Report On

Functions of Quality Assurance Department of a pharmaceutical Industry in Bangladesh

By

Pratiti Roy
Student ID: 20264051

An internship report submitted to the Graduate School of Management in partial fulfillment of the requirements for the degree of
[Master of Business Administration]

Graduate School of Management
Brac University
February 2023

Declaration

It is hereby assured that

1. The internship report which is submitted is my own effort to complete for the fulfillment of degree at BRAC University.
2. The internship report is not copied from any kind of journal which is already published however it is properly cited and referencing as per the required criteria set for the report.
3. The report does not contain any kind of similarities which has already been submitted and accepted for the degree accomplishment within BRAC university and other institution.
4. This report will add value to learn more about the pharmaceutical Industry in Bangladesh.

Student's Full Name & Signature:

_____

Pratiti Roy
Student ID: 20264051

Supervisor's Full Name & Signature:

_____

Dr. Md Shamimul Islam
Assistant Professor, Operations Management and Information Management
Brac Business School, Brac University

Letter of Transmittal

Dr. Md Shamimul Islam

Assistant Professor,

Operations Management and Information Management

BRAC University

66 Mohakhali, Dhaka-1212

Subject: Submission an Internship Report on Functions of Quality Assurance Department of a pharmaceutical Industry in Bangladesh

Dear Sir,

With due respect and great pleasure, I would like to approach you that, The Internship report is submitted as titled "Functions of Quality Assurance Department of a pharmaceutical Industry in Bangladesh" for the accomplishment of my degree.

I worked on this topic, since the day you I have been assigned. My experience throughout the internship journey is really great. From where I got to know so much about different organizations working culture and functions of the specific department of the pharmaceutical industry. During preparing the report, I have taken care about the fact that, I have not violated the rules and regulations set by the BRAC Business School for the Internship and used all the authentic source to complete my report.

Your acceptance is highly required by analysis my work which will motivate me a lot. I will definitely be available to justify the information that I have added in the report.

Sincerely yours,

_____

Pratiti Roy

ID: 20264051

BRAC Business School

BRAC University

2 February, 2023

Non-Disclosure Agreement

As Ms. Pratiti Roy gets access to the confidential information of Synovia Pharma PLC. in Bangladesh so She is required to sign this NDA in order to safeguard the "Confidential Information". Trade secrets, proprietary information, customer information, customer lists, methods, plans, documents, data, drawings, notebooks, reports, models, inventions, formulas, processes, software, information systems, contracts, negotiations, strategic planning, proposals, business alliances, and training materials are just a few examples of information that may be considered confidential.

I have read the above definition of "Confidential Information" and understand it. I thus promise not to share or discuss any confidential information with anyone at any time, including during and after my internship at Synovia Pharma.

IN WITNESS WHEREOF, this agreement has been signed by me, the intern, and Synovia Pharma PLC. (ex-Sanofi Bangladesh Limited) in the month of February 2023.

Acknowledgement

First and foremost, I am grateful to my Supervisor Dr. MD. Shamimul Islam and Co-supervisor Dr. Suman Paul Chowdhury for their tremendous guidance throughout the period.

My special gratitude goes to Mr. Salman Ahmed, Manager of Quality Assurance from Quality Operations Department of Synovia Pharma PLC. for his tremendous support and fastidious supervision to carry out the work superbly.

Without the excellent help of all departmental personnel, I am not hesitant to admit that it would be difficult to complete this report properly.

I'm thrilled to have such a terrific job opportunity with Synovia Pharma PLC (formerly Sanofi Bangladesh Limited) and such excellent guidance from my supervisor and co-supervisor.

Executive Summary

This paper clarifies how a huge Quality operations Department in a pharmaceutical Industry runs by facing different ups and downs and how they are ensuring Quality in every aspect to provide best quality products to cure disease of the patients. Explains how we can operate the day-to-day operation using a hybrid strategy. This demonstrates how to manage quality control in-depth operationally and how to deliver both imported and exported medicines. To fill the gap in lead time, how prepared to supervise & control the operational planning of different phases with a convincing argument and visual representation. This study provides a detailed understanding of how Oracle, Phenix, and Geode interact with one another. Additionally, this study gave us firsthand knowledge with the profound plunge of real organizational operational process under sound management. In this study, a few potential research areas are suggested as recommendations.

Keywords: Quality Operations, Quality Assurance; Deviation; Risk Assessment; Change control; CAPA; PQR; In-process control; BMR; BPR; BAR.

Table of Contents

List of Tables

List of Figures

List of Acronyms

PQR	Product Quality Review
CCR	Change Control
BMR	Batch Manufacturing Record
BPR	Batch Packaging Record
BAR	Batch Analytical Record
QCR	Quality Control Request
COA	Certificate of Analysis
EIQC	Electrical Industrial Quality Compliance
QC	Quality Control
QA	Quality Assurance
PD	Product Development
CAPA	Corrective Action Preventive Action
SOP	Standard Operating Procedure
QMS	Quality Management System
ASL	Approved Supplier List
OOS	Out of Specification
OOT	Out of Trend
PTC	Product Technical Call

IPC	In-Process Checking
IPQA	In-Process Quality Assurance
LOD	Loss On Drying
KF	Karl Fisher
MLT	Microbiological Limit Test
PFS	Powder for Suspension
OEB	Occupational Exposure Band
RAR	Raw materials Analytical Record
PO	Process Order
AWB	Airway bill
COO	Certificate of Origin

Glossary

Process Capability	The ability of a process to produce output within specification limits, which is determined by a comparison of the actual performance of a process to its specifications limits by using capability indices.
AWB	When the products are delivered to a predefined location, a receipt of shipment is issued which is known as AWB (Air Way Bill)
Product Quality Review	It is also referred to as annual quality review. Periodic evaluation to make sure a process is consistent, examine trends, identify modifications that may be necessary to standards, manufacture, and methods of control, assess the need for verification, and enable the quality improvement process.
Batch Records	Documentation necessary to trace the complete cycle of manufacture of a batch of product, from dispensing of materials through all processing, testing and subsequent packaging to the dispatch for sale and supply of the finished product. This documentation includes quality control, quality assurance and environmental data specific to the batch.
Certificate of Analysis	Document which reflects that the batch meets the product specification described in the regulatory dossier or established document.

CPK	An estimation of the process's production capacity given that the process mean might not be perfectly centered between the specification boundaries.
Issuance	Quality Assurance department is responsible for issuance of checklist required for batch documents release, training record sheet, any kind of appendix within the Pharmaceutical Plant.
Freight Certificate	It is one kind of document which proves that during -shipping all the payments have paid from the buyers end.

Logbook	The logbook can be defined as a full defined chronological activity undertaken in a given area and or in a given equipment covering it's use/operation, cleaning and maintenance or any other quality critical monitoring data.
Recall	It is a process to prevent use or further use due to a defect or potential defect in production, distribution, product stability, safety or efficacy, or any other reason such as a change in business contract due to local regulations that renders the product unfit for use on the market, it is a process of retrieving one or more batches of product from the distribution network or from the market.

Chapter 1: Overview of Internship

1.1 Student Information

Student Name: Pratiti Roy

Student ID: 20264051

Program: MBA

Major: Operations Management

1.2 Internship Information

1.2.1 Employee Information

Employee Name:	Pratiti Roy
Designation:	Executive
Department:	Quality Assurance, Quality Operations
Job Location	Synovia Pharma PLC., Tongi IA site
Report to:	Salman Ahmed, manager, Quality Assurance
Joining Date	15.12.21
Job Experience	1+ year

1.2.2 Supervisor's Information

Employee Name:	Salman Ahmed
Designation:	Manager
Department:	Quality Assurance, Quality Operations
Job Location	Synovia Pharma PLC., Tongi ia site
Report to:	Md. Badrul Haider Chowdhury, Assistant General Manager, Quality Operations
Job Experience	13+ year

1.2.3 Job Description

Job purpose
Qualified Person in performing the floor level IPQA (In Process Quality Assurance) and maintaining quality, compilation and review of batch records for batches manufactured by site in accordance to regulatory requirements and Synovia guidelines and policies, performing investigation, and ensuring the quality and regulatory compliance throughout product shelf life.

Duties and Responsibilities
Quality Oversight in Site Premises 1 Ensuring cGMP compliance and assuring amelioration of floor level activities such as in the production floor, quality operations, and warehouse according to the Synovia guidelines and the local regulatory agency. 2 Performing IPC in a timely manner in accordance with relevant SOPs and Synovia Guidelines. 3 Ensure compliance of Containment Policies and Practices in day-to-day activities. 4 Execute Quality Gemba Visit in day-to-day activities. 5 Prevention of contamination, cross-contamination, mix-up and minimization of human error in day-to-day floor level activities. Qualified Person for Review of Batch Records: 1 Responsible for Batch Record Review and compilation of Batch Manufacturing Record (BMR), Batch Packaging Record (BPR), Batch Analytical Record (BAR), Microbiological Report for batch analysis. Implementation and Management of Quality Systems in the Site 6 Responsible for Imported Product Management. 7 Responsible for conducting investigations and reporting of events such as deviations, out of specifications. 8 Ensure notification and escalation of pharmacovigilance related identified issues. 9 Responsible to perform Risk Assessment.

Duties and Responsibilities
10 Preparation of Standard Operating Procedure and conduct training to related personnel 11 Preparation and management of Product Quality Review (PQR). HSE activities 12 Carry out all activities complying the Sanofi's HSE policy, requirements, standards, SOPs and relevant local laws. 13 Always remain vigilant in conducting activities to ensure preservation of natural resources and prevention of environmental damage and pollution. 14 Identify HSE concerns, risks and alerts; communicate in appropriate channel and act accordingly to ensure safety and security of human health and company assets.

1.3 Internship Outcomes

1.3.1 Contribution to the company:

a. CAPA 95.00% in whole year for 2022. b. RFT 100% for 2022. c. Deviations ongoing overdue Nil (0.00%) in 2022 e. PTC: 0.5 ppm in 2022 f. Number of repeat deviations: 6.89% in 2022 g. Quality Cycle Time: 9.18 days on average in 2022 h. Change Control on-time closure: 88.9% in 2022.
1. Ensure cGMP compliance and development of floor level activities at T4 Solid Manufacturing and packaging area from 25 JAN 2022-28 MAR 2022. 2. Regular IPC performing at Solid manufacturing and Packaging area from 25th JAN 2022-28th MAR 2022, Penicillin area from 29 th March-30th May and Sterile and Semi-solid from 01 June-continuing. 3. Ensure Floor compliance and IPC performing at Penicillin area from 29 MAR 2022-Present. 4. Shop floor compliance during site transaction. 5. Logbook and batch documents issuance

1. Number of executed PQR on 2022: 25.
2. Number of deviation investigations performed on 2022: 21.
3. Trained as a qualified batch records reviewer.
4. Trained for imported product receiving and management from MAY 2022.
5. Trained on Management of Annual Product Quality Review.
6. Number of Monthly PQR Summary Report completed Q1-Q4: 03.
7. Annual PQR Plan for 2023.

1.3.2 Benefits to the student

1. Gathered more knowledge regarding quality operations of a pharmaceutical industry
2. Co-relate whole process flow with the academic knowledge.
3. Build more confidence as Quality Assurance monitor and supervise all of the departments function so could learn cross functional department work.
4. Problem solving by Ishikawa and Fishbone Diagram, analytical thinking, time management skill, on-time delivery, multi-tasing these are some qualitied that I could adapt from Synovia Pharma PLC.

1.3.3 Problems/Difficulties (faced during the internship period)

1 During the 1 year, several issued have been raised regarding manufacturing facilities. As source changes of raw materials for multiple products have been occurred during the site transition period so at that time multiple products could not delivered on time as a result workload increased.

1 Due to the excessive workload and less rewards and remuneration facilities, retention rate is very poor in all the departments and extremely poor in quality operations department.

2 As there is no software available for documents soft copy archival so all the hardcopy documents need to archive for 10 years which consume so many spaces as well as it is very risky as documents may destroy at any time.

3 As there are no night shift facilities for women and female employees are more than 80% in the quality operations department so not able to run the analysis on night shift so need to take maximum load on day shift which impacts health.

1.3.4 Recommendations (to the company on future internships)

Pharmaceutical Quality department is always a great place to learn in depth. I would recommend that if anyone wants to learn in-depth functions of Quality Assurance then they should definitely try to avail the opportunity because only Synovia Pharma is the only Pharmaceutical Industry where learning scope is huge. Here young enthusiastic employees can definitely learn so many things within a very short period of time.

CHAPTER 2: ORGANIZATION PART (SYNOVIA PHARMA PLC. IN BANGLADESH)

2.1 Introduction

The pharma industry in Bangladesh is fastest growing sector which has capability to fulfill all the need of a country and it has also potential to fulfill 98% countries total demand for the medicines. In addition to meeting domestic demand, the enterprises export pharmaceuticals. During the 2019–20 fiscal year, Bangladesh made 136 million from the export of pharmaceuticals. In terms of pharmaceutical exports, Bangladesh is rated 71st out of 134 countries worldwide. In addition to allopathic medicines, Bangladesh also makes homeopathic, unani, and ayurvedic ones. There are currently 257 pharmaceutical companies in Bangladesh, of which 80 percent make generic drugs, indigenous firms like Square, Beximco, Reneta, healthcare, Radiant, Drug International, ACI, ACME currently control the pharmaceutical industry.

The pharmaceutical industry in Bangladesh is expanding and has great promise since 98% of the nation's total medical demand is met by local institutions. In addition to meeting domestic demand, the enterprises export pharmaceuticals. During the 2019–20 fiscal year, Bangladesh made 136 million from the export of pharmaceuticals. In terms of pharmaceutical exports, Bangladesh is rated 71st out of 134 countries worldwide.

In addition to allopathic medicines, Bangladesh also makes homeopathic, Unani, and ayurvedic ones. Currently, 257 pharmaceutical companies are located in Bangladesh of which 80 percent produce generic medications. In Bangladesh, indigenous firms like Square, Beximco, Reneta, and Opsonin currently control the pharmaceutical industry.

Some MNCs and local businesses launched Bangladesh's pharmaceutical sector in the 1950s. Bangladesh was designated a least developed country under the British Patents and Designs Act of 1911 and given patent exemption in the pharmaceutical industry after gaining independence in 1971. As a result, the country's production of generic medicines began to increase. However, the pharmaceutical sector began to grow in the 1980s. In 1981, Bangladesh had 166 licensed pharmaceutical producers. However, 75% of the nation's pharmaceutical manufacture at the time was provided by eight foreign companies, including Glaxo, Pfizer, and Hoechst. At that time, 133 companies generated the remaining 10%, with 25 medium-sized domestic pharmaceutical organizations producing the final 15%.

2.2 Overview of the Company:

Formerly known as Sanofi Bangladesh Limited, Synovia Pharma PLC was a division of Sanofi S.A., a multinational biopharmaceutical corporation. In 1958, As a branch of the British chemical company May & Baker, Sanofi Bangladesh first started conducting business in Bangladesh. After a string of mergers and acquisitions (including those involving the British firm Fisons, the French firm Rhône-Poulenc, and the German firm Hoechst Marion Roussel), it adopted the name Sanofi-Aventis in 2004 and changed its name to Sanofi Bangladesh Limited in 2013. There have been four name changes for it.

