QRM C&Q Key Deliverables Examples

The ISPE C&Q Community of Practice formed a Task Team of industry SMEs to prepare example deliverable documents that apply the concepts presented in *ISPE Baseline® Guide: Commissioning and Qualification (Second Edition)*. The example document packages include User Requirements Specification, System Risk Assessment, Design Qualification, and Acceptance and Release Report (excluding test scripts) for a Single-Use Bioreactor, Primary Packaging for a Tablet Blister Pack, and Secondary Packing of the Tablet Blisters. These examples are a supplement to those already included in the Baseline Guide Appendices.

The Quality Risk Management C&Q process establishes the focus for systems and equipment being suitable for the intended purpose and qualified to support PQ and PPQ (as applicable). It establishes the appropriate level of Quality oversight, through the preparation of these key deliverable documents, along with owner, SME, and Quality unit approvals. The formats shown in the example documents are suggestions for how to compile these deliverables. The example content, presented across the different documents, provides an approach that is efficient, repeatable, and error proof. The approach shown should be modified for use as directed by each company's procedures and documentation practices.

Example Document Packages

The *ISPE Baseline® Guide: Commissioning and Qualification (Second Edition)* example documents are provided for your convenience. The examples are free to use and may be modified for internal use within your organization only; however, they remain the property of ISPE, should not be used for commercial purposes, and are not available for resale. These examples are provided in Adobe® PDF format only and are not editable.

These materials consist of:

1. Single-Use Bioreactor
   - Overview
   - URS Bioreactor
   - SRA Bioreactor
   - DQ Bioreactor
   - QSAR Bioreactor
2. Primary Packaging System (for a Tablet Blister Pack)
   - Overview
   - URS Primary Packaging
   - SRA Primary Packaging
   - DQ Primary Packaging
   - QSAR Primary Packaging
3. Secondary Packaging System (of the Tablet Blisters)
   - Overview
   - URS Secondary Packaging
   - SRA Secondary Packaging
   - DQ Secondary Packaging
   - QSAR Secondary Packaging

This example documents package applies the concepts presented in the *ISPE Baseline® Guide: Volume 5 – Commissioning and Qualification (Second Edition)* to the primary deliverable documents (excluding test scripts) for a **Single-Use Bioreactor**.

The Risk Based C&Q process requires the compilation and approval of certain elements by the system owner, SME and quality units. The formats shown in the single use bioreactor example documents are one suggestion of how to compile these requirements. These requirements can be presented across the different documents in a manner that is most efficient, repeatable and error proof as directed by each company's procedures and documentation practices.

Bio Reactor Document	Content Description	Comments
URS	Follows content and format of example in BG 5. Includes and categorizes all quality impacting and non-quality impacting user requirements. User Requirements define what is required and can be tested/verified.	1. Further levels of sub-categories could be used to distinguish the four categories of quality impacting URs, (i.e., CQA, CPP, Regulatory, Company Quality System). GEP URs could be further categorized as E/H/S and business operational. 2. A table could be included that precedes the UR listing table that documents the CPPs that will be subject of risk assessment. Note: A Traceability Matrix may be initiated following URS approval and act as a tool to summarize the relevant data generated in the documents that follow in this table.
SRA	Follows content and format of example in BG 5 Appendix 5. Impact on CQAs by associated CPPs is evaluated. Engineering and automation design control elements (CAs) are identified so that an evaluation of quality risk can be assigned. As appropriate, procedural controls and any available critical design elements in place to implement CAs are also verified. If unacceptable risk is identified additional controls are added to mitigate risk to an acceptable level. The additional CAs are communicated to the vendor and the procedures are added to that overall qualification process. An additional output of the SRA process is identification of critical alarms and associated instruments.	1. The example presented applies to a single piece of equipment. It is also possible to conduct SRA the basis of defined systems or manufacturing areas. 2. Other risk assessment tools can be used. However, the outputs of the RA process must include all CAs needed to mitigate risk and supporting procedures needed to support the manufacturing process.
DQ	Confirmation by SME and QA approval that: 1. DQ prerequisites have been met. 2. Associated test acceptance criteria are established for each CA and CDE in the form of an abbreviated trace matrix 3. DQ conclusion which confirms the design contain the documented CAs and CDEs and will adequately controls risks to product quality and patient safety as identified in the System Risk Assessment.	DQ conclusion statement which references information presented in other documents (i.e., design review (DR) summaries, SRA, detailed trace matrix)
Qualification Summary, Acceptance and Release Report	Combined Qualification Summary and Acceptance and Release Report: 1. Shows traceability that CDEs have passed acceptance criteria, 2. deviations are closed, 3. quality system elements are in place 4. system can be released.	Elements of the Acceptance and release can be documented separately. Ex: • Commissioning summary report which documents traceability and deviation closure. • Acceptance and release report.

User Requirements Specification Example

Note: Gray text is informational only and must be deleted before document review.

The template text coloration includes:

1. *Gray italicized text* provides directions, guidance, and suggestions on how to develop various portions of the URS document – to be removed once completed.

2. <*Black italicized text in brackets*> provides sample text that may be modified to meet the needs of the system.

3. Black text is for section headings and to provide the template format that should not be changed or removed because it is language and formatting that is consistent from URS to URS.

Gray text must be deleted or changed to black. Applicable black text should remain unchanged prior to printing the document for pre-approval signatures.

Project teams must determine the need for system user requirements specification on a project-specific basis.

The User Requirements Specification is a living document that serves several purposes during the lifecycle of the system:

- *For new systems or equipment, the URS initiates system design and defines the basic requirements that the system must meet.*

- *The URS is the defining document for traceability in support of verification and qualification.*

The URS defines the requirements that must be met for a system to meet its intended purpose; not how the requirements are met. A system URS brings together multidisciplinary system requirements into a single document to support system design, commissioning, verification, operations and maintenance.

- *Compliance to the requirements must be verifiable*

- *The requirements must clearly distinguish business requirements from quality requirements*

- *Critical Quality Attributes of the system product (output) and associated Critical Process Parameters must be identified in the requirements document*

- *This document is the basis for the design, commissioning and where appropriate verification of the system*

EXAMPLE: A filling line with multiple systems could have multiple URS documents (e.g., one URS for the Isolator, one for the Capper and one for the Filling Line if they are different vendors) or a single URS for the entire filling line.

EXAMPLE: Several identical chromatography columns could have multiple URS documents (one for each column) or a single URS for the identical columns.

EXAMPLE: Several similar chromatography columns could have multiple URS documents (one for each column) or a single URS with sections describing the different requirements for each system.

The URS document provides input to the System Risk Assessment process, the URS may be in draft form. After the Quality Risk Assessment is the URS is updated to include CDEs identified in the risk assessment.

For modifications to existing systems, the URS may be updated to include new requirements or existing requirements may be modified to ensure that the system will reflect the process and/or system changes.

For Qualified systems the URS must be maintained in a controlled location.

For commissioned systems the URS may be stored initially in the project documentation site with the appropriate approvals. The URS for commissioned systems may then be included in the system Turnover Package (TOP) and maintained in the site engineering document repository. For ease of retrieval, a numbering format may be defined such as: Site reference – Building number – System number – Sub-system identification number.

1.1 URS documents must include the following sections:

1.1.1 Purpose and Scope: Identify the system(s) the URS will cover.

1.1.2 System Overview: Describe the system. Appropriate process flow diagrams, data flow diagrams, network diagrams, etc. may be referenced.

1.1.3 Definitions, Abbreviations, References: Populate tables for definitions, abbreviations, and references as they appear and are used in the body of the URS.

1.1.4 Requirements: Populate the template with information identified below.

1.2 Requirements must be classified as Quality or Business in the type column.

1.3 Include the following requirement categories. If a category is not applicable, enter "not applicable" in the template with a justification:

- *Process Requirements*
- *Automation and records*
- *Design and Construction*
- *Operations and Maintenance*
- *Miscellaneous (e.g., documentation, procedural)*

User Requirements Specification Bioreactor

Building Number, Site: *<Insert text>*
Document Number: *<XXXXX-XXX-XXX>*

The Review and Approval Table and Confidentiality Statement may be deleted if the user requirements document will be maintained in a system with appropriate electronic signatures. Note: If Quality has previously approved the quality requirements (CQAs/CPPs/Regulatory/Company Quality documents) then a Quality signature is not required.

Review and Approval				
Role	**Name**	**Department**	**Signature**	**Date**
System Owner (to confirm relevant business requirements are included)	*<Insert text>*	*<Insert text>*	*<Insert text>*	*<DD-MMM-YYYY>*
SME (to confirm relevant technical requirements are included, and they are classified correctly)	*<Insert text>*	*<Insert text>*	*<Insert text>*	*<DD-MMM-YYYY>*
Quality (to confirm relevant quality requirements are included, and they are classified correctly)	*<Insert text>*	*<Insert text>*	*<Insert text>*	*<DD-MMM-YYYY>*

1. Purpose and Scope

The purpose of this document is to define the user requirements for the *< Bioreactor System insert system and name here >*.

The scope of this document applies to the *<insert system name>* at the *<insert site and building or facility name as applicable>*.

Revise this document as necessary throughout the entire system or equipment lifecycle. Use it as the basis to assess changes to the system.

2. Definitions and Abbreviations

Include definitions where they assist the reader – it is not necessary to define standard terms.

Add rows as needed below to supplement the Definitions, Abbreviations, and References.

Term	**Definition**
<Insert text>	*<Insert text>*

Abbreviation	**Definition**
<ESS>	*<Engineering Standards and Specifications>*
<PRD>	*<Process and Product Requirements Document>*
<PRJD>	*<Project Requirements Document>*
<SRA>	*<System Risk Assessment>*

3. References

Document Identifier	**Title**
<Insert document number>	*<Insert title>*

4. System Description

Provide a simple system description and show how it interfaces with other systems. List inputs and outputs as applicable. The appropriate process flow diagrams, data flow diagrams, network diagrams, etc. may be referenced.

List piping and instrumentation diagrams if necessary, to clearly define the scope of the user requirements.

5. User Requirements

The < *Bioreactor System insert system name*> user requirements are defined in the tables below.

Each table contains user requirements for a functional area or discipline such as Process, Design and Construction, Operations and Maintenance, etc.

The tables are structured as follows:

- ID Number *(a unique requirement number that is auto generated in the table)*
- Requirements *(examples in black italicized bracketed text – good, bad, and why)*
- Type: A drop down menu allowing the author to select Quality, HSE, or Business, or Other as the type of attribute
- Source *(identify the source of the requirements)*

In the Requirement column, specify the requirement as a condition that must be satisfied for the system to meet its intended purpose. Requirements should define and describe what is required without being prescriptive as to how the requirements are met (design solutions) unless the method of meeting the requirement is also a requirement. Requirements shall be specific and verifiable.

Use the Type column to select the type of the requirement. The Type column specifies which requirements are quality critical and which are not.

List the source of each requirement in the Source column. The source should indicate the direct source and version number. Use actual document numbers, titles, and section numbers wherever possible so that the source of the requirement is absolutely clear and traceable.
Input to the URS may come from a number of sources:

- *Project Requirements Document/Charter*
- *Process and Product Requirements Document (PRD)*
- *Quality System Risk Assessment*
- *National, local and site requirements*
- *Legacy equipment evaluations*
- *SME input*

Source documents do not need to be approved to be used as references. Changes and revisions to these source documents may require revision to the URS.

The columns in the table have example text showing both appropriate and inappropriate requirements.

If a section is not used, delete the table but retain the section header and add "Not applicable." after the text. For example, if the URS contained no physical product properties, the table in section 3.2 would be deleted and the section title changed to: "3.2 Process Requirements – Physical Product Properties – N/A"

Subject Matter Experts (SME) should establish their requirements through the project documentation such as the PRD.

(Values are for illustrational purposes only.)

6. Process Requirements – Capacity

ID No.	Requirement	Type	Source
6.1	The bioreactor system must have a single use bag holder with capacity range of 400-500 liters	Business	Project Charter
6.2	The system must be able to empty at a flow rate of 4 Kg/min with a range of ± 2 kg/min	Business	Operations

7. Process Requirements – Product Physical Properties

ID No.	Requirement	Type	Source
7.1	The equipment will be capable of handling a range of products with the following key Physical properties. Density: 0.9 – 1.2 g/ml Viscosity: 1 - 20 cP	Business	Product and process requirements

8. Process Requirements – Critical Quality Attributes and Critical Process Parameters

ID No.	Requirement	Type	Source
8.1	Control, trend and alarm the process fluid at a predefined temperature between 20-30 degrees C with a range of ±2 degrees C.	Quality	Product and process requirements
8.2	Control, trend and alarm agitation between 0 to 100 RPM with an accuracy of ± 5 RPM	Quality	Product and process requirements
8.3	Control, trend and alarm the flow of oxygen to maintain a Dissolved Oxygen (DO) level as specified in the recipe with an accuracy of 5%	Quality	Product and process requirements
8.4	Control, trend and alarm nutrient flow between 0-100 g/min with an accuracy of ±10 g/min.	Quality	Product and process requirements
8.5	Control, trend and alarm pH at a predefined range of 4-12 pH.	Quality	Product and process requirements

9. Automation and Records

ID No.	Requirement	Type	Source
9.1	Each authorized user must have a unique user ID and an associated password.	Quality	21 CFR part 11
9.2	The automation system must provide ability to configure segregation of roles to provide access control.	Quality	21 CFR part 11
9.3	The automation system must provide an audit trail.	Quality	21 CFR part 11
9.4	The automation system must provide tools and utilities for configuring, categorizing, prioritizing, logging, annunciating, displaying, acknowledging, disabling, and reporting alarms and events.	Business	Manufacturing
9.5	Reports shall be generated via the company reporting system	Business	Company Standard
9.6	The vent filter heater must have a high and low temperature alarm, (see ID10.3).	Business	Manufacturing

10. Design and Considerations

ID No.	Requirement	Type	Source
10.1	Product contact materials of construction must not be reactive, additive or absorptive with the product or the following cleaning solutions: x, y and z as to alter product quality.	Quality	21 CFR 211 / Eudralex
10.2	All product contact elastomers and gasket materials shall be pharmaceutical grade, animal derivative free and compliant with USP Sec <88> Class V1 and CFR 177.2600.	Quality	Company Quality Standard
10.3	The system must be fitted with a 0.2-micron vent filter, with a heating system to maintain a predefined temperature of 40-150 degrees C with an accuracy of ±4 degrees C.	Business	Company Standard
10.4	The equipment must be of hygienic design, smooth, cleanable, impervious, non-reactive, non-additive and resistant to cleaning/sterilizing agents.	Quality	21 CFR 211 / Eudralex
10.5	The system must be mobile, with non-marking wheels, and wheel locks.	Business	N/A
10.6	The design must comply with the company manual handling requirements.	EHS	Company EHS Standards
10.7	Noise levels generated by the equipment shall be less than 75 dba.	EHS	Company EHS Standard
10.8	The skid shall have a hard-wired emergency stop to immediately shut down the skid when triggered and release all stored energy.	EHS	Company EHS Standard

ID No.	Requirement	Type	Source
10.9	The system must be able to operate from the utility supply. In the event of power failure, it must auto restart when the backup supply is available.	Business	Company Engineering Standard
10.10	The system and instrument shall not lose configuration when power is cycled.	Business	Company Engineering Standard

11. Utilities Available

This section describes the utilities that are available for the system to use, with capacities where they are known; for a greenfield site these would be N/A – the designer would define the requirements.

