

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.

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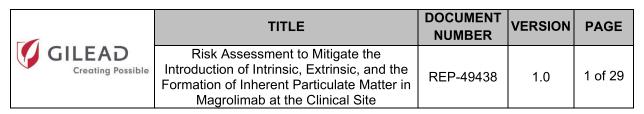


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Clinical Operations Approval

Name	SignatureDocuSigned by Tyler Prater	Date
Tyler Prater	Julia Pratu I approve t	nis document ruary 12, 2024

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Doc. Status Approved

CONFIDENTIAL INFORMATION Document No. MEMO-16025 GVault Ver. No. 1.0 Legacy Doc. No.

Approved Date 12 Feb 2024 **Date Printed** 29 Sep 2025

	TITLE	DOCUMENT NUMBER	VERSION	PAGE
GILEAD Creating Possible	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	2 of 29

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

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Revision	Description of Change	Justification
1.0	New document	New document

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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

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Risk Assessment Team Members					
Area	Name	Title			
Team Lead/Facilitator	Kristie Taber	Sr Director, Quality			
Facilitator	Joseph Rogers	Sr Manager, Quality Systems			
	Jeff Hoinowski	Sr Director, External QA Biologics Development			
Quality Assurance Representative	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			
	Yajie Zhang	Sr Research Scientist I, FPD			
Technical Representative	Marco Rodriquez	Sr Supply Chain Specialist			
	Brandy Searcy	Sr Associate Scientist, FPD			

Risk Analysis

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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		Failure has no impact on patient health, system, product quality or regulatory compliance.	Minor compliance deviations with no quality impact
3	Low	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

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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	

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.

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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		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.

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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 Identif				
	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		
Risk Type					Sub-Totals	TOTAL
High: Requires Risk						
Control Action	0	0	0	0	0	
	15	6	34	2	57	58

¹The 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.

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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.



Mitigation Plan 5.

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:

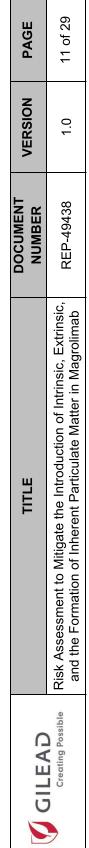
#	PID1	Cause of Failure	Mitigation Plan	Target Implementation	CAPA	Anticipated Risk Rating Post- Implementation
_	23	Low concentration of surfactant in drug-infusion solution.	Action Item: Allowance of 100 mL infusion bag for the preparation of low concentration drug infusion solution.	28Feb 2024	QE-183389	Гом
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	Гом
3	27	Multiple vials required resulting in multiple instances of septum being punctured by needle.	Action Item: Update to $Pharmacy\ Manua^{\mathcal{P}}$ to instruct to use new needle on each drug product vial.	28Feb 2024	QE-183389	Гом
4	28	Multiple introductions of drug product into the same infusion bag required.	Action Item: Update to <i>Pharmacy ManuaP</i> to instruct to use new needle on each drug product vial.	28Feb 2024	QE-183389	Low
2	29	Dulling of syringe needle as a result of multiple septum puncture instances.	Action Item: Update to $Pharmacy\ Manua^{\it L}$ to instruct to use new needle on each drug product vial.	28Feb 2024	QE-183389	Low
9	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 <i>Pharmacy ManuaR</i> 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 <i>Pharmacy ManuaP</i> to instruct the large volume additions.	30May2024	QE-183695	Low



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CAPA Anticipated Risk Rating Post- Number Implementation	QE-183389 Low	QE-183389 Low	QE-183389 Low	QE-183389 Low	QE-183389 Low	QE-183389 Low	QE-183389 Low		QE-183389 Low
Target Implementation	28Feb 2024	28Feb 2024	28Feb 2024	28Feb 2024	28Feb 2024	28Feb 2024	28Feb 2024		28Feb 2024
Mitigation Plan	Action Item: Update to Pharmacy Manual ² to instruct on drug product vial equilibration to room temperature before 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.	Action Item: Update to Pharmacy Manual ^e for the preparation and instruct on inspection of empty bag prior to preparation of drug infusion solution.	Action Item: Update to Pharmacy Manual ^e to instruct on ensuring no debris present on septum after cleaning with an alcohol wipe.	Action Item: Update to <i>Pharmacy ManuaP</i> to ensure alcohol is dried prior to puncturing the vial septum with the needle.	Action Item: Update to Pharmacy Manua $^{\mu}$ to ensure alcohol is dried prior to puncturing the vial septum with the needle.	Action Item: Update to Pharmacy Manual ² to perform visual inspection on drug infusion solution immediately prior to administration to patient.	A attended to the land of the state of the s	perform visual inspection on drug infusion solution immediately prior to administration to patient.
Cause of Failure	Vial is not allowed to equilibrate to room temperature prior to preparation of drug-infusion solution.	Vial is not allowed to equilibrate to room temperature prior to preparation of drug-infusion solution.	Particulate Matter present in the empty bag prior to dose preparation.	Alcohol swab debris present on drug product septum introduced to drug infusion solution.	Alcohol present on stopper from cleaning septum introduced into drug product vial.	Alcohol present on stopper from cleaning septum introduced into drug product vial.	Drug infusion mixture stored beyond allowable timeframe beyond recommended storage condition.	Drug infusion mixture stored beyond	allowable timeframe beyond recommended storage condition.
PID1	40	41	43	44	45	46	53	27	5
#	8	6	10	11	12	13	14	15	



Process ID

²Update 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.

Risk Review/Maintenance Plan ဖ

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 Consistent with FDA recommendation listed in the guidance of the Risk Management Plans (RMP), GSI will conduct a risk review of the mitigating actions, changes to the ratings of risk factors, and any new identified risks.

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This

		PAGE	12 of 29		Comments / Action Items		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.	Risk is acceptable as is and no additional actions will be taken.	There are currently effective controls and detection mechanisms	risk at the clinical facility.	Risk is acceptable as is and no additional	actions will be taken. There are currently	detection mechanisms in place to reduce the risk at the clinical	facility.	Risk is acceptable as is and no additional actions will be taken.	There are currently effective controls and detection mechanisms in place to require the	risk at the clinical facility.
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		>			Detectability (D)			က			က			~	,			က	
		DOCUMENT NUMBER	REP-49438		Rationale for D		Per SOP-05382 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 he detected within the	step.	Per SOP-05362 Quality and Compliance Risk	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.	Per SOP-05362 Quality and Compliance Risk	Management (V 5.U) 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.	Per SOP-05362 Quality and Compliance Risk Management (v. 50 Table 3:	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.
		DOC			Monitoring Plan		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 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	reported to Gilead Sciences upon discovery.	Per GS-US-586-6144 Pharmacy Manual (v 8.0) the drug product is	packaged and shipped with temperature monitoring devices (Temperature monitoring	(Templates): Templatation monitoring device data is reviewed by the Clinical site and excursions are reported to Gilead Sciences mon	discovery.	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 Chinical city and exemptance of chinical city and exemptance.	reported to Gilead Sciences upon discovery.
					Occurrence (O)			ო			က			~	,			က	
	Operations		Magrolimab		Rationale for O		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.	Per SOP-05362 Quality and Compliance Risk Management (v 5.0) Table 2: Probability of	Scale: Scale: Effective routine manual process interventions	and/or preventative controls are in place through procedural and labeling controls.	Per SOP-05362 Quality and Compliance Risk Management (v.5.0)	l able Z: Probability of Occurrence Rating Scale:	Effective routine manual process interventions and/or preventative	controls are in place through procedural and labeling controls.	Per SOP-05362 Quality and Compliance Risk Management (v 5.0) Table 2: Probability of	Scale: Scale: Effective routine manual process interventions	and/or preventative controls are in place through procedural and labeling controls.
	External Quality Operations	ш	and the Formation of Inherent Particulate Matter in Magrolimab		Controls		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	Section 4.3, Drug Product is to be stored at 2–8 °C.	Drug product is packaged in a pre-qualified shipping container to maintain storage conditions.	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.	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.	Drug product is packaged in a pre-qualified shipping container to maintain storage conditions.	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.
		TITLE	sic, and the Formation c		Cause of Failure		Drug product left at receiving area for	extended duration and storage temperature not maintained.		Drug product left at	extended duration and storage temperature not	maintained.	-	Drug product left at receiving area for extended duration	and storage temperature not maintained.		Drug product left at	extended duration and storage temperature not	maintained.
			Extrins		Severity (S)			9			7			Ę	2			7	
			Risk Assessment to Mitigate the Introduction of Intrinsic, Extrinsic,	386-6144	Rationale for S	acility	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	resulting in severity rating	Per SOP-05362 Quality and Compliance Risk Management (v 5.0)	Table 1: Severity Rating Scale: Loss of product	quality leading to adverse events.	Per SOP-05362 Quality and Compliance Risk Management (v 5.0)	l able 1: Severity Rating Scale: Introduction of	particulate matter to patient intravenously may result in serious	adverse events resulting in severity rating	Per SOP-05362 Quality and Compliance Risk Management (v 5.0)	Table 1: Severity Rating Scale: Loss of product	quality leading to adverse events.
:12530981			ssessment to Mitigate th	Appendix 1 – FMEA Risk Assessment for GS-US-586-6144	Effect of Failure	Receipt and Storage of Magrolimab at the Clinical Facility	Formation of particulate matter (protein) in drug product.	Particulate matter introduced to patient intravenously resulting in carious	adverse event.	Formation of	particulate matter (protein) in drug product. Reduction		Formation of particulate matter	(protein) in drug product. Particulate matter	introduced to patient intravenously	resulting in serious adverse event.	Formation of	particulate matter (protein) in drug product. Reduction	. Corporation of the corporation
O O O O O O O O O O O O O O O O O O O			sible	MEA Risk Asses	Failure Mode	Receipt and Storage of Magrolimab at the Cli		Drug product	subjected to elevated	remperatures above recommended storage conditions of 2–8 °C					חמים מיים ס	subjected to decreased	temperatures below recommended storage conditions of 2–8 °C		
ID: CAFF9AC8-91(Creating	\ppendix 1 – FI	Process Step							Drug product arrives at the	and is sent to pharmacy.						
elope	_4	Ĺ			OI	Ref # 1.0		-	, <i>,</i> , — ·	10 10	٥ •			٣	י			4	
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	Occurrence (O)	ю	m		
Magrolimab	Rationale for O	Per SOP-05362 Quality and Compliance Risk Management (v. 5.0) Table 2: Probability of Cocurnere Rating Scale: Effective noutine manual process interventions and/or preventative controls are in place through procedural controls.	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.		
Risk Assessment to Mitigate the Introduction of Intrinsic, Extrinsic, and the Formation of Inherent Particulate Matter in Magnolimab	Controls	Per GS-US-588-6144 Pharmacy Manual (v 8.0) Section 4.3, states "Do not shake" the drug product.	Per GS-US-586-6144 Pharmacy Manual (v 8.0) Section 4.3, states "Do not shake" the drug product.		
sic, and the Formation o	Cause of Failure	Drug product is mishandled upon receipt at the clinical facility.	Drug product is mishandled upon receipt at clinical facility.		
Extrins	Severity (S)	10	7		
ne Introduction of Intrinsic,	Rationale for S	Per SOP-05362 Quality and Compliance Risk Management (v. 5.0) Table 1: Seventy Raffing Scale: Introduction of particulate matter to particulate matter to particulate matter to particulate matter of	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.		
sessment to Mitigate th	Effect of Failure	Formation of particulate matter (protein) in drug product. Particulate matter introduced to patient intravenously resulting in serious adverse event.	Formation of particulate matter (protein) in drug product. Od drug efficacy.		
Risk As	J ode	luct is	oration.		

