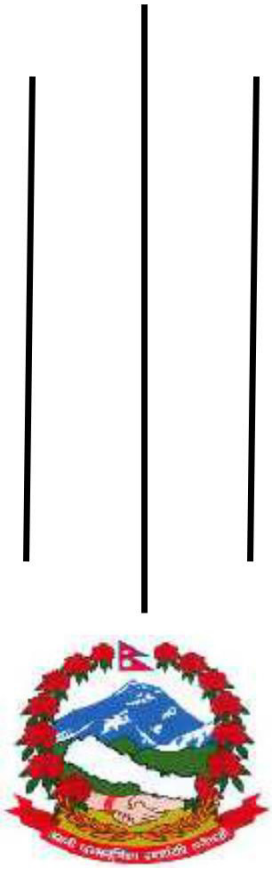
Medicine Registration Guidance

(Issued under Drug Registration Regulation 2038)



Government of Nepal

Ministry of Health

Department of Drug Administration

Bijulibazar, Kathmandu, Nepal

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Preface

Medicines registration is the process by which a national regulatory authority approves the use of a medicine in a country, having considered evidence of the Medicine's safety, quality and efficacy. It is thus primarily concerned with protecting public health. Product assessment and registration are carried out by the drug regulatory authority to ensure that the pharmaceutical products meet appropriate standards of safety, efficacy and quality. There are different divisions under Department of Drug Administration (DDA) namely Registration, Management and Inspection division. Under each division there are different sections. These sections are responsible to carry out the regular regulatory and administrative function under DDA. The development of the guideline was felt need towards better management of regulatory system. The present registration guidance document encompasses the drug registration requirements and processes applicable to all kinds of medicines manufacturing and marketing authorization, importation recommendation and different permission, pharmacy registration. The guidance document is also expected to promote accountability and transparency of the regulatory processes and facilitate communication between the regulatory authority, the pharmaceutical industries, importers, media, health care stakeholders, and the public.

Compliance to this guideline will facilitate the speedy processing and evaluation of the applications and subsequent registration of the medical products and help to promote good regulatory practice leading to better governance of the sector.

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Balkrishna Khakurel

Director General

Department of Drug Administration

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Annex-A:

- Application for recommendation letter for establishment of drug industry (Schedule-1)
- Recommendation letter for establishment of drug industry (Schedule-2)
- Application for product license (Schedule-3)
- Registration book (Schedule-4)
  Application for drug sale and distribution registration certificate (Schedule-4A^{+})
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- Drug import registration certificate (Schedule-4E)
- Product license (Schedule-5)
- Application for drug export/import recommendation letter (Schedule-6)
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- Application for license to have publicity and advertisement of drug (Schedule-10)
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- Application for license to conduct clinical trial (Schedule-12)
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Annex B: Essential contents of feasibility study report
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Annex D: Summary of product characteristics (SPC)
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Background

Tools to deliver services and regulatory compliance are required to make working procedure more transparent and efficient. Various guidance and procedures including Standards for Pharmaceutical Regulation and Care, 2000 were already developed but there is needed to collate them for easy and handy referencing. A consolidated and up-to-date guidance on manufacture, sale-distribution and import of medicines should be in place as reference document for use by all concerned parties. The regulatory process is under automation. Once completed this guidance document shall take a form of quality manual of the Department of Drug Administration (DDA) and promote good regulatory practice in the country. Appropriate and effective conduct of regulatory process is an essential prerequisite for introducing medicinal product to the market and keeping it there in compliance with legal, scientific, ethical and administrative standards, norms and other requirements.

The medicine registration guidance document is developed to complement the working procedure (Karyabiddhi) of the Department of Drug Administration, 2065.

Regulatory Framework:

Preamble of the Drug Act 1978 (2035) includes;

In order to prohibit the misuse or abuse of drugs and allied pharmaceutical materials as well as the false or misleading information relating to efficacy and use of drugs and control the production, marketing, distribution, export-import, storage and utilization of those drugs which are not safe for use by people, efficacious and of standard quality, the Drug Act 1978 (2035) is enacted and implemented throughout the country.

For the purpose of the Drug Act 1978 (2035) the '**drug**' has been defined as "*any substance to be used for the diagnosis, cure, mitigation, treatment or prevention of a disease in a human being, animal or bird or to be used to destruct vermin or insects which cause diseases in the human being, animal or bird or any substance used to affect the structure or any physiologic function of the body of a human being, animal or bird or allied ingredients or components to be used for the preparation of such substance.*"

To implement and fulfill the objectives of the National Drug Policy 1995 (2051) and the Drug Act 1978 activities related to drug production, import, export, storage, supply, sales, distribution, quality assessment, regulatory control, rational use and information flow are carried out as per the law.

To enforce and implement regulatory measures Drug Advisory Committee and Drug Consultative Council are provisioned with duties and responsibilities. Some important regulations and organizational set up are in place for the effective implementation. The main regulations include:

- Regulation on Constitution of Drug Consultative Council and Drug Advisory Committee 1979
- Drug Registration Regulation 1981,
- Drug Investigation and Inspection Regulation 1983,
- Codes on Drug Manufacturing, 1984,
- Drug Standard Regulation, 1985.
- Code on sale-distribution of drugs, 2015

All these regulatory instruments become effective only when they are efficiently enforced, evaluated and updated.

An efficient organization and procedural guidance are needed for ensuring effectiveness of regulations. The principle organization, the Department of Drug Administration (DDA) is in existence as per the clause 5 of the Act. National Medicine Laboratory (NML) is set up as a principal organization for testing quality standards of drug in the country. These organizations are entrusted with the responsibility of continually evolving a regulatory system which can effectively ensure that regulatory compliance is upheld and there is efficiency, effectiveness, transparency, clarity and equity in the functioning of the organization complying fully with the legislative and regulatory framework, and that the stakeholders would be in a position to bring about mutual benefit for all the customer and the patients.

Manufacture, sale-distribution, export and import of drugs are regulated as per the section 7, 8, 8a, 9, 10, 10a, and 11 of the Act. The subsequent sections of this guidance may be referred as requirements for obtaining recommendation letters or registration certificate or product license or marketing authorization whichever seems relevant for the applicant in pursuant to section 28 of the Drug Act 2035.

Currently DDA performs its function from the Department in Kathmandu and three of its branch offices one each in Biratnagar, Birgunj and Nepalgunj.

New organization and management, expansion of regulatory scope to regulate health technological products, sampling and testing of products from user's point and e-regulation are some of the recent initiatives undertaken by the Department.

Chapter I: Medicine manufacturing industry establishment procedure

1.1 Recommendation letter for establishment of industry

An applicant requiring to establish a pharmaceutical industry should have recommendation letter (Schedule 2) as per the Drug Registration Regulation 1981. The applicant should submit an application for this purpose with following document:

1.1.1 Application as prescribed in Schedule-1 of drug registration regulation (Annex A)

1.1.2 A detailed feasibility study report as per given format (Annex B)

1.1.3 Citizenship/registration certificate of the applicant(s) (authorized person from among board of directors)

1.1.4 Registration fee as prescribed in the Schedule-14 (Annex A) to be paid after departmental approval.

1.2 Pre-requisites for manufacture of medicines

An applicant should abide by the following conditions while constructing a pharmaceutical industry building.

1.2.1 Manufacturing plant Layout

The applicant should get approval of layout design of the proposed manufacturing premises prior to begin any construction from the Department. An applicant wishing to get layout design approval from the department should fulfill the following requirements;

- Building lay out (UDF) should be designed with the provision of F &D. Production, Quality Control, stability study, contrl sample, microbiology, store (RM &FG), Quarantine, QA (documentation, validation and qualification etc), Utilities (HVAC, water, ETP, maintenance, powersupply, air compressor, equipment store, rest rooms, canteen recreation etc), Site Planning, & BMS as per WHO-GMP guideline.
- Applicant should consider the nature of product and probable risk prior to the approval and implementation of construction work.
- Submission of detail layout design of pharmaceutical manufacturing facility should be prepared and signed and stamped by legally qualified & competent firm or personnel who have knowledge on design control of pharmaceutical manufacturing industry. The submission should qualify applicable standards like WHO, USFDA or EU or MHRA or PICS or TGA GMP guidelines and name of such applicable standard(s) should be mentioned in the layout itself. Only approved layout will be considered for regulatory purpose.

1.2.1.1 Formulation industry

1. Separate building facility for manufacture of Penicillin, sex hormone and oncology (cytotoxic) groups with AHU/HVAC system. Sex hormone will require special category of personnel.
2. Dedicated and self contained facility for cephalosporin, steroid and immunosuppressant groups.
3. Non-penicillin block may be used to manufacture external dosage forms like cream/ointment containing steroid/hormones in low strength in campaign basis. AHU system should be appropriate to implement this provision.
4. External liquid preparation can be manufactured in the non-penicillin block if a separate/dedicated line is provisioned. These products are not allowed to be manufactured at non-penicillin oral liquid section.
5. A separate self-contained, dedicated block is required for non penicillin injectable. Ear/Eye drops can be manufactured at the injectable facility. Eye/Ear drop preparation may be formulated at grade C and filled under grade A (WHO classification) provided with background grade D and B respectively.
6. Veterinary preparation consisting of ingredients for human use e.g; Albendazole may be manufactured at human product manufacturing facility but products containing ingredients for veterinary use only cannot be manufactured at the same facility. For this a self-contained & dedicated area should be provisioned.
7. Lay out plan should be unidirectional with respect to flow of man, material and processes as per the concept of WHO GMP.
8. Process area should be demarcated in line with process steps and flow and should be sufficient to carry out the intended process(s).
9. The layout design should clearly depict the clean classification of different areas as per the qualification requirement. This should include pressure differential between the interfaces and provisions of appropriate air locks. Construction materials and finishing should be consistent with these area classification and qualification requirements.
10. Design Parameters of HVAC system likes; temperature, pressure & humidity applicable for different processing & non-processing areas within the manufacturing premises should be depicted and relevant schedule and qualification requirement should support them.

11. Purified/WFI water purification distribution loop design meeting pharmacopoeial specification and qualification requirements.
12. Appropriate service floor (mezzanine or walkable floor) and pendant system should be provided to utilities like light, air conduction, water, compressed air, pharmaceutical gases including their repair and maintenance etc.
13. Additional requirements for hazardous substances such as certain steroids, cytotoxics, biological, blood products, hormones, APIs, traditional medicines, radiopharmaceuticals shall apply as per the WHO/GMP guidelines as applicable.

Self-contained area is premises which provide complete and total seggregation of all aspects of an operation, including personnel and equipment movement, with established procedures, controls and monitoring. This includes physical barriers as well as separate air handling systems, but does not necessarily imply separate buildings.

Additional clarification: *The layout design of the proposed manufacturing area should be appended with site plot, covered/uncovered land area ratio, activities being conducted in adjoining areas and environmental aspects. The design related document should be signed & approved by key personnel of the industry. The person or form responsible for preparing such engineering design jobs should be mentioned and signed thereof to take charge and responsibility of ensuring compliance with the state of art pharm. Technology and current WHO-GMP Guidelines and applicable international standards and norms.*

1.2.1.2 Repacking Industry for manufacturing a few conventional externally used products

A person or firm intending to establish a repacking industry should have valid recommendation letter as prescribed in the Drug Registration Regulation. (Same as 1.1)

NB: *Repacking is an act of dividing a bulk into small quantities and filling in a unit pack and subsequently sealing, labeling and packaging.*

Following arrangements should be provisioned to establish a repacking industry:

- Own infrastructure as described in the section 1.2.1 above.
- RCC or equivalent structure for premises/building with approved layout design (man, material, and process flow) from the Department.
- The manufacturing activities should be undertaken and supervised by person with qualification, experience and expertise in related work.
- Adequate air handling units should be installed at least with 10 micron terminal filters supplying air to the units intended for external repacking.
- Quality control activities should be carried out in-house. If this is not feasible, products can be tested from authorized drug testing laboratory as per formal agreement (contract analysis) between the company & the laboratory.
- The company should submit application in a prescribed format with details of product, label, mfg. lic, repacking procedures prior approval. The applicant should provide details as per Schedule-3 & 4 (A) of the Drug Registration Regulation 2038 in stepwise manner.

1.3 Manufacturing License

1.3.1 Prerequisites for manufacturing license

1.3.1.1 Compliance with the terms and condition (as appended with Schedule-2)

1.3.1.3 Industry registration certificate

1.3.1.4 Site visit (optional)

1.3.1.5 Approved layout of the concerned section and plant.

1.3.2 Application and issue of manufacturing license (Schedule-5)

1.3.2.1 Application as prescribed by drug registration regulation in the form of Schedule-3 signed by authorized person. To obtain the brand name in Schedule 5, the brand name (Trade mark registration) certificate (received from Department of Industry) should be submitted to DDA along with Schedule-3 otherwise generic license will be provided.

1.3.2.2 Official letter along with F & D evidence document and analytical testing capacity as specified in the recognized pharmacopoeia as per Regulation on Standard of Drug 2043 should be submitted.

1.3.2.3 If dosage form is not mentioned in official pharmacopoeia the manufacturing company should develop their own in-house method and that method should be validated by company and submit to DDA along with Schedule-3 with Summary of Product Characteristics (SPC) for the purpose of recognition by DAC.

1.3.2.4 Application should be submitted separately for different strength, and dosage form and pack size of a same active pharmaceutical entity or a combination.

