REGISTERED No. M - 302
L.-7646

The Gazette of Pakistan

EXTRAORDINARY
PUBLISHED BY AUTHORITY

ISLAMABAD, SATURDAY, JUNE 9, 2018

PART II

Statutory Notifications (S.R.O.)

GOVERNMENT OF PAKISTAN

MINISTRY OF NATIONAL HEALTH SERVICES, REGULATIONS & COORDINATION

(Drug Regulatory Authority of Pakistan)

NOTIFICATION

Islamabad, the 8th June, 2018

S. R. O. 713 (I)/2018.—In exercise of the powers conferred by section 23 of the Drug Regulatory Authority of Pakistan Act, 2012 (XXI of 2012), read with clause (a) of section 7 thereof and section 43 of the Drugs Act, 1976 (XXXI of 1976), the Drug Regulatory Authority of Pakistan, with the approval of the Federal Government, is pleased to direct that in the Drugs (Licensing, Registering and Advertising) Rules, 1976, the following further amendments shall be made, the same having been previously published *vide* S.R.O. No.932(I)/2017, dated the 18th September, 2017 as required by sub-section (3) of the said section 43, namely:—

In the aforesaid Rules,—

(1) in rule (26), in sub-rule (1),—

Price Rs : 20.00

[6074 (2018) Ex. Gaz.]

(a) after the word "drug", at the end, the expression "or on Form 5-F (Common Technical Document) as notified by the Drug Regulatory Authority of Pakistan; and the Registration Board may issue necessary explanations and exemptions in this regard if needed" shall be inserted; and

(b) for the full stop, at the end, a colon shall be substituted and thereafter the following provision shall be added, namely:—

"Provided that an applicant may submit registration application on existing forms (Form 5 or 5-A or 5-D or 5-E) for a period of 6 months, which may be extended, on justifiable reasons, for further period as determined by DRAP, after notification of Form 5-F by DRAP."; and

(2) in Schedule A, after Form 5(E), the following new Form shall be added, namely:—

FORM 5-F

[See rule 26 (1)]

Common Technical Document (CTD) for Registration of Human Drugs

Module 1: Administrative Part

Section	Sub-Section	Heading
1.1		Covering Letter and Fee Deposit Slip
1.2		Table of Contents (From Module 1 to Module 5)
1.3		**Applicant Information:**
	1.3.1	Name, address and contact details of Applicant / Marketing Authorization Holder:
	1.3.2	Name, address and contact details of Manufacturing site.
	1.3.3	Specify whether the Applicant is: a. ❑ Manufacturer b. ❑ Importer c. ❑ Is involved in none of the above (contract giver)
	1.3.4	Valid Drug Manufacturing License (DML) of manufacturer/ Applicant or Drug Sale License, whichever is applicable.
	1.3.5	Evidence of approval of manufacturing facility / Approved Section from Licensing Authority.
	1.3.6	List of already approved registered drugs in this section.

Section	Sub-Section	Heading
	1.3.7	Identification of Signature(s) of authorized persons, Incharge Production, Quality Control and Incharge Quality Assurance.
	1.3.8	Manufacturer's Site Master File and Credential (for importer)
1.4		**Type of Application:**
	1.4.1	Application is for the registration of: ❑ New Drug Product (NDP) ❑ Generic Drug Product (GDP)
	1.4.1	Pharmaceutical product is intended for: ❑ Domestic sale. ❑ Export sale. ❑ Domestic and Export sales.
	1.4.2	For imported products, please specify one of following: ❑ Finished Pharmaceutical Product Import. ❑ Bulk Import and local repacking (specify status of bulk). ❑ Bulk Import Local Repacking for Export purpose only.
	1.4.3	Contract Manufacturing as per Rule 20-A of Drugs (Licensing, Registering and Advertising) Rules, 1976. ❑ Domestic Manufacturing. ❑ Export Purpose Only.
1.5		**Detailed Information of Drug, Dosage From & Labelling Claims:**
	1.5.1	Generic name with chemical name & synonyms of the applied drug.
	1.5.2	Strength / concentration of Active Pharmaceutical ingredient (API) per unit.
	1.5.3	The proposed proprietary name / brand name under which the drug is intended to be sold with trade mark certification / clearance.
	1.5.4	Proposed Pack size and Proposed unit price of drug e.g., per tablet/ capsule. Maximum Retail Price (MRP) per pack shall also be mentioned.
	1.5.5	Pharmacotherapeutic Group of Active Pharmaceutical Ingredient (API)
	1.5.6	Pharmacopoeial reference / Status of applied formulation.
	1.5.7	Route of administration.
	1.5.8	For Generic Drug Product, reference of other similar approved medicines with information pertaining to Manufacturer name, brand name, strength, composition, registration number & dosage form, Pack size and Price.

