1. REVIEW APPROVALS

FUNCTION	NAME	SIGNATURE	DATE
Product Risk Management Owner (PRMO)/Author	**ANUPAM CHOUBEY**	**SEE ELECTRONIC SIGNATURE**	
Product Design Owner (PDO)	**DEEPAK MISHRA**	**SEE ELECTRONIC SIGNATURE**	
Therapeutic Area (Medical)	**JIAN WU**	**SEE ELECTRONIC SIGNATURE**	
Quality Representative	**ANN MILLIMAN**	**SEE ELECTRONIC SIGNATURE**	
Verifier	**ANBARASAN S**	**SEE ELECTRONIC SIGNATURE**	

2. PURPOSE

The purpose of this document is to provide a high-level summary of the potential risks resulting from the design, intended use, reasonably foreseeable misuse, and manufacture of the product. This captures results of GQP-10-02 Risk assessment and Reduction. Each subsection provides a description of the potential risk, discusses the foreseeable sequences of events that may lead to hazardous situations, and an overview of the risk control strategy taken to minimize the risk so that it is reduced as far as possible. A table of hazards, hazardous situations, severities of harms, estimates of probabilities for foreseeable events that may lead to hazardous situations, the mitigations implemented to control them, and the residual risk can be found in the Risk Assessment and Control Table (RACT) associated with this document

3. SCOPE

Product Family Name: Ahmedabad Vials and Bottles

Product Family Definition: This product family include both products made in Vials and Bottles manufactured in Ahmedabad. The products included are utilized for the following therapies: Analgesic, Anesthesia, Anti-Convulsant, Anti-Infective, Anti-Sedative, Cardiovascular, Diuretic, Iron Deficiency Anemia, Nutrition, Oncology and Supportive Care, and Sedative.

This product family contains glass containers that are either clear or amber colored glass for supporting light sensitive products. The packaging for these products may include plastic trays for individual vials as an intermediate packaging layer prior to the secondary packaging. For products without the plastic trays, partitions are included in the secondary packaging between the glass containers. The secondary packaging is contained within the carton shipper in packaging configurations dependent on the quantity and marketing requirements.

3. SCOPE

Product Name: Vial

Product Description: Vials are among the container closure systems that are in typical use in the pharmaceutical industry and are used for many therapies. Vials hold sterile drugs. A vial is closed with a stopper that is sealed with an aluminum skirt and covered by a flip cap. The vial in glass and stopper are the primary packaging components that are in direct contact with the dosage form. The aluminum skirt is used to hold the stopper onto the vial. The flip cap is used to keep the stopper clean until use and is removed just prior to use. Access to the drug is through a needle attached to a syringe that is inserted through the stopper. Vial products are not used for direct infusion. Vials are available for use as single dosing or multiple dosing.

The Vials manufactured in Ahmedabad are sterilized through terminal sterilization. The drug products in the vial are in the form of liquid. A vial drug can be used as an injection in which the drug is administered directly from the syringe used to withdraw the drug from the vial. With an infusion, the vial drug is diluted first into a second container with a base solution which is then infused into a patient over the specific time indicated in the prescribing information.

Product Name: **Bottle**

Product Description: Bottles have the same components as vials with the difference being in a larger vial typically ≥ 50 mL. A bottle in glass may also contain an integrated hanger (not shown) used to hang products during infusion. Bottles contain liquid solution and are typically sterilized with terminal sterilization. Bottles in contrast to vials can be used for direct infusion into a patient and accessed with an administration set.

In some cases, the same product in the vial/bottle can be used as a bottle (infusion) or vial (injection). Also, some multi-dose vials can be ≥ 50 mL.

Therapy and Intended Use: Refer Ahmedabad Vials and Bottles Product Risk Management Plan (BXU579479)

3. SCOPE

Description of the Use Environment for the Product Family: The use environment is a hospital, clinic, or alternate care setting where medication is administered under medical supervision.

List or Attach List of Product Code(s) Covered Under This Risk Assessment:

Product Code	Product Name/Description
Product codes in scope include all Vials/Bottles product codes manufactured at the Ahmedabad. The final list of product codes is referenced in the Ahmedabad Vials and Bottles Product Trending Table (PTT) BXU585343 issued in accordance with GQP-10-04 (Post Market Risk Monitoring).	

4. REFERENCES

GQR-10/K	PRODUCT RISK MANAGEMENT
GQP-10-02/E	RISK ASSESSMENT AND REDUCTION
GG-10-01/D	P1 DEVELOPMENT
ISO 13485:2016	MEDICAL DEVICES – QUALITY MANAGEMENT SYSTEMS
BXU585343/H	Ahmedabad Vials and Bottles Product Trending Table (PTT)
BXU579479/C	AHMEDABAD VIALS AND BOTTLES PRODUCT RISK MANAGEMENT PLAN
HSHA-PIT/J	PARENTERAL INFUSION THERAPY HAZARDOUS SITUATION AND HARM ANALYSIS
GQI-05-87/E	PHARMACEUTICALS PRODUCT PROBLEM CODES AND COMPONENT CODES FOR GLOBAL COMPLAINT MANAGEMENT SYSTEM
GQI-05-03/V	INDEX OF GUIDANCE DOCUMENTS, CODING DOCUMENTS, AND CALL SCRIPTS
STDA-PHARMACEUTICALS/G	PHARMACEUTICALS END EFFECT AND STANDARD ALLOCATION ANALYSIS

4. REFERENCES	
BXU571529/C	VIAL AND BOTTLE USE ERROR ANALYSIS (UEA)
BXU563057/A	AHMEDABAD SVP-AQUEOUS LINE - ACICLOVIR DISPENSING AND MIXING PROCESS FAILURE MODE AND EFFECT ANALYSIS (PFMEA)
BXU565396/A	AHMEDABAD SVP LINE -AQUEOUS LINE - ADENOSINE DISPENSING AND MIXING PROCESS FAILURE MODE AND EFFECT ANALYSIS (PFMEA)
BXU538015/A	AMD - AQUEOUS LINE - CIPROFLOXACIN INJECTION USP, DISPENSING AND MIXING PROCESS FAILURE MODE AND EFFECT ANALYSIS (PFMEA)
BXU538437/G	AMD-AQUEOUS LINE PFMEA
BXU567697/B	AHMEDABAD BA2 PLANT RECEIVING AND INSPECTION (R&I) PROCESS FAILURE MODE AND EFFECT ANALYSIS (PFMEA)
BXU566616/B	VIAL LINE-BUPIVACAINE INJECTION(2.5 MG/ML & 5MG/ML) - DISPENSING & MIXING PFMEA
BXU567392/B	AHMEDABAD AQUEOUS LINE –PARACETAMOL DISPENSING AND MIXING PROCESS FAILURE MODE AND EFFECT ANALYSIS (PFMEA)
BXU566097/B	AHMEDABAD PFE-1 & PFE-2 LINE – PROPOFOL LCT MCT DISPENSING AND MIXING PROCESS FAILURE MODE AND EFFECT ANALYSIS (PFMEA)
BXU563113/C	AHMEDABAD PFE-1 & PFE-2 LINE – PROPOFOL DISPENSING AND MIXING PROCESS FAILURE MODE AND EFFECT ANALYSIS (PFMEA)
BXU538320/A	AMD-R&I-PFMEA
BXU567594/D	AHMEDABAD BA2 VIAL LINE PROCESS FAILURE MODE EFFECT ANALYSIS (PFMEA)
BXU566623/B	VIAL LINE-BUPIVACAINE HYDROCHLORIDE 5MG/ML INJECTION BP DISPENSING AND MIXING PFMEA

4. REFERENCES	
BXU565556/C	AHMEDABAD AQUEOUS LINE -FLUCONAZOLE DISPENSING AND MIXING PROCESS FAILURE MODE AND EFFECT ANALYSIS (PFMEA)
BXU538274/A	AMD - SVP LINE - FLUMAZENIL INJECTION USP, DISPENSING AND MIXING PROCESS FAILURE MODE AND EFFECT ANALYSIS (PFMEA)
BXU567469/B	VIAL LINE-FUROSEMIDE (10 MG/ML) INJECTION USP DISPENSING AND MIXING PFMEA
BXU537622/B	AMD - SVP-AQUEOUS LINE - FUROSEMIDE DISPENSING AND MIXING PROCESS FAILURE MODE AND EFFECT ANALYSIS (PFMEA)
BXU537623/B	AMD - SVP-AQUEOUS LINE - BUPIVACAINE HYDROCHLORIDE DISPENSING AND MIXING PROCESS FAILURE MODE AND EFFECT (PFMEA) ANALYSIS
BXU565300/A	AHMEDABAD SVP LINE – IRON SUCROSE DISPENSING AND MIXING PROCESS FAILURE MODE AND EFFECT ANALYSIS (PFMEA)
BXU566892/B	AHMEDABAD VIAL LINE – IRON SUCROSE INJECTION USP, 20 MG ELEMENTAL IRON/ML DISPENSING AND MIXING PFMEA
BXU567599/B	AHMEDABAD VIAL LINE - KETAMINE INJECTION 50 MG/ML DISPENSING AND MIXING PROCESS FAILURE MODE AND EFFECT ANALYSIS (PFMEA)
BXU566738/B	AHMEDABAD AQUEOUS LINE – LEVOFLOXACIN DISPENSING AND MIXING PROCESS FAILURE MODE AND EFFECT ANALYSIS (PFMEA)
BXU537621/B	AMD - SVP-AQUEOUS LINE - METOPROLOL TARTRATE DISPENSING AND MIXING PROCESS FAILURE MODE AND EFFECT ANALYSIS (PFMEA)
BXU566836/B	AHMEDABAD AMPOULE LINE – MIDAZOLAM 1MG/ML INJECTION DISPENSING AND MIXING PROCESS FAILURE MODE AND EFFECT ANALYSIS (PFMEA)

4. REFERENCES	
BXU566833/B	PFMEA DISPENSING AND MIXING: MIDAZOLAM INJECTION USP 1 MG/ML & MIDAZOLAM INJECTION USP 5 MG/ML
BXU566831/B	AHMEDABAD VIAL LINE – MIDAZOLAM 1MG/ML INJECTION DISPENSING AND MIXING PROCESS FAILURE MODE AND EFFECT ANALYSIS (PFMEA)
BXU567554/B	AHMEDABAD VIAL LINE – ONDANSETRON (SINGLE DOSE) DISPENSING AND MIXING PROCESS FAILURE MODE AND EFFECT ANALYSIS (PFMEA)
BXU575006/D	AHMEDABAD BA1 PLANT RECEIVING AND INSPECTION (R&I) PROCESS FAILURE MODE AND EFFECT ANALYSIS (PFMEA) FOR PFE AND PFE-2 LINE
BXU565471/E	AHMEDABAD PFE 2 LINE PROCESS FAILURE MODE AND EFFECT ANALYSIS (PFMEA)
BXU563347/F	AHMEDABAD PFE 1 LINE PROCESS FAILURE MODE AND EFFECT ANALYSIS (PFMEA)
BXU538272/A	AMD - SVP LINE - ONDANSETRON INJECTION USP (SINGLE DOSE), DISPENSING AND MIXING PROCESS FAILURE MODE AND EFFECT ANALYSIS (PFMEA)
BXU538438/H	AMD - SVP LINE PFMEA
BXU537420/B	AMD - SVP-AQUEOUS LINE - TOBRAMYCIN MIXING AND DISPENSING PFMEA

5. GLOSSARY – TERMS AND ACRONYMS	
AMD	Ahmedabad
SME	Subject Matter Expert
RACT	Risk Assessment and Control Table
HAZOP	Hazard and Interoperability Assessment
HSHA	Hazardous Situation and Harm Analysis

5. GLOSSARY – TERMS AND ACRONYMS

UEA	Use Error Analysis
PFMEA	Process Failure Modes and Effects Analysis
UCL	Upper Control Limit
PTT	Product Trending Table
P1	Probability of a Hazardous Situation occurring
P2	Probability of a Hazardous Situation leading to harm
FSOE	Foreseeable Sequence of Events
TcU	Team Center Unified
RR	Risk Reduction
N/A	Not Applicable

6. ASSUMPTIONS

This document is the summation for all Hazards, Hazardous Situations, Harms, and severities for this global product family. Any further information or inquiries pertaining to the meaning of the Hazards, Hazardous Situations, Harms, and severities in the RACT can be found in Parenteral Infusion Therapy Hazardous Situation and Harm Analysis (HSHA-PIT).