ID No.	Requirement	Type	Source
11.1	Potable water is available at 5 bar.	N/A	Site Engineering Records
11.2	Site steam is available at 6 bar.	N/A	Site Engineering Records
11.3	Single and three phase power is available 240/380v 50 hz	N/A	Site Engineering Records

12. Operations and Maintenance

ID No.	Requirement	Type	Source
12.1	*Ex: Downtime requirements*	*Business*	
12.2	*Ex: Maintenance accessibility, lock out tagout requirements* *All serviceable instrumentation must be accessible from a height of 6 feet (2 meters) or less.*	*Business*	

13. Miscellaneous

ID No.	Requirement	Type	Source
13.1			
13.2			
13.3			

Change Summary

(Required section and content) List each current change for this version, including step number references as applicable. Each change must include a justification. Add or delete rows as needed.

Change	Justification
<Insert change. State "NEW" for new document.>	*<Insert reason/justification for change.>*

SYSTEM RISK ASSESSMENT	*Single-Use Bioreactor*
BUILDING, SITE	*Building, Site*

REVIEW AND APPROVALS

Function	Printed Name	Signature	Date
Engineering	*Approver Name*	*Approver Signature*	*DD-MMM-YYYY*
System Owner	*Approver Name*	*Approver Signature*	*DD-MMM-YYYY*
Quality	*Approver Name*	*Approver Signature*	*DD-MMM-YYYY*
SME	*Approver Name*	*Approver Signature*	*DD-MMM-YYYY*

REVISION HISTORY

Version	Author Name	Description of Change	Date
1.0	*Document Author Name*	*Initial Draft*	*DD-MM-YYYY*

TABLE OF CONTENTS

1. Purpose

The purpose of this document is to risk assess the equipment design and use, with respect to impact on product quality and Regulatory compliance of *Equipment Name & ID* as it is pertains to the manufacture of *xxx*.

2. System Description

Provide a high-level equipment / system description which detail the overall operation, major components, and intended use.

The material of construction for the single-use bag is out of scope and subject to separate qualification.

3. References

List the Document ID, Version/Revision and Title of all reference documents (e.g., System Risk Assessment SOP, User Requirement Specification, Functional Specification, Process risk assessments, vendor documentation, Etc.).

Document ID	Version / Revision	Title
Document ID	*Version / Revision*	*Document Title*
Document ID	*Version / Revision*	*Document Title*
Document ID	*Version / Revision*	*Document Title*
Document ID	*Version / Revision*	*Document Title*

4. System Risk Assessment

#	Operations Sequence/ Process Flow	Process Description	CQA	CPP	How CQA can be Impacted	Design Controls (CAs or CDEs as appropriate)	Recipe Parameter	Associated Alarm	Procedural Controls	Comments	Residual Risk Determination
1.	Heat/Cool Contents	Heat/Cool to maintain temperature of product	Cell uniformity	Temperature	High temperature may inhibit cell uniformity (growth)	Temperature Control High Temperature Alarm	Temperature is maintained between 20-30 degrees C with a range of ±2 degrees C.	High Alarm	Operation SOP Calibration SOP Alarm Response SOP	Low temperature will slow growth (no impact)	Low
2.	Aeration of Contents	Agitation to provide aeration and nutrient distribution among contents	Concentration/ viable cell density	Agitation	Inadequate or non-uniform oxygen or nutrient availability may affect cell culture expansion	Agitation Control Agitation High/Low Alarms	control agitation between 0 to 100 RPM with an accuracy of ± 5 RPM	High/Low Alarm	Operation SOP Calibration SOP Alarm Response SOP		Low
3.	DO control of Environment	Provide measurable aeration of contents	Concentration/ viable cell density	DO	Undersupply or over saturation of oxygen may affect cell culture expansion	DO Control, DO high/low alarm	Dissolved Oxygen (DO) level as specified in the recipe with an accuracy of 5%	High/Low Alarm	Operation SOP Calibration SOP Alarm Response SOP		Low
4.	Nutrient Additions	Additions to promote growth	Concentration/ viable cell density	Flow rate	In adequate nutrient availability may negatively affect Concentration/ viable cell density	Nutrient pump control, Flow high/low alarm	flow is maintained between 0-100 g/min with an accuracy of ±10 g/min.	High/Low Alarm	Operation SOP Calibration SOP Alarm Response SOP		Low
5.	pH control of Contents	Maintain pH of product	Concentration/ viable cell density free from living organisms other than the species required	pH	High or low pH may provide hostile environment to cells or favorable environment to foreign growth	pH Control pH trend data pH high/low alarms	Control pH at a predefined range of 4-12 pH .	High/Low Alarm	Operation SOP Calibration SOP Alarm Response SOP		Low
6.	Product Contact	Product Contact Parts	Identity, strength, quality, or purity of the product	MOC	Additive contamination may affect cell culture expansion	The material of construction for the single-use bag is out of scope and subject to separate qualification.	N/A	N/A	N/A	Verification of product contact material Identity for the vessel, pH sensors, transmitters, gaskets, elastomers etc	Low
7	Data Integrity	Regulatory security and data collection requirements	Data Integrity	Data Integrity	Data Integrity Compromised	Data integrity is out of scope and subject to separate qualification.	N/A	N/A	Operational SOP	Cross references with GAMP automation URS and included in automation verification	Low

DESIGN QUALIFICATION	*Bioreactor*
BUILDING, SITE	*Building, Site*

REVIEW AND APPROVALS

Function	Printed Name	Signature	Date
Engineering	*Approver Name*	*Approver Signature*	*DD-MMM-YYYY*
System Owner	*Approver Name*	*Approver Signature*	*DD-MMM-YYYY*
Quality	*Approver Name*	*Approver Signature*	*DD-MMM-YYYY*
SME	*Approver Name*	*Approver Signature*	*DD-MMM-YYYY*

REVISION HISTORY

Version	Author Name	Description of Change	Date
1.0	*Document Author Name*	*Initial Draft*	*DD-MM-YYYY*

1. Purpose

The purpose of this document is to record the design qualification for the *Equipment Name & ID* Direct Impact System. Design Qualification (DQ) Objective: Establish that the design of the facility and equipment meets quality impacting and Regulatory requirements and that the system/ equipment is designed to be suitable for intended purpose. Equipment DQ verifies that the equipment/system has applied QRM and QbD concepts and is adequately designed to reliably produce product meeting established quality specifications in accordance with GMPs. Approval of this design qualification report signifies the design is suitable for intended purpose.

2. Design Qualification Process

2.1. Design Qualification Prerequisites

- Approved URS
- Functional requirements (for automated systems)
- System Risk Assessments with identification of design (CAs/CDEs) and procedural controls that will be used to mitigate the unacceptable risks
- Completed DRs, with verification that all open design issues that affect CAs/CDEs, CPPs, and CQAs are closed and included in the final design

List the Document ID, Version/Revision and Title of all reference documents as noted above.

Document ID	Version / Revision	Title
Document ID	*Version / Revision*	*Document Title*
Document ID	*Version / Revision*	*Document Title*
Document ID	*Version / Revision*	*Document Title*
Document ID	*Version / Revision*	*Document Title*

2.2. CA/ CDE and Acceptance Criteria

Attachment A lists the Critical Aspects, Critical Design Elements and respective Acceptance Criteria for verification of suitability for intended use. Acceptance Criteria describe the required system design or controls response that must be demonstrated through objective evidence.

As appropriate, during the verification execution document preparation, issued for fabrication/construction drawings and engineering and automation design documentation and specifications will be referenced for verification of as-built configuration, (i.e. components, instruments, MOC, etc.) and operation (i.e., functional control, alarms, data management, etc.). Traceability of acceptance criteria to C&Q testing documentation will be documented in the supporting traceability matrix.

2.3. Design Qualification Conclusion

Design review by the multidisciplinary team of SMEs, including the Quality Unit, confirmed that all approved User Requirements specifications, including the regulatory and quality, requirements, have been met, confirmed the design will adequately controls risks to product quality and patient safety as identified in the System Risk Assessment and the verified the CAs/CDEs necessary to implement the risk controls are present.

Pre-requisites for Design Qualification have been met and the design of the direct impact system will result in a system that is suitable for intended purpose.

Attachment A
Critical Aspects, Critical Design Elements and Acceptance Criteria for *Equipment Name & ID*

**These columns have been repeated from the SRA and are optional to include in this document*
*** Reference document if these have been approved in another quality approved document.*

#	* Operations Sequence/ Process Flow	* Process Description	CQA/ Regulatory	CPP	*How CQA can be Impacted	Design Controls (CAs)	*Recipe Parameter (Specification)	*Associated Alarm (CDE)	CDE	**Acceptance Criteria
1.	Heat/Cool Contents	Heat/Cool to maintain temperature of product	Cell uniformity	Temperature	High temperature may inhibit cell uniformity (growth)	Temperature Control High Temperature Alarm	Temperature is maintained between 20-30 degrees C with an accuracy of ±2 degrees C.	High Alarm	1. Product contact surface materials of construction: gaskets, thermowell, temperature element 2. Measurement accuracy across the operating range 3. Control across the recipe range 4. Alarm as specified 5. Temperature instrument	1. Demonstrate conformance to approved material specifications of identity and surface finish of sensors/transmitters product contact material. (specify material) 2. Calibration across the range. 3. Temperature control is within range and tolerance. 4. Alarm activates at limit. 5. Temperature instrument in calibration program and meets requirements of calibration SOPs (or reference specifications)
2.	Aeration of Contents	Agitation to provide aeration and nutrient distribution among contents	Concentration/ viable cell density	Agitation	Inadequate or non-uniform oxygen or nutrient availability may affect cell culture expansion	Agitation Control Agitation High/Low Alarms	control agitation between 0 to 100 RPM with an accuracy of ± 5 RPM	High/Low Alarm	1. Product contact surface materials of construction: gaskets, agitator shaft and blades 2. Measurement accuracy across the operating range 3. Agitation direction 4. Control across the recipe range 5. Alarm as specified 6. RPM instrument	1. Demonstrate conformance to approved material specifications of identity and surface finish of sensors/transmitters product contact material. (specify material) 2. Calibration across the range 3. Agitational direction is verified per blade angle 4. Agitation control is within range and tolerance. 5. Alarm activates at limit. 6. RPM instrument in calibration program and meets requirements of calibration SOPs (or reference specifications)
3.	DO control of Environment	Provide measurable aeration of contents	Concentration/ viable cell density	DO	Undersupply or over saturation of oxygen may affect cell culture expansion	DO Control, DO high/low alarm	Dissolved Oxygen (DO) level as specified in the recipe with an accuracy of 5%	High/Low Alarm	1. Product contact surface materials of construction: gaskets, measuring element 2. Measurement accuracy across the operating range 3. Control across the recipe range 4. Alarm as specified 5. DO Instrument	1. Demonstrate conformance to approved material specifications of identity and surface finish of sensors/transmitters product contact material. (specify material) 2. Calibration across the range 3. DO control is within range and tolerance. 4. Alarm activates at limit. 5. DO instrument in calibration program and meets requirements of calibration SOPs (or reference specifications)
4.	Nutrient Additions	Additions to promote growth	Concentration/ viable cell density	Flow rate	In adequate nutrient availability may negatively affect Concentration/ viable cell density	Nutrient pump control, Flow high/low alarm	flow is maintained between 0-100 g/min with an accuracy of ±10 g/min.	High/Low Alarm	1. Product contact surface materials of construction: gaskets, flow meter path and sensing element 2. Measurement accuracy across the operating range 3. Control across the recipe range 4. Alarm as specified 5. Flow instrument	1. Demonstrate conformance to approved material specifications of identity and surface finish of sensors/transmitters product contact material. (specify material) 2. Calibration across the range 3. Flow control is within range and tolerance. 4. Alarm activates at limit 5. Flow instrument in calibration program and meets requirements of calibration SOPs (or reference specifications).

#	* Operations Sequence/ Process Flow	* Process Description	CQA/ Regulatory	CPP	*How CQA can be Impacted	Design Controls (CAs)	*Recipe Parameter (Specification)	*Associated Alarm (CDE)	CDE	**Acceptance Criteria
5.	pH control of Contents	Maintain pH of product	Concentration/ viable cell density free from living organisms other than the species required	pH	High or low pH may provide hostile environment to cells or favorable environment to foreign growth	pH Control pH trend data pH high/low alarms	Control pH at a predefined range of 4-12 pH.	High/Low Alarm	1. Product contact surface materials of construction: gaskets, measuring element 2. Measurement accuracy across the operating range 3. Control across the recipe range 4. Alarm as specified 5. pH instrument	1. Demonstrate conformance to approved material specifications of identity and surface finish of sensors/transmitters product contact material. (specify material) 2. Calibration across the range (user standardized per operating procedures) 3. pH control is within range and tolerance. 4. Alarm activates at limit. 5. Instrument in calibration program and meets requirements of calibration SOPs (or reference specifications)
6.	Product Contact	Product Contact Parts	Identity, strength, quality, or purity of the product	MOC	Additive contamination may affect cell culture expansion	. The material of construction for the single-use bag is out of scope and subject to separate qualification.	N/A	N/A	N/A	N/A
7	Data Integrity (Use this for integrated verification of GAMP)	Regulatory security and data collection requirements	Data Integrity	Data Integrity	Data Integrity Compromised	Each authorized user must have a unique user ID and an associated password. The automation system must provide ability to configure segregation of roles to provide access control. The automation system must provide an audit trail	N/A	N/A	1. Unique user ID's and Passwords. 2. Segregation of roles 3. Audit trail	1. Unique user ID's and Passwords are assigned. 2. Segregation of roles is assigned. 3. Audit trail is accurate and contemporaneous.
7	Data Integrity (Use this for separate verification of GAMP)	Regulatory security and data collection requirements	Data Integrity	Data Integrity	Data Integrity Compromised	Data integrity is out of scope and subject to separate qualification.	N/A	N/A	N/A	N/A

QUALIFICATION SUMMARY, ACCEPTANCE AND RELEASE REPORT	*Bioreactor*
BUILDING, SITE	*Building, Site*

REVIEW AND APPROVALS

Function	Printed Name	Signature	Date
Engineering	*Approver Name*	*Approver Signature*	*DD-MMM-YYYY*
System Owner	*Approver Name*	*Approver Signature*	*DD-MMM-YYYY*
Quality	*Approver Name*	*Approver Signature*	*DD-MMM-YYYY*
SME	*Approver Name*	*Approver Signature*	*DD-MMM-YYYY*

REVISION HISTORY

Version	Author Name	Description of Change	Date
1.0	*Document Author Name*	*Initial Draft*	*DD-MM-YYYY*

TABLE OF CONTENTS

1. Purpose

The purpose of this document is to summarize the qualification activities and conclude acceptance and release for the *Equipment Name & ID* Direct Impact System.