Modern manufacturing facilities owned by Sanofi Bangladesh have been passed down to Synovia Pharma, including a PIC/s certified facility for the production of cephalosporin antibiotics. The 25 acres of the cephalosporin area are located in Tongi, Gazipur, Bangladesh. The corporate headquarters are in Shegunbagicha, Dhaka. (PLC., 2022). In Bangladesh, Synovia Pharma is still producing and selling Sanofi goods just as before. In addition, Synovia Pharma PLC. also re-launching some products which were discontinued at Sanofi's time. They have launched two new products such as Ertu 5 and 15 mg tablet which is newest generic (Ertugliflozin L-Pyroglutamic Acid) ever in Bangladesh and Luzol 10 g cream (Anti-fungal). New company will provide an expanded portfolio of products to address the unmet medical needs of the patients. Synovia Pharma remains committed to value creation via synergy of strengths of the two ethical entities and will continue to bring hope, health and happiness in the lives of people. There are more than 70 products are manufactured in Synovia Pharma. They have 6 toller companies (Beximco, Novarties, ACI, Healthcare, Radiant and DBL) who also manufactured different dosage form in Synovia Pharma. The manufacturing plant comprises of several departments such as Administration, HR, Supply Chain, Commercial, Finance, Health Safety & Environment (HSE), Engineering, Manufacturing, Product development (PD), Quality Operations, Marketing and so on. All of these department individually doing their job with inter-organizational support. Synovia Pharma PLC. have more than 100 products manufactured such as anti-biotics, anti-diabetic, anti-fungal, anti-viral, probiotic, narcotics, anti-diarrheal and so on.

2.3 Management Practices:

Synovia Pharma PLC. ensure 6 best management practices. They are discussing below-

Hiring right candidates: Synovia former Sanofi Bangladesh Limited is very professional to recruit any candidate. Maximum productivity comes from efficient employees and Synovia hire efficient employees by different competitive viva process. Employees skill need to enhance for the benefit of the company. Only proper assessment can bring a perfect match for the company, so Synovia Pharma is very serious about recruiting candidates.

Consistent action: When an employee knows the expectations of the company then they try to fulfill all the expectations. Without a consistent leader, employee will not able to do better performance at the same time they will feel stressed which will impact their productivity and will be the reason for poor performance.

Effective communication: Without proper communication, no team will able to fulfill target. Communication should be clear and accurate so that expected outcome can be achieved. Written and verbal communication is considered one of the effective way of communication. For individual and organizational target accomplishment there is no alternative way for effective communication. Human Resource department of Synovia Pharma arrange training program for the employees whereas per requirements employees need to participate in different training program.

Active listening and providing constructive feedback: We as a human love to say more rather than listen which sometimes the main reason for our poor performance. Synovia Pharma provide these basic training and give detail information how we can practice to-hear from others because until we listen properly, we will not able to solve the problem and until we solve the problem, we will not able to gather knowledge and implement it to our workplace. Constructive feedback is another weapon which makes an employee confident. Constructive feedback means providing feedback about their specific performance about the work. It should be provided in a positive way. (Czerwanka, 2023)

2.4 Manufacturing Practices:

Safety instructions:

1. If the product is under Occupational Exposure Band (OEB) 2 then full gown must be wear in manufacturing area
2. Use Protective clothing, Latex/surgical gloves, and safety glasses with eye protection shields during material handling.

3. Wear cloth mask (during Inspection), HFNP mask (during dispensing).

4. If material is accidentally released or spilled, gather the Avoid the hazard region, keep spilled material out of sewers and water sources, isolate it, and lock the area to bar personnel from entering.

First aid measures:

1. Avoid contact with skin, eyes and inhalation and accidental ingestion through mouth.
2. In case of skin contacts wash with soap and water for 15 minutes.
3. If chemicals are contact with eye, then flush with plenty of water for atleast15 minutes.
4. For accidental ingestion get immediate medical attention.
5. In case of inhalation remove to uncontaminated area and provide facilities for artificial respiration consult site first aid center.

Manufacturing Process flow chart of different dosage forms are given below-

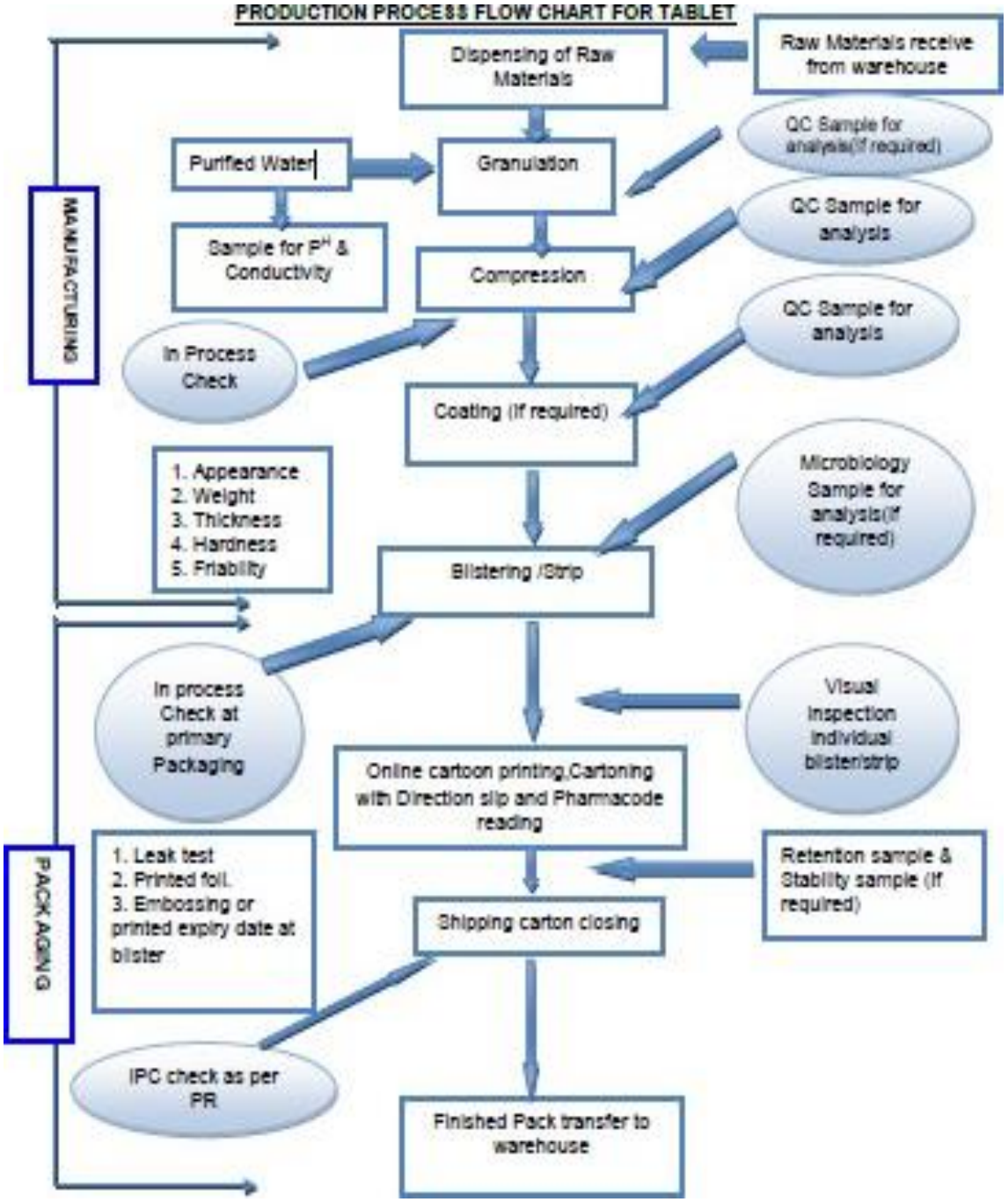


Figure 1: Manufacturing Process Flow chart for different dosage form

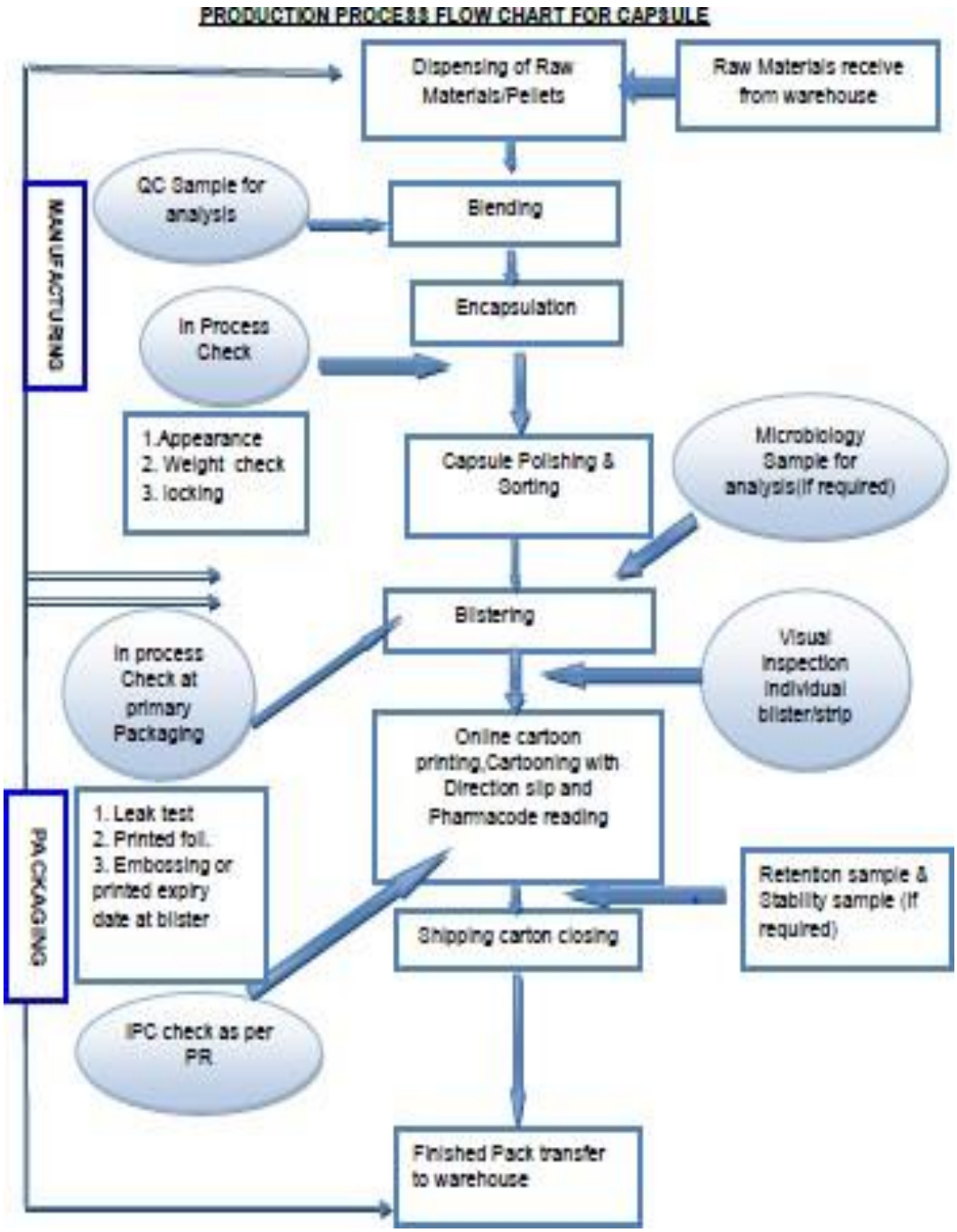
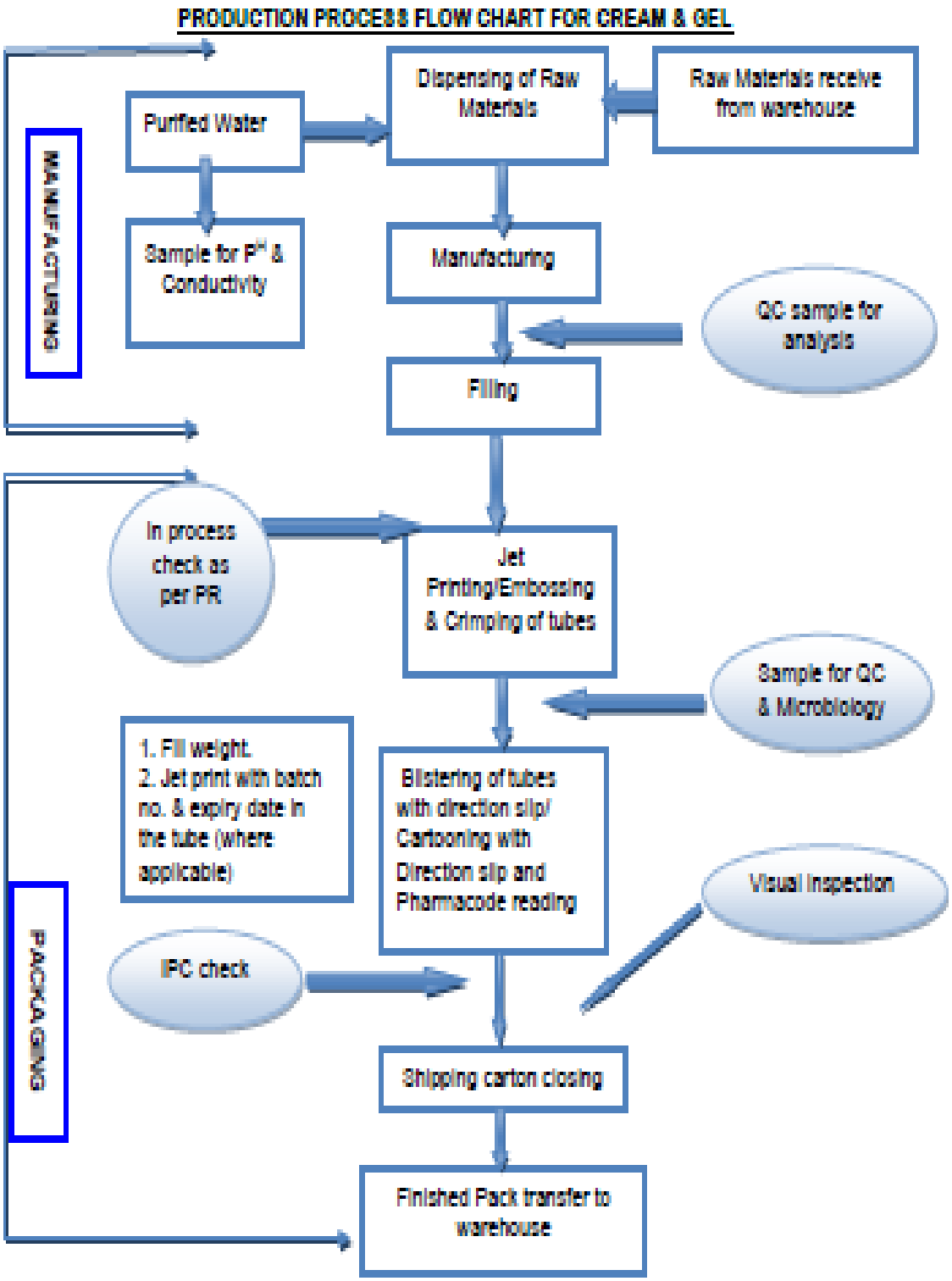