This is a living document that will be updated via the remediation of existing product documents and during lifecycle management which includes New Product Development (NPD) and Change Control projects.

The following section describes the assumptions and process that was used to create the Global Risk Assessment and Control Table (RACT), ‘Appendix A - GLOBAL RACT’.

Note 1: Risk Identification (Therapy Level) (columns B through E), Risk Analysis (Therapy Level) (columns F through H): The PARENTERAL INFUSION THERAPY HAZARDOUS SITUATION AND HARM ANALYSIS (HSHA-PIT) was leveraged and then modified to develop P2s specific for AMD. The ranges noted in the Risk Analysis (Therapy Level) have been converted to qualitative values as shown in ‘Appendix B – P2 Conversion’.

Note 2: Foreseeable Sequence of Events – FSOE (column I): This column references ‘Appendix G – MOR’ (column B) and was populated utilizing the Effects on Product identified in ‘Appendix D - Data Summary’ based on a joint effort by

6. ASSUMPTIONS

the team where the content was derived from Subject Matter Expertise. The relationships between FSOE / Effects on Product are also outlined in STDA-PHARMACEUTICALS.

Note 3: Risk Reduction (column J): This column references 'Appendix G – MOR' (column C, E, G, I, K, M, O, Q, S, U, W, Y, AA, AC, AE, AG, AI, AK, AM, AO, AQ, AS, AU, AW, AY, BA, BC, BE, BG, BI, BK, BM and BO) includes or references the use, process, and safety information that have been committed to or completed and that form the basis for the risk reduction for applicable systems or subsystems. A full listing of process and labelling controls can be found in the documents referenced by this column. NOTE: For Use Risk Reductions in Attachment 1, HS.PIT.1.4-7 risk reduction "Training" was based off the specific HS ID RR in HAZOP BXU566192/A.

Note 4: Demonstration of Effectiveness (column K): This column references 'Appendix G – MOR' (column D, F, H, J, L, N, P, R, T, V, X, Z, AB, AD, AF, AH, AJ, AL, AN, AP, AR, AT, AV, AX, AZ, BB, BD, BF, BH, BJ, BL, BN and BP) and includes or references the process, and safety information that have been committed to or completed and that form the basis for the demonstration of effectiveness for applicable systems or subsystems. A full listing of process and labelling controls can be found in the documents referenced by this column.

Note 5: Probability of Hazardous Situation (P1) (column L): This column was calculated based on the current state of products in the field which includes risk control measures that are currently in place and represents the occurrence of the Hazardous Situation in units of occurrence per million. The P1 values can be found in 'Appendix C - P1 Table'. See Section 8 below for the methodology of determining P1 values for this Risk File.

Note 6: Risk Evaluation (Product Level) (columns M through O): The Probability of Occurrence of Harm identified in these columns is calculated based on the Risk Analysis (Therapy Level) (i.e., P2) and the Probability of Hazardous Situation (i.e., P1). These calculations are found in 'Appendix E – PHarm Table' of the RACT.

Note 7: The worst case Predicted P1 values from 'Appendix D – Data Summary' can be found in 'Appendix F – Data Pivot' with the appropriate "Hazardous Situation ID" and respective "Max of Predicted P1" value.

7. CONVERTED P2 VALUES

Severity and Probability of Harm Definitions are documented in the Parenteral Infusion Therapy Hazardous Situation and Harm Analysis (HSHA-PIT).

Assessment of the severity of harm associated with each Hazardous Situation shall be based on the potential or known consequences. The severity shall be categorized according to the HSHA.

HSHA-PIT was filtered for HS IDs applicable to Therapeutic Drug. When multiple P2 values of the same HSID were present, it was defaulted to the lines applicable to the therapy with the highest P2 overall criticality dependent on applicability of therapy in the product family.

All applicable HS.IDs were used in the generation of the STDA aside from those listed below:

7. CONVERTED P2 VALUES

HS.ID.	Hazardous Situation	Non-Applicability Rationale
HS.PIT.3.5	Patient experiences bodily fluid loss (CSF)	This hazardous situation does not apply to products within the scope of this file as these are not utilized for spinal infusions.
HS.PIT.6.1	End user is exposed to a product's hot surface or hot fluid leaking from a product	Not applicable to Vial or Bottle. Applicable for Pre-mix Frozen category only.
HS.PIT.20.4	Patient's tissue is exposed to shear stress during therapy	Not applicable to Vial or Bottle products as they are in rigid containers and are not used under pressure infusion.
HS.PIT.21.1	End User is exposed to bodily tissue	Not applicable to Vial or Bottle. Applicable for Premix and Pre-filled syringes only.
HS.PIT.24.2	Patient is exposed to a product with a pH of < 7 or > 8	Not applicable to Vial or Bottle. Applicable for Premix only.
HS.PIT.25.1	Patient is infused with a product at higher than intended temperatures (> 43°C / 109.4°F)	Not applicable to AMD Vial or Bottle. Applicable for Premix Frozen only.
HS.PIT.27.2	End User is entangled or entrapped by the product or product components	Not applicable to Vial or Bottle products as they do not have an overpouch that would cause potential for injury to the user if they were entangled/entrapped by the product.

A new end effect described as "Separation of Solution" has been included, specific to the emulsifying product Propofol, and is in alignment with STDA PARENTERAL NUTRITION. There will be an allocation of 3 for HS.PIT.28.1, Patient is exposed to an unstable drug emulsion, and 3, 3, 3, 1, 1 for HS.PIT.5.1, HS.PIT.5.2, HS.PIT.5.3, HS.PIT.5.4, and HS.PIT.5.5 respectively. If the effect is identified early in the setup process, it may sometimes be quickly resolved. However, if the effect is not noticed just prior to administration to the patient, there may be an increased amount of time required to obtain new supplies. Delay Split (%): 20 / 50 / 25 / 3 / 2.

In addition, HS.PIT.28.1 has also been made applicable to Discoloured and Incorrect Storage end effects for this risk file, with an allocation of 3 and 5 respectively, due to the presence of the emulsifying agent, Propofol and in alignment with the STDA PARENTERAL NUTRITION allocations for emulsion with these end effects.

Standard Delay, Standard Interruption, Individually Investigate, Problem Code does not relate to Product Family Code, and No directly resulting Hazardous Situation/End Effect are end effects that result in mutually exclusive hazardous situations but are not directly affects on products themselves. They are building blocks for other end effects in the STDA and are included in other end effects that impact the product directly. Therefore, the end effects themselves are excluded in the RACT.

The P2 value in the HSHA represents the probability of a Hazardous Situation leading to harm at a specific severity level, regardless of the cause. The P2 assumes the HS has occurred and does not consider any clinical sequence of events which may prevent the HS from occurring. The P2 values are converted using table 1 below:

7. CONVERTED P2 VALUES

Table 1 – Therapy Occurrence Conversions

Therapy Occurrences (HSHA)		
Qualitative		**Quantitative (OPM)**
Expected	7	> 500,000
Likely	6	>240,000 to <= 500,000
Often	5	> 100,000 to <= 240,000
Periodic	4	> 10,000 to <= 100,000
Occasional	3	> 100 to <= 10,000
Rare	2	> 1 to <= 100
Exceptional	1	> 0 to <= 1

The probability of the Hazardous Situation (P1) occurring will leverage occurrence rankings based on information from multiple sources, including but not limited to: SME expertise, UEA, and pFMEAs. For each Hazardous Situation, the probability of occurrence of harm for this product family will be evaluated based on the consideration of both P1 and P2 (P1 x P2). See next section for P1 methodology.

8. P1 METHODOLOGY

The guidance outlined in GG-10-01, P1 development, was utilized to create the P1 table for this product family. The purpose of this section is to provide a detailed summary of the inputs to the analysis conducted. The documents and software listed in Table 2 were utilized to determine a predicted P1.

Table 2 – Data/Tools Used in this Analysis

Reference Number	Document Title / Source	Revision	Archival Location
HSHA-PIT	PARENTERAL INFUSION THERAPY HAZARDOUS SITUATION AND HARM ANALYSIS	J	TcU+
STDA-PHARMACEUTICALS	PHARMACEUTICALS END EFFECT AND STANDARD ALLOCATION ANALYSIS	G	TcU+
BXU566192	HAZARD AND INTEROPERABILITY ASSESSMENT (HAZOP) PHARMA-GLASS_BOTTLES	A	TcU+
Attachment 1_Vial and Bottle UEA BXU571529	VIAL AND BOTTLE USE ERROR ANALYSIS (UEA)	B	TcU+
Attachment 2_Aciclovir BA 1 (SVP)_pFMEA_BXU563057	AHMEDABAD SVP-AQUEOUS LINE - ACICLOVIR DISPENSING AND MIXING PROCESS FAILURE MODE AND EFFECT ANALYSIS (PFMEA)	B	TcU+
Attachment 3_Adenosine BA 1 SVP Aqueous Line (Vial)_pFMEA_BXU565396	AHMEDABAD SVP LINE -AQUEOUS LINE - ADENOSINE DISPENSING AND MIXING PROCESS FAILURE MODE AND EFFECT ANALYSIS (PFMEA)	B	TcU+
Attachment 4_AMD - Aqueous Line - Ciprofloxacin Injection USP Dispensing and Mixing_pFMEA_BXU538015	AMD - AQUEOUS LINE - CIPROFLOXACIN INJECTION USP, DISPENSING AND MIXING PROCESS FAILURE MODE AND EFFECT ANALYSIS (PFMEA)	B	TcU+
Attachment 5_AMD - Aqueous Line_pFMEA_BXU538437	AMD-AQUEOUS LINE PFMEA	B	TcU+
Attachment 6_AMD - BA2 Plant Receiving and Inspection (RI)_pFMEA_BXU567697	AHMEDABAD BA2 PLANT RECEIVING AND INSPECTION (R&I) PROCESS FAILURE MODE AND EFFECT ANALYSIS (PFMEA)	B	TcU+
Attachment 7_AMD - Bupivacaine 2.5mgmL & 5mgmL pFMEA - B2 Vial line_pFMEA_BXU566616	VIAL LINE-BUPIVACAINE INJECTION(2.5 MG/ML & 5MG/ML) - DISPENSING & MIXING PFMEA	B	TcU+
Attachment 8_AMD - Bupivacaine Dispensing and Mixing_pFMEA_BXU537623	AMD - SVP-AQUEOUS LINE - BUPIVACAINE HYDROCHLORIDE DISPENSING AND MIXING PROCESS FAILURE MODE AND EFFECT (PFMEA) ANALYSIS	B	TcU+