Section	Sub-Section	Heading
	1.5.9	The registration status of applied drug in same molecule and salt, strength, dosage form, container closure system, indications and route of administration etc. in other countries. The status in reference regulatory authorities is mandatory to mention.
	1.5.10	Dosage form of applied drug.
	1.5.11	Proposed label [outer (secondary) & inner (primary)] & colour scheme in accordance.
		with Drug (Labelling & Packing) Rules, 1986 along with specimens.
	1.5.12	Description of Batch numbering system.
	1.5.13	Training evidence of technical staff with respect of manufacturing of applied drug (mandatory in case of specially designed pharmaceutical product / Novel Dosage
	1.5.14	Summary of Product Characteristics (SmPC) including Prescribing Information (PI) along with Patient information Leaflet (PIL) of the Finished Pharmaceuticals Product (FPP).
	1.5.15	Commitment/Undertaking that after registration of applied drug, the Pharmacovigilance department of the applicant / manufacture is liable to impose similar restrictions, addition of any clinical information (like in Indications, Contra- indications, Side effects, Precautions, Dosage & Adverse Drug Reactions etc. in Summary of Product Characteristics (SmPC), Labelling & Promotional material) or withdraw the drug from market in Pakistan within fourteen days after knowing that such information (which was not available or approved by the DRAP at the time of registration)/ actions taken (for safety reasons) by any reference / stringent drug regulatory agency / authority & also inform the DRAP (Drug Regulatory Authority of Pakistan) for further action in this regard.
	1.5.16	Commitment / Undertaking that the applicant shall recall the defective Finished Pharmaceutical Products (FPP) and notify the compliance to the authority along with detail of actions taken by him as soon as possible but not more than ten days. The level of recall shall also be defined.
	1.5.17	Commitment / Undertaking that in case of any false claim/ concealing of information, the DRAP has the right to reject the application at any time, before and even after approval or registration of the product in case if proved so.
	1.5.18	Commitment / Undertaking that the firm shall follow the official pharmacopoeia specifications for product / substance as published in the latest edition & shall update its specification as per latest editions of the same. In case, the specifications of product/ substance not present in any official pharmacopoeia the firm shall establish the specifications. In both cases, the validation of specifications shall be done by the applicant.

Section	Sub-Section	Heading
	1.5.19	Commitment / Undertaking that in case of any post approval change, the applicant shall ensure that the product with both approvals shall not be available in the market at the same time. And the product with new approvals shall be marketed only after consumption / withdrawal of stock with previous approvals. The company shall be liable to inform the same regarding marketing status of product to the DRAP after getting such post-registration approvals.
	1.5.20	Other commitment *e.g.*, regarding stability studies etc.
	1.5.21	Protocols along with the commitment to follow Good Laboratory Practices (GLP) by the Manufacturer.
	1.5.22	Protocols to implement Good Pharmacovigilance Practice by the Pharmacovigilance department / section of the Manufacturer / Company.
1.6		**Miscellaneous Information:**
	1.6.1	Information on Prior-related Applications.
	1.6.2	Appendix.
	1.6.3	Electronic Review Package.
	1.6.4	QIS (Quality Information Summary).
	1.6.5	Drug Substance related Document including following: a. Name and address of API manufacturer. b. Approval of manufacturing facility of API by regulatory body of country & validity. c. Vendor qualification / audit is ❑ Document based ❑ Site inspection based d. Reason for point c.

