SQUARE SQUARE	***SQUARE* PHARMACEUTICALS LIMITED** **DHAKA UNIT**

Standard Operating Procedure	**TITLE**			
	FORMULATION DEVELOPMENT OF NEW DRUG PRODUCT			
Document No.	**Issue Date**	**Effective Date**	**Review Due**	**PAGE**
SOP/PD/002/10				1 OF 8

DISTRIBUTION

1. Head of Quality Assurance
2. GM, Production Operation
3. AGM, Quality Assurance
4. AGM, Production
5. Sr. Manager, Product Development
6. Sr. Manager, PMD
7. Sr. Manager, Regulatory Affairs
8. Sr. Executive, Product Development
9. Manager, Quality Control
10. Archive Copy

Name		**Designation**	**Signature**	**Date**
Prepared by	Kazi Akramuddaula	Sr. Executive, Product Development		
Reviewed by	A. T. M. Masud	Sr. Manager, Product Development		
Approved by	Dr. Md. Zahurul Hossain	AGM, Quality Assurance		

1. PURPOSE

To develop stable product through cost effective formulation so that degradation reaction do not take place in marketed product up to its declared shelf life and ensure the safety, efficacy of finished products.

2. SCOPE

This procedure is applicable for the formulation & process development of new products or modification of the existing products covering the various dosage forms such as solid products (GPB & SFrL) and Sterile products (SVP&O, LVP, Insulin & MDI) of Square Pharmaceuticals Limited. Dhaka unit for local market and overseas market.

3. RESPONSIBILITIES

3.1 Sr. Manager, Product Development is responsible to supervise the product development activities.

3.2 Sr. Executive/ Executive, Product Development is responsible for carry out individual product development activities.

3.3 Sr. Executive/Executive, Method development & Validation is responsible for analysis of the sample.

3.4 PMD is responsible for providing the Project paper & innovators sample.

3.5 TSD is responsible for providing the DMF and RM sample for analysis and trial.

4. TRAINING REQUIREMENTS

Sr. Executive / Executive of Product Development.

Sr. Executive / Executive of Method Development and Validation

Lab Attendant of Product Development.

5. ASSOCIATED DOCUMENTS

Procedure for procurement of raw materials for new product - SOP/PD/004/XX

Procedure for batch size determination of trial batch, pilot batch or process Development (optimization) batch-SOP/PD/021/XX

Preparation, review and approval of Process Development Protocol- SOP/PD/005/XX

Procedure for Technical Feasibility study for new product development - SOP/QC/022/XX.

Procedure for Preformulation study - SOP/PD/015/XX

Procedure for drug - excipient compatibility study - SOP/PD/014/XX

6. ABBREVIATIONS AND DEFINITIONS

Drug Product: The finished dosage form that contains a drug substance, generally, but not necessarily in association with other active or inactive ingredients.

Project Paper: The project paper is the document provided by PMD used for new product Launching. It includes (a) Product proposal form (b) Technical feasibility report (c) Proposed Product brief & (d) GANTT chart.

Product Brief: Product brief describes the proposed brand name, generic name, dosage form, strength, physical appearance, primary and secondary packaging requirements etc. of a product. The product brief is to reflect the identified customer needs that product needs to Fulfill for the market.

TSD	: Technical Service Department.
QC	: Quality Control
API	: Active Pharmaceutical Ingredient
AGM	: Assistant General Manager
GM	: General Manager
SVP&O	: Small Volume Parenterals and Ophthalmics.
LVP	: Large Volume Parenterals
PMD	: Product Management Department
MDI	: Metered Dose Inhaler
INN	: International Non Proprietary Name
DMF	: Drug Master File
MACO	: Maximum allowable carryover
CQA	: Critical Quality attributes
QTPP	: Quality Target Product Profile
SPL	: Square Pharmaceutical limited.
DTL	: Drug Testing laboratory

7. PRECAUTIONS

None

8. PROCEDURE

8.1 The Product Management Department (PMD) provides project paper to the Product Development Laboratory.

8.2 Give necessary input into project paper & send back to PMD.

8.3 Ask brand sample to TSD and initiate Preformulation study as per SOP/PD/015/XX.

8.4 Identify the Quality Target Product Profile (QTPP) of the drug product with justification upon evaluation of the brand product and reviewing the Preformulation study report.

8.5 Perform technical feasibility for formulation development, analysis and manufacturing of the product as per SOP/PD/022/XX.

8.6 Ask for initial QC analysis sample of the RM (API & new excipients) that are not available SPL to TSD according to SOP/PD/004/XX.

8.7 Collect DMF from API manufacturer.

8.8 Review and study the DMF and collect necessary information to design the formulation.

8.9 Develop or Select manufacturing and packing Tooling.

Check and design for necessary compression, encapsulation, and blister tools.

(i) Solid dosage Form :

Compression/encapsulation /powder filling/packaging change parts (e.g. die-punches, dossetor, blister format, printing or labeling change parts etc.)

(ii) For Liquid/ lyophilized/ MDI Products.

Liquid filling and filtration change parts (e.g. filling nozzle for different volume, BFS change parts, blister format, printing or labeling change parts etc.)

8.10 Perform initial risk assessment of the drug substance (API) attributes on drug product critical quality attributes (CQA) with justification.

8.11 Prepare a provisional specification of the API on the basis of initial QC analysis report.

8.12 Ask for laboratory trial sample of the RM with three different lots to TSD according to SOP/PD/004/XX.

8.13 Design experiments to minimize the high and medium risk drug substance attributes to low risk.

8.14 Conduct laboratory trial of the designed experiments and identify the required specification of the RM with low risk.