Attachment 9_AMD - Paracetamol Mixing and Dispensing_pFMEA_BXU567392	AHMEDABAD AQUEOUS LINE – PARACETAMOL DISPENSING AND MIXING PROCESS FAILURE MODE AND EFFECT ANALYSIS (PFMEA)	B	TcU+
Attachment 10_AMD - Propofol LCT MCT Mixing and Dispensing_pFMEA_BXU566097	AHMEDABAD PFE-1 & PFE-2 LINE – PROPOFOL LCT MCT DISPENSING AND MIXING PROCESS FAILURE MODE AND EFFECT ANALYSIS (PFMEA)	B	TcU+
Attachment 11_AMD - Propofol_pFMEA_BXU563113	AHMEDABAD PFE-1 & PFE-2 LINE – PROPOFOL DISPENSING AND MIXING PROCESS FAILURE MODE AND EFFECT ANALYSIS (PFMEA)	B	TcU+
Attachment 12_AMD - R&I_pFMEA_BXU538320	AMD-R&I-PFMEA	B	TcU+
Attachment 13_BA 2 Vial Line_pFMEA_BXU567594	AHMEDABAD BA2 VIAL LINE PROCESS FAILURE MODE EFFECT ANALYSIS (PFMEA)	B	TcU+
Attachment 14_Bupivacaine BA 2 (Vial Line) Vial_pFMEA_BXU566623	VIAL LINE-BUPIVACAINE HYDROCHLORIDE 5MG/ML INJECTION BP DISPENSING AND MIXING PFMEA	B	TcU+
Attachment 15_Fluconazole Mixing and Dispensing_pFMEA_BXU565556	AHMEDABAD AQUEOUS LINE - FLUCONAZOLE DISPENSING AND MIXING PROCESS FAILURE MODE AND EFFECT ANALYSIS (PFMEA)	B	TcU+
Attachment 16_Flumazenil SVP Vial_pFMEA_BXU538274	AMD - SVP LINE - FLUMAZENIL INJECTION USP, DISPENSING AND MIXING PROCESS FAILURE MODE AND EFFECT ANALYSIS (PFMEA)	B	TcU+
Attachment 17_Furosemide BA 2 (Vial line)_pFMEA_BXU567469	VIAL LINE-FUROSEMIDE (10 MG/ML) INJECTION USP DISPENSING AND MIXING PFMEA	B	TcU+
Attachment 18_Furosemide_pFMEA_BXU537622	AMD - SVP-AQUEOUS LINE - FUROSEMIDE DISPENSING AND MIXING PROCESS FAILURE MODE AND EFFECT ANALYSIS (PFMEA)	B	TcU+
Attachment 19_Iron Sucrose BA 1 (SVP)_pFMEA_BXU565300	AHMEDABAD SVP LINE – IRON SUCROSE DISPENSING AND MIXING PROCESS FAILURE MODE AND EFFECT ANALYSIS (PFMEA)	B	TcU+
Attachment 20_Iron Sucrose BA2 Vial_pFMEA_BXU566892	AHMEDABAD VIAL LINE – IRON SUCROSE INJECTION USP, 20 MG ELEMENTAL IRON/ML DISPENSING AND MIXING PFMEA	B	TcU+
Attachment 21_Ketamine BA 2 (Vial line)_pFMEA_BXU567599	AHMEDABAD VIAL LINE - KETAMINE INJECTION 50 MG/ML DISPENSING AND	B	TcU+

	MIXING PROCESS FAILURE MODE AND EFFECT ANALYSIS (PFMEA)		
Attachment 22_Levofloxacin - Aqueous line_pFMEA_BXU566738	AHMEDABAD AQUEOUS LINE – LEVOFLOXACIN DISPENSING AND MIXING PROCESS FAILURE MODE AND EFFECT ANALYSIS (PFMEA)	B	TcU+
Attachment 23_Metoprolol_pFMEA_BXU537621	AMD - SVP-AQUEOUS LINE - METOPROLOL TARTRATE DISPENSING AND MIXING PROCESS FAILURE MODE AND EFFECT ANALYSIS (PFMEA)	B	TcU+
Attachment 24_Midazolam BA 2 (Ampoule line)_pFMEA_BXU566836	AHMEDABAD AMPOULE LINE – MIDAZOLAM 1MG/ML INJECTION DISPENSING AND MIXING PROCESS FAILURE MODE AND EFFECT ANALYSIS (PFMEA)	B	TcU+
Attachment 25_Midazolam BA 2 (Vial line) Midazolam 1 mgmL & 5mgmL Injection USP pFMEA Vial Line Appendix-B_pFMEA_BXU566833	PFMEA DISPENSING AND MIXING: MIDAZOLAM INJECTION USP 1 MG/ML & MIDAZOLAM INJECTION USP 5 MG/ML	B	TcU+
Attachment 26_Midazolam BA 2 (Vial line)_pFMEA_BXU566831	AHMEDABAD VIAL LINE – MIDAZOLAM 1MG/ML INJECTION DISPENSING AND MIXING PROCESS FAILURE MODE AND EFFECT ANALYSIS (PFMEA)	B	TcU+
Attachment 27_Ondansetron BA 2 (Vial line)_pFMEA_BXU567554	AHMEDABAD VIAL LINE – ONDANSETRON (SINGLE DOSE) DISPENSING AND MIXING PROCESS FAILURE MODE AND EFFECT ANALYSIS (PFMEA)	B	TcU+
Attachment 28_PFE & PFE-2 R&I_pFMEA_BXU575006	AHMEDABAD BA1 PLANT RECEIVING AND INSPECTION (R&I) PROCESS FAILURE MODE AND EFFECT ANALYSIS (PFMEA) FOR PFE AND PFE-2 LINE	B	TcU+
Attachment 29_PFE 2 Line_pFMEA_BXU565471	AHMEDABAD PFE 2 LINE PROCESS FAILURE MODE AND EFFECT ANALYSIS (PFMEA)	B	TcU+
Attachment 30_PFE Line_pFMEA_BXU563347	AHMEDABAD PFE 1 LINE PROCESS FAILURE MODE AND EFFECT ANALYSIS (PFMEA)	B	TcU+
Attachment 31_SVP Line - Ondansetron Injection USP (Single dose) Dispensing and Mixing pFMEA_BXU538272	AMD - SVP LINE - ONDANSETRON INJECTION USP (SINGLE DOSE), DISPENSING AND MIXING PROCESS FAILURE MODE AND EFFECT ANALYSIS (PFMEA)	B	TcU+
Attachment 32_SVP Line_pFMEA_BXU538438	AMD-SVP LINE PFMEA	B	TcU+
Attachment 33_Tobramycin pFMEA_BXU537420	AMD - SVP-AQUEOUS LINE - TOBRAMYCIN MIXING AND DISPENSING PFMEA	B	TcU+

Attachment 34_Manufacturing Process FMEA Equivalency Assessment Report	MANUFACTURING PROCESS FMEA EQUIVALENCY ASSESSMENT REPORT	B	Baxter AMD site-doc cell
Attachment 35_Initial_PTT_Ahmedabad	Vial and Bottle Initial Product Trending Table (PTT)	B	TcU+
Attachment 36_UCL	Vial and Bottle Upper Control Limit (UCL)	B	TcU+
Attachment 37_UCL Memo	Vial and Bottle UCL Memo	B	TcU+

+TcU = Teamcenter Unified

The following process was used to determine a P1 value:

1. Establish a list of Effects on Product due to Process and Use related failures.
   a. A list of End Effects has already been established in the STDA-PHARMACEUTICALS, filtered with 'Vial & Bottle Qualitative' applicability. Allocation ranges are defined as follows:

Table 3 – Allocation Conversions

Allocation Factors	
Qualitative	**Quantitative (%)**
5	>= 80% to <= 100%
3	>= 11% to <= 79%
1	<= 10%

   b. For Use related End Effects, use the 'STDA End Effect' column in VIAL AND BOTTLE USE ERROR ANALYSIS (UEA) document, Attachment 1.
   c. For Process related End Effects, map in the 'STDA End Effect' column in the PFMEAs to the appropriate End Effect from the STDA-PHARMACEUTICALS.

2. For the UEA:
   Line75 in the UEA with Use Steps "Dispose Administration Materials" mapped to "Loose Components" end effect will also be mapped as end effect "Product not used as single dose only". The improper disposal of administration material would allow a product to not be used as a single dose only with the probability rating of 1 taken from row 75 of the UEA. In addition, line 59 Use Step "Prepare Infusion / Injection" with Use Sub-Step "Prime administration set (if applicable)" will also be mapped to "Introduction of Air into fluid Path". The line is noted as "N/A - Out of Scope because this step does not have an interaction between the USER and VIAL / BOTTLE, VIAL CARTON or PRODUCT." In the UEA, it should be applicable to the product as Vial products are used for direct administration. Therefore, it is assigned a probability rating of 3, based off the occurrence value for "Introduction of Air into fluid Path" in HAZOP BXU566192/A. Document the relationship between the ' STDA End Effect' to the applicable Hazardous Situations in 'Appendix D - Data Summary' of the RACT as "Use" source. Generalized 'Effect Types' and their mappings to appropriate Hazardous Situations for AMD are found in the STDA-PHARMACEUTICALS. Note: Multiple Effects on Product may lead to the same Hazardous Situations and multiple Hazardous Situations may lead to the same Effect on Product.

a. Data Roll Up of the 'STDA End Effect' and maximum Probability Rating are provided in the "End Effects Max Probability" tab of Attachment 1_Vial and Bottle UEA BXU571529.

3. For pFMEAs:
   Comparable pFMEAs, found in Attachment 34, were utilized in circumstances where a specific mixing pFMEA was not available.

   For Process related End Effects, map in the 'STDA End Effect' column in the pFMEAs to the appropriate End Effect on Product from STDA-PHARMACEUTICALS.
   a. Calculate the Occurrence x Detection (O x D) value using the chart below to determine the predicted failure rate for each row in the pFMEA.

Qualitative Detection		
Category	**Rank**	**Definition**
Improbable	5	It is unlikely that the detection control will detect the defect
Low	4	There is low probability the detection control will detect the defect
Moderate	3	The detection control will detect about half of the defects in the population
High	2	The detection control will detect a significant portion of the defects
Almost Certain	1	The detection control will detect almost all defects

O X D		Detection				
		1	**2**	**3**	**4**	**5**
Occurrence	**1**	1	1	1	1	1
	2	1	1	1	1	2
	3	1	2	2	2	3
	4	1	3	3	3	4
	5	2	4	4	4	5

   b. Data Roll Up of the End Effect and maximum O x D for each pFMEA is provided in the "P1 Pivot" tab of Attachments 2-33.
   c. Document the relationship between the 'STDA End Effect' for each pFMEA to the applicable Hazardous Situations in 'Appendix D - Data Summary' of the RACT as each respective "Process" pFMEA source column.
4. Then populate the worst-case failure rate (WC failure rate) with the highest value between the pFMEA and the UEA for each Hazardous Situation.
5. Use the following table to determine the predicted P1 for each End Effect – Hazardous Situation combination by comparing the worst-case failure rate determined in Step 4 and the allocation factor (1-3-5) determined in STDA-PHARMACEUTICALS:

Table 5 – P1 Calculations

FR x AF		Allocation Factor		
		1	**3**	**5**
Failure Rate	**1**	1	1	1
	2	1	1	2
	3	1	3	3

	4	1	3	4
	5	1	5	5

Then record the worst case P1 for each hazardous situation in "Data Summary Derived P1" column of 'Appendix C – P1 Table.'

6. Convert the UCLs (Upper Control Limits) from Complaint Data (seen in Attachment 36) to qualitative according to GG-10-01 Appendix 1 Table A1--5, provided below.