1.3.2.5 In-vitro, in-vivo drug release, BE study with rationality/justification/reference should be provided for new drug, new dosage forms, modified dosage forms and those with narrow therapeutic index. (WHO BCS Classification may be referred). It is advised to refer guidance on BE requirement issued by the department (Refer to Section 2.10 and 2.11). For new molecule or combination product with already registered active pharmaceutical entities in the similar dosage form, rationality/justification/references in the form prescribed by the Department should be submitted together with Summary of Product Characteristics (SPC)-Annex-D.

1.3.2.6 Bioavailability/Bioequivalence requirement for domestic/imported medicine

I. For drugs which have low therapeutic index, low bioavailability, non linear kinetics, poor dissolution profile, variable bioavailability/bioequivalence, modified release dosage form having blood steady state concentration such as sodium valproate, valproic acid, carbamazepine, antibiotics etc, the comparative in-vivo bioequivalence test profile should be submitted during registration.

II. For drugs which are comparatively safer and have wider therapeutic index such as NSAIDs, analgesic, antipyretic and OTC products, the comparative in-vitro dissolution test profile along with real time stability data may be accepted instead of BA/BE study report.

III. For molecules having modified release API (pellets) like Omeprazole, Indomethacin, Tamsulosin etc, bioequivalence test profile from API manufacturers can be submitted. If BA/BE test profile from API manufacturer could not be made available then depending upon the nature of drugs decision will be made by DDA during registration whether to submit BA/BE test profile as mentioned in point I or dissolution test profile as mentioned in point II above.

IV. In-vivo BA/BE profile or in-vitro dissolution profile should be compared with Innovator/leading/comparator brand of the product. Leading/comparator brands should be approved from DDA.

1.3.2.7 Brand name of the products should be proposed by the applicant however the department shall check for its similarity with the other already registered brand. If the proposed Brand name, in any case, registered in the department is found SALA (sound alike and look alike) with another brand which is already registered in the department, the department shall write off the latest brand and a new brand name shall be given if relevant with the consent of the applicant. Preference will be given to brand name registered as per the existing Act. For brand naming and other labeling requirement, the applicant should refer the INN guideline and labeling guidelines issued by the department. Applicant should declare that the proposed name is not used/registered by other companies nationally and internationally to the best of their knowledge and consultation to available international sources.

1.3.2.8 A tentative format of the product manufacturing processes in line with requirement of BMR

1.3.2.9 The applicant should submit additional evidences of physical as well as technical capability for manufacture of new dosage forms or products needing specific requirement

1.3.2.10 The applicant industry should have its own full-fledged testing laboratory however only one or two tests which are not regularly done and not feasible due to high cost may be carried out from accredited laboratory with formal contract. Such test should be spelled out and contract document should be submitted.

1.3.2.11 Upon reviewing the documents submitted by the applicant for its completeness and its capability for formulation and manufacturing such dosage, the department registers the drug in the registration book (Schedule-4) and issues medicine manufacturing license as

prescribed in the form of Schedule-5 of the Drug Registration Regulation (1981) 2038.

1.3.2.12 The Inspection report of DDA (Purpose, observations, remarks, conclusion, date, Signature) should be submitted by the applicant.

1.3.2.13 Manufacturing license will be automatically cancelled if the marketing authorization Schedule-4B could not obtained for commercial purpose within 2 years of issuance of it however the manufacturer is liable to clear any due on renewal charges.

Note: The application along with relevant document thus submitted should be duly signed by the authorized personnel. The signatory should have name and the NPC Reg No. The complete application should be submitted in the form of dossier hardcopy/online with content index. Authorized person should report to the department with valid credentials and get approval for the purpose of certain skills and knowledge of manufacturing techniques. The complete dossier will be a confidential document and stay safe in DDA document repository section.

1.4 Marketing authorization (Schedule- 4B)

The dossier file of commercial batch should be submitted along with own laboratory report and other prescribed documents. On the basis of these documents DDA will provide the marketing approval letter for commercial purpose. The sample of same batch is also sent to NML for testing purpose. However, pretesting of R&D batch in NML may be made optional. This condition will be applicable only for valid GMP certified company. For those not holding valid GMP certificate will have to get tested from NML. For this provision parameters especially Primary RS, Product quality review, Analytical method/ process validation, (as per pharmacopoeial, ICH standards), building/machinaries qualification, F&D facility/capability, DMF of raw materials, ETP etc. should be monitored during marketing approval.

For those companies who have not received GMP certification and those who still have deficiencies will get marketing authorization letter only after receiving testing report of the commercial batch from NML. But this approach shall be considered only for a period of maximum 2 years.

An applicant (industry) should submit application by fulfilling following requirement to obtain medicine marketing authorization (Schedule- 4B) as per Drug Registration Regulation:

1.4.1 Application in the form of Schedule- 4 A of the Drug Registration Regulation.

1.4.2. 0, 3, 6 months' accelerated stability test report and also real time stability test report as per stability test guideline issued by the Department as applicable. Expiry/Shelf life should be based on the stability test report of three non-commercial batches as far as practicable (ICH guideline). The chromatogram of respective stability testing should be attached with the documents. The applicable stability condition is Zone IV (b).

1.4.3 A copy of method of analysis

1.4.4 Recent analytical test report for commercial batch from the National Medicines Laboratory should be submitted or NML receipt of sample submission for testing in case of products requiring longer time for test and analysis. The data of R & D or scale up manufacturing documents should be submitted during marketing approval, the size of pilot batch is minimum 1/8 of the commercial batches. On the basis of above documents and or parametric basis, DDA will issue the marketing license. For such product and other registered product PMS and sampling plan will be developed by inspection division. Sampled product will be sent to NML for test and analysis.

1.4.5 Batch manufacturing records of the commercial batch, with details of excipients, color and packaging and their test reports.

1.4.6 The product specification with complete analytical test report as per pharmacopoeial monograph (Refer Chapter I, Section 1.8).

1.4.7 A copy of valid medicine manufacturing license (Schedule-5)

1.4.8 Product samples (of commercial batch)-minimum quantity to be submitted is as follows:

- Strip/blister-one box, bottles/tubes/sachet/pouch/vials/ampoules-5units for physical evaluation only.

1.4.9 If drug is extended/sustained/prolonged release products, the invitro dissolution test should be done with comparator brand and their dissolution profile report should be submitted to DDA along with official letter. A comparator brand can be selected as per WHO referenced list or a list issued by the department for this purpose.

1.4.10 Each industry should establish own Research and Development section.

1.4.11 The package inserts of each medical product should be submitted during marketing authorization. The package inserts of Group "Ga" medicines should be in Nepali language and for other groups it can either be in Nepali or English or Both as needed.

1.4.12 Applicant should submit BA/BE study report as applicable. (Refer section 2.10 and 2.11 of Chapter II: Guideline on import registration)

Note: The labeling information on or with the product should be as per Drug Standard Regulation (Schedule-5) and as issued by the Department.

1.5 Raw Material (starting and packaging material) import recommendation letter (Schedule-7)

The medicine manufacturing industries registered in the department shall apply and receive import recommendation letter for raw material including packaging material as per the Drug Registration Regulation.

The documents required for such recommendation letter are as follows:

1.5.1 Application as prescribed in the drug registration regulation in the form of Schedule-6

1.5.2 Specification and standards in DMF format (if non pharmacopoeial product in-house specification should be submitted similar to pharmacopoeial format).

1.5.3 Copy of Schedule-5

1.5.4 Source (manufacturer/supplier/certificate of origin and release profile of modified RM, Vendor qualification)

1.5.5 R&D special import, an applicant should apply in writing, expressing the quantity required, the source (as section 1.54), standard and proposed dosage under development, and material safety data of the material.

1.5.6 For recommendation of machine/equipment/instruments importation, machineries specification, qualification, source and cost should be submitted along with proforma invoice.

1.5.7 The required quantity and specifications of packing material (primary and secondary)

1.6 Renewal of licenses, recommendation letter and certificate

1.6.1 Raw material (Schedule-7)

1.6.1.1 Application requesting renewal of Schedule-7

1.6.1.2 Original recommendation letter (Schedule-7)

1.6.1.3 Consumption/Quantity and projected requirement (Annex E)

1.6.1.4 Fee as applicable after approval.

1.6.1.5 In case of API real time stability data (ongoing) or report.

1.6.2 Manufacturing license (Schedule-5)

1.6.2.1 Application for renewal of Schedule-5

1.6.2.2 Original Schedule-5

1.6.2.3 Compliance with terms and condition of Schedule-5

1.6.2.4 Fee as applicable after approval.

1.6.3 Marketing authorization (Schedule-4 B)

1.6.3.1 Real time stability study report with statistical analysis of shelf life/expiry date as per ICH guideline/or DDA guidelines.

1.6.3.2 Commercial product sample-one unit of market presentation.

1.6.3.3 Original Schedule-4 (B)

1.6.3.4 Latest product specification with sample

1.6.3.5 Changes in price or Latest MRP approved from DDA

1.6.3.6 Report of deviation, product withdrawal and any change control made within the period.

1.6.3. 7 Annual product review during the renew of marketing authorization.

1.6.3.8 Stability chamber data logger with online computerized system print out paper, stress factors, data logger, document.

1.6.3.9 Cosumption in terms of quantity/price for quantification purpose. (Annex-G)

1.6.3.10 Declaration on ADR reporting of the product.

1.6.4 Export/Import recommendation letter (Schedule-7)

1.6.4.1 Application-Schedule-6

1.6.4.2 Schedule-5

1.6.4.3 Schedule-4 (B)

1.6.4.4 Certificate of pharmaceutical products (Annex F)

1.6.4.5 WHO-Good Manufacturing Practices certificate issued from the department

1.6.4.6 Site Master File along with copy of approved layout.

1.6.4.7 Quantity exported.

1.7 Variations (Schedule-5, 4-B, Schedule-7)

1.7.1 Application should be submitted to DDA for any variation in the certificates along with the justification for changes.

1.7.2 No changes will be made in the certificates without any valid scientific reason once it is issued.

1.8 General guidelines on test and analysis of products (both Public ad Private sector)

1.8.1 NML follows the official standard pharmacopoeia for testing. For non pharmacopoeial product, the validated analytical method should be developed by manufacturer and approved by DDA/NML (DAC) for their reliability. The traceability of method and reference standard used should also be mentioned.

1.8.2 Before sending any drug sample to the recognized laboratory for analysis sample should be submitted to DDA to obtain the registration number. The testing laboratory should include this registration number in their analytical report with complete compliance/noncompliance information. Laboratory shall report DDA the result of all registered samples tested by it. Incomplete test report will not be accepted for further processes. The analytical report should be released by laboratory as soon as possible within stipulated time defined in their work procedure. Sample risk based and parametric approach may also be followed as determined in SOP.

1.8.3 The drug testing laboratory will be periodically accreditated from NML and obtain GLP Certificate. The analytical report from non accreditated laboratory will not be accepted

for drug registration and marketing authorization purpose. Generally the laboratory must renew their accreditation or GLP certificate audited by NML once a year. The list of accreditated or non accreditated laboratory will be published in DDA website. WHO good practice guideline on pharmaceutical quality control and microbiology laboratory will be followed as the basis for accreditation or certification.

1.8.4 For registration and marketing authorization of any new molecule, new combination, modified and new dosage form product, health and new technology product, analytical report issued by NML will be required. The applicant must be responsible for making available all the required reference standard, biological standard, validated method to NML.

1.9 Quality standard and GMP certification

1.9.1 GMP certificate or CPP from DDA will be issued only if there is no critical deficiency. If minor deficiencies are found during audit it should be addressed and CAPA should be made before submitting audit report. If not possible during audit the deficiencies can be corrected after audit and CAPA report should be submitted to DDA for GMP certification processes. During GMP recertification, Annual Product Review, product complaint and recall, primary reference standard, microbiology with clean room, ETP, validation and qualification (Facility, utility, machines), real time data, F & D, BE study, RM DMF/REMS/ADR reporting, price comparability/competitiveness SPC of the product, product performance like aspects shall be monitored. The company who does not have GMP certification/Recertification will not be issued any new manufacturing licenses and marketing authorization till certification. Certificate and license of critical products (Group Ka & Kha) may be suspended or may not be renewed.

1.9.2 The manufacturer should apply for recertification within 6 months from their GMP certification expiration. If the applicant is not certified with GMP compliance within this period, the certificate will automatically cancelled and will automatically cancelled and the company cannot claim WHO/GMP certification in their product, label, any form or format. While issuing new product license, new manufacturing license, new market license, raw material import license, the department will take into account their status of GMP certification and validity. Similarly, the foreign company product will not be

registered, renewed if GMP and COPP is not recertified and their product also will not be imported. The notification will be published in DDA website.

1.10 Sale-distribution of registered products and good practice certification

The manufacturer or importer &/or their distributor shall not sale or distribute their product to any firm or business outlet or person who is not a valid wholesaler or retailer as per the provision of Drug Act 2035. Only registered product can enter into distribution chain. Integrity of distribution chain shall be maiantained to prevent entry of SSFFC into the distribution chain. Storage condition and traceability of the product shall be maintained during transportation, warewhousing, storage and use. Risk evaluation and mitigation strategy (REMS) and risk-based approach shall be applied in the distribution, dispensing and use of the products.