8.15 Perform initial risk assessment of the formulation variables (e.g. type of process, PSD specification of API & Excipients, excipients grade and quantity, etc.) on drug product critical quality attributes (CQA) with justification.

8.16 Design a prototype formulation upon reviewing the literature of the brand product and Preformulation study report.

8.17 Perform Drug excipient compatibility study as per SOP/PD/014/XX.

8.18 Design experiments to minimize the high and medium risk formulation variables to low risk.

8.19 Conduct laboratory trial of the designed experiments and identify the required specification of the formulation variables with low risk to develop the optimized formula.

8.20 Prepare bulk and finished product specification.

8.21 Manufacture at least three laboratory batches as per optimized formula and specification with standard batch size according to SOP/PD/021/XX to conduct stability study.

8.22 Prepare packaging instruction of the trial product as per packaging mode proposed in the product brief and according to Preformulation study report.

8.23 Pack the trial products according to the packaging instruction.

8.24 Prepare stability study protocol of the trail products and perform stability study of the trial products (optimized formula) according to the stability study protocol.

8.25 Forward the sample to PMD for assessment.

8.26 Order RM for pilot batches and process optimization batches upon getting satisfactory stability report of the trial batches.

8.27 Perform initial risk assessment of each process steps (e.g. sieving, mixing, filtration, filling, etc.) and their variables (e.g. screen or filter pore size, order of material addition, mixing speed and duration, etc.) on drug product critical quality attributes (CQA) with justification.

8.28 Prepare pilot scale protocol and batch manufacturing document.

8.29 Conduct pilot scale batches at laboratory or at pilot facility considering same operating principal at commercial scale to minimize the high and medium risk process variables to low risk.

8.30 Prepare a pilot scale batch manufacturing report after successful manufacturing of the pilot scale batches.

8.31 Prepare process development protocol and batch manufacturing document to optimize the manufacturing process parameter at commercial facility.

8.32 Ask validation department to calculate MACO value of the API and perform cleaning validation of the product if the MACO value exceed the validated limit.

8.33 Conduct process development batch (es) to optimize the manufacturing process and manufacture continue until getting satisfactory process parameters at commercial scale.

8.34 Establish process capability index (Cpk) value upon statistical analysis of the data generated during pilot scale batch and process optimization batch manufacturing as reference data for Cpk analysis of commercial batches.

8.35 Prepare process development report and master manufacturing report as per SOP/PD/007/xx

8.36 Handover the Process Development Report & Master Manufacturing Report to QA.

8.37 Perform stability study of the process development batches as per approved protocol.

8.38 Prepare the technical data and send it to RA (Regulatory Affairs) for recipe submission.

8.39 Prepare DTL sample for INN product according to the optimized formula and specification.

8.40 Prepare Pharmaceutical development report of the drug product.

9. REFERENCES

9.1. ICH Guideline - Q8 (R2): Pharmaceutical Development.

9.2 ICH Guideline – Q9: Quality Risk Management.

9.3 ICH Guideline – Q10: Pharmaceutical Quality System.

10. APPENDICES

A. FLOW CHART OF NEW DRUG PRODUCT DEVELOPMENT

11. CHANGE HISTORY

DATE	REVISION	DESCRIPTION OF CHANGE
03-09-2006	01	Original Document
05-11-2007	02	1. Distribution list is modified. 2. Changes in steps 3.1, 8.2, 8.3, 8.5, 8.6, 8.8, 8.9 and 8.13 3. SOP updating as per current format.
10 Sep' 08	03	1 Purpose and Scope is modified. 2. Addition of information by step 8.7, 8.10, 8.11, 8.12, 8.14, 8.16, 8.17, 8.18 and 8.19. 3. Change of content in steps 8.10 and 8.13.
03 Mar' 09	04	1. Distribution list is modified. 2. Changes in SOP title and step 3.1, 4, 8.15 3. Addition of information in steps3.3, 3.4, 6, 8.2, 8.6, 8.7, 8.11, 8.16 and Appendix A
19 May'09	05	1. Title, purpose, scope & Associate document is modified. 2. Changes in steps 8.11, 8.18, 8.19 3. Changes in Appendix A
22 Feb' 10	06	1. Change the document to SOP/PD002/06 2. Changed the SOP format as per SOP/QA/002/11, Ref. No.CDR 273/10
31 Jul' 11	07	1. Distribution list is modified. 2. Changes in steps 4, 8.14, 8.17, 8.19, 8.20 and 8.21 3. Addition of step 8.15.
21 Jul' 12	08	1. Distribution list is modified 2. Change in step 8.21 3. Change in Appendix A
18 Jun '14	09	1. Change in step 8.11

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DATE	REVISION	DESCRIPTION OF CHANGE
12 Oct'14	11	1. Title of the SOP is changed to Formulation Development of New Drug product instead of Carryout Product Development Activities. 2. Distribution list is changed. 3. In section 3; responsibility for Executive of Method Development and Validation is incorporated. 4. In section 4; Training requirement for Executive of Method Development and Validation is incorporated. 5. In section 5; associated document list is updated. 6. In section 6; definition of new product is incorporated and abbreviation for QTPP, CQA, MDI, SPL, LVP,SVP&O, DMF, MACO and DTL is incorporated. 7. In section 8; the whole procedure is modified to perform risk assessment and process capability study. 8. In section 8.10; risk assessment for drug substance is incorporated. 9. In section 8.15; risk assessment for formulation variables are incorporated. 10. In section 8.27; risk assessments for process steps are incorporated. 11. In section 8.34; Establishment of process capability index (Cpk) is incorporated. 12. Change in Appendix – A. 13. Authorized by signing option is omitted. (Ref. No. CDR/FU1/0443/14)

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