shaking/vibration.	Formation of particulate matter (protein) in drug product. Particulate matter introduced to patient intravenously resulting in serious adverse event.	Per SOP-05362 *Quality and Compliance Risk Management* (v 5.0) Table 1: Severity Rating Scale: Introduction of particulate matter to patient intravenously may result in serious adverse events resulting in severity rating	**10**	Drug product is mishandled upon receipt at the clinical facility.	Per GS-US-586-6144 *Pharmacy Manual* (v 8.0) Section 4.3, states "Do not shake" the drug product.	Per SOP-05362 *Quality and Compliance Risk Management* (v 5.0) Table 2: Probability of Occurrence Rating Scale: Effective routine manual process interventions and/or preventative controls are in place through procedural controls.	**3**	Per GS-US-586-6144 *Pharmacy Manual* (v 8.0) section 4.3, mishandled product is to be quarantine until sponsor disposition for use or destruction. Site submits FRM-11946 *Investigational Medicinal Products (IMPs) Event Reporting for Clinical Sites, Distributors, and other Contract Organizations.* Per *GS-US-586-6144 Pharmacy Manual (v 8.0)* section 4.6.2 step 5, vials are inspected for discoloration or foreign particulate prior to use. Discovery of discoloration or foreign particulate are reported via FRM-06432 *Investigational Medicinal Product (IMP) Complaint Form*	Per SOP-05362 *Quality and Compliance Risk Management* (v 5.0) Table 3: Probability of Detection Rating Scale: There is a manual inspection of the failure and there is a high probability that the failure will be detected within the step.	**3**	**90**	Risk is acceptable as is and no additional actions will be taken. There are currently effective controls and detection mechanisms in place to reduce the risk at the clinical facility.
15			Formation of particulate matter (protein) in drug product. Reduction of drug efficacy.	Per SOP-05362 *Quality and Compliance Risk Management* (v 5.0) Table 1: Severity Rating Scale: Loss of product efficacy or product quality leading to adverse events.	**7**	Drug product is mishandled upon receipt at the clinical facility.	Per GS-US-586-6144 *Pharmacy Manual* (v 8.0) Section 4.3, states "Do not shake" the drug product.	Per SOP-05362 *Quality and Compliance Risk Management* (v 5.0) Table 2: Probability of Occurrence Rating Scale: Effective routine manual process interventions and/or preventative controls are in place through procedural controls.	**3**	Per GS-US-586-6144 *Pharmacy Manual* (v 8.0) section 4.3, mishandled product is to be quarantine until sponsor disposition for use or destruction. Site submits FRM-11946 *Investigational Medicinal Products (IMPs) Event Reporting for Clinical Sites, Distributors, and other Contract Organizations.* Per *GS-US-586-6144 Pharmacy Manual (v 8.0)* section 4.6.2 step 5, vials are inspected for discoloration or foreign particulate prior to use. Discovery of discoloration or foreign particulate are reported via FRM-06432 *Investigational Medicinal Product (IMP) Complaint Form*	Per SOP-05362 *Quality and Compliance Risk Management* (v 5.0) Table 3: Probability of Detection Rating Scale: There is a manual inspection of the failure and there is a high probability that the failure will be detected within the step.	**3**	**63**	Risk is acceptable as is and no additional actions will be taken. There are currently effective controls and detection mechanisms in place to reduce the risk at the clinical facility.
16		Product is exposed to excessive light.	No impact to product quality or patient safety as determined in REP-27687.	Per SOP-05362 *Quality and Compliance Risk Management* (v 5.0) Table 1: Severity Rating Scale: Failure has no impact on patient health or product quality	**1**	Drug product is not stored per light requirements at the clinical facility.	Per GS-US-586-6144 *Pharmacy Manual* (v 8.0) Section 4.3, states "Protect from light" in regard to product storage.	Per SOP-05362 *Quality and Compliance Risk Management* (v 5.0) Table 2: Probability of Occurrence Rating Scale: Effective routine manual process interventions and/or preventative controls are in place through procedural controls.	**3**	Per GS-US-586-6144 *Pharmacy Manual* (v 8.0) section 4.3, mishandled product is to be quarantine until sponsor disposition for use or destruction. Site submits FRM-11946 *Investigational Medicinal Products (IMPs) Event Reporting for Clinical Sites, Distributors, and other Contract Organizations.* Per *GS-US-586-6144 Pharmacy Manual (v 8.0)* section 4.6.2 step 5, vials are inspected for discoloration or foreign particulate prior to use. Discovery of discoloration or foreign particulate are reported via FRM-06432 *Investigational Medicinal Product (IMP) Complaint Form*	Per SOP-05362 *Quality and Compliance Risk Management* (v 5.0) Table 3: Probability of Detection Rating Scale: There is a manual inspection of the failure and there is a high probability that the failure will be detected within the step.	**3**	**9**	Risk is acceptable as is and no additional actions will be taken. There are currently effective controls and detection mechanisms in place to reduce the risk at the clinical facility.

PID	Process Step	Failure Mode	Effect of Failure	Rationale for S	Severity (S)	Cause of Failure	Controls	Rationale for O	Occurrence (O)	Monitoring Plan	Rationale for D	Detectability (D)	RPN	Comments / Action Items
Ref # 2.0	**Transport of Drug Product Vial Between Clinical Facilities**													
17	The vials may be transported within 8 hours at refrigerator temperature (2–8 °C) storage for up to 190 miles by motor vehicle.	Drug product subjected to elevated temperatures above recommended storage conditions of 2–8 °C.	Formation of particulate matter (protein) in drug product. Particulate matter introduced to patient intravenously resulting in serious adverse event.	Per SOP-05362 *Quality and Compliance Risk Management* (v 5.0) Table 1: Severity Rating Scale: Introduction of particulate matter to patient intravenously may result in serious adverse events resulting in severity rating	**10**	Drug product not stored at recommended temperature of 2–8 °C during transport between clinical facilities.	Per GS-US-586-6144 *Pharmacy Manual* (v 8.0) Section 4.3, Drug Product is to be stored at 2–8 °C.	Per SOP-05362 *Quality and Compliance Risk Management* (v 5.0) Table 2: Probability of Occurrence Rating Scale: Effective routine manual process interventions and/or preventative controls are in place through procedural and labeling controls.	**3**	Per GS-US-586-6144 *Pharmacy Manual* (v 8.0) section 4.3, mishandled product is to be quarantine until sponsor disposition for use or destruction. Site submits FRM-11946 Investigational Medicinal Products (IMPs) Event Reporting for Clinical Sites, Distributors, and other Contract Organizations. Per GS-US-586-6144 *Pharmacy Manual* Section 4.3 storage temperature should be monitored and documented on a temperature log. Per GS-US-586-6144 *Pharmacy Manual* (v 8.0) section 4.6.2 step 5, vials are inspected for discoloration or foreign particulate prior to use. Discovery of discoloration or foreign particulate are reported via FRM-06432 Investigational Medicinal Product (IMP) Complaint Form	Per SOP-05362 *Quality and Compliance Risk Management* (v 5.0) Table 3: Probability of Detection Rating Scale: There is a manual inspection of the failure and there is a high probability that the failure will be detected within the step.	**3**	**90**	Risk is acceptable as is and no additional actions will be taken. There are currently effective controls and detection mechanisms in place to reduce the risk at the clinical facility.
18			Formation of particulate matter (protein) in drug product. Reduction of drug efficacy.	Per SOP-05362 *Quality and Compliance Risk Management* (v 5.0) Table 1: Severity Rating Scale: Loss of product efficacy or product quality leading to adverse events.	**7**	Drug product not stored at recommended temperature of 2–8 °C during transport between clinical facilities.	Per GS-US-586-6144 *Pharmacy Manual* (v 8.0) Section 4.3, Drug Product is to be stored at 2–8 °C. Drug vials are labeled with temperature storage requirements.	Per SOP-05362 *Quality and Compliance Risk Management* (v 5.0) Table 2: Probability of Occurrence Rating Scale: Effective routine manual process interventions and/or preventative controls are in place through procedural and labeling controls.	**3**	Per GS-US-586-6144 *Pharmacy Manual* (v 8.0) section 4.3, mishandled product is to be quarantine until sponsor disposition for use or destruction. Site submits FRM-11946 Investigational Medicinal Products (IMPs) Event Reporting for Clinical Sites, Distributors, and other Contract Organizations. Per GS-US-586-6144 *Pharmacy Manual* Section 4.3 storage temperature should be monitored and documented on a temperature log. Per GS-US-586-6144 *Pharmacy Manual* (v 8.0) section 4.6.2 step 5, vials are inspected for discoloration or foreign particulate prior to use. Discovery of discoloration or foreign particulate are reported via FRM-06432 Investigational Medicinal Product (IMP) Complaint Form	Per SOP-05362 *Quality and Compliance Risk Management* (v 5.0) Table 3: Probability of Detection Rating Scale: There is a manual inspection of the failure and there is a high probability that the failure will be detected within the step.	**3**	**63**	Risk is acceptable as is and no additional actions will be taken. There are currently effective controls and detection mechanisms in place to reduce the risk at the clinical facility.