Qualitative		Quantitative
Frequent	5	X >1000 OPM
Probable	4	1000 ≥ X > 100 OPM
Occasional	3	100 ≥ X > 10 OPM
Remote	2	10 ≥ X >1 OPM
Improbable	1	< 1 OPM

   Then record qualitative values in the "UCL" column of 'Appendix C – P1 Table' for all applicable Hazardous Situations. Note: UCLs were calculated using the upper limit of the Allocation Factor Range, to be conservative. An allocation of 1 was represented as 10%, an allocation of 3 was represented as 79%, and an allocation of 5 was represented as 100%.
7. Evaluate the worst case P1 between the "Data Summary Derived P1" and "UCL" data to record in the P1 column of 'Appendix C – P1 Table' the final P1 value.
   Note: SME establishes P1 value with Rationale, if appropriate, in 'Appendix C – P1 Table' in the P1 Predicted by Subject Matter Expertise and Selected P1 Rationale columns.
8. Next, record the P2 Conversion and P1 values for each Hazardous Situation in 'Appendix E – PHarm Table'. Calculate PHarm for each Hazardous Situation by multiplying P1 x P2 at each severity level. Convert the PHarm values to Qualitative using Table 6 below:

Table 6 – PHarm Conversions

Individual Residual Risk		Severity (Qualitative)		
		Critical	Moderate	Minor
P1 x P2	0	N/A	N/A	N/A
	1-7	Medium	Low	Low
	8 – 18	High	Medium	Low
	19 – 35	High	High	Medium

9. Record the P1 values and PHarm Qualitative values, per each severity level, for all Hazardous Situations in ‘Appendix A – Global RACT’.

9. RISK ASSESSMENT AND CONTROL TABLE

☒ RACT attached or ☐ Reference:

In BXU579481_Rev B.xlsx

Cover Page Details (Computer details, OS and Excel version, References)
Sites (List of Plants involved in the Product Family Risk File)
Appendix A – Global Risk Assessment and Control Table (RACT)
Appendix B – P2 Conversion
Appendix C – P1 Table
Appendix D – Data Summary
Appendix E – PHarm Table
Appendix F – Pivot Table
Appendix G - MOR

Attachment 1_Vial and Bottle UEA BXU571529
Attachment 2_Aciclovir BA 1 (SVP)_pFMEA_BXU563057
Attachment 3_Adenosine BA 1 SVP Aqueous Line (Vial)_pFMEA_BXU565396
Attachment 4_AMD - Aqueous Line - Ciprofloxacin Injection USP Dispensing and Mixing_pFMEA_BXU538015
Attachment 5_AMD - Aqueous Line_pFMEA_BXU538437
Attachment 6_AMD - BA2 Plant Receiving and Inspection (RI)_pFMEA_BXU567697
Attachment 7_AMD - Bupivacaine 2.5mgmL & 5mgmL pFMEA - B2 Vial line_pFMEA_BXU566616
Attachment 8_AMD - Bupivacaine Dispensing and Mixing_pFMEA_BXU537623
Attachment 9_AMD - Paracetamol Mixing and Dispensing_pFMEA_BXU567392
Attachment 10_AMD - Propofol LCT MCT Mixing and Dispensing_pFMEA_BXU566097
Attachment 11_AMD - Propofol_pFMEA_BXU563113
Attachment 12_AMD - R&I_pFMEA_BXU538320
Attachment 13_BA 2 Vial Line_pFMEA_BXU567594
Attachment 14_Bupivacaine BA 2 (Vial Line) Vial_pFMEA_BXU566623
Attachment 15_Fluconazole Mixing and Dispensing_pFMEA_BXU565556
Attachment 16_Flumazenil SVP Vial_pFMEA_BXU538274
Attachment 17_Furosemide BA 2 (Vial line)_pFMEA_BXU567469
Attachment 18_Furosemide_pFMEA_BXU537622
Attachment 19_Iron Sucrose BA 1 (SVP)_pFMEA_BXU565300
Attachment 20_Iron Sucrose BA2 Vial_pFMEA_BXU566892
Attachment 21_Ketamine BA 2 (Vial line)_pFMEA_BXU567599
Attachment 22_Levofloxacin - Aqueous line_pFMEA_BXU566738
Attachment 23_Metoprolol_pFMEA_BXU537621
Attachment 24_Midazolam BA 2 (Ampoule line)_pFMEA_BXU566836
Attachment 25_Midazolam BA 2 (Vial line) Midazolam 1 mgmL & 5mgmL Injection USP pFMEA Vial Line Appendix-B_pFMEA_BXU566833
Attachment 26_Midazolam BA 2 (Vial line)_pFMEA_BXU566831
Attachment 27_Ondansetron BA 2 (Vial line)_pFMEA_BXU567554
Attachment 28_PFE & PFE-2 R&I_pFMEA_BXU575006
Attachment 29_PFE 2 Line_pFMEA_BXU565471
Attachment 30_PFE Line_pFMEA_BXU563347
Attachment 31_SVP Line - Ondansetron Injection USP (Single dose) Dispensing and Mixing pFMEA_BXU538272
Attachment 32_SVP Line_pFMEA_BXU538438

Attachment 33_Tobramycin pFMEA_BXU537420
Attachment 34_Manufacturing Process FMEA Equivalency Assessment Report
Attachment 35_Initial_PTT_Ahmedabad
Attachment 36_UCL
Attachment 37_UCL Memo

10. HAZARDOUS SITUATION MITIGATION OVERVIEW

To demonstrate the risk has been reduced as far as possible (AFAP), the mitigation overview addresses how the product meets one or more of the following criteria (reference GQP-10-02):

Case I. Conformance to a harmonized standard.

Case II. Compliant to a local country standard or commensurate to published literature, in the absence of a harmonized standard.

Case III. Demonstration that no further mitigations are technically practical when considering:
- Best medical practices
- State of the art technology
- Performance of predicate and competitive products

Case IV. Demonstration that further mitigations will not improve safety*

End Effect:	Breach in Aseptic Technique - Administration	**Hazardous Situation(s):**	HS.PIT.21.3
Acceptability Assessment:	☐ Case I	☐ Case II	☒ Case III ☐ Case IV
Product labeling clearly instructs that aseptic technique must be used throughout use of the product. Aseptic Technique is dependent on standard good clinical practice. Individual residual risk for this hazardous situation is reduced as far as possible (AFAP) considering the generally acknowledged state of the art.			
Residual Risk is:	☒ Acceptable	☐ Acceptable with cRBA	☐ Unacceptable

End Effect:	Breach in Aseptic Technique - Compounding	**Hazardous Situation(s):**	HS.PIT.21.4
Acceptability Assessment:	☐ Case I	☐ Case II	☒ Case III ☐ Case IV
Product labeling clearly instructs that aseptic technique must be used throughout use of the product. Aseptic Technique is dependent on standard good clinical practice. Individual residual risk for this hazardous situation is reduced as far as possible (AFAP) considering the generally acknowledged state of the art.			
Residual Risk is:	☒ Acceptable	☐ Acceptable with cRBA	☐ Unacceptable

End Effect:	Compounding - Base Solution Concentration Incorrect	**Hazardous Situation(s):**	HS.PIT.22.1 HS.PIT.22.2 HS.PIT.5.1 HS.PIT.5.2 HS.PIT.5.3

			HS.PIT.5.4 HS.PIT.5.5	
Acceptability Assessment:	☐ Case I	☐ Case II	☒ Case III	☐ Case IV
Product labeling includes product concentration and volume informing the clinician. Packaging inserts are designed to instruct the user about correct dose volume and compatible IV solutions. Process controls are in place to ensure labeling accuracy. Individual residual risk for these hazardous situations is reduced as far as possible (AFAP) considering the generally acknowledged state of the art.				
Residual Risk is:	☒ Acceptable	☐ Acceptable with cRBA	☐ Unacceptable	

End Effect:	Compounding - Diluent Concentration Incorrect	**Hazardous Situation(s):**	HS.PIT.22.1 HS.PIT.22.2 HS.PIT.5.1 HS.PIT.5.2 HS.PIT.5.3 HS.PIT.5.4 HS.PIT.5.5

Acceptability Assessment:	☐ Case I	☐ Case II	☒ Case III	☐ Case IV
Product labeling includes product concentration, diluent concentration and volume informing the clinician. Packaging inserts are designed to instruct the user about correct dose volume and compatible IV solutions along with appropriate diluent concentration. Process controls are in place to ensure labeling accuracy. Individual residual risk for these hazardous situations is reduced as far as possible (AFAP) considering the generally acknowledged state of the art.				
Residual Risk is:	☒ Acceptable	☐ Acceptable with cRBA	☐ Unacceptable	

End Effect:	Compounding - Incorrect Base Solution	**Hazardous Situation(s):**	HS.PIT.11.1 HS.PIT.22.1 HS.PIT.22.2 HS.PIT.23.1 HS.PIT.23.2 HS.PIT.5.1 HS.PIT.5.2 HS.PIT.5.3 HS.PIT.5.4 HS.PIT.5.5

Acceptability Assessment:	☐ Case I	☐ Case II	☒ Case III	☐ Case IV
Product labeling includes product concentration and volume informing the clinician. Packaging inserts are designed to instruct the user about correct dose volume and compatible IV solutions. Process controls are in place to ensure labeling accuracy. Individual residual risk for these hazardous situations is reduced as far as possible (AFAP) considering the generally acknowledged state of the art.				
Residual Risk is:	☒ Acceptable	☐ Acceptable with cRBA	☐ Unacceptable	

End Effect:	Compounding - Incorrect Diluent	**Hazardous Situation(s):**	HS.PIT.11.1 HS.PIT.22.1 HS.PIT.22.2 HS.PIT.23.1 HS.PIT.23.2 HS.PIT.5.1 HS.PIT.5.2 HS.PIT.5.3 HS.PIT.5.4 HS.PIT.5.5

Acceptability Assessment:	☐ Case I	☐ Case II	☒ Case III	☐ Case IV

Product labeling includes correct diluent for reconstitution and dilution informing the clinician. Packaging inserts are designed to instruct the user about correct and compatible IV solutions. Process controls are in place to ensure labeling accuracy. Individual residual risk for these hazardous situations is reduced as far as possible (AFAP) considering the generally acknowledged state of the art.

Residual Risk is:	☒ Acceptable	☐ Acceptable with cRBA	☐ Unacceptable

End Effect:	Cosmetic defects	**Hazardous Situation(s):**	HS.PIT.5.1 HS.PIT.5.2 HS.PIT.5.3 HS.PIT.5.4 HS.PIT.5.5

Acceptability Assessment:	☐ Case I	☐ Case II	☒ Case III	☐ Case IV

Processes are validated and machine setup activities are performed in order to reduce the introduction of defects. Units are visually inspected for defects in-process and during packing. Final release visual inspections include inspection for cosmetic defects. Individual residual risk for these hazardous situations is reduced as far as possible (AFAP) considering the generally acknowledged state of the art.

Residual Risk is:	☒ Acceptable	☐ Acceptable with cRBA	☐ Unacceptable

End Effect:	Damaged – Carton	**Hazardous Situation(s):**	HS.PIT.5.1 HS.PIT.5.2 HS.PIT.5.3 HS.PIT.5.4 HS.PIT.5.5 HS.PIT.27.3

Acceptability Assessment:	☐ Case I	☐ Case II	☒ Case III	☐ Case IV

Packaging Materials are designed and validated to withstand distribution and handling conditions. The stretch wrapping pallets are inspected for damage prior to shipment. Shipping studies assess for physical damage of the product and secondary packaging. These ensure the carton functions as intended.