Figure 1: Manufacturing Process Flow chart for different dosage form



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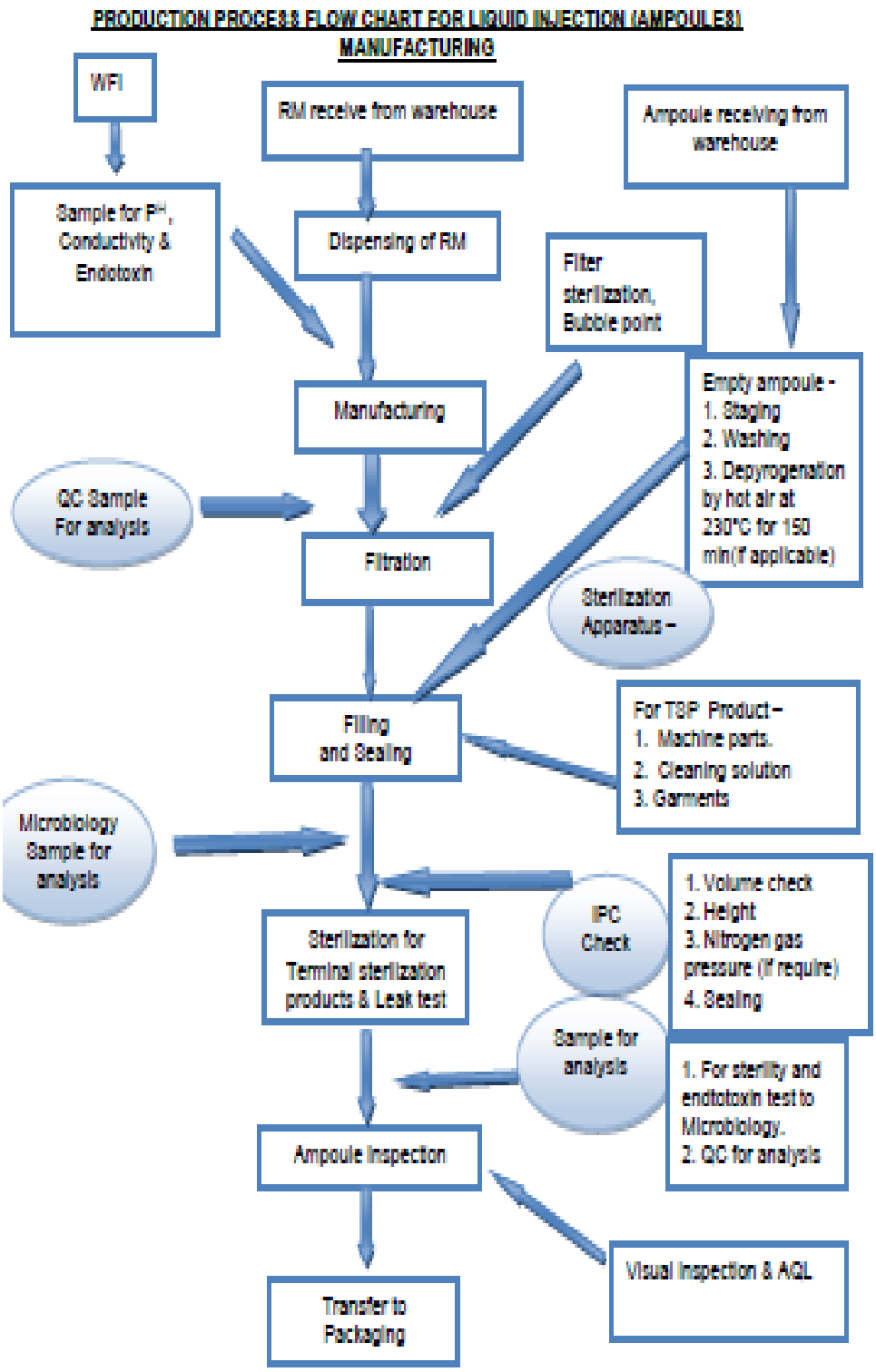
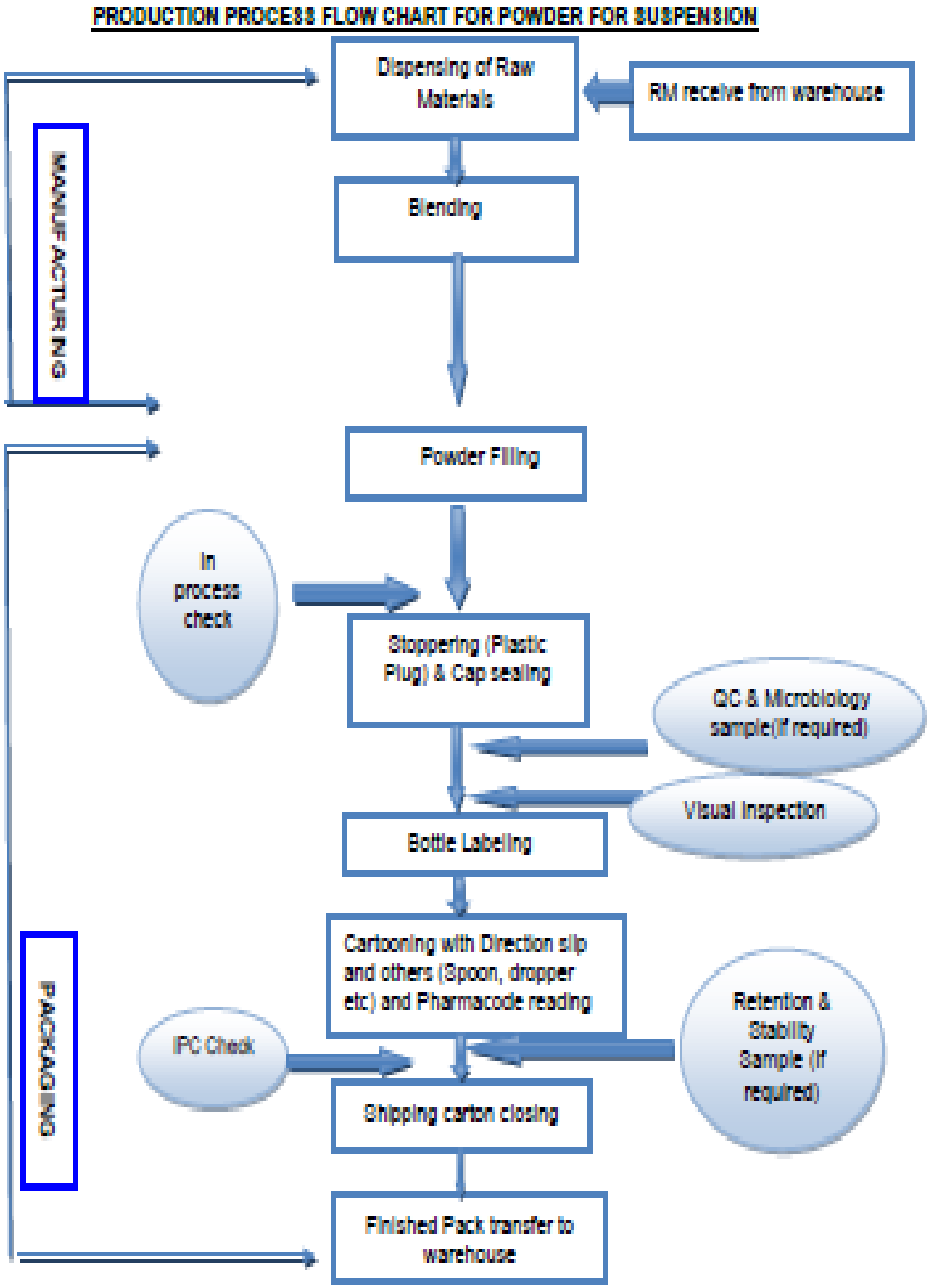


Figure 1: Manufacturing Process Flow chart for different dosage form



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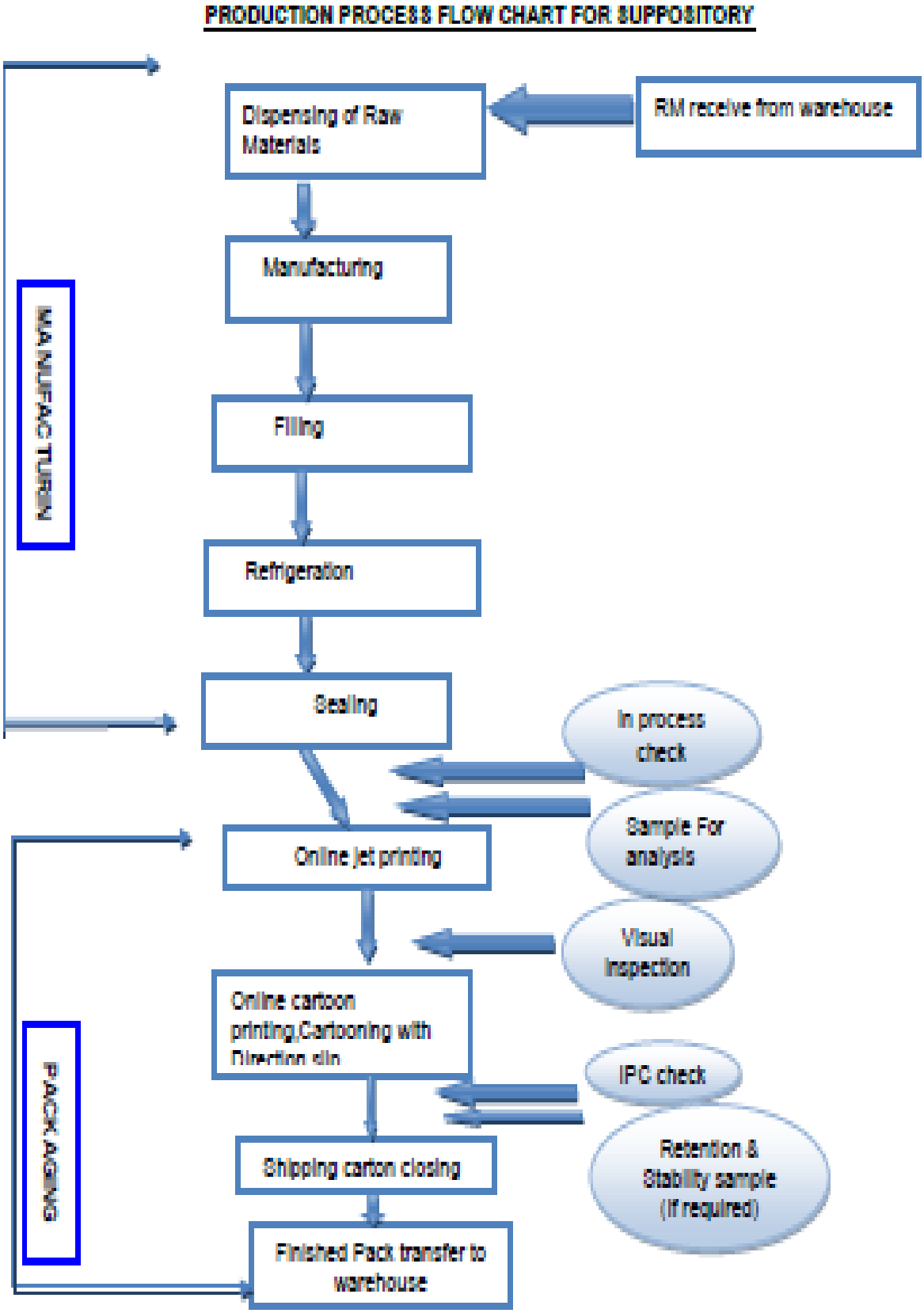


Figure 1: Manufacturing Process Flow chart for different dosage form

2.5 Quality Assurance Functions: It is the sum total of the organized arrangement made with the object of ensuring that the product will fulfill all the requirement according to their expectations. The core functions of quality assurance departments are discussed below-

2.5.1 In-Process Control Test: The main objective is to ensure quality in each step of manufacturing and packaging, to assure batch uniformity and integrity of the pharmaceutical product, a systemic and periodic control is undertaken during the manufacturing and packaging production process. In-process control testing basically conduct to check the physical parameters (Average weight, hardness, disintegration time, thickness, uniformity of weight). It helps to identify any quality related impact on products and if any flaws observed during test then investigation required to identify the root cause of the flaws.

2.5.2 Quality Management System (QMS): Quality Assurance ensures product are manufactured as per quality standards for the use of patients. The main purpose of GMP are prevention of cross contamination and mix-up. All the steps are systematically monitored to maintain quality of the pharmaceutical product, process.

2.5.3 Batch document and logbook issuance: This is the major function of Quality Assurance to ensure quality by keeping control over batch documents (BMR, BPR, BAR & RAR) and also ensure the process, batch no, dosage form, manufacturing, expiry date is correctly recorded and then handed over to manufacturing department because without issuance a batch by Quality Assurance, manufacturing is unable to start. Logbook format is designed as per SOP.

Front page of the logbook will contain relevant information as per below label-

Figure 2: Front page of Logbook

LOGBOOK NAME	
DEPARTMENT NAME	

INDEX	
DESCRIPTION	PAGE NO.

SOP REF. NO.	
QA REF. NO.	
ROOM NO.	
TOTAL NO. OF PAGES	

QA ISSUED BY (Sign & Date):	
Logbook Closing by QA (Sign & Date):	

Figure 3: Logbook Format

The master list of the GMP logbook is also prepared by Quality Assurance department and the list is approved by respective department designee. The list should be updated annually at a minimum and versioned in case of requirements within a year.

Master List of GMP Logbook Document ref:
Department Name:

Sl No.	Logbook Name	Logbook Ref no:	Room No./Equipment name & ID	Remarks

Figure 4: Master list Logbook Format

2.5.4 Batch record review, compilation and finished product release: Quality team are responsible for Batch manufacturing record, batch packaging record, Analytical and microbiological record checking, compilation of the documents as per sequence and finally release the product from manufacturing plant for patient consumption so that patient can cure as soon as possible. Sanofi Bangladesh Limited used SAP software for batch release but after introducing oracle system and EIQC system, before final batch release, QC and micro need to authorize after verifying the product information such as testing date, product name, batch no, manufacturing and expiry date, batch size, spec-SM reference no etc. A file (hard copy or soft copy) contains all the data that is produced while a pharmaceutical product is being manufactured. At the conclusion of the manufacturing process, it informs us

of all pertinent information pertaining to the manufacture of the product (e.g., timing of the process, ingredients, environmental conditions, people involved, etc.). Pharma products are finally made available for distribution and sale.

All QC test results are associated with the batch record. After the pharmaceutical product is created and packaged, the duty of QA is to check that the product is safe for market or not.

1. After verifying the safety of the product and confirming that all calculations linked to that batch are accurate, the QA representative will authorize.

2 Product stability testing and shelf-life assessment:

The QA department is in charge of conducting stability tests on pharmaceutical items produced in their factory. In order to prevent complaints from the market, make sure the product's shelf life is the same as stated in the study and on the product.

3. Ensuring appropriate storage of finished good.

4. All the criteria necessary to prevent product decontamination during storage are ensured by the QA person since storage conditions play a significant influence in the stability of pharmaceutical products.