2. References

List the Document ID, Version/Revision and Title of all C&Q documents (e.g. User Requirements, Design Qualification, FAT, SAT, Initial stage of PQ for WFI, Commissioning Summary Reports, etc.) associated with the verification activities of the equipment.

Document ID	Version / Revision	Title
Document ID	*Version / Revision*	*Document Title*
Document ID	*Version / Revision*	*Document Title*
Document ID	*Version / Revision*	*Document Title*
Document ID	*Version / Revision*	*Document Title*

3. Summary Results

3.1. Verification of Critical Aspects/Critical Design Elements

***These columns have been repeated from the DQ and are optional to include in this document.*

#	**Design Controls (CAs)	**Recipe Parameter (Specification)	**Associated Alarm (CDE)	CA/CDE	**Acceptance Criteria	Verification Test Reference Doc. ID, Test ID.
1.	Temperature Control High Temperature Alarm	Temperature is maintained between 20-30 degrees C with an accuracy of ±2 degrees C.	High Alarm	1. Product contact surface materials of construction: gaskets, thermowell, temperature element 2. Measurement accuracy across the operating range 3. Control across the recipe range 4. Alarm as specified 5. Temperature instrument	1. Demonstrate conformance to approved material specifications of identity and surface finish of sensors/transmitters product contact material. 2. Calibration across the range. 3. Temperature control is within range and tolerance. 4. Alarm activates at limit. 5. Temperature instrument in calibration program	1. Doc IDXXX Section xx.xx 2. Doc IDXXX Section xx.xx 3. Doc IDXXX Section xx.xx 4. Doc IDXXX Section xx.xx 5. Doc IDXXX Section xx.xx
2.	Agitation Control Agitation High/Low Alarms	control agitation between 0 to 100 RPM with an accuracy of ± 5 RPM	High/Low Alarm	1. Product contact surface materials of construction: gaskets, agitator shaft and blades 2. Measurement accuracy across the operating range 3. Agitation direction 4. Control across the recipe range 5. Alarm as specified 6. RPM instrument	1. Demonstrate conformance to approved material specifications of identity and surface finish of sensors/transmitters product contact material. 2. Calibration across the range 3. Agitational direction is verified per blade angle 4. Agitation control is within range and tolerance. 5. Alarm activates at limit. 6. RPM instrument in calibration program	1. Doc IDXXX Section xx.xx 2. Doc IDXXX Section xx.xx 3. Doc IDXXX Section xx.xx 4. Doc IDXXX Section xx.xx 5. Doc IDXXX Section xx.xx 6. Doc IDXXX Section xx.xx
3.	DO Control, DO high/low alarm	Dissolved Oxygen (DO) level as specified in the recipe with an accuracy of 5%	High/Low Alarm	1. Product contact surface materials of construction: gaskets, measuring element 2. Measurement accuracy across the operating range 3. Control across the recipe range 4. Alarm as specified 5. DO Instrument	1. Demonstrate conformance to approved material specifications of identity and surface finish of sensors/transmitters product contact material. 2. Calibration across the range 3. DO control is within range and tolerance. 4. Alarm activates at limit. 5. DO instrument in calibration program	1. Doc IDXXX Section xx.xx 2. Doc IDXXX Section xx.xx 3. Doc IDXXX Section xx.xx 4. Doc IDXXX Section xx.xx 5. Doc IDXXX Section xx.xx
4.	Nutrient pump control, Flow high/low alarm	flow is maintained between 0-100 g/min with an accuracy of ±10 g/min.	High/Low Alarm	1. Product contact surface materials of construction: gaskets, flow meter path and sensing element 2. Measurement accuracy across the operating range 3. Control across the recipe range 4. Alarm as specified 5. Flow instrument	1. Demonstrate conformance to approved material specifications of identity and surface finish of sensors/transmitters product contact material. 2. Calibration across the range 3. Flow control is within range and tolerance. 4. Alarm activates at limit 5. Flow instrument in calibration program.	1. Doc IDXXX Section xx.xx 2. Doc IDXXX Section xx.xx 3. Doc IDXXX Section xx.xx 4. Doc IDXXX Section xx.xx 5. Doc IDXXX Section xx.xx
5.	pH Control pH trend data pH high/low alarms	Control pH at a predefined range of 4-12 pH.	High/Low Alarm	1. Product contact surface materials of construction: gaskets, measuring element 2. Measurement accuracy across the operating range 3. Control across the recipe range 4. Alarm as specified 5. pH instrument	1. Demonstrate conformance to approved material specifications of identity and surface finish of sensors/transmitters product contact material. 2. Calibration across the range (user standardized per operating procedures) 3. pH control is within range and tolerance. 4. Alarm activates at limit. 5. instrument in calibration program	1. Doc IDXXX Section xx.xx 2. Doc IDXXX Section xx.xx 3. Doc IDXXX Section xx.xx 4. Doc IDXXX Section xx.xx 5. Doc IDXXX Section xx.xx
6.	.The material of construction for the single-use bag is out of scope and subject to separate qualification.	N/A	N/A	N/A	N/A	N/A
7	Each authorized user must have a unique user ID and an associated password. The automation system must provide ability to configure segregation of roles to provide access control. The automation system must provide an audit trail	N/A	N/A	1. Unique user ID's and Passwords. 2. Segregation of roles 3. Audit trail	1. Unique user ID's and Passwords are assigned. 2. Segregation of roles is assigned. 3. Audit trail is accurate and contemporaneous.	1. Doc IDXXX Section xx.xx 2. Doc IDXXX Section xx.xx 3. Doc IDXXX Section xx.xx
7	Data integrity is out of scope and subject to separate qualification.	N/A	N/A	N/A	N/A	N/A

3.2. Quality System Elements

Quality system elements per *Document Number* have been implemented.
Consider the following

- *Availability of SOPs for operation of the system*
- *Calibration/maintenance system and associated procedures*
- *Mechanism for tracking system use and maintenance (e.g., logbook)*
- *Vendor documentation (e.g., maintenance requirements, spare parts)*
- *Operator training within the training quality system*
- *Completion of any other organization requirements to add the system into the operating facility*

3.3. Quality Related Discrepancies and Engineering Changes

All quality related changes have been implemented and closed. Refer to Commissioning Summary Reports in Section 2.

4. Acceptance and Release

Check the appropriate box in the table below to indicate whether the equipment is subject to full release, conditional release or not suitable for release.

<table>
<tr><th colspan="6">Statement of Release</th></tr>
<tr><td>☐</td><td colspan="5">FULL RELEASE – Review of the testing and verification performed for the system verified that all acceptance criteria were satisfied successfully, demonstrating that the equipment was installed and operates according to the intended design and Company Name requirements. All installation and quality system elements are completed. The system has been successfully installed and is fully operational. The system is fully released for GMP use.</td></tr>
<tr><td>☐</td><td colspan="5">CONDITIONAL RELEASE - Per Policy Number,
Ex: following situations may be eligible for conditional approval (i.e. conditional release): Redline drawing; Redline Operating Procedures with an approved Change Request; Incomplete spare parts list; Incomplete Preventative Maintenance (PM) program/procedures; Statement by Metrology of satisfactory post-calibration results.

If the equipment is subject to conditional release, identify the open item(s) and target date for completing the conditional item(s). Per Policy Number, conditional approvals must be closed within XX calendar days.
<table>
<tr><th>Section No.</th><th>Item No.</th><th>Open Item</th><th>Target Completion Date</th></tr>
<tr><td></td><td></td><td></td><td></td></tr>
<tr><td></td><td></td><td></td><td></td></tr>
<tr><td></td><td></td><td></td><td></td></tr>
</table></td></tr>
<tr><td>☐</td><td colspan="5">NOT SUITABLE FOR RELEASE - Executed test(s) for verification of critical aspects and/or quality system elements failed acceptance criteria. Additional testing is required per comments below.
Record Open Discrepancies and Engineering Change Management items here</td></tr>
<tr><td colspan="6">Comments:</td></tr>
</table>

Completed By:	Date:

END OF DOCUMENT

This example documents package applies the concepts presented in the *ISPE Baseline® Guide: Volume 5 – Commissioning and Qualification (Second Edition)* to the primary deliverable documents (excluding test scripts) for a Tablet Blister **Secondary Packaging** (Cartoning and Case Packing) System.

This example has combined cartoner and case packer in one document for application of an inclusive verification (lifecycle C&Q testing) approach. Often, companies have separated C&Q boundaries for each machine/operation.

The Risk Based C&Q process requires the compilation and approval of certain elements by the system owner, SME and quality units. The formats shown in these example documents are one suggestion of how to compile these requirements. These requirements can be presented across the different documents in a manner that is most efficient, repeatable and error proof as directed by each company's procedures and documentation practices.

Tablet Blister Secondary Packaging	**Content Description**	**Comments**
URS	Follows content and format of example in BG 5. Includes and categorizes all quality impacting and non-quality impacting user requirements. User Requirements define what is required and can be tested/verified.	As presented in the Guide, the focus for secondary packaging are quality related requirements and fall in the sub-classification of being Regulatory/compliance/patient safety and focused on presence of correct labeling, patient information, and product label claim. Since all blister packs moved forward into secondary packaging operations meet quality requirements related to product purity, over the stated expiry date, there is not impact on product CQAs.
SRA	Follows content and format of example in BG 5 Appendix 5. Impact on CQAs by associated CPPs is evaluated. For secondary packaging, the Regulatory (Reg.) are treated the same as product CQAs. CPPs are not often associated with secondary packaging and the focus is on the controls (CAs) that are supported by the engineering and automation design control elements (CDEs) identified so that an evaluation of Regulatory/compliance risk can be evaluated. As appropriate, procedural controls and any available critical design elements in place to implement CAs are also verified. If unacceptable risk is identified additional controls are added to mitigate risk to an acceptable level. The additional CAs are communicated to the vendor and the procedures are added to that overall qualification process. An additional output of the SRA process is identification of detection controls, critical alarms and associated instruments.	1. The example presented applies to an integrated packaging system including two pieces of equipment. It is also possible to conduct SRA the basis of single pieces of equipment, defined systems or manufacturing areas. 2. Other risk assessment tools can be used. However, the outputs of the RA process must include all CAs needed to mitigate risk and supporting procedures needed to support the manufacturing process. 3. Model SRAs can be executed against "families of equipment" and applied to specific equipment per use. 4. Data integrity and access security risks, related to the automation/PCS, are excluded from this example with the assumption that these risks are addressed separately under the supervisory automation control system. Data integrity and access security risks can also be incorporated into the SRA if these features are dedicated to this system.
DQ	Confirmation by SME and QA approval that: 1. DQ prerequisites have been met. 2. Associated test acceptance criteria are established for each CA and CDE in the form of an abbreviated trace matrix 3. DQ conclusion which confirms the design contain the documented CAs and CDEs and will adequately controls risks to product	DQ conclusion statement which references information presented in other documents (i.e., design review (DR) summaries, SRA, detailed trace matrix). List acceptance criteria within the DQ or reference documents if acceptance criteria have been approved in other quality approved documents.

Tablet Blister Secondary Packaging	Content Description	Comments
	quality and patient safety as identified in the System Risk Assessment.	
Qualification Summary, Acceptance and Release Report	Combined Qualification Summary and Acceptance and Release Report: 1. Shows traceability that CDEs have passed acceptance criteria, 2. deviations are closed, 3. quality system elements are in place, 4. system can be released.	Elements of the Acceptance and release can be documented separately. Ex: • Commissioning summary report which documents traceability and deviation closure. • Acceptance and release report.

User Requirements Specification Example

Note: Gray text is informational only and must be deleted before document review.

The template text coloration includes:

1. *Gray italicized text* provides directions, guidance, and suggestions on how to develop various portions of the URS document – to be removed once completed.

2. <*Black italicized text in brackets*> provides sample text that may be modified to meet the needs of the system.

3. Black text is for section headings and to provide the template format that should not be changed or removed because it is language and formatting that is consistent from URS to URS.

Gray text must be deleted or changed to black. Applicable black text should remain unchanged prior to printing the document for pre-approval signatures.

Project teams must determine the need for system user requirements specification on a project-specific basis.

The User Requirements Specification is a living document that serves several purposes during the lifecycle of the system:

- *For new systems or equipment, the URS initiates system design and defines the basic requirements that the system must meet.*

- *The URS is the defining document for traceability in support of verification and qualification.*

The URS defines the requirements that must be met for a system to meet its intended purpose; not how the requirements are met. A system URS brings together multidisciplinary system requirements into a single document to support system design, commissioning, verification, operations and maintenance.

- *Compliance to the requirements must be verifiable*

- *The requirements must clearly distinguish business requirements from quality requirements*

- *Critical Quality Attributes of the system product (output) and associated Critical Process Parameters must be identified in the requirements document*

- *This document is the basis for the design, commissioning and where appropriate verification of the system*

EXAMPLE: A filling line with multiple systems could have multiple URS documents (e.g., one URS for the Isolator, one for the Capper and one for the Filling Line if they are different vendors) or a single URS for the entire filling line.

EXAMPLE: Several identical chromatography columns could have multiple URS documents (one for each column) or a single URS for the identical columns.

EXAMPLE: Several similar chromatography columns could have multiple URS documents (one for each column) or a single URS with sections describing the different requirements for each system.

The URS document provides input to the System Risk Assessment process, the URS may be in draft form. After the Quality Risk Assessment is the URS is updated to include CDEs identified in the risk assessment.

For modifications to existing systems, the URS may be updated to include new requirements or existing requirements may be modified to ensure that the system will reflect the process and/or system changes.

For Qualified systems the URS must be maintained in a controlled location.

For commissioned systems the URS may be stored initially in the project documentation site with the appropriate approvals. The URS for commissioned systems may then be included in the system Turnover Package (TOP) and maintained in the site engineering document repository. For ease of retrieval, a numbering format may be defined

such as: Site reference – Building number – System number – Sub-system identification number.

1.1 URS documents must include the following sections:

1.1.1 Purpose and Scope: Identify the system(s) the URS will cover.

1.1.2 System Overview: Describe the system. Appropriate process flow diagrams, data flow diagrams, network diagrams, etc. may be referenced.

1.1.3 Definitions, Abbreviations, References: Populate tables for definitions, abbreviations, and references as they appear and are used in the body of the URS.