Drug product is subjected to shaking/vibration.

Drug product arrives at the clinical facility and is sent to pharmacy.

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actions will be taken.
There are currently
effective controls and
detection mechanisms
in place to reduce the
risk at the clinical

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Rating Scale:

There is a manual inspection of the failure and there is a high probability that the failure will be detected within the

Contract Organizations.
Per GS-US-S06-614 Pharmacy
Manual (v. 80.) section 4.6.2 step 5,
visis are inspected for discoloration
or foreign particulate prior to use.
Discovery of discoloration or foreign
particulate are reported via FRM06429. Investigational Medicinal

Risk is acceptable as is

Per SOP-05362 Quality and Compliance Risk Management (v 5.0) Table 3: Probability of Detection

for use or destruction. Site submits FRM-11946 Investigational Medicinal Products (IMPs) Event Reporting for Clinical Sites, Distributors, and other

quarantine until sponsor disposition

mishandled product is to be

Manual (v 8.0) section 4.3,

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External Quality Operations

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Sont States (Section 1998)

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Comments / Action Items

RPN

efectability (D)

Rationale for D

Monitoring Plan

Failure Mode

Process Step

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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.

90

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Rating Scale:

Compliance Risk
Management (v 5.0) Table 3:
Probability of Detection

quarantine until sponsor disposition for use or destruction. Site submits FRM-11946 investigational Medicinal Products (IMPs) Event Reporting for Clinical Sites, Distributors, and other

Per SOP-05362 Quality and

There is a manual inspection of the failure and there is a high probability that the failure will be detected within the

or foreign particulate prior to use.
Discovery of discoloration or foreign
particulate are reported via FRM06422 Investigational Medicinal
Product (IMP) Complaint Form

vials are inspected for discoloration

Manual (v 8.0) section 4.6.2 step 5

Contract Organizations. Per GS-US-586-6144 Pharmacy

Per SOP-05362 Quality
and Compliance Risk
Management (v. 5.0)
Table 2: Probability of
Occurrence Rating
Scale:
Scale:
Failure not expected to
occur often.

Historical review of complaints related to damaged vials for Magrolimab upon receipt at the clinical facility from Oxpa2020 to Oxpa2020 to Axpa2020 tound 1 complaint related to damaged vials, therefore failure is not expected to occur offen.

Drug product is mishandled upon receipt at the clinical facility.

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Per SOP-05362 Quality and Compliance Risk Management (v 5.0) Table 1: Severity Rating Scale: Introduction of particulate matter to particulate matter to particulate matter adverse events resulting in severity

Introduction of particulate matter (glass) to the drug product. Particulate matter introduced to patient intravenously resulting in serious adverse event.

Vials are damaged/broken

Pharmacy cross-checks packing list and performs initial visual inspection of vials for damage.

rating

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.

63

Compliance Risk Management (v 5.0) Table 3: Probability of Detection

quarantine until sponsor disposition for use or destruction. Site submits FRM-11946 investigational Medicinal Products (IMPs) Event Reporting for Clinical Sites, Distributors, and other

Product (IMP) Complaint Form Per GS-US-586-6144 Pharmacy Manual (v 8.0) section 4.3,

mishandled product is to be

Contract Organizations. Per GS-US-586-6144 Pharmacy

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Rating Scale:

Per SOP-05362 Quality and

There is a manual inspection of the failure and there is a high probability that the failure will be detected within the

Manual (v 8.0) section 4.6.2 step 5, vials are inspected for discoloration of foreign particulate prior to use. Discovery of discoloration or foreign particulate are reported with FRM-06432 Investigational Medicinal

Product (IMP) Complaint Form Per GS-US-586-6144 Pharmacy Manual (v 8.0) section 4.3,

mishandled product is to be

Risk is acceptable as is

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PAGE	14 of 29	Comments / Action Items	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.	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.		
VERSION	1.0	RPN	90 0 d d d d d d d d d d d d d d d d d d	63 		
VEF		Detectability (D)	m	ო		
DOCUMENT NUMBER	REP-49438	Rationale for D	Per SOP-05362 Ouality and Compliance Risk Management (* 50.) 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.	Per SOP-05362 Quality and Compliance Risk Management (v. 50.) 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.		
1300		Monitoring Plan	Per (S.C.)L-Se96-14th Pharmacy Manual (v. 8.0) section 4.3 mishandled product is to be quarantine until sponsor of deposition for use or destruction. Site submits FRM-1146 investigational Medicinal Products (MPS) Event Reporting for Clinical Sites, Distributors, and other Contract Organizations. Per CS-US-886-6144 Pharmacy Manual Section 4.3 storage and documented on a temperature per GS-US-886-6144 Pharmacy Per GS-US-886-6144 Pharmacy Per GS-US-886-6144 Pharmacy Per GS-US-886-6144 Pharmacy wais are inspected for discoloration of freigin particulate prior to use. Discovery of discoloration of freigin particulation of foreign Model (MPS) Complaint Form Product (MPS)	Per (S.C.)LS-686-6144 Pharmacy Manual (v. 8.0) section 4.3 mishandled product is to be quarantine until sponsor of deposition for use or destruction. Site submits FRM-1146 investigational Medicinal Products (MPS) Event Reporting for Contract Organizations. Per CS-US-886-6144 Pharmacy Manual Section 4.3 storage Manual Section 4.3 storage amd documented on a temperature should be monitored and documented on a temperature of the contract of the		
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perations	Magrolimab	Rationale for O	Per SOP-05362 Quality and Compilance 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.	Per SOP-05362 Quality and Compilance Risk Management (v. 5.0). Table 2: Probability of Occurrence Rating Scale: Scale: produces interventions and/or preventative controls are in place through procedural and labeling controls.		
External Quality Operations	Risk Assessment to Mitigate the Introduction of Intrinsic, Extrinsic, and the Formation of Inherent Particulate Matter in Magnolimab	Controls	Per GS-US-586-6144 Pharmacy Manual (v 8.0) Section 4.3 Drug Product is to be stored at 2-8 °C. Drug wist are labeled with temperature storage requirements.	Per GS-US-586-6144 Pharmacy Manual (V 8.0) Section 4.3 Drug Product is to be stored at 2-8° C Drug visia are labeled with temperature storage requirements.		
ТШ	ic, and the Formation of	Cause of Failure	Drug product not stored at recommended temperature of 2–8 °C or removed from recommended temperature for longer than allowed per storage conditions.	Drug product not stored at recommended temperature of 2-8° C or removed from recommended temperature for longer than allowed per storage conditions.		
	Extrins	Severity (S)	10	۲		
	ne Introduction of Intrinsic,	Rationale for S	Per SOP-05382 Quality and Compliance Risk Management (v. 5.0) Table 1: Severity Rating Scale: Introduction of particulate matter to patient intravenously may result in servous adverse events resulting in severity	Per SOP-05362 Quality and Compliance Risk Management (v. 5.0) Table 1: Severity Rating Scale: Rass of product efficacy or product efficacy or product quality leading to adverse events.		
12530981	ssessment to Mitigate tl	Effect of Failure	Formation of particulate matter (protein) in drug product. Particulate matter infroduced to patient infravenously resulting in serious adverse event.	Formation of particulate matter (protein) in drug product. Reduction of drug efficacy.		
Doc. Status Selope ID: CAFF9AC8-91CE-49AE-A1CD-F1BC12530981	sible	Failure Mode	Drug product subjected to elevated to	in prefativity and a commanded storage conditions of 2–8 °C		
ID: CAFF9AC8-91	GILEAD Creating Pos	Process Step	Maintain accountability of drug lots for necepit to destruction. - Date received. - Qty of study of	- Date/Patient Number/Study number dispensed - Date, Qiy Used, and Unused study drug returned. Initial/Date of individual		
Doc. Status Approved Document No. MEMO-16025 Approved Date 12 Feb 2024 Date Printed 29 Sep 2025 Legacy Doc. No.						

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PAGE	15 of 29	Comments / Action Items		Risk is acceptable as is and no additional actions will be laken. There are currently effective controls and detection nechanisms in place to reduce the risk at the clinical facility.	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.
VERSION	1.0	RPN		90 R 4 a d d d d d d d d d d d d d d d d d d	63 A 1 2 2 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1
VEF	Ì	Detectability (D)		ო	ო
DOCUMENT NUMBER	REP-49438	Rationale for D		Per SOP-05362 Quality and Complance Risk Management (v. 5.0) Table 3: Probability of Detection Retiring Scale: There is a manual inspection of the failure and there is a high probability that the failure will be detected within the step.	Per SOP-05362 Quality and Compliance Risk Management (v. 50) 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.
1300		Monitoring Plan	Per GS-US-586-6144 Pharmacv	Manual (v 8.0) section 4.3, aminated products to be quarantine until sponsor disposition for use or destruction. Sile submits FRM-11946 investigational Medicinal Products (MHPs) Event Reporting for Clinical Siles, 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 Per GS-US-586-6144 Pharmacy Manual (v 8.0) section 4.6.2 step 5, will see inspected for discoloration or foreign particulate prior to use. Discovery of discoloration or foreign particulate prior to use. Discovery of discoloration of organizational Medicinal Product (IMP) Complaint Form	Per GS.U-5:886-614 Pharmacy Manual (v. 8.0) section 4.3 mishandled product is to be quarantine until spoors of disposition for use or destruction. Site submits FRM-1146 investigational Medicinal Products (IMPs) Event Reporting for Clinical Sites. Distributors, and other GS-US-586-6144 Pharmacy Manual Section 4.3 storage and documented on a temperature Per GS-US-586-6144 Pharmacy Manual (v. 80) section 4.6.2 step 5, will see in respected for discoloration of breiging particulate prior to use. Discovery of discoloration or foreign particulate are reported via FRM- 06432 investigational Medicinal Product (IMP) Complaint Form
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perations	Magrolimab	Rationale for O		Per SOP-05362 Quality and Compilance Risk Management (v. 5.0) Table 2: Probability of Occurrence Rating Occurrence Rating Scale: Effective routine nanual process interventions and/or preventative controls are in place through procedural and labeling controls.	Per SOP-05362 Quality and Compliance Risk Management (v. 5.0). Table 2. Probability of Occurrence Rating Scale: Scale: produce interventions and or preventions and or preventions are interventions are in the controls are in place through procedural and labeling controls.
External Quality Operations	mation of Inherent Particulate Matter in Magrolimab	Controls	•	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 elabed with temperature storage requirements.	Per GS-US-586-6144 Pharmacy Manual (v 8.0) Section 4.3. Drug Product is to be stored at 2-8 °C. Drug vidis are labeled with remperature storage requirements.
ТШ	ic, and the Formation of	Cause of Failure		Drug product not stored at stored at stored at tenommended temperature of 2–8 °C or removed from recommended from leteroperature for loteroperature for longer than allowed per storage conditions.	Drug product not stored at recommended temperature of 2-8° Cor removed from recommended temperature for longer than allowed per storage conditions.
	Extrins	Severity (S)		10	2
	Risk Assessment to Mitigate the Introduction of Intrinsic, Extrinsic, and the For	Rationale for S		Per SOP-05362 Quality and Compliance Risk Management (v 5.0) Table 1: Severity Rating Scale: Introduction of particulate matter for patient intravenously may result in serious adverse events resulting in severity rating	Per SOP-05362 Quality and Compliance Risk Management (v 5.0) Table 1: Severity Rating Scale: Ross of product efficacy or product quality leading to adverse events.
212530981	ssessment to Mitigate th	Effect of Failure	Ą	Formation of particulate matter (protein) in drug product. Particulate matter introduced to patient intravenously resulting in serious adverse event.	Formation of particulate matter (protein) in drug product. Reduction of drug efficacy.
Doc. article 49AC8-91CE-49AE-A1CD-F1BC12530981	sible	Failure Mode	Storage at the Clinical Facility	Drug product subjected to elevated temperatures above recommended storage conditions of 2–8 °C.	Drug product subjected to elevated temperatures above recommended storage conditions of 2–8 °C.
ID: CAFF9AC8-9'	CILEAU Creating Pos	Proces		Store in a secure and controlled environment with limited access.	Store in a secure and controlled environment with limited access.
Doc. Status Approved Date Printed	e 12	₽ proved Feb 2024 Sep 2025	Ref # 1.2	Document No. MEMO- GVault Ver. No. 1,0 Legacy Doc. No.	5 16025