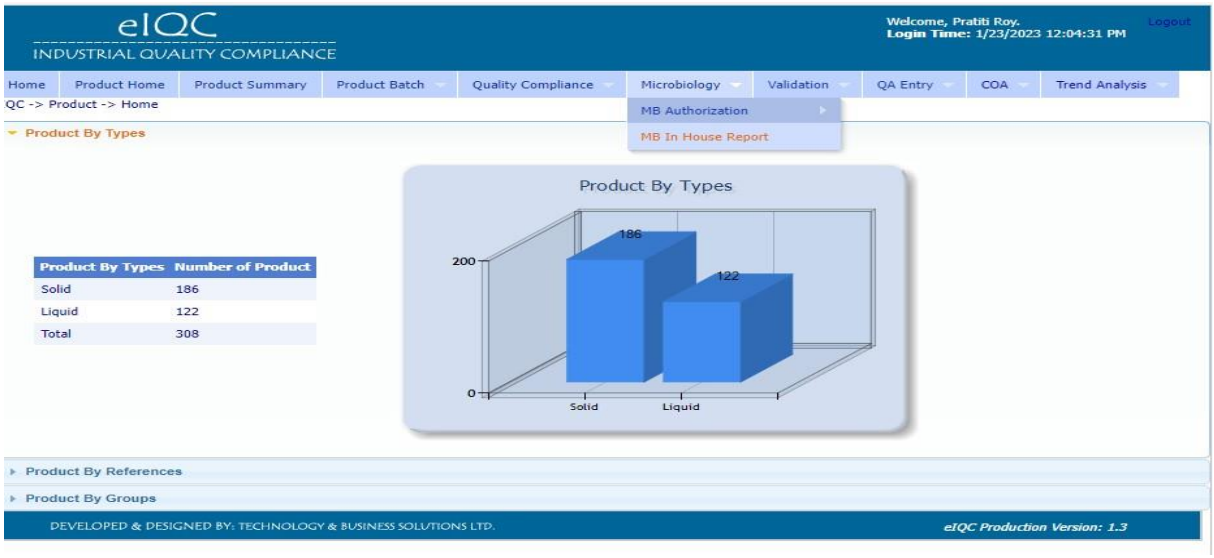


Figure 5: Visual Representation of EIQC

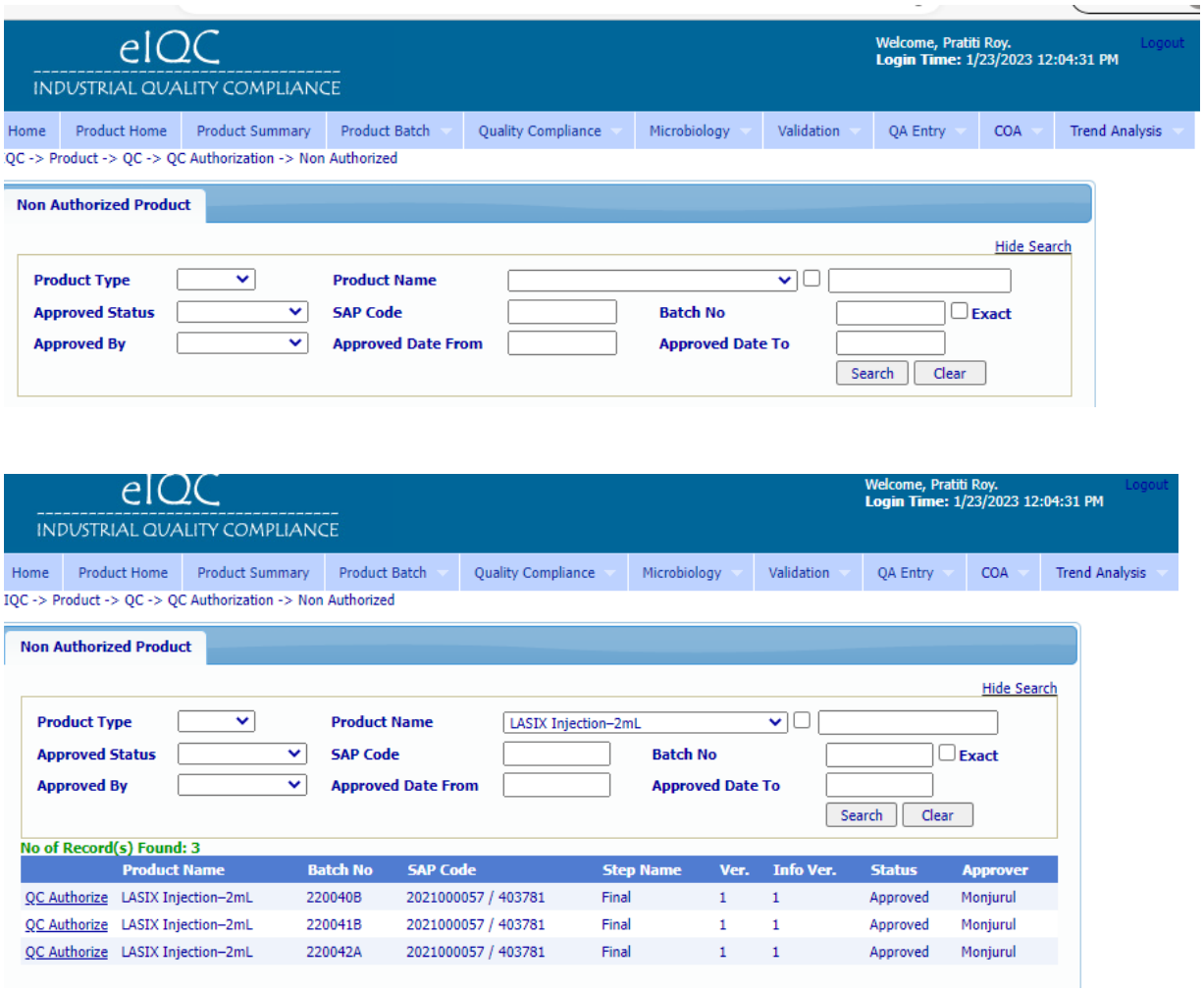
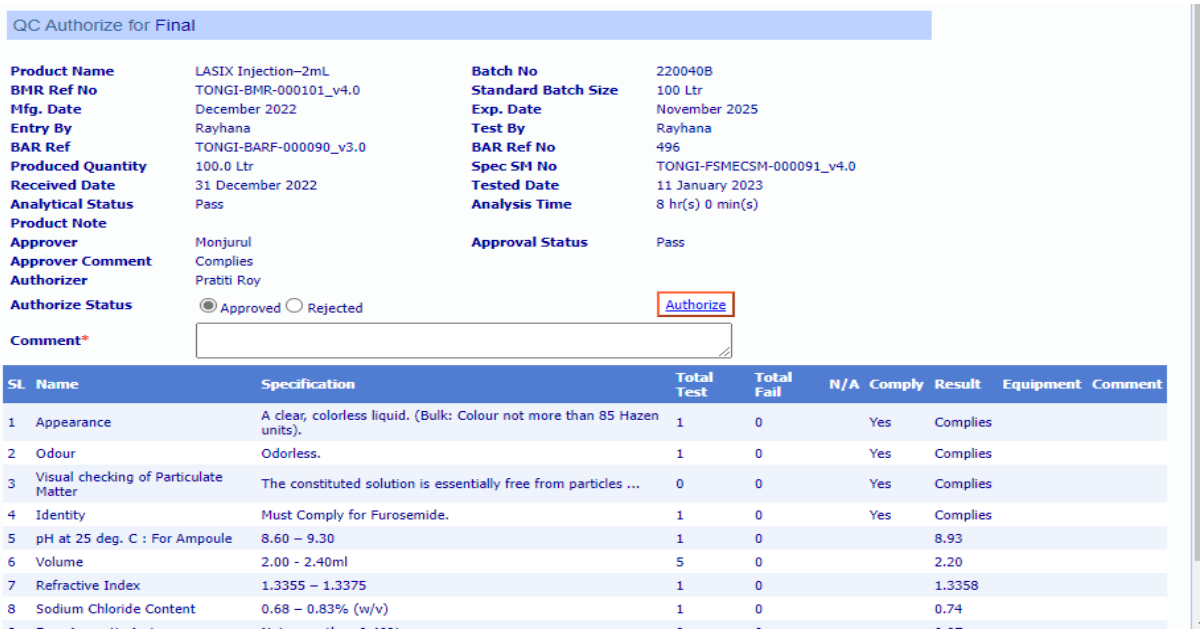


Figure 6: QC report Approval system

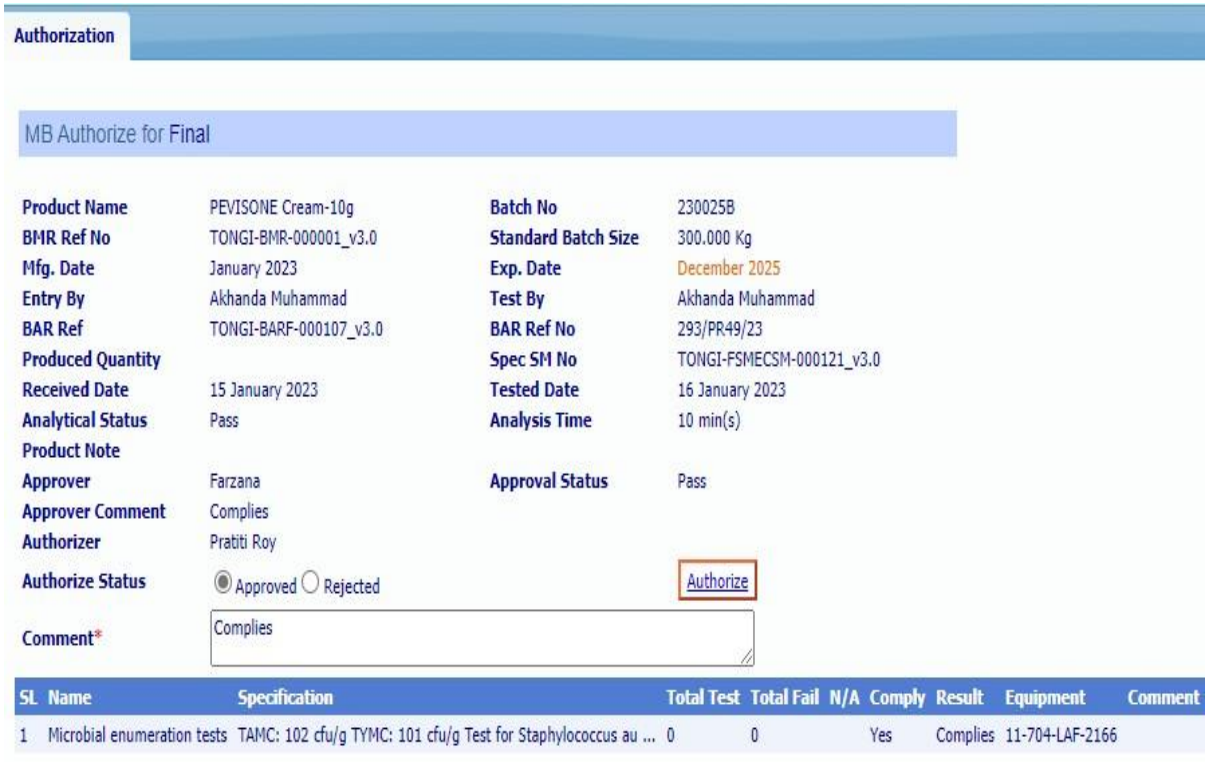


QC Authorize for Final

Product Name	LASIX Injection–2mL	**Batch No**	220040B
BMR Ref No	TONGI-BMR-000101_v4.0	**Standard Batch Size**	100 Ltr
Mfg. Date	December 2022	**Exp. Date**	November 2025
Entry By	Rayhana	**Test By**	Rayhana
BAR Ref	TONGI-BARF-000090_v3.0	**BAR Ref No**	496
Produced Quantity	100.0 Ltr	**Spec SM No**	TONGI-FSMECSM-000091_v4.0
Received Date	31 December 2022	**Tested Date**	11 January 2023
Analytical Status	Pass	**Analysis Time**	8 hr(s) 0 min(s)
Product Note			
Approver	Monjurul	**Approval Status**	Pass
Approver Comment	Complies		
Authorizer	Pratiti Roy		
Authorize Status	Approved / Rejected	Authorize	
Comment*			

SL	Name	Specification	Total Test	Total Fail	N/A	Comply	Result	Equipment	Comment
1	Appearance	A clear, colorless liquid. (Bulk: Colour not more than 85 Hazen units).	1	0		Yes	Complies		
2	Odour	Odorless.	1	0		Yes	Complies		
3	Visual checking of Particulate Matter	The constituted solution is essentially free from particles ...	0	0		Yes	Complies		
4	Identity	Must Comply for Furosemide.	1	0		Yes	Complies		
5	pH at 25 deg. C : For Ampoule	8.60 – 9.30	1	0			8.93		
6	Volume	2.00 - 2.40ml	5	0			2.20		
7	Refractive Index	1.3355 – 1.3375	1	0			1.3358		
8	Sodium Chloride Content	0.68 – 0.83% (w/v)	1	0			0.74		

Here we can see, after QC analysis, Quality Control department cannot directly release the QC report before QA approval. If all the above criteria fulfill then QA will comment complies and authorize the report and then hard copy will be sent to the QA department.



Authorization

MB Authorize for Final

Product Name	PEVISONE Cream-10g	**Batch No**	230025B
BMR Ref No	TONGI-BMR-000001_v3.0	**Standard Batch Size**	300.000 Kg
Mfg. Date	January 2023	**Exp. Date**	December 2025
Entry By	Akhanda Muhammad	**Test By**	Akhanda Muhammad
BAR Ref	TONGI-BARF-000107_v3.0	**BAR Ref No**	293/PR49/23
Produced Quantity		**Spec SM No**	TONGI-FSMECSM-000121_v3.0
Received Date	15 January 2023	**Tested Date**	16 January 2023
Analytical Status	Pass	**Analysis Time**	10 min(s)
Product Note			
Approver	Farzana	**Approval Status**	Pass
Approver Comment	Complies		
Authorizer	Pratiti Roy		
Authorize Status	Approved / Rejected	Authorize	
Comment*	Complies		

SL	Name	Specification	Total Test	Total Fail	N/A	Comply	Result	Equipment	Comment
1	Microbial enumeration tests	TAMC: 102 cfu/g TYMC: 101 cfu/g Test for Staphylococcus au ...	0	0		Yes	Complies	11-704-LAF-2166	

Figure 7: Microbiology test Approval Step

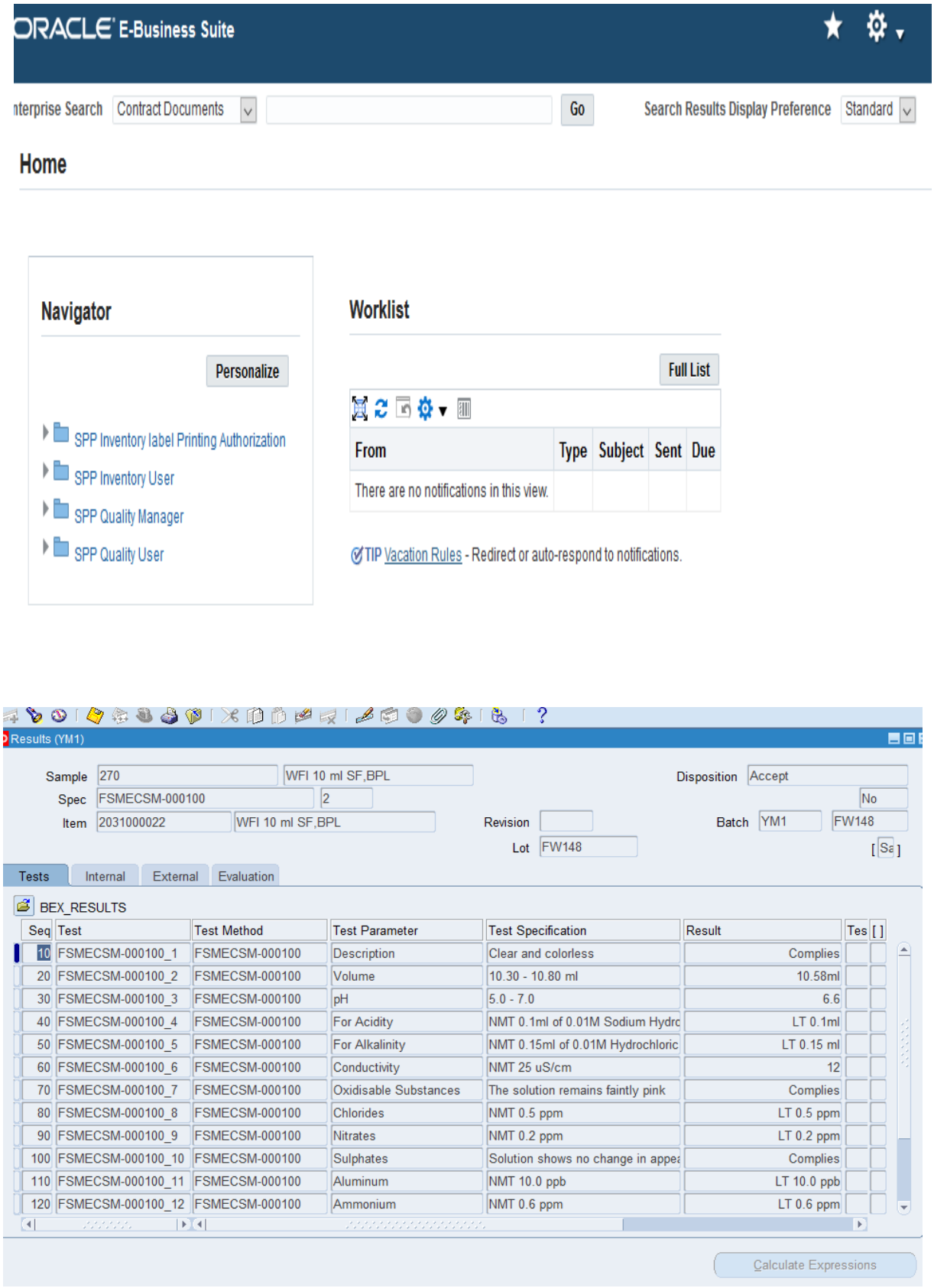


Figure 8: Oracle QC result authorize system

2.5.5 Management and preparation of Annual Product quality Review:

Product quality reviews are carried out to confirm the consistency of the process and the product's quality, to analyse trends, to ascertain the necessity of spec changes, and to assess the need for revalidation. According to the annual plan, PQR need to perform on yearly basis to check if the product meets the specifications, if any changes required for active pharmaceutical ingredients and excipients source, check the robustness of the process, find out critical process parameters, validation and qualification status and analytical equipments are calibrated or not and trend of the API, microbiological test parameters complies or not, if stability study are performed for the drug or not. Stability study is performed to check how many days the product remains without any quality impact. The study performed both 30–40-degree Celsius temperature to varify if the product have no impact on quality during it's shelf life.

