DEPARTMENT OF PHARMACEUTICAL SERVICES
MINISTRY OF HEALTH
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BDMCA/DPS/02/B

APPLICATION OF REGISTRATION OF MEDICINAL PRODUCTS

QUALITY REQUIREMENTS FOR DRUG PRODUCT (PART II – SECTION 2)

PRODUCT: REF.NO.

N.B. This is the recommended format for Part II – Section 2. Spacing should be adjusted by Applicant as and when necessary. Extension sheets for details and supporting documents should be appropriately numbered and referenced.

SECTION A

Table of contents for the filed application.

SECTION B

Checklist of tabulated information required for registration of medicinal product.

SECTION C

P1. DRUG PRODUCT

P1.1 Description (Physical Characteristics)

P1.2 Composition (Complete Formula)

P1.2.1 Active Ingredient(s)
Name of Active Ingredient(s) Content

P1.2.2 Other Ingredients
(adjunct, excipients, colour, preservative, flavour, etc)
Name of Ingredient(s) Content Function

P1.2.3 Overages (where applicable)

Name of Ingredient(s)	Overage (To include reasons for including overage)

P1.3 Description of Reconstitution Diluents, if applicable

P1.4 Type of Container Closure System / Pack Size (Briefly)

P2. PHARMACEUTICAL DEVELOPMENT

P2.1 Information on Development Studies
(Applicable to NCE and Biotechnological Products Only)

P2.1.1 Product Development and its Manufacturing Process

P2.1.2 Bibliography of Development Studies

P2.2 Component of Drug Product

P2.2.1Drug Substance

State briefly the characteristics-performance relationship of the drug substance, mentioning also, where applicable, and its compatibility with excipients listed in Item P2.1.1 and other drugs in the same formulation.

P2.2.2 Excipients

State briefly the concentration and characteristics of excipients that can influence product performance, also mentioning, compatibility of the excipients with each other.

P2.3 Drug Product

P2.3.1 Formulation Development

i) State briefly structure-active relationship of drug substance putting

into consideration the proposed route of administration and usage.

ii) Highlight evolution of formulation design from initial concept to final design of drug substance.

iii) Summarise all formulations used, including changes made, between proposed commercial formulation and those used in pivotal clinical batches and primary stability batches. Also provide the rationale for changes made, if any.

iv) Manufacturer's comparative in-vitro studies and standards, as well as in-vivo studies and standards for the release of active ingredients. (For example, dissolution, diffusion, etc.)

v) Identification of special design features and rationale for their use.

vi) Rationale for special formulations.

Detail of tests, analytical methods and test protocols enclosed. [ ]

Summary of in-vitro and in-vivo studies on release rates of product by other investigators. [ ]

Details of test/studies, analytical methods, test protocols reports of studies, and supporting documents enclosed. [ ]

Bibliography of comparative in-vitro and in-vivo studies for release rates. [ ]

P2.3.2 Overages

P2.3.3 Physicochemical and Biological Properties

P2.4 Manufacturing Process Development

P2.4.1 Development of Manufacturing Process for Commercial Production Batches

P2.4.2 Differences between Manufacturing Process(es) Used for Pivotal Clinical Batches and Commercial Production Batches that can Influence Performance and Manufacturability of Drug Product

P2.5 Container Closure System

P2.5.1 Suitability of Container Closure System

P2.5.2 Performance of Dosing Device

P2.6 Microbiological Attributes

P2.6.1 Non-Sterile Products

P2.6.2 Selection of Preservative Systems

P2.6.3 Container Closure System of Sterile Preparation

P2.7 Compatibility

Summary of compatibility studies of drug product with primary container closure system, product accessories and reconstitution diluents.

P3. MANUFACTURE OF PRODUCT

P3.1 Batch Manufacturing Master Formula

Name of Ingredients (Active and otherwise)	Quantities Used per Batch	Batch Size

Stages of Manufacturing

P3.2 Manufacturing Process & Process Control

P3.2.1 Brief Description and Principles

Detailed manufacturing process enclosed [ ]

P3.2.2 In-process Quality Control (IPQC)

Tests performed during manufacturing process and sampling protocols.

Tests	Stage at which test is done	Frequency of sampling	Quality of sample taken each time

Details of test, test protocols, analytical methods specification limits and sampling plans enclosed [ ]

P3.3 Controls of Critical Steps and Intermediates

P3.3.1 Critical Steps

Critical Steps	Control Specifications	Acceptance Limits

P3.3.2 Intermediates

Intermediates	Control Specifications	Acceptance Limits

P3.4 Process Validation and/or Evaluation

P4. QUALITY CONTROL OF EXCIPIENTS

P4.1 Specification for Excipients

Name of Excipients	Specifications (State whether B.P/ U.S.P/ manufacturer's, etc)	Acceptance Limits (Manufacturer and country of origin)	Source

Details of specifications tests, test protocols, analytical methods, sampling protocols, etc. enclosed. [ ]

P4.2 Analytical Procedures
(Refer to Annex A)

P4.2.1 Description of Analytical Procedures

P4.2.2 Source of Compliance

State whether quality control is done in part or solely by the manufacturer's own quality control department or an external laboratory.

If quality control tests are done by an external laboratory, state the following:

i) Name and address of the laboratory;
ii) Tests done by the external laboratory;
iii) Reasons why the tests are not done by the manufacturer;
iv) Whether the manufacturer or the external laboratory is responsible for deciding if a batch of product is suitable for release for marketing.