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PAGE	16 of 29	Comments / Action Items	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.	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.
VERSION	1.0	RPN N	90 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	63 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1
VEF		Detectability (D)	m	ო
DOCUMENT NUMBER	REP-49438	Rationale for D	Per SOP-05362 Ouality and Compliance Risk Management (v. 50) Table 3: Probability of Detection Rafing Scale: There is a manual inspection of the failure and there is a high probability that the failure will be detected within the step.	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.
)00d	ш	Monitoring Plan	Per (S.C.)LS-686-614 Pharmacy Manual (v. 8.0) section 4.3. mishandled product is to be quarantine until sponsor disposition for use or destruction. Site submits FRM-1146 investigational Medicinal Products (MPPs) Event Reporting for Contract Organizations. Per CS-US-886-6144 Pharmacy Manual Section 4.3 storage Amarual Section 4.3 storage amd documented on a temperature should be monitored and documented on a temperature of the storage of	Per (S.C.)LS-866 let H. Pharmacy Manual (v 8.0) section 4.3. mishandled product is to be quarantine until sponsor of deposition for use or destruction. Site submits FRM-1146 investigational Medicinal Products (MPS) Event Reporting for Clinical Sites, Distributors, and other Contract Organizations. Per GS-US-886-6144 Pharmacy Manual Section 4.3 storage and documented on a temperature should be monitored and documented on a temperature per GS-US-886-6144 Pharmacy Manual (v 8.0) section 4.6.2 step 5, walls are inspected for discoloration of froeign particulate prior to use. Discovery of discoloration of froeign particulation or foreign particulation or foreign particulation or foreign particulation or foreign particulation of foreign and Product (MPI) Complaint Form Froduct (MPI) Complaint Form
		Occurrence (O)	ო	ო
perations	//dgrolimab	Rationale for O	Per SOP-05382 Quality and Compilance 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.	Per SOP-05362 Quality and Compilance Risk Management (v. 5.0). Table 2: Probability of Occurrence Rating Scale: Scale: produce as interventions and opposes interventions and opposes interventions are in place through procedural and labeling controls.
External Quality Operations	Risk Assessment to Mitigate the Introduction of Intrinsic, Extrinsic, and the Formation of Inherent Particulate Matter in Magnolimab	Controls	Per GS-US-586-6144 Pharmacy Manual (v 8.0) Section 4.3. Drug Product is to be stored at 2-8 °C. Drug visits are labeled with remperature storage requirements.	Per GS-US-586-6144 Pharmacy Manual (v. 8.0) Section 4.3 Drug Product is to be stored at 2-8°C. Drug visia are labeled with temperature storage requirements.
	ic, and the Formation o	Cause of Failure	Drug product not stored at recommended temperature of 2–8 °C or removed from recommended temperature for longer than allowed per storage conditions.	Drug product not stored at recommended temperature of 2-8 °C or removed from recommended temperature for longer than allowed per storage conditions.
	Extrins	Severity (S)	10	۲
	ne Introduction of Intrinsic,	Rationale for S	Per SOP-05382 Quality and Compliance Risk Management (v 5.0) Table 1: Severity Rating Scale: Introduction of particulate matter to patient intravenously may result in services adverse events resulting in seventy	Per SOP-05362 Quality and Compliance Risk Management (v. 5.0) Table 1: Severity Rating Scale: Sess of product efficacy or product quality leading to adverse events.
:12530981	ssessment to Mitigate the	Effect of Failure	Formation of particulate matter (particulate matter product. Particulate matter introduced to patient intravenously resulting in serious adverse event.	Formation of particulate matter (protein) in drug product. Reduction of drug efficacy.
Doc. Status Dade ID: CAFF9AC8-91CE-49AE-A1CD-F1BC12530981	sible	Failure Mode	Drug product subjected to decreased	eniperatures below recommended storage conditions of 2–8°C.
ID: CAFF9AC8-91CE	Creating	Process Step	Store in a secure and controlled	environment with limited access.
Doc. status Approved Date Date Printed	12	₽ proved Feb 2024 Sep 2025	Document No. MEMO GVault Ver. No. 1.0 Legacy Doc. No.	⊊ D-16025

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	PAGE	17 of 29	Comments / Action Items	Risk is acceptable as is and no additional actions will be taken. Theirs are currently deflective controls and deflection mechanisms in place to reduce the risk at the clinical facility.	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.	Risk is acceptable as is and no additional actions will be taken. There are currently effective controls and effective controls and detection mechanisms in place to reduce the risk at the clinical facility.
	VERSION	1.0	RPN	06	89	6
	VE		Detectability (D)	m	т	m
	DOCUMENT NUMBER	REP-49438	Rationale for D	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.	Per SOP-05862 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.	Per SOP-05362 Quality and Compliance Risks Management (v.5.0) Table 3: Probability of Detection Rating Scale: There is a manual inspection of the failure and there is a manual inspection of the failure and there is a high probability that the failure will be detected within the step.
	DOC		Monitoring Plan	Per CS. U.S586 et 4th Pharmacy Manual (v 8.0) section 4.3. mishandled product is to be quarantine until sponsor disposition for use or destruction. Site submits FRM-1146 investigational Medicinal Products (IMPS) Event Reporting for Contract Organizations. Per CS-US-886 ef 44 Pharmacy Manual (v 8.0) section 4.6.2 step 5, walls are inspected for discoloration of foreign particulate prior to use. Discovery of discoloration or foreign particulate prior to use. Discovery of discoloration of foreign particulate prior to use. Product (IMP) Complaint Form Product (IMP) Complaint Form Product (IMP) Complaint Form Product (IMP) Complaint Form	Per GS. U.S866-614 F. Pharmacy Manual (V. 8.0) section 4.3, mishanded product is to be quarantine until sponsor disposition frou use or destruction. Site submits FRM-1146 Investigational Medicinal Products (IMPS) Event Reporting for Clinical Sites, Distributors, and other Contract Organizations. Per GS-U.S866-6144 Pharmacy Manual (V. 8.0) section 4.6.2 step 5, walls are inspected for discoloration of foreign particulate prior to use Discovery of discoloration or foreign particulate are reported via FRM- Deduct (IMPS) Complaint Form Product (IMPS) Complaint Form	Per (S.C.).S-866 lt4 Pharmacy Manual (v. 8.0) section 4.3 mishandled product is to be quarantine until sponsor disposition frou use or destruction. Site submits FRM-11486 investigational Medicinal Products (IMPS) Event Reporting for Clinical Sites Distributions, and other Contract Organizations. Per GS-US-586-6144 Pharmacy Manual (v. 8.0) section 4.6.2 step 5, wills are inspected for discoloration of foreign particulate prior to use. Discovery of discoloration or foreign particulate are resported via FRM- G0432 Investigational Medicinal Product (IMP) Compaint Form
			Occurrence (O)	м	м	м
Operations		Magrolimab	Rationale for O	Per SOP-05382 Quality and Compliance Risk Management (6.50). Table 2: Probability of Courance Rating Scale: Effective outline manual process interventions and/or preventative controls are in place through procedual controls.	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 procedual	Per SOP-05382 Quality and Compliance Risk Management (v. 5.0) Table 2: Probability of Courance Rating Scale: Effective outine manual process interventions and/or preventative controls are in place through procedual controls.
External Quality Operations	В	Risk Assessment to Mitigate the Introduction of Intrinsic, Extrinsic, and the Formation of Inherent Particulate Matter in Magnolimab	Controls	Per GS-US-586-6144 Pharmacy Manual (v 8.0) Section 4.3, states "Do not shake" the drug product.	Per GS-US-586-6144 Pharmacy Manual (v 8.0) Section 4.3, states "Do not shake" the drug product.	Per GS-US-566-6144 Pharmaco Manual (v. 8.0) Section 4.3, states "Protect from light" in regat to product storage.
	TIT.	ic, and the Formation c	Cause of Failure	Drug product is mishandled upon receipt at the clinical facility.	Drug product is mishandled upon receipt at the clinical facility.	Drug product is not stored per light requirements at the clinical facility.
		Extrins	Severity (S)	10		-
		ne Introduction of Intrinsic,	Rationale for S	Per SOP-05362 Quality and Compliance Risk Managament (v. 5.0) Table 1: Seventy Rating Scale: Introduction of particulate matter to p	Per SOP-05362 Ouality and Compliance Risk Managament (v. 5.0) Table 1: Severity Table 1: Severity Earling Scale: Loss of product efficacy or product quality learned out addiverse events.	Per SOP-05382 Quality and Compliance Risk Management (* 5.0) Table 1: Severity Table 1: Severity Table 1: Severity Table 1: Severity Table 1: Severity Table 1: Severity Table 2: Severity Table 2: Severity Table 3: Severity Table 4: Severity Table 5: Severity Table
C12530981		ssessment to Mitigate tl	Effect of Failure	Formation of particulate matter (protein) in drug product. Particulate matter introduced to patient intravenously resulting in serious adverse event.	Formation of particulate matter (protein) in drug product. Reduction of drug efficacy.	No impact to product quality or product quality or patient asfery as determined in REP-27687.
Sont at the control of the control o		sible	Failure Mode	Drug product is	subjecter to shaking/vibration.	Product is exposed to excessive light.
ID: CAFF9AC8-9′		GILEAD Creating Pos	Process Step		Store in a secure and controlled environment with limited access.	
yelope I			Old	41	55	91
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	PAGE	18 of 29	Comments / Action Items		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.	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.
	VERSION	1.0	A T S		<u> </u>	- - 8
	N.		Detectability (D)		м	m
	DOCUMENT NUMBER	REP-49438	Rationale for D		Per SOP-05862 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.	Per SOP-05362 Quality and Compliance Risk Maragement (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.
	DOG		Monitoring Plan		Per (GS-US-686-6144 Pharmacy Manual (v 8 0) section 4.3, mishandled product is to be quarantine until sponsor of deposition frou se or destruction. Site submits FRM-1496 investigational Medicinal Products (IMPs) Event Reporting for Clinical Sites, Distributors, and other. Per GS-US-866-6144 Pharmacy Manual Section 4.3 storage of Manual Section 4.3 storage and documented on a temperature Per GS-US-866-6144 Pharmacy Per GS-US-866-6144 Pharmacy wilst are inspected for discoloration or foreign particulate prior to use Discovery of discoloration or foreign particulate prior to use Discovery of discoloration or foreign particulate are reported via FRM- leads. 2 Investigational Medicinal Product (IMP) Complaint Form	Per (CS-US-686-6144 Pharmacy Manual (v 8 0) section 4.3, mishandled product is to be quarantine until sporsor disposition frou use or destruction. Site submits FRM-11946 investigational Madicinal Products (IMPS) Exem Reporting for Clinical Sites, Distributors, and other Per GS-US-686-614 Ammacy Manual Section 4.3 storage Manual Section 4.3 storage and documented on a temperature should be monitored or foreign particulate prior to use. Discovery of discoloration or foreign particulate are reported via FRM- G423 investigational Medicinal Porvair (IMP).
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Onerations		Magrolimab	Rationale for O		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 noted procedural and labeling controls.	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.
External Quality	External Quality Operations	TILLE mation of Inherent Particulate Matter in Magrolimab	Controls		Per GS-US-586-6144 Pharmacy Manual (V 8.0) Section 4.3. Drug Product is to be stored at 2–8 °C.	Per GS-US-586-6144 Pharmacy Manual (v 8.0) Section 4.2. Drog Product is to be stored at 2-8 °C. Drug vidas are labeled with temperature storage requirements.
	TITLE	ic, and the Formation c	Cause of Failure		Drug product not stored at recommended temperature of 2–8 °C during transport between clinical between clinical facilities.	Drug product not stored at recommended temperature of 2-8 °C during transport between clinical facilities.
		, Extrins	Severity (S)		10	7
		Risk Assessment to Mitigate the Introduction of Intrinsic, Extrinsic, and the Fon	Rationale for S	acilities	Per SOP-05362 Quality and Compilares 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 resulting	Per SOP-05362 Quality and Compilations Risk Management (v 5.0) Table 1: Severity Rating Scale: Loss of product efficacy or product quality leading to adverse events.
C12530981		ssessment to Mitigate th	Effect of Failure	Transport of Drug Product Vial Between Clinical Facilities	Formation of particulate matter (protein) in drug product. Particulate matter introduced to patient intravenced to patient intravenced sadverse event.	Formation of particulate matter (protein) in drug product. Reduction of drug efficacy.
DOC.		sible	Failure Mode	ort of Drug Product V	Drug product subjected to elevated	emperatures above recommended storage conditions of 2–8 °C.
ID: CAFF9AC8-9		GILEAD Creating Pos	Process Step		The vials may be transported within 8 hours at refrigerator	(emperature (emperature (emperature (emperature (emperature (emperature emperature emper
Doc. Statu Appr ved Date Printe	Dui	te 12	₽ proved Preb 2024 Sep 2025	Ref # 2.0	Document No. MEMO-1 GVault Ver. No. 1.0 Legacy Doc. No.	© 6025