Process Capability Indices

Process capacity analysis is predicated on the fundamental premise that the process must be under statistical control. Without statistical control, the process is unpredictable and it is impossible to meaningfully assess distribution-related values like probabilities, percentiles, and competence indices.

The process distribution must be normal, or at least somewhat normal, in order for any of the conventional process capability indices to be valid. To evaluate the dataset's distribution, a normality test must be run.

Calculations can be used to assess process capability for populations that are not regularly distributed (e.g., nonparametric capability, CNp and CNpK indices). Process capacity indices allow processes to be compared in terms of how well they are managed by determining how much "natural variation" a process experiences in relation to its specification limitations. All batches produced should be included in the process capability exercise (including out of specification batches).

Cp: An evaluation of the process's production capacity and whether the process mean would be in the middle of the specification range is provided by a process capability index.

Cpk: An estimation of the process's production capacity given that the process mean might not be perfectly centered between the specification boundaries.

USL : Upper Specification Limit $\bar{X}$: Mean of individual measurements

LSL : Lower Specification Limit σ : Standard Deviation

$Cp = (USL - LSL) / 6\sigma$

$Cpku = (USL - \bar{X}) / 3\sigma$ $Cpkl = (\bar{X} - LSL) / 3\sigma$

The overall process Cpk is the lower value of Cpku and Cpkl. Process capability analysis assessing for selected parameters intra-batch and inter batch variability should be based on total (intra and inter batch) dispersion characteristics (Cp_{total} indice) and the total (intra and inter batch) dispersion and centering characteristics (CpK_{total} indice) with regard to specification limits.

Cp_{Total} and Cpk_{Total} are calculated with σ_{Total} (obtained with variance analysis)

Acceptability thresholds

Should be fixed based on the process with typical expectation of at least $Cpk \geq 1.0$

Values $Cpk < 1.0$ need to be justified and explained and an overall process performance assessment must be conducted.

For calculations of Cpk, 10 data points are to be considered as a minimum and 30 data points are recommended for a better precision.

If the number of produced batches is below 10 for the considered annual period, batches produced during last 2 or 3 years could be integrated for the process capability evaluation.

If process capability cannot be evaluated for a given parameter or release test, it remains necessary to demonstrate that the process is in statistical control using statistical process control analysis (e.g., control chart). This approach should be appropriately justified and documented.

Frequency and Extent of Product Quality Review

The product quality review must cover a one-year rolling period but does not have to coincide with a calendar year. For example, January 2020 to December 2020 or July 2020 to June 2020. The review must be completed within ninety (90) calendar days after this period ends which means if the review period ends on March 2020, the PQR must be completed by June 2020.

The batches to be considered are the batches manufactured or released during the agreed annual period and the minimum is 10 batches. If less than 10 batches are produced per year, a product quality review must still be conducted. This review should incorporate data from batches from preceding production years, or that is otherwise justified.

In cases where no or only a reduced number of batches were manufactured in the defined period, a PQR (in a similar format as a complete PQR) is still mandatory for monitoring of activities of the review period (e.g., Stability Studies, Complaints, Change Controls, CAPA). The parts which cannot be filled (e.g., data trending) would only mention as 'Not applicable'.

PQR can be finished by classifying products according to a characteristic. The grouped products should be created using the same machinery, be of the same pharmaceutical form, and include the same active ingredients and excipients.

The same dosage forms with the same ingredients and primary packaging but different strengths, as well as final presentations that are the same but with distinct marketed regions and/or product registrations, are examples of groupings related to the finished products. All product batches, regardless of whether they were released, rejected, or destroyed within the time period under consideration, must be included in the product quality review.

For environmental monitoring and for each water quality grade (such as bulk purified water, water for injection) generated on site, a product quality review must be provided.

It is necessary to either conduct a separate product quality assessment for important utilities like heating, ventilation, air conditioning (HVAC), and gases, or to include a particular chapter in the involved product quality evaluations. Monthly Follow-up of PQR to be performed and to be reported through monthly report. A summary report to be prepared quarterly as per Appendix III.

Logbook, Reference Number and Version Control

A yearly logbook (Appendix I) must follow prior to generate a PQR. Necessary information including PQR reference number to be recorded.

PQR reference number (For In-house products) will be as followed– PQR/AAA/DF/STR/YY/NNN/XX/PQR = Product Quality Review AAA Product Name (e.g., Fimoxyclav, Amaryl) DF = Dosage Form (e.g., PFS for Powder for Suspension.

2.5.6 Deviation Investigation & management: Deviation means any kind of error that has critical, major or impact on quality. From manufacturing to packaging each step are recorded. So, if any error occurred then it, Quality Assurance department form an investigation team to find out the root cause of the deviation and by applying 6M rule (Manpower, Machine, Material, Method, Medium, Measurement). (Pharma Articles, 2018)

Role and responsibilities of the deviation investigation team are discussed below-

Role	Responsibility
Event Creator	Any site associate to whom authority is given by the PHENIX site administrator. ➢ The event creator creates and sends events within the system. ➢ The event creator can change the name of the person responsible for the sector which has been entered by default in the system.
Area Responsible /designee	This is any person who is responsible for a unit or activity at a site. Following are the responsibility of the Area Responsible/designee. ➢ Can modify the contents of a declared event before its evaluation, reject it, request more information on the event, accept it and evaluate it. ➢ Can change the name of the person responsible for the sector and the experts entered by default in the system. ➢ Can read the contents of an event, a CAPA or an ER, and can read and create queries.
Expert (QA/HSE)	This is anyone who is responsible for Quality and who is a member of the Quality team on the site. ➢ This person may enter information in the common part of the investigation. ➢ The expert evaluates events in his or her domain of expertise and declares whether it is necessary to carry out an investigation. ➢ He or she may designate another expert as a substitute. ➢ The expert may assign a person other than the one designated by the system to take charge of the investigation and may add other people to the investigation team. ➢ The expert may add steps to the investigation and edit interim reports. ➢ He or she approves or rejects CAPAs, may request specific document signatories to do the same, and may confirm CAPA implementation. ➢ The expert may request an ER from the appropriate person and

	set the deadline for a report on work done in order to ascertain whether a CAPA has been effective or not. ➢ Finally, the expert concludes the investigation and edits the corresponding report.
Investigation Leader	This is anyone who is responsible for a given sector and who is a member of the quality management system team. ➢ The investigation team leader may enter information in the common part of the investigation, create an investigation that is pertinent to the domain, evaluate the event according to his or her area of expertise, add investigation steps, edit intermediate reports, conclude an investigation and edit the corresponding report. ➢ The investigation team leader may enter information in the common part of the investigation as soon as he or she has been designated by the system or the expert. ➢ He or she may evaluate the event. ➢ The investigation team leader may designate another person to take charge of the investigation and may add other persons to the investigation team. ➢ He or she may add investigation steps and edit in term reports. ➢ Finally, the investigation team leader concludes the investigation and edits the corresponding report. ➢ He or she may read the contents of an event, a CAPA or an ER an read and create queries. Approval of the investigation after conclusion and approval of interim reports.
Investigation Team Member	This is a member of the Quality team, or any person designated at the site. 2 Members of the investigation team may indicate the results of investigation steps and add further steps if necessary. 3 These persons may read the contents of an event, a CAPA or an ER and read and create queries. A notification is sent to investigation team member when he is added.

CAPA Creator	This is a person from the sector concerned by CAPA implementation. ➢ A CAPA creator identifies which CAPAs need to be implemented, designates someone to carry out implementation and defines a deadline for this implementation. ➢ He or she sends a CAPA to the person responsible for implementation so that this person can evaluate it and the expert can approve it. The CAPA creator can read the contents of an event, a CAPA or an ER and Read and create queries.
Empowered CAPA Creator	This is someone from the sector who is concerned with CAPA implementation. This user has evaluation and approval rights for creating CAPAs. ➢ A CAPA creator with evaluation rights identifies CAPAs that need to be implemented, designates someone to be responsible for their implementation and defines an implementation deadline. ➢ He or she submits a CAPA, evaluates it and approves it in one operation and may also request confirmation of implementation by an expert. The empowered CAPA creator may read the contents of an event, a CAPA or an ER and read and create queries.
CAPA	This should preferably be someone who works in the sector. In the detailed CAPA flow, someone who is responsible for implementing CAPA'S may evaluate CAPAS proposed by CAPA creators before approval by an expert.
CAPA creator	This is a person from the sector concerned by CAPA implementation. ➢ A CAPA creator identifies which CAPAs need to be implemented, designates someone to carry out implementation and defines a deadline for this implementation. ➢ He or she sends a CAPA to the person responsible for implementation so that this person can evaluate it and the expert

	can approve it. The CAPA creator can read the contents of an event, a CAPA or an ER and readand create queries.
Implementation Leader	However, the CAPA implementation leader may not perform this evaluation in astandard CAPA flow. ➢ He or she is responsible for implementing the CAPA on the deadline set by theCAPA creator. The CAPA implementation leader may read the contents of an event, a CAPA oran ER and read and create queries.
Specific signatory	This is anyone who has rights within the system. ➢ A specific signatory may approve or reject a CAPA if requested to do so by theexpert. ➢ He or she may also sign or reject a report if requested to do so by the expert andthe investigation team leader. The specific signatory may read contents of an event, a CAPA or an ER.
ER Responsible	This is a person working in a sector who is concerned by CAPAs that have been implemented. ➢ On a chosen date, the ER head reviews CAPA effectiveness according to ➢ criteria defined by the expert. ➢ The ER head may read the contents of an event, a CAPA or an ER and read andcreate queries. ➢ The person associated to a CAPA that have been implemented. ➢ The ER Responsible is responsible for: Reviewing the effectiveness of the CAPA as per the criteria defined by the expert.
Reader	These are the people who have reading rights. They can read the contents of an event, a CAPA or an ER and read and create queries.
KPI	These are the people in site or corporate people. They can execute KPI regarding their rights.

Site Manager	This is the person who manages the site. ➢ The site manager is notified if a Quality event has a major or critical severity levelwhen the expert chooses to launch an investigation. ➢ According to site and expertise parameters, the site manager may also be calledupon for budget approval of CAPA processing. The site manager may read the contents of an event, a CAPA or an ER and readand create queries.
Deviation–Site Administrator	This is someone from the Quality teams who is responsible for recording all site profilesand equipment. ➢ The administrator may modify site user rights and change local parameters. ➢ To modify site settings, site messages and has access to audit trail at site ➢ Manage site equipment, items created on the site (Only for site Without interface) & execute user report (Technical queries).
PHENIX Global Administrator	The Global Administrator is responsible of PHENIX system administration(management of roles and access of site administrator, global settings etc.)

Manpower: People who are engaged in manufacturing process to delivery the product, sometimes may impact the quality by not following the defined manufacturing process as a result deviation may occur.

Machine: Sometimes, due to the breakdown of the machine or any time of functional error, manufacturing process may impact. For example, if the grease or lubricants not applied in upper and lower punch and die of the compression machines, then granules sticking problem arise as a result, do not compressed and tables not shaped accordingly. As a result, accurate tablet weight may increase or decrease which will not cure disease so for this type of problem investigation team as a solution advice to apply appropriate proportion of lubricants to prevent the sticking problem of the tablets.

Material: If any default found in API, excipients, primary and secondary packaging materials then deviation will be raised to find the reason of the quality impact in supplier's source because in some times the raw materials may degrade in terms of their quality if they are not properly stored within proper temperature and humidity.

Method: Any process related fault or error needs to correct immediately in a Pharma industry and quality Assurance ensures it.

2.5.7 Imported product management: Quality Assurance department are engaged in imported product management. If any product is import from different country then quality team are responsible for monitoring if the product are reached to the manufacturing plant without excessive temperature excursion because any temperature excursion are high than the limit, it will damage quality of the product. It has different parts. Commercial department receive shipping information (COA. COO, Freight Certificate, AWB, Form 9 which is a shipment license, packing list, radioactivity certificate and so on) before receiving the product to Tongi IA Site. Synovia have licensed to bring 24 products and 2 medical devices from different countries. Commercial department after receiving the shipping information share it with Quality Assurance department. This shipping information need to archive by QA and then mfg., exp date and other information need to cross-check by QA. Products receive after some days interval of shipping information receive. Synovia has vaccine, insulin, food supplements, anti-cancer, anti-arthritis, anti-viral, antibiotics and so many imported items. Their storage facilities are different. All vaccines and some insulins need to store below 8-degree temperature which are cold chain product. Some Insulins need to store below 25 degree and so on. Synovia have 2 Warehouse AC and DC. AC warehouse means after receiving raw materials it needs to store in AC warehouse. DC warehouse means after manufacturing, finished goods needs to keep there and then final product will be sent to depot from DC warehouse. After receiving imported product, mail communication is mandatory because no product can be release without manufacturer decision. For mail communication data logger report, temperature report, sentitech record, Tag alert all of these need to send as attachment.

Temptale Report of Taxotere

QOD-Pratiti Roy

Reply | Reply All | Forward | ...

To FRA DP Quality Distribution Compliance /DE

Thu 12/22/2022 4:36 PM

Cc Foo, Yin Ping /SG; Eamlikitkuakul, Nareenuch /TH; AsiaBD.Quality; SCM-A S M Abdullah; QOD-Salman Ahmed; QOD-Muhammad Badrul Haider Chowdhury; MFG-Ishtiaq Ahmed; **+6 others**

KH14N1R7V0_0.pdf 14 KB

KH14N1R7V0_0.ttv 22 KB

KH14N19AH0_0.ttv 23 KB

KH14N19AH0_0.pdf 16 KB

CCM Alert Frankfurt Shipment Status: Conform

Dear Concern,

We have received the following products on 22.11.22 at 16:00 to 16:18 am with 02 data loggers.

Sl	Product Name	Batch/Lot no.	Qty (Packs)	Remarks
1	Taxotere 20 mg Inj 1 vial	2F493A	1500	-
2	Taxotere 80 mg1 vial	2F497A	60	-
3	Taxotere 80 mg 1 vial	2F506A	900	-

Immediately we have stopped the data loggers and the products have been stored .The TempTale reports are attached herewith for your kind evaluation and feed back.