Module 2: (Overviews and Summaries)

Module	Section	Sub-section	Contents
2	2.1		Overall CTD Table of Content
	2.2		CTD Introduction
	2.3		Quality Overall Summary (QOS)*
		2.3	Introduction
		2.3.S	Drug Substance
		2.3.P	Drug Product
		2.3.A	Appendices
		2.3.R	Regional Information

Module	Section	Sub-section	Contents
	2.4		Non-Clinical Overview
	2.5		Clinical Overview
	2.6		Non-Clinical Written and Tabulated Summaries (Normally not required for generics)
	2.7		Clinical Summary

*QOS has been explained by a WHO QOS - PD template MODULE 2.3

Module 3: (Quality / CMC)

Module	Section	Sub-section	Contents
3	3.2.S		DRUG SUBSTANCE
		3.2.S.1	General Information
		3.2.S.2	Manufacture
		3.2.S.3	Characterization
		3.2.S.4	Control of Drug Substance
		3.2.S.5	Reference Standards or Materials
		3.2.S.6	Container Closure System
		3.2.S.7	Stability
	3.2.P		DRUG PRODUCT
		3 .2.P.1	Description and Composition of Drug Product
		3.2.P.2	Pharmaceutical Development
		3.2.P.3	Manufacture
		3.2.P.4	Control of Excipient
		3.2.P.5	Control of Drug Product
		3.2.P.6	Reference Standards or Materials
		3.2.P.7	Container Closure System
		3.2.P.8	Stability

Module 3 has been explained by following guidelines M4Q-R1 3, 4_Quality_ Questions_Answers_R1 (Location Issues), WHO TRS 970 annexure 4.

Details of Module: 3 (Quality/CMC)

- 3.1 Table of Contents of Module 3
- 3.2 Body of Data
- **3.2.S Drug Substance**
  - ❖ **3.2.S.1 General Information**
    - — 3.2.S.1.1 Nomenclature
    - — 3.2.S.1.2 Structure
    - — 3.2.S.1.3 General Properties

- **3.2.S.2 Manufacture**
  - 3.2.S.2.1 Manufacturer(s)
  - 3.2.S.2.2 Description of Manufacturing Process and Process Controls
  - 3.2.S.2.3 Control of Materials
  - 3.2.S.2.4 Controls of Critical Steps and Intermediates
  - 3.2.S.2.5 Process Validation and/or Evaluation
  - 3.2.S.2.6 Manufacturing Process Development
- **3.2.S.3 Characterisation**
  - 3.2.S.3.1 Elucidation of Structure and other Characteristics
  - 3.2.S.3.2 Impurities
- **3.2.S.4 Control of Drug Substance**
  - 3.2.S.4.1 Specification
  - 3.2.S.4.2 Analytical Procedures
  - 3.2.S.4.3 Validation of Analytical Procedures
  - 3.2.S.4.4 Batch Analyses
  - 3.2.S.4.5 Justification of Specification
- **3.2.S.5 Reference Standards or Materials**
- **3.2.S.6 Container Closure System**
- **3.2.S.7 Stability**
  - 3.2.S.7.1 Stability Summary and Conclusions
  - 3.2.S.7.2 Post-approval Stability Protocol and Stability Commitment
  - 3.2.S.7.3 Stability Data