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PAGE 19 of 29	Comments / Action Items	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.	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.			
VERSION 1.0	RP N	<u>-</u> 86	- 63			
VE	Detectability (D)	т	м			
DOCUMENT NUMBER REP 49438	Rationale for D	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.	Per SOP-05362 Quality and Compliance Risk Management (v. 50.) 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.			
DOOG	Monitoring Plan	Per GS-US-Se6-Gild Pharmacy Manual (v 8 to) section 0.3, mishandled product is to be quaranthie until sporator disposition for use or destruction. Site submits FRM-1496 investigational Medicinal Products (IMPs) Event Reporting for Clinical Sites, Distributors, and other Contract Organizations. Per GS-US-86-Gild Pharmacy Manual (v 8.t) section at temperature should be monitored and documented on a temperature and documented on a temperature Per GS-US-Se6-Gild Pharmacy Pharmacy Per GS-US-Se6-Gild Pharmacy Pharmacy Per GS-US-Se6-Gild Pharmacy Pharmacy Per GS-US-Se6-Gild Pharmacy Phar	Per GS-US-Se6-Gild A Pharmacy Manual (v 8 to) section 4.3, mishandled product is to 4.3, quaranthie until sporator disposition for use or destruction. Site submits FRM-14946 investigational Medicinal Products (IMPs) Event Reporting for Clinical Sites, Distributors, and other Contract Organizations. Per GS-US-86-6144 Pharmacy Manual (v 8 to) section 4.3 storage temperature should be monitored and documented on a temperature Per GS-US-Se6-6144 Pharmacy Manual (v 8 to) 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-0943. Investigational Medicinal Peroduct (IMP) Complaint Form			
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Operations Magrolimab	Rationale for O	Per SOP-05382 Quality and Compliance Risk Management (v. 5.0) Table, 2. Probability of Occurence Rating Scale: Effective routine manual process interventions and/or preventative controls are in place through procedural and labeling controls.	Per SOP-05382 Quality and Compliance Risk Management (v. 5.0) Table C. Probability of Occurrence Rating Scale: Effective routine manual process interventions and processing procedural and labeling controls.			
External Quality Operations TITLE mation of Inherent Particulate Matter in Magrolimab	Controls	Per GS-US-586-6144 Pharmacy Manual (v 8.0) Section 4.3. Drug Product is to be stored at 2-8 °C. Drug vilsia are labeled with temperature storage requirements.	Per GS-US-586-6144 Pharmacy Manual (v 8.0) Section 4.3 Drug Product is to be stored at 2-8° C. Drug Visia are labeled with temperature storage requirements.			
TITL	Cause of Failure	Drug product not stored at recommended temperature of 2-8 °C during transport between dirical facilities.	Drug product not stored at recommended temperature of 2-8 °C during transport between the control of the control facilities.			
Extrins	Severity (S)	10	۲			
9-F1BC12530981	Rationale for S	Per SOP-05382 Quality and Compilatione Risk Management (v 5.0) Table 1: Severity Rating Scale: Introduction of particulate matter to patient intravenously may seault in servent advirse events resulting in seventry	Per SOP-05362 Quality and Compliance Risk Management (v. 5.0) Table 1: Severity Rating Scale: Cass of product efficacy or product quality leading to adverse events.			
C12530981	Effect of Failure	Formation of particulate matter (protein) in drug product. Particulate matter introduced to patient intravenously resulting in serious adverse event.	Formation of particulate matter (protein) in drug product. Reduction of drug efficacy.			
49AE-A1CE	Failure Mode	Drug product subjected to decreased	renperatures between temperatures between temperatures of the storage conditions of 2–8 °C.			
ID: CAFF9AC8-91CE	Process Step	The vials may be transported within 8 hours at refrigerator	compensation (2–8°C) storage for up to 190 miles by motor vehicle.			
Door	<u> </u>	Dogument No. MEM	2 16026			
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.						

	PAGE	20 of 29	Comments / Action Items	Risk is acceptable as is and no additional actions will be taken. There are currently deflective controls and deflective controls and deflection mechanisms in place to reduce the risk at the falling.	Risk is acceptable as is and no additional actions will be taken. There are currently detection mechanisms in place to reduce the risk are the clinical facility.		There is no lower weight limit for patient. Action them: Allowance of 100 mL infusion bag for the preparation of low concentration drugs infusion solution.
	VERSION	1.0	RPN	06	<u>8</u>		300 A A A
	ΥE		Detectability (D)	ε	ь		ъ
	DOCUMENT NUMBER	REP-49438	Rationale for D	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.	Per SOP-05382 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.		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.
	DOC		Monitoring Plan	Per CS. U.S586 et 4th Pharmacy Manual (v 8.0) section 4.3. mishandled product is to be quarantine until sponsor disposition for use or destruction. Site submits FRM-1146 investigational Medicinal Products (IMPS) Event Reporting for Contract Organizations. Per CS-US-886 ef 44 Pharmacy Manual (v 8.0) seatch 4.6. 2 step 5, walls are inspected for discoloration of treging particulate prior to use. Discovery of discoloration or foreign particulate prior to use. Discovery of discoloration or foreign particulate prior to use. Product (IMR) Complaint FRM-0642 investigational Medicinal Product (IMR) Complaint Form	Per (S.C.)LS-686 e144 Pharmacy Manual (v. 8.0) section 4.3. mishandled product is to be quarantine until sponsor desposition for use or destruction. Site submits FRM-1146 investigational Medicinal Products (IMPS) Event Reporting for Contract Organizations. Per GS-US-886 e144 Pharmacy Manual (v. 8.0) section 4.6.2 step 5, walls are inspected for discoloration of foreign particulation or foreign foreign and product (IMPS).		Per GS-US-586-6144 Pharmacy Manual (v 8.0) section 4.6.2 step 9, infusion beg is inspected for discoloration or foreign particulate prior to use. Discovery of discoloration or foreign particulate are reported via FRM-06-432 Investigational Medicinal Product (IMP) Complaint Form
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Operations		Magrolimab	Rationale for O	Per SOP-05382 Quality and Compliance Risk Management (v. 5.0). Table 2: Probability of Coursene Rating Scale: Effective outline manual process indeventaive controls are in place through procedual controls.	Per SOP-05362 Quality and Compliance Risk Management (v. 5.0) Table 2: Probability of Courante Rating Scale: Effective outline manual process interventions and/or preventative controls are in place through procedual controls.		Per SOP-05362 Quality and Compliance Risk and Compliance Risk Managament (v. 50) Table 2: Probability of Occurrence Rating Scale: No preventiative controls are in place. Low concentration of surfactant in duug- infusion solution is almost certain to occur as part of nomal operations.
External Quality Operations	Е	Risk Assessment to Mitigate the Introduction of Intrinsic, Extrinsic, and the Formation of Inherent Particulate Matter in Magnolimab	Controls	Per GS-US-586-6144 Pharmacy Manual (v 8.0) Section 4.3, states "Do not shake" the drug product.	Per GS-US-586-6144 Pharmacy Manual (v 8.0) Section 4.3, states "Do not shake" the drug product.		GS-US-586-6144 Pharmacy Manual (v 8.0) section 4.5 provides dosing information and calculation guidance for pharmacy.
	TIT	c, and the Formation c	Cause of Failure	Drug product is mishandled during transport between clinical facilities.	Drug product is mishandled during transport between clinical facilities.		Low concentration of orfractar in drug-initiasin solution.
		Extrinsi	Severity (S)	10	٨		10
		e Introduction of Intrinsic,	Rationale for S	Per SOP-05382 Quality and Compliance Risk Management (v. 5.0). Table 1: Severity Rating Scale: Introduction of particulate matter to particulate matter to particulate matter to particulate matter adverse events resulting in severity result in serious adverse events resulting in severity rating	Per SOP-05382 Quality and Compliance Risk Managament (v. 5.0) Table 1: Severity Table 2: Severity Loss of product efficacy or product efficacy or product quality leading to adverse events.		Per SOP-05362 Quality and Compilance Risk Management (v. 5.0) Table 1: Severity Rating Scale: Introduction of particulate matter to resulting in severity rating
C12530981		Assessment to Mitigate th	Effect of Failure	Formation of particulate matter (protein) in drug product. Particulate matter introduced to patient intravenously resulting in serious adverse event.	Formation of particulate matter (particulate matter particulate matter product. Reduction of drug efficacy.	n Solution	Particulate matter (proferin) introduced to patient intravenously resulting in a serious adverse event.
Sond Discarrance 49AE-A1CD-F1BC12530981		sible	Failure Mode	Drug product is	shaking/vibration.	Preparation of Drug-Infusion Solution	Formation of particulate matter (protein) in the drug-infusion solution.
ID: CAFF9AC8-9		CILEAU Creating Pos	Process Step	The vials may be transported within 8 hours at refrigerator temperature (2-8°C) storage for up to 190 miles. by motor vehicle.	The vials may be transported within 8 hours at refrigerator temperature (2-8°C) stonger for up to 190 miles. by motor vehicle.		Dosage preparation for low concentration of drug product († mg/kg)
Doo & totue	Ĺ		E Proved	Nocument No	NEMO 16025	Ref # 3.0	23
Approved D	uı	e 12	proved Feb 2024 Sep 2025	Document No. GVault Ver. No. Legacy Doc. No.	MEMO-16025 1.0		