Figure 9: Mail Communication for Imported Product

Figure 10: Tag Alert

Figure 11: Data Logger

Data logger and Tag alert comes with imported product which keeps temperature record during transportation and transit of product. If any product reveived under damage condition then these these quantity will need to reject in Oracle and for that reason Rejection certificate need to prepare where reason for rejection, product name, batch no, mfg and exp date, rejection quantity need to write and finally need approval of Quality Head to reject it.

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Synovia Pharma PLC.
A subsidiary of RENATA PHARMACEUTICALS LIMITED
6/2/A, Segun Bagicha, Dhaka-1000, Bangladesh
Tel : +880 9678000777 | Fax : +880 2223380009

To: Sr. Manager Warehouse
From: Quality Operations
Copy: Chief Operating Officer
Sr. Manager Commercial
Ref.: ANC/DOC-22/096/01
Date: 21.09.22

Sub. : **Rejection Statement of Enterogermina 5 ml Suspension (B/N:1I072)**

Product Name : Enterogermina 5 ml Suspension
Batch No : 1I072
Mfg. Date : March, 2021
Exp. Date : February, 2023
Rejected Quantity : 02

With due respect this is to inform you that, 02 Packs of Enterogermina 5 ml Suspension (B/N:1I072) has been rejected due to, one shipment damaged and another damage found during printing.

This is for your information and necessary action please.

Prepared by	Reviewed by	Approved by
Pratiti Roy Management Trainee, Quality Assurance	Salman Ahmed Manager, Quality Assurance	Muhammad Badrul Haider Chowdhury Assistant General Manager, Quality Operations

Figure 12: Rejection Certificate of Imported Product

After rejecting the quantity in oracle system, as per requirements label need provide to finished goods warehouse so that, rejected quantity specified and keep separately.

REJECTED		
Item	Enterogermina Suspension	
SAP Code Number	4021000009	
SAP Lot/Batch No.	NA	
Batch / Challan No.	FS125	
Lab. Ref. No.	NA	
Manufacture	Synovia Pharma PLC.	
Quantity / Packs	5	
Rejected Date	16.01.24	
Remarks	Due to shipment damage.	
Synovia Pharma PLC.		**Authorized By**

Figure 13: Rejected Label

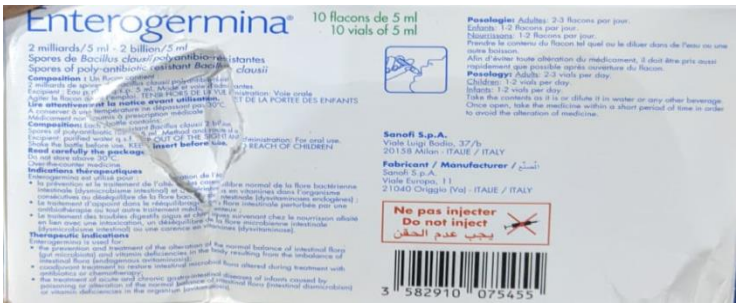


Figure 14: Rejected Printed Carton and Label

2.5.8 Change control: Any kind of changes related to the pharmaceutical process, system, method needs to implement by raising change control in Phenix. For example, if any sources of any API, excipients or packaging materials changes then it should be gone through by requesting change control because if from starting the raw materials source was France and now the company found another source like Singapore to get better Quality API with less cost, it should be implemented. Investigation leader form a cross-functional team with different members and find out the root cause of the complaint. After investigation, cross-functional team suggest the corrective action if required and ensure implementation of CAPA and train the relevant personnel after implementation. (Chowdhury, 2018)

2.5.9 Management of Recall/Counterfeit: Sometimes it is seen that some complaints are falsified that means the product, which is not manufactured in Synovia, but to somewhere others but in printed carton-manufactured details written as synovia. Counterfeit mainly occurred when some dishonest businessmen produce duplicate medicines which do not have therapeutic impact, they target renowned company's name and logo to sale their products under the company's name.

2.5.10 Management of SOP: Standard Operating Procedure is the guideline where all the manufacturing process, method, all the responsibilities of the departments are written as per global guidelines and run the pharma operations accordingly so quality Operations or specifically quality assurance department are responsible to manage all the SOP so that all of these are controlled as per standard quality.

2.5.11 Management of CAPA: It results from any kind of quality events, correction or prevention of known issue or resulting from a proactive improvement must be implemented to ensure the compliance of products and processes in accordance with Good Manufacturing Practices, Good Distribution practices, applicable both for international and local regulatory requirements. CAPA is the key tool for continuous improvement process.

2.5.12 Supplier Audit: Quality Assurance department are also responsible for the supplier Audit because raw materials source has direct impact on products quality. So, whether the materials are brought from authentic source which will maintain quality of the pharmaceutical product, quality assurance department also ensure it.

2.5.13 Toll Communication: Pharmaceuticals have multiple toller companies. Toll means other pharma industries who do not have the specific facilities to manufacture different kinds of dosage form so they manufacture that particular dosage form in the other pharmaceutical company and pay according. For example, Synovia Pharma PLC. have multiple toller companies such as Beximco, Healthcare, ACI, Radiant, Unimed and uniheath, Aristropharma. They manufacture some dosage form in Synovia Plant. On the other hand, synovia Pharma do not have liquid dosage form manufacturing facility so they manufacture liquid oral dosage form (Flagyl Suspension, Epilim Syrup, Avil syrup in Beximco and Incepta pharmaceutical).

2.5.14 Retention sample management: Retention sample means the quantity of the sample of the pharmaceutical Product that are stored within controlled temperature and humidity according to the products shelf life so that if any market complaint raise then samples are taken to test the reason behind quality impact and if the complaint is valid or it is counterfeit. We have cool, cold and ambient temperature retention room. According to product storage conditions these retention samples are kept in the retention sample room.

2.5.15 Out of specification investigations

Any time a pharmaceutical product's testing results differ from what was anticipated, and the final results are outside of the accepted range, the QA department launches an inquiry to identify the underlying cause using the relevant SOP.

2.5.16 Handling of Change Control Systems

Any other than validated step/ activity required to fix in any document and process is taken through the change control system. A documented process to apply change in the pharmaceutical industries. Change control system finally review by the QA department for approval. (Pharma Beginners Website, 2023)

2.5.17 Archival of Batch documents

The released batches documents need to archive for 10 years by the quality assurance department for audit purpose so that during inspections, documents are cross checked to varify the quality of the released batches. Apart from them, quality Assurance department also ensure quality of the pharmaceutical industry by Six Sigma strategy.

Six Sigma is one kind of quality tools by which the pharmaceutical industry can reduce defects by increasing process capabilities and improving quality. (Pharmatutor Webpage, n.d.)

It can be acquired by PDSA cycle. First of all, strategic plan should be ensured, secondly ensuring availability of the resources, after that analysis which drivers are required to increase the quality by reducing defects and finally implementing the strategy by increasing process consistency and improving quality.

CHAPTER 3: PROJECT PART

3.1 Introduction

For the project part, Qualitative analysis is performed where the challenging functions have been discussed which is manufacturing defects, the reason of the pharmaceutical defects, types of defects how Quality Assurance deal to minimize the quality defects along with multiple technical market complaint. and There are three subs-sections of quality operations department. Qualitative analysis is conducted by presenting real life example of complaints from different depot for both toll in, toll out and local products manufactured by Synovia Pharma. The main purpose of the analysis is to create real life example of managing complaints to minimize regulatory impact and for the sake of customers health. In the pharmaceutical plant, technical complaint is the prestigious issue,
so action plan is defined for some complaints to stop product technical complaint in future.

3.1.1 Literature Review

Johann Wolfgang once claimed that "some faults are necessary for the existence of individuality," yet this is not what is anticipated in medicinal products. (G, et al., 2020). Pharmaceutical items are known as the "golden sword" for treating illnesses, and any flaws would endanger priceless human life. A flaw is "A fault or difficulty in something or someone that spoils that item or person or causes it, him, or her to not work correctly," according to the Cambridge Dictionary. Defects in pharmaceutical products have a very different connotation because they are vital to saving lives. Any modification to a pharmaceutical product that outweighs the advantages of the drug qualifies as a fault. (G, et al., 2020).

3.1.2 Objectives

The objective of this project is to

a) Know more about the functions of quality Assurance Department of Synovia Pharma PLC. and how they are running their operations on a regular basis as a pharmaceutical industry

b) What kind of problems related to quality they are facing and how they are overcoming the problem and fulfill the product requirements for a large number of populations by maintaining quality from each manufacturing steps.

c) How to reduce quality defect from each step and deal with PTC (Product Technical Complaints).

3.1.3 Significance

This explains how Quality Assurance department manage all the functional activity in a pharmaceutical industry. This shows how we are managing all the defect which impacts quality which results in market complaint and in which area we are facing difficulties to reduce cost.

3.2 Methodology

For identifying the operational functions of Quality Assurance, Qualitative method has been conducted. Here all the manufacturing problems related issued and how we deal with this problem on a regular basis have been discussed. Here all the method has been discussed based on the functional observations. For Toll products, PTC needs to deal by the cross-functional departments of the toller company. Here I have discussed the source of Product Technical Complaints and the investigation process flow of the QA and also the measurable action plan to reduce the recurrence of these incident. As investigation of market complaint needs to complete within 30 calendar days by identifying the root cause so I have provided available information of two products from which source market complaint raised, the reason of the complaint, how QA team defined action plan to prevent such incident. CAPA is discussed as well and all of the study conducted by observing the problem, investigation and providing necessary measures.

3.3 Operational Analysis of Quality Assurance Department

Market complain is the main problem to deal with for quality assurance department because there is huge difference between real life quality defects with textbook recorded defects.

Types of Defects in Pharmaceutical Industry

1. Manufacturing Defects in the Pharmaceutical Industry: These are Defects that Occur during Production or for the negligence of the Quality Assurance Department. A production batch of packed-broken tablets which may bring market complaint if released the batch for commercial use.

2. Design-related faults: If these are not resolved, the entire production process may have flaws. The created product differs from the required specifications in terms of design or content. For instance, the homogeneity of dispersion was changed by amoxicillin trihydrate dispersible tablet.

3. System failure-related flaws: When producing, every industry must abide by the same regulatory standards. This type of issue arises when the manufacturing system disregards those regulations.

Comparison of real-life pharmaceutical defects and textbooks recorded defects: Our educational approach equips students pursuing a degree in pharmacy with the necessary skills to meet the difficulties facing the pharmaceutical industry. The unpleasant truth is that reality differs greatly from what one expects. We'd like to give an illustration for the aforementioned sentences. Table 1 compares flaws that are actual and happen in the pharmaceutical sector with defects that are reported in standard books. Table 1 compares real-world pharmaceutical flaws to those noted in textbooks. dose form kind Errors found in textbooks Real-world flaws Forms of solid dosage Tabs with an enteric coating orange peel effect when picking Lamination that rattles Blooming two impressions 9 softened/melted pills in a blister Eight uncoated pills Intact blister contains a hair follicle. 8 tablets with film coating creation of dust inside.

Consequences of pharmaceutical defects:

Customer complaints: When a customer complaint is received, it simply means that there is a problem with the sold goods and the customer is dissatisfied. Market complaints in the pharmaceutical industry are vocal or written expressions of displeasure with the clinical indication, product quality, or packaging.

Types of complaints:

1. Quality-related: This type of complaints relates to the product's physical, chemical, or biological standards, as well as the labeling and packaging.

2. Adverse medication reactions: A doctor or patient should notify the Pharmacovigilance department of any harmful or unexpected drug effects.

3. Other: Inadequate clinical effectiveness or reaction.

1. Market complaints' fate: The travel of a market complaint is governed by the company's Standard

Operating Procedure (SOP). The complaint is submitted through a customer complaint communication form with all necessary complaint-related information. The QA head evaluates papers such analytical records, sampling and release records, and other raw data in collaboration with the QC head. If there is a sizable discrepancy between the recorded values and the values of the complying product, the QA head confirms compliance. The QA head examines the stability data, and if no problems are found, he processes the compliance to the R&D head and the QC head. When the inputs from the various departments are received, the QA head must write a summary of findings and share it with the customers.

2. Drug recall or Product recall: Recalling a drug or product is a process of removing it from the market if it was not produced in accordance with FDA guidelines in order to safeguard the public's health from such faulty items or to protect the public from harmful products, companies have chosen to return all currently on the market defective products at FDA's request or on a voluntary basis.

Depending on who is ordering the product recall, drug recalls can also be categorized: a) Firm-initiated or voluntary recall: When a company thinks a product issued to the public poses a risk, it tells the FDA to issue a public alert. b) Involuntary or FDA-initiated recall: This is only done in cases of extreme emergency.

Management of market Complaints and product recalls

If a customer complaint arrives at the factory where the product is made, the QA department is in charge of responding to it and making sure the proper steps are taken. Likewise, if a customer complaint necessitates a product recall, the QA department starts the recall procedure and makes sure all the products associated with the complaint batch are recalled.

1. The SOP is used to make all of these decisions.

Managing Change Control Systems -

3. The change control system is used for each step or action that must be performed in a document or process that is not already validated.

4. There is a procedure in place for implementing change in the pharmaceutical industries. The QA department has finally reviewed and approved the change control system.

Complaint: A complaint is a declaration that something is flawed or inadequate. In the pharmaceutical sector, concerns are frequently made about the quality of the drugs themselves. Complaints may relate to the product's aspect and effect, such as "there is no effect," "the tablet or solution color is different," "the tablet is broken," and so forth. They may also relate to the packaging material, such as "the bottle is leaking," "the cap is difficult to open," "the label color is fading," or "one tablet in the blister is missing." A complaint, regardless of what it is about, demonstrates consumer unhappiness with a product and, consequently, with a business. Internal or external customers are also possible. An

internal client is a person who uses your goods or services within your organization. (Audumber, Ritesh, Ashpak, & Jyatiram, 2015)

CLASSIFICATION OF COMPLAINTS

1. A-Type Complaints: Serious complaints that necessitate the removal of a product from sale. Adverse drug reactions are one example. • A serious health risk that results in permanent disability or death. • Safety and purity. • Strength. • Product Robustness

2. B-Type Complaints: Serious grievances such as • An issue with the product's initial packing; • A problem with the product's chemical or physical characteristics; • Extraneous contamination, mix-ups, etc.

3. C-Type Concerns: Minor complaints include a. A labeling or coding issue with the batch information. b. Scarcity. (G, et al., 2020)

Steps of Complaint:

Step 1: Receiving complaint from market/depot.