Individual residual risk for these hazardous situations is reduced as far as possible (AFAP) considering the generally acknowledged state of the art.			
Residual Risk is:	☒ Acceptable	☐ Acceptable with cRBA	☐ Unacceptable

End Effect:	Damaged - Closure System	**Hazardous Situation(s):**	HS.PIT.5.1 HS.PIT.5.2 HS.PIT.5.3 HS.PIT.5.4 HS.PIT.5.5 HS.PIT.21.3

Acceptability Assessment:	☐ Case I	☐ Case II	☒ Case III	☐ Case IV
The closure is intended to maintain a sterile fluid path until the point of use when it is intended to be removed. Materials selected for the closure are intended to provide a bond which can ensure that the sterile barrier is maintained, and the closure can still be removed at time of use. The ability of the bond to maintain the sterile barrier is verified during design. Product is additionally 100% visually inspected for presence of closure and proper seal. Individual residual risk for these hazardous situations is reduced as far as possible (AFAP) considering the generally acknowledged state of the art. These controls represent state of the art technology available of the time of design.				
Residual Risk is:	☒ Acceptable	☐ Acceptable with cRBA	☐ Unacceptable	

End Effect:	Damaged - Other	**Hazardous Situation(s):**	HS.PIT.5.1 HS.PIT.5.2 HS.PIT.5.3 HS.PIT.5.4 HS.PIT.5.5 HS.PIT.18.1 HS.PIT.18.2 HS.PIT.18.3 HS.PIT.18.4 HS.PIT.18.5

Acceptability Assessment:	☐ Case I	☐ Case II	☒ Case III	☐ Case IV
Parts are evaluated during receiving and inspection. Processes are validated and machine setup activities are performed in order to reduce the introduction of defects. Units are visually inspected for defects in-process and during packing. Final release visual inspections include inspection for cosmetic defects. Individual residual risk for these hazardous situations is reduced as far as possible (AFAP) considering the generally acknowledged state of the art.				
Residual Risk is:	☒ Acceptable	☐ Acceptable with cRBA	☐ Unacceptable	

End Effect:	Damaged - Rigid Components	**Hazardous Situation(s):**	HS.PIT.5.1 HS.PIT.5.2

			HS.PIT.5.3 HS.PIT.5.4 HS.PIT.5.5 HS.PIT.27.3
Acceptability Assessment:	☐ Case I	☐ Case II	☒ Case III	☐ Case IV
Parts are evaluated during receiving and inspection. Processes are validated and machine setup activities are performed in order to reduce the introduction of defects. Units are visually inspected for defects in-process and during packing. Individual residual risk for these hazardous situations is reduced as far as possible (AFAP) considering the generally acknowledged state of the art.			
Residual Risk is:	☒ Acceptable	☐ Acceptable with cRBA	☐ Unacceptable

End Effect:	Damaged - Secondary Packaging	**Hazardous Situation(s):**	HS.PIT.5.1 HS.PIT.5.2 HS.PIT.5.3 HS.PIT.5.4 HS.PIT.5.5 HS.PIT.11.1 HS.PIT.13.5 HS.PIT.13.6 HS.PIT.13.7 HS.PIT.27.3
Acceptability Assessment:	☐ Case I	☐ Case II	☒ Case III	☐ Case IV
Shipping studies have been performed to provide evidence that the secondary packaging protects the product from damage. These controls represent state of the art technology available of the time of design.			
Residual Risk is:	☒ Acceptable	☐ Acceptable with cRBA	☐ Unacceptable

End Effect:	Difficult to Use	**Hazardous Situation(s):**	HS.PIT.5.1 HS.PIT.5.2 HS.PIT.5.3 HS.PIT.5.4 HS.PIT.5.5 HS.PIT.27.6
Acceptability Assessment:	☒ Case I	☐ Case II	☐ Case III	☐ Case IV
The products are designed to be ergonomically easy to use. Product container is sourced by suppliers with design in conformance to the harmonized standard. The supplier certificate analysis conformance provides this evidence. Design requirements for testing the product manually are in place to ensure that the product is functionally easy to use. Individual residual risk for these hazardous situations is reduced as far as possible (AFAP) considering the generally acknowledged state of the art.			
Residual Risk is:	☒ Acceptable	☐ Acceptable with cRBA	☐ Unacceptable

End Effect:	Difficult to Use - Access Ports or Stoppers	**Hazardous Situation(s):**	HS.PIT.5.1 HS.PIT.5.2 HS.PIT.5.3 HS.PIT.5.4 HS.PIT.5.5 HS.PIT.27.4 HS.PIT.27.6

Acceptability Assessment:	☒ Case I	☐ Case II	☐ Case III	☐ Case IV
The products are designed to be ergonomically easy to use. Product container is sourced by suppliers with design in conformance to the harmonized standard. The supplier certificate analysis conformance provides this evidence. Design requirements for testing the product manually are in place to ensure that the product is functionally easy to use. The instructions for use for the products make it clear and easy to the end user to follow and use the proper technique for drug admixing with these products. The labelling of the product has been verified to ensure that it is meeting the product requirements.				
Residual Risk is:	☒ Acceptable	☐ Acceptable with cRBA	☐ Unacceptable	

End Effect:	Discolored	**Hazardous Situation(s):**	HS.PIT.5.1 HS.PIT.5.2 HS.PIT.5.3 HS.PIT.5.4 HS.PIT.5.5 HS.PIT.11.1 HS.PIT.28.1

Acceptability Assessment:	☐ Case I	☐ Case II	☒ Case III	☐ Case IV
The manufacturing process is designed and validated to ensure that the drug product is produced to ensure appropriate composition and purity. Vials and Bottles are 100% visual inspected for discolored solution. Individual residual risk for these hazardous situations is reduced as far as possible (AFAP) considering the generally acknowledged state of the art.				
Residual Risk is:	☒ Acceptable	☐ Acceptable with cRBA	☐ Unacceptable	

End Effect:	Embedded Material - Non-Solution Path Contact	**Hazardous Situation(s):**	HS.PIT.5.1 HS.PIT.5.2 HS.PIT.5.3 HS.PIT.5.4 HS.PIT.5.5

Acceptability Assessment:	☐ Case I	☐ Case II	☒ Case III	☐ Case IV
Processes are validated and machine setup activities are performed in order to reduce the introduction of defects. Units are visually inspected for defects in receiving and inspection, in-process and during packing. During the release of packaging materials, inspection for presence of extraneous matter is performed. Final release visual inspections include inspection for cosmetic defects.				

Individual residual risk for these hazardous situations is reduced as far as possible (AFAP) considering the generally acknowledged state of the art.			
Residual Risk is:	☒ Acceptable	☐ Acceptable with cRBA	☐ Unacceptable

End Effect:	Embedded Material - Solution Path Contact	**Hazardous Situation(s):**	HS.PIT.5.1 HS.PIT.5.2 HS.PIT.5.3 HS.PIT.5.4 HS.PIT.5.5 HS.PIT.11.1

Acceptability Assessment:	☐ Case I	☐ Case II	☒ Case III	☐ Case IV
Processes are validated and machine setup activities are performed in order to reduce the introduction of defects. Units are visually inspected for defects in receiving and inspection, in-process and during packing. During the release of packaging materials, inspection for presence of extraneous matter is performed. Final release visual inspections is also performed. Individual residual risk for these hazardous situations is reduced as far as possible (AFAP) considering the generally acknowledged state of the art.				
Residual Risk is:	☒ Acceptable	☐ Acceptable with cRBA	☐ Unacceptable	

End Effect:	Expired Product	**Hazardous Situation(s):**	HS.PIT.5.1 HS.PIT.5.2 HS.PIT.5.3 HS.PIT.5.4 HS.PIT.5.5 HS.PIT.11.1 HS.PIT.13.5 HS.PIT.13.6 HS.PIT.13.7 HS.PIT.19.1 HS.PIT.24.1

Acceptability Assessment:	☐ Case I	☐ Case II	☒ Case III	☐ Case IV
Stability testing are performed to determine appropriate expiry dating (see ICH Q1A-Q1F for stability testing conditions). Verification at variable print setup as well as at release testing ensures that the expiry date is accurately applied at manufacturing. Instructions for use specify not to use the product after expiry. Individual residual risk for these hazardous situations is reduced as far as possible (AFAP) considering the generally acknowledged state of the art.				
Residual Risk is:	☒ Acceptable	☐ Acceptable with cRBA	☐ Unacceptable	

End Effect:	Excessive Bolus or Therapy	**Hazardous Situation(s):**	HS.PIT.10.1 HS.PIT.10.2

			HS.PIT.10.3	
Acceptability Assessment:	☐ Case I	☒ Case II	☐ Case III	☐ Case IV
The labeling identifies the volume and strength of the product. The product labeling instructs the timing to deliver the product which correlates to the appropriate flow rate. Process controls are in place to ensure labeling accuracy. Appropriate administration is dependent on good clinical practice. Labelling content is designed to contain correct information, and is aligned with approved internal labelling and specific country regulatory requirements. Print correctness and quality inspections are performed during in-process and final release testing using validated methods. Individual residual risk for these hazardous situations is reduced as far as possible (AFAP) considering the generally acknowledged state of the art.				
Residual Risk is:	☒ Acceptable	☐ Acceptable with cRBA	☐ Unacceptable	

End Effect:	Falling Product		**Hazardous Situation(s):**	HS.PIT.3.1 HS.PIT.3.2 HS.PIT.3.3 HS.PIT.3.4 HS.PIT.18.1 HS.PIT.18.2 HS.PIT.18.3 HS.PIT.18.4 HS.PIT.18.5 HS.PIT.20.3 HS.PIT.27.3 HS.PIT.27.7
Acceptability Assessment:	☐ Case I	☐ Case II	☒ Case III	☐ Case IV
Secondary Packaging Materials are designed and validated to withstand distribution and handling conditions. Shipping studies, assess for physical damage of the product and secondary packaging. For the Bottle, Hanger is designed to meet product design requirements and was qualified through product design verification. The design of the product is a standard commercial design. Handling of products in a clinical setting is dependent on standard good clinical practice. Individual residual risk for this hazardous situation is reduced as far as possible (AFAP) considering the generally acknowledged state of the art.				
Residual Risk is:	☒ Acceptable	☐ Acceptable with cRBA	☐ Unacceptable	

End Effect:	Falling Product - Carton		**Hazardous Situation(s):**	HS.PIT.27.7
Acceptability Assessment:	☐ Case I	☐ Case II	☒ Case III	☐ Case IV

Packaging Materials are designed and validated to withstand distribution and handling conditions. The stretch wrapping pallets are inspected for damage prior to shipment. Shipping studies assessed for physical damage of the product and secondary packaging. These ensure the carton functions as intended.

Individual residual risk for this hazardous situation is reduced as far as possible (AFAP) considering the generally acknowledged state of the art.

Residual Risk is:	☒ Acceptable	☐ Acceptable with cRBA	☐ Unacceptable

End Effect:	Final product contains sub-visible particulate matter	**Hazardous Situation(s):**	HS.PIT.23.1

Acceptability Assessment:	☒ Case I	☐ Case II	☐ Case III	☐ Case IV

This product is tested in compliance with USP <788> Particulate Matter in Injections (sub-visible) and regional pharmacopeia requirements. Methods and limits conform to pharmacopeias and/or local and federal regulations.

Individual residual risk for this hazardous situation is reduced as far as possible (AFAP) considering the generally acknowledged state of the art.