1.11 Certificate of Pharmaceutical Products (CPP) Annex-F

An industry shall receive certificate of pharmaceutical products from the department if it wishes to export drug products into the international commerce. Following document should be submitted for issuing CPP from the department:

1.11.1 Current WHO-GMP certificates issued from the department

1.11.2 Process validation report of the concerned product(s)

1.11.3 Validated Method of analysis of the concerned product(s)

1.11.4 A copy of Drug marketing authorization certificate

1.11.5 Updated Site Master File (SMF)

1.11.6 Approved layout

ANNEX-I

Annex-A:

- Application for recommendation letter for establishment of industry (Schedule-1)
- Recommendation letter for establishment of industry (Schedule-2)
- Application for product license (Schedule-3)
- Registration book (Schedule-4)
- Application for drug sale and distribution registration certificate (Schedule-4A)
- Drug sale and distribution registration certificate (Schedule-4B)
- Product license (Schedule-5)
- Application for drug export/import recommendation letter (Schedule-6)
- Drug export/import recommendation letter (Schedule-7)

Annex B: Essential contents of feasibility study report

Annex-C: Registration and renewal fees (Schedule 14)

Annex D: Summary of product characteristics (SPC)

Annex E: Raw Material consumption report

Annex F: Certificate of Pharmaceutical Products

Annex G: Quality of a product produced and imported during the reported FY period.

ANNEXES

Annex-A:

- Application for recommendation letter for establishment of industry (Schedule-1)
- Recommendation letter for establishment of industry (Schedule-2)
- Application for product license (Schedule-3)
- Registration book (Schedule-4)
- Application for drug sale and distribution registration certificate (Schedule-4A)
- Drug sale and distribution registration certificate (Schedule-4B)
- Product license (Schedule-5)
- Application for drug export/import recommendation letter (Schedule-6)
- Drug export/import recommendation letter (Schedule-7)

Schedule-1

(Relating to Sub-rule (1) of Rule 3)

Application for recommendation letter of establishment of drug industry

The Administrator,

Department of Drugs Administration.

Subject: Request for recommendation letter for establishment of drug industry.

Sir,

Whereas, I/we intend to establish the following drug industry; Now, therefore, I/we make this application, affixing a stamp of one rupee hereto, and setting out the following details, to obtain a recommendation letter for the same.

1. Proposed drug industry's:
   (a) Name:
   (b) Place where it is established: (Also mention the name and ward number of the District and Municipality or Village Development Committee)
   (c) Estimated capital and source of that capital:
   (d) Where a preliminary study report carried out on the establishment is attached or not:
   (e) Whether a sketch and map of the plan also showing the area where the industry is to be established is attached or not:

S.N.	**Of the drug to be manufactured by the proposed**				**Remarks**
	Name	System (et out whether it is Allopathic , Homeopathic, *Ayurvedic,* Unani etc.	Group or sub-group	Composition (set out whether it is a tablet, injection, capsule etc.)	

2. For the manufacturing of drug by proposed industry:

(a) Description of required raw materials and source thereof:

(b) Whether a machine is required or not, if so required, possible details thereof:

(c) Of the required house or building:

(1) Whether sketch and map is attached or not:

(2) What will be its composition:

(3) Whether outside environment will be polluted, neat and clean or otherwise, mention it:

(4) Whether the air can pass through the room or not: Mention why and for what reasons such room has to be so built that the air can or cannot so pass through it:

(5) Whether the sun or light can enter the room or not: Mention why and for what reasons such room has to be so built that the sun or light can or cannot so enter it:

Applicant's:

Signature:

Name, surname:

Address:

Date:

Schedule-2

(Relating to Sub-rule (2) of Rule 3)

Government of Nepal

Ministry of Health Department of Drugs Administration

Recommendation letter for establishment of drug industry

This recommendation letter is hereby issued, setting out the following matters, for the establishment of the following drug industry, subject to the Drugs Act, 2035 (1978) and the Drugs Registration Rules, 2038 (1981).

1. Of the drug industry recommended for establishment:
   (a) Name:
   (b) Place where it is established:
   (c) Estimated capital:
2. Of the drug that can be manufactured by the drug industry after having obtained the product license:

Of the drug				Remarks
Name	System	Group of sub-group	Composition	

3. Recommendation letter receiving person's:
   (a) Name and surname:
   (b) Address:
4. Validity period of recommendation letter:

   Signature of the recommendation letter receiving person:

Date:

Recommendation letter issuing officer's:

Signature:

Name and surname:

Designation:

Date:

(The matters to be written on the back side of this recommendation letter)

Renewal of the recommendation letter

Recommendation letter					
Validity extension period		Renewing Officer's signature and date	Renewal fees	Department's Seal	Remarks
From	To				

Schedule-3

(Relating to Sub-rule (1) of Rule 4)

Application for product license

The Administrator,

Department of Drugs Administration.

Sir,

Whereas, in order to manufacture the following drugs by the following drug industry already established after having obtained the following recommendation letter and license, I/we intend to obtain the product license by having the drugs registered;

Now, therefore, I/we have made this application, affixing a stamp of one rupee hereto, to obtain the product license. The duplicate copies of the recommendation letter and license are attached herewith.

1. Serial number of the recommendation letter of that Department and date thereof:
2. Date of license obtained from-----Department:
3. Drug industry:
   (a) Name:
   (b) Place of establishment: (Also mention the name and ward number of the district, Municipality and Village Development Committee.)

Drug to be manufactured										
S.N.	**Name**	**System**	**Group or sub-group**	**Composition**	**Type of kind**	**Colour**	**Weight per unit**	**Active ingredient**		**Disease to be cured from consumption**
								Name	**Quantity**	

5. Whether the required materials related with the manufacture of drugs are available in an adequate quantity or not:

Applicant's:
Signature:
Name and surname:
Address:

Date:

Schedule-4

(Relating to Sub-rule (2) of Rule 4-----)

Registration book

The following drug has been registered as follows for its manufacture,subject to the Drugs Act, 2035(1978) and the Drugs Registration Regulation, 2038(1981).

Registration No	Of the drug										
	Name	System	Group or sub-group	Composition	Type or kind	Colour	Active ingredient		Disease to be cured from its consumption	Name manufacturing company and country	Registering officer's signature and date
							Name	Quantity			

Deleted by the First Amendment.
Inserted by the First Amendment.

Schedule-4A

(Relating to Sub-rule (1) of Rule 4)

Application for drug sale and distribution registration certificate

The Administrator,
Department of Drugs Administration.

Dear sir,

Whereas, the drug as referred to in the product license, bearing number....., issued by that Department is appropriate for sale and distribution; Now, therefore, I/we have made this application, setting out the following details and affixing a stamp of five rupees hereto, to obtain the sale registration certificate, pursuant to Sub-rule (2) of Rule 4A. of the Drugs Registration Rules, 2038(1981).

1. Drug of which sale registration certificate is intended to be obtained:
   (a) Name:
   (b) System:
   (c) Group or sub-group:
   (d) Composition:
   (e) Active ingredient and quantity (per unit):
   (f) Expiry date:
   (g) Pharmacopoeia standard:
   (h) Retail price:
   (i) Laboratory having conducted analysis and test, and the analysis and test report issued by that laboratory and date thereof:

Inserted by the First Amendment.

2. Other details:

(a) Whether the product specification setting down the size, color, measurement or weight, taste and flavor of drug, method of packing and details mentioned in its label is attached or not:

(b) Whether the method of analyzing and testing the drug is attached or not:

(c) Whether the label, cartoon and sample of drug is attached or not:

Applicant's:

Signature:

Name and surname:

Address:

Date:

Schedule-4B
(Relating to Sub-rule (2) of Rule 4A.)

Government of Nepal

Ministry of Health Department of Drugs Administration

Drug sale and distribution registration certificate

Sale and distribution registration certificate number:

Sir,

The sale and distribution registration certificate has been issued for the following drug, pursuant to Sub-section (1) of section 8A of the Drugs Act, 2035(1978) and Sub-rule (2) of Rule 4A of the Drugs Registration Rules, 2038 (1981).

1. Of the drug:
   (a) Name:
   (b) System:
   (c) Group and sub-group:
   (d) Composition:
   (e) Active ingredient and quantity (per unit):
   (f) Expiry date:
2. Product specification (certified copy is attached):
3. Fees received for the sale registration certificate: Rs.---
4. Validity period of certificate:

Certificate receiver's:
Name and surname:
Address:
Signature:
Date:

Certificate issuing officer's:

Signature:

Name and surname:

Designation:

Date:

Inserted by the First Amendment.

Note bene: Prior approval has to be obtained from the Department if any alteration is to be made in the product specification and label submitted to the department and in the above-mentioned details:

Amendment to the certificate

Date	Details o Amendment

Renewal

Period of extension of validity		Fees	Officer's signature	Remarks
From	To			

Schedule-5

(Relating to Sub-rules (2) and (3) of Rule 4)

Government of Nepal

Ministry of Health

Department of Drugs Administration

Serial number:

Product license

This product license is hereby issued setting out the following matters, allowing the-------industry already established in -------, based on the following recommendation letter and the license, subject to the Drugs Act, 2035(1978) and the Drugs Registration Rules, 2038(1981).

1. Serial number of the recommendation letter of this Department and date thereof:
2. Date of license obtained from-----Department:
3. Drug industry:
   (a) Name:
   (b) Place of establishment: (Also mention the name and ward number of the district, Municipality and Village Development Committee.)

S.N.	Drug licensed for Manufacture									Remarks
	Registration No	System	Group or sub-group	Composition	Type or kind	Colour	Weight and measurement per unit	Active ingredient		
								Name	Quantity	

4. Product license obtainer's:
   (a) Name and surname:
   (b) Address:
5. Fees received for the issuance of product license: Rs.---
6. Validity period of product license:

Product license receiver's:

Signature:

Date:

Product license issuing officer's:

Signature:

Name and surname:

Designation:

Date:

(The matters to be written on the reverse side of this product license)

Renewal of the product license

Products license				Department's Seal	Remarks
Validity extension period		Renewing officer's signature and date	Renewal fees		
From	To				

Schedule-6

(Relating to Sub-rule (1) of Rule 5)

Application for drug export/import recommendation letter

The Administrator,
Department of Drugs Administration.

Sir,

Whereas, I/we intend to obtain a recommendation letter to export/import the following drug;

Now, therefore, I/we have made this application, setting out the following matters and affixing a stamp of one rupee hereto, to obtain the recommendation letter.

Drug to be exported/imported							
S.N.	Name	System	Group or sub-group	StandardComposition	Active ingredient's		Name of manufacturing company and country
					Name	Quantity	

Applicant's:

Signature:

Name and surname:

Address:

Date:

Schedule-7

(Relating to Sub-rule (2) of rule 5)

Government of Nepal

Ministry of Health

Department of Drugs Administration

Drug export/import recommendation letter

This recommendation letter is hereby issued, setting out the following matters, to export/import the following drug, subject to the Drugs Act, 2035(1978) and the Drugs Registration Rules, 2038 (1981).

1.

Drug recommended to be exported/imported							
S.N.	Name	System	Group or sub-group	StandardComposition	Active ingredient's		Name of manufacturing company and country
					Name	Quantity	

2. Recommendation letter obtainer's:

   (a) Name and surname:

   (b) Address:

3. Validity period of recommendation letter:

4. Recommendation letter receiver's:

Signature:

Date:

Recommendation letter issuing officer's:

Signature:

Name and surname:

Designation:

Date:

(The matters to be written on the reverse side of this recommendation letter.)

Renewal of the recommendation letter

Recommendation letter		Renewing officer's signature and date	Renewal fees	Department's Seal	Remarks
Validity extension period					
From	To				

Annex B

Essential contents of feasibility study report

- The name of the person/firm responsible for carrying the feasibility studies both technical and financial part should be provided along with their qualification, experience and expertise (full CV) and the references used in the report.
- Physical infrastructure including land, road accessibility, electricity, building, equipment, and utilities of the proposed venture as per the type and nature of dosage form. The standards of building material and equipment, plant layout and finishes should be inconsistent with WHO-GMP requirement
- Financial analysis including, BEP, IRR. Sensitivity analysis, NPV, payback period, loan repayment , working capital required, fixed asset investment financial analysis shall be presented with 10 years projected period with relevant assumption
- Technical aspects including, list of finished products/presentation/price/reference personnel (category, qualification, experience/skill, required number), process flow diagram, material specification/source and vendor requirement GACP/GSP/GDP etc, quality management system including chemical reference material, QA, QC, and environment consistent with WHO GMP Guideline.
- In case of traditional medicines the following should be provided:
  i) API name (Scientific and Vernacular), reference and sources: collection/procurement/transportation/strategy; identification and QC testing parameters; supplier/vendor qualification; reference specimen/marker compound; approval/rejection criteria; storage requirement and method etc.
  ii) Reference test for classical formulations/products and clinical trial report/ reference document/ reference product in case of proprietary product/formulation and patent registration certificate in case of patent product, marketed products of similar nature and market size.
  iii) Labeling sample consistent with the requirement of Drug Act 2035.

- A Tentative format for the report is as follows:

  Front page

  Project Highlight

  1. Introduction
  2. Objectives
  3. Market Analysis
  4. Existing market Structure
  5. Market Strategies
  6. Technical Aspects
  7. Quality Assurance and Quality control
  8. Engineering and maintenance
  9. Project Management
  10. Land Building and infrastructure
  11. Financial Explanation
  12. Conclusion on feasibility status based on technical and financial sensitivity analysis.