Step 2: Technical Investigation

Step 3: Corrective and preventive actions and feedback to the customers

Step 4: Monthly reports and trend analysis. (G, et al., 2020)

3.3.1 Findings and Analysis of Product Technical Complaint: 2022

PTC Ref no	**Product name and batch no**	**Complaint Receive date**	**Origin of complaint**	**Description of PTC & class of defects**	**Investigation Closing date**	**Root cause**	**Action plan**	**Implementation Timeline/ Status**
SBL/PTC-22/01	Incrit M 500 mg tablet: H1	01.03.22	Pharmacy, Dada Vie Pharmacy, Distelleri Road, Gandaria, Sutrapur	Torn Pocket found in Blister: IV	31.03.22	• Based on the human error analysis tool it can be said that due to distraction/ lack of concentration of the	1.Awareness training to be conducted for all the operator who are responsible for inspection during secondary packaging	Jul-22

						operators involved in the blister checking this failure had occurred. • Due to the roughness of blister forming plugs with the forming pocket results in torn pocket.	operation. 2. The identified set of Forming plug of Incrit M 500mg Tablet to be changed	
SBL/PTC-22/02	Fimoxyclav 625 mg tablet: E13 & E20	09.03.22	Pharmacy, Kapasia Bazar, Gazipur	Air pocket formation within the intact blister: III	07.04.22	Based on the investigation data available the following root causes has been identified 1. Due to API moisture sensitivity, tablet absorbed moisture within blister pocket as a result the blister swollen up 2.	1.Tablet of Fimoxyclav SKUs to be packed in Alu pouch with silica gel 2. Purging of Nitrogen gas to be ensured in product processing stage. (CAPA ref: TNGD22A0021 is already in place)	Jul-23

						Packaging mode of the product is not adequate to prevent moisture from atmosphere 3. During manufacturing & packaging no extra precaution like purging inert gas was taken to prevent moisture absorption from different manufacturing & packaging step.		
SBL/PTC-22/03	Carbanem 500 mg Injection:H2	27.03.22	Hospital: BRB Hospital Limited, Panthapath, Dhaka	Discolored & clotted powder observed within intact vial	28.04.22	Based on the available investigation data, it can be concluded that due to crack on the bottom of the vial, moisture entered into the vial and	PVC glass clear film with thickness of 400 to 450 micron to be developed for Carbanem 1 g IV Injection, Carbanem 500mg IV Injection, Fimoxyclav 1.2 g	Dec-22

						made the powder reddish and sticky. And the vial may be cracked during handling & transportation due to poor quality of vial & low thickness of PVC film.	IV injection, Fimoxyclav 0.6 g IV injection.	
LOCAL /PTC-22/04	Fimoxyclav 625 mg tablet: H20	02.06.22	Hospital: Evercare Hospital Dhaka.	Missing Tablet in Blister	10.06.22	Based on the investigation data available the following root causes has been identified -Due to absence of Sensor/Camera detector in Buchon Blister Packaging Machine (ID: 04-006-BPM-	a. Necessary awareness Training to be conducted to the relevant primary packaging operator considering this complaint b.Fimoxyclav 625 mg tablet to be transferred to HoongA Blister Packing Machine (04-006-BPM-004) having CAMER	Dec-22

						003) for detection of empty pocket (for tablet), there is manual checker who checks the blister pocket. As it is manual checking system, so there is a chance of missing tablets inside the blister.	A DETECTOR AND REJECTOR SYSTEM. Timeline: NA (As BPR has been updated already & to be implemented from next commercial batch) c.Install functioning camera on the Buchon Blister Packaging Machines situated within the site listed below: 1. ID: 03-006-BPM-008- Non-antibiotic Solid (T4) Packaging Area 2. ID: 03-006-BPM-010- Non-antibiotic Solid (T4) Packaging Area 3. ID: 04-006-BPM-003- Penicillin	

							area 4.ID: 06-006-BPM-002-Cephalosporin area (Timeine: DEC 2022 (CAPA ref: TNGD20A0537)	
LOCAL/PTC-22/05	Fimoxyclav 1 g tablet:E2	05.06.22	Pharmacy: GreenHill Pharma, Morzal, Belabo, Narsingdi	Air pocket formation within the intact blister: III	05.07.22	Based on the investigation data available the following root causes has been identified. 1. Due to API moisture sensitivity, tablet absorbed moisture within blister pocket as a result the blister swollen up 2. Packaging mode of the product is not adequate to prevent moisture from	1.Tablet of Fimoxyclav SKUs to be packed in Alu pouch with silica gel 2. Purging of Nitrogen gas to be ensured in product processing stage. (CAPA ref: TNGD22A0021 is already in place)	23-Jul

						atmosphere 3. During manufacturing & packaging no extra precaution like purging inert gas was taken to prevent moisture absorption from different manufacturing & packaging step.		
LOCAL /PTC-22/06	Betanol 50 mg tablet: H4	12.09.22	Hospital: Asgar Ali Hospital, Gandaria, Dhaka	Broken pieces of tablet found on a blister pocket: IV	10.10.22	Due to attention error of the concern personnel responsible for blister checking & counting, could not identify the defective blister pocket during packaging operation	Necessary awareness Training to be conducted to the relevant secondary packaging operator considering this complaint	

Table 1: PTC 2022 for local products

PTC Ref number	Product name & Batch	Complaint Receive date	Origin of complaint	Description of PTC	Class of defects	Investigation Closing date	Root cause	Action plan
TI/APL/PTC-22/01	Stafoxin 500 mg capsule: 21K0230	03.02.22	Keranigan j Distribution centre	No blisters found within inner carton of Stafoxin 500 mg capsule	IV	23.02.22	- Due to attention error of the concern personnel responsible for blister inserting & shipping carton filling could not identify the empty inner carton during packaging	Necessary awareness Training to be conducted to the relevant secondary packaging operators considering this complaint.

TI/APL/ PTC-22/02	Stafoxin 500 mg capsule	08.03.22	Paltan Distribution centre & Narayanganj Distribution centre	No blisters found within inner carton of Stafoxin 500 mg capsule	IV	07.04.22	- Due to attention error of the concern personnel responsible for blister inserting & shipping carton filling could not identify the empty inner carton during packaging operation.	Necessary awareness Training to be conducted to the relevant secondary packaging operators considering this complaint.

Table 2: PTC 2022 for TOLL-IN products

PTC Ref number	Product name & Batch no	Compalint Receive date	Origin of complaint	Description of PTC	Class of defects	Investigation Closing date	Root cause	Action plan
DC/PTC-22/01	Pevisone 10g Cream: K45	23.06.22	Distribution center, Uttara Depot	One Tube missing in Blister	IV	21.07.22	Based on the investigation data available the following root causes has been identified: Due to absence of challenge test procedure of Detection & Rejection system after breaktime, it cannot be verified /checked whether the switch of Detection & Rejection system is turned “on” or “off” by the operator.	1.Ensure visual identification/label representing the “On or Off” status of Detection & Rejection system switch in Hoong-A Blister Packer (ID: 01-006-BPM-001). After that ensure necessary awareness training to the concern operators. 2. BPR of Pevisone 10 g Cream to be updated to include

							Ø It is also noted that due to lack of visual identification /label, the "On or Off" status of Detection & Rejection system cannot be easily detected by the operator.	the following: Challenge test frequency of Detection & Rejection system to be included after any breaktime or machine breakdown along with existing frequency.

Figure 3: PTC from Distribution Centre

PTC Ref number	**Product name & Batch No.**	**Compalint Receive date**	**Origin of complaint**	**Description of PTC**	**Class of defects**
EM/IPL/PTC-22/01	Telfast Suspension 50 ml	26.12.22	Gazipur Distribution center	Missing batch panel information in Printed carton	IV

Figure 4: PTC for Toll-out product

(Real life complaints and outcome)

Case 1: PTC investigation for Telfast Suspension (B/N: K3)

1. Description of Complaint:

A complaint was received for Telfast Suspension 50 ml (Batch Number: K3) from Synovia Pharma PLC, Station Road, Tongi, Gazipur-1710, Bangladesh. As per the complainant, Batch Print Information (e.g., Batch No., Mfg. Date, Exp. Date, and Price) was missing on one inner carton. Total one unit box is received as complaint sample. The bottle, leaflet and spoon are present in a unit box and bottle is found intact. Batch Print Information (e.g., Batch No., Mfg. Date, Exp. Date, Price, Pharma code) is found on the bottle label.

2. Previous History:

Previously, no similar complaint was received for Telfast Suspension 50 ml regarding this issue or any other issue.

3. Comparison with Retention Sample:

Complaint Sample Checking:

1. Physical appearance of inner carton of the complaint sample is found okay but batch print was missing.
2. Physical appearance of sticker of the sample is found okay and batch printing details is found clear and legible.
3. Physical appearance of leaflet is found okay.
4. Physical appearance of spoon is found okay.

Figure 15: Picture of complaint sample

Retention Sample Checking:

• Retention sample of Batch No. K3 was checked physically and no anomalies like complaint sample was identified.

Figure 16: Picture of Retention sample

4. Action Taken Immediately after Receiving the Complaint:

1. The complainant was acknowledged about the receipt of the complaint. The related personnel of Quality Assurance (QA) and Production were informed regarding the complaint.

2. A cross functional investigation team has been formed.

3. Batch document of respective batch have been reviewed and no anomalies were found. The complaint batch is released in the domestic market.

Root Cause Analysis Perspective (not limited to):

a) Man:

• Production and Quality Compliance personnel who performed line clearance, in-process checking, individual process review, finished goods inspection and batch release were found trained.

• All the operators involved in carton printing and packing operation were found trained and qualified.

So, Man has no contribution to this complaint.

b) Material:

• All the secondary packaging materials used in the complaint batch was found QA approved.

• The batch document confirms that right materials with right quantity were used for the packing of the complaint batch.

• During investigation, existing inner carton (Material Batch. No.: 11298361) of Telfast Sus (50ml) (Synovia) was checked and some sticked inner carton was found (Please see the Attachment-2). There is a possibility that double inner carton may pass through the machine due to the stickiness of inner carton. To resolve this stickiness of inner carton, Synovia Pharma PLC will be communicated to inform the supplier and ensure to deliver the inner carton without stickiness.

So, Material may have contribution to this complaint.

c) Machine:

All machine used in carton printing and packing are found qualified and calibrated.

• Preventive maintenance for the machine or equipment used in production process was done as per preventive maintenance schedule (Please see the Attachment-4).

• Operation & Maintenance logbook of respective machines has been reviewed and no record of machine breakdown during operation of the complaint batch was found (Please see the Attachment-5) The batch document confirms that machine setting was done as per the parameters mentioned in the respective SOP and found maintaining during the operation of the complaint batch.

• During investigation, a machine trial has been performed with the same lot (Material Batch. No.: 11298361) of carton Telfast suspension 50 ml (synovia) of complaint batch. During trial operation it was observed that, when the operator manually inserting cartons into the machine, double inner carton passed through the machine. For this reason, the batch print was only done on the upper carton but not on the lower carton. However, it is found that, there was no provision in machine to detect the double inner carton.

So, Machine has contribution to this complaint.

However, others machine of U05 and others unit of plant (1100) have been checked and found that the system already in place in those machines to detect the double inner carton passing through machine.

d) Method:

• In-process check was performed as per the SOP for 'In-Process Control of All Dosage Forms, Ref. Doc. No.: SOP/11/QA/009.

• Packaging operation was performed as per respective SOP for 'Control of Packaging Operation, Ref. Doc. No.: SOP/11/PR/073"and the approved instructions of batch document.

• After packaging finished goods release were performed as per respective SOP for 'Procedure for Finished Goods Release', Ref. Doc. No.: SOP/11/QA/026"and no anomalies were found.

So, Method has no contribution to this complaint.

e) Measurement:

• In-Process checking parameters are well defined and was performed and recorded in the respective batch document by the trained and qualified production personnel and quality compliance personnel as per SOP for "In-process Control of All Dosage Forms"

So, Measurement has no contribution to this complaint.

f) Mother Nature (Environment): Not applicable.

Root Cause:

From the above investigation it is suspected that, during batch printing operation of inner carton, two inner cartons were passed through the machine at a time. As a result, batch printing was done only in the upper carton but missing in the lower carton. As there was no provision in machine to detect the double IC during batch printing operation, unprinted inner carton was come to packaging area and packed in master carton and subsequently dispatched in the depot.

Conclusion:

Based on the root-cause analysis, this complaint is categorized as 'Confirmed' and therefore, CAPA has been defined. As batch panel were missing in the printed carton and from the available data it is found out that batch panel size is small as a result Z printer camera could not identify the missing printing record. So below mentioned CAPA must be ensured-

Action	**Description**	**Timeline**	**Responsible**
Corrections	NA	NA	NA
Corrective action	Training is to be provided to relevant personnel on who were responsible for packaging.	Immediate	Quality Assurance
Preventive action	Ensure supplier audit for changing source of batch panel.	August 2023	Quality Assurance

Case 2: Investigation Report

SOP Reference No. TONGI-SOP-000804

Local PTC No: SBL/PTC-22/01

COMPLAINT DESCRIPTION:

Torn Pocket found in Blister of Incrit-M 500 mg Tablet (B/N: H1)

Product Name	Incrit-M 500 mg Tablet
Batch No	H1
Quantity Involved	2 Tablets
Criticality of Defect	IV
Received Date of Complaint Sample	06.03.22
Origin of the Complaint	Pharmacy, Dada Vie Pharmacy, Distelleri Road, Gandaria, Sutrapur
Used by Patient	No
Global PTC Number	NA

IMMEDIATE ACTIONS:

Preliminary assessment was performed by the Quality Officer. Retention samples, batch document were reviewed.

BRIEF DESCRIPTION OF THE PRODUCT:

Manufacturing Information :

Product Name (local/International trademark)	Incrit-M 500 mg Tablet
INN / API / Antigen	Sitagliptin Phosphate Monohydrate & Metformin Hydochloride
Dosage Form / Dosage Strength / Presentation	Tablet/500mg/Alu-Alu Blister
Packaging	2X10’s
Shelf Life	2 years
Therapeutic Indication	Hypoglycaemic agent
Presentations and Registration Countries	Bangladesh

Batch Information:

Product	Incrit-M 500 mg Tablet
Batch Number	H1
Batch Size **(Bulk and/or Finished Product)**	119.00 Kg (Uncoated) 124.242 Kg (Coated)
Manufacturing Date	June, 2021
Packaging Date	Primary Packaging:05.07.21 Secondary Packaging: 05.07.21
Date of release	13.07.21
Expiry Date	May, 2023
Countries of Distribution	Bangladesh

Distribution Information:

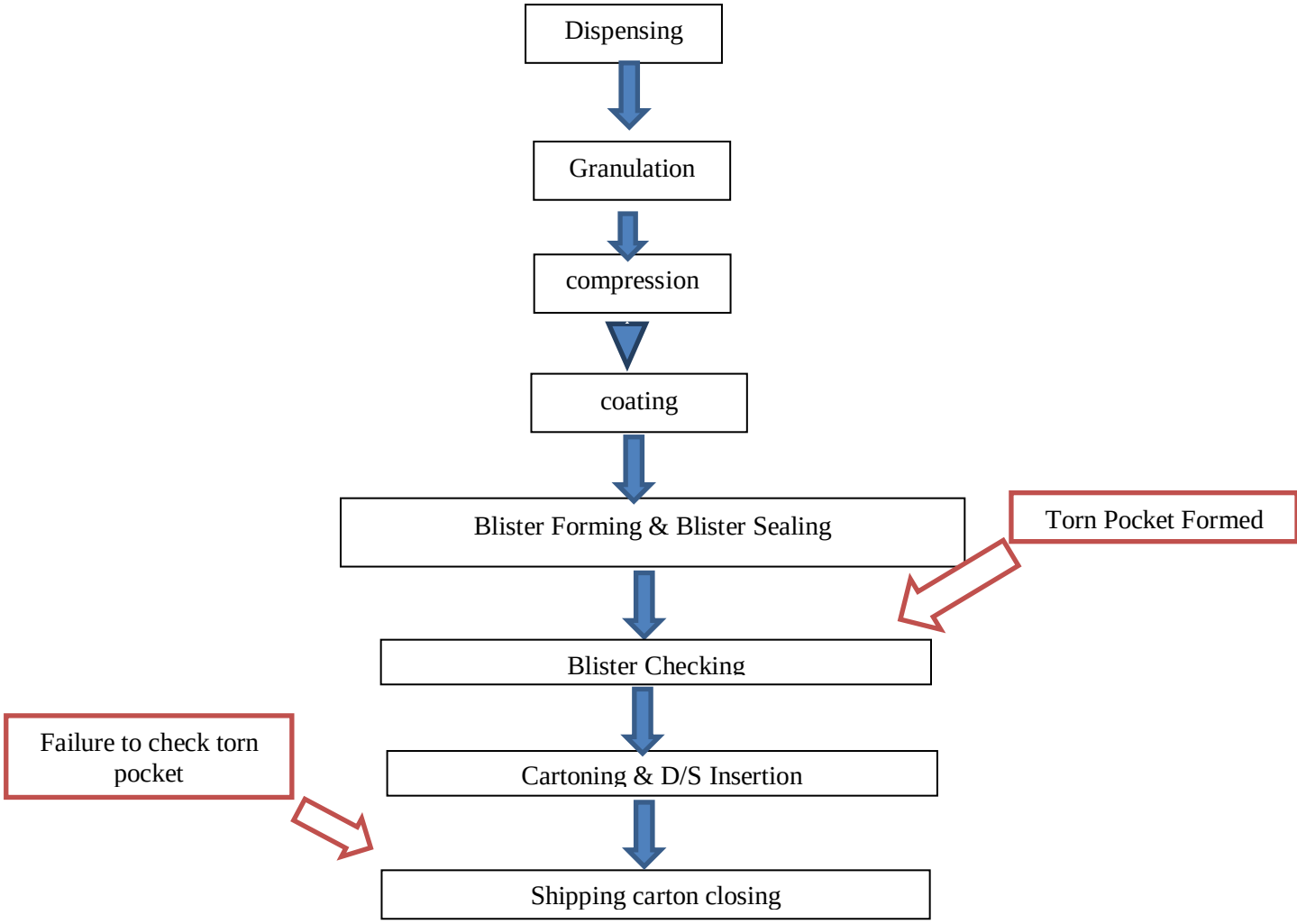
Batch Number	H1
Release Date	13.07.21
Number of Units Distributed	8214 Packs
Current Stocks	Nil
Countries of Distribution	Bangladesh

RESPONSIBILITIES:

Manufacturing and Packaging operations of all these products were performed in the T4 manufacturing and packaging area of Sanofi Bangladesh Limited respectively.