Residual Risk is:	☒ Acceptable	☐ Acceptable with cRBA	☐ Unacceptable

End Effect:	Final product contains visible particulate matter	**Hazardous Situation(s):**	HS.PIT.5.1 HS.PIT.5.2 HS.PIT.5.3 HS.PIT.5.4 HS.PIT.5.5 HS.PIT.18.1 HS.PIT.18.2 HS.PIT.18.3 HS.PIT.18.4 HS.PIT.18.5 HS.PIT.23.2

Acceptability Assessment:	☒ Case I	☐ Case II	☐ Case III	☐ Case IV

Baxter controls the presence of loose visible particulate matter through a series of prevention controls, detection controls, and release testing including:

- Raw material handling controls including container cleaning and inspections
- Visual tank inspections
- Solution filtered before filling along with routine checks of the filter integrity
- Personnel controls (e.g. Gowning, cleaning, and qualification) and environmental controls (air handling, filtration).

This product is tested in compliance with USP<1> and USP <790>. Methods and limits conform to local pharmacopeias, regional pharmacopeias and/or local and federal regulations.

Individual residual risk for these hazardous situations is reduced as far as possible (AFAP) considering the generally acknowledged state of the art.			
Residual Risk is:	☒ Acceptable	☐ Acceptable with cRBA	☐ Unacceptable

End Effect:	Flow rate greater than intended	**Hazardous Situation(s):**	HS.PIT.10.1 HS.PIT.10.2 HS.PIT.10.3

Acceptability Assessment:	☐ Case I	☐ Case II	☒ Case III	☐ Case IV
Appropriate administration is dependent on good clinical practice. Vials and Bottles are included in the situation where they are used to compound an infusion product where the flow rate is dependent on the set/infusion products. For the direct infusion with a bottle the product labeling instructs the timing to deliver the product which correlates to the appropriate flow rate. No further controls are feasible. Individual residual risk for these hazardous situations is reduced as far as possible (AFAP) considering the generally acknowledged state of the art.				
Residual Risk is:	☒ Acceptable	☐ Acceptable with cRBA	☐ Unacceptable	

End Effect:	Flow rate less than intended	**Hazardous Situation(s):**	HS.PIT.16.1 HS.PIT.16.2 HS.PIT.16.3

Acceptability Assessment:	☐ Case I	☐ Case II	☒ Case III	☐ Case IV
Appropriate administration is dependent on good clinical practice. Vials and Bottles are included in the situation where they are used to compound an infusion product where the flow rate is dependent on the set/infusion products. For the direct infusion with a bottle the product labeling instructs the timing to deliver the product which correlates to the appropriate flow rate. No further controls are feasible. Individual residual risk for these hazardous situations is reduced as far as possible (AFAP) considering the generally acknowledged state of the art.				
Residual Risk is:	☒ Acceptable	☐ Acceptable with cRBA	☐ Unacceptable	

End Effect:	Incorrect Storage	**Hazardous Situation(s):**	HS.PIT.11.1 HS.PIT.13.5 HS.PIT.13.6 HS.PIT.13.7 HS.PIT.19.1 HS.PIT.24.1 HS.PIT.28.1

Acceptability Assessment:	☐ Case I	☐ Case II	☒ Case III	☐ Case IV
Labeling and package inserts clearly indicate the appropriate storage conditions of the product. Process controls are in place to ensure labeling accuracy. Proper storage of product is dependent on good clinical practice.				

Individual residual risk for these hazardous situations is reduced as far as possible (AFAP) considering the generally acknowledged state of the art.			
Residual Risk is:	☒ Acceptable	☐ Acceptable with cRBA	☐ Unacceptable

End Effect:	Insufficient Bolus or Therapy	**Hazardous Situation(s):**	HS.PIT.16.1 HS.PIT.16.2 HS.PIT.16.3
Acceptability Assessment:	☐ Case I	☐ Case II	☒ Case III ☐ Case IV
System contains intended volume which is maintained by process controls. The labeling identifies the volume and strength of the product. Process controls are in place to ensure labeling accuracy. Appropriate administration is dependent on good clinical practice. Individual residual risk for these hazardous situations is reduced as far as possible (AFAP) considering the generally acknowledged state of the art.			
Residual Risk is:	☒ Acceptable	☐ Acceptable with cRBA	☐ Unacceptable

End Effect:	Introduction of Air into fluid Path	**Hazardous Situation(s):**	HS.PIT.1.4 HS.PIT.1.5 HS.PIT.1.6 HS.PIT.1.7
Acceptability Assessment:	☐ Case I	☐ Case II	☒ Case III ☐ Case IV
This is applicable only to products in this product family that are in a bottle and used with direct infusion. This is dependent on the priming of the set prior to infusion of the solution. Proper priming is dependent on good clinical practice. Individual residual risk for these hazardous situations is reduced as far as possible (AFAP) considering the generally acknowledged state of the art.			
Residual Risk is:	☒ Acceptable	☐ Acceptable with cRBA	☐ Unacceptable

End Effect:	Label - Drug Identifying	**Hazardous Situation(s):**	HS.PIT.2.1 HS.PIT.5.1 HS.PIT.5.2 HS.PIT.5.3 HS.PIT.5.4 HS.PIT.5.5 HS.PIT.10.1 HS.PIT.10.2 HS.PIT.10.3 HS.PIT.13.1 HS.PIT.13.2 HS.PIT.13.3 HS.PIT.13.4 HS.PIT.13.5

			HS.PIT.13.6 HS.PIT.13.7 HS.PIT.14.1 HS.PIT.16.1 HS.PIT.16.2 HS.PIT.16.3

Acceptability Assessment:	☐ Case I	☒ Case II	☐ Case III	☐ Case IV

Once received material, storage and release of the material is controlled. Representative units of finished product are selected from each batch for final testing. The labeling indicates the composition of the product. Instructions for Use and the product label specify route of administration.

Label content is approved by each regulatory authority. Preprinted labels are inspected at R&I and use of the correct label is verified prior to batch manufacturing. For labeling printed during the manufacturing process, correct print information and quality are verified at set-up. Print correctness and quality inspections are performed during in-process and final release testing using validated methods and 100% visual inspection.

Labels are compliant to a local or country standard or commensurate to published literature, in the absence of a harmonized standard.

Individual residual risk for these hazardous situations is reduced as far as possible (AFAP) considering the generally acknowledged state of the art.

Residual Risk is:	☒ Acceptable	☐ Acceptable with cRBA	☐ Unacceptable

End Effect:	Label - Instructions for Use (Includes warnings/cautions)	**Hazardous Situation(s):**	HS.PIT.2.1 HS.PIT.5.1 HS.PIT.5.2 HS.PIT.5.3 HS.PIT.5.4 HS.PIT.5.5 HS.PIT.15.1

Acceptability Assessment:	☐ Case I	☒ Case II	☐ Case III	☐ Case IV

The labeling indicates the composition of the product, the instructions for use and the route of administration. Labelling content is designed to contain correct information, and is aligned with approved internal labelling and specific country regulatory requirements. Preprinted labels are inspected at R&I and use of the correct label is verified prior to batch manufacturing.
Labels are compliant to a local or country standard or commensurate to published literature, in the absence of a harmonized standard.

Individual residual risk for these hazardous situations is reduced as far as possible (AFAP) considering the generally acknowledged state of the art.

Residual Risk is:	☒ Acceptable	☐ Acceptable with cRBA	☐ Unacceptable

End Effect:	Label - Other information and redundant	**Hazardous Situation(s):**	HS.PIT.5.1 HS.PIT.5.2 HS.PIT.5.3 HS.PIT.5.4 HS.PIT.5.5

Acceptability Assessment:	☐ Case I	☐ Case II	☒ Case III	☐ Case IV

Processes are validated and machine setup activities are performed in order to reduce the introduction of defects. Units are visually inspected for defects in-process and during packing. Final release visual inspections include inspection for cosmetic defects. Individual residual risk for these hazardous situations is reduced as far as possible (AFAP) considering the generally acknowledged state of the art.

Residual Risk is:	☒ Acceptable	☐ Acceptable with cRBA	☐ Unacceptable

End Effect:	Leachables	**Hazardous Situation(s):**	HS.PIT.19.1

Acceptability Assessment:	☐ Case I	☒ Case II	☐ Case III	☐ Case IV

Vial and Bottle materials were selected to reduce extractables and leachables.
Material conformity is ensured during receiving and inspection activities.
Design controls to reduce the presence of raw material organic or non-organic contaminants include material and supplier certification. Requirements are in place to control the materials to be used in these products.
Trace metal levels are also evaluated as part of the chemical testing when qualifying the material as per local pharmacopoeias and/or local and federal regulations.
Stability is also a product requirement which ensures through design verification that the product remains sterile, safe to use and maintains its functionality through the whole period of its shelf life.
This product is in compliance with USP <1663> and <1664> and regional pharmacopeia requirements.
Individual residual risk for this hazardous situation is reduced as far as possible (AFAP) considering the generally acknowledged state of the art.

Residual Risk is:	☒ Acceptable	☐ Acceptable with cRBA	☐ Unacceptable

End Effect:	Leak	**Hazardous Situation(s):**	HS.PIT.6.2 HS.PIT.6.3 HS.PIT.18.1 HS.PIT.18.2 HS.PIT.18.3 HS.PIT.18.4 HS.PIT.18.5 HS.PIT.21.3 HS.PIT.21.5 HS.PIT.27.8 HS.PIT.27.9

Acceptability Assessment:	☐ Case I	☐ Case II	☒ Case III	☐ Case IV

Material selection and glass container parameters are designed to maintain container closure integrity during manufacturing, distribution and use. Design is verified with distribution and use testing. Vials and Bottles are

inspected for leakages during manufacturing. Manufacturing controls and specifications are in place to ensure that the product is manufactured as per the respective specification and to ensure that its integrity is maintained throughout the entire shelf-life.
Verification of the design ensures the components and materials are tested to demonstrate that the product meets the product requirements.
Manufacturing mitigations include packaging material incoming inspections, in-process testing, and 100% visual inspection to ensure that the product meets all specifications.

Individual residual risk for these hazardous situations is reduced as far as possible (AFAP) considering the generally acknowledged state of the art.

Residual Risk is:	☒ Acceptable	☐ Acceptable with cRBA	☐ Unacceptable

End Effect:	Leak - After completion of therapy	**Hazardous Situation(s):**	HS.PIT.6.2 HS.PIT.6.3 HS.PIT.27.8 HS.PIT.27.9

Acceptability Assessment:	☐ Case I	☐ Case II	☒ Case III	☐ Case IV

Material selection and container parameters are designed to maintain container integrity during manufacturing, distribution and use. This design is verified with distribution. Disconnecting the vial or bottle from a set/syringe requires standard clinical practice to prevent a leak after therapy.

Individual residual risk for these hazardous situations is reduced as far as possible (AFAP) considering the generally acknowledged state of the art.

Residual Risk is:	☒ Acceptable	☐ Acceptable with cRBA	☐ Unacceptable

End Effect:	Leak - Prior to initiation of therapy	**Hazardous Situation(s):**	HS.PIT.5.1 HS.PIT.5.2 HS.PIT.5.3 HS.PIT.5.4 HS.PIT.5.5 HS.PIT.6.2 HS.PIT.6.3 HS.PIT.27.8 HS.PIT.27.9

Acceptability Assessment:	☐ Case I	☐ Case II	☒ Case III	☐ Case IV

Material selection and container parameters are designed to maintain container integrity during manufacturing, distribution. This design is verified with distribution. Vials and Bottles are inspected for leakages during manufacturing and use.
Verification of the design ensures the components and materials are tested to demonstrate that the product meets the product requirements.
Manufacturing mitigations include raw material incoming inspections, in-process testing, and final physical release testing to ensure that the product meets all specifications.