1.1.4 Requirements: Populate the template with information identified below.

1.2 Requirements must be classified as Quality or Business in the type column.

1.3 Include the following requirement categories. If a category is not applicable, enter "not applicable" in the template with a justification:

- *Process Requirements*
- *Automation and records*
- *Design and Construction*
- *Operations and Maintenance*
- *Miscellaneous (e.g., documentation, procedural)*

User Requirements Specification Tablet Thermoforming Blister Packaging System

Building Number, Site: *<Insert text>*
Document Number: *<XXXXX-XXX-XXX>*

The Review and Approval Table and Confidentiality Statement may be deleted if the user requirements document will be maintained in a system with appropriate electronic signatures. Note: If Quality has previously approved the quality requirements (CQAs/CPPs/Regulatory/Company Quality documents) then a Quality signature is not required.

Review and Approval				
Role	**Name**	**Department**	**Signature**	**Date**
System Owner (to confirm relevant business requirements are included)	*<Insert text>*	*<Insert text>*	*<Insert text>*	*<DD-MMM-YYYY>*
SME (to confirm relevant technical requirements are included, and they are classified correctly)	*<Insert text>*	*<Insert text>*	*<Insert text>*	*<DD-MMM-YYYY>*
Quality (to confirm relevant quality requirements are included, and they are classified correctly)	*<Insert text>*	*<Insert text>*	*<Insert text>*	*<DD-MMM-YYYY>*

1. Purpose and Scope

The purpose of this document is to define the user requirements for the < Tablet Thermoforming Blister Packaging System >.

The scope of this document applies to the Tablet Thermoforming Blister Packaging System at the *<insert site and building or facility name as applicable>*.

Revise this document as necessary throughout the entire system or equipment lifecycle. Use it as the basis to assess changes to the system.

2. Definitions and Abbreviations

Include definitions where they assist the reader – it is not necessary to define standard terms.

Add rows as needed below to supplement the Definitions, Abbreviations, and References.

Term	**Definition**
<Insert text>	*<Insert text>*

Abbreviation	**Definition**
<ESS>	*<Engineering Standards and Specifications>*
<PRD>	*<Process and Product Requirements Document>*
<PRJD>	*<Project Requirements Document>*
<SRA>	*<System Risk Assessment>*

3. References

Document Identifier	Title
<Insert document number>	*<Insert title>*

4. System Description

Provide a simple system description and show how it interfaces with other systems. List inputs and outputs as applicable. The appropriate process flow diagrams, data flow diagrams, network diagrams, etc. may be referenced.

The Tablet Thermoforming Blister Packaging System thermoforms blisters from approved film commodities. After the forming of the blister, a feeding system places approved tablets into the thermoformed pockets of the blister and applies and seals a lidding material printed with variable data such as product identification and expiry dating. Finished blister packs are die-cut for use in secondary packaging operations. Secondary packaging is covered by a separate URS.

A vision system inspects the contents of the blister to inspect for product and blister pack defects such as: blister integrity, empty pockets; proper tablet (i.e., shape and color); tablet integrity (i.e., whole or broken). Blisters which are not identified as good are rejected prior to transfer to secondary packaging.

List piping and instrumentation diagrams if necessary, to clearly define the scope of the user requirements.

5. User Requirements

The Tablet Thermoforming Blister Packaging System user requirements are defined in the tables below.

Each table contains user requirements for a functional area or discipline such as Process, Design and Construction, Operations and Maintenance, etc.

The tables are structured as follows:

- ID Number *(a unique requirement number that is auto generated in the table)*
- Requirements *(examples in black italicized bracketed text – good, bad, and why)*
- Type: A drop down menu allowing the author to select Quality, HSE, or Business, or Other as the type of attribute
- Source *(identify the source of the requirements)*

In the Requirement column, specify the requirement as a condition that must be satisfied for the system to meet its intended purpose. Requirements should define and describe what is required without being prescriptive as to how the requirements are met (design solutions) unless the method of meeting the requirement is also a requirement. Requirements shall be specific and verifiable.

Use the Type column to select the type of the requirement. The Type column specifies which requirements are quality critical and which are not.

List the source of each requirement in the Source column. The source should indicate the direct source and version number. Use actual document numbers, titles, and section numbers wherever possible so that the source of the requirement is absolutely clear and traceable.
Input to the URS may come from a number of sources:

- *Project Requirements Document/Charter*
- *Process and Product Requirements Document (PRD)*
- *Quality System Risk Assessment*
- *National, local and site requirements*
- *Legacy equipment evaluations*

- *SME input*

Source documents do not need to be approved to be used as references. Changes and revisions to these source documents may require revision to the URS.

The columns in the table have example text showing both appropriate and inappropriate requirements.

If a section is not used, delete the table but retain the section header and add "Not applicable." after the text. For example, if the URS contained no physical product properties, the table in section 3.2 would be deleted and the section title changed to: "3.2 Process Requirements – Physical Product Properties – N/A"

Subject Matter Experts (SME) should establish their requirements through the project documentation such as the PRD.

(Values are for illustrational purposes only.)

6. Process Requirements – Capacity

ID No.	Requirement	Type	Source
6.1	Equipment will be capable of delivering the required package configurations at a peak speed of XXX blisters per minute (XXcpm), with the respective blister designs in a XXX layout. (may have several depending on multiproduct machine)	Business	Operational Physical Requirements
6.2	Minimum speed for the package configurations = XXX packages per minute (XXcpm) This is optional based your equipment downstream requirements (timing of downstream automation operations, commodities, etc.)	Business	Operational Physical Requirements

7. Process Requirements – Product Physical Properties

Reference product data sheets for physical specification of material being packaged

8. Process Requirements – Critical Quality Attributes and Critical Process Parameters

ID No.	Requirement	Type	Source
8.1	Product purity/stability over shelf life: Equipment shall be capable of identifying process errors which may affect blister integrity and rejecting the following defects): - Malformed blisters - Holes in blister - Wrong tablet in the blister - inadequate sealing - inadequate punching	Quality	CQA
8.2	Equipment shall be capable of detecting and rejecting the following defects: - Product color and size of individual tablets in each pocket - Broken or damaged tablets - Empty pockets	Quality	CQA
Note: Temperature, Pressure, Dwell/Sealing Time, Speed will have specific recipe values based on each approved commodity SKU. Some companies define these parameters as CPPs. However, since individual parameter ranges, are defined based each commodity, they may be designated as an impacting attribute protecting CQAs (e.g. Blister integrity to protect product purity/stability over shelf life). *Refer to BG5 Section 1.6.2 Terminology for Product Impacting Attributes*			
	Temperature forming and sealing (will have specific recipe values based on commodity SKU)	Quality	Impacting Attribute/CPP
	Pressure (will have specific recipe values based on commodity SKU)	Quality	Impacting Attribute/CPP
	Dwell/Sealing Time (will have specific recipe values based on commodity SKU)	Quality	Impacting Attribute/CPP

ID No.	Requirement	Type	Source
	Speed (will have specific recipe values based on commodity SKU)	Quality	Impacting Attribute/CPP
8.3	Printed variable data content should meet Regulatory Requirements (i.e lot, expiration date, serialization data, etc)	Quality	Regulatory
8.4	Equipment shall be capable of printing variable data at designated locations on pre-printed or inline printed lidding stock.	Business	Business
8.5	Equipment shall be capable of verifying the presence and accuracy of printed variable data.	Quality	Company Quality
8.6	Equipment shall be capable of verifying automatic rejection or manual removal of all packages not positively verified for acceptance.	Business	Business
8.7	Equipment shall be capable of preventing mix up between good and rejected products (i.e. tracking rejection along the line and enforcing rejection of blisters with defects).	Quality	Regulatory / Quality

9. Automation and Records

ID No.	Requirement	Type	Source
9.1	Each authorized user must have a unique user ID and an associated password.	Quality	21 CFR part 11
9.2	The automation system must provide ability to configure segregation of roles to provide minimum 3 levels of access control.	Quality	21 CFR part 11
9.3	The automation system must provide an audit trail.	Quality	21 CFR part 11
9.4	The automation system must provide tools and utilities for configuring, categorizing, prioritizing, logging, annunciating, displaying, acknowledging, disabling, and reporting alarms and events.	Business	Manufacturing
9.5	Reports shall be generated via the company reporting system	Business	Company Standard
9.6	Equipment shall be capable of saving and recalling format-specific recipes.	Quality	Data Monitoring And Recording Requirements
9.7	Equipment shall be capable of protecting recipe parameters from unauthorized changes.	Quality	Data Monitoring And Recording Requirements

10. Design and Considerations

ID No.	Requirement	Type	Source
10.1	Product contact materials of construction must not be reactive, additive or absorptive with the product or the following cleaning solutions: x, y and z as to alter product quality.	Quality	21 CFR 211 / Eudralex
10.2	The equipment must be smooth, cleanable, impervious, non-reactive, non-additive and resistant to cleaning/sterilizing agents.	Quality	21 CFR 211 / Eudralex
10.3	All drive components and moving assembly tooling shall be adequately guarded to eliminate all pinch points and other exposed danger areas. Note: Fault message should display which door is opened for easy diagnosing.	EHS	Company EHS Standards
10.4	Noise levels generated by the equipment shall be less than 75 dba.	EHS	Company EHS Standard
10.5	The system shall have a hard-wired emergency stop to immediately shut down the system when triggered and release all stored energy.	EHS	Company EHS Standard

ID No.	Requirement	Type	Source
10.6	The system must be able to operate from the utility supply. In the event of power failure (no UPS), it must stop to a failsafe/controlled state and allow for manual restart when the backup supply is available.	Business	Company Engineering Standard
10.7	The system and instruments shall not lose configuration when power is cycled.	Business	Company Engineering Standard

11. Utilities Available

This section describes the utilities that are available for the system to use, with capacities where they are known; for a greenfield site these would be N/A – the designer would define the requirements.

ID No.	Requirement	Type	Source
11.1	Process Air available at 5 bar.	N/A	Site Engineering Records
11.3	Single and three phase power is available 240/380v 50 hz	N/A	Site Engineering Records

12. Operations and Maintenance

ID No.	Requirement	Type	Source
12.1	*Ex: Downtime requirements, product changeover without special tools*	*Business*	
12.2	*Ex: Maintenance accessibility, lock out tagout requirements All serviceable instrumentation must be accessible from a height of 6 feet (2 meters) or less.*	*Business*	

13. Miscellaneous

ID No.	Requirement	Type	Source
13.1			
13.2			
13.3			

Change Summary

(Required section and content) List each current change for this version, including step number references as applicable. Each change must include a justification. Add or delete rows as needed.

Change	Justification
<Insert change. State "NEW" for new document.>	*<Insert reason/justification for change.>*

SYSTEM RISK ASSESSMENT	**Tablet Thermoforming Blister Packaging System**
BUILDING, SITE	*Building, Site*

REVIEW AND APPROVALS

Function	Printed Name	Signature	Date
Engineering	*Approver Name*	*Approver Signature*	*DD-MMM-YYYY*
System Owner	*Approver Name*	*Approver Signature*	*DD-MMM-YYYY*
Quality	*Approver Name*	*Approver Signature*	*DD-MMM-YYYY*
SME	*Approver Name*	*Approver Signature*	*DD-MMM-YYYY*

REVISION HISTORY

Version	Author Name	Description of Change	Date
1.0	*Document Author Name*	*Initial Draft*	*DD-MM-YYYY*

TABLE OF CONTENTS

1. Purpose

The purpose of this document is to risk assess the equipment design and use, with respect to impact on product quality and Regulatory compliance of *Equipment Name & ID*.

2. System Description

See Tablet Thermoforming Blister Packaging System URS Document No. XXXXX, Version X.X for system description.

3. References

List the Document ID, Version/Revision and Title of all reference documents (e.g. System Risk Assessment SOP, User Requirement Specification, Functional Specification, Process risk assessments, vendor documentation, Etc.).

Document ID	Version / Revision	Title
Document No. XXXXX	Version X.X	System URS
Document ID	*Version / Revision*	*Document Title*
Document ID	*Version / Revision*	*Document Title*
Document ID	*Version / Revision*	*Document Title*

4. System Risk Assessment

** temperature pressure etc., will have specific recipe values for each commodity SKU

#	Operations Sequence/ Process Flow	Process description	CQA / Reg.	CPP/ Impacting Attribute	How CQA can be Impacted	Design Controls (CAs or CDEs as appropriate)	Recipe Parameter**	Associated Alarm	Procedural Controls	Comments
1.	Blister Formation	Heat film and form pockets	Product Stability (blister integrity)	Temperature Control	Over or under heated forming results in malformed blister, holes in blister	Temperature Control, Low and High Temperature Alarm, Reject Register	Temperature range TBD at specified tolerance ±Z°C	Low Alarm High Alarm	Operation SOP Calibration SOP Alarm Response SOP	
2.	Blister Formation	Heat film and form pockets	Product Stability (blister integrity)	Time Control	Over or under heated forming results in malformed blister, holes in blister	Dwell Time Control, Low and High Dwell Time Alarm, Reject Register	Time value range TBD	Low Alarm High Alarm	Operation SOP Calibration SOP Alarm Response SOP	
3	Blister Formation	Heat film and form pockets	Product Stability (blister integrity)	Pressure Control	Over or under pressure results in malformed blister, holes in blister	Pressure Control, Low and High Pressure Alarm, Reject Register	Pressure range TBD at specified tolerance ±Z bar	Low Alarm High Alarm	Operation SOP Calibration SOP Alarm Response SOP	
4	Blister Filling	Feed tablets into pockets	Product identification, defect free verification	N/A	Incorrect product in hopper empty pockets; improper tablet shape or color; bad tablet integrity (whole or broken)	Product Verification Reject Register Vision System	N/A	N/A	Operational SOP (system set-up and in-process challenge verification)	
5	Lidding	Lid with variable data is applied to Film	Product identification and stability data (Potency)	N/A	Missing or inaccuracy data.	Accuracy Detection Reject Register Vision System	N/A	N/A	Operational SOP (system set-up and in-process challenge verification)	
6	Sealing	Sealing of Film and Foil	Integrity of seal (Potency/product stability)	Temperature Control	Over or under heated sealing resulting in insufficient sealing of blisters	Temperature Control Low and High Temperature Alarm Reject Register	Temperature range TBD at specified tolerance ±Z°C	Low Alarm High Alarm	Operation SOP Calibration SOP Alarm Response SOP	
7	Sealing	Sealing of Film and Foil	Integrity of seal (Potency/product stability)	Pressure Control	Over or under pressure results in malformed blister, holes in blister	Pressure Control Low and High Pressure Alarm Reject Register	Pressure range TBD at specified tolerance bar ±Z bar	Low Alarm High Alarm	Operation SOP Calibration SOP Alarm Response SOP	
8	Blister card cutting	Die cut blisters for secondary packaging	Product Stability (Blister card integrity)	N/A	Splices in lid or foil too close to product	Splice detection Lid foil lateral/edge control Pocket detection Reject Register Vision System	N/A	N/A	Operational SOP (system set-up and in-process challenge verification)	
9	Reject Sorting	Good blisters are transferred to the downstream machine for secondary packaging	Rejected blisters are segregated (Regulatory)	N/A	Mix up between good and rejected products Low-pressure at reject station results Blisters with defects are not segregated	Air pressure Low Pressure Alarm, Reject Station with Reject Register	Air pressure is maintained above XX bar	Low Pressure Alarm, Rejection Alarm, System Stop	Operation SOP (system set-up and in-process challenge verification) Calibration SOP Alarm Response SOP	Alarms and stops system if an identified reject is not removed from line
10.	Product Contact	Product contact parts	Identity, strength, quality, or purity of the product	MOC	Additive contamination may affect content	material of construction.	N/A	N/A	N/A	Verification of product contact material Identity for the, gaskets, elastomers etc
11.	Data Integrity	Regulatory security and data collection requirements	Data Integrity	Data Integrity	Data Integrity Compromised	Data integrity is out of scope and subject to separate qualification.	N/A	N/A	Operational SOP	Cross references with GAMP automation URS and included in automation verification

DESIGN QUALIFICATION	**Tablet Thermoforming Blister Packaging System**
BUILDING, SITE	*Building, Site*

REVIEW AND APPROVALS

Function	Printed Name	Signature	Date
Engineering	*Approver Name*	*Approver Signature*	*DD-MMM-YYYY*
System Owner	*Approver Name*	*Approver Signature*	*DD-MMM-YYYY*
Quality	*Approver Name*	*Approver Signature*	*DD-MMM-YYYY*
SME	*Approver Name*	*Approver Signature*	*DD-MMM-YYYY*

REVISION HISTORY

Version	Author Name	Description of Change	Date
1.0	*Document Author Name*	*Initial Draft*	*DD-MM-YYYY*

1. Purpose

The purpose of this document is to record the design qualification for the Tablet Thermoforming Blister Packaging System *Equipment Name & ID* Direct Impact System. Design Qualification (DQ) Objective: Establish that the design of the facility and equipment meets quality impacting and Regulatory requirements and that the system/ equipment is designed to be suitable for intended purpose. Equipment DQ verifies that the equipment/system has applied QRM and QbD concepts and is adequately designed to reliably produce product meeting established quality specifications in accordance with GMPs. Approval of this design qualification report signifies the design is suitable for intended purpose.