- **3.2. P Drug Product**
  - **3.2.P.1 Description and Composition of the Drug Product**
  - **3.2.P.2 Pharmaceutical Development**
    - 3.2.P.2.1 **Components of the Drug Product**
      - 3.2.P.2.1.1 Drug Substance
      - 3.2.P.2.1.2 Excipients
    - 3.2.P.2.2 **Drug Product**
      - 3.2.P.2.2.1 Formulation Development
      - 3.2.P.2.2.2 Overages
      - 3.2.P.2.2.3 Physicochemical and Biological Properties
  - **3.2.P.2.3 Manufacturing Process Development**
  - **3.2.P.2.4 Container Closure System**
  - **3.2P.2.5 Microbiological Attributes**
  - **3.2.P.2.6 Compatibility**
  - **3.2.P.3 Manufacture**
    - 3.2.P.3.1 Manufacturer(s)
    - 3.2.P.3.2 Batch Formula
    - 3.2.P.3.3 Description of Manufacturing Process and Process Controls
    - 3.2.P.3.4 Controls of Critical Steps and Intermediates
    - 3.2.P.3.5 Process Validation and/or Evaluation

- **3.2.P.4 Control of Excipients**
  - 3.2.P.4.1 Specifications
  - 3.2.P.4.2 Analytical Procedures
  - 3.2.P.4.3 Validation of Analytical Procedures
  - 3.2.P.4.4 Justification of Specifications
  - 3 .2.P.4.5 Excipients of Human or Animal Origin
  - 3.2.P.4.6 Novel Excipients
- **3.2.P.5 Control of Drug Product**
  - 3.2.P.5.1 Specification(s)
  - 3.2.P.5.2 Analytical Procedures
  - 3.2.P.5.3 Validation of Analytical Procedures
  - 3.2.P.5.4 Batch Analyses - for **Biologics Drugs & for Pharmaceutical Drugs**
  - 3.2.P.5.5 Characterisation of Impurities
  - 3.2.P.5.6 Justification of Specification(s)
- **3.2.P.6 Reference Standards or Materials**
- **3.2.P.7 Container Closure System**
- **3.2.P.8 Stability**
  - 3.2.P.8.1 Stability Summary and Conclusions
  - 3.2.P.8.2 Post-approval Stability Protocol and Stability Commitment
  - 3.2.P.8.3 Stability Data

- **3.2.A Appendices**
  - 3.2A.1 Facilities and Equipment
  - 3.2.A.2 Adventitious Agents Safety Evaluation
  - 3.2.A.3 Excipients
- **3.2.R Regional Information**
  - 3.2.R.1 Production Documentation Human Blood Product with required supporting documents
  - 3.2.R.2 TSE Checklist with required supporting documents
  - 3.2.R.3 Product Interchangeability (Bioequivalence Study Reports)
    - BE test product uses same DS and DP manufactured at same site as proposed in application
    - Reference product used in BE study
    - If BE RP not from same DP site then bridging data (comparative dissolution) will be required
    - Batch size, manufacturing date & expiry date for test product are stated.
    - Expiry date & manufacturing site for BE RP (Reference product) are stated.
    - CoA of both test product and BE RP are provided
    - IRB & protocol approval are provided
    - Analytical validation reports are provided
    - BE inspection report is provided

- If BE study is not provided, then justification for bio-wavier is required, with supporting documents
- Lot Release Documentation (for Biological Drugs)

➢ 3.2.R.4 Blank Production Batch Record

- Yearly Biologic Product Reports (Biological Drugs only)

- **3.3 Literature References**

➢ **Bioequivalence or Comparative Dissolution Testing is discussed in 3.2.P.2.2.1 Formulation Development and 3.2.R.3 Product Interchangeability**

Module 4: (Non-clinical / Safety)