  Annexures

  I. Financial Structure

  II. Fixed Assets Investment

  III. Annual Operating Cost

  IV. Break Even Point Calculation

  V. Working Capital Estimation

  VI. Sales Revenue

  VII. Long Term Loan Repayment

  VIII. Annual Production Cost

  IX. Profit and Loss Statement

  X. Cash Flow Projection

  XI. Balance Sheet

  XII. Calculation of Payback Period

  XIII. Financial Ratio

XIV. Cash Flow for Discounting

XV. Net Present Value

XVI. Sensitivity Analysis

XVII. List of Equipments-Utilities, manufacturing, quality control purposes

XVIII. Raw Materials & Packaging Materials with applicable pharmacopoeial standards XIX. Process flow diagram, QC specification and relevant references

XX. List of documents referred and consulted with details for verification.

Annex-C Registration Renewal and fees (Schedule 14)

Annex C: Schedule 14

Annex C (1): Sample required for submission of application for analytical services to National Medicines Laboratory (NML)

Annex C (2) Medicine analysis fee structure of National Medicine Laboratory

Schedule-14

(Relating to Sub-rule (2) of Rule 3, Sub-rule (2) of Rule 4, Sub-rule (2) of Rule 4A, Sub-rule (3) of Rule 4B, Sub-rule (2) of Rule 5, Sub-rule (2) of Rule 6, Sub-rule (2) of Rule 7, Sub-rule (2) of Rule 8, Rule 9, and Sub-rule (2) of Rule 10)

Fees			
SN	**Description**	**Initial fees Rs.**	**Renewal fees Rs.**
1.	For the recommendation letter for the establishment of an industry pursuant to Sub-rule (2) of Rule 3.	200/-	-
2.	For the product license pursuant to Sub-rule (2) of Rule 4 .	200/-	50/-
3.	For the sale and distribution registration certificate pursuant to Sub-rule (2) of Rule 4A.	100/-	50/-
4.	For the import registration certificate pursuant to Sub-rule (2) of Rule 4B.	200/-	100/-
5.	For the export/import recommendation letter pursuant to Sub-rule (2) of Rule 5.	200/-	100/-
6.	For the shop registration certificate pursuant to Sub-rule (2) of Rule 5:		
	(a) Capital not exceeding fifty thousand rupees	200/-	100/-
	(b) Capital from fifty thousand one rupees to one hundred thousand rupees	500/-	250/-
	(c) Capital from one hundred thousand one rupees to five hundred thousand rupees	1000/-	500/-
	(d) Capital exceeding five hundred thousand one rupees	2000/-	1000/-
7.	For the publicity and advertisement license pursuant to Sub-rule (2) of Rule 7:		
	(a) For the license for publicity and advertisement	5000/-	2500/-

Fees			
SN	**Description**	**Initial fees Rs.**	**Renewal fees Rs.**
	through television		
	(b) For the license for publicity and advertisement through printing or other media	2000/-	1000/-
8.	For the clinical trial license pursuant to Sub-rule (2) of Rule 8.	5000/-	-
9.	For duplicate copies of license, certificate and recommendation letter pursuant to Sub-rule (2) of Rule 10.		
	(a) For the first time	50/-	-
	(b) For the second time or each time more than that	100/-	-

Annex C (1)

Sample required for submission of application for analytical services

to

National Medicines Laboratory (NML)

The following is the requirements for submitting a sample for analysis for Marketing Authorization.

A. Quantity of samples required

S. No.	Particular	Quantity
1.	Tablets/ Capsules	100 Tab/Cap
2.	Dry Syrup	15 bottles
3.	Liquid/Tube	15 bottles/tube
4.	Powder (Oral and External)	25 Pkt
5.	Injection/Solution/Suspension	
	Less than 10 ml	40 vials
	10 ml to less than 100 ml	20 vials
	100 ml or more	16 vials/bottle

* The quantity mentioned here may slightly vary on case to case basis as required by the parameters to be tested and type of analyte.

B. Documents Required

1. Product Specification/Protocol
2. Analytical Report (In-house)
3. Method of Analysis
4. Stability test report (Accelerated)
5. Reference standard

Annex C (2)

MEDICINE ANALYSIS FEE STRUCTURE OF NATIONAL MEDICINE LABORATORY

ANALYSIS TEST	FEES (Rs.)
Test for Finish Product	
A. Each medicine + one active chemical for simple test	800
B. For added each active chemical +A	400
C. Dissolution test for different stage	
D. For A+ 1st added active chemical	400
E. For each added active chemical	
F. For the content uniformity addition in A	1400
G. For pyrogene or LAL test addition in A	700
H. For Sterility test addition in A	600
I. For vaccination test	1800
Other analysis tests for each n every sample:	
A. Chemical Analysis	
1 Quality test for each	100
2 Quality test for each	500
B. Physical/pharmacognoical test	**600**
C. Micro-organism bioassay and	
1. Analyzation test + A	300
2. Bioassay analysis	800
3. Every quality test with the use of animal	800
4. Test with use of more animal	800
5. Mice or for guinea pig or 3 rabbit	800
Scientific tools/equipments used for test	
1. Use of UV/visual with standard and Disintegration with 6 tablets	250
A. IR spectrometer, gas chromatography	400
B. HPLC method	800
Report fees	
2. Report processing without investigation or	
A. For without analysis for any product	100
B. Attested for each test certificate	50

* The fees or charges are applicable as per revision from time to time.

Annex D

Additional information required to register new molecule

The following information along with this form is submitted for the registration of new molecule previously not registered and/or not included in recognized Pharmacopoeias.

Name of the product (brand & generic): ……

Name & address of the Manufacturer: ……

1	Summary of Product Characteristics (SPC) as per guidelines of European countries or WHO (section 1 to 12) www.**ema.europa.eu/**pdfs	Remarks (√) or (x)
2	Summary of the information containing the following: a) Where and when the drug had been introduced including the patent status (if relevant). b) Name of the countries where the drug is marketed. c) List of the other drugs (already marketed) having similar indication (s). d) Therapeutic benefits and risks over the existing drugs listed in section C above. e) Price comparison with other available drugs listed in section C above. f) Comparative adverse drug reaction and safety profile (within the members of the same therapeutic group) g) Summary SPC sections 4 (clinical particulars) and 5 (pharmacological properties). h) Relevant references (unbiased publication, trial reports)	

I hereby certify that the above-mentioned documents have been submitted.

Signature:
Name:
Designation
(Stamp of Manufacturer) Manufacturer
Address:
Phone no, Fax, e-mail:

Note:

1. *The documents should be signed by authorized person and stamp of the manufacturer / importer should be in each and every page.*

2. *Domestic industry will be encouraged to produce new molecules through fast track processing with respect to raw material recommendation, product license, laboratory testing of trial products considering the applicant's R&D capacity (technical know how, manpower expertise& strength, traceability and full testing facilities including related substances).*

Annex E

Consumption report

Fiscal year:

Name and pharmacopoeial reference of raw material

……
……

Import			**Used in**			**Total consumption Kg**	**Balance quantity Kg**
Date	**Source**	**Quantity (Kg)**	**Product**	**Batch Number**	**Quantity (Kg)**		

Name of applicant:

Signature:

Stamp:

Date:

Annex F

Certificate of a pharmaceutical product

No. of certificate

Exporting (certifying country):

Importing (requesting country):

1. Name and dosage form of the product:

1.1. Active ingredient(s)[2] and amount(s) per unit dose[3]:

For complete composition including excipients, see attached[4]:

1.2. Is this product licensed to be placed on the market for use in the exporting country?[5] (yes/no)

1.3 Is this product actually on the market in the exporting country?

If the answer to 1.2. is yes, continue with section 2A and omit section 2B.

If the answer to 1.2 is no, omit section 2A and continue with section 2B[6]:

2.A.1. Number of product licence[7] and date of issue:

2.A.2. Product licence holder (name and address):

2.A.3. Status of product licence holder[8]: (Key in appropriate category as defined in note 8)

2.A.3.1. For categories b and c the name and address of the manufacturer producing the dosage form is[9]:

2.A.4. Is a summary basis for approval appended?[10] (yes/no)

2.A.5. Is the attached, officially approved product information complete and consonent with the licence?[11] (yes/no/not provided)

2.A.6. Applicant for certificate, if different from licence holder (name and address)[12]:

2.B.1. Applicant for certificate (name and address):

2.B.2. Status of applicant: (Key in appropriate category as defined in footnote 8)

2.B.2.1. For categories (b) and (c) the name and address of the manufacturer producing the dosage form is:[9]

2.B.3. Why is marketing authorization lacking? (not required/not requested/under consideration/refused)

2.B.4. Remarks[13]:

3. Does the certifying authority arrange for periodic inspection of the manufacturing plant in which the dosage form is produced? (yes/no/not applicable)[14]

If not or not applicable, proceed to question 4.

3.1. Periodicity of routine inspections (years):

3.2. Has the manufacture of this type of dosage form been inspected? (yes/no)

3.3 Do the facilities and operations conform to GMP as recommended by the World Health Organization?[15] (yes/no/not applicable)[14]

4. Does the information submitted by the applicant satisfy the certifying authority on all aspects of the manufacture of the product[16]: (yes/no?)

If no, explain:

Address of certifying authority:

Telephone:

Fax:

Name of authorized person:

Signature

Stamp and date

Note: Documents referred on the superscription 1-16, refer WHO model certificate of pharmaceutical products

(Refer:http://www.who.int/medicines/areas/quality_safety/regulation_legislation/certification/modelcertificae/en/)

Annex G

Production report

(Price and Quantity)

Fiscal year:

Name of the product, composition and reference

……
……

Production			**Price**	**Total Units (No. and quantity)**
Batch No.	**Date**	**Unit of production (Bottle/strip/cartoon/tube)**		**Million tab/cap/bottle**
				(Equivalent Kg)

Name of applicant:

Signature:

Stamp:

Date:

Chapter II: Import registration

2.1 Introduction

Since the promulgation of Drug Act 2035 and formation of rules there under, the import regulation begun in an improved manner in Nepal. Import of majority of products came under book and companies manufacturing them were listed. The drug registry now became source of authentic registration information and illegal import became under control. Over 7000 brands (including branded generics) have been in the drug registry from the import mode and about 300 foreign companies are listed and approved for drug import into the country.

The framework law of drug import regulation is more than 35 years old. Since then, there have been tremendous changes in regulatory concepts and practices. It is now being regarded as a science. Thus regulation of drug import has become a science and is dynamic subject to rapid development in drug, therapies and dosage form concepts. With changes in concept, there is inherent need of improvement in drug laws, procedures and practices. The Drug Act was revised twice during this period. Rules made under the act need further clarity on the purpose and understanding through guidance in relevant areas. In the past, the Department of Drug Administration (DDA) has issued various directives through Government of Nepal's decision to streamline the drug import regulation.

Few such interventions include:

- Compulsory requirement of WHO-GMP certification of the company for concerned drug product intended to be imported in Nepal
- On-site inspection prior to drug product registration for compliance of WHO-GMP guidelines by the company of non-Stringent Regulatory Authority (nSRA) countries
- Compulsory requirement of Notarized copy of Certificate of Pharmaceutical Products (CPP) as prescribed by WHO
- BA/BE report of modified release dosage forms
- Clinical study report on safety and efficacy of new drug
- Drug product specification with quality control parameter, analytical methods and reports with the drug registration application
- Summary Product Characteristics (SPC) requirement for new drug products registration

Drug product registration and issuing recommendation letter to importer has been improved since the beginning, however the overall drug evaluation capacity and content is not up to the international standards. It is even not as per with that of WHO recommended standards. Thus, improvement on the part of guidance document for drug import regulation is must to safeguard the public health and ensure quality, safety and efficacy of drug product to the patient. The current guidance is intended to make import regulation transparent, predictable, evidence-focused and efficient and handy for the regulatory staff as well as those concerned with drug importation activities.