2. Design Qualification Process

2.1. Design Qualification Prerequisites

- Approved URS
- Functional requirements (for automated systems)
- System Risk Assessments with identification of design (CAs/CDEs) and procedural controls that will be used to mitigate the unacceptable risks
- Completed DRs, with verification that all open design issues that affect CAs/CDEs, CPPs, and CQAs are closed and included in the final design

List the Document ID, Version/Revision and Title of all reference documents as noted above.

Document ID	Version / Revision	Title
Document No. XXXXX	Version X.X	URS
Document No. XXXXX	Version X.X	SRA
Document ID	*Version / Revision*	*Document Title*
Document ID	*Version / Revision*	*Document Title*

2.2. CA/ CDE and Acceptance Criteria

Attachment A lists the Critical Aspects, Critical Design Elements and respective Acceptance Criteria for verification of suitability for intended use. Acceptance Criteria describe the required system design or controls response that must be demonstrated through objective evidence.

As appropriate, during the verification execution document preparation, issued for fabrication/construction drawings and engineering and automation design documentation and specifications will be referenced for verification of as-built configuration, (i.e. components, instruments, MOC, etc.) and operation (i.e., functional control, alarms, data management, etc.). Traceability of acceptance criteria to C&Q testing documentation will be documented in the supporting traceability matrix.

2.3. Design Qualification Conclusion

Design review by the multidisciplinary team of SMEs, including the Quality Unit, confirmed that all approved User Requirements specifications, including the regulatory and quality, requirements, have been met, confirmed the design will adequately controls risks to product quality and patient safety as identified in the System Risk Assessment and the verified the CAs/CDEs necessary to implement the risk controls are present.

Pre-requisites for Design Qualification have been met and the design of the direct impact system will result in a system that is suitable for intended purpose.

Attachment A
Critical Aspects, Critical Design Elements and Acceptance Criteria for *Equipment Name & ID*

**These columns have been repeated from the SRA and are optional to include in this document*
*** Reference document if these have been approved in another quality approved document.*
**** temperature pressure etc., will have specific recipe values based on commodity SKU*

#	* Operations Sequence/ Process Flow	* Process Description	CQA/ Regulatory	CPP/ Impacting Attribute	*How CQA can be Impacted	Design Controls (CAs or CDEs as appropriate)	*Recipe Parameter (Specification) ***	*Associated Alarm (CDE) Specify light, audible horn, print-out, notification, or combination; Specify machine response	CDE	**Acceptance Criteria
1.	Blister Formation	Heat film and form pockets	Product Stability (blister integrity)	Temperature Control	Over or under heated forming results in malformed blister, holes in blister	Temperature Control, Low and High Temperature Alarm, Reject Register	Temperature range TBD at specified tolerance ±Z°C	Low Alarm High Alarm	1. Measurement accuracy across the operating range 2. Control across the recipe range 3. Alarm response is as specified 4. Temperature instrument 5. Rejection accuracy	1. Calibration across the range. 2. Temperature control is within range and tolerance. 3. Alarm activates at limit; machine response is as specified. 4. Temperature instrument which fails to alarm state and is in calibration program and meets requirements of calibration SOPs (or reference specifications) 5. Reject register is accurate: Identifies for rejection the blister formed with the wrong temperature
2.	Blister Formation	Heat film and form pockets	Product Stability (blister integrity)	Time Control	Over or under heated forming results in malformed blister, holes in blister	Dwell Time Control, Low and High Dwell Time Alarm, Reject Register	Time value range TBD	Low Alarm High Alarm	1. Alarm response is as specified 2. Time verification 3. Rejection accuracy	1. Alarm activates at limit; machine response is as specified. 2. Timer is accurate and not dependent on scan rate 3. Reject register is accurate: Identifies for rejection the blister formed with film dwelling too long/short in the heating station
3.	Blister Formation	Heat film and form pockets	Product Stability (blister integrity)	Pressure Control	Over or under pressure results in malformed blister, holes in blister	Pressure Control, Low and High Pressure Alarm, Reject Register	Pressure range TBD at specified tolerance ±Z bar	Low Alarm High Alarm	1. Measurement accuracy across the operating range 2. Control across the recipe range 3. Alarm response is as specified 4. Pressure Instrument 5. Rejection accuracy	1. Calibration across the range 2. Pressure control is within range and tolerance. 3. Alarm activates at limit; machine response is as specified. 4. Pressure instrument which fails to alarm state and is in calibration program and meets requirements of calibration SOPs (or reference specifications) 5. Reject register is accurate: Identifies for rejection the blister formed with over or under pressure (ex: Forming Air Pressure, plug Assist Air Pressure)
4.	Blister Filling	Feed tablets into pockets	Product identification, defect free verification	N/A	Incorrect product in hopper empty pockets; improper tablet shape or color; bad tablet integrity (whole or broken)	Product Verification Reject Register Vision System	N/A	N/A	1. Camera setup for rejection accuracy: Dimension of blisters, labels. etc	1. Verify camera setup (setting type and number, shutter, calibration, light and color adjustment, picture formats) 2. Reject register is accurate: Identifies for rejection the blister with defects, Incorrect product in hopper, empty pockets; improper tablet shape or color; bad tablet integrity (whole or broken)
5.	Lidding	Lid with variable data is applied to Film	Product identification and stability data (Potency)	N/A	Missing or inaccurate data.	Accuracy Detection Reject Register Vision System	N/A	N/A	1. Camera setup for rejection accuracy: Lid foil print verification.	1. Verify camera setup (setting type and number, shutter, calibration, light and color adjustment, picture formats) 2. Reject register is accurate: Identifies for rejection the blister with altered presence or inaccuracy of variable data

#	* Operations Sequence/ Process Flow	* Process Description	CQA/ Regulatory	CPP/ Impacting Attribute	*How CQA can be Impacted	Design Controls (CAs or CDEs as appropriate)	*Recipe Parameter (Specification) ***	*Associated Alarm (CDE) Specify light, audible horn, print-out, notification, or combination; Specify machine response	CDE	**Acceptance Criteria
6.	Sealing	Sealing of Film and Foil	Integrity of seal (Potency/product stability)	Temperature Control	Over or under heated sealing resulting in insufficient sealing of blisters	Temperature Control Low and High Temperature Alarm Reject Register	Temperature range TBD at specified tolerance ±Z°C	Low Alarm High Alarm	1. Measurement accuracy across the operating range 2. Control across the recipe range 3. Alarm response is as specified 4. Temperature instrument 5. Rejection accuracy	1. Calibration across the range. 2. Temperature control is within range and tolerance. 3. Alarm activates at limit; machine response is as specified. 4. Temperature instrument which fails to alarm state and is in calibration program and meets requirements of calibration SOPs (or reference specifications) 5. Reject register is accurate: Identifies for rejection the blister formed with the wrong temperature
7.	Sealing	Sealing of Film and Foil	Integrity of seal (Potency/product stability)	Pressure Control	Over or under pressure results in malformed blister, holes in blister	Pressure Control Low and High Pressure Alarm Reject Register	Pressure range TBD at specified tolerance bar ±Z bar	Low Alarm High Alarm	1. Measurement accuracy across the operating range 2. Control across the recipe range 3. Alarm response is as specified 4. Pressure Instrument 5. Rejection accuracy	1. Calibration across the range 2. Pressure control is within range and tolerance. 3. Alarm activates at limit; machine response is as specified. 4. Pressure instrument which fails to alarm state and is in calibration program and meets requirements of calibration SOPs (or reference specifications) 5. Reject register is accurate: Identifies for rejection the blister formed with the wrong pressure
8.	Cutting	Die cut blisters for secondary packaging	Product Stability (Blister card integrity)	N/A	Splices in lid or foil too close to product	Splice detection Lid foil lateral/edge control Pocket detection Reject Register Vision System	N/A	N/A	1. Camera setup for rejection accuracy: Splice detection	1. Verify camera setup (setting type and number, shutter, calibration, light and color adjustment, picture formats) 2. Reject register is accurate: Identifies for rejection the blister with pocket edge not detected after the punching station
9.	Reject Sorting	Good blisters are transferred to the downstream machine for secondary packaging	Rejected blisters are segregated (Regulatory)	N/A	Mix up between good and rejected products Low-pressure at reject station results Blisters with defects are not segregated	Air pressure Low Pressure Alarm, Reject Station with Reject Register	Air pressure is maintained above XX bar	Low Pressure Alarm, Rejection Alarm, System Stop	1. Measurement accuracy across the operating range 2. Alarm response is as specified 3. Pressure Instrument 4. Rejection accuracy 5. Rejection separation and alarm	1. Calibration across the range 2. Alarm activates at limit. 3. Pressure instrument/sensor which fails to alarm state and is in calibration program and meets requirements of calibration SOPs (or reference specifications) 4. Rejects blisters are identified for rejection such that good and faulty blisters are removed from the line in different positions. 5. Alarms and stops system if an identified reject is not removed from line
10.	Product Contact	Product contact parts	Identity, strength, quality, or purity of the product	MOC	Additive contamination may affect content	material of construction.	N/A	N/A	1. Product contact surface materials of construction	1. Demonstrate conformance to approved material specifications of identity and surface finish of sensors/transmitters product contact material
11.	Data Integrity	Regulatory security and data collection requirements	Data Integrity	Data Integrity	Data Integrity Compromised	Data integrity is out of scope and subject to separate qualification.	N/A	N/A	N/A	N/A

QUALIFICATION SUMMARY, ACCEPTANCE AND RELEASE REPORT	**Tablet Thermoforming Blister Packaging System**
BUILDING, SITE	*Building, Site*
REVIEW AND APPROVALS	

Function	Printed Name	Signature	Date
Engineering	*Approver Name*	*Approver Signature*	*DD-MMM-YYYY*
System Owner	*Approver Name*	*Approver Signature*	*DD-MMM-YYYY*
Quality	*Approver Name*	*Approver Signature*	*DD-MMM-YYYY*
SME	*Approver Name*	*Approver Signature*	*DD-MMM-YYYY*

REVISION HISTORY

Version	Author Name	Description of Change	Date
1.0	*Document Author Name*	*Initial Draft*	*DD-MM-YYYY*

TABLE OF CONTENTS

1. Purpose

The purpose of this document is to summarize the qualification activities and conclude acceptance and release for the Tablet Thermoforming Blister Packaging System *Equipment Name & ID* Direct Impact System.

2. References

List the Document ID, Version/Revision and Title of all C&Q documents (e.g. User Requirements, Design Qualification, FAT, SAT, Commissioning Summary Reports, etc.) associated with the verification activities of the equipment.

Document ID	Version / Revision	Title
Document No. XXXXX	Version X.X	URS
Document No. XXXXX	Version X.X	SRA
Document No. XXXXX	Version X.X	DQ
Document ID	*Version / Revision*	*Document Title*