Operations	
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		PAGE	21 of 29	Comments / Action Items	There is no lower weight limit for patient Action Item. Allowance of 100 mt. Intision bag for the preparation of low concentration drug infusion solution	There is no upper weight limit for the patient. Allowance to dose patient without saline dilution. Saline dilution stakes actions will be taken. There are currently effective controls and detection mechanisms in place to reduce the risk at the clinical actions will be set to the same actions will be taken. There are currently effective controls and detection mechanisms in place to reduce the risk at the clinical facility.	There is no upper weight limit for the patient. Allowarnce 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.	Action Item: Update to GS-US-588-6144 Pharmago Waanual to instruct on change of needle after each addition of drug to initision bag.														
		VERSION	1.0	A A S	210	06	63	150														
		3		Detectability (D)	e	ε	r	ю														
		DOCUMENT NUMBER	REP-49438	Rationale for D	Per SOP-05382 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 manual inspection of the failure and there is a high probability that the failure will be detected within the step.	Per SOP-05382 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.	Per SOP-05382 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.	Per SOP-05382 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 multip probability that the failure will be detected within the step.														
		DOCU	500	2000 H		200	Monitoring Plan	Per GS-US-588-6144 Pharmacy Manual (r & B) seaton 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-0843.2 Investigational Medicinal Froduct (IMP) Complaint Form	Per GS-US-588-6144 Pharmacy Manual (r 8.0) seaton 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-0843.2 Investigational Medicinal Froduct (IMP) Complaint Form	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 (MP) Complaint Form	Per GS-US-586-6144 Pharmacy Maruel (* 8.0) Sector 4.6.2 step 9. infusion bag is inspected for disoloration or foreign particulate prior to use. Discovery of discoloration or foreign particulate are reported via FRM-6842 are reported via FRM-6842 investigational Medicinal Frount (IMP) Complaint Form											
				Occurrence (O)	10	ဗ	ဗ	rs.														
	or City	Operations	n Magrolimab	ı Magrolimab	Magrolimab	Magrolimab	Magrolimab	Magrolimab	Magrolimab	Magrolimab	Magrolimab	Magrolimab	Magrolimab	Magrolimab	Magrolimab	n Magrolimab	in Magrolimab	Rationale for O	Per SOP-05582 Quality and Occupations 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 is solution is almost certain to occur as part of frommal as part of fromal operations.	Per SOP-05362 Quality and Compliance Risk Management (v. 5.0) Table 2: Probability of Cocurrence Rating Scale: Effective routine manual process interventians and/or preventative controls are in place through procedual	Per SOP-05382 Quality and Compliance Risk Management (v. 5.0) Table, 2. Probability of Occurrence Rating Scale: Effective routine manual process interventions and/or preventiative controls are in place through procedural	Per SOP-05/362 Quality and Complaince Risk Management (1 5.0) Table 5.2 Probability of Occurence Rating Occasional non-routine manual process interventions are in place as the needle may be changed as needled however it is not required.
	External Oriality Onerations		Formation of Inherent Particulate Matter in Magrolimab	Controls	GS-US-586-6144 Pharmacy Manual (v.8.0) section 45 provides dosing information metological information metological guidance for pharmacy,	GS-US-586-6144 Pharmacy Manual (v 8.) section 4.5 provides dosing information and calculation guidance for pharmacy. Per GS-US-566-6144 Pharmacy Manual (v 8.) section 4.7 requires use of 500 mL infusion bag for 500 mL infusion bag for concentrations.	GS-US-586-6144 Pharmacy Manual (v 8.0) section 4.5 provides desing information and calculation guidance for plannacy. Per GS-US-586-6144 Pharmacy Manual (v 8.0) section 4.7 requires use of 500 mL infusion hag for high dosage concentrations.	GS-US-586-6144 Pharmacol (W. 8.0) section 4.6.2 step 8. "Exchange needle as needle as														
		TILE		Cause of Failure	Low concentration of surfactant in drug-infusion solution.	High concentration of drug product material in drug-infusion material.	High concentration of drug product material in drug-infusion material.	Multiple vials required resulting in multiple instances of septum being purctured by needle.														
			Extrins	Severity (S)	2	10	2	10														
			Risk Assessment to Mitigate the Introduction of Intrinsic, Extrinsic, and the	Rationale for S	Per SOP-05382 Quality and Compliance Risk Managament (v 5.0) Table 1: Severity Table 2: Severity Esting Scale: Loss of product efficacy or product quality leading to adverse events.	Per SOP-05382 Quality and Compliance Risk Management (v. 5.0) Table 1: Seventy Rating Scale: Introduction of particulate matter to particulate matter to particulate matter to particulate matter or particulate matter or south in serious may result in serious resulting in seventy resulting in seventy rating	Per SOP-05382 Quality and Compliance Risk Management (v. 5.0) Table 1: Severity Rating Scale: Loss of product efficacy or product quality leading to adverse events.	Per SOP-05382 Quality and Compliance Risk Managament (v 5.0) Table 1: Seventh Tintavenously may result in serious adverse events resulting in seventh Talling														
	:12530981		ssessment to Mitigate th	Effect of Failure	Particulate matter (protein) in drug product. Reduction of drug efficacy.	Particulate matter introduced to patient patient intravenously resulting in a serious adverse event.	Particulate matter (protein) in drug product. Reduction of drug efficacy.	Particulate matter (vial septum material) introduced to patient intravenously resulting in a serious diverse event.														
	2 O O O O O O O O O O O O O O O O O O O		sible	sible	sible	sible	Failure Mode	Formation of particulate matter (protein) in the drug-infusion solution.	Formation of particulate matter	(protein) in the drug-infusion solution.	Introduction of particulate matter (vial septum material) in the drug infusion solution.											
	ID: CAFF9AC8-91		GILEAD Creating Pos	Process Step	Dosage preparation for low concentration of drug product (1 mg/kg)		Dosage preparation for high concentration of drug product (30–60 mg/kg)															
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		PAGE	22 of 29	Comments / Action Items	Action Item: Update to GS-US-586-6144 Pharmacy Manual to instruct on change of needle after each addition of drug to infusion bag.	Action Item: Update to GS-US-586-6144 Pharmacy Manual to instruct on change of needle after each addition of drug to infusion bag.	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.	Risk is acceptable as is and or additional actions will be taken. There are currently effective controls and detection mechanisms in place to reduce the risk at the clinical facility.
		VERSION	1:0	RPN	150	150	90 3	69
		5		Detectability (D)	m	ო	е	ю
		DOCUMENT NUMBER	KEP-49438	Rationale for D	Per SOP-05382 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.	Per SOP-05382 Quality and Compliance Risk Management (v. 5.0) Table 3: Probability of Deecdon 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.	Per SOP-05382 Quality and Compliance Risk Management V. 65.0 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.	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.
		DOC		Monitoring Plan	Per GS-US-586-6144 Pharmacy Manual (v 8.0) seaton 4.6.2 step 9. infusion hag 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 GS-US-586-6144 Pharmacy Manual (1 k B), seaton 4.6.2 step 9, infusion bag is inspected for discoloration or foreign particulate profit to use. Discovery of discoloration or foreign particulate are reported via FRM-06432 Investigational Medicinal Product (IMP) Complaint Form	Per GS-US-586-6144 Pharmacy Manual (v. 8.0) section 4.6.2 step 9, infusion bag is inspected for infusion bag is inspected for discoloration of toeign particulate prior to use. Discovery of discoloration of toeign particulate are reported via FRW-06432 Investigational Medicinal Product (MP) Complaint Form	Per CS-UIS-586-6144 Pharmacy Manuel (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
				Occurrence (O)	ro	ro	ဗ	က
	Operations		Magrolimab	Rationale for O	Per SOP-05382 Quality Aand Compliance Risk Management (v. 5.0) Table 2: Probability of Occurrence Rating Scale: Cocasional non-routine manual process interventions are in place as the needle may be changed as needed, however it is not required.	Per SOP-05382 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.	Per SOP-05362 Cuality Per ACO-05362 Cuality Management (v 5.0) Table 2: Probability of Occurrence Rating Cocurrence Rating Scale: Effective routine manual process interventions and/or preventiative controls are in place through procedural controls:	Per SOP-05362 Quality and Compilance Risk Management (v. 5.0). Table 2: Probability of Occurrence Rating Scale: Effective routine manual process interventions and/or preventiative controls are in place through procedural controls.
	External Quality Operations		Formation of Inherent Particulate Matter in Magrolimab	Controls	GS-US-586-6144 Pharmacy Manual (v 8 0) section 4.6.2 step 8, "Exchange needle as needled"	GS-US-586-6144 Praemacy Manual (v 8.0) section 4.6.2 step 8, "Exchange needle as needled"	GS-US-586-6144 Phermacy Manual (v 8.0) section 4.6.2 step 8. instructs pharmacy to use 19G or larger bore needed	GS-US-586-6144 Prammacy Manual (v.8.0) section 4.6.2 step 8, instructs pharmacy to use 19G or larger bore needed
				Cause of Failure	Multiple introductions of drug product into the same infusion bag required.	Dulling of syringe needle as a result of multiple septum puncture instances.	Use of needle bore size smaller than 19G.	Use of needle bore size smaller than 19G.
			Extrinsi	Severity (S)	10	10	10	۲
			Kisk Assessment to Mitigate the Introduction of Intrinsic, Extrinsic, and the	Rationale for S	Per SOP-05362 Quality and Compliance Risk Managament (v. 50) Table 1: Severity Raffing Scale: Raffing Scale: Introduction of particulate matter to a mat	Per SOP-05382 Quality and Compliance Risk Management (v 5.0) Table 1: Severity Rating Scale: Introduction of particulate matter to result in serious adverse events resulting in severity resulting in severity	Per SOA-D5382 Quality Annagement (v. 5.0) Table 1: Seventy Rating Scale: Introduction of particulate matter to patient intravenously may seault in serious adverse eventis resulting in severity rating in severity	Per SOP-16:382 Quality and Compilance Risk Management (v. 5.0) Table 1: Severity Table 1: Severity Table 5: Severity Table 6: Severity Table 7: Severity Table 7: Severity Table 7: Severity Table 6: Severity Table 7: Severity Tab
12530981			sessment to Mitigate ti	Effect of Failure	Particulate matter (infusion bag septum material) introduced to patient intravenously resulting in a serious adverse event.	Particulate matter (vial infusion bag septum material) introduced to introduced to intravenously resulting in a serious adverse event.	Particulate matter (protein) introduced to patient intravenously resulting adverse event.	Particulate matter (protein) in drug product. Reduction of drug efficacy.
DO CO DO CO CAFF9AC8-91CE-49AE-A1CD-F1BC12530981			sible	Failure Mode	Introduction of particulate matter (Infusion bag septum material) in the drug infusion solution.	Introduction of particulate matter (politiculate matter (politiculate matter) septum material) in the drug infusion solution.	Drug addition exhibits shear stress on drug	product resulting in formation of particulate matter (protein).
D: CAFF9AC8-91(GILEAD	Creating Possible	Process Step		Dosage preparation for high concentration	on and 60 mg/kg)	
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		23 of 29	Comments /	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.	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.	Action Item: Update to GS-US-866-6144 Pharmacy Manual to instruct on order of addition for multiple drug addition for multiple lowest addition first for high dose preparation.	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.
		VERSION 1.0	N N	06	83	300	210
		>	Detectability (D)	м	ю	м	က