Certificate of Analysis for Compliance of Purchase Specifications [ ]

P4.3 Excipients of Human and Animal Origin

P4.3.1 Description

P4.3.2 Specification

P4.3.3 Sources

P4.3.4 Viral Safety Data

P4.4 Novel Excipients

P4.4.1 Manufacture of Excipients

P4.4.2 Safety Characteristics

P5. QUALITY CONTROL OF FINISHED PRODUCT

P5.1 Specifications for Ingredients
(active and otherwise)

Name of Ingredients	Specifications (State whether B.P/U.S.P/ manufacturer's, etc)	Acceptance Limits	Source (Manufacturer and country of origin)

Details of specifications tests, test protocols, analytical methods, sampling protocols, etc. enclosed. [ ]

Certificate of Analysis of two recent batches of finished product enclosed. [ ]

P5.2 Analytical Procedures
(Refer to Annex A)

State whether quality control is done in part or solely by the manufacturer's own quality control department or an external laboratory.

If quality control tests are done by an external laboratory, state the following:

i) Name and address of the laboratory;
ii) Tests done by the external laboratory;
iii) Reasons why the tests are not done by the manufacturer;
iv) Whether the manufacturer or the external laboratory is responsible for deciding if a batch of product is suitable for release for marketing.

Certificate of Analysis for Compliance to Purchase Specification [ ]

P5.3 Validation of Analytical Procedures Used
(Refer to Annex C)

P5.4 Batch Analyses Report

P5.4.1 Description of Batches Analysed

P5.4.2 Results of Tests Conducted on All Relevant Batches

Analytical reports of recent batches of finished product which are representative of product seeking registration. [ ]

P5.5 Characterisation of Impurities

Summary of impurities monitored or tested for during and after manufacture of drug product.

Impurities Monitored	Analytical Method Used (E.g. TLC, HPLC, chemical test, IR spectroscopy, atomic absorption, etc)	Acceptance Limits

Analytical reports for batches used for toxicity tests and clinical work submitted in support of the drug registration application, if different from the above [ ]

P5.6 Justification of Specification

Specification	Analytical Procedure	Acceptance Limits	Justification

P6. REFERENCE STANDARDS OR MATERIALS

P6.1 Reference Standards or Materials Used for Testing

P6.2 Purity
(Measurement by Quantitative Procedures)

P7. CONTAINER CLOSURE SYSTEM / PACKAGING

P7.1 Immediate Container Closure System / Primary Packaging

Type:

Material :

Capacity (where applicable):

Closure and liner (type and material) :
(where applicable)

Name and Address of Manufacturer:

Specifications:

P7.2 Outer Container(s) / Secondary Packaging(s)

Type:

Material :

Capacity (where applicable):

Closure and liner (type and material) :
(where applicable)

Name and Address of Manufacturer:

Specifications:

Product Accessories

Description/Type:

Material :

P7.3 Packaging Inclusions
(Dose-measuring device/applicators/administration set/desiccant/ fillers/ etc., if any)

Description:

Material and Composition:

Reasons for Inclusion:

Capacity (where applicable):

Name and address of Manufacturer:

Specification:

Duration of Satisfactory Performance:
(where applicable)

Instruction to users:

P7.4 Other Supporting Data

The application must have ready details of containers and packaging materials - composition of material and added substances, technical properties and specifications, methods for testing relevant properties/specifications, safety or toxicity of material and added substances, efficacy of closures in manufacturing sterile products, compatibility of inclusions with finished product, etc.

However, DO NOT enclose such details and supporting documents. The applicant shall be notified when such details are needed; they shall be made available to the Authority immediately on request.

Suitability information should be referred under Item P2.5.

P8. PRODUCT STABILITY

P8.1 Storage Conditions Included on Label

P8.2 Proposed Shelf-life of Product

P8.3 Stability Studies Summary and Conclusion

Completed Stability Studies
(Summary of stability studies, characteristics and degradation products monitored, results and conclusions of completed stability studies). Results of studies on at least 2 batches are required.

Details of completed stability studies, place of study, protocols, analytical methods, results and conclusions, etc. enclosed. [ ]

P8.4 Post-approval Stability Protocol and Stability Commitment

On-going / Proposed Stability Studies
(Outline of on-going or proposed stability studies)

Details of on-going/proposed stability studies, protocols, analytical methods, etc. enclosed. [ ]

N.B. Results and conclusions of studies shall be submitted to The Authority on completion of such studies.

P8.5 Stability Data Reports

Report on stability study that include batches examined, conditions of storage, container closure systems, duration of study, monitoring of changes, analytical methods, results of study, and conclusion.

P9. PRODUCT INTERCHANGEABILITY
(Applies to Major Variation and Generic Products Only)

P9.1 Type of Studies Conducted

P9.2 Protocols Used & Result of Studies Conducted

SECTION D

Summary of Other Data

Bibliography of Relevant Data

N.B. Details of data particulars, full reports of studies including methodology, protocols, analytical methods, results, interpretation, conclusion, copies of papers, articles, etc. referenced and relevant supporting documents shall be kept by the applicant and submitted to the Authority immediately on request.

Manufacturer

SIGNATURE : .....

NAME : .....

OFFICIAL DESIGNATION: .....

Applicant

SIGNATURE : .....

NAME : .....

DATE : .....