PID	Process Step	Failure Mode	Effect of Failure	Rationale for S	Severity (S)	Cause of Failure	Controls	Rationale for O	Occurrence (O)	Monitoring Plan	Rationale for D	Detectability (D)	RPN	Comments / Action Items
19	The vials may be transported within 8 hours at refrigerator temperature (2–8 °C) storage for up to 190 miles by motor vehicle.	Drug product subjected to decreased temperatures below recommended storage conditions of 2–8 °C.	Formation of particulate matter (protein) in drug product. Particulate matter introduced to patient intravenously resulting in serious adverse event.	Per SOP-05362 *Quality and Compliance Risk Management* (v 5.0) Table 1: Severity Rating Scale: Introduction of particulate matter to patient intravenously may result in serious adverse events resulting in severity rating	**10**	Drug product not stored at recommended temperature of 2–8 °C during transport between clinical facilities.	Per GS-US-586-6144 *Pharmacy Manual* (v 8.0) Section 4.3, Drug Product is to be stored at 2–8 °C. Drug vials are labeled with temperature storage requirements.	Per SOP-05362 *Quality and Compliance Risk Management* (v 5.0) Table 2: Probability of Occurrence Rating Scale: Effective routine manual process interventions and/or preventative controls are in place through procedural and labeling controls.	**3**	Per GS-US-586-6144 *Pharmacy Manual* (v 8.0) section 4.3, mishandled product is to be quarantine until sponsor disposition for use or destruction. Site submits FRM-11946 Investigational Medicinal Products (IMPs) Event Reporting for Clinical Sites, Distributors, and other Contract Organizations. Per GS-US-586-6144 *Pharmacy Manual* Section 4.3 storage temperature should be monitored and documented on a temperature log. Per GS-US-586-6144 *Pharmacy Manual* (v 8.0) section 4.6.2 step 5, vials are inspected for discoloration or foreign particulate prior to use. Discovery of discoloration or foreign particulate are reported via FRM-06432 Investigational Medicinal Product (IMP) Complaint Form	Per SOP-05362 *Quality and Compliance Risk Management* (v 5.0) Table 3: Probability of Detection Rating Scale: There is a manual inspection of the failure and there is a high probability that the failure will be detected within the step.	**3**	**90**	Risk is acceptable as is and no additional actions will be taken. There are currently effective controls and detection mechanisms in place to reduce the risk at the clinical facility.
20			Formation of particulate matter (protein) in drug product. Reduction of drug efficacy.	Per SOP-05362 *Quality and Compliance Risk Management* (v 5.0) Table 1: Severity Rating Scale: Loss of product efficacy or product quality leading to adverse events.	**7**	Drug product not stored at recommended temperature of 2–8 °C during transport between clinical facilities.	Per GS-US-586-6144 *Pharmacy Manual* (v 8.0) Section 4.3, Drug Product is to be stored at 2–8 °C. Drug vials are labeled with temperature storage requirements.	Per SOP-05362 *Quality and Compliance Risk Management* (v 5.0) Table 2: Probability of Occurrence Rating Scale: Effective routine manual process interventions and/or preventative controls are in place through procedural and labeling controls.	**3**	Per GS-US-586-6144 *Pharmacy Manual* (v 8.0) section 4.3, mishandled product is to be quarantine until sponsor disposition for use or destruction. Site submits FRM-11946 Investigational Medicinal Products (IMPs) Event Reporting for Clinical Sites, Distributors, and other Contract Organizations. Per GS-US-586-6144 *Pharmacy Manual* Section 4.3 storage temperature should be monitored and documented on a temperature log. Per GS-US-586-6144 *Pharmacy Manual* (v 8.0) section 4.6.2 step 5, vials are inspected for discoloration or foreign particulate prior to use. Discovery of discoloration or foreign particulate are reported via FRM-06432 Investigational Medicinal Product (IMP) Complaint Form	Per SOP-05362 *Quality and Compliance Risk Management* (v 5.0) Table 3: Probability of Detection Rating Scale: There is a manual inspection of the failure and there is a high probability that the failure will be detected within the step.	**3**	**63**	Risk is acceptable as is and no additional actions will be taken. There are currently effective controls and detection mechanisms in place to reduce the risk at the clinical facility.

PID	Process Step	Failure Mode	Effect of Failure	Rationale for S	Severity (S)	Cause of Failure	Controls	Rationale for O	Occurrence (O)	Monitoring Plan	Rationale for D	Detectability (D)	RPN	Comments / Action Items
21	The vials may be transported within 8 hours at refrigerator temperature (2–8 °C) storage for up to 190 miles by motor vehicle.	Drug product is subjected to shaking/vibration.	Formation of particulate matter (protein) in drug product. Particulate matter introduced to patient intravenously resulting in serious adverse event.	Per SOP-05362 *Quality and Compliance Risk Management* (v 5.0) Table 1: Severity Rating Scale: Introduction of particulate matter to patient intravenously may result in serious adverse events resulting in severity rating	**10**	Drug product is mishandled during transport between clinical facilities.	Per GS-US-586-6144 *Pharmacy Manual* (v 8.0) Section 4.3, states "Do not shake" the drug product.	Per SOP-05362 *Quality and Compliance Risk Management* (v 5.0) Table 2: Probability of Occurrence Rating Scale: Effective routine manual process interventions and/or preventative controls are in place through procedural controls.	**3**	Per GS-US-586-6144 *Pharmacy Manual* (v 8.0) section 4.3, mishandled product is to be quarantine until sponsor disposition for use or destruction. Site submits FRM-11946 *Investigational Medicinal Products (IMPs) Event Reporting for Clinical Sites, Distributors, and other Contract Organizations.* *Per GS-US-586-6144 Pharmacy Manual (v 8.0)* section 4.6.2 step 5, vials are inspected for discoloration or foreign particulate prior to use. Discovery of discoloration or foreign particulate are reported via FRM-06432 *Investigational Medicinal Product (IMP) Complaint Form*	Per SOP-05362 *Quality and Compliance Risk Management* (v 5.0) Table 3: Probability of Detection Rating Scale: There is a manual inspection of the failure and there is a high probability that the failure will be detected within the step.	**3**	**90**	Risk is acceptable as is and no additional actions will be taken. There are currently effective controls and detection mechanisms in place to reduce the risk at the clinical facility.
22	The vials may be transported within 8 hours at refrigerator temperature (2–8 °C) storage for up to 190 miles by motor vehicle.		Formation of particulate matter (protein) in drug product. Reduction of drug efficacy.	Per SOP-05362 *Quality and Compliance Risk Management* (v 5.0) Table 1: Severity Rating Scale: Loss of product efficacy or product quality leading to adverse events.	**7**	Drug product is mishandled during transport between clinical facilities.	Per GS-US-586-6144 *Pharmacy Manual* (v 8.0) Section 4.3, states "Do not shake" the drug product.	Per SOP-05362 *Quality and Compliance Risk Management* (v 5.0) Table 2: Probability of Occurrence Rating Scale: Effective routine manual process interventions and/or preventative controls are in place through procedural controls.	**3**	Per GS-US-586-6144 *Pharmacy Manual* (v 8.0) section 4.3, mishandled product is to be quarantine until sponsor disposition for use or destruction. Site submits FRM-11946 *Investigational Medicinal Products (IMPs) Event Reporting for Clinical Sites, Distributors, and other Contract Organizations.* *Per GS-US-586-6144 Pharmacy Manual (v 8.0)* section 4.6.2 step 5, vials are inspected for discoloration or foreign particulate prior to use. Discovery of discoloration or foreign particulate are reported via FRM-06432 *Investigational Medicinal Product (IMP) Complaint Form*	Per SOP-05362 *Quality and Compliance Risk Management* (v 5.0) Table 3: Probability of Detection Rating Scale: There is a manual inspection of the failure and there is a high probability that the failure will be detected within the step.	**3**	**63**	Risk is acceptable as is and no additional actions will be taken. There are currently effective controls and detection mechanisms in place to reduce the risk at the clinical facility.
Ref # 3.0	**Preparation of Drug-Infusion Solution**													
23	Dosage preparation for low concentration of drug product (1 mg/kg)	Formation of particulate matter (protein) in the drug-infusion solution.	Particulate matter (protein) introduced to patient intravenously resulting in a serious adverse event.	Per SOP-05362 *Quality and Compliance Risk Management* (v 5.0) Table 1: Severity Rating Scale: Introduction of particulate matter to patient intravenously may result in serious adverse events resulting in severity rating	**10**	Low concentration of surfactant in drug-infusion solution.	GS-US-586-6144 *Pharmacy Manual* (v 8.0) section 4.5 provides dosing information and calculation guidance for pharmacy.	Per SOP-05362 *Quality and Compliance Risk Management* (v 5.0) Table 2: Probability of Occurrence Rating Scale: No preventative controls are in place. Low concentration of surfactant in drug-infusion solution is almost certain to occur as part of normal operations.	**10**	Per GS-US-586-6144 *Pharmacy Manual* (v 8.0) section 4.6.2 step 9, infusion bag is inspected for discoloration or foreign particulate prior to use. Discovery of discoloration or foreign particulate are reported via FRM-06432 Investigational Medicinal Product (IMP) Complaint Form	Per SOP-05362 *Quality and Compliance Risk Management* (v 5.0) Table 3: Probability of Detection Rating Scale: There is a manual inspection of the failure and there is a high probability that the failure will be detected within the step.	**3**	**300**	There is no lower weight limit for patient. **Action Item:** Allowance of 100 mL infusion bag for the preparation of low concentration drug infusion solution.