2.2. Important legal provisions on registration

Following provisions are made for registration regulation of medicines for import in the Drug Act 2035:

SN	Ref. Section or Clause of the Act	Provisions
i	Drug Act 2035 clause[8.(ka]:	Provisions the requirement of drug registration as prescribed prior to import
ii	Drug Act 2035 clause[9]:	Provisions the requirement of drug import recommendation as prescribed
iii	Drug Act 2035 clause [11]:	Provisions the validity and renewal of drug import licenses and recommendation letter. Such licenses and recommendation letter certificate remain valid for two years for the first time, should renewed within thirty five days from the date of expiration every year, can be renewed within three months of expiration upon payment of amount prescribed as fine, but remain invalid if not renewed within three months of expiration
iv	Drug act 2035, section-5, clause [12,13,14,15,16,17,18 and 19]:	Provision the required standard of drug to made available for use in Nepal.
v	Drug act 2035 section-6, clause [20, 21..]:	Provision the power to inspect and investigate on drug import, sales, distribution, manufacture and sales of medicines for public use.
vi	Drug Act 2035 section-7, clause 25:	Provisions the power to the government of Nepal prohibit, manufacture, sales-distribution, storage**,** importation, transportation and use.
vii	Drug Act 2035 section-7, clause 29:	Provisions to restrict act of adulteration, counterfeiting or selling substandard and harmful medicines for any treatment or use.
viii	Drug Act 2035 section-7, clause 30:	Provisions of prohibition of sales and distribution of expired drug
ix	Drug Act 2035 section-7, clause 31:	Provisions for requirement of permission as prescribe by the department for conducting clinical trials on patient or other person for the use of new drug.
x	Drug Act 2035 section-7, clause [34, 35]:	Provision for penalty and fines for offences if proved by the court of law

Following important provisions are made in relevant rules under the Drug Act 2035:

SN	Regulation ,Rule	Provisions
i	Drug Registration Rule 2038, rule(4-B):	Provisions the requirements for acquiring Drug Registration license(as Schedule-4E)
ii	Drug Registration Rule 2038, rule(5):	Provisionsthe requirements for acquiring drug import recommendation letter (as Schedule-7)
iii	Drug Registration Rule 2038, rule(7):	Provisions the requirements for acquiring permit for advertising drug product.
iv	Drug Registration Rule 2038, rule(8):	Provisions the requirements for acquiring permit of conducting clinical trial for new drug use.
v	Drug Registration Rule 2038, rule(9):	Provisions the requirement for fees/revenues to acquire various permits, recommendation letter, licenses and certificates as prescribed in Schedule 14 of the rule.
vi	Drug Registration Rule 2038, rule(10):	Provisions to provide duplicate copy of the licenses, recommendation letter, permits and certificate issued by the department
vii	Drug Registration Rule 2038, rule (11):	Provisions the duty of those beholding licenses, permits, recommendation letter of certificate duly issued by the department to observe codes issued by the Department.
viii	Drug Standards rule 2043, rule [3.4.5]:	Define the official standards applicable for drug in Nepal. The Nepalese official compendia being the official standards for drug and in its absence Schedule-1 of the rule defines the official compendia for drug standards applicable., these are ; Ph.Int, Ph.Eur, IP, BP, USP, The pharmacopoeia of Russian confederation, JP, IPC , BPC, and US-NF
ix	Drug Standards rule 2043, rule [8]:	Provisions to provide compensation in case any person inflicted with harms, death following administration of the medicine. It defines various health related harms or death verses compensation liable to be paid to the person near heir
x	Drug Standards rule 2043, rule [9]:	Provisions for the requirements to furnish deed of guarantee from the manufacturer (applies for those intend to export to Nepal)
xi	Drug Standards rule 2043, rule [12 and 13]:	Provisions the need to label and package insert as prescribed in Schedule-5 and 6 of the rule on the container of the medicine. Labelling in Nepali and English are required. It may be in languages as approved by the Government of Nepal

2.3. Framework laws and document on import registration

i. Drug Act 2035
ii. Drug Registration Rule 2038
iii. Drug Standards Rule 2043
iv. Guidance document circulars and official communiqué issued from time to time by the Department

2.4. Procedural guideline

(Supplementary guidelines and requirement approved by the Government of Nepal (Secretary Level) decision dated 2071.02.26 as in Annex- 1 is currently valid wherever applicable until further notice)

2.4.1 Procedure to get approval of manufacturing company

a. Pharmaceutical company

2.4.1.1 Any person intended to import drug in Nepal from a new manufacturing company needs to apply for approval of the company with following documents:

i) Application by the company (with intention and purpose) on its own letterhead.
ii) Letter of authority to the importer issued by the responsible person of the company.(refer to *Annex-2*)
iii) Site Master File (*as per PICS guidelines*)
iv) Up to date manufacturing license.
v) List of products intended to be registered in Nepal.
vi) Letter of warranty (*refer Annex-3*).
vii) Latest GMP internal audit report.
viii) Photocopy of firm registration as wholesaler (*of Nepalese importer*).
ix) A complete dossier of one product intended to register (*as minimum*).
x) Approval letter from the Department on WHO-GMP compliance (*applicable for non SRA, Non-UN prequalified product and company*)
xi) Risk evaluation and mitigation strategy including PV and post marketing surveillance

b. Vaccine and Biological company

2.4.1.2 Any person intended to import vaccines, sera, blood and blood products and other biologicals manufactured by a new manufacturing company into Nepal needs to apply for approval of the company with following documents:

i. Application by the company (with intention and purpose) on its own letterhead.

ii. Letter of authority to the importer (Nepalese owner of a drug wholesale form) issued by the responsible person of the company.(*refer to Annex-2*)

iii. Site Master File (as per PICS guidelines)

iv. Up to date manufacturing license.

v. List of products intended to be registered in Nepal.

vi. Letter of warranty (*refer to Annex-3*).

vii. Latest GMP internal audit report.

viii. Photocopy of firm registration as wholesaler (*of Nepalese importer*).

ix. A complete dossier of one product intended to be imported to Nepal.

x. Approval letter from the Department on WHO-GMP compliance (*not applicable for SRA, WHO-PQed product*)

xi. Risk evaluation and mitigation strategy (*PV and post marketing surveillance*)

2.4.1.3 If the company is SRA approved or UN prequalified, upon evaluation of these documents, the Departments may approve and communicate in writing to the company for registration of its intended product.

2.4.1.4 If it is not SRA approved, and non UN-prequalified company then the company shall be scheduled for inspection provided it manufactures drug product applicable for import registration in Nepal [*Please refer the notice published on **2071.04.01, in Gorkhapatra** daily for class and type of products applicable for import registration in Nepal*]

2.4.1.5 In case of guidance no 4.1.4 above, the company inspected should have acceptable compliances of WHO-GMP guidelines. In this scenario, the company shall be approved along with evaluation of the documents listed in guidance no 4.1.1 or 4.1.2 above, whichever applicable.

2.4.1.6 The approval letter is issued by the Department in favour of the applying company.

2.4.2 Procedure to obtain product license (Schedule –4E) and import recommendation letter (Schedule-7)

a. Pharmaceutical products

2.4.2.1 An applicant shall apply for drug product registration and import recommendation letter with the following documents as prescribed in the drug registration rule 2038 and directives issued by the Department from time to time:

- **i.** An Application in the form of *Schedule **4 'C'*** for product registration as per Drug Registration Regulation of Drug Act 1978 (*Available in the Department*).
- **ii.** An application in the form *Schedule **6*** for product import recommendation letter as per Drug Registration Regulation of Drug Act, 1978 (*Available in the DDA website*).
- **iii.** Up-to-date manufacturing license issued by the concerned Drug Regulatory Authority (*Drug License*)
- **iv.** Attested copy of valid Certificate of Pharmaceutical Product (*CPP*) as recommended by WHO (*Attested by Drug Regulatory Authority or Notary Public with valid license in Nepal*).
- **v.** Detail formulation including excipients, colour, flavour, etc.
- **vi.** In case of new drug combination / new molecule (*document in the format designed by the Department*).
- **vii.** In case of controlled & sustained release dosage forms additional documents as prescribed (as devised by the Department*)*.
- **viii.** BA/BE report (*bio waivers can be requested as per biowaiver guidances mentioned in the following section*)
- **ix.** Product specification.
- **x.** Method of Analysis (*official compendia methods are accepted however other methods must be validated for precision, accuracy,*

repeatability/specificity, ruggedness, limit of detection, limit of quantitation. For this, latest WHO guidelines on analytical method validation may be followed and substantiated with report).

xi. Samples of label and carton.

xii. Sample of the product (*equivalent quantity as defined by NML for 2 complete tests*).

xiii. Analytical report from company's own laboratory and from any of the following Laboratories for the same batch: a) Government Laboratory of the exporting country or, b) National Medicine Laboratory, Nepal; or c) from other national or foreign laboratories approved by the Department.

xiv. Real Time Stability Testing Report for the period of claimed shelf-life (*refer to Annex-4*)

xv. A letter of attorney in favour of the authorised importer (in format as A*nnex-5*)

xvi. Undertaking that the proposed products is not supplied in higher prices than in the exporting country

xvii. Submission of prices of at least 5 competitor brand, this may not be mandatory in case of fewer brands that 5 available in the market

b. Vaccine and Biological

2.4.2.2 An applicant shall apply for vaccine or biological products registration and import recommendation letter with the following documents as prescribed in the drug registration rule 2038 and directives issued by the Department from time to time:

i. Schedule **4 'C'** Application form for product registration as per Drug Registration Regulation of Drug Act 1978 (*Available in the Department*).

ii. Schedule **6** Application Form for product recommendation letter as per Drug Registration Regulation of Drug Act, 1978 (*Available in the Department*).

iii. Up-to-date manufacturing license issued by the concerned Drug Regulatory Authority (*Drug License*)

iv. Attested copy of valid Certificate of Pharmaceutical Product (CPP) as recommended by WHO (Attested by Drug Regulatory Authority or Notary Public).

v. Detail vaccine of biological batch formulation including excipients, colour, flavour, etc.

vi. Bio-similarity report (for biosimilars follow guidance *issued form the department for this purpose*)

vii. Vaccine or biological Product specification.

viii. Method of Analysis (*official compendia methods are accepted however other methods must be validated for precision, accuracy, repeatability/specificity, ruggedness, limit of detection, limit of quantitation, latest WHO guidelines on analytical method validation may be followed and substantiated with report*) .

ix. Samples of label and carton.

x. Sample of the product (equivalent quantity as defined by NML for 2 complete tests.

xi. Analytical report from company's own laboratory and from any of the following Laboratories for the same batch: a) Government Laboratory of the exporting country or, b) National Medicine Laboratory, Nepal; or c) from other national or foreign laboratories approved by the Department.

xii. Real Time Stability Testing Report for the period of claimed shelf-life (*refer Annex-4)*

xiii. A letter of attorney in favour of the authorised importer form of the letter of attorney as Annex-5)

xiv. Undertaking that the proposed products is not supplied in higher prices than in the exporting country

xv. Submission of prices of at least 5 competitor brand, this may not be mandatory in case of fewer brands that 5 available in the market

2.4.2.3 The Following the evaluation of the submitted application document the drug /vaccine/biological product is noted in drug registry as prescribed in Schedule 4-D and product license in the form Schedule4E is issued in favour of the authorised importer of the company. Similarly upon receiving the application in the form as prescribed in Schedule-6, import recommendation letter in favour of

the company's authorised imported in the form prescribed as Schedule-7 is issued

c. Import recommendation as per rule 4B sub-rule(4)

2.4.2.4 Live saving medicines with prescription of medical doctor, when applied with evidences, the department shall issue import recommendation letter for the drug/vaccine/biological product in required quantity.

2.4.2.5 The Department shall issue import recommendation letter for Drug/Vaccine/Biological intended to be imported by governmental or non-governmental agencies through donation*.

2.4.5.6 The department shall issue import recommendation letter for the drug/vaccine/biological products and quantity intended to be imported through international competitive bidding,

2.4.5.7 Following documents are required to issue import recommendation letter as per rule 4B sub-rule (4):

a) An application with purpose and justification
b) The prescription of registered practitioner for personal use with quantity (for personal use only).
c) Recommendation letter with justification by the concerned Drug & Therapeutic Committee (DTC) of the Hospitals (including medical colleges hospitals) and Nursing Homes(for hospital use)
d) Additional clarification or document as decided by the Drug Evaluation Committee of DDA.
e) Payment voucher as prescribed in Schedule 14 of the Drug Registration Rule 2038

*(Please refer to **Donation Guidelines** post at our official webpage ***www.dda.gov.np.)***

2.5 Application for importation of products and restrictions

Any person fulfilling following requirements may apply for drug product importation in Nepal

2.5.1 Any Nepali drug wholesale firms registered with DDA authorised by the manufacturing company in foreign company can apply for drug import registration in Nepal

2.5.2 The company should have issued letter of attorney in favour of the authorised importer

2.5.3 Authenticated documents as described in the Section 4 above

Restricitons

2.5.4 Company not having authorised wholesaler in Nepal

2.5.5 Those having importation interest outside the provisions mentioned in the departmental communiqué *dated 2071.04.01 in Gorkhapatra daily*

2.5.6 Those barred by the law of the land

2.6 Sample application dossier

WHO-PQ programme has adopted common technical document (CTD) format for product dossier assessment in its focused programme products, which is equally relevant for other products also. Any person applying for new or generic product registration in the department may submit application as prescribed (Schedule-4C and 6) along with the product dossier. (For further detail of the sample dossier may be referred to WHO guidelines document: WHO technical series 961, Annex 15/ or refer to WHO website.

2.7 Sample master file:

WHO guiding document to prepare site master file is given in the WHO Technical Series 961, Annex 14

2.8 Stability requirement

A guiding document is published in the DDA website and reproduced in this document (*Annex-3*)

2.9 BA/BE requirement

2.9.1 An applicant is required to submit reports on bioavailability and bioequivalence study. The methods and approaches to conduct such studies may be followed as per WHO guidelines or equivalent (US FDA guidance, EU guidance).

2.9.2 Bioavailability and BE study is not required for drug products intended to use as IV injection.

2.9.3 An applicant can request BCS biowaiver for orally administered solid dosage forms(*detailed guidelines on BCS –based biowaiver and BE study may be refered to WHO Technical Series 937 Annex 7*)

2.9.4 Conditions requiring BE study report are:

a) Locally applied, systemically acting products
b) Non-oral immediate release forms with systemic action
c) Modified release products; e.g.; sustained release tablet
d) Transdermal products
e) Narrow therapeutic drugs, drugs with low bioavailability, non linear kinetics, poor dissolution profile, variable bioavailability/bioequivalence, modified release dosage form having blood steady state concentration such as sodium valproate, valproic acid, carbamazepine, antibiotics etc,
f) Oral products intended to be absorbed in the oral cavity
g) In-vivo BA/BE profile or in-vitro dissolution profile should be compared with Innovator/leading/comparator brand of the product.