4.1 Table of Contents
4.2 Study Reports
4.2.1 Pharmacology
4.2.1.1 Primary Pharmacodynamics
4.2.1.2 Secondary Pharmacodynamics
4.2.1.3 Safety Pharmacology
4.2.1.4 Pharmacodynamic Drug Interactions
4.2.2 Pharmacokinetics
4.2.2.1 Analytical Methods and Validation Reports
4.2.2.2 Absorption
4.2.2.3 Distribution
4.2.2.4 Metabolism
4.2.2.5 Excretion
4.2.2.6 Pharmacokinetic Drug Interactions (non-clinical)
4.2.2.7 Other Pharmacokinetic Studies
4.2.3 Toxicology
4.2.3.1 Single-Dose Toxicity (in order by species, by route)
4.2.3.2 Repeat-Dose Toxicity (in order by species, by route, by duration; including
4.2.3.3 supportive toxicokinetics evaluations)
4.2.3.3 Genotoxicity
4.2.3.3.1 In vitro
4.2.3.3.2 In vivo (including supportive toxicokinetics evaluations)
4.2.3.4 Carcinogenicity (including supportive toxicokinetics evaluations)
4.2.3.4.1 Long-term studies (in order by species; including range-finding studies that cannot appropriately be included under repeat-dose toxicity or pharmacokinetics)
4.2.3.4.2 Short- or medium-term studies (including range-

finding studies that cannot appropriately be included under repeat-dose toxicity orpharmacokinetics)

4.2.3.4.3 Other studies

4.2.3.5 Reproductive and Developmental Toxicity (including range-finding studies and supportive toxicokinetics evaluations) (If modified study designs are used, the following sub-headings should be modified accordingly.)

4.2.3.5.1 Fertility and early embryonic development

4.2.3.5.2 Embryo-fetal development

4.2.3.5.3 Prenatal and postnatal development, including maternal function

4.2.3.5.4 Studies in which the offspring (juvenile animals) are dosed and/or further evaluated.

4.2.3.6 Local Tolerance

4.2.3.7 Other Toxicity Studies(if available)

4.2.3.7.1 Antigenicity

4.2.3.7.2 Immunotoxicity

4.2.3.7.3 Mechanistic studies (if not included elsewhere)

4.2.3.7.4 Dependence

4.2.3.7.5 Metabolites

4.2.3.7.6 Impurities

4.2.3.7.7 Other

4.3 List of Literature References

Module 5: (Clinical / Efficacy)

- **5.1 Table of Contents of Module 5**
- **5.2 Tabular Listing of All Clinical Studies**
- **5.3 Clinical Study Reports**
- **5.3.1 Reports of Biopharmaceutic Studies**

5.3.1.1 Bioavailability (BA) Study Reports

5.3.1.2 Comparative BA and Bioequivalence (BE) Study Reports

5.3.1.3 *In vitro-In vivo* Correlation Study Reports

5.3.1.4 Reports of Bioanalytical and Analytical Methods for Human Studies

5.3.2 Reports of Studies Pertinent to Pharmacokinetics using Human Biomaterials

5.3.2.1 Plasma Protein Binding Study Reports

5.3.2.2 Reports of Hepatic Metabolism and Drug Interaction Studies

5.3.2.3 Reports of Studies Using Other Human Biomaterials

5.3.3 Reports of Human Pharmacokinetic (PK) Studies

5.3.3.1 Healthy Subject PK and Initial Tolerability Study Reports

5.3.3.2 Patient PK and Initial Tolerability Study Reports

5.3.3.3 Intrinsic Factor PK Study Reports

5.3.3.4 Extrinsic Factor PK Study Reports

5.3.3.5 Population PK Study Reports

5.3.4 Reports of Human Pharmacodynamic (PD) Studies

5.3.4.1 Healthy Subject PD and PK/PD Study Reports

5.3.4.2 Patient PD and PK/PD Study Reports

5.3.5 Reports of Efficacy and Safety Studies

5.3.5.1 Study Reports of Controlled Clinical Studies Pertinent to the Claimed Indication

5.3.5.2 Study Reports of Uncontrolled Clinical Studies

5.3.5.3 Reports of Analyses of Data from more than one study

5.3.5.4 Other Clinical Study Reports

5.3.6 Reports of Post-Marketing Experience

5.3.7 Case Report Forms and Individual Patient Listings

5.4 Literature References

[No. F.2-2/2017(Reg-I)/DRAP.]

AAMAR LATIF,
Deputy Director (Legal Affairs).

PRINTED BY THE MANAGER, PRINTING CORPORATION OF PAKISTAN PRESS, ISLAMABAD.
PUBLISHED BY THE DEPUTY CONTROLLER, STATIONERY AND FORMS, UNIVERSITY ROAD, KARACHI.