3. Summary Results

3.1. Verification of Critical Aspects/Critical Design Elements

***These columns have been repeated from the DQ and are optional to include in this document.*

#	Design Controls (CAs or CDEs as appropriate)	*Recipe Parameter (Specification) ***	*Associated Alarm (CDE) Specify light, audible horn, print-out, notification, or combination; Specify machine response	CDE	**Acceptance Criteria	Verification Test Reference Doc. ID, Test ID.
1.	Temperature Control, Low and High Temperature Alarm, Reject Register	Temperature range TBD at specified tolerance ±Z°C	Low Alarm High Alarm	Measurement accuracy across the operating range Control across the recipe range Alarm response is as specified Temperature instrument Rejection accuracy	1. Calibration across the range. 2. Temperature control is within range and tolerance. 3. Alarm activates at limit; machine response is as specified. 4. Temperature instrument which fails to alarm state and is in calibration program and meets requirements of calibration SOPs (or reference specifications) 5. Reject register is accurate: Identifies for rejection the blister formed with the wrong temperature	1. Doc IDXXX Section xx.xx 2. Doc IDXXX Section xx.xx 3. Doc IDXXX Section xx.xx 4. Doc IDXXX Section xx.xx 5. Doc IDXXX Section xx.xx
2.	Dwell Time Control, Low and High Dwell Time Alarm, Reject Register	Time value range TBD	Low Alarm High Alarm	Alarm response is as specified Time verification Rejection accuracy	1. Alarm activates at limit; machine response is as specified. 2. Timer is accurate and not dependent on scan rate 3. Reject register is accurate: Identifies for rejection the blister formed with film dwelling too long/short in the heating station	1. Doc IDXXX Section xx.xx 2. Doc IDXXX Section xx.xx 3. Doc IDXXX Section xx.xx
3.	Pressure Control, Low and High Pressure Alarm, Reject Register	Pressure range TBD at specified tolerance ±Z bar	Low Alarm High Alarm	Measurement accuracy across the operating range Control across the recipe range Alarm response is as specified Pressure Instrument Rejection accuracy	1. Calibration across the range 2. Pressure control is within range and tolerance. 3. Alarm activates at limit; machine response is as specified. 4. Pressure instrument which fails to alarm state and is in calibration program and meets requirements of calibration SOPs (or reference specifications) 5. Reject register is accurate: Identifies for rejection the blister formed with over or under pressure (ex: Forming Air Pressure, plug Assist Air Pressure)	1. Doc IDXXX Section xx.xx 2. Doc IDXXX Section xx.xx 3. Doc IDXXX Section xx.xx 4. Doc IDXXX Section xx.xx 5. Doc IDXXX Section xx.xx
4.	Product Verification Reject Register Vision System	N/A	N/A	Camera setup for rejection accuracy: Dimension of blisters, labels. etc	1. Verify camera setup (setting type and number, shutter, calibration, light and color adjustment, picture formats) 2. Reject register is accurate: Identifies for rejection the blister with defects, Incorrect product in hopper, empty pockets; improper tablet shape or color; bad tablet integrity (whole or broken)	1. Doc IDXXX Section xx.xx 2. Doc IDXXX Section xx.xx
5.	Accuracy Detection Reject Register Vision System	N/A	N/A	Camera setup for rejection accuracy: Lid foil print verification.	1. Verify camera setup (setting type and number, shutter, calibration, light and color adjustment, picture formats) 2. Reject register is accurate: Identifies for rejection the blister with altered presence or inaccuracy of variable data	1. Doc IDXXX Section xx.xx 2. Doc IDXXX Section xx.xx
6.	Temperature Control Low and High Temperature Alarm Reject Register	Temperature range TBD at specified tolerance ±Z°C	Low Alarm High Alarm	Measurement accuracy across the operating range Control across the recipe range Alarm response is as specified Temperature instrument Rejection accuracy	1. Calibration across the range. 2. Temperature control is within range and tolerance. 3. Alarm activates at limit; machine response is as specified. 4. Temperature instrument which fails to alarm state and is in calibration program and meets requirements of calibration SOPs (or reference specifications) 5. Reject register is accurate: Identifies for rejection the blister formed with the wrong temperature	1. Doc IDXXX Section xx.xx 2. Doc IDXXX Section xx.xx 3. Doc IDXXX Section xx.xx 4. Doc IDXXX Section xx.xx 5. Doc IDXXX Section xx.xx
7.	Pressure Control Low and High Pressure Alarm Reject Register	Pressure range TBD at specified tolerance bar ±Z bar	Low Alarm High Alarm	Measurement accuracy across the operating range Control across the recipe range Alarm response is as specified Pressure Instrument Rejection accuracy	1. Calibration across the range 2. Pressure control is within range and tolerance. 3. Alarm activates at limit; machine response is as specified. 4. Pressure instrument which fails to alarm state and is in calibration program and meets requirements of calibration SOPs (or reference specifications) 5. Reject register is accurate: Identifies for rejection the blister formed with the wrong pressure	1. Doc IDXXX Section xx.xx 2. Doc IDXXX Section xx.xx 3. Doc IDXXX Section xx.xx 4. Doc IDXXX Section xx.xx 5. Doc IDXXX Section xx.xx
8.	Splice detection Lid foil lateral/edge control Pocket detection Reject Register Vision System	N/A	N/A	Camera setup for rejection accuracy: Splice detection	1. Verify camera setup (setting type and number, shutter, calibration, light and color adjustment, picture formats) 2. Reject register is accurate: Identifies for rejection the blister with pocket edge not detected after the punching station	1. Doc IDXXX Section xx.xx 2. Doc IDXXX Section xx.xx

#	Design Controls (CAs or CDEs as appropriate)	*Recipe Parameter (Specification) ***	*Associated Alarm (CDE) Specify light, audible horn, print-out, notification, or combination; Specify machine response	CDE	**Acceptance Criteria	Verification Test Reference Doc. ID, Test ID.
9.	Air pressure Low Pressure Alarm, Reject Station with Reject Register	Air pressure is maintained above XX bar	Low Pressure Alarm, Rejection Alarm, System Stop	Measurement accuracy across the operating range Alarm response is as specified Pressure Instrument Rejection accuracy Rejection separation and alarm	1. Calibration across the range 2. Alarm activates at limit. 3. Pressure instrument/sensor which fails to alarm state and is in calibration program and meets requirements of calibration SOPs (or reference specifications) 4. Rejects blisters are identified for rejection such that good and faulty blisters are removed from the line in different positions. 5. Alarms and stops system if an identified reject is not removed from line	1. Doc IDXXX Section xx.xx 2. Doc IDXXX Section xx.xx 3. Doc IDXXX Section xx.xx 4. Doc IDXXX Section xx.xx 5. Doc IDXXX Section xx.xx
10.	Material of construction.	N/A	N/A	Product contact surface materials of construction	1. Demonstrate conformance to approved material specifications of identity and surface finish of sensors/transmitters product contact material	1. Doc IDXXX Section xx.xx
11.	Data integrity is out of scope and subject to separate qualification.	N/A	N/A	N/A	N/A	

3.2. Quality System Elements

Quality system elements per *Document Number* have been implemented.

Consider the following:

- *Availability of SOPs for operation of the system*
- *Calibration/maintenance system and associated procedures*
- *Mechanism for tracking system use and maintenance (e.g., logbook)*
- *Vendor documentation (e.g., maintenance requirements, spare parts)*
- *Operator training within the training quality system*
- *Completion of any other organization requirements to add the system into the operating facility*

3.3. Quality Related Discrepancies and Engineering Changes

All quality related changes have been implemented and closed. Refer to Commissioning Summary Reports in Section 2.

4. Acceptance and Release

Check the appropriate box in the table below to indicate whether the equipment is subject to full release, conditional release or not suitable for release.

<table>
<tr><th colspan="6">Statement of Release</th></tr>
<tr><td>☐</td><td colspan="5">FULL RELEASE – Review of the testing and verification performed for the system verified that all acceptance criteria were satisfied successfully, demonstrating that the equipment was installed and operates according to the intended design and Company Name requirements. All installation and quality system elements are completed. The system has been successfully installed and is fully operational. The system is fully released for GMP use.</td></tr>
<tr><td rowspan="5">☐</td><td colspan="5">CONDITIONAL RELEASE - Per Policy Number,
Ex: following situations may be eligible for conditional approval (i.e. conditional release): Redline drawing; Redline Operating Procedures with an approved Change Request; Incomplete spare parts list; Incomplete Preventative Maintenance (PM) program/procedures; Statement by Metrology of satisfactory post-calibration results.

If the equipment is subject to conditional release, identify the open item(s) and target date for completing the conditional item(s). Per Policy Number, conditional approvals must be closed within XX calendar days.</td></tr>
<tr><td>Section No.</td><td>Item No.</td><td colspan="2">Open Item</td><td>Target Completion Date</td></tr>
<tr><td></td><td></td><td colspan="2"></td><td></td></tr>
<tr><td></td><td></td><td colspan="2"></td><td></td></tr>
<tr><td></td><td></td><td colspan="2"></td><td></td></tr>
<tr><td>☐</td><td colspan="5">NOT SUITABLE FOR RELEASE - Executed test(s) for verification of critical aspects and/or quality system elements failed acceptance criteria. Additional testing is required per comments below.
Record Open Discrepancies and Engineering Change Management items here</td></tr>
<tr><td colspan="6">Comments:</td></tr>
</table>

Completed By:	Date:

END OF DOCUMENT

This example documents package applies the concepts presented in the *ISPE Baseline® Guide: Volume 5 – Commissioning and Qualification (Second Edition)* to the primary deliverable documents (excluding test scripts) for a Tablet Blister **Secondary Packaging** (Cartoning and Case Packing) System.

This example has combined cartoner and case packer in one document for application of an inclusive verification (lifecycle C&Q testing) approach. Often, companies have separated C&Q boundaries for each machine/operation.

The Risk Based C&Q process requires the compilation and approval of certain elements by the system owner, SME and quality units. The formats shown in these example documents are one suggestion of how to compile these requirements. These requirements can be presented across the different documents in a manner that is most efficient, repeatable and error proof as directed by each company's procedures and documentation practices.

Tablet Blister Secondary Packaging	**Content Description**	**Comments**
URS	Follows content and format of example in BG 5. Includes and categorizes all quality impacting and non-quality impacting user requirements. User Requirements define what is required and can be tested/verified.	As presented in the Guide, the focus for secondary packaging are quality related requirements and fall in the sub-classification of being Regulatory/compliance/patient safety and focused on presence of correct labeling, patient information, and product label claim. Since all blister packs moved forward into secondary packaging operations meet quality requirements related to product purity, over the stated expiry date, there is not impact on product CQAs.
SRA	Follows content and format of example in BG 5 Appendix 5. Impact on CQAs by associated CPPs is evaluated. For secondary packaging, the Regulatory (Reg.) are treated the same as product CQAs. CPPs are not often associated with secondary packaging and the focus is on the controls (CAs) that are supported by the engineering and automation design control elements (CDEs) identified so that an evaluation of Regulatory/compliance risk can be evaluated. As appropriate, procedural controls and any available critical design elements in place to implement CAs are also verified. If unacceptable risk is identified additional controls are added to mitigate risk to an acceptable level. The additional CAs are communicated to the vendor and the procedures are added to that overall qualification process. An additional output of the SRA process is identification of detection controls, critical alarms and associated instruments.	1. The example presented applies to an integrated packaging system including two pieces of equipment. It is also possible to conduct SRA the basis of single pieces of equipment, defined systems or manufacturing areas. 2. Other risk assessment tools can be used. However, the outputs of the RA process must include all CAs needed to mitigate risk and supporting procedures needed to support the manufacturing process. 3. Model SRAs can be executed against "families of equipment" and applied to specific equipment per use. 4. Data integrity and access security risks, related to the automation/PCS, are excluded from this example with the assumption that these risks are addressed separately under the supervisory automation control system. Data integrity and access security risks can also be incorporated into the SRA if these features are dedicated to this system.
DQ	Confirmation by SME and QA approval that: 1. DQ prerequisites have been met. 2. Associated test acceptance criteria are established for each CA and CDE in the form of an abbreviated trace matrix 3. DQ conclusion which confirms the design contain the documented CAs and CDEs and will adequately controls risks to product	DQ conclusion statement which references information presented in other documents (i.e., design review (DR) summaries, SRA, detailed trace matrix). List acceptance criteria within the DQ or reference documents if acceptance criteria have been approved in other quality approved documents.

Tablet Blister Secondary Packaging	Content Description	Comments
	quality and patient safety as identified in the System Risk Assessment.	
Qualification Summary, Acceptance and Release Report	Combined Qualification Summary and Acceptance and Release Report: 1. Shows traceability that CDEs have passed acceptance criteria, 2. deviations are closed, 3. quality system elements are in place, 4. system can be released.	Elements of the Acceptance and release can be documented separately. Ex: • Commissioning summary report which documents traceability and deviation closure. • Acceptance and release report.

User Requirements Specification Example

Note: Gray text is informational only and must be deleted before document review.

The template text coloration includes:

1. *Gray italicized text* provides directions, guidance, and suggestions on how to develop various portions of the URS document – to be removed once completed.

2. <*Black italicized text in brackets*> provides sample text that may be modified to meet the needs of the system.

3. Black text is for section headings and to provide the template format that should not be changed or removed because it is language and formatting that is consistent from URS to URS.

Gray text must be deleted or changed to black. Applicable black text should remain unchanged prior to printing the document for pre-approval signatures.

Project teams must determine the need for system user requirements specification on a project-specific basis.

The User Requirements Specification is a living document that serves several purposes during the lifecycle of the system:

- *For new systems or equipment, the URS initiates system design and defines the basic requirements that the system must meet.*

- *The URS is the defining document for traceability in support of verification and qualification.*

The URS defines the requirements that must be met for a system to meet its intended purpose; not how the requirements are met. A system URS brings together multidisciplinary system requirements into a single document to support system design, commissioning, verification, operations and maintenance.

- *Compliance to the requirements must be verifiable*

- *The requirements must clearly distinguish business requirements from quality requirements*

- *Critical Quality Attributes of the system product (output) and associated Critical Process Parameters must be identified in the requirements document*

- *This document is the basis for the design, commissioning and where appropriate verification of the system*

EXAMPLE: A filling line with multiple systems could have multiple URS documents (e.g., one URS for the Isolator, one for the Capper and one for the Filling Line if they are different vendors) or a single URS for the entire filling line.

EXAMPLE: Several identical chromatography columns could have multiple URS documents (one for each column) or a single URS for the identical columns.

EXAMPLE: Several similar chromatography columns could have multiple URS documents (one for each column) or a single URS with sections describing the different requirements for each system.

The URS document provides input to the System Risk Assessment process, the URS may be in draft form. After the Quality Risk Assessment is the URS is updated to include CDEs identified in the risk assessment.

For modifications to existing systems, the URS may be updated to include new requirements or existing requirements may be modified to ensure that the system will reflect the process and/or system changes.

For Qualified systems the URS must be maintained in a controlled location.

For commissioned systems the URS may be stored initially in the project documentation site with the appropriate approvals. The URS for commissioned systems may then be included in the system Turnover Package (TOP) and

maintained in the site engineering document repository. For ease of retrieval, a numbering format may be defined such as: Site reference – Building number – System number – Sub-system identification number.

1.1 URS documents must include the following sections:

1.1.1 Purpose and Scope: Identify the system(s) the URS will cover.

1.1.2 System Overview: Describe the system. Appropriate process flow diagrams, data flow diagrams, network diagrams, etc. may be referenced.

1.1.3 Definitions, Abbreviations, References: Populate tables for definitions, abbreviations, and references as they appear and are used in the body of the URS.

1.1.4 Requirements: Populate the template with information identified below.

1.2 Requirements must be classified as Quality or Business in the type column.

1.3 Include the following requirement categories. If a category is not applicable, enter "not applicable" in the template with a justification:

- *Process Requirements*
- *Automation and records*
- *Design and Construction*
- *Operations and Maintenance*
- *Miscellaneous (e.g., documentation, procedural)*

User Requirements Specification Tablet Blister Secondary Packaging (Cartoning and Case Packing) System

Building Number, Site: *<Insert text>*
Document Number: *<XXXXX-XXX-XXX>*

The Review and Approval Table and Confidentiality Statement may be deleted if the user requirements document will be maintained in a system with appropriate electronic signatures. Note: If Quality has previously approved the quality requirements (CQAs/CPPs/Regulatory/Company Quality documents) then a Quality signature is not required.

Review and Approval				
Role	**Name**	**Department**	**Signature**	**Date**
System Owner (to confirm relevant business requirements are included)	*<Insert text>*	*<Insert text>*	*<Insert text>*	*<DD-MMM-YYYY>*
SME (to confirm relevant technical requirements are included, and they are classified correctly)	*<Insert text>*	*<Insert text>*	*<Insert text>*	*<DD-MMM-YYYY>*
Quality (to confirm relevant quality requirements are included, and they are classified correctly)	*<Insert text>*	*<Insert text>*	*<Insert text>*	*<DD-MMM-YYYY>*

1. Purpose and Scope

The purpose of this document is to define the user requirements for Tablet Blister Secondary Packaging (Cartoning and Case Packing).