2.10 Conditions when bio waiver can be permitted

The objectives of BCS based biowaiver consideration are:

I) To improve the efficiency of drug development and the review process by recommending a strategy for identifying expendable clinical bioequivalence tests.

II) To recommend a class of immediate-release (IR) solid oral dosage forms for which bioequivalence may be assessed based on in vitro dissolution tests.

III) To recommend methods for classification according to dosage form dissolution, along with the solubility and permeability characteristics of the drug substance

Accepted Bio waiver conditions:

- Injectable, ophthalmic and otic solutions- provided that the active and inactive ingredients are qualitatively and quantitatively same as the reference listed drug.
- Oral and topical solutions- provided that differences in inactive ingredients are characterized and do not affect absorption of active ingredient of the product.
- Immediate-release drug products with a determination of efficacy. The regulatory authority may request in vitro dissolution testing for oral solid dosage forms. Examples include acetaminophen and codeine tablets, folic acid tablets, hydrocortisone cream and ointment, triamcinolone ointment, cytarabine injectable and dacarbazine injectables.
- Drugs which are comparatively safer and have wider therapeutic index such as NSAIDs, analgesic, antipyretic and OTC products, the comparative in-vitro dissolution test profile along with real time stability data can also be submitted instead of BA/BE study report.
- BCS class 1 drugs, e.g., metoprolol and few BCS class III drug
- Pharamcopoieal immediate release solid dosage drug products with comparable dissolution profile with comparater drug product (f2 test as per WHO guidelines)

2.10.1 What data required for bio waiver request by the applicant?

- Drug substance highly soluble over the entire physiological pH range (pH 1.2, pH 4.5 acetate buffer and pH 6.8 phosphate buffer)
- Drug substance highly permeable
- Drug product very/ rapidly dissolves rapidly over the entire physiological pH range can be considered for Biowaiver is found equivalent through comparable dissolution profile (f2 test as per WHO guidelines) with reference drug product.

Option 1: Very rapidly dissolving products

- Not less than 85 % of labeled amount are dissolved within 15 min in each of three buffers (pH 1.2, pH 4.5 acetate buffer, pH 6.8 phosphate buffer) – no further profile comparison of T and R is required

Option 2: Rapidly dissolving products

- Not less than 85 % of labeled amount are dissolved within 30 min in each of three buffers (pH 1.2, pH 4.5 acetate buffer, pH 6.8 phosphate buffer)
- Not a drug with narrow therapeutic index
- For Generic products, also demonstrate similar dissolution profiles of test and reference (comparator)
- BCS class I and some BCS III class drug containing products can be considered for biowaiver
- Class III drugs (low solubility, high permeability) with weak acidic properties may be considered based on revised WHO Criteria.

2.11 Clinical study requirements

An applicant for multisource generic products needs to submit product dossier in a format prescribed (currently WHO guidelines as per *Generic Guidelines_PDS_CTD* format is accepted) and for new products ICH guidelines as recommended in M4E may be followed.

2.12 Renewal of licenses, recommendation letter and certificate

2.12.1 Imported product registration certificate (Schedule-4E)

2.12.1.1 Application for renewal of Schedule-4E

2.12.1.2 original Schedule-4E

2.12.1.3 compliance with terms and condition of Schedule-4E

2.12.1.4 Valid certificate of pharmaceutical products (Notarized and in the format as recommended by WHO Valid licenses issued by the exporting country's regulatory authority

2.12.1.5 Payment voucher as per Schedule 14 of Drug Registration Regulation

2.12.2 Drug product Import/ export recommendation letter (Schedule-7)

2.12.2.1 Application-Schedule-6

2.12.2.2 Original product registration certificate Schedule-5 (for export only, applicable for products manufactured in the country)

2.12.2.3 Original product registration certificate (Schedule-4(E)

2.12.2.4 Valid certificate of pharmaceutical products (Notarized and in the format as recommended by WHO)

2.12.2.5 Valid licenses issued by the exporting country's competent regulatory authorities

2.12.2.6 Approval of variations made during the period

2.12.2.7 Valid WHO-Good Manufacturing Practices certificate or equivalent from SRA as applicable issued from the concerned competent authority

2.12.2.8 Sample of drug product to be renewed

2.12.2.9 Evidence of export to SRA(s) in case of drug product registered under conditions of export to SRA country.

2.12.2.10 Payment voucher as per Schedule 14 of Drug Registration Regulation

2.12.2.11 Annual Product Review

2.12.2.12 Stability informations in case of changes with report of data logger sheets.

2.12.2.13 Declaration on ADR reporting on the product

2.13 Re-registration of the drug product (Schedule 4E) and re-issue of import recommendation letter (Schedule7)

The products which are registered in the Department but the importer failed to renew within 125 days after the validity period can still renew their drug product registration certificates and import recommendation letter upon payment of fines as prescribed and after furnishing following documents. If the manufacturer has not renewed its products licenses or recommendation letters for last two years, the company will not be considered for renewal of its products. The pending fees and fines will be recovered from the company on outstanding revenue.

2.13.1 Up to date drug product manufacturing license issued in favour of the manufacturer.

2.13.2 Notarized copy of valid Certificate of Pharmaceutical Product (CPP).

2.13.3 Approval of variations during the period.

2.13.4 If substantive variations were done document supporting expiration period

2.13.5 Method of Analysis

2.13.6 Valid GMP certificate issued by DDA or competent authority of the exporting country.

2. 14. Variations in licenses, recommendation letter, product specification/standards

2.14.1 The applicant shall apply with scientific justification of any variation required to be done in the master/batch formula and composition, such variation if found justified shall be allowed in the drug manufacturing license, such variation should be mentioned in the drug marketing authorization certificate/ import registration also for this, following documents are required:

- Variation requested and justification
- Revised product specification (with proposed variations)
- Analytical test report from own testing laboratory
- Product sample with labelling specimens

Note: Standards of non-pharmacopoeial products should be authorized through the recommendation of drug advisory committee. For this the concerned applicant should apply to the Department however, standards of any article or products if mentioned in any of the official pharmacopoeia should be revised accordingly. For such revision, however, prior authorization is recommended from the Department.

The change control mechanism must address the variation in average weight, shape, size, color, packing material, label but such changes or variations must be recorded in the drug manufacturing license, marketing authorization certificates and relevant product's master document through variation authorization from the departmenVariations like packing sizes (eg. Liquids in different volume, tablets in 1x10x10's, 15x10x10's,20x10x10's) may be done with application and sample of the packing size(s). These changes or addition shall be recorded in the drug manufacturing license but if there is a change in unit price then separate manufacturing license shall be issued upon request made by the industry. Variation like brand name, pharmacopoeial standard and other statements mistakenly recorded during registration shall be made if requested so from the industry.

2.14.2 Variation of Name of the industry and address shall be made if application for such variation along with evidences of changes made at company registrar's office, department of industry and department of cottage industry are submitted at the department.

Note: Variation like one dosage form to another consisting of same active pharmaceutical ingredient cannot made. Addition or deletion of active pharmaceutical ingredient(s) shall be allowed but the stability requirement for marketing authorization are applied and such changes in the drug marketing authorization certificate shall be allowed after receiving at least 6 months' stability test reports.

2.15 Import recommendation letter in case of non-registered medicine

2.15.1 Medicine(s) as per the prescription of registered practitioner for personal use of patient.

2.15.2 Medicine(s) recommended by the Drug & Therapeutic Committee (DTC) of the hospitals (including medical colleges) and nursing homes for hospital use.

2.16 Medicines from donation sources

Please refer to **Donation Guidelines**. For this, visit ***www.dda.gov.np*.**

2.17 Permission for publicity and advertisement Schedule-11

2.17.1 Application in Schedule-10

2.17.2 Copy of manufacturing licence

2.17.3 Copy of marketing authorization

2.17.4 Material (audio-visual) suitable for TV, Radio, Printed media etc consistent with the provision of clause 19 of Drug Act and WHO Ethical criteria for medicinal drug promotion,1988

2.17.5 Independent reference (s) supporting the clain(s)

2.18 Permission to conduct clinical trial (Schedule-13)

2.18.1 Application in Schedule-12

2.18.2 Approval of Nepal Health Research Council (NHRC) and other government approved agencies.

2.18.3 Clinical trial protocol

2.18.4 Independent reference(s) supporting the objectives and hypothesis of the clinical trial.

***Stringent regulatory Authority (SRA)**

A stringent regulatory authority is:

• The medicines regulatory authority in the country which is:(a) a member of the International Conference on Harmonization(ICH)(European Union(EU), Japan and the United Stated of America); or(b) an ICH observer, being the European Free Trade Association(EFTA) as represented by Swiss Medic and Health Canada(as may be updated from time to time); or (c) a regulatory authority associated with an ICH member through a legally-binding, mutual recognition agreement including Australia, Iceland, Liechtenstein and Norway(as may be updated from time to time)

• Only in relation to good manufacturing practices (GMP) inspection; a medicines regulatory authority that is a member of the Pharmaceutical Inspection Co-operation Scheme (PIC/S) as specified at htt://www.picshcheme.org

Appendix1: Supplementary guidelines on recent import intervention effective from Shrawan 1st 2071

1. Strict Regulatory Authorities up to the date are mentioned below. This list may change if the categories (related with the provision no 1):

1) Austria: Austrian Agency for health and food safety http://www.ages.at/ages/ueber-uns/English-what-is-ages/
2) Belgium: Federal agency for medicines and health products: http://www.fagg-afmps.be/
3) Bulgaria: Bulgarian Drug Agency: http://www.bda.bg/
4) Croatia: Agency for medicinal products and medical device of Croatia: http://www.almp.hr/?ln=en&w=o_agenciji
5) Cyprus: Ministry of Health-pharmaceutical services :http://www.moh.gov.cy/moh/phs/phs.nsf/dmlindex_en/dmlindex_en?open document
6) Czech Republic :State Institute for drug control: http://www.sukl.cz/
7) Denmark: Danish Health and medicines authority: http://www.dkma.dk/
8) Estonia: State agency for Medicines :http://www.sam.ee/
9) Finland: Finnish Medicines agency: http://www.nam.fi/
10) France: national Agency for safety of medicines and Health products: http://www.afssaps.fr/
11) Germany: Federal Institute for Drug and medical devices: http://www.bfarm.de/gb_ver/ and: http://www.zlg.nrw.de/ and
12) Greece: National organization of Medicines: http://www.eof.gr/web/guest/home
13) Hungary: National Institute of Pharmacy: http://www.ogyi.hu/main_page/
14) Ireland: Health products regulatory authority: http://www.imb.ie/
15) Italy: Italian Medicines agency: http://www.aifa.gov.it/ and http://www.agenziafarmaco.it/section8983.html
16) Latvia: State agency of Medicines: http://www.vza.gov.lv/index.php?setlang=en&large
17) Lithuania: State Medicines control agency: http://www.vvkt.lt/index.php?3327723903
18) Luxembourg: Ministry of Health: http://www.ms.public.lu/fr/activites/pharmacie-
19) Malta: Medicines authority: http://www.medicinesauthority.gov.mt/
20) Netherlands: Healthcare inspectorate : http://www.cbg-meb.nl/
21) Poland: Office of registration of medicinal products, medical devices and Biocidal products: http://www.urpl.gov.pl/
22) Portugal: National Authority of Medicines and Health products: http://www.infarmed.pt/
23) Romania: National Medicines agency: http://www.anm.ro/en/home.html
24) Slovakia: State Institute for Drug control: http://www.sukl.sk/en
25) Slovenia: Agency for medicinal products and medical devices of republic of Slovenia: http://www.jazmp.si/index.php?id=56
26) Spain: Spanish agency for medicines and health products: http://www.agemed.es/en/actividad/sgInspeccion/home.htm
27) Sweden: medical products agency: http://www.lakemedelsverket.se/english/
28) United Kingdom: Medicines and healthcare products regulatory agency: UKMHRA:

Other ICH member

1. United states of America:US Food and Drug Administration (USFDA): http://www.usfda.gov
2. Japan: Japanese Pharamceuticals and medical device Agency(PDMA) :http://www.pmda.go.jp/index.html

ICH Observer

3. Switzerland: SWISS AGENCY FOR THERAPEUTIC PRODUCTS (Swiss Medic): http://www.swissmedic.ch/index.html?lang=en
4. Canada: Health Canada

Authorities having legally-binding, mutual recognition agreement with an ICH member

5. Australia: Australian Therapeutic goods Administration(TGA): http://www.tga.gov.au/
6. Iceland: Iceland Medicines agency: http://www.imca.is/
7. Liechtenstein: http://www.llv.li/
8. Norway :Norwegian medicines agency(NOMA): http://www.legemiddelverket.no/Sider/default.aspx

2. Following products or product types are considered technology based modified release formulations (related *to provision no 4 and 8*):

- Transdermal drug delivery system based drug products
- Lyophilised injectable drug products
- sustained release drug products
- Nanotechnology and liposomal delivery system and drug products containing liposomes, neosomes
- biotechnology based drug products including Biosimilar,
- blood and blood products
- gene/genome based therapies/drug products

3. Those not manufactured in Nepal and orphan medicines (*related to provisions no 6*)

Allergenic extracts (e.g. for allergy shots and tests), blood and blood components, gene therapy products. Devices and test kits. Human tissue and cellular products used in transplantation. Vaccines. monoclonal antibodies designed as targeted therapies in cancer and other diseases cytokines (types of proteins involved in immune response), growth factors (proteins that affect the growth of a cell), enzymes (types of proteins that speed up biochemical reactions), such as thrombolytics (used to dissolve blood clots), immunomodulators (agents that affect immune response), antibiotics like; Tigecycline, Meropenam injection, contraceptives and drug product technologies like; drug plus device products, inhalers, prefilled syringes etc.