PID	Process Step	Failure Mode	Effect of Failure	Rationale for S	Severity (S)	Cause of Failure	Controls	Rationale for O	Occurrence (O)	Monitoring Plan	Rationale for D	Detectability (D)	RPN	Comments / Action Items
24	Dosage preparation for low concentration of drug product (1 mg/kg)	Formation of particulate matter (protein) in the drug-infusion solution.	Particulate matter (protein) in drug product. Reduction of drug efficacy.	Per SOP-05362 *Quality and Compliance Risk Management* (v 5.0) Table 1: Severity Rating Scale: Loss of product efficacy or product quality leading to adverse events.	**7**	Low concentration of surfactant in drug-infusion solution.	GS-US-586-6144 *Pharmacy Manual* (v 8.0) section 4.5 provides dosing information and calculation guidance for pharmacy.	Per SOP-05362 *Quality and Compliance Risk Management* (v 5.0) Table 2: Probability of Occurrence Rating Scale: No preventative controls are in place. Low concentration of surfactant in drug-infusion solution is almost certain to occur as part of normal operations.	**10**	Per GS-US-586-6144 *Pharmacy Manual* (v 8.0) section 4.6.2 step 9, infusion bag is inspected for discoloration or foreign particulate prior to use. Discovery of discoloration or foreign particulate are reported via FRM-06432 Investigational Medicinal Product (IMP) Complaint Form	Per SOP-05362 *Quality and Compliance Risk Management* (v 5.0) Table 3: Probability of Detection Rating Scale: There is a manual inspection of the failure and there is a high probability that the failure will be detected within the step.	**3**	**210**	There is no lower weight limit for patient. **Action Item:** Allowance of 100 mL infusion bag for the preparation of low concentration drug infusion solution
25	Dosage preparation for high concentration of drug product (30–60 mg/kg)	Formation of particulate matter (protein) in the drug-infusion solution.	Particulate matter introduced to patient intravenously resulting in a serious adverse event.	Per SOP-05362 *Quality and Compliance Risk Management* (v 5.0) Table 1: Severity Rating Scale: Introduction of particulate matter to patient intravenously may result in serious adverse events resulting in severity rating	**10**	High concentration of drug product material in drug-infusion material.	GS-US-586-6144 *Pharmacy Manual* (v 8.0) section 4.5 provides dosing information and calculation guidance for pharmacy. Per GS-US-586-6144 *Pharmacy Manual* (v 8.0) section 4.7 requires use of 500 mL infusion bag for high dosage concentrations.	Per SOP-05362 *Quality and Compliance Risk Management* (v 5.0) Table 2: Probability of Occurrence Rating Scale: Effective routine manual process interventions and/or preventative controls are in place through procedural controls.	**3**	Per GS-US-586-6144 *Pharmacy Manual* (v 8.0) section 4.6.2 step 9, infusion bag is inspected for discoloration or foreign particulate prior to use. Discovery of discoloration or foreign particulate are reported via FRM-06432 Investigational Medicinal Product (IMP) Complaint Form	Per SOP-05362 *Quality and Compliance Risk Management* (v 5.0) Table 3: Probability of Detection Rating Scale: There is a manual inspection of the failure and there is a high probability that the failure will be detected within the step.	**3**	**90**	There is no upper weight limit for the patient. Allowance to dose patient without saline dilution. Risk is acceptable as is and no additional actions will be taken. There are currently effective controls and detection mechanisms in place to reduce the risk at the clinical facility.
26			Particulate matter (protein) in drug product. Reduction of drug efficacy.	Per SOP-05362 *Quality and Compliance Risk Management* (v 5.0) Table 1: Severity Rating Scale: Loss of product efficacy or product quality leading to adverse events.	**7**	High concentration of drug product material in drug-infusion material.	GS-US-586-6144 *Pharmacy Manual* (v 8.0) section 4.5 provides dosing information and calculation guidance for pharmacy. Per GS-US-586-6144 *Pharmacy Manual* (v 8.0) section 4.7 requires use of 500 mL infusion bag for high dosage concentrations.	Per SOP-05362 *Quality and Compliance Risk Management* (v 5.0) Table 2: Probability of Occurrence Rating Scale: Effective routine manual process interventions and/or preventative controls are in place through procedural controls.	**3**	Per GS-US-586-6144 *Pharmacy Manual* (v 8.0) section 4.6.2 step 9, infusion bag is inspected for discoloration or foreign particulate prior to use. Discovery of discoloration or foreign particulate are reported via FRM-06432 Investigational Medicinal Product (IMP) Complaint Form	Per SOP-05362 *Quality and Compliance Risk Management* (v 5.0) Table 3: Probability of Detection Rating Scale: There is a manual inspection of the failure and there is a high probability that the failure will be detected within the step.	**3**	**63**	There is no upper weight limit for the patient. Allowance to dose patient without saline dilution. Risk is acceptable as is and no additional actions will be taken. There are currently effective controls and detection mechanisms in place to reduce the risk at the clinical facility.
27		Introduction of particulate matter (vial septum material) in the drug infusion solution.	Particulate matter (vial septum material) introduced to patient intravenously resulting in a serious adverse event.	Per SOP-05362 *Quality and Compliance Risk Management* (v 5.0) Table 1: Severity Rating Scale: Introduction of particulate matter to patient intravenously may result in serious adverse events resulting in severity rating	**10**	Multiple vials required resulting in multiple instances of septum being punctured by needle.	GS-US-586-6144 *Pharmacy Manual* (v 8.0) section 4.6.2 step 8, "Exchange needle as needed"	Per SOP-05362 *Quality and Compliance Risk Management* (v 5.0) Table 2: Probability of Occurrence Rating Scale: Occasional non-routine manual process interventions are in place as the needle may be changed as needed, however it is not required.	**5**	Per GS-US-586-6144 *Pharmacy Manual* (v 8.0) section 4.6.2 step 9, infusion bag is inspected for discoloration or foreign particulate prior to use. Discovery of discoloration or foreign particulate are reported via FRM-06432 Investigational Medicinal Product (IMP) Complaint Form	Per SOP-05362 *Quality and Compliance Risk Management* (v 5.0) Table 3: Probability of Detection Rating Scale: There is a manual inspection of the failure and there is a high probability that the failure will be detected within the step.	**3**	**150**	**Action Item:** Update to GS-US-586-6144 *Pharmacy Manual* to instruct on change of needle after each addition of drug to infusion bag.