The scope of this document applies to Tablet Blister Secondary Packaging (Cartoning and Case Packing)
Revise this document as necessary throughout the entire system or equipment lifecycle. Use it as the basis to assess changes to the system.

2. Definitions and Abbreviations

Include definitions where they assist the reader – it is not necessary to define standard terms.

Add rows as needed below to supplement the Definitions, Abbreviations, and References.

Term	**Definition**
<Insert text>	*<Insert text>*

Abbreviation	**Definition**
<ESS>	*<Engineering Standards and Specifications>*
<PRD>	*<Process and Product Requirements Document>*
<PRJD>	*<Project Requirements Document>*
<SRA>	*<System Risk Assessment>*

3. References

Document Identifier	**Title**
<Insert document number>	*<Insert title>*

Document Identifier	Title

4. System Description

Provide a simple system description and show how it interfaces with other systems. List inputs and outputs as applicable. The appropriate process flow diagrams, data flow diagrams, network diagrams, etc. may be referenced.

The Cartoner automatically erects, fills, seals, and prints specified Regulatory information on cartons intended for delivery to end users. Each carton contains blister packages and product-specific literature.

Cartons are inspected, and non-conforming cartons are rejected prior to proceeding to case packing.

Blister packages are delivered to an infeed conveyor from the thermoforming blister packing system. Carton blanks and product literature (inserts) are manually loaded into magazines at the cartoner.

The cartoner performs the following basic unit operations.

- Pick and erect carton blank
- Verify and place literature into carton
- Assemble and place blister packages from the infeed into carton
- Close and seal cartons with glue
- Print regulatory information on the carton
- Inspect finished carton for conformance
- Reject non-conforming cartons

Finished conforming cartons are automatically conveyed to downstream equipment.

The Case Packer is designed to pack cartons into cases, print specified Regulatory information on and apply case labels. Conforming cartons are delivered to the machine and assembled at the stacking station, into a specified configuration, for insertion into the case.

Applied case labels are inspected for conformance and non-conforming cases are rejected.

The Thermoforming Blister Packaging System will accommodate various carton and case sizes and operate at speeds as specified.

Note: There are no risks to product quality (CQAs) in secondary packaging operations; the main focus is on meeting Regulatory quality/compliance requirements and to ensure patient safety. These are mostly related to labeling, lot code and expiration dating, and counterfeit verification measures if applied.

List piping and instrumentation diagrams if necessary, to clearly define the scope of the user requirements.

5. User Requirements

The Tablet Blister Secondary Packaging (Cartoning and Case Packing) user requirements are defined in the tables below.

Each table contains user requirements for a functional area or discipline such as Process, Design and Construction, Operations and Maintenance, etc.

The tables are structured as follows:

- ID Number *(a unique requirement number that is auto generated in the table)*
- Requirements *(examples in black italicized bracketed text – good, bad, and why)*
- Type: A drop down menu allowing the author to select Quality, HSE, or Business, or Other as the type of attribute
- Source *(identify the source of the requirements)*

In the Requirement column, specify the requirement as a condition that must be satisfied for the system to meet its intended purpose. Requirements should define and describe what is required without being prescriptive as to how the

requirements are met (design solutions) unless the method of meeting the requirement is also a requirement. Requirements shall be specific and verifiable.

Use the Type column to select the type of the requirement. The Type column specifies which requirements are quality critical and which are not.

List the source of each requirement in the Source column. The source should indicate the direct source and version number. Use actual document numbers, titles, and section numbers wherever possible so that the source of the requirement is absolutely clear and traceable.
Input to the URS may come from a number of sources:

- *Project Requirements Document/Charter*
- *Process and Product Requirements Document (PRD)*
- *Quality System Risk Assessment*
- *National, local and site requirements*
- *Legacy equipment evaluations*
- *SME input*

Source documents do not need to be approved to be used as references. Changes and revisions to these source documents may require revision to the URS.

The columns in the table have example text showing both appropriate and inappropriate requirements.

If a section is not used, delete the table but retain the section header and add "Not applicable." after the text. For example, if the URS contained no physical product properties, the table in section 3.2 would be deleted and the section title changed to: "3.2 Process Requirements – Physical Product Properties – N/A"

Subject Matter Experts (SME) should establish their requirements through the project documentation such as the PRD.

(Values are for illustrational purposes only.)

6. Process Requirements – Capacity

ID No.	Requirement	Type	Source
6.1	The upstream therforming blister machine will deliver blister packs at a rate of XX to XX per minute to deliver filled/finished cartons at a rate of XX to XX cartons per minute.	Business	Operational Physical Requirements
6.2	The case packer must achieve an output range determined by the output of the cartoner and configuration of the case per the specified product configuration.	Business	Operational Physical Requirements

7. Process Requirements – Component Specifications

Reference data sheets for specifications of material/components used for packaging.

8. Process Requirements – Critical Quality Attributes and Critical Process Parameters

ID No.	Requirement	Type	Source
Cartoner			
8.2	Verify the presence and accuracy at designated carton locations of printed variable data.	Quality	Company Quality
8.1	Printing variable data on label stock.	Business	Business
8.3	Verify the presence and accuracy of inserts (i.e., PI, instructions, etc.).	Quality	Company Quality

ID No.	Requirement	Type	Source
8.4	Verify automatic rejection or manual removal of all cartons not positively verified for acceptance.	Business	Business
8.5	Prevent mix up between good and rejected cartons (i.e., tracking and rejecting cartons with defects).	Quality	Regulatory / Quality
Case Packer			
8.7	Verify the presence and accuracy of printed variable data.	Quality	Company Quality
8.6	Print variable data at designated locations on label stock or on cases.	Business	Business
8.8	Verify automatic rejection or manual removal of all cases not verified for acceptance.	Business	Business
8.9	Prevent mix up between good and rejected cases (i.e., tracking and rejecting cases with defects).	Quality	Regulatory / Quality

9. Automation and Records

ID No.	Requirement	Type	Source
9.1	Each authorized user must have a unique user ID and an associated password.	Quality	21 CFR part 11
9.2	The automation system must provide ability to configure segregation of roles to provide minimum 3 levels of access control.	Quality	21 CFR part 11
9.3	The automation system must provide an audit trail.	Quality	21 CFR part 11
9.4	The automation system must provide tools and utilities for configuring, categorizing, prioritizing, logging, annunciating, displaying, acknowledging, disabling, and reporting alarms and events.	Business	Manufacturing
9.5	Reports shall be generated via the company reporting system.	Business	Company Standard
9.6	Equipment shall be capable of saving and recalling format-specific recipes.	Quality	Data Monitoring And Recording Requirements
9.7	Equipment shall be capable of protecting recipe parameters from unauthorized changes.	Quality	Data Monitoring And Recording Requirements

10. Design and Considerations

ID No.	Requirement	Type	Source
10.1	A full format changeover (all change parts and adjustments) should take 1 operator no more than XX minutes.	Business	Operational Physical Requirements
10.2	All drive components and moving assembly components shall be adequately guarded to eliminate all pinch points and other exposed danger areas. Note: Fault message should display which door is opened for easy diagnosing.	EHS	Company EHS Standards
10.3	Noise levels generated by the equipment shall be less than 75 dba.	EHS	Company EHS Standard
10.4	The system shall have a hard-wired emergency stop to immediately shut down the system when triggered and release all stored energy.	EHS	Company EHS Standard
10.5	The system must be able to operate from the utility supply. In the event of power failure (no UPS), it must stop to a failsafe/controlled state and allow for manual restart when the backup supply is available.	Business	Company Engineering Standard

ID No.	Requirement	Type	Source
10.6	The system and instruments shall not lose configuration when power is cycled.	Business	Company Engineering Standard

11. Utilities Available

This section describes the utilities that are available for the system to use, with capacities where they are known; for a greenfield site these would be N/A – the designer would define the requirements.

ID No.	Requirement	Type	Source
11.1	Process Air available at 5 bar.	N/A	Site Engineering Records
11.3	Single and three phase power is available 240/380v 50 hz	N/A	Site Engineering Records

12. Operations and Maintenance

ID No.	Requirement	Type	Source
12.1	*Ex: Downtime requirements, product changeover without special tools*	*Business*	
12.2	*Ex: Maintenance accessibility, lock out tagout requirements All serviceable instrumentation must be accessible from a height of 6 feet (2 meters) or less.*	*Business*	

13. Miscellaneous

ID No.	Requirement	Type	Source
13.1			
13.2			
13.3			

Change Summary

(Required section and content) List each current change for this version, including step number references as applicable. Each change must include a justification. Add or delete rows as needed.

Change	Justification
<Insert change. State "NEW" for new document.>	*<Insert reason/justification for change.>*

SYSTEM RISK ASSESSMENT	**Tablet Blister Secondary Packaging (Cartoning and Case Packing)**
BUILDING, SITE	*Building, Site*

REVIEW AND APPROVALS

Function	Printed Name	Signature	Date
Engineering	*Approver Name*	*Approver Signature*	*DD-MMM-YYYY*
System Owner	*Approver Name*	*Approver Signature*	*DD-MMM-YYYY*
Quality	*Approver Name*	*Approver Signature*	*DD-MMM-YYYY*
SME	*Approver Name*	*Approver Signature*	*DD-MMM-YYYY*

REVISION HISTORY

Version	Author Name	Description of Change	Date
1.0	*Document Author Name*	*Initial Draft*	*DD-MM-YYYY*

TABLE OF CONTENTS

1. Purpose

The purpose of this document is to risk assess the equipment design and use, with respect to impact on product quality and Regulatory compliance of *Equipment Name & ID*.

2. System Description

See Tablet Blister Secondary Packaging System URS
Document No. XXXXX, Version X.X for system description.

3. References

List the Document ID, Version/Revision and Title of all reference documents (e.g. System Risk Assessment SOP, User Requirement Specification, Functional Specification, Process risk assessments, vendor documentation, etc.).

Document ID	Version / Revision	Title
Document No. XXXXX	Version X.X	Tablet Blister Secondary Packaging System URS
Document ID	*Version / Revision*	*Document Title*
Document ID	*Version / Revision*	*Document Title*
Document ID	*Version / Revision*	*Document Title*

4. System Risk Assessment

#	Operations Sequence/ Process Flow	Process description	CQA / Reg.	CPP/ Impacting Attribute	How CQA can be Impacted	Design Controls (CAs or CDEs as appropriate)	Recipe Parameter	Associated Alarm	Procedural Controls	Comments
Cartoner										
1.	Carton is loaded with insert(s)	Pick required literature and accessories from magazines then place into carton	Patient Safety (Reg.)	N/A	Missing inserts results in incomplete package to patient	Insert Verification Reject Register Vision System	N/A	Missing or incorrect inserts	Operation SOP Alarm Response SOP	
2.	Carton is loaded with blister package	Product identification, pick blister packages from the infeed conveyor, orient and place into carton	Misbranded Product (Reg.)	N/A	Missing blister results in incomplete package to patient	Blister Verification Reject Register Vision System	N/A	Missing product blisters	Operation SOP Alarm Response SOP	
3.	Carton is printed	Variable data is applied to carton	Data Integrity (Reg.)	N/A	Missing or inaccuracy of data.	Printed Data Verification Reject Register Vision System	N/A	N/A	Operational SOP (system set-up and in-process challenge verification)	
5.	Reject Sorting	Good cartons are transferred to the downstream machine for case packing	Rejected cartons are segregated (Reg.)	N/A	Mix up between good and rejected cartons Low-pressure at reject station results cartons with defects are not segregated	Reject Station with Reject Register Air pressure Low Pressure Alarm,	Air pressure is maintained above XX bar	Rejection Alarm, System Stop Low Pressure Alarm	Operation SOP (system set-up and in-process challenge verification) Calibration SOP Alarm Response SOP	Alarms and stops system if an identified reject is not removed from line
Case Packer										
1.	Print label	Accuracy of printed variable data	Data Integrity (Reg.)	N/A	Missing or inaccuracy of data.	Printed Data Verification Reject Register Vision System	N/A	Missing cartons	Operation SOP Alarm Response SOP	Alarms and stops system if an identified reject is not removed from line
2.	Apply label	Presence of label	Misbranded Product (Reg.)	N/A	Missing label	Label Verification Reject Register Vision System	N/A	Missing cartons	Operation SOP Alarm Response SOP	Alarms and stops system if an identified reject is not removed from line
3.	Reject Sorting	Good cases are transferred to the downstream	Rejected cases are segregated (Reg.)	N/A	Mix up between good and rejected cases Low-pressure at reject station results cases with defects are not segregated	Reject Station with Reject Register Air pressure Low Pressure Alarm,	Air pressure is maintained above XX bar	Rejection Alarm, System Stop Low Pressure Alarm	Operation SOP (system set-up and in-process challenge verification) Calibration SOP Alarm Response SOP	Alarms and stops system if an identified reject is not removed from line
Data Integrity / Access Control										
1.	Data Integrity	Regulatory security and data collection requirements	Data Integrity (Reg.)	Data Integrity	Data Integrity Compromised	Data integrity is out of scope and subject to separate qualification.	N/A	N/A	Operational SOP	Cross references with GAMP automation URS and included in automation verification

DESIGN QUALIFICATION	**Tablet Blister Secondary Packaging (Cartoning and Case Packing)**
BUILDING, SITE	*Building, Site*

REVIEW AND APPROVALS

Function	Printed Name	Signature	Date
Engineering	*Approver Name*	*Approver Signature*	*DD-MMM-YYYY*
System Owner	*Approver Name*	*Approver Signature*	*DD-MMM-YYYY*
Quality	*Approver Name*	*Approver Signature*	*DD-MMM-YYYY*
SME	*Approver Name*	*Approver Signature*	*DD-MMM-YYYY*

REVISION HISTORY

Version	Author Name	Description of Change	Date
1.0	*Document Author Name*	*Initial Draft*	*DD-MM-YYYY*

1. Purpose

The purpose of this document is to record the design qualification for the Tablet Blister Secondary Packaging System *& ID* Direct Impact System. Design Qualification (DQ) Objective: Establish that the design of the facility and equipment meets quality impacting and Regulatory requirements and that the system/ equipment is designed to be suitable for intended purpose. Equipment DQ verifies that the equipment/system has applied QRM and QbD concepts and is adequately designed to reliably produce product meeting established quality specifications in accordance with GMPs. Approval of this design qualification report signifies the design is suitable for intended purpose.

2. Design Qualification Process

2.1. Design Qualification Prerequisites

- Approved URS
- Functional requirements (for automated systems)
- System Risk Assessments with identification of design (CAs/CDEs) and procedural controls that will be used to mitigate the unacceptable risks
- Completed DRs, with verification that all open design issues that affect CAs/CDEs, CPPs, and CQAs are closed and included in the final design

List the Document ID, Version/Revision and Title of all reference documents as noted above.