4. Critical Care Products (related *to provision no 9*)

Including some of category in no 3 above following products are considered critical care products:

(A list published by DDA in collaboration with professional organization related to hospital pharmacy like Hospital Pharmacist Association Nepal (HosPaN).

5. Products identified for submission of art-work of label are as follows (*related to provision no 11*):

Samuha Ga products and minimum labelling and package insert requirement in Nepali (as per provision 10 of the notice)

1. Albendazole
2. Paracetamol
3. Paracetamol and Ibuprofen combinaton
4. Metronidazole
5. Metronidazole and Diloxanide Furoate combination
6. Mebendazole
7. Ranitidine
8. Omeprazole
9. Pantoprazole
10. Vitamin B complex
11. Enzyme(tablet, liquid)
12. Cough expectorant
13. Cough suppressant
14. Oral Rehydration Solution
15. Antacid formulation(tablet, suspension)
16. Diclofenac oint/gel
17. Cetrizine tablet/suspension
18. Indomethacin capsule(immediate release)
19. Tinidazole
20. Povidone Iodine

Following minimum requirements required on the primary and secondary labels of the Samuha Ga products listed above

i. Product name(brand name in not generic)
ii. Direction for use
iii. Classification (Ga) and warning /precaution/directions
iv. MRP
v. Manufacturing date
vi. Expiry date
vii. Batch No

1. Product dossier as per WHO recommended format(*related to provision no 13*)- as recommended by WHO expert committee and amended thereof from time to time for generic pharmaceutical products the latest dossier format and details are found in **WHO TRS 961**
   Annex 15 - ***Guidelines on submission of documentation for a multisource (generic) finished product. General format: preparation of product dossiers in common technical document format***.

Annex-2: Letter of Authorization

Date:

The Chief Drug Administrator
Department of Drug Administration
Bijuli Bazar Kathmandu.

Sub: Letter of Authorization

We, M/S.....hereby authorize the undersigned import firm M/S.....of....., DDA registration No..... to import the drug products attached here with and as amended later through mutual agreement and represent us before the court of law or any other agency (ies) deemed necessary. The true copy/or a notarized copy of the agreement between us(both the parties, the manufacturer and the importer) is attached herewith and carries validity until its expiry and shall be renewed time to time through mutual agreement and copy of new agreement or revision will be submitted to the Department on time.

We solemnly accept the deed or any actions for or against us through the authorized importer and would bear the accountability and responsibility of any liabilities as our duty and for the best of the customer of our drug products. The true seal and signature of the authorized person is as mentioned below.

SEAL OF THE COMPANY
(Manufacturer)

Signature:

Name:
Designation
Company (Manufacturer)
Address:
Phone no,
Fax,
Email:

SEAL of THE IMPORTER

Signature:
Name:
Designation
Importer
Address:
Phone no,
Fax,
Email:

Annex-3: Letter of Warranty

Date:

The Chief Drug Administrator
Department of Drug Administration

Bijuli Bazar Kathmandu.

Sub: Letter of Warranty

We hereby certify that the products manufactured by us are of standard quality, efficacious and safe. All the products manufactured and supplied by us comply with all the required quality control parameters. In case of non-conformity with the quality we shall abide by the Drug Act 1978 and Rules & Regulations there under.

Stamp of Company

(Manufacturer)

Signature:
Name:
Designation
Company (Manufacturer)
Address:
Phone no:
Fax:
Email:

Annex-4: Guidelines on Stability of Products, 2007(as amended in 2015)

DDA has been implementing the WHO guidelines on stability testing in phased manner. Cooperation of the industry and progress made in implementing the stability requirement is praiseworthy. All manufacturers are requested to adopt the WHO working document QAS/06.179/Rev.1 on "Stability testing of active pharmaceutical ingredients and pharmaceutical products, 2007" as far as possible. However the following is the minimum requirement that has to be complied for applying for marketing authorization of the product on or after Shrawan 1, 2064.

a. Accelerated stability testing on two batches should be conducted, one of which must be either commercial batch or a pilot-scale batch. A pilot batch should not be smaller than one eighth of the commercial batch. If accelerated stability testing was carried out on one laboratory batch, which was produced by similar manufacturing process and has the same composition of active ingredient/s and excipient/s as for the commercial batch, accelerated stability test on single commercial or pilot-scale batch should be acceptable. Accelerated stability testing should be done on 0, 3 and 6 months.
b. Initially real time stability testing should be conducted on two batches for the expected shelf-life of the product, one of which should be commercial batch. One batch can be a pilot scale batch. Continuing real time stability study should be carried out on subsequent batches, as per the schedule and standard operating procedure approved by quality assurance department of the industry, taking into consideration any changes like equipment, process and source of raw material etc. Real time stability testing should be done on 0, 3, 6, 9 and 12 months on first year, every six-month on second year and once every year afterwards.
c. Stability testing should be conducted on the dosage form packaged in the container closure system proposed for marketing (including, as appropriate, any secondary packaging and container label).
d. Stability studies should include testing of those attributes of the pharmaceutical product that are susceptible to change during storage and are likely to influence quality, safety, and efficacy. The testing should cover, as appropriate, the physical, chemical, biological and microbiological attributes, preservative content (e.g. antioxidant, antimicrobial preservative). Analytical procedures should be fully validated and stability indicating.
e. One initial batch of the pharmaceutical product should be tested for antimicrobial preservative effectiveness (in addition to preservative content) at the proposed shelf-life for verification purposes.
f. If significant change occurs between three and six months' testing at the accelerated storage condition, the proposed shelf-life should be based on the real-time data available from the long- term storage condition.

In general, "significant change" for a pharmaceutical product is defined as:

g. A 5% change in assay from its initial value, or failure to meet the acceptance criteria for potency when using biological or immunological procedures.
h. Any degradation product exceeding its acceptance criterion.
i. Failure to meet the acceptance criteria for appearance and physical attributes (e.g. colour, phase separation, resuspendability, caking, and hardness). However, some changes in physical attributes (e.g. softening of suppositories, melting of creams, and partial loss of adhesion for transdermal products) may be expected under accelerated conditions.

j. Failure to meet the acceptance criterion for pH (for liquid preparation).
k. Failure to meet the acceptance criteria for dissolution for 12 dosage units (tablet and capsule).
l. Stability studies for products stored in impermeable containers can be conducted under any controlled or ambient humidity condition.
m. If no significant change occurs during six-month's accelerated and real time stability testing, the product will be allowed to place in the market with a provisional shelf-life of up to twenty-four months. However, real time stability testing should be continued up to the proposed shelf-life. The manufacturer should have a system of recall in place so that the sale any batch which does not remain within the limit of approved product specification be stopped within twenty-four hours.

Expiry date

The date given on the individual container (usually on the label) of a product up to and including which the product is expected to remain within specifications, if stored correctly. It is established for each batch by adding the shelf-life to the date of manufacture.

n. Once the pharmaceutical product has been registered, additional stability studies are required whenever variations that may affect the stability of the active pharmaceutical substance or pharmaceutical product are made, such as major variations like the following:

i) Change in the manufacturing process.

ii) Change in the composition of the pharmaceutical product.

iii) Change of the immediate packaging.

o. The ongoing stability programme should be described in a written protocol, and results formalized as a report.
p. Condition of Climatic zone IV A will be applicable for Nepal, though the WHO document mentions Climatic Zone II. Condition for real time stability testing: 30°C ± 2°C/75% RH ± 5% RH; condition for accelerated stability testing: 40°C ± 2°C/75% RH ± 5% RH.
q. Testing protocols for Biologicals including vaccine: refer to the ICH document "Stability testing of Biotechnological/Biologicals(Q5C):

Long term	Accelerated	Stress
≤-20±5 ^{0}C	+5±3 ^{0}C and / or +25±2 ^{0}C/60^{0}RH	Temperature, pH, light, oxidation, shaking, freeze/thaw
+5±3 ^{0}C	+25±2 ^{0}C/60^{0}RH	
+25±2 ^{0}C/60^{0}RH Or +30±2 ^{0}C/65^{0}RH	+40±2 ^{0}C/75^{0}RH	

Recommended Testing frequency

Parameters for stability testing

The following list of parameters for each dosage form is presented as a guide for the types of tests to be included in a stability study. In general, - appearance, - assay and - degradation products should be evaluated for all dosage forms, as well as preservative and antioxidant content if applicable.

The microbial quality of multiple-dose sterile and non-sterile dosage forms should be controlled. Challenge tests should be carried out at least at the beginning and at the end of the shelf-life.

The list of tests presented for each dosage form is not intended to be exhaustive, nor is it expected that every listed test be included in the design of a stability protocol for a particular pharmaceutical product (for example, a test for odour should be performed only when necessary and with consideration for the analyst's safety).

1. Tablets

Dissolution (or disintegration, if justified), water content and hardness/friability. For coated and colour tablets additional tests may require for texture and colour stability.

2. Capsules

Hard gelatin capsules: brittleness, dissolution (or disintegration, if justified), water content, and level of microbial contamination.

3. Emulsions

Phase separation, pH, viscosity, level of microbial contamination, and mean size and distribution of dispersed globules.

4. Oral solutions and suspensions

Formation of precipitate, clarity for solutions, pH, viscosity, extractables, level of microbial contamination.

Additionally for suspensions, redispersibility, rheological properties, mean size and distribution of particles should be considered. Also, polymorphic conversion may be examined, if applicable.

5. Powders and granules for oral solution or suspension Water content, and reconstitution time. Reconstituted products (solutions and suspensions) should be evaluated as described in "Oral solutions and suspensions" above, after preparation according to the recommended labelling, through the maximum intended use period.

6. Nasal sprays: solutions and suspensions

Clarity (for solution), level of microbial contamination, pH, particulate matter, unit spray

medication content uniformity, number of actuations meeting unit spray content uniformity per container, droplet and/or particle size distribution, weight loss, pump delivery, microscopic evaluation (for suspensions), foreign particulate matter and extractable/leachable from plastic and elastomeric components of the container, closure and pump.

7. Topical, ophthalmic and otic preparations
Included in this broad category are ointments, creams, lotions, paste, gel, solutions, eye drops, and cutaneous sprays.

Topical preparations should be evaluated for clarity, homogeneity, pH, resuspendability (for Lotions), consistency, viscosity, particle size distribution (for suspensions, when feasible), level of microbial contamination/sterility and weight loss (when appropriate).

Evaluation of ophthalmic or otic products (e.g. creams, ointments, solutions and suspensions) should include the following additional attributes: sterility, particulate matter and extractable.

Evaluation of cutaneous sprays should include: pressure, weight loss, net weight dispensed, delivery rate, level of microbial contamination, spray pattern, water content, and particle size distribution (for suspensions).

8. Suppositories
Softening range, dissolution (at 37°C).

9. Small volume parenterals (SVPs)
Colour, clarity (for solutions), particulate matter, pH, sterility, endotoxins.

Stability studies for powders for injection solution should include monitoring for colour, reconstitution time and water content. Specific parameters to be examined at appropriate intervals throughout the maximum intended use period of the reconstituted drug product, stored under condition(s) recommended in labelling, should include clarity, colour, pH, sterility, pyrogen/endotoxin and particulate matter.

The stability studies for Suspension for injection should include, in addition, particle size distribution, redispersibility and rheological properties.

The stability studies for Emulsion for injection should include, in addition, phase separation, viscosity, mean size and distribution of dispersed phase globules.

10. Large volume parenterals (LVPs)
Colour, clarity, particulate matter, pH, sterility, pyrogen/endotoxin, and volume.

Minimum requirement for applying for the marketing authorization of the product

1. Accelerated stability test results of three batches of which at least one commercial batch, or pilot-scale batch intended to be placed in the market and produced using the same equipment and process approved for commercial batch. Accelerated stability testing should be done on 0, 3 and 6 months.
2. Real time stability study reports for 0, 3 and 6 month of three batches of which one as the same batch for which accelerated stability testing is carried out and two more consecutive batches for commercial use.
3. Real time and accelerated stability test report should be self-explanatory and conclusion should be mentioned on the report.
4. Report of analysis from National Medicines Laboratory for the same batch for which accelerated stability report is being submitted.

Guidelines issued on Friday, Asadh 1, 2064(June 15, 2007) and as amended in this document

Annex-5: Format of a Letter of Attorney

POWER OF ATTORNEY FOR ISSUE OF PRODUCT LICENSE AND/OR IMPORT RECOMMENDATION LETTER FOR IMPORT OF DRUGS IN NEPAL

Whereas, M/s. **……**, having Registered Office at **……..**, (Telephone ……., Fax ……..., email: ……) hereinafter to be known as Authorised Agent / Manufacturer of us intends to apply for a registration of product license and/or Import recommendation letter under the Drug Act 3035, chapter 4 and Drugs registration Rules, 2038, for the import, use and marketing into Nepal, the **……**, Manufactured by **…….** hereafter to be known as the Manufacturer, having the factory premises at **……..**, hereby delegate Power of Attorney that for the duration of the said product Registration and /or recommendation letter period:-

(1) The said applicant shall be our Authorized Agent for the drug product Registration and/or Import recommendation letter of drugs imported into Nepal, under rule 4-Kha and 5 of the Drugs Registration Rules, 2038; respectively for the purposes of representations and /or signing of the drug product Registration Applications in Form as in Schedule 4(Ga), Schedule 6, undertaking and /other allied documents.