PID	Process Step	Failure Mode	Effect of Failure	Rationale for S	Severity (S)	Cause of Failure	Controls	Rationale for O	Occurrence (O)	Monitoring Plan	Rationale for D	Detectability (D)	RPN	Comments / Action Items
28	Dosage preparation for high concentration of drug product (30–60 mg/kg)	Introduction of particulate matter (Infusion bag septum material) in the drug infusion solution.	Particulate matter (infusion bag septum material) introduced to patient intravenously resulting in a serious adverse event.	Per SOP-05362 *Quality and Compliance Risk Management* (v 5.0) Table 1: Severity Rating Scale: Introduction of particulate matter to patient intravenously may result in serious adverse events resulting in severity rating	**10**	Multiple introductions of drug product into the same infusion bag required.	GS-US-586-6144 *Pharmacy Manual* (v 8.0) section 4.6.2 step 8, "Exchange needle as needed"	Per SOP-05362 *Quality and Compliance Risk Management* (v 5.0) Table 2: Probability of Occurrence Rating Scale: Occasional non-routine manual process interventions are in place as the needle may be changed as needed, however it is not required.	**5**	Per GS-US-586-6144 *Pharmacy Manual* (v 8.0) section 4.6.2 step 9, infusion bag is inspected for discoloration or foreign particulate prior to use. Discovery of discoloration or foreign particulate are reported via FRM-06432 Investigational Medicinal Product (IMP) Complaint Form	Per SOP-05362 *Quality and Compliance Risk Management* (v 5.0) Table 3: Probability of Detection Rating Scale: There is a manual inspection of the failure and there is a high probability that the failure will be detected within the step.	**3**	**150**	**Action Item:** Update to GS-US-586-6144 *Pharmacy Manual* to instruct on change of needle after each addition of drug to infusion bag.
29		Introduction of particulate matter (vial or Infusion bag septum material) in the drug infusion solution.	Particulate matter (vial infusion bag septum material) introduced to patient intravenously resulting in a serious adverse event.	Per SOP-05362 *Quality and Compliance Risk Management* (v 5.0) Table 1: Severity Rating Scale: Introduction of particulate matter to patient intravenously may result in serious adverse events resulting in severity rating	**10**	Dulling of syringe needle as a result of multiple septum puncture instances.	GS-US-586-6144 *Pharmacy Manual* (v 8.0) section 4.6.2 step 8, "Exchange needle as needed"	Per SOP-05362 *Quality and Compliance Risk Management* (v 5.0) Table 2: Probability of Occurrence Rating Scale: Occasional non-routine manual process interventions are in place as the needle may be changed as needed, however it is not required.	**5**	Per GS-US-586-6144 *Pharmacy Manual* (v 8.0) section 4.6.2 step 9, infusion bag is inspected for discoloration or foreign particulate prior to use. Discovery of discoloration or foreign particulate are reported via FRM-06432 Investigational Medicinal Product (IMP) Complaint Form	Per SOP-05362 *Quality and Compliance Risk Management* (v 5.0) Table 3: Probability of Detection Rating Scale: There is a manual inspection of the failure and there is a high probability that the failure will be detected within the step.	**3**	**150**	**Action Item:** Update to GS-US-586-6144 *Pharmacy Manual* to instruct on change of needle after each addition of drug to infusion bag.
30		Drug addition exhibits shear stress on drug product resulting in formation of particulate matter (protein).	Particulate matter (protein) introduced to patient intravenously resulting adverse event.	Per SOP-05362 *Quality and Compliance Risk Management* (v 5.0) Table 1: Severity Rating Scale: Introduction of particulate matter to patient intravenously may result in serious adverse events resulting in severity rating	**10**	Use of needle bore size smaller than 19G.	GS-US-586-6144 *Pharmacy Manual* (v 8.0) section 4.6.2 step 8, instructs pharmacy to use 19G or larger bore needed	Per SOP-05362 *Quality and Compliance Risk Management* (v 5.0) Table 2: Probability of Occurrence Rating Scale: Effective routine manual process interventions and/or preventative controls are in place through procedural controls.	**3**	Per GS-US-586-6144 *Pharmacy Manual* (v 8.0) section 4.6.2 step 9, infusion bag is inspected for discoloration or foreign particulate prior to use. Discovery of discoloration or foreign particulate are reported via FRM-06432 Investigational Medicinal Product (IMP) Complaint Form	Per SOP-05362 *Quality and Compliance Risk Management* (v 5.0) Table 3: Probability of Detection Rating Scale: There is a manual inspection of the failure and there is a high probability that the failure will be detected within the step.	**3**	**90**	Risk is acceptable as is and no additional actions will be taken. There are currently effective controls and detection mechanisms in place to reduce the risk at the clinical facility.
31			Particulate matter (protein) in drug product. Reduction of drug efficacy.	Per SOP-05362 *Quality and Compliance Risk Management* (v 5.0) Table 1: Severity Rating Scale: Loss of product efficacy or product quality leading to adverse events.	**7**	Use of needle bore size smaller than 19G.	GS-US-586-6144 *Pharmacy Manual* (v 8.0) section 4.6.2 step 8, instructs pharmacy to use 19G or larger bore needed	Per SOP-05362 *Quality and Compliance Risk Management* (v 5.0) Table 2: Probability of Occurrence Rating Scale: Effective routine manual process interventions and/or preventative controls are in place through procedural controls.	**3**	Per GS-US-586-6144 *Pharmacy Manual* (v 8.0) section 4.6.2 step 9, infusion bag is inspected for discoloration or foreign particulate prior to use. Discovery of discoloration or foreign particulate are reported via FRM-06432 Investigational Medicinal Product (IMP) Complaint Form	Per SOP-05362 *Quality and Compliance Risk Management* (v 5.0) Table 3: Probability of Detection Rating Scale: There is a manual inspection of the failure and there is a high probability that the failure will be detected within the step.	**3**	**63**	Risk is acceptable as is and no additional actions will be taken. There are currently effective controls and detection mechanisms in place to reduce the risk at the clinical facility.

PID	Process Step	Failure Mode	Effect of Failure	Rationale for S	Severity (S)	Cause of Failure	Controls	Rationale for O	Occurrence (O)	Monitoring Plan	Rationale for D	Detectability (D)	RPN	Comments / Action Items
32	Dosage preparation for high concentration of drug product (30–60 mg/kg)	Slow introduction of drug product to infusion bag leads to formation of particulate matter (protein).	Particulate matter (protein) introduced to patient intravenously resulting in a serious adverse event.	Per SOP-05362 *Quality and Compliance Risk Management* (v 5.0) Table 1: Severity Rating Scale: Introduction of particulate matter to patient intravenously may result in serious adverse events resulting in severity rating	**10**	Use of needle bore size smaller than 19G.	GS-US-586-6144 *Pharmacy Manual* (v 8.0) section 4.6.2 step 8, instructs pharmacy to use 19G or larger bore needed	Per SOP-05362 *Quality and Compliance Risk Management* (v 5.0) Table 2: Probability of Occurrence Rating Scale: Effective routine manual process interventions and/or preventative controls are in place through procedural controls.	**3**	Per GS-US-586-6144 *Pharmacy Manual* (v 8.0) section 4.6.2 step 9, infusion bag is inspected for discoloration or foreign particulate prior to use. Discovery of discoloration or foreign particulate are reported via FRM-06432 Investigational Medicinal Product (IMP) Complaint Form	Per SOP-05362 *Quality and Compliance Risk Management* (v 5.0) Table 3: Probability of Detection Rating Scale: There is a manual inspection of the failure and there is a high probability that the failure will be detected within the step.	**3**	**90**	Risk is acceptable as is and no additional actions will be taken. There are currently effective controls and detection mechanisms in place to reduce the risk at the clinical facility.
33			Particulate matter (protein) in drug product. Reduction of drug efficacy.	Per SOP-05362 *Quality and Compliance Risk Management* (v 5.0) Table 1: Severity Rating Scale: Loss of product efficacy or product quality leading to adverse events.	**7**	Use of needle bore size smaller than 19G.	GS-US-586-6144 *Pharmacy Manual* (v 8.0) section 4.6.2 step 8, instructs pharmacy to use 19G or larger bore needed	Per SOP-05362 *Quality and Compliance Risk Management* (v 5.0) Table 2: Probability of Occurrence Rating Scale: Effective routine manual process interventions and/or preventative controls are in place through procedural controls.	**3**	Per GS-US-586-6144 *Pharmacy Manual* (v 8.0) section 4.6.2 step 9, infusion bag is inspected for discoloration or foreign particulate prior to use. Discovery of discoloration or foreign particulate are reported via FRM-06432 Investigational Medicinal Product (IMP) Complaint Form	Per SOP-05362 *Quality and Compliance Risk Management* (v 5.0) Table 3: Probability of Detection Rating Scale: There is a manual inspection of the failure and there is a high probability that the failure will be detected within the step.	**3**	**63**	Risk is acceptable as is and no additional actions will be taken. There are currently effective controls and detection mechanisms in place to reduce the risk at the clinical facility.
34		Low concentration of drug product exhibited during multiple vial addition preparation resulting in formation of particulate matter (protein)	Particulate matter (protein) introduced to patient intravenously resulting in a serious adverse event.	Per SOP-05362 *Quality and Compliance Risk Management* (v 5.0) Table 1: Severity Rating Scale: Introduction of particulate matter to patient intravenously may result in serious adverse events resulting in severity rating	**10**	Pharmacy adds lowest volume of drug product to infusion bag first during multiple vial addition preparation.	No current instruction on the controls.	Per SOP-05362 *Quality and Compliance Risk Management* (v 5.0) Table 2: Probability of Occurrence Rating Scale: No preventative controls are in place. Volume addition of the lowest volume for multiple vial additions is almost certain to occur as part of normal operations.	**10**	Per GS-US-586-6144 *Pharmacy Manual* (v 8.0) section 4.6.2 step 9, infusion bag is inspected for discoloration or foreign particulate prior to use. Discovery of discoloration or foreign particulate are reported via FRM-06432 Investigational Medicinal Product (IMP) Complaint Form	Per SOP-05362 *Quality and Compliance Risk Management* (v 5.0) Table 3: Probability of Detection Rating Scale: There is a manual inspection of the failure and there is a high probability that the failure will be detected within the step.	**3**	**300**	**Action Item:** Update to GS-US-586-6144 *Pharmacy Manual* to instruct on order of addition for multiple drug additions to avoid lowest addition first for high dose preparation.
35			Particulate matter (protein) in drug product. Reduction of drug efficacy.	Per SOP-05362 *Quality and Compliance Risk Management* (v 5.0) Table 1: Severity Rating Scale: Loss of product efficacy or product quality leading to adverse events.	**7**	Pharmacy adds lowest volume of drug product to infusion bag first during multiple vial addition preparation.	No current instruction on the controls.	Per SOP-05362 *Quality and Compliance Risk Management* (v 5.0) Table 2: Probability of Occurrence Rating Scale: No preventative controls are in place. Volume addition of the lowest volume for multiple vial additions is almost certain to occur as part of normal operations.	**10**	Per GS-US-586-6144 *Pharmacy Manual* (v 8.0) section 4.6.2 step 9, infusion bag is inspected for discoloration or foreign particulate prior to use. Discovery of discoloration or foreign particulate are reported via FRM-06432 Investigational Medicinal Product (IMP) Complaint Form	Per SOP-05362 *Quality and Compliance Risk Management* (v 5.0) Table 3: Probability of Detection Rating Scale: There is a manual inspection of the failure and there is a high probability that the failure will be detected within the step.	**3**	**210**	**Action Item:** Update to GS-US-586-6144 *Pharmacy Manual* to instruct on order of addition for multiple drug additions to avoid lowest addition first for high dose preparation.