Explanatory Notes

Section	Sub-Section	Heading
1.1		• Covering letter on the Applicant company / manufacturer / importer letter head in context to the application for the registration of the Pharmaceutical Drug Product shall be submitted, which should be dully signed by owner/ authorized person on behalf of company/ manufacturer/ importer. • An original cash deposit slip endorsed by Budget & Accounts Division, DRAP of prescribed fee as per Schedule F for specified category shall be attached therewith.
1.2		• A comprehensive Table of Contents shall contain Module and sub module heading with page number on the pharmaceutical dossier. The contents of all the Module from 1 to 5 shall be covered. Comprehensive Table of Contents is different form individual table of contents in the beginning of each Module. • Also, a complete list of all documents provided in the application dossier by Module, Section and sub-section shall be included • For hardcopy submissions, the location of each document should be identified by the volume number and tab identifiers (name of document or section heading according to PDF format)
1.3		**Applicant Information**
	1.3.1	• In this section, administrative information related to the applicant is required. • It is necessary to provide the complete particulars of the applicant, which shall contain: ▪ Name of Licensed Pharmaceutical Manufacturer / Licensed Importer having Drug Sale License by respective licensing authority ▪ Manufacturing Site Address of Pharmaceutical Company ▪ Contact details, including postal address, telephone contact number, Fax number, website and email address.
	1.3.2	
	1.3.3	The applicant must select one of the above mentioned options. A manufacturer will provide all the requisite information as per Registration procedure of Pakistan, subsequently mentioned in 1.3.4-1.3.5. ▪ An importer shall provide Drug Manufacturing License from respective Licensing authorities in the country of origin, Certificate of Pharmaceutical Product (CoPP) confirming Market authorization / Free Sale and GMP status of the Manufacturer firm in this section. ▪ c is for Contract Manufacturing as per Rule 20-A of Drugs (Licensing, Registering and Advertising) Rules, 1976.
	1.3.4	▪ To be provided if selected ***a, b or c*** of sub-section 1.3.3 (Attested copy of valid DML or Drug Sale License / renewal of DML or Drug Sale License including initial date of grant of license and subsequent renewals.
	1.3.5	▪ To be provided if selected ***a*** of sub-section 1.3.3 (Attach New Section / Area Approval, if applicable), which should be verified from the data given by the Licensing Division.)
	1.3.6	▪ List of already approved registered drugs with brand names, generic, registration number, strength, dosage form along with finished product specification and current granted price. Section / manufacturing facility wise of approved drugs shall be followed. ▪ To be provided irrespective of selection of option in sub-section 1.3.2 and mandatory for all type of Applicants.
	1.3.7	▪ The List of the name and designation of the signatory with specimen Signatures, present in any part of the Pharmaceutical Dossier.