BRIEF DESCRIPTION OF THE PROCESS:

The process flow of manufacturing and packaging of Incrit-M 500 mg Tablet is given below:



SUMMARY OF ROOT CAUSE ANALYSIS:

Review of Complaint Sample(s):

The complaint sample has been checked and found that the defect did occur, and two pockets were found torn in one blister.

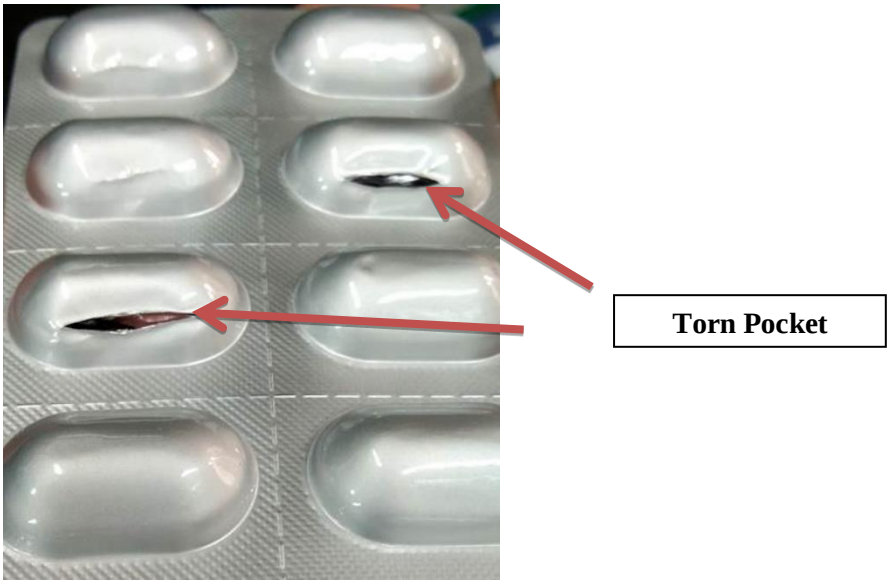


Figure 17: Complaint Sample photograph

Review of Retention Samples:

Based on preliminary investigation, the retention sample of the batch number has immediately checked and observed that no such defect was identified.

Figure 18: Picture of Retention Sample

Review of Batch Record and related documentation:

The Batch Manufacturing Record, Batch Packaging Record of Incrit M 500, Batch no: H1 has been checked. In-process data was found to have no anomalies.

Methodology:

By 6M analysis (Ishikawa/fish-bone diagram): (Applicable: Yes No)

Manpower:	**Contributing Factor**	
	Yes	**No**
Training to the equipment used	√	
Respect of the training SOP evaluation: initial – annual – re-training		√
Is the operator used to work on this equipment?	√	
Is there any history of deviations on same subject with the same operator?		√
Respect of the SOPs		√

Remarks:

Primary and secondary packaging operations was performed on 05.07.21. During primary packing operation some blisters found with torn pocket which were supposed to be checked and sorted out during secondary packing.

The personnel responsible for Primary packaging are as below:

Activity	**ID of personnel**
Machine Operator	S1709
Feeding and Tablet loader	SP5037, SP5118
Inspection	RS43

The personnel responsible for secondary packaging are as below:

Activity	ID of personnel
Laying	-
Inspection	S1201, S1675
Counting	S1201, S1675
Carton Making	S0438, S2291
Blister Inserting, D/S inserting and flap closing	S0463, S0419, S1012, S1607
Inner carton Batch Print Check, Closing and outer numbering	S0429, S1695, S2291, S2294
Charge Hand	S1701, S1710

Secondary packaging operation was performed on 05.07.21. During secondary operation the blisters with torn pockets were supposed to be checked and sorted out and this function was performed by ID: S1201 and S1675. Nevertheless, as the packaging mode of the product is ALU-ALU, the torn pockets can be visibly detected which the packaging operators failed to detect, hence eventually went to the market.

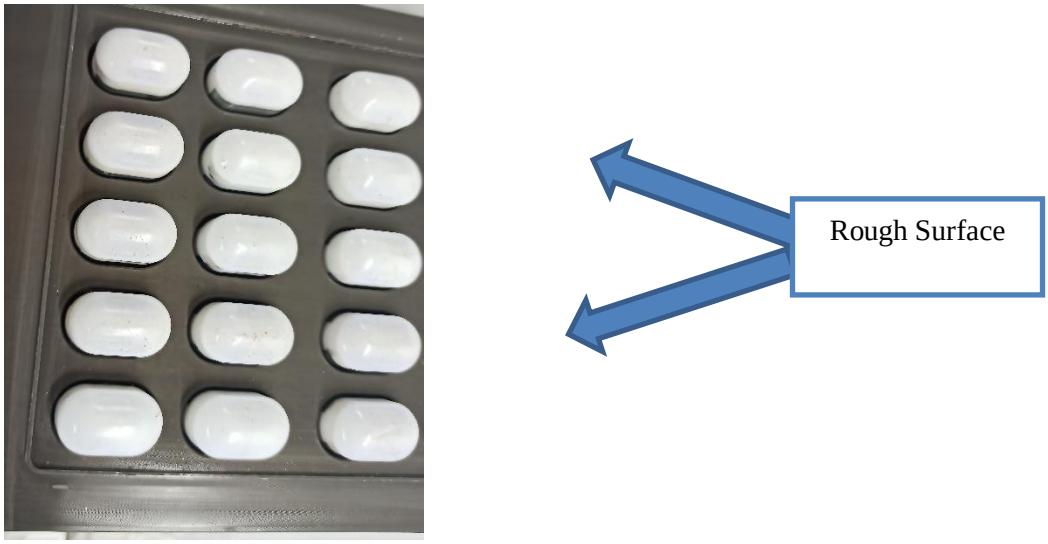
Means:

	Contributing Factor	
	Yes	**No**
Compliance of IQ/OQ/PQ		√
Last requalification: compliance / respect of the planning		√
Last maintenance: compliance / respect of the planning		√
Calibration of other control equipment: compliance / respect of the planning		√
Compliance of utilities systems (water, steam, compressed air, electricity)		√
Deviations observed during process		√

Remarks:

Upon interview with the section supervisor, as well as with the section in-charge, they informed that the roughness of the forming plug could result in torn pocket in a blister.

After physically checking the forming plug it has been identified that the surface of two forming plugs was rough.



Picture 19: Plug Formation

Medium:

	Contributing Factor	
	Yes	**No**
Conformity of working conditions: temperature/ humidity / light / pressures / particulates controls		√
Conformity of storage conditions (raw materials, packaging articles, intermediates and finished products, standards) : temperature / humidity		√

Remarks:

Moreover, Fluctuation in supplied compressed air pressure could result in insufficiency in pocket formation and as a consequence formation of torn pockets. But after reviewing the PR it has been

identified that 7.0 bar compressed air pressure was used during the beginning of the operation which is within the range (6.5-9.0 Bar)

Materials:

	Contributing Factor	
	Yes	**No**
Raw materials: agreed suppliers, compliance of reception controls, checking of suppliers results, checking of expiry date (suppliers, site), history of OOS		√
Utilities: compliance of water results / steam / compressed air		√
Conformity of incorporation of raw materials		√

Remarks: Two lots of aluminum bottom foil (1853501 & 1853067) has been used in this batch. After reviewing the QC result of these two lots, all the results are found with in specification.

Methods:

	Contributing Factor	
	Yes	**No**
Respect of instructions: production, control		√
Respect of instructions: sampling, storage		√
Process validation - respect of validated parameters		√
Cleaning validations		√

Remarks:

Method is not a contributing factor here.

Measures:	Contributing Factor	
	Yes	**No**
Checking and conformity of calculations		√
Trend analysis of results		√

Remarks:

The above-mentioned factors have no impact on the complaint sample

5 WHY MATRICES (Applicable: Yes No):

'SWISS CHEESE MODEL' (Applicable: Yes No):

HUMAN ERROR ANALYSIS TOOL (Applicable Yes No):

DAY OF WEEK (circle one):	SHIFT (circle one): NA	START/END OF SHIFT (circle):
Su M Tu W Th F Sa	1st 2nd 3rd	Start Middle End

Learning analysis (Applicable: Yes No):

Was employee trained on the applicable task or procedures?	**Yes No N/A**
Is this the first time the employee performs the task?	**Yes No N/A**
Length of time from previous execution of task?	days month months year >1 yr N/A
Has employee performed the task(s) previously free of error?	**Yes No N/A**
How often does the employee perform this task?	Regular basis as backup not often N/A
Was this a recurring error for the employee?	**Yes No N/A**

Procedural analysis (Applicable: Yes No):

Does the task require employee to follow a sequence of steps?	**Yes No N/A**
Did the employee miss the step(s)?	**Yes No N/A**
Did employee refer to the procedure/record to confirm activity steps?	**Yes No N/A**
Is procedure/record clear and well understood to employee?	**Yes No N/A**
Are there any job-aids (tools, signs, etc.) available?	**Yes No N/A**
Are procedures / job-aids in the immediate area?	**Yes No N/A**
Are job-aids needed or further instructions required?	**Yes No N/A**

Procedure consistencies ((Applicable: Yes No):

Does the procedure reflect current practices and all steps?	**Yes No N/A**
If the procedure does not reflect current practices or include all the steps, was this a factor in the event?	**Yes No N/A**
Does procedure identify required resources to perform task?	**Yes No N/A**

Application (Applicable: Yes No):

Were several tasks involved simultaneously?	**Yes No N/A**
Is this task possible with the resources that were available at the time of the event?	**Yes No N/A**
Was employee distracted while performing the task?	**Yes No N/A**
Was sufficient staffing available to support the task or process?	**Yes No N/A**
Did employee feel that they were under pressure or time constraints?	**Yes No N/A**

Time & Environment (Applicable: Yes No):

Did this error occur prior to or after a holiday or vacation?	**Yes No N/A**
Did this error occur prior to or after a break or shift change?	**Yes No N/A**
Was the environment or conditions very busy	**Yes No N/A**

Decision (Applicable: Yes No):

Was this a new situation for the employee?	**Yes No N/A**
Did the employee have to make a decision?	**Yes No N/A**
Was another employee informed or consulted?	**Yes No N/A**
Was the event or circumstance covered on the procedure?	**Yes No N/A**
Was this a routine activity or troubleshooting	**Routine activity troubleshooting**

Based on the analysis, the human error resulted from a (check one):

The incident that took place due to **"Distraction"** of the packing operator that resulted in human error.

Learning gap	Employee is unaware of requirements (i.e., did not remember the requirement at all)
Omission/Memory Gap	Remembers the requirement but failed to complete (i.e., skipped step but understood requirements)
Misinterpretation / Misunderstanding	Employee did not understand the requirement
Application error	Employee did not execute task/instruction as intended (i.e., inattention to detail, did not recognize nonconformance)
Decision error	Employee made incorrect / improper judgment (i.e., employee accepted nonconformance)
Distraction	Employee was distracted due to carrying out too many tasks in the timeframe
Documentation error	Documented wrong or revised data incorrectly

Action Plan:

Action	Description	Timeline	Responsible
Corrections	Awareness training to be conducted for all the operator who are responsible for inspection during secondary packaging operation.	Immediate	Manufacturing
Corrective action	The identified set of Forming plug of Incrit M 500mg Tablet to be changed	April, 2023	Manufacturing
Preventive action	NA	NA	NA

CONCLUSION:

Based on the investigation data available it can be concluded that the due to the roughness of the forming plug resulted in the scattered event of pocket rupture of blister of Incrit M 500mg Tablet. As the complaint was identified before administration, therefore no impact on patient safety is foreseen.

3.4 Summary and Conclusions

The functions of Quality Assurance department in any pharmaceutical industry in Bangladesh like (Synovia Pharma PLC.) is very critical and covers vast area. In Synovia, we have Quality Operations department where Quality Assurance is sub-section and still it has to play significant role by monitoring each and every individual department. Everything must be planned out by the QA department. Therefore, managing everything on time is difficult. The most important aspect is to meet the material in-house date deadline. It is also difficult to manage and monitor all the components involved in QA still from Supplier audit to Market Complaint all the functions are carefully supervised by QA. The office time is another important factor because most of our time is lost in heavy traffic. Sometimes on time delivery become impossible still due to product urgency QA needs to release the product working extra hours to finish the work on time. Sometimes breaking the law is necessary to handle an emergency but doing so has an impact on compliance and increases the likelihood of being discovered during internal or external auditing. We must compromise between these things. Additionally, we must handle market complaints, which is quite difficult.

When a delay occurs at one point, it has an impact on every component throughout the entire manufacturing facility. Therefore, it is possible that occasionally, as a result of the manufacturing delay, the customer may experience a severe product market crisis as we may have suffered a significant loss. When there is a great deal of product urgency and CAPA, deviation, and CR need to close on time at the same time, toll management can be challenging. For a timely product, we must manage both internal and external departments. This department is under intense workload pressure and has several ways to manage the vendor. Time management is crucial at Synovia because we have to oversee not only our own department but also the other internal departments.

Market complaint handling is very challenging for QA people because most of the times some complaints that arise is vague and, in that cases, supports from cross-functional teams are required for CAPA and some defects are not man made which are technical in that case huge time required to provide a solution.

3.5 Recommendations

There is a constant lack of labor. Single people must manage several things, which is why many mistakes happen. Error results in financial loss, which occasionally exceeds the wage of the new job. But people consistently try to avoid it. We constantly put the short-term gain ahead of the long-term gain. Below are my recommendations for Synovia Pharma PLC in Bangladesh:

1. In order to complete the work on time and deliver the product for use, teamwork is essential within the department and within internal cross-functional departments.

2. Employ a larger workforce.

3. A change in the distribution of authority

4. Establish a work schedule for internal departments as well, such as manufacturing, microbiology, and quality control.

5. Re-engineering of processes.

6 Quality Assurance department ensure quality as it's their core job responsibility, but quality implementation is not possible without manufacturing so quality assurance department should give proper solution so that not only quality is ensured but also cost reduction can be ensured by minimizing defects.

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