PID	Process Step	Failure Mode	Effect of Failure	Rationale for S	Severity (S)	Cause of Failure	Controls	Rationale for O	Occurrence (O)	Monitoring Plan	Rationale for D	Detectability (D)	RPN	Comments / Action Items
36	Select materials for preparation of IMP and administration of IMP that are compatible with Magrolimab per *Pharmacy Manual*.	Excessive headspace in infusion bag heads to formation of particulate matter (protein)	Particulate matter (protein) introduced to patient intravenously resulting in a serious adverse event.	Per SOP-05362 *Quality and Compliance Risk Management* (v 5.0) Table 1: Severity Rating Scale: Introduction of particulate matter to patient intravenously may result in serious adverse events resulting in severity rating	**10**	Drug-infusion solution prepared in bag that is too large.	GS-US-586-6144 *Pharmacy Manual* (v 8.0) section 4.7 provides instruction on appropriate infusion bag size of 250 mL or 500 mL.	Per SOP-05362 *Quality and Compliance Risk Management* (v 5.0) Table 2: Probability of Occurrence Rating Scale: Effective routine manual process interventions and/or preventative controls are in place through procedural controls.	**3**	Per GS-US-586-6144 *Pharmacy Manual* (v 8.0) section 4.6.2 step 9, infusion bag is inspected for discoloration or foreign particulate prior to use. Discovery of discoloration or foreign particulate are reported via FRM-06432 Investigational Medicinal Product (IMP) Complaint Form	Per SOP-05362 *Quality and Compliance Risk Management* (v 5.0) Table 3: Probability of Detection Rating Scale: There is a manual inspection of the failure and there is a high probability that the failure will be detected within the step.	**3**	**90**	Risk is acceptable as is and no additional actions will be taken. There are currently effective controls and detection mechanisms in place to reduce the risk at the clinical facility.
37			Particulate matter (protein) in drug product. Reduction of drug efficacy.	Per SOP-05362 *Quality and Compliance Risk Management* (v 5.0) Table 1: Severity Rating Scale: Loss of product efficacy or product quality leading to adverse events.	**7**	Drug-infusion solution prepared in bag that is too large.	GS-US-586-6144 *Pharmacy Manual* (v 8.0) section 4.7 provides instruction on appropriate infusion bag size of 250 mL or 500 mL.	Per SOP-05362 *Quality and Compliance Risk Management* (v 5.0) Table 2: Probability of Occurrence Rating Scale: Effective routine manual process interventions and/or preventative controls are in place through procedural controls.	**3**	Per GS-US-586-6144 *Pharmacy Manual* (v 8.0) section 4.6.2 step 9, infusion bag is inspected for discoloration or foreign particulate prior to use. Discovery of discoloration or foreign particulate are reported via FRM-06432 Investigational Medicinal Product (IMP) Complaint Form	Per SOP-05362 *Quality and Compliance Risk Management* (v 5.0) Table 3: Probability of Detection Rating Scale: There is a manual inspection of the failure and there is a high probability that the failure will be detected within the step.	**3**	**63**	Risk is acceptable as is and no additional actions will be taken. There are currently effective controls and detection mechanisms in place to reduce the risk at the clinical facility.
38		Component interaction with drug-infusion solution leads to formation of particulate matter (Intrinsic/Extrinsic)	Particulate matter (intrinsic/extrinsic) introduced to patient intravenously resulting in serious adverse event.	Per SOP-05362 *Quality and Compliance Risk Management* (v 5.0) Table 1: Severity Rating Scale: Introduction of particulate matter to patient intravenously may result in serious adverse events resulting in severity rating	**10**	Use of incompatible component during preparation and/or administration.	GS-US-586-6144 *Pharmacy Manual* (v 8.0) section 4.6.1 provides compatibility information for Magrolimab and infusion bag and administration components.	Per SOP-05362 *Quality and Compliance Risk Management* (v 5.0) Table 2: Probability of Occurrence Rating Scale: Effective routine manual process interventions and/or preventative controls are in place through procedural controls.	**3**	Per GS-US-586-6144 *Pharmacy Manual* (v 8.0) section 4.6.2 step 9, infusion bag is inspected for discoloration or foreign particulate prior to use. Discovery of discoloration or foreign particulate are reported via FRM-06432 Investigational Medicinal Product (IMP) Complaint Form Clinical practices are routinely reviewed by CRA/Monitor to ensure compliance with GS-US-586-6144 *Pharmacy Manual*. Review is inclusive of use of compatible materials and documented in CTMS.	Per SOP-05362 *Quality and Compliance Risk Management* (v 5.0) Table 3: Probability of Detection Rating Scale: There is a manual inspection of the failure and there is a high probability that the failure will be detected within the step.	**3**	**90**	Risk is acceptable as is and no additional actions will be taken. There are currently effective controls and detection mechanisms in place to reduce the risk at the clinical facility.
39		Component interaction with drug-infusion solution leads to formation of particulate matter (Intrinsic/Extrinsic)	Presence of Particulate Matter (intrinsic/extrinsic) in components. Particulate Matter introduced to patient intravenously resulting in a serious adverse event.	Per SOP-05362 *Quality and Compliance Risk Management* (v 5.0) Table 1: Severity Rating Scale: Introduction of particulate matter to patient intravenously may result in serious adverse events resulting in severity rating	**10**	Use of poor quality component during preparation and/or administration.	GS-US-586-6144 *Pharmacy Manual* (v 8.0) section 4.6.1 provides compatibility information for Magrolimab and infusion bag and administration components.	Per SOP-05362 *Quality and Compliance Risk Management* (v 5.0) Table 2: Probability of Occurrence Rating Scale: Effective routine manual process interventions and/or preventative controls are in place through procedural controls.	**3**	Per GS-US-586-6144 *Pharmacy Manual* (v 8.0) section 4.6.2 step 9, infusion bag is inspected for discoloration or foreign particulate prior to use. Discovery of discoloration or foreign particulate are reported via FRM-06432 Investigational Medicinal Product (IMP) Complaint Form Clinical practices are routinely reviewed by CRA/Monitor to ensure compliance with GS-US-586-6144 *Pharmacy Manual*. Review is inclusive of use of compatible materials and documented in CTMS.	Per SOP-05362 *Quality and Compliance Risk Management* (v 5.0) Table 3: Probability of Detection Rating Scale: There is a manual inspection of the failure and there is a high probability that the failure will be detected within the step.	**3**	**90**	Risk is acceptable as is and no additional actions will be taken. There are currently effective controls and detection mechanisms in place to reduce the risk at the clinical facility.

PID	Process Step	Failure Mode	Effect of Failure	Rationale for S	Severity (S)	Cause of Failure	Controls	Rationale for O	Occurrence (O)	Monitoring Plan	Rationale for D	Detectability (D)	RPN	Comments / Action Items
40	Equilibration of drug product vials to room temperature prior to preparation of drug infusion solution.	Formation of particulate matter (protein) in the drug-infusion solution.	Particulate matter (protein) introduced to patient intravenously resulting in a serious adverse event.	Per SOP-05362 *Quality and Compliance Risk Management* (v 5.0) Table 1: Severity Rating Scale: Introduction of particulate matter to patient intravenously may result in serious adverse events resulting in severity rating	**10**	Vial is not allowed to equilibrate to room temperature prior to preparation of drug-infusion solution.	No current controls are in place.	Per SOP-05362 *Quality and Compliance Risk Management* (v 5.0) Table 2: Probability of Occurrence Rating Scale: No preventative controls are in place. There is no guidance provided to pharmacy to allow for vial to equilibrate to room temperature prior to preparation of drug-infusion solution.	**10**	Per GS-US-586-6144 *Pharmacy Manual* (v 8.0) section 4.6.2 step 9, infusion bag is inspected for discoloration or foreign particulate prior to use. Discovery of discoloration or foreign particulate are reported via FRM-06432 Investigational Medicinal Product (IMP) Complaint Form	Per SOP-05362 *Quality and Compliance Risk Management* (v 5.0) Table 3: Probability of Detection Rating Scale: There is a manual inspection of the failure and there is a high probability that the failure will be detected within the step.	**3**	**300**	**Action Item:** Update to GS-US-586-6144 *Pharmacy Manual* to instruct on allowing drug product vial to allow for equilibration to room temperature before preparation of drug infusion solution.
41			Particulate matter (protein) in drug product. Reduction of drug efficacy.	Per SOP-05362 *Quality and Compliance Risk Management* (v 5.0) Table 1: Severity Rating Scale: Loss of product efficacy or product quality leading to adverse events.	**7**	Vial is not allowed to equilibrate to room temperature prior to preparation of drug-infusion solution.	No current controls are in place.	Per SOP-05362 *Quality and Compliance Risk Management* (v 5.0) Table 2: Probability of Occurrence Rating Scale: No preventative controls are in place. There is no guidance provided to pharmacy to allow for vial to equilibrate to room temperature prior to preparation of drug-infusion solution.	**10**	Per GS-US-586-6144 *Pharmacy Manual* (v 8.0) section 4.6.2 step 9, infusion bag is inspected for discoloration or foreign particulate prior to use. Discovery of discoloration or foreign particulate are reported via FRM-06432 Investigational Medicinal Product (IMP) Complaint Form	Per SOP-05362 *Quality and Compliance Risk Management* (v 5.0) Table 3: Probability of Detection Rating Scale: There is a manual inspection of the failure and there is a high probability that the failure will be detected within the step.	**3**	**210**	**Action Item:** Update to GS-US-586-6144 *Pharmacy Manual* to instruct on allowing drug product vial to allow for equilibration to room temperature before preparation of drug infusion solution.
42	**Empty IV Bag:** Preparation of a saline solution using an empty bag.	Introduction of Particulate Matter (Intrinsic/Extrinsic) during filling of infusion and drug product solution in the bag.	Particulate matter (intrinsic/extrinsic) introduced to patient intravenously resulting in serious adverse event.	Per SOP-05362 *Quality and Compliance Risk Management* (v 5.0) Table 1: Severity Rating Scale: Introduction of particulate matter to patient intravenously may result in serious adverse events resulting in severity rating	**10**	Particulate Matter introduced from environment pharmacy personnel.	GS-US-586-6144 *Pharmacy Manual* (v 8.0) section 4.4 step 2 provides instruction to use aseptic technique throughout the preparation process.	Per SOP-05362 *Quality and Compliance Risk Management* (v 5.0) Table 2: Probability of Occurrence Rating Scale: Effective routine manual process interventions and/or preventative controls are in place through procedural controls.	**3**	Per GS-US-586-6144 *Pharmacy Manual* (v 8.0) section 4.6.2 step 9, infusion bag is inspected for discoloration or foreign particulate prior to use. Discovery of discoloration or foreign particulate are reported via FRM-06432 Investigational Medicinal Product (IMP) Complaint Form	Per SOP-05362 *Quality and Compliance Risk Management* (v 5.0) Table 3: Probability of Detection Rating Scale: There is a manual inspection of the failure and there is a high probability that the failure will be detected within the step.	**3**	**90**	Risk is acceptable as is and no additional actions will be taken. There are currently effective controls and detection mechanisms in place to reduce the risk at the clinical facility.
43		Introduction of Particulate Matter (Intrinsic/Extrinsic) during filling of infusion and drug product solution in the bag.	Particulate matter (intrinsic/extrinsic) introduced to patient intravenously resulting in serious adverse event.	Per SOP-05362 *Quality and Compliance Risk Management* (v 5.0) Table 1: Severity Rating Scale: Introduction of particulate matter to patient intravenously may result in serious adverse events resulting in severity rating	**10**	Particulate Matter present in the empty bag prior to filling.	No current controls in place.	Per SOP-05362 *Quality and Compliance Risk Management* (v 5.0) Table 2: Probability of Occurrence Rating Scale: No preventative controls are in place. There is no guidance to inspect empty infusion bag for particulate matter prior to preparation of drug-infusion solution.	**10**	Per GS-US-586-6144 *Pharmacy Manual* (v 8.0) section 4.6.2 step 9, infusion bag is inspected for discoloration or foreign particulate prior to use. Discovery of discoloration or foreign particulate are reported via FRM-06432 Investigational Medicinal Product (IMP) Complaint Form	Per SOP-05362 *Quality and Compliance Risk Management* (v 5.0) Table 3: Probability of Detection Rating Scale: There is a manual inspection of the failure and there is a high probability that the failure will be detected within the step.	**3**	**300**	**Action Item:** Update to GS-US-586-6144 *Pharmacy Manual* for preparation and instruct on inspection of empty bag prior to preparation of drug infusion solution.