Document ID	Version / Revision	Title
Document No. XXXXX	Version X.X	Tablet Blister Secondary Packaging System URS
Document No. XXXXX	Version X.X	Tablet Blister Secondary Packaging System SRA
Document ID	*Version / Revision*	*Document Title*
Document ID	*Version / Revision*	*Document Title*

2.2. CA/ CDE and Acceptance Criteria

Attachment A lists the Critical Aspects, Critical Design Elements and respective Acceptance Criteria for verification of suitability for intended use. Acceptance Criteria describe the required system design or controls response that must be demonstrated through objective evidence.

As appropriate, during the verification execution document preparation, issued for fabrication/construction drawings and engineering and automation design documentation and specifications will be referenced for verification of as-built configuration, (i.e. components, instruments, MOC, etc.) and operation (i.e., functional control, alarms, data management, etc.). Traceability of acceptance criteria to C&Q testing documentation will be documented in the supporting traceability matrix.

2.3. Design Qualification Conclusion

Design review by the multidisciplinary team of SMEs, including the Quality Unit, confirmed that all approved User Requirements specifications, including the regulatory and quality, requirements, have been met, confirmed the design will adequately controls risks to product quality and patient safety as identified in the System Risk Assessment and the verified the CAs/CDEs necessary to implement the risk controls are present.

Pre-requisites for Design Qualification have been met and the design of the direct impact system will result in a system that is suitable for intended purpose.

Attachment A
Critical Aspects, Critical Design Elements and Acceptance Criteria for *Equipment Name & ID*

**These columns have been repeated from the SRA and are optional to include in this document*
*** Reference document if these have been approved in another quality approved document.*

#	* Operations Sequence/ Process Flow	* Process Description	CQA/ Regulatory	CPP/ Impacting Attribute	*How CQA can be Impacted	Design Controls (CAs or CDEs as appropriate)	*Recipe Parameter (Specification) ***	*Associated Alarm (CDE) Specify light, audible horn, print-out, notification, or combination; Specify machine response	CDE	**Acceptance Criteria
Cartoner										
1.	Carton is loaded with insert(s)	Pick required literature and accessories from magazines then place into carton	Patient Safety (Reg.)	N/A	Missing inserts results in incomplete package to patient	Insert Verification Reject Register Vision System	N/A	Missing or incorrect inserts	1. Camera setup for rejection accuracy: Dimension, data. etc.	1. Verify camera setup (setting type and number, shutter, calibration, light and color adjustment, picture formats) 2. Reject register is accurate: Identifies for rejection the carton with defects
2.	Carton is loaded with blister package	Product identification Pick blister packages from the infeed conveyor, orient and place into carton	Misbranded Product (Reg.)	N/A	Missing blister results in incomplete package to patient	Blister Verification Reject Register Vision System	N/A	Missing product blisters	1. Camera setup for rejection accuracy: Dimension, data. etc.	1. Verify camera setup (setting type and number, shutter, calibration, light and color adjustment, picture formats) 2. Reject register is accurate: Identifies for rejection the carton with defects
3.	Carton is printed	Variable data is applied to carton	Data Integrity (Reg.)	N/A	Missing or inaccuracy of data.	Printed Data Verification Reject Register Vision System	N/A	N/A	1. Camera setup for rejection accuracy: Dimension, labels. etc.	1. Verify camera setup (setting type and number, shutter, calibration, light and color adjustment, picture formats) 2. Reject register is accurate: Identifies for rejection the carton with defects
4.	Reject Sorting	Good cartons are transferred to the downstream machine for case packing	Rejected cartons are segregated (Reg.)	N/A	Mix up between good and rejected cartons Low-pressure at reject station results cartons with defects are not segregated	Reject Station with Reject Register Air pressure Low Pressure Alarm,	Air pressure is maintained above XX bar	Rejection Alarm, System Stop Low Pressure Alarm	1. Measurement accuracy across the operating range 2. Alarm response is as specified 3. Pressure Instrument 4. Rejection accuracy 5. Rejection separation and alarm	1. Calibration across the range 2. Alarm activates at limit. 3. Pressure instrument/sensor which fails to alarm state and is in calibration program and meets requirements of calibration SOPs (or reference specifications) 4. Rejects are identified for rejection such that good and faulty cartons are removed from the line in different positions. 5. Alarms and stops system if an identified reject is not removed from line
Case Packer										
1.	Print label	Accuracy of printed variable data	Data Integrity (Reg.)	N/A	Missing or inaccuracy of data.	Printed Data Verification Reject Register Vision System	N/A	Missing data/ Inaccurate Label	1. Camera setup for rejection accuracy: Dimension, data. etc.	1. Verify camera setup (setting type and number, shutter, calibration, light and color adjustment, picture formats) 2. Reject register is accurate: Identifies for rejection the carton with defects
2.	Apply label	Presence of label	Misbranded Product (Reg.)	N/A	Missing label	Label Verification Reject Register Vision System	N/A	Missing Label	1. Camera setup for rejection accuracy: Dimension, data. etc.	1. Verify camera setup (setting type and number, shutter, calibration, light and color adjustment, picture formats) 2. Reject register is accurate: Identifies for rejection the carton with defects

#	* Operations Sequence/ Process Flow	* Process Description	CQA/ Regulatory	CPP/ Impacting Attribute	*How CQA can be Impacted	Design Controls (CAs or CDEs as appropriate)	*Recipe Parameter (Specification) ***	*Associated Alarm (CDE) Specify light, audible horn, print-out, notification, or combination; Specify machine response	CDE	**Acceptance Criteria
3.	Reject Sorting	Good cases are transferred to the downstream	Rejected cases are segregated (Reg.)	N/A	Mix up between good and rejected cases Low-pressure at reject station results cases with defects are not segregated	Reject Station with Reject Register Air pressure Low Pressure Alarm,	Air pressure is maintained above XX bar	Rejection Alarm, System Stop Low Pressure Alarm	1. Measurement accuracy across the operating range 2. Alarm response is as specified 3. Pressure Instrument 4. Rejection accuracy 5. Rejection separation and alarm	1. Calibration across the range 2. Alarm activates at limit. 3. Pressure instrument/sensor which fails to alarm state and is in calibration program and meets requirements of calibration SOPs (or reference specifications) 4. Rejects are identified for rejection such that good and faulty cases are removed from the line in different positions. 5. Alarms and stops system if an identified reject is not removed from line
Data Integrity / Access Control										
11.	Data Integrity	Regulatory security and data collection requirements	Data Integrity	Data Integrity	Data Integrity Compromised	Data integrity is out of scope and subject to separate qualification.	N/A	N/A	N/A	N/A

QUALIFICATION SUMMARY, ACCEPTANCE AND RELEASE REPORT	**Tablet Blister Secondary Packaging (Cartoning and Case Packing)**
BUILDING, SITE	*Building, Site*

REVIEW AND APPROVALS

Function	Printed Name	Signature	Date
Engineering	*Approver Name*	*Approver Signature*	*DD-MMM-YYYY*
System Owner	*Approver Name*	*Approver Signature*	*DD-MMM-YYYY*
Quality	*Approver Name*	*Approver Signature*	*DD-MMM-YYYY*
SME	*Approver Name*	*Approver Signature*	*DD-MMM-YYYY*

REVISION HISTORY

Version	Author Name	Description of Change	Date
1.0	*Document Author Name*	*Initial Draft*	*DD-MM-YYYY*

TABLE OF CONTENTS

1. Purpose

The purpose of this document is to summarize the qualification activities and conclude acceptance and release for the Tablet Blister Secondary Packaging System *& ID* Direct Impact System.

2. References

List the Document ID, Version/Revision and Title of all C&Q documents (e.g. User Requirements, Design Qualification, FAT, SAT, Commissioning Summary Reports, etc.) associated with the verification activities of the equipment.

Document ID	Version / Revision	Title
Document No. XXXXX	Version X.X	Tablet Blister Secondary Packaging System URS
Document No. XXXXX	Version X.X	Tablet Blister Secondary Packaging System SRA
Document No. XXXXX	Version X.X	Tablet Blister Secondary Packaging System DQ
Document No. XXXXX	Version X.X	Tablet Blister Secondary Packaging System Commissioning Summary Report

3. Summary Results

3.1. Verification of Critical Aspects/Critical Design Elements

***These columns have been repeated from the DQ and are optional to include in this document.*

#	Design Controls (CAs or CDEs as appropriate)	*Recipe Parameter (Specification) ***	*Associated Alarm (CDE) Specify light, audible horn, print-out, notification, or combination; Specify machine response	CDE	**Acceptance Criteria	Verification Test Reference Doc. ID, Test ID.
Cartoner						
1.	Insert Verification Reject Register Vision System	N/A	Missing or incorrect inserts	1. Camera setup for rejection accuracy: Dimension, data. etc	1. Verify camera setup (setting type and number, shutter, calibration, light and color adjustment, picture formats) 2. Reject register is accurate: Identifies for rejection the carton with defects	1. Doc IDXXX Section xx.xx 2. Doc IDXXX Section xx.xx
2.	Blister Verification Reject Register Vision System	N/A	Missing product blisters	1. Camera setup for rejection accuracy: Dimension, data. etc	1. Verify camera setup (setting type and number, shutter, calibration, light and color adjustment, picture formats) 2. Reject register is accurate: Identifies for rejection the carton with defects	1. Doc IDXXX Section xx.xx 2. Doc IDXXX Section xx.xx
3.	Printer Data Verification Reject Register Vision System	N/A	N/A	1. Camera setup for rejection accuracy: Dimension, labels. etc	1. Verify camera setup (setting type and number, shutter, calibration, light and color adjustment, picture formats) 2. Reject register is accurate: Identifies for rejection the carton with defects	1. Doc IDXXX Section xx.xx 2. Doc IDXXX Section xx.xx
4.	Reject Station with Reject Register Air pressure Low Pressure Alarm,	Air pressure is maintained above XX bar	Rejection Alarm, System Stop Low Pressure Alarm	1. Measurement accuracy across the operating range 2. Alarm response is as specified 3. Pressure Instrument 4. Rejection accuracy 5. Rejection separation and alarm	1. Calibration across the range 2. Alarm activates at limit. 3. Pressure instrument/sensor which fails to alarm state and is in calibration program and meets requirements of calibration SOPs (or reference specifications) 4. Rejects are identified for rejection such that good and faulty cartons are removed from the line in different positions. 5. Alarms and stops system if an identified reject is not removed from line	1. Doc IDXXX Section xx.xx 2. Doc IDXXX Section xx.xx 3. Doc IDXXX Section xx.xx 4. Doc IDXXX Section xx.xx 5. Doc IDXXX Section xx.xx
Case Packer						
1.	Print Verification Reject Register Vision System	N/A	Missing data/ Inaccurate Label	1. Camera setup for rejection accuracy: Dimension, data. etc	2. Verify camera setup (setting type and number, shutter, calibration, light and color adjustment, picture formats) 3. Reject register is accurate: Identifies for rejection the carton with defects	1. Doc IDXXX Section xx.xx 2. Doc IDXXX Section xx.xx
2.	Label Verification Reject Register Vision System	N/A	Missing Label	1. Camera setup for rejection accuracy: Dimension, data. etc	1. Verify camera setup (setting type and number, shutter, calibration, light and color adjustment, picture formats) 2. Reject register is accurate: Identifies for rejection the carton with defects	1. Doc IDXXX Section xx.xx 2. Doc IDXXX Section xx.xx
3.	Reject Station with Reject Register Air pressure Low Pressure Alarm,	Air pressure is maintained above XX bar	Rejection Alarm, System Stop Low Pressure Alarm	1. Measurement accuracy across the operating range 2. Alarm response is as specified 3. Pressure Instrument 4. Rejection accuracy 5. Rejection separation and alarm	1. Calibration across the range 2. Alarm activates at limit. 3. Pressure instrument/sensor which fails to alarm state and is in calibration program and meets requirements of calibration SOPs (or reference specifications) 4. Rejects are identified for rejection such that good and faulty cases are removed from the line in different positions. 5. Alarms and stops system if an identified reject is not removed from line	1. Doc IDXXX Section xx.xx 2. Doc IDXXX Section xx.xx 3. Doc IDXXX Section xx.xx 4. Doc IDXXX Section xx.xx 5. Doc IDXXX Section xx.xx
Data Integrity / Access Control						
1.	Data integrity is out of scope and subject to separate qualification.	N/A	N/A	N/A	N/A	N/A

3.2. Quality System Elements

Quality system elements per *Document Number* have been implemented.

Consider the following:

- *Availability of SOPs for operation of the system*
- *Calibration/maintenance system and associated procedures*
- *Mechanism for tracking system use and maintenance (e.g., logbook)*
- *Vendor documentation (e.g., maintenance requirements, spare parts)*
- *Operator training within the training quality system*
- *Completion of any other organization requirements to add the system into the operating facility*

3.3. Quality Related Discrepancies and Engineering Changes

All quality related changes have been implemented and closed. Refer to Commissioning Summary Reports in Section 2.

4. Acceptance and Release

Check the appropriate box in the table below to indicate whether the equipment is subject to full release, conditional release or not suitable for release.

<table>
<tr><th colspan="6">Statement of Release</th></tr>
<tr><td>☐</td><td colspan="5">FULL RELEASE – Review of the testing and verification performed for the system verified that all acceptance criteria were satisfied successfully, demonstrating that the equipment was installed and operates according to the intended design and Company Name requirements. All installation and quality system elements are completed. The system has been successfully installed and is fully operational. The system is fully released for GMP use.</td></tr>
<tr><td rowspan="5">☐</td><td colspan="5">CONDITIONAL RELEASE - Per Policy Number,
Ex: following situations may be eligible for conditional approval (i.e. conditional release): Redline drawing; Redline Operating Procedures with an approved Change Request; Incomplete spare parts list; Incomplete Preventative Maintenance (PM) program/procedures; Statement by Metrology of satisfactory post-calibration results.

If the equipment is subject to conditional release, identify the open item(s) and target date for completing the conditional item(s). Per Policy Number, conditional approvals must be closed within XX calendar days.</td></tr>
<tr><td>Section No.</td><td>Item No.</td><td colspan="2">Open Item</td><td>Target Completion Date</td></tr>
<tr><td></td><td></td><td colspan="2"></td><td></td></tr>
<tr><td></td><td></td><td colspan="2"></td><td></td></tr>
<tr><td></td><td></td><td colspan="2"></td><td></td></tr>
<tr><td>☐</td><td colspan="5">NOT SUITABLE FOR RELEASE - Executed test(s) for verification of critical aspects and/or quality system elements failed acceptance criteria. Additional testing is required per comments below.
Record Open Discrepancies and Engineering Change Management items here</td></tr>
<tr><td colspan="6">Comments:</td></tr>
</table>

Completed By:	Date:

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