Connecting the vial or bottle to a set/syringe requires standard clinical practice to prevent a leak prior to therapy. Individual residual risk for these hazardous situations is reduced as far as possible (AFAP) considering the generally acknowledged state of the art.			
Residual Risk is:	☒ Acceptable	☐ Acceptable with cRBA	☐ Unacceptable

End Effect:	Loose Components		**Hazardous Situation(s):**	HS.PIT.27.1 HS.PIT.27.8
Acceptability Assessment:	☐ Case I	☐ Case II	☒ Case III	☐ Case IV
Product is integrated to include a stopper and flip cap. The flip cap is required to be removed prior to use by a clinical professional. The bottle hanger is included for direct infusion and is handled by clinical professionals. Appropriate disposal of therapy components is required to ensure components like the stopper, flip cap or bottle hanger are disposed and requires good standard clinical practice. Individual residual risk for these hazardous situations is reduced as far as possible (AFAP) considering the generally acknowledged state of the art.				
Residual Risk is:	☒ Acceptable	☐ Acceptable with cRBA	☐ Unacceptable	

End Effect:	Manufacturing - Concentration Out of Specification		**Hazardous Situation(s):**	HS.PIT.13.1 HS.PIT.13.2 HS.PIT.13.3 HS.PIT.13.5 HS.PIT.13.6 HS.PIT.13.7
Acceptability Assessment:	☐ Case I	☒ Case II	☐ Case III	☐ Case IV
Multiple preventative controls are in place to prevent the addition of incorrect quantities of active drug substance(s) during mixing. Calibrated scales and measurement systems are used and verified during active drug substance(s) weighing. Additionally, mixing parameters are controlled on qualified equipment with validated process parameters. Continuous monitoring and visual inspection are employed to ensure that the parameters are met. Solution concentration is verified via in process testing prior, as well as finished product testing. Representative units of finished product are selected from each batch for final testing. The labeling indicates the composition of the product. Methods and limits conform to pharmacopeias, regional pharmacopeias and/or local and federal regulations. Individual residual risk for these hazardous situations is reduced as far as possible (AFAP) considering the generally acknowledged state of the art.				
Residual Risk is:	☒ Acceptable	☐ Acceptable with cRBA	☐ Unacceptable	

End Effect:	Manufacturing - Excipient out of specification or use of incorrect excipient	**Hazardous Situation(s):**	HS.PIT.11.1 HS.PIT.22.1 HS.PIT.22.2 HS.PIT.13.5 HS.PIT.13.6 HS.PIT.13.7

Acceptability Assessment:	☐ Case I	☒ Case II	☐ Case III	☐ Case IV

Multiple preventative controls are in place to prevent the addition of incorrect quantities of raw materials during mixing as per applicable batch records. Calibrated scales and measurement systems are used and verified during raw material weighing. Additionally, mixing parameters are controlled on qualified equipment with validated process parameters. Continuous monitoring and visual inspection are employed to ensure that the parameters are met. Solution concentration is verified via finished product testing for functional excipients, as applicable.

Representative units of finished product are selected from each batch for final testing.

The labeling indicates the composition of the product.

Methods and limits conform to pharmacopeias, regional pharmacopeias and/or local and federal regulations.

Individual residual risk for these hazardous situations is reduced as far as possible (AFAP) considering the generally acknowledged state of the art.

Residual Risk is:	☒ Acceptable	☐ Acceptable with cRBA	☐ Unacceptable

End Effect:	Manufacturing - Organic contaminant is above threshold value	**Hazardous Situation(s):**	HS.PIT.11.1

Acceptability Assessment:	☐ Case I	☒ Case II	☐ Case III	☐ Case IV

Controls are in place to reduce the presence of raw material contaminants including material selection, receiving and inspection activities, and supplier certification.

Methods and limits conform to pharmacopeias, regional pharmacopeias and/or local and federal regulations. Manufacturing controls and specifications are in place to ensure that products are manufactured as per the respective specifications and to ensure that it maintains the product quality, safety, and efficacy throughout the entire shelf-life. The products have been developed in accordance with applicable standards to meet the established impurities requirement.

Also, the respective stability studies ensure that the test result remains within the established limits during shelf life. Thus, it is unlikely to have the impurities being out of accepted criteria from product process.

Individual residual risk for these hazardous situations is reduced as far as possible (AFAP) considering the generally acknowledged state of the art.

Residual Risk is:	☒ Acceptable	☐ Acceptable with cRBA	☐ Unacceptable

End Effect:	Manufacturing - pH Extremes	**Hazardous Situation(s):**	HS.PIT.11.1 HS.PIT.13.5 HS.PIT.13.6 HS.PIT.13.7 HS.PIT.24.1

Acceptability Assessment:	☐ Case I	☒ Case II	☐ Case III	☐ Case IV

Design controls are in place to target and maintain product pH throughout shelf life. Requirements are in place to control the materials to be used in these products.

Methods for pH conform to local pharmacopeias and/or local and federal regulations or published literature.
As there are product formulations within this product family that are outside the range of 6 to 9, the P1 for HS.PIT.24.1 is 1,000,000. The RBA will further discuss the risk benefit analysis regarding this hazardous situation.

There are formulations within this product family where the pH of the product is outside the range of 6-9. Therefore inherently the patient may always have exposure to this set of hazardous situations when receiving therapy. The efficacy of this therapy is dependent on the formulation at the specified pH. Although further mitigations may be available, it will not allow for the product to provide the therapy as intended if formulated to be within the range of 6-9. Therefore further mitigations will not improve patient safety.

Individual residual risk for these hazardous situations is reduced as far as possible (AFAP) considering the generally acknowledged state of the art.

Residual Risk is:	☒ Acceptable	☐ Acceptable with cRBA	☐ Unacceptable

End Effect:	Manufacturing - Product is not sterile	**Hazardous Situation(s):**	HS.PIT.21.5

Acceptability Assessment:	☐ Case I	☐ Case II	☒ Case III	☐ Case IV

The sterilization process is validated to a SAL of 10^{-6}. The product is designed to be contained in sterile primary packaging to be protected from external contamination. Verification of the design ensures the components and materials, including the primary packaging, are tested to demonstrate that the product meets product requirements. The product is designed with materials and interfaces so that it allows for complete sterilization without deterioration to the product itself or of its packaging.
Sterilization cycles are validated and monitored to ensure that product components and packaging are not damaged or deteriorated during the cycle. Specifically, sterilization parameters are set to produce a sterile product while not damaging or degrading the packaging or the product itself. Finished product sterility test is performed before product release.

Individual residual risk for these hazardous situations is reduced as far as possible (AFAP) considering the generally acknowledged state of the art.

Residual Risk is:	☒ Acceptable	☐ Acceptable with cRBA	☐ Unacceptable

End Effect:	Manufacturing - Product is pyrogenic	**Hazardous Situation(s):**	HS.PIT.7.1

Acceptability Assessment:	☐ Case I	☒ Case II	☐ Case III	☐ Case IV

Endotoxin and pyrogen are mainly introduced from raw materials and components. Endotoxins are controlled for raw material and components to reduce endotoxin/pyrogen introduction. Bioburden tests are performed to limit endotoxin in-process. Besides, endotoxin is tested on finished product to reduce the risk.
For solution products endotoxin control is demonstrated by performing the Limulus Amebocyte Lysate (LAL) test. Baxter performs LAL testing in accordance with USP Chapter <85>. Endotoxin limits for solution products are set in accordance with the pharmacopeia and are compliant with both the intended use of the product (i.e. maximum posology) and any compendial limits (monographs). All methods are appropriately validated prior to implementation in accordance with applicable standards.

Methods and limits conform to local pharmacopeias and/or local and federal regulations.

Individual residual risk for these hazardous situations is reduced as far as possible (AFAP) considering the generally acknowledged state of the art.

Residual Risk is:	☒ Acceptable	☐ Acceptable with cRBA	☐ Unacceptable

End Effect:	Manufacturing - Residual solvent is above threshold value	**Hazardous Situation(s):**	HS.PIT.11.7 HS.PIT.11.8 HS.PIT.11.9 HS.PIT.11.10

Acceptability Assessment:	☐ Case I	☐ Case II	☒ Case III	☐ Case IV

Residual solvents in drug products are mainly introduced from raw material (API and excipients). Procedures are in place (raw material specifications, release testing of materials before use) to ensure residual solvents are at levels below established limits.
Thus, it is unlikely to have residual solvents in products beyond established limits as per applicable pharmacopeias, regional pharmacopeias and/or local and federal regulations

Individual residual risk for these hazardous situations is reduced as far as possible (AFAP) considering the generally acknowledged state of the art.

Residual Risk is:	☒ Acceptable	☐ Acceptable with cRBA	☐ Unacceptable

End Effect:	Manufacturing - Solution contains transmissible spongiform encephalopathies (TSEs and BSEs)	**Hazardous Situation(s):**	HS.PIT.4.1

Acceptability Assessment:	☐ Case I	☒ Case II	☐ Case III	☐ Case IV

Controls to reduce the presence of raw material contaminants include material selection, receiving and inspection activities, and supplier certification.

Material selections conform to local pharmacopeias and/or local and federal regulations.

The evaluation of incoming raw materials, manufacturing materials, primary packaging materials and disposable equipment from outside suppliers for Baxter manufactured products adhere to GQP-12-08 or supplier harmonized template, Evaluation of TSE and Virus Risks for Materials Used in Baxter Processes and are confirmed during client audits and periodic checks.

Individual residual risk for this hazardous situation is reduced as far as possible (AFAP) considering the generally acknowledged state of the art.

Residual Risk is:	☒ Acceptable	☐ Acceptable with cRBA	☐ Unacceptable

End Effect:	Manufacturing - Solution is not free of allergen contaminants	**Hazardous Situation(s):**	HS.PIT.2.1

Acceptability Assessment:	☐ Case I	☒ Case II	☐ Case III	☐ Case IV

Controls to reduce the presence of raw material allergens include material selection, receiving and inspection activities, and supplier certification.

Methods and limits conforms to pharmacopeias, regional pharmacopeias and/or local and federal regulations.

Individual residual risk for these hazardous situations is reduced as far as possible (AFAP) considering the generally acknowledged state of the art.

Residual Risk is:	☒ Acceptable	☐ Acceptable with cRBA	☐ Unacceptable

End Effect:	Manufacturing - System does not contain defined volume - High	**Hazardous Situation(s):**	HS.PIT.5.1 HS.PIT.5.2 HS.PIT.5.3 HS.PIT.5.4 HS.PIT.5.5 HS.PIT.10.1 HS.PIT.10.2 HS.PIT.10.3 HS.PIT.21.5 HS.PIT.24.1

Acceptability Assessment:	☐ Case I	☐ Case II	☒ Case III	☐ Case IV

Fill Volume is a validated process parameter. During filling, the fill volume is checked regularly at pre-determined intervals. Fill volume measurement is performed during in-process and final release testing using validated methods.

Individual residual risk for these hazardous situations is reduced as far as possible (AFAP) considering the generally acknowledged state of the art.

Residual Risk is:	☒ Acceptable	☐ Acceptable with cRBA	☐ Unacceptable

End Effect:	Manufacturing - System does not contain defined volume - Low	**Hazardous Situation(s):**	HS.PIT.5.1 HS.PIT.5.2 HS.PIT.5.3 HS.PIT.5.4 HS.PIT.5.5 HS.PIT.11.1 HS.PIT.16.1 HS.PIT.16.2 HS.PIT.16.3 HS.PIT.24.1

Acceptability Assessment:	☐ Case I	☐ Case II	☒ Case III	☐ Case IV

Fill Volume is a validated process parameter. During filling, fill volume is checked regularly at pre-determined intervals Fill volume measurement is performed during in-process and final release testing using validated methods.