PID	Process Step	Failure Mode	Effect of Failure	Rationale for S	Severity (S)	Cause of Failure	Controls	Rationale for O	Occurrence (O)	Monitoring Plan	Rationale for D	Detectability (D)	RPN	Comments / Action Items
44	Remove the plastic cap from the Magrolimab vial(s) and swab the top(s) with alcohol pads.	Introduction of particulate matter (alcohol swab debris) into the drug infusion solution	Particulate matter (intrinsic/extrinsic) introduced to patient intravenously resulting in serious adverse event.	Per SOP-05362 *Quality and Compliance Risk Management* (v 5.0) Table 1: Severity Rating Scale: Introduction of particulate matter to patient intravenously may result in serious adverse events resulting in severity rating	**10**	Alcohol swab debris present on drug product septum introduced to drug infusion solution.	No controls in place to prevent.	Per SOP-05362 *Quality and Compliance Risk Management* (v 5.0) Table 2: Probability of Occurrence Rating Scale: No preventative controls are in place. There is no guidance to inspect vial septum for alcohol swab debris prior to puncturing the septum with the syringe.	**10**	Per GS-US-586-6144 *Pharmacy Manual* (v 8.0) section 4.6.2 step 9, infusion bag is inspected for discoloration or foreign particulate prior to use. Discovery of discoloration or foreign particulate are reported via FRM-06432 Investigational Medicinal Product (IMP) Complaint Form	Per SOP-05362 *Quality and Compliance Risk Management* (v 5.0) Table 3: Probability of Detection Rating Scale: There is a manual inspection of the failure and there is a high probability that the failure will be detected within the step.	**3**	**300**	**Action Item:** Update to GS-US-586-6144 *Pharmacy Manual* to instruct on ensuring no debris present on septum after cleaning with an alcohol wipe.
45		Formation of particulate matter (protein) in the drug-infusion solution.	Particulate matter (protein) introduced to patient intravenously resulting in a serious adverse event.	Per SOP-05362 *Quality and Compliance Risk Management* (v 5.0) Table 1: Severity Rating Scale: Introduction of particulate matter to patient intravenously may result in serious adverse events resulting in severity rating	**10**	Alcohol present on from cleaning septum introduced into drug product vial.	No current control in place.	Per SOP-05362 *Quality and Compliance Risk Management* (v 5.0) Table 2: Probability of Occurrence Rating Scale: No preventative controls are in place. There is no guidance to ensure alcohol is dried prior to puncturing the septum with the syringe.	**10**	Per GS-US-586-6144 *Pharmacy Manual* (v 8.0) section 4.6.2 step 9, infusion bag is inspected for discoloration or foreign particulate prior to use. Discovery of discoloration or foreign particulate are reported via FRM-06432 Investigational Medicinal Product (IMP) Complaint Form	Per SOP-05362 *Quality and Compliance Risk Management* (v 5.0) Table 3: Probability of Detection Rating Scale: There is a manual inspection of the failure and there is a high probability that the failure will be detected within the step.	**3**	**300**	**Action Item:** Update to GS-US-586-6144 *Pharmacy Manual* to ensure alcohol is dried prior to puncturing the vial septum with the needle.
46			Particulate matter (protein) in drug product. Reduction of drug efficacy.	Per SOP-05362 *Quality and Compliance Risk Management* (v 5.0) Table 1: Severity Rating Scale: Loss of product efficacy or product quality leading to adverse events.	**7**	Alcohol present on from cleaning septum introduced into drug product vial.	No current control in place.	Per SOP-05362 *Quality and Compliance Risk Management* (v 5.0) Table 2: Probability of Occurrence Rating Scale: No preventative controls are in place. There is no guidance to ensure alcohol is dried prior to puncturing the septum with the syringe.	**10**	Per GS-US-586-6144 *Pharmacy Manual* (v 8.0) section 4.6.2 step 9, infusion bag is inspected for discoloration or foreign particulate prior to use. Discovery of discoloration or foreign particulate are reported via FRM-06432 Investigational Medicinal Product (IMP) Complaint Form	Per SOP-05362 *Quality and Compliance Risk Management* (v 5.0) Table 3: Probability of Detection Rating Scale: There is a manual inspection of the failure and there is a high probability that the failure will be detected within the step.	**3**	**210**	**Action Item:** Update to GS-US-586-6144 *Pharmacy Manual* to ensure alcohol is dried prior to puncturing the vial septum with the needle.
47	Record the start time of preparation (when Magrolimab vials are initially pierced)	Drug product subjected to elevated temperatures above recommended storage conditions of 2–8 °C.	Formation of particulate matter (protein) in drug product. Particulate matter introduced to patient intravenously resulting in serious adverse event.	Per SOP-05362 *Quality and Compliance Risk Management* (v 5.0) Table 1: Severity Rating Scale: Introduction of particulate matter to patient intravenously may result in serious adverse events resulting in severity rating	**10**	Start time of preparation not documented or duration of preparation takes longer than allowed.	GS-US-586-6144 *Pharmacy Manual* (v 8.0) section 4.6.2 step 10, instructs on allowable durations to hold drug infusion solution for refrigerated and room temperatures prior to administration.	Per SOP-05362 *Quality and Compliance Risk Management* (v 5.0) Table 2: Probability of Occurrence Rating Scale: Effective routine manual process interventions and/or preventative controls are in place through procedural controls.	**3**	Clinical facility documents preparation time (dosing preparation worksheet) and time of administration (subject accountability log). CRA reviews worksheets to ensure they align with GS-US-586-6144 *Pharmacy Manual* (v 8.0) requirements. Protocol deviation initiated if not followed.	Per SOP-05362 *Quality and Compliance Risk Management* (v 5.0) Table 3: Probability of Detection Rating Scale: There is a manual inspection of the failure and there is a high probability that the failure will be detected within the step.	**3**	**90**	Risk is acceptable as is and no additional actions will be taken. There are currently effective controls and detection mechanisms in place to reduce the risk at the clinical facility.