		DOCUMENT NUMBER REP-49438	Rationale for D	Per SOP-05362 Quality and Management (v. 6.0) Table 3: Probability of Detection Rating Scale: There is a manual inspection of the fallure and there is a high probability that the fallure will be detected will be detected within the step.	Per SOP-05362 Quality and Compilance 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.	Per SOP-05382 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.	Per SOP-05362 Quality and Compliance Risk Management (v 5.0) Table 3: Probability of Detection There is a manual inspection of the fallure and there is a high probability that the fallure will be detected within the sitep.
	_	ŏ	Monitoring Plan	Per GS-US-586-6144 Pharmacy Manual (v. 8.0.) section 4.6.2 step 9, influsion bag is inspected for discoloration of theeing particulate prior to use. Discovery of discoloration of theeing particulate are reported via FRM-06432 Investigational Medicinal Product (IMP) Complaint Form	Per GS-US-586-6144 Pharmacy Manual (v. 8.0) section 4.6.2 step 9, influsion bag is inspected for discoloration of toeign particulate prior to use. Discovery of discoloration of toeign particulate are reported via FRM-06432 Investigational Medicinal Product (IMP) Comptaint Form	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 port to use. Discovery of discoloration or foreign particulate are reported via FRM-08432 Investigational Medicinal Product (IMP) Complaint Form	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 RRM-06422 Investigational Medicinal Product (MP) Complaint Form
			(O) eourrence	т	е	10	10
	Operations	Magrolimab	Rationale for O	Per SOP-05-852 Quality and Compliance Risk Managament (v. 50) Table 2: Probability of Occurrence Rating Scale: Effective routine manual process interventions and/or preventiarve controls are in place through procedural controls are in place through procedural	Per SOP-05382 Outling and Compleance Risk Managament (* 5.0) Table 2: Probability of Occurrence Rating Scale: Effective routine manual process interventions and/or preventative controls are in place through procedural controls are in place	Per SOP-05362 Quality and Compliance Risk Management (v 5.0) Table 2: Probability of Occurrance 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.	Per SOP-05382 Quality and Compliance Risk Managament (v. 50) Table 2: Probability of Occurrence Rating Occurrence Rating No preventative controls are in place. Volume addition of the lowest volume for multiple val additions is almost certain to occur as part of normal operations.
External Quality Operations	External Quality	TITLE Formation of Inherent Particulate Matter in Magrolimab	Controls	GS-US-586-6144 Phamacy Manuel (v. 8.0) section 4, 6, 2, 8tep 8, instructs pharmacy to use 19G or larger bore needed	GS-US-586-6144 Phamacy Manual (v. 8.0) section 4,6,2,518p.6, instructs pharmacy to use 19G or larger bore needed	No current instruction on the controls.	No current instruction on the controls.
		TITL nsic, and the Formation of	Cause of Failure	Use of needle bore size smaller than 19G.	Use of needle bore size smaller than 19G.	Pharmacy adds lowest volume of drug product to infusion beginst during multiple vial addition preparation.	Pharmacy adds lowest volume of drug product to intusion beginst during multiple val addition preparation.
		, Extri	Severity (S)	9		10	
		Risk Assessment to Mitigate the Introduction of Intrinsic, Extrinsic, and the	Rationale for S	Per SOP-05362 Quality and Compliance Risk Management (v. 50) Table 1: Severity Rating Scale: Introduction of particular ematter to patient intravenously may result in serious adverse events resulting in serious rating in serious	Per SOP-05362 Quality and Compilarace Risk Management (v 5.0) Table 1: Severity Rating Scale: Loss of product efficacy or product quality leading to adverse events.	Per SOP-05362 Quality and Compliance Risk Management (v 5.0) Table 1. Swerting Rating Scale: Introduction of particulate matter to patient intravenously may result in serious adverse events resulting in sevents resulting in sevents	Per SOP-05362 Quality and Compilance Risk Management (v. 50) Table 1: Severity Table 1: Severity Starling Scale: Loss of product efficacy or product quality leading bedresse events.
712530981		ssessment to Mitigate t	Effect of Failure	Particulate matter (protein) introduced into patient intravenously resulting in a serious adverse event.	Particulate matter (protein) in drug product. Reduction of drug efficacy.	Particulate matter (protein) introduced to patient intravenously resulting in a serious adverse event.	Particulate matter (protein) in drug product. Reduction of drug efficacy.
DOC Proper ID: CAFF9AC8-91CE-49AE-A1CD-F1BC12530981		sible	Failure Mode	Slow introduction of intropproduct to infusion bad leads	to formation of particulate matter (protein).	Low concentration of ording product exhibited during multiple vial	acounting preparation acounting the particular ameter (protein) (protein)
ID: CAFF9AC8-91		GILEAD Creating Pos	Process Step		Dosage preparation	concentration of drug product (30– 60 mg/kg)	
velope	. [<u> </u>	32	88	8	35
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		PAGE	24 of 29	Comments / Action Items	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.	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.	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.	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.
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		VE		Detectability (D)	e e	en en	м	м
		DOCUMENT NUMBER	REP-49438	Rationale for D	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.	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.	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.	Per SOP-05362 Quality and Compliance Risk Managemen (v. 50) 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.
		DOC		Monitoring Plan	Per GS-US-586-6144 Pharmacy Manual (v 6.0) 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 GS-US-586-6144 Pharmacy Manual (v & D) 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 CS-US-596-6144 Pharmacy Manual (v 8.0) section 4.6.2 step 9, infusion bag is inspected for discoloration of relegion particulate prior to use. Discovery of discoloration of rotein particulate are reported via FRM-06432 Investigational Medicinal Product (MIP) Complaint Form Clinical practices are routinely reviewed by CRAMonitor to ensure compliance with GS-US-66-6144 Pharmacy Manual. Review is inclusive of use of compatible	Per GS-US-586-6144 Pharmacy Manual (v 8.0) section 4.6.2 step 9, infusion beg is inspected for discoloration of foreign particulate prior to use. Discovery of discoloration of foreign particulate are reported via FRM-06432 Investigational Medicinal Product (infu?) complaint Form Clinical practices are routinely reviewed by CRAMontior to ensure compliance with GS-US-586-6144 Pharmacy Manual. Review is inclusive of use of compatible materials and documented in CTMS.
				Occurrence (O)	ဗ	ю	ю	м
1	Operations		Magrolimab	Rationale for O	Per SOP-D5582 Cuality and Compleane Risk Management (v. 5.0) Table 2: Probability of Courrence Rating Courrence Rating Effective routine manual process interventions and/or preventions controls are in place through procedural controls are in place	Per SOP-DSSeZ Ovality and Complemen Risk Managament (v. 50) Table 5. Probability of Courrence Rating Courrence Rating Effective routine manual process interventions and/or preventative controls are in place through procedural controls are in place	Per SOP-05362 Quality and Compliance Risk Management (v. 5) Table (z. Probability of Occurrence Rating Vocurrence Rating Scale: Effective routine manual process interventions and/or preventions and/or preventiative controls are in place through procedural controls are in place through procedural controls.	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 preventainve controls are in place through procedural controls are in place
•	External Quality Operations	ш	ormation of Inherent Particulate Matter in Magrolimab	Controls	GS-US-586-6144 Pharmacy Manual (v 8.0) section 4.7 provides instruction on appropriate influsion bag size of 250 mL or 500 mL.	GS-US-588-6144 Pharmacy Manual (v 8.0) section 4.7 provides instruction on appropriate influsion bag size of 250 mL or 500 mL.	GS-US-586-6144 Pharmacy Manual (v 8.0) section 4.6.1 provides compatiblity information for Magolimab and infusion bag and administration components.	GS-US-566-6144 Phamacy Manual (v 8.0) section 4.6.1 provides compatiblity information for Magolimas and infusion bag and administration components.
		TIL		Cause of Failure	Drug-infusion solution prepared in bag that is too large.	Drug-infusion solution prepared in bag that is too large.	Use of incompatible component during preparation and/or administration.	Use of poor quality component during preparation and/or administration.
			Extrinsi	Severity (S)	10	2	10	10
•			Risk Assessment to Mitigate the Introduction of Intrinsic, Extrinsic, and the	Rationale for S	Per SOD-DGSSZ Quality and Compliance Risk Management (v. 5.0) Table 1: Severity Rating Scale: Introduction of particulate matter to particulate matter to patient intraverously may result in serious adverse events resulting in severity rating in severity	Per SOP-05362 Quality and Compulance Risk Management (v. 5.0) Table 1: Severity Rating Scale: Loss of product efficacy or product quality leading to adverse events.	Per SOP-05382 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	Per SOP-05382 Quality and Compliance Risk Management (v. 5.0). Table 1: Severity Rating Scale: Introduction of patient intravenously may result in serious adverse events resulting in severity falling
	512530981		ssessment to Mitigate th	Effect of Failure	Particulate matter (protein) introduced to patient intravenously resulting in a serious adverse event.	Particulate matter (protein) in drug product. Reduction of drug efficacy.	Particulate matter (intrinsic/extrinsic) introduced to patient intravenously resulting in serious adverse event.	Presence of Particulate Matter (intrinsic/aktrinsic) in components. In components particulate Matter introduced to patient intravenously resulting in a serious adverse event.
	DOC.		sible	Failure Mode	Excessive headspace in infusion bag heads	to formation of particulate matter (protein)	Component interaction with drug-infusion solution leads to formation of particulate matter (Intrinsic/Extrinsic)	Component interaction with drug-infusion solution leads to formation or particulate mater (Intrinsio/Extrinsic)
	ID: CAFF9AC8-91		GILEAD Creating Pos	Process Step		Select materials for preparation of	IMP and administration of IMP that of IMP that compatible with Magrolimab per Pharmacy Manual.	
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	PAGE	25 of 29	Comments / Action Items	Action Item: Update to CS-US-S86-6144 Pharmacy Manual to instruct on allowing drug product val to allow for equilibration to room temperature before preparation of drug infusion solution.	Action Item: Update to CS-US-S86-6144 Pharmacy Manual to instruct on allowing drug product vall to allow for equilibration to room temperature before preparation of drug infusion solution.	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.	Action Item: Update to GS-US-586-6144 Pharmaco Manuel for preparation and instruct on inspection of empty bag prior to preparation of drug infusion solution.
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	>		Detectability (D)	ю	м	ю	ო
	DOCUMENT NUMBER	REP-49438	Rationale for D	Per SOP-05382 Quality and Compliance Risk Management (v. 5.0) Table 3: Probability of Derection Probability of Derection There is a manual inspection of the failure and there is a high probability that the failure will be detected within the step.	Per SOP-05362 Quality and Compliance Risk Management (v. 5.0) Table 3: Probability of Derection There is a manual inspection of the failure and there is a high probability that the failure will be detected within the sitep.	Per SOP-05382 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.	Per SOP-05382 Quality and Compliance Risk Management (v.5.0) Table 3: Probability of Detection There is a manual inspection of the failure and there is a high probability that the failure will be detected within the sitep.