Individual residual risk for these hazardous situations is reduced as far as possible (AFAP) considering the generally acknowledged state of the art.

Residual Risk is:	☒ Acceptable	☐ Acceptable with cRBA	☐ Unacceptable

End Effect:	Manufacturing - Trace metal is above threshold value	**Hazardous Situation(s):**	HS.PIT.11.3 HS.PIT.11.4 HS.PIT.11.5 HS.PIT.11.6

Acceptability Assessment:	☐ Case I	☒ Case II	☐ Case III	☐ Case IV

Design controls to reduce the presence of raw material organic or non-organic contaminants include material and supplier certification. Requirements are in place to control the materials to be used in these products.
Trace metal levels are also evaluated as part of the chemical testing when qualifying the material as per local pharmacopoeias and/or local and federal regulations. A risk-based approach has been adopted for elemental impurities to determine which control and frequency need to be put in place to ensure the product compliance in regards to the elemental impurity requirements.

Individual residual risk for these hazardous situations is reduced as far as possible (AFAP) considering the generally acknowledged state of the art.

Residual Risk is:	☒ Acceptable	☐ Acceptable with cRBA	☐ Unacceptable

End Effect:	Manufacturing - Use of Incorrect Drug	**Hazardous Situation(s):**	HS.PIT.14.1

Acceptability Assessment:	☐ Case I	☐ Case II	☒ Case III	☐ Case IV
Design controls to reduce the use of incorrect API include material and supplier certification. Requirements are in place to control the materials to be used in these products. Process controls include batch record verification for material codes to ensure correct drug. Individual residual risk for these hazardous situations is reduced as far as possible (AFAP) considering the generally acknowledged state of the art.				
Residual Risk is:	☒ Acceptable	☐ Acceptable with cRBA	☐ Unacceptable	

End Effect:	Overfill of container during compounding	**Hazardous Situation(s):**	HS.PIT.10.1 HS.PIT.10.2 HS.PIT.10.3

Acceptability Assessment:	☐ Case I	☐ Case II	☒ Case III	☐ Case IV
Product labeling includes product concentration and volume informing the clinician. Packaging inserts are designed to instruct the user about correct dose volume and compatible IV solutions. Individual residual risk for these hazardous situations is reduced as far as possible (AFAP) considering the generally acknowledged state of the art.				
Residual Risk is:	☒ Acceptable	☐ Acceptable with cRBA	☐ Unacceptable	

End Effect:	Potency Impact - Concentration	**Hazardous Situation(s):**	HS.PIT.13.3 HS.PIT.13.4 HS.PIT.13.7

Acceptability Assessment:	☐ Case I	☒ Case II	☐ Case III	☐ Case IV
Once received material, storage and release of the material is controlled. Representative units of finished product are selected from each batch for final testing. The labeling indicates the composition of the product. Label content is approved by each regulatory authority and are compliant to a local or country standards. Preprinted labels are inspected at R&I and use of the correct label is verified during batch manufacturing. For labeling printed during the manufacturing process, correct print information and quality are verified at set-up. Print correctness and quality inspections are performed during in-process and 100% visual inspection. Individual residual risk for these hazardous situations is reduced as far as possible (AFAP) considering the generally acknowledged state of the art.				
Residual Risk is:	☒ Acceptable	☐ Acceptable with cRBA	☐ Unacceptable	

End Effect:	Product not used as single dose only	**Hazardous Situation(s):**	HS.PIT.21.5 HS.PIT.23.1 HS.PIT.23.2

Acceptability Assessment:	☐ Case I	☐ Case II	☒ Case III	☐ Case IV
Label states: Discard after single use. Discard any unused portion. Do not reconnect partially used bottles. Preprinted labels are inspected at R&I and use of the correct label is verified prior to batch manufacturing Disposal of therapy components is dependent on standard good clinical practice. Individual residual risk for these hazardous situations is reduced as far as possible (AFAP) considering the generally acknowledged state of the art.				
Residual Risk is:	☒ Acceptable	☐ Acceptable with cRBA	☐ Unacceptable	

End Effect:	Separation of Solution	**Hazardous Situation(s):**	HS.PIT.5.1 HS.PIT.5.2 HS.PIT.5.3 HS.PIT.5.4 HS.PIT.5.5 HS.PIT.28.1

Acceptability Assessment:	☐ Case I	☐ Case II	☒ Case III	☐ Case IV
The manufacturing process is designed and validated to ensure that the drug product is produced to ensure appropriate composition and purity. Vials and Bottles are 100% visually inspected. Stability studies have been performed to indicate stability of the emulsion products. Individual residual risk for these hazardous situations is reduced as far as possible (AFAP) considering the generally acknowledged state of the art.				
Residual Risk is:	☒ Acceptable	☐ Acceptable with cRBA	☐ Unacceptable	

End Effect:	Shipping Issue	**Hazardous Situation(s):**	HS.PIT.5.5

Acceptability Assessment:	☐ Case I	☐ Case II	☒ Case III	☐ Case IV
The product's shipping packaging is designed to facilitate user handling and prevent damage during shipping and transportation. The product is designed to have a specific number of products per shipping carton. Design Verification includes distribution testing, which evaluates the presence of product in the packaging, checks the quantity of items placed in the packaging, and verifies the overall packaging design. Manufacturing mitigations include incoming inspections for raw material and carton boxes, in-process testing, and 100% visual inspection to ensure that the product meets all specifications. Individual residual risk for these hazardous situations is reduced as far as possible (AFAP) considering the generally acknowledged state of the art.				

Residual Risk is:	☒ Acceptable	☐ Acceptable with cRBA	☐ Unacceptable

End Effect:	System does not contain intended volume - High	Hazardous Situation(s):	HS.PIT.10.1 HS.PIT.10.2 HS.PIT.10.3 HS.PIT.5.1 HS.PIT.5.2 HS.PIT.5.3 HS.PIT.5.4 HS.PIT.5.5

Acceptability Assessment:	☐ Case I	☒ Case II	☐ Case III	☐ Case IV

Product container labels and carton labels are designed to convey the correct volume of the system. Controls are in place to ensure accuracy of product labelling. Preprinted labels are inspected at R&I and use of the correct label is verified prior to batch manufacturing.
Further, the product is designed to confirm that correct volumes are delivered. Controls are in place to ensure the correct volume is used during manufacturing, Qualified equipment with validated process parameters are used for container filling. Continuous monitoring and visual inspection are employed to ensure that the parameters are met.
Representative units of the finished product are selected from each batch for final testing.
Methods and limits conform to local pharmacopeia and/or local and federal regulations
Stability study verified extractable volumes during shelf life.
Individual residual risk for these hazardous situations is reduced as far as possible (AFAP) considering the generally acknowledged state of the art.

Residual Risk is:	☒ Acceptable	☐ Acceptable with cRBA	☐ Unacceptable

End Effect:	System does not contain intended volume - Low	Hazardous Situation(s):	HS.PIT.16.1 HS.PIT.16.2 HS.PIT.16.3 HS.PIT.5.1 HS.PIT.5.2 HS.PIT.5.3 HS.PIT.5.4 HS.PIT.5.5

Acceptability Assessment:	☐ Case I	☒ Case II	☐ Case III	☐ Case IV

Product container labels and carton labels are designed to convey the correct volume of the system. Controls are in place to ensure accuracy of product labelling. Preprinted labels are inspected at R&I and use of the correct label is verified prior to batch manufacturing.
Further, product is designed to confirm that correct volumes are delivered. Controls are in place to ensure the correct volume is used during manufacturing, Qualified equipment with validated process parameters are used for container filling. Continuous monitoring and visual inspection are employed to ensure that the parameters are met.
Representative units of finished product are selected from each batch for final testing.
Methods and limits conform to local pharmacopeia and/or local and federal regulations
Stability study verified extractable volumes during shelf life.

Individual residual risk for these hazardous situations is reduced as far as possible (AFAP) considering the generally acknowledged state of the art.			
Residual Risk is:	☒ Acceptable	☐ Acceptable with cRBA	☐ Unacceptable

End Effect:	System does not deliver intended volume	**Hazardous Situation(s):**	HS.PIT.16.1 HS.PIT.16.2 HS.PIT.16.3 HS.PIT.18.1 HS.PIT.18.2 HS.PIT.18.3 HS.PIT.18.4 HS.PIT.18.5
Acceptability Assessment:	☐ Case I	☒ Case II	☐ Case III ☐ Case IV
Product is designed to confirm that correct volumes can be extracted and delivered. Controls are in place to ensure the correct volume is used during manufacturing, Qualified equipment with validated process parameters are used for container filling. Continuous monitoring and visual inspection are employed to ensure that the parameters are met. Representative units of finished product are selected from each batch for final testing. Methods and limits conform to local pharmacopeia and/or local and federal regulations Stability study verified extractable volumes during shelf life. Individual residual risk for these hazardous situations is reduced as far as possible (AFAP) considering the generally acknowledged state of the art.			
Residual Risk is:	☒ Acceptable	☐ Acceptable with cRBA	☐ Unacceptable

End Effect:	Underfill of container during compounding	**Hazardous Situation(s):**	HS.PIT.16.1 HS.PIT.16.2 HS.PIT.16.3
Acceptability Assessment:	☐ Case I	☐ Case II	☒ Case III ☐ Case IV
Product labeling includes product concentration and volume informing the clinician. Packaging inserts are designed to instruct the user about correct dose volume and compatible IV solutions. Individual residual risk for these hazardous situations is reduced as far as possible (AFAP) considering the generally acknowledged state of the art.			
Residual Risk is:	☒ Acceptable	☐ Acceptable with cRBA	☐ Unacceptable

Conclusion:

☒ All Hazardous Situations have been addressed in this Risk Assessment

11. CHANGE HISTORY

Revision	Description of change
A	Refer to Revision A Change History form for BXU579481 document
B	Refer to Revision B Change History form for BXU579481 document

Baxter

TcU ELECTRONIC SIGNATURE REPORT

REVISION INFORMATION

Item ID: BXU579481	**Revision ID:** B
Item Name: Ahmedabad Vials and Bottles Risk Assessment and Control Table (RACT)	**Release Date:** 19-Sep-2024
Description: Ahmedabad Vials and Bottles Risk Assessment and Control Table (RACT)	

CHANGE INFORMATION

CN/CR Number (if applicable):

Description of Change (This field will be blank if required data is not available):

The Risk Assessment and Control Table is updated to align with:

- Latest GQT-10-02-01 Template
- Latest UEA document
- New UCL data received for last 2 years
- Latest PFMEA End Effect mapping
- Latest STDA and HSHA-PIT

Reason for Change (This field will be blank if required data is not available):

Risk Assessment and Control Table needs to be updated to align with latest GQT-10-02-01 Template, UEA, PFMEA, STDA, HSHA as necessary for the Periodic Risk Review

APPROVALS & SIGNATURES for Document Release

Name	Role	Workflow Step	Date of Signature	Decision Taken
S, Anbarasan	Author	Initiate Review	06-Sep-2024	Approved
Wu, Jian	Clinical	Document Review - SME & Quality	06-Sep-2024	Approved
Choubey, Anupam Kumar	SME	Document Review - SME & Quality	09-Sep-2024	Approved
Mishra., Deepak	SME	Document Review - SME & Quality	11-Sep-2024	Approved
Milliman, Ann M.	Quality	Document Review - SME & Quality	18-Sep-2024	Approved
Johnson, Thomas	Change Specialist 3	Release Document(s)	19-Sep-2024	Approved
Johnson, Thomas	Change Specialist 3	Set Effectivity	19-Sep-2024	Approved