PID	Process Step	Failure Mode	Effect of Failure	Rationale for S	Severity (S)	Cause of Failure	Controls	Rationale for O	Occurrence (O)	Monitoring Plan	Rationale for D	Detectability (D)	RPN	Comments / Action Items
48	Record the start time of preparation (when Magrolimab vials are initially pierced)	Drug product subjected to elevated temperatures above recommended storage conditions of 2–8 °C.	Formation of particulate matter (protein) in drug product. Reduction of drug efficacy.	Per SOP-05362 *Quality and Compliance Risk Management* (v 5.0) Table 1: Severity Rating Scale: Introduction of particulate matter to patient intravenously may result in serious adverse events resulting in severity rating	**7**	Start time of preparation not documented or duration of preparation takes longer than allowed.	GS-US-586-6144 *Pharmacy Manual* (v 8.0) section 4.6.2 step 10, instructs on allowable durations to hold drug infusion solution for refrigerated and room temperatures prior to administration.	Per SOP-05362 *Quality and Compliance Risk Management* (v 5.0) Table 2: Probability of Occurrence Rating Scale: Effective routine manual process interventions and/or preventative controls are in place through procedural controls.	**3**	Clinical facility documents preparation time (dosing preparation worksheet) and time of administration (subject accountability log). CRA reviews worksheets to ensure they align with GS-US-586-6144 *Pharmacy Manual* (v 8.0) requirements. Protocol deviation initiated if not followed.	Per SOP-05362 *Quality and Compliance Risk Management* (v 5.0) Table 3: Probability of Detection Rating Scale: There is a manual inspection of the failure and there is a high probability that the failure will be detected within the step.	**3**	**63**	Risk is acceptable as is and no additional actions will be taken. There are currently effective controls and detection mechanisms in place to reduce the risk at the clinical facility.
49	Slowly add the dose volume of Magrolimab solution to the infusion bag. Slowly and gently invert the bag 3-6 times to mix.Avoid creating foam and bubbles.	Formation of particulate matter (protein) in the drug-infusion solution.	Particulate matter (protein) introduced to patient intravenously resulting in a serious adverse event.	Per SOP-05362 *Quality and Compliance Risk Management* (v 5.0) Table 1: Severity Rating Scale: Introduction of particulate matter to patient intravenously may result in serious adverse events resulting in severity rating	**10**	Harsh mixing of drug infusion solution.	GS-US-586-6144 *Pharmacy Manual* (v 8.0) section 4.6.2 step 9, instructs to slowly and gently invert bag 4-6 times to mix.	Per SOP-05362 *Quality and Compliance Risk Management* (v 5.0) Table 2: Probability of Occurrence Rating Scale: Effective routine manual process interventions and/or preventative controls are in place through procedural controls.	**3**	Per GS-US-586-6144 *Pharmacy Manual* (v 8.0) section 4.6.2 step 9, infusion bag is inspected for discoloration or foreign particulate prior to use. Discovery of discoloration or foreign particulate are reported via FRM-06432 Investigational Medicinal Product (IMP) Complaint Form	Per SOP-05362 *Quality and Compliance Risk Management* (v 5.0) Table 3: Probability of Detection Rating Scale: There is a manual inspection of the failure and there is a high probability that the failure will be detected within the step.	**3**	**90**	Risk is acceptable as is and no additional actions will be taken. There are currently effective controls and detection mechanisms in place to reduce the risk at the clinical facility.
50			Formation of particulate matter (protein) in drug product. Reduction of drug efficacy.	Per SOP-05362 *Quality and Compliance Risk Management* (v 5.0) Table 1: Severity Rating Scale: Loss of product efficacy or product quality leading to adverse events.	**7**	Harsh mixing of drug infusion solution.	GS-US-586-6144 *Pharmacy Manual* (v 8.0) section 4.6.2 step 9, instructs to slowly and gently invert bag 4-6 times to mix.	Per SOP-05362 *Quality and Compliance Risk Management* (v 5.0) Table 2: Probability of Occurrence Rating Scale: Effective routine manual process interventions and/or preventative controls are in place through procedural controls.	**3**	Per GS-US-586-6144 *Pharmacy Manual* (v 8.0) section 4.6.2 step 9, infusion bag is inspected for discoloration or foreign particulate prior to use. Discovery of discoloration or foreign particulate are reported via FRM-06432 Investigational Medicinal Product (IMP) Complaint Form	Per SOP-05362 *Quality and Compliance Risk Management* (v 5.0) Table 3: Probability of Detection Rating Scale: There is a manual inspection of the failure and there is a high probability that the failure will be detected within the step.	**3**	**63**	Risk is acceptable as is and no additional actions will be taken. There are currently effective controls and detection mechanisms in place to reduce the risk at the clinical facility.
51		Formation of particulate matter (protein) in the drug-infusion solution.	Particulate matter (protein) introduced to patient intravenously resulting in a serious adverse event.	Per SOP-05362 *Quality and Compliance Risk Management* (v 5.0) Table 1: Severity Rating Scale: Introduction of particulate matter to patient intravenously may result in serious adverse events resulting in severity rating	**10**	Inadequate mixing of drug-infusion solution leading to formation of particulate matter (protein)	GS-US-586-6144 *Pharmacy Manual* (v 8.0) section 4.6.2 step 9, instructs to slowly and gently invert bag 4-6 times to mix.	Per SOP-05362 *Quality and Compliance Risk Management* (v 5.0) Table 2: Probability of Occurrence Rating Scale: Effective routine manual process interventions and/or preventative controls are in place through procedural controls.	**3**	Per GS-US-586-6144 *Pharmacy Manual* (v 8.0) section 4.6.2 step 9, infusion bag is inspected for discoloration or foreign particulate prior to use. Discovery of discoloration or foreign particulate are reported via FRM-06432 Investigational Medicinal Product (IMP) Complaint Form	Per SOP-05362 *Quality and Compliance Risk Management* (v 5.0) Table 3: Probability of Detection Rating Scale: There is a manual inspection of the failure and there is a high probability that the failure will be detected within the step.	**3**	**90**	Risk is acceptable as is and no additional actions will be taken. There are currently effective controls and detection mechanisms in place to reduce the risk at the clinical facility.
52			Formation of particulate matter (protein) in drug product. Reduction of drug efficacy.	Per SOP-05362 *Quality and Compliance Risk Management* (v 5.0) Table 1: Severity Rating Scale: Loss of product efficacy or product quality leading to adverse events.	**7**	Inadequate mixing of drug-infusion solution leading to formation of particulate matter (protein)	GS-US-586-6144 *Pharmacy Manual* (v 8.0) section 4.6.2 step 9, instructs to slowly and gently invert bag 4-6 times to mix.	Per SOP-05362 *Quality and Compliance Risk Management* (v 5.0) Table 2: Probability of Occurrence Rating Scale: Effective routine manual process interventions and/or preventative controls are in place through procedural controls.	**3**	Per GS-US-586-6144 *Pharmacy Manual* (v 8.0) section 4.6.2 step 9, infusion bag is inspected for discoloration or foreign particulate prior to use. Discovery of discoloration or foreign particulate are reported via FRM-06432 Investigational Medicinal Product (IMP) Complaint Form	Per SOP-05362 *Quality and Compliance Risk Management* (v 5.0) Table 3: Probability of Detection Rating Scale: There is a manual inspection of the failure and there is a high probability that the failure will be detected within the step.	**3**	**63**	Risk is acceptable as is and no additional actions will be taken. There are currently effective controls and detection mechanisms in place to reduce the risk at the clinical facility.