	DOG		Monitoring Plan	Per GS-US-586-6144 Pharmacy Manuel (v. 8.) seaton 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 FRN-06432 Investigational Medicinal Product (MP) Complaint Form	Per GS-US-586-6144 Pharmacy Manuel (v. 8.) 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 vise TRN-06432 Investigational Medicinal Product (MP) Complaint Form	Per GS-US-586-6144 Pharmacy Manual (v 8.0) section 4.6.2 step 9, infusion bag is inspected for discolation or foreign particulate prior to use. Discovery of discolation or foreign particulate are reported via FRM-06432 Investigational Medicinal Product (IMP) Complaint Form	Per GS-US-586-6144 Pharmacy Manual (* 8.0) sector 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 vise TRN-06432 Investigational Medicinal Product (MP) Complaint Form
			Occurrence (O)	10	10	ဗ	10
Onerations		Magrolimab	Rationale for O	Per SOD-05382 Quality Annagement (1.5.0) Table 2: Probability of Cocurrence Rating Occurrence Rating No preventative controls are in place. There is no guidance provided to pharmacy to allow for viat to equilibrate to room tamperature prior to perpendition of drug- infusion solution.	Per SOD-D5382 Quality Annagement (v. 5.0) Table S. Probability of Cocurrence Rating No preventative controls are in place. There is no guidance provided to pharmacy to allow for viat to equilibrate to room tamperature prior to perpendition of drug- infusion solution.	Per SOA-DisSay Quality and Compilaron 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 are in place	Per SOP-05382 Quality and Compliance Risk Managament (* 5.0) Table 2: Probability of Occurence Rating No preventative controls are in place. There is no guidance to inspect empty infusion bag for particulate matter prior to preparation of drug-
External Quality Onerations	E E	Formation of Inherent Particulate Matter in Magrolimab	Controls	No current controls are in place.	No current controls are in place.	GS-US-586-6144 Pharmacy Manual (v 8.0) section 4. step 2 provides instruction to use aseptic technique throughout the preparation process.	No current controls in place.
	E		Cause of Failure	Vial is not allowed to quilibrate to room temperature prior to preparation of drug-infusion solution.	Vial is not allowed to quilibrate to room temperature prior to preparation of drug-infusion solution.	Particulate Matter introduced from environment pharmacy personnel.	Particulate Matter present in the empty bag prior to filling.
		Extrinsi	Severity (S)	10	۷	10	10
		Risk Assessment to Mitigate the Introduction of Intrinsic, Extrinsic, and the	Rationale for S	Per SOP-05382 Quality and Compliance Risk Management (v. 5.0) Table 1: Severity Rating Scale: Introduction of particulate matter to particulate matter to particulate matter to particulate matter or particulate matter or particulate matter or severity may result in serious advierse events resulting in severity rating	Per SOP-05382 Quality and Compliance Risk Managament (v. 5.0) Table 1: Severity Table 1: Severity Enting Scale: Loss of product efficacy or product quality leading to adverse events.	Per SOLP-05382 Quality and Compilance Risk Managament (v. 5.0) Table 1: Severity Rating Scale: Introduction of particulate matter to patient intravenously may exell it is serious adverse events resulting in seventry rating	Per SOP-05362 Quality and Compliance Risk Managament (v. 5.0) Table 1: Severity Raffing Scale: Introduction of particulate matter to particulate matter to particulate matter to particulate matter of
:12530981		ssessment to Mitigate th	Effect of Failure	Particulate matter (protein) introduced intravenously resulting in a serious adverse event.	Particulate matter (protein) in drug product. Reduction of drug efficacy.	Particulate matter (intrinsic/extrinsic) introduced to patient intravenously resulting in serious adverse event.	Particulate matter (intrinsic/extrinsic) introduced to patient intravenously resulting in serious adverse event.
DOC The Pyelope ID: CAFF9AC8-91CE-49AE-A1CD-F1BC12530981		ssible	Failure Mode	Formation of particular matter	Chorenty In the Christian solution.	Introduction of Particulate Matter (Intrinsice/Extrinsic) during filling of infusion and drug product solution in the bag.	Introduction of Particulate Matter (Intrinsic/Extrinsic) during filling of infusion and drug product solution in the bag.
D: CAFF9AC8-91		GILEAD Creating Pos	Process Step	Equilibration of drug product viels	terriperature prior to preparation of drug infusion solution.	Empty IV	rreparation or assiline an empty bag.
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	PAGE	26 of 29	Comments / Action Items	Action Item: Update to GS-US-566-6144 Pharmacy Manual to instruct on resuming no debris present on septum after cleaning with an alcohol wipe.	Action Item: Update to GS-US-S66-6144 Pharmacy Manual to ensure alcohol is dried prior to puncturing the vial septum with the needle.	Action Item: Update to GS-US-566-6144 Phermacy Manual to ensure alcohol is dried prior to puncturing the vial septum with the needle.	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.																				
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	ΛEI		Detectability (D)	m	ю	n	м																				
	DOCUMENT NUMBER	REP-49438	Rationale for D	Per SOP-05382 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.	Per SOP-05362 Quality and Compliance Risk Management (v. 50.) 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.	Per SOP-05362 Quality and Compliance Risk Management (v. 50.) 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.	Per SOP-05362 Quality and Compliance Risk Management (v. 50.) 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.																				
	DOCI		Monitoring Plan	Per GS-US-586-6144 Pharmacy Manuel (1 & B), Seep 9, Manuel (1 & B), Seep 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 CS-US-586-6144 Pharmacy Manual (v. 8.0) section 4.6.2 step 9, influsion 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 CS-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 facility documents preparation time (dosing preparation worksheet) and time of administration (subject accountability 0g). CRA reviews worksheets to ensure they align with GSL-S86-6144 Pharmacy Manual (v 8.0) requirements. Protocol deviation initiated if not followed.																				
			Occurrence (O)	10	10	10	n																				
Operations		. Magrolimab	ı Magrolimab	Magrolimab	Magrolimab	Magrolimab	Magrolimab	Magrolimab	Magrolimab	Magrolimab	Magrolimab	Magrolimab	Magrolimab	Magrolimab	Magrolimab	Magrolimab	Magrolimab	Magrolimab	n Magrolimab	n Magrolimab	Magrolimab	ı Magrolimab	Rationale for O	Per SOD-05382 Quality and Compliance Risk Management (v. 5.0) Table 2: Probability of Occurrence Rating No preventative controls Scale: No preventative controls spelm for alrea is no guidance to inspect vial septum for accord swab debris prior to puncturing the septum with the syringe.	Per SOP-D5582 Quality and Compliance Risk Management (v. 5.0). Table C. Probability of Occurence Rating Scale. No preventative controls are in place. There is no quidance to ensure alcohol is dried prior to puncturing the septum with the syringe.	Per SOCP-05:382 Quality and Compilarce Risk Managament (v. 5.0) Table 12: Probability of Occurrence Rating No preventative controls are in place. There is no guidance to ensure alcohol is dried prior to puncturing the septum with the syringe.	Per SOP-05332 Quality and Compliance Risk Managament (v. 5.0) Table (s. Probability of Occurrence Rating Scale: Effective routine manual process interventions and for preventative controls are in place through procedural controls are in place.
External Quality Operations		Formation of Inherent Particulate Matter in Magrolimab	Controls	No controls in place to prevent.	No current control in place.	No current control in place.	GS-US-586-6144 Pharmacy Manual (v 8.0) section 4.6.2 step 10, instructs on allowable durations to hold drug influsions solution for refrigerated and room temperatures prior to administration.																				
	TITLE		Cause of Failure	Alcohol swab debris present on drug product septum introduced to drug infusion solution.	Alcohol present on from cleaning septum introduced into drug product vial.	Alcohol present on from cleaning septum introduced into drug product vial.	Start time of preparation not documented or duration of preparation takes longer than allowed.																				
		Extrins	Severity (S)	10	10	7	10																				
		Risk Assessment to Mitigate the Introduction of Intrinsic, Extrinsic, and the	Rationale for S	Per SOP-05362 Quality and Compliance Risk Managament (v 5.0) Table 1: Severity Rating Scale: Introduction of particulate matter to particulate matter to particulate matter to particulate matter adverse events resultin serious reduting in severity resulting in severity rating	Per SOD-05532 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 sevents rating in sevents.	Per SOP-05382 Quality and Compilance Risk Management (v 5.0) Table 1: Severity Rating Scale: Loss of product efficacy or product quality leading to adverse events.	Per SOP-05:382 Quality and Compliance Risk Management (v. 5.0) Table 1: Severity Rating Scale: Introduction of particulate matter to partient intravenously may result in serious adverse events resulting in sevenity rating																				
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Son Service 19: CAFF9AC8-91CE-49AE-A1CD-F1BC12530981		ssible	Failure Mode	Introduction of particulate matter (alcorota wab debn's) into the drug infusion solution	Formation of particulate matter	(process) in the drug-infusion solution.	Drug product subjected to elevated temperatures above recommended storage conditions of 2–8 °C.																				
D: CAFF9AC8-91	1	Creating Pos	Process Step		Remove the plastic cap from the Magrolimab vial(s) and swal (s) and such top(s) with alcohol pads.		Record the start time of preparation (when Magrolimab vials are initially pierced)																				
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	PAGE	27 of 29	Comments / Action Items	Risk is acceptable as is and no additional actions will be taken. There are controls and detection mechanisms in place to reduce the risk at the clinical facility.	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.	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.	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.	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.		
	VERSION	1.0	RPN	63	06	63	06			
	VEF		Detectability (D)	ဗ		ဗ	٣	m		
	DOCUMENT NUMBER	REP-49438	Rationale for D	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.	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.	Per SOP-05362 Quality and Compliance Risk Management (v. 6.0) 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.	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.	Per SOP-05362 Ouality and Compliance Risk Management (v. 50) Table 3: Protability of Detection Rafing Scale: There is a manual inspection of the failure and there is a high probability that the failure will be detected within the step.		
	DOCI		Monitoring Plan	Clinical facility documents preparation in (dosing preparation worksheet) and time of administration (subject accountability log). CRA reviews worksheets to ensure they align with CS-US-2686-6144 Pharmacy Manual (v 8.0) requirements. Protocol deviation initiated if not followed.	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 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 GS-US-586-6144 Pharmacy Manual (v 8.0) section 4.6.2 slep 9, infusion bag is inspected for discoloration of foreign particulate prior to use. Discovery of discoloration or foreign particulate are reported via FRM-06432 Investigational Medicinal Product (MP) Complaint Form	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-064.22 Investigational Medicinal Product (IMP) Complaint Form		
			Occurrence (O)	ю	ဗ	ဗ	м	ო		
Operations	-	Magrolimab	Rationale for O	Per SOD-OSSEX Quality and Compliance Risk Management (v. 5.0). Table S. Probability of Occurrence Rating Scale: Effective routine manual process interventions and process interventions controls are in place through procedural countryls procedural controls are in place.	Per SOD-OSSRZ Ouality and Compulance Risk Management (v. 5.0) Table S. Probability of Occurrence Rating Scale: Effective routine manual process interventions and too preventative controls are in place through procedural controls are in place	Per SOD-OSSR2 Quality and Compliance Risk Management (v. 5.0) Table S. Probability of Occurrence Rating Scale: Effective routine manual process interventions and/or preventative controls are in place through procedural controls are in place	Per SOD-GSS2D Quality and Compliance Risk Management (v. 5.0). Table S. Probability of Cocurrence Rating Cocurrence Rating Scale: Effective routine manual process interventions and/or preventative controls are in place through procedural controls.	Per SOD-DGSAZ 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.		