	1.3.8	▪ Site master file contains information regarding Management, Human Resource (Technical Staff), Layout Plan, HVAC, Water Treatment Facilities, List of Analytical Equipment, List of Manufacturing Equipment, Storage Facilities (both for API and Finished Product), Fire Management and Risk Management Plan. ▪ ISO certification and any other accreditations (if applicable). ▪ Relevant SOPs dually approved by the management and Technical Head of the production facility. Each page of the Site Master File/Credential shall be dully signed by respective technical heads.
1.4		**Type of Application**
	1.4.1	▪ New Drug Product include New Molecule/ New strength / Novel dosage form/ New Formulation / New Container Closure System ▪ It is important to specify here whether the Applicant has submitted the CTD for a New Drug Product Registration or a Generic Drug Product. The information in the subsequent dossier and exemptions in provision of relevant information depends upon the type of application. ▪ In case of a New Drug Product (New Drug Product contains New Molecule/ New strength / Novel dosage form/ New Formulation/ New Container Closure System), which is not already registered in the country, the information to be provided shall be comprehensive fulfilling all the parameters of Safety, Efficacy and Quality as per international requirements endorsed and recommended by ICH.
	1.4.1	-
	1.4.2	-
	1.4.3	Specify the names of Contract acceptor along with DML, Recent GMP, Evidence of Section / facility approval from CLB and notarized copy of Contract between the parties as per Rule 20A of Drugs (L,R & A) Rules, 1976.
1.5		**Detailed Information of Drug, Dosage From & Labelling Claims**
	1.5.1	• The following necessary information shall be provided in this sub-section: (a) (Recommended) International Non-proprietary name (INN): (b) Compendial name, if relevant: (c)Chemical name(s): (d)Company or laboratory code: (e) Other non-proprietary name(s) (e.g. national name, USAN, BAN): (f) Chemical Abstracts Service (CAS) registry number:
	1.5.2	• Strength of Active ingredient should be stated clearly. In case API is in the form of salt, specify the equivalent strength of the base e.g., AAA sodium 50 mg (equivalent to AAA) etc. • For example, each tablet contains, each ml contains in case of Injectable. However, description like each ampoule / vial contains should be avoided, or in case of syrup / suspension/dry powder for suspension each 5 ml (after reconstitution) contains etc.
	1.5.3	• The proposed brand name should be justified along with an assessment / analysis report considering the LASA (Look alike and Sound alike) with specific emphasis on prefix, mid-name and suffix. • The FDA guidance namely "Best Practices in Developing Proprietary Names for Drugs" may also be consulted. An undertaking in this regard that the applicant shall be responsible to change the name in case the name after approval will resemble with already approved / registered names. • The company should also submit the approval of Trade Mark before submitting the proposed brand name.
	1.5.4	
	1.5.5	• Indicate Pharmacological class of the API with proper reference. Also, state WHO ATC code for each distinct therapeutic indication. • There should be no spacing in between the characters.

		• If WHO ATC code is not available at the time of application submission, pending status should be mentioned in this section.
	1.5.6	• Attach reference monograph from respective Pharmacopeia). This should also include the reason / justification of following the specific pharmacopoeia or manufacturer's specification in the light of Drugs (Specification) Rules, 1978.
	1.5.7	-
	1.5.8	-
	1.5.9	• Reference regulatory authorities include: United States Food Drug Administration USFDA, Health Canada, European Medicine Agency (EMA), Therapeutic Goods Administration (TGA) Australia, PMDA Japan, MHRA, Regulatory authorities of Germany, France, Switzerland, Netherlands, Austria, Denmark, Sweden and Norway, Drugs registered in at least three European Union counties.
	1.5.10	• Dosage form of applied drug shall be mentioned clearly, with complete description of a unit like "Film Coated Tablet" & "Sugar Coated Tablet" etc. • Also description of the tablet shape, dimensions, capsule color schemes, diameters, ampoule color and dimensions, granular powder for Dry Suspension, color of solution for reconstitution in amber glass bottle with Aluminum cap, etc. shall be provided.
	1.5.11	• In case, where secondary packaging is done on other site, the name of "Secondary Packager" should be added on the label after the name of manufacturer. For products intended to be marketed outside Pakistan (for Export purpose) labels should be in accordance with the requirements of importing country (for which an undertaking should be submitted by the company.
	1.5.12	-
	1.5.13	-
	1.5.14	i) Following format may be used with appropriate modifications / amendments for development of SmPC & PI. This should also include **black box warnings** & **highlights of prescribing information** in conformity with US FDA. 1. Name of Medicinal Product along with dosage forms 2. Composition of Product 3. Pharmaceutical Form 4. Clinical Particulars 4.1. Therapeutic Indications 4.1.1. Adults 4.1.2. Children & Adolescent 4.2. Posology & Method of Administration 4.2.1. Adults 4.2.2. Children & Adolescent 4.2.3. Geriatric Patients 4.2.4. Renal & hepatic impairment 4.2.5. Pregnant women 4.2.6. Method of Administration 4.2.7. Appearance of reconstituted product 4.3. Contraindication 4.4. Special warning & precautions for use 4.5. USE IN SPECIFIC POPULATIONS 4.5.1 Pregnancy 4.5.2 Paediatric Use 4.5.3 Geriatric Use 4.5.4 Renal impairment 4.5.5 Hepatic impairment 4.6. Interactions 4.5.1 Drug- Drug 4.5.2 Drug-Food