PID	Process Step	Failure Mode	Effect of Failure	Rationale for S	Severity (S)	Cause of Failure	Controls	Rationale for O	Occurrence (O)	Monitoring Plan	Rationale for D	Detectability (D)	RPN	Comments / Action Items
53	Drug infusion mixture can be stored in refrigerated conditions for up to 16 hours or stored at room temperature for 8 hours.	Formation of particulate matter (protein) in the drug-infusion solution.	Particulate matter (protein) introduced to patient intravenously resulting in a serious adverse event.	Per SOP-05362 *Quality and Compliance Risk Management* (v 5.0) Table 1: Severity Rating Scale: Introduction of particulate matter to patient intravenously may result in serious adverse events resulting in severity rating	**10**	Drug infusion mixture stored beyond allowable timeframe for beyond recommended storage conditions	GS-US-586-6144 *Pharmacy Manual* (v 8.0) section 4.6.2 step 10, states that drug infusion solution can be stored refrigerated 2–8 °C for up to 16 hours, room temperature for up to 8 hours.	Per SOP-05362 *Quality and Compliance Risk Management* (v 5.0) Table 2: Probability of Occurrence Rating Scale: Effective routine manual process interventions and/or preventative controls are in place through procedural controls.	**3**	No current requirement to perform visual inspection after refrigerating the solution in the bag.	Per SOP-05362 *Quality and Compliance Risk Management* (v 5.0) Table 3: Probability of Detection Rating Scale: There is no established inspection, testing, or monitoring in place to detect the failure.	**10**	**300**	**Action Item:** Update to GS-US-586-6144 *Pharmacy Manual* to perform visual inspection on drug infusion solution immediately prior to administration to patient.
54			Formation of particulate matter (protein) in drug product. Reduction of drug efficacy.	Per SOP-05362 *Quality and Compliance Risk Management* (v 5.0) Table 1: Severity Rating Scale: Loss of product efficacy or product quality leading to adverse events.	**7**	Drug infusion mixture stored beyond allowable timeframe for beyond recommended storage conditions	GS-US-586-6144 *Pharmacy Manual* (v 8.0) section 4.6.2 step 10, states that drug infusion solution can be stored refrigerated 2–8 °C for up to 16 hours, room temperature for up to 8 hours.	Per SOP-05362 *Quality and Compliance Risk Management* (v 5.0) Table 2: Probability of Occurrence Rating Scale: Effective routine manual process interventions and/or preventative controls are in place through procedural controls.	**3**	No current requirement to perform visual inspection after refrigerating the solution in the bag.	Per SOP-05362 *Quality and Compliance Risk Management* (v 5.0) Table 3: Probability of Detection Rating Scale: There is no established inspection, testing, or monitoring in place to detect the failure.	**10**	**210**	**Action Item:** Update to GS-US-586-6144 *Pharmacy Manual* to perform visual inspection on drug infusion solution immediately prior to administration to patient.
55	**If stored at refrigerated temperature**, the prepared drug solution should be equilibrated to room temperature for at least 1 hour.	Formation of particulate matter (protein) in the drug-infusion solution.	Particulate matter (protein) introduced to patient intravenously resulting in a serious adverse event.	Per SOP-05362 *Quality and Compliance Risk Management* (v 5.0) Table 1: Severity Rating Scale: Introduction of particulate matter to patient intravenously may result in serious adverse events resulting in severity rating	**10**	Drug infusion mixture was not allowed to equilibrate for long enough.	GS-US-586-6144 *Pharmacy Manual* (v 8.0) section 4.6.2 step 10, states that drug infusion solution shall be allowed to equilibrate for a minimum of 1 hour prior to administration.	Per SOP-05362 *Quality and Compliance Risk Management* (v 5.0) Table 2: Probability of Occurrence Rating Scale: Effective routine manual process interventions and/or preventative controls are in place through procedural controls.	**3**	No current requirement to perform visual inspection after refrigerating the solution in the bag. No requirement to review documentation of time out of temperature.	Per SOP-05362 *Quality and Compliance Risk Management* (v 5.0) Table 3: Probability of Detection Rating Scale: There is no established inspection, testing, or monitoring in place to detect the failure.	**10**	**300**	**Action Item:** Update to GS-US-586-6144 *Pharmacy Manual* to perform visual inspection on drug infusion solution immediately prior to administration to patient. **Action Item:** Update to GS-US-586-6144 *Pharmacy Manual* to ensure time out of temperature range is documented.
56	**If stored at refrigerated temperature**, the prepared drug solution should be equilibrated to room temperature for at least 1 hour.		Formation of particulate matter (protein) in drug product. Reduction of drug efficacy.	Per SOP-05362 *Quality and Compliance Risk Management* (v 5.0) Table 1: Severity Rating Scale: Loss of product efficacy or product quality leading to adverse events.	**7**	Drug infusion mixture was not allowed to equilibrate for long enough.	GS-US-586-6144 *Pharmacy Manual* (v 8.0) section 4.6.2 step 10, states that drug infusion solution shall be allowed to equilibrate for a minimum of 1 hour prior to administration.	Per SOP-05362 *Quality and Compliance Risk Management* (v 5.0) Table 2: Probability of Occurrence Rating Scale: Effective routine manual process interventions and/or preventative controls are in place through procedural controls.	**3**	No current requirement to perform visual inspection after refrigerating the solution in the bag. No requirement to review documentation of time out of temperature.	Per SOP-05362 *Quality and Compliance Risk Management* (v 5.0) Table 3: Probability of Detection Rating Scale: There is no established inspection, testing, or monitoring in place to detect the failure.	**10**	**210**	**Action Item:** Update to GS-US-586-6144 *Pharmacy Manual* to perform visual inspection on drug infusion solution immediately prior to administration to patient. **Action Item:** Update to GS-US-586-6144 *Pharmacy Manual* to ensure time out of temperature range is documented.

PID	Process Step	Failure Mode	Effect of Failure	Rationale for S	Severity (S)	Cause of Failure	Controls	Rationale for O	Occurrence (O)	Monitoring Plan	Rationale for D	Detectability (D)	RPN	Comments / Action Items
Ref # 4.0	**Transportation of Prepared Magrolimab Infusion Bags**													
57	Infusion bags may be transported, for up to 16 hours at refrigerator temperature (2–8 °C) storage, up to 340 miles by a motor vehicle.	Drug infusions solution subjected to elevated temperatures above recommended storage conditions of 2–8 °C.	Formation of inherent particulate matter in drug infusions solution. Particulate matter introduced to patient intravenously resulting in a serious adverse event.	Per SOP-05362 *Quality and Compliance Risk Management* (v 5.0) Table 1: Severity Rating Scale: Introduction of particulate matter to patient intravenously may result in serious adverse events resulting in severity rating	**10**	Drug infusions solution not stored at recommended temperature of 2–8 °C during transport between clinical facilities.	GS-US-586-6144 *Pharmacy Manual* (v 8.0) section 4.6.4 provides guidance on allowable transportation storage temperatures and distances.	Per SOP-05362 *Quality and Compliance Risk Management* (v 5.0) Table 2: Probability of Occurrence Rating Scale: Effective routine manual process interventions and/or preventative controls are in place through procedural controls.	**3**	No current requirement to perform visual inspection after transporting the solution in the bag.	Per SOP-05362 *Quality and Compliance Risk Management* (v 5.0) Table 3: Probability of Detection Rating Scale: There is no established inspection, testing, or monitoring in place to detect the failure.	**10**	**300**	**Action Item:** Update to GS-US-586-6144 *Pharmacy Manual* to perform visual inspection on drug infusion solution immediately prior to administration to patient.
58			Formation of particulate matter (protein) in drug product. Reduction of drug efficacy.	Per SOP-05362 *Quality and Compliance Risk Management* (v 5.0) Table 1: Severity Rating Scale: Loss of product efficacy or product quality leading to adverse events.	**7**	Drug infusions solution not stored at recommended temperature of 2–8 °C during transport between clinical facilities.	GS-US-586-6144 *Pharmacy Manual* (v 8.0) section 4.6.4 provides guidance on allowable transportation storage temperatures and distances.	Per SOP-05362 *Quality and Compliance Risk Management* (v 5.0) Table 2: Probability of Occurrence Rating Scale: Effective routine manual process interventions and/or preventative controls are in place through procedural controls.	**3**	No current requirement to perform visual inspection after transporting the solution in the bag.	Per SOP-05362 *Quality and Compliance Risk Management* (v 5.0) Table 3: Probability of Detection Rating Scale: There is no established inspection, testing, or monitoring in place to detect the failure.	**10**	**210**	**Action Item:** Update to GS-US-586-6144 *Pharmacy Manual* to perform visual inspection on drug infusion solution immediately prior to administration to patient.

DocuSign

Certificate Of Completion

Envelope Id: CAFF9AC891CE49AEA1CDF1BC12530981 Status: Completed

Subject: Complete with DocuSign: REP-49438 Risk Assessment to Mitigate the Introduction of Intrinsic, Ex...

Source Envelope:

Document Pages: 29 Signatures: 1 Envelope Originator:

Certificate Pages: 1 Initials: 0 Kristie Taber

AutoNav: Enabled 333 Lakeside Dr

EnvelopeId Stamping: Enabled Foster City, CA 94404-1147

Time Zone: (UTC-08:00) Pacific Time (US & Canada) Kristie.Taber@gilead.com

IP Address: 24.206.69.80

Record Tracking

Status: Original Holder: Kristie Taber Location: DocuSign

2/12/2024 1:16:42 PM Kristie.Taber@gilead.com

Signer Events	Signature	Timestamp
Tyler Prater tyler.prater@gilead.com Director, Clinical Operations Security Level: Email, Account Authentication (Required), Login with SSO	 Signature Adoption: Pre-selected Style Signature ID: 198B3D4C-50A6-4F12-B068-D3CBFD0ABBBD Using IP Address: 24.206.84.52 With Signing Authentication via DocuSign password With Signing Reasons (on each tab): I approve this document	Sent: 2/12/2024 1:21:01 PM Viewed: 2/12/2024 3:19:47 PM Signed: 2/12/2024 3:21:03 PM

Electronic Record and Signature Disclosure:
Not Offered via DocuSign

In Person Signer Events	Signature	Timestamp

Editor Delivery Events	Status	Timestamp

Agent Delivery Events	Status	Timestamp

Intermediary Delivery Events	Status	Timestamp

Certified Delivery Events	Status	Timestamp

Carbon Copy Events	Status	Timestamp

Witness Events	Signature	Timestamp

Notary Events	Signature	Timestamp

Envelope Summary Events	Status	Timestamps
Envelope Sent	Hashed/Encrypted	2/12/2024 1:21:01 PM
Certified Delivered	Security Checked	2/12/2024 3:19:47 PM
Signing Complete	Security Checked	2/12/2024 3:21:03 PM
Completed	Security Checked	2/12/2024 3:21:03 PM

Payment Events	Status	Timestamps

Document Approval Information

Document No.: **MEMO-16025** Document Version: **1.0**

Name: **MEMO-16025 MEMO to document REP-48438 Clincal Operations Approval**

Document Type: **Memo**

Document Subtype: **Quality & Compliance**

Classification:

Title: **MEMO to document REP-48438 Clincal Operations Approval**

Approved By | Verdict	Capacity | Date Approved
Kristie Taber, Sr Director, Quality Approve	Author Approval 12-Feb-2024 23:44:18 GMT+0000