External Quality Operations		f Inherent Particulate Matter ir	Controls	GS-US-586-6144 Pharmacy Manual (v 8.0) section 4.6.2 step 10, instructs on allowable durations to hold arug infusion solution for refigerated and room temperatures prior to administration.	GS-US-586-6144 Pharmacy Manual (v 8.0) section 4.6.2 step 9, instructs to slowly and gentty invert bag 4-6 times to mix.	GS-US-586-6144 Pharmacy Manual (v 8.0) section 4.6.2 step 9, instructs to slowly and gentty invert bag 4-6 times to mix.	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.	GS-US-586-6144 Pharmacy Manual (v.8.0) section 46.2 ktep 9, instructs to slowly and gentty invert bag 4-6 times to mix.		
	TITL	Risk Assessment to Mitigate the Introduction of Intrinsic, Extrinsic, and the Formation of Inherent Particulate Matter in Magrolimab	usic, and the Formation o	nsic, and the Formation	Cause of Failure	Start time of preparation not documented or duration of preparation takes longer than allowed.	Harsh mixing of drug infusion solution.	Harsh mixing of drug infusion solution.	Inadequate mixing of drug-infusion solution leading to formation of particulate matter (protein)	Inadequate mixing of drug-infusion solution leading to formation of particulate matter (protein)
			Severity (S)	.	10	۲				
			he Introduction of Intrinsic,	Rationale for S	Per SOD-OGS&S counting and Compulance Risk Management (v 5.0) Table f. Severity Rating Scale: Introduction of particulate matter to patient intravenously may result in serious advorse events resulting in sevenity rating	Per SOD-OGS&Z Oualing and Compulance Risk Management (v. 5.0) Table 1: Severity Rating Scale: Introduction of particulate matter to partient intravenously may result in serious advorse events resulting in severity resulting in severity	Per SOP-05362 Ouality and Compliance Risk Management (v. 5.0) Table 1: Severty Rating Scale: Cass of product efficacy or product quality leading to adverse events.	Per SOD-OGS&S country Annagement (v. 5.0) Table 1. Severity Rating Scale: Introduction of particulate matter to partient intravenously may result in serious advorse events resulting in severity resulting in serious	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.	
:12530981		ssessment to Mitigate t	Effect of Failure	Formation of particulate matter (protein) in drug product. Reduction of drug efficacy.	Particulate matter (protein) introduced to patient intravenously resulting in a serious adverse event.	Formation of particulate matter (protein) in drug product. Reduction of drug efficacy.	Particulate matter (protein) introduced to patient intravenously resulting in a serious adverse event.	Formation of particulate matter (protein) in drug product. Reduction of drug efficacy.		
DOC. OAFF9AC8-91CE-49AE-A1CD-F1BC12530981		sible	Failure Mode	Drug product subjected to elevated temperatures above recommended storage conditions of 2–8 °C.	Formation of particulate matter	choosing in the drug-influsion solution.	Formation of particulate matter	drugs-inflation drugs-inflation solution.		
) ID: CAFF9AC8-91	C. V. I. I. J.	Creating	Process Step	Record the start time of preparation (when Magnolimab vials are initially pierced)		Slowly add the dose volume of Magrolimab solution to the ritusion bag-	Stowy and gently invert the bag 3-6 times to mix. Avoid creating foam and bubbles.			
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PAGE	28 of 29	Comments / Action Items	Action Item: Update to GS-US-586-6144 Phermacy Manual to Perform visual inspection on drug influsion soution immediately prior to administration to administration to	Action Item: Update to GS-US-588-6144 Phermacy Manual to perform visual inspection on drug influsion soution immediately prior to administration to administration to	Action Item; Update to CSC-US-566-6144 Pharmacy Manual to perform visual inspection on drug infusion solution infusion solution immediately prior to administration to patient. Action Item: Update to GS-US-686-6144 Pharmacy Manual to ensure time out of ensure time out of emergener range is documented.	Action Item; Update to CSC-US-588-6144 Pharmacy Manual to perform visual inspection on drug influsion solution immediately prior to administration to patient. Action Item: Update to CS-US-586-6144 Pharmacy Manual to ensure fine out of temperature range is documented.	
VERSION	1.0	A N	300	210	300	210	
VE		Detectability (D)	10	10	10	10	
DOCUMENT NUMBER	REP-49438	Rationale for D	Per SOP-05382 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.	Per SOP-05382 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.	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.	Per SOP-05362 Quality and Compliance Risk Management (r S. 6) Table 3: Probability of Detection Rating Scale: There is no established inspection, testing, or monitoring in place to detect the failure.	
900 -		Monitoring Plan	No current requirement to perform visual inspection after refrigerating the solution in the bag.	No current requirement to perform visual inspection after refrigerating the solution in the bag.	No current requirement to perform visual inspection after refrigerating the solution in the bag. No requirement to review documentation of time out of temperature.	No current requirement to perform visual inspection after refrigerating the soution in the bag. No requirement to review documentation of time out of temperature.	
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Operations	Magrolimab	Rationale for O	Per SOP-D6382 Outlify and Compliance Risks 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.	Per SOP-DiSSEZ 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.	Per SOP-05382 Quality and Compilare Risk Management (v. 5.0) Table 2. Probability of Occurence Rating Scale: Effective routine manual process interventions and/or preventiative controls are in place through procedural controls are in place through procedural controls are in place.	Per SOP-05382 Quality and Compilance 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 are in place through procedural controls.	
External Quality Operations	Formation of Inherent Particulate Matter in Magrolimab	Controls	GS-US-586-6144 Pharmacy Manual (v 8.0) section 4.6.2 step 10, states that drug infusion solution can be stored eringerated 2-8° C for up, to 16 hours, room temperature for up to 8 hours.	GS-US-588-6144 Pharmacy Manual (v 8.0) section 4.6.2 step 1.0 states that drug infusion solution can be stored refrigerated 2-8° C for up to 16 hours, room temperature for up to 8 hours.	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.	GS-US-566-6144 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.	
1111		Cause of Failure	Drug infusion mixture stored beyond allowable timeframe for beyond recommended storage conditions	Drug infusion mixture stored beyond allowable timeframe for beyond recommended storage conditions	Drug infusion mixture was not allowed to equilibrate for long enough.	Drug influsion mixture was not allowed to equilibrate for long enough.	
	Extrinsi	Severity (S)	10	7	10	7	
	Risk Assessment to Mitigate the Introduction of Intrinsic, Extrinsic, and the	Rationale for S	Per SOP-DGSRZ Ouality and Compliance Risk Management (v 5.0) Table 1: Severity Rating Scale: Introduction of particulate matter to patient intravenously may result in serious advorse events resulting in seventy rating	Per SOP-05362 Quality and Compliance Risk Management (v. 5.0) Table 1: Severity Rating Scale: Class of product efficacy or product quality leading to adverse events.	Per SOP-05382 Quality and Compilance Risk Management (v 5.0) Table 1: Seventh Rating Scale: Introduction of particulate matter to patient intravenously may sexult in serious adverse evenths resulting in seventhy rating	Per SOP-05362 Quality and Compilance Risk. Management (v 5.0) Table 1: Severity Rating Scale: Loss of product efficacy or product quality leading to adverse events.	
012530981	ssessment to Mitigate t	Effect of Failure	Particulate matter (protein) introduced to patient intravenously resulting in a serious adverse event.	Formation of particulate matter (protein) in drug product. Reduction of drug efficacy.	Particulate matter (protein) introduced to patient intravenously resulting in a serious adverse event.	Formation of particulate matter (profesi) in drug product. Reduction of drug efficacy.	
Son State of CE-49AE-A1CE-49AE-A1CD-F1BC12530981	GILEAD Risk A Creating Possible	Failure Mode	Formation of applicable marter (concern) to the	drug-fulfish in the drug-fulfish on solution.	Formation of particulate matter (profes) in the drug-infusion solution.		
ID: CAFF9AC8-91		Process Step	Drug infusion mixture can be stored in refrigerated conditions for	up to 16 hours or stored at room temperature for 8 hours.	If stored at refrigerated temperature, the prepared drug soution should be equilibrated to room form at least 1 hour.	If stored at refrigerated temperature, the prepared drug solution should be equilibrated to room temperature for at least 1 hour.	
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PAGE	PAGE	29 of 29	Comments / Action Items		Action Item: Update to GS-US-566-6144 Pharmacy Manual to perform visual inspection on drug infusion solution immediately prior to administration to patient.	Action Item: Update to CS-US-386-6144 Pharmacy Manual to perform visual inspection not drug infusion solution immediately prior to administration to patient.
NO	KSION	1.0	RPN		300	210
5	5		Detectability (D)		10	10
DOCIMENT NIMBED	UMENI NUMBER	KEP-49438	Rationale for D		Per SOP-05382 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.	Per SOP-105382 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.
	500		Monitoring Plan		No current requirement to perform visual inspection after transporting the solution in the bag.	No current requirement to perform visual inspection after transporting the solution in the bag.
			Occurrence (O)		r	m
Operations		Magrolimab	Rationale for O		Per SOp-GSS&2 Quality and Compliance Risk Management (v. 5.0) Table 2: Probability of Occurrence Rating Cocurrence Rating Effective routine manual process interventions and/or preventative controls are in place through procedural controls.	Per SOP-05:362 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.
External Quality Operations	III LE Risk Assessment to Mitigate the Introduction of Intrinsic, Extrinsic, and the Formation of Inherent Particulate Matter in Magnolimab	Inherent Particulate Matter in	Controls		GS-US-586-6144 Pharmacy Manual (v 8.0) section 4.6 4 provides guidance on allowable transportation storage temperaturos and distances.	GS-US-586-6144 Pharmacy Manual (v 8.0) section 4.6 provides guidance on allowable transportation storage temperatures and distances.
i i		ic, and the Formation of	Cause of Failure		Drug infusions solution not stored the commended temperature of 2-8° C during transport between the transport between the transport and facilities.	Drug infusions solution not stored at recommended temperature of 2-8 °C during transport between clinical facilities.
		Extrins	Severity (S)		10	7
		ne Introduction of Intrinsic, E	Rationale for S	ags	Per SOA-D5322 Outlifty Anna Compiliance Risk Managament (v. 5.0) Tablin 1: Sevenity Rating Scale: Introduction of particulate matter to patient intravenously may result in serious adverse eventis resulting in sevenity rating	Per SOP-16582 Quality and Compilance Risk Managament (* 5.0) Table 1: Severity Rating Scale: Loss of product efficacy or product efficacy or product quality leading to adverse events.
C12530981		Assessment to Mitigate the	Effect of Failure	Magrolimab Infusion Ba	Formation of inherent particulate matter in drug infusions solution. Particulate matter introduced to patient intravenously resulting in a sentus adverse event.	Formation of particulate matter (protein) in drug product. Reduction of drug efficacy.
Solution Discretes and E-41CD-F1BC12830981 and Dec. 2000 Discrete	GILEAD Creating Possible		Property of the state of the st		Drug infusions solution subjected the repared temperatures above recommended storage conditions of Z-8°C.	recommended storage conditions of 2–8 °C.
) ID: CAFF9AC8-91					lemperature (2-8 °C) storage, up to 340 miles by a motor vehicle.	
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