		4.5.3 Drug-Laboratory 4.7. Pregnancy & lactation 4.7.1. Pregnancy 4.7.2. Lactation 4.8. Effects on ability to drive & use machine 4.9. Undesirable effects &/or Adverse Drug Reactions 4.10. Overdose 5. Pharmacological Properties 5.1. Pharmacodynamics 5.2. Pharmacokinetics 5.2.1. Absorption 5.2.2. Distribution 5.2.3. Metabolism 5.2.4. Elimination 5.3. Clinical Pharmacology 5.4. Preclinical Safety data 6. Pharmaceutical Particulars 6.1. List of Excipeints 6.2. Incompatibilities 6.3. Shelf Life 6.4. Special precautions for storage 6.5. Nature & contents of container 6.6. Special precautions for disposal & other handling 7. Name & Address of manufacturer 8. Product Registration Number 9. Date of Registration & Last Renewal 10. Date of Last Revision of text ➢ Following format may be used with appropriate alterations / adjustments for development of PIL. 1. Brief description of medicine 2. How does it work? 3. Who should take this medicine? 4. Do not take this drug if you are taking ___ medicine or ___food. 5. What should I tell my doctor / health care provider before taking this medicine? 6. How should I take this medicine? 7. What should I avoid while taking this medicine? 8. What are possible side effects of this medicine? 9. How should I store this medicine? 10. What are the ingredients (actives / inactives) of this medicine?
	1.5.15	-
	1.5.16	-
	1.5.17	-
	1.5.18	-
	1.5.19	-
	1.5.20	-
	1.5.21	-
	1.5.22	-
1.6		**Miscellaneous Information**
	1.6.1	-
	1.6.2	-
	1.6.3	-
	1.6.4	-
	1.6.5	• COA of API. • Importation Documents of API.

Exemptions

Module	Section	Sub-section	New Drug Product	Generic Drug Product
2	2.4	Non-Clinical Overview	Not Exempted	Exempted
	2.5	Clinical Overview	Not Exempted	Exempted
	2.6	Non-Clinical Written and Tabulated Summaries	Not Exempted	Exempted
	2.7	Clinical Summary	Not Exempted	Exempted
3 (3.2.S)	3.2.S.2 Drug Substance	3.2.S.2.2 Description of Manufacturing Process and Process Controls	Not Exempted	Exempted
		3.2.S.2.3 Control of Materials	Not Exempted	Exempted
		3.2.S.2.4 Control of critical steps and Intermediates (Closed Part)	Exempted	Exempted
		3.2.S.2.5 Process Validation and/or Evaluation	Not Exempted	Exempted
		3.2.S.2.6 Manufacturing Process Development	Exempted	Exempted
3 (3.2.P)	Drug Product	3.2.P.2.2.1 Formulation Development (Pharmaceutical Equivalence through Comparative Dissolution Profile)	Not Exempted	Not Exempted
	3.2.R	3.2.R.3 Product Interchangeability (Bioequivalence Study Reports)	Exempted	Exempted
		Bioequivalence	Exempted	Exempted
4	4.2.3	4.2.3.3 Genotoxicity	Exempted	Exempted
		4.2.3.4 Carcinogenicity	Exempted	Exempted
		4.2.3.5 Reproductive and Developmental Toxicity	Exempted	Exempted
		4.2.3.6 Local Tolerance	Exempted	Exempted
		4.2.3.7 Other toxicity studies	Exempted	Exempted
5	Clinical Studies	Innovator (In-house and Published)	Not Exempted	Not Applicable
		New Drug Generic version (Published data)	Not Applicable	Not Exempted