(2) We shall comply with all the conditions imposed on the drug product Registration license and/or Import recommendation Letter, with relevant rules of the Drugs registration rules, 2038.

(3) We declare that we are carrying on the manufacture of the drugs mention in this letter of attorney, at the premises specified above, and we shall from time to time report and seek approval of any change of premises on which manufacture will be carried on and in cases where manufacture is carried on in more than one factory any change in the distribution of functions between the factories:

(4) We shall comply with the provisions of Drug standard rule 2043 and similar guidelines issued by the Department from time to time with regards to labelling requirements.

(5) Every drug manufactured by us for import under the Registration Certificate and import recommendation letter into Nepal shall be as regard strength, quality and purity conforms with the provisions of Chapter 5 of Drug Act 2035 and provisions and their amendments from time to time of the Drug standard rules 2043

(6) We shall from time to time report for any change of manufacturing process, or in packaging, or in labelling, or in testing, or in documentation of any of the drugs, pertaining to the drug product Registration license, to be granted to us. Where any change in respect of any of the drugs under the drug product registration license and Import recommendation letter has taken place, in respect of any of the above matters, we shall inform the same to the Department, in writing within 30 days from the date of such changes. In such cases, where there will be any major change/modification in manufacturing or in processing or in testing, or in documentation, as the case may be, at

the discretion of the Department, we shall obtain necessary approval within 30 days by submitting a separate application.

(7) We shall from time to time report for any administrative action taken due to adverse reaction, viz. market withdrawal regulatory restriction, or cancellation of authorization and/or "not of standard quality report" of any drug pertaining to the drug product license and/or Import recommendation letter declared by any Regulatory Authority of any country where the drug is marketed/sold or distributed. The dispatch and marketing of the drug in such cases shall be stopped immediately and the licensing authority shall be informed immediately. Further action in respect of stop marketing of drug shall be taken as per the directions of the licensing authority. In such cases, action equivalent to that taken with reference to the concerned drug(s) in the country of origin or in the country of marketing will be followed in Nepal also, in consultation with the Department. The Department may direct any further modification to this course of action, including the withdrawal of the drug from Nepali market within 48 hours' time period.

(8) We shall comply with such further requirements, if any, as may be specified, by the Government of Nepal, under the Act and the rules, made there under.

(9) We shall allow the Department and/or any person authorized by him in that behalf to enter and inspect the manufacturing premises and to examine the process/procedure and documents in respect of any drug manufactured by us for which the application for drug product license and/or Import recommendation letter has been made.

(10) We shall allow the Department or any person authorized by him in that behalf to take samples of the drugs concerned for test, analysis or examination, if considered necessary by the Department.

(11) We shall comply with, the any, instructions or directions for the purpose of registration and Import of drugs in the country given by the Department.

NAME OF THE DRUGS

Signature on behalf of manufacturer, with name, designation, date and place.

(Authentic seal of the manufacturer)	Name: Place: Date: Signature*:

(* Signatory Authority should be authorized by the Board of the Company/Directors)

Signature on behalf of Authorised Agent in Nepal with name, designation, date and place.

(Authentic seal of the authorised Agent (Nepal))	Name: Place: Date: Signature:

Annex-6

- Schedule 4B
- Schedule 4C
- Schedule 4D
- Schedule 4E
- Schedule-6
- Schedule-7
- Schedule-10
- Schedule-11
- Schedule-12
- Schedule-13
- Schedule-14

Schedule-4B
(Relating to Sub-rule (2) of Rule 4A.)

Government of Nepal

Ministry of Health Department of Drugs Administration

Drug sale and distribution registration certificate

Sale and distribution registration certificate number:

Sir,

The sale and distribution registration certificate has been issued for the following drug, pursuant to Sub-section (1) of section 8A of the Drugs Act, 2035(1978) and Sub-rule (2) of Rule 4A of the Drugs Registration Rules, 2038 (1981).

1. Of the drug:
   (a) Name:
   (b) System:
   (c) Group and sub-group:
   (d) Composition:
   (e) Active ingredient and quantity (per unit):
   (f) Expiry date:
2. Product specification (certified copy is attached):
3. Fees received for the sale registration certificate: Rs.---
4. Validity period of certificate:

Certificate receiver's:
Name and surname:
Address:
Signature:
Date:

Certificate issuing officer's:

Signature:

Name and surname:

Designation:

Date:

Inserted by the First Amendment.

Note bene: Prior approval has to be obtained from the Department if any alteration is to be made in the product specification and label submitted to the department and in the above-mentioned details:

Amendment to the certificate

Date	Details o Amendment

Renewal

Period of extension of validity		Fees	Officer's signature	Remarks
From	To			

Schedule-4C

(Relating to Sub-rule (1) of Rule 4B)

Application for drug import registration certificate

The Administrator,
Department of Drugs Administration.

Sir,

I/we have made this application, setting out the following details and affixing a stamp of five rupees hereto, to obtain the drug import registration certificate, pursuant to Sub-section (2) of Section 8A. of the Drugs Act, 2035(1978) and Sub-rule (1) of Rule 4B of the Drugs Registration Rules, 2038 (1981).

1. Drug of which import registration certificate is intended to be obtained:
   (a) Name:
   (b) System:
   (c) Group and sub-group:
   (d) Composition:
   (e) Active ingredient and quantity (per unit):
   (f) Expiry date:
   (g) Pharmacopoeia standard:
   (h) Retail price:
   (i) Laboratory having conducted analysis and test, and the analysis and test report issued by that laboratory and date thereof:

Inserted by the First Amendment.

2. Other details:

(a) Whether the product specification setting down the size, color, measurement or weight, taste and flavor of drug, method of packing and details mentioned in its label is attached or not:

(b) Whether the method of analyzing and testing the drug is attached or not:

(c) Whether the label, cartoon and sample of drug are attached or not:

Applicant's:

Signature:

Name and surname:

Address:

Date:

Schedule-4D

(Relating to Sub-rule (3) of Rule 4B)

Registration book

The following drug has been registered as follows for its import, subject to the Drugs Act, 2035(1978) and the Drugs Registration Rules, 2038(1981).

Registration No	Of the drug											
	Name	System	Group or sub-group	Composition	Type or kind	Colour	Active ingredient		Disease to be cured from its consumption	Name manufacturing company and country	Registering officer's signature and date	Remarks
							Name	Quantity				

Inserted by the First Amendment.

Schedule-4E

(Relating to Sub-rule (3) of Rule 4B)

Government of Nepal

Ministry of Health

Department of Drugs Administration

Drug import registration certificate

Import registration certificate number:

Sir,

The drug import registration certificate has bee issued, setting out the following details, pursuant to Sub-section (2) of Section 8A of the Drugs Act, 2035(1978) and Sub-rule (3) of Rule 4B. of the Drugs Registration Rules, 2038(1981).

1. Of the drug:
   - (a) Name:
   - (b) System:
   - (c) Group and sub-group:
   - (d) Composition:
   - (e) Active ingredient and quantity (per unit):
   - (f) Expiry date:
2. Manufacturer's:
   - (a) Name:
   - (b) Address and country:
3. Fees received for the import registration certificate: Rs.---
4. Validity period of certificate:

Import registration certificate obtainer's:

Name and surname:

Address:

Import registration certificate receiver's:

Signature:

Name and surname:

Address:

Date:

Certificate issuing officer's:

Signature:

Name and surname:

Designation: Date:

Note bene: Prior approval has to be obtained from the Department if any alteration is to be made in the product specification and label submitted to the department and in the above-mentioned details:

Amendment to the certificate

Date	Details of Amendment

Renewal

Period of extension of validity		Fees	Officer's signature	Remarks
From	To			

Inserted by the First Amendment.

Schedule-6

(Relating to Sub-rule (1) of Rule 5)

Application for drug export/import recommendation letter

The Administrator,
Department of Drugs Administration.

Sir,

Whereas, I/we intend to obtain a recommendation letter to export/import the following drug;

Now, therefore, I/we have made this application, setting out the following matters and affixing a stamp of one rupee hereto, to obtain the recommendation letter.

Drug to be exported/imported							
S.N.	Name	System	Group or sub-group	StandardComposition	Active ingredient's		Name of manufacturing company and country
					Name	Quantity	

Applicant's:

Signature:

Name and surname:

Address:

Date:

Schedule-7

(Relating to Sub-rule (2) of rule 5)

Government of Nepal

Ministry of Health

Department of Drugs Administration

Drug export/import recommendation letter

This recommendation letter is hereby issued, setting out the following matters, to export/import the following drug, subject to the Drugs Act, 2035(1978) and the Drugs Registration Rules, 2038 (1981).

1.

Drug recommended to be exported/imported							
S.N.	Name	System	Group or sub-group	StandardComposition	Active ingredient's		Name of manufacturing company and country
					Name	Quantity	

2. Recommendation letter obtainer's:

   (a) Name and surname:

   (b) Address:

3. Validity period of recommendation letter:

4. Recommendation letter receiver's:

Signature:

Date:

Recommendation letter issuing officer's:

Signature:

Name and surname:

Designation:

Date:

(The matters to be written on the reverse side of this recommendation letter.)

Renewal of the recommendation letter

Recommendation letter		Renewing officer's signature and date	Renewal fees	Department's Seal	Remarks
Validity extension period					
From	To				

Schedule-10

(Relating to Sub-rule (1) of rule 7)

Application for license to have publicity and advertisement of drug

The Administrator,
Department of Drugs Administration.

Sir,

Whereas, I/we intend to publicize or advertise the following drug; Now, therefore, I/we have made this application, setting out the following matters and affixing a stamp of one rupee hereto, to obtain the license for the same.

1.

S N	Of the drug to be publicized or advertised									Remarks
	Name	System	Group or sub-group	Composition	Type or kind	Active ingredient's		Name of manufacturing company and country	Disease to be cured by consumption	
						Name	Quantity			

2. Means of publicity or advertisement of drug:

(a) In which language:

(b) By which means: (poster, motion picture, newspapers, mobile demonstration etc.)----------

3. Description relating to the words or symbols to be used for publicity and advertisement of drug:
4. Area where the drug is publicized or advertised:

Applicant's:

Signature:

Name and surname:

Address:

Date:

Schedule-11

(Relating to Sub-rules (2) and (3) of Rule 7)

Government of Nepal

Ministry of Health

Department of Drugs Administration

License for publicity and advertisement of drug

This license is hereby issued, setting out the following matters, allowing the following person to publicize and advertise the following drug, subject to the Drugs Act, 2035(1978) and the Drugs Registration Rules, 2038(1981).

S N	Of the drug licensed for publication or advertisement									Remarks
	Name	System	Group or sub-group	Composition	Type or kind	Active ingredient's		Name of manufacturing company and country	Disease to be cured by consumption	
						Name	Quantity			

2. Allowed for publicity and advertisement of drug:
   (a) Means:
   (b) Words or symbols:
   (c) Area:
3. Licensee's:
   (a) Name and surname:
   (b) Address:
   (c) Occupation:
4. Fees received for the issuance of license: Rs.

5. Validity period of the license:

License receiver's: Signature:

Date:

License issuing officer's:

Signature:

Name and surname:

Designation:

Date:

(The matters to be written on the reverse side of this license.)

Renewal of the license

Certificate				Department's Seal	Remarks
Validity extension period		Renewing officer's signature and date	Renewal fees		
From	To				

Schedule-12

(Relating to Sub-rule (1) of Rule 8)

Application for license to conduct clinical trial

The Administrator,
Department of Drugs Administration.

Sir,

Whereas, I/we intend to conduct the clinical trial of the following drug; Now, therefore, I/we have made this application, setting out the following matters and affixing a stamp of one rupee hereto, to obtain the license for the same.

1. Of the new drug of which clinical trial is to be conducted:

Name	System	Group or sub-group	Composition	Type or kind	Active ingredient's		Remarks
					Name	Quantity	

2. Of the disease to be suffered by a patient or person on whom clinical trial is conducted:
   (a) Name:
   (b) Method of diagnosis:

3. Of the consumption of the new drug to be administered in the course of clinical trial:
   (a) Method:
   (b) Mode:
   (c) Dosage (daily):
   (d) Period:
4. Mode of clinical trial:--
5. Place where clinical trial is or intended to be conducted:
   (a) Name and address of hospital:
   (b) Name and address of other doctor:
6. Of the person on whom clinical trial is intended to be conducted:
   (a) Name and surname:
   (b) Address:
   (c) Occupation:
   (d) Qualifications:
7. Mention whether the following details of the new drug are attached or not:
   (a) Toxicological report:
   (b) Quality control method:
   (c) Other necessary matters:

Applicant's:
Signature:
Name and surname:
Address:

Date:

Schedule-13

(Relating to Sub-rule (2) of Rule 8)

Government of Nepal

Ministry of Health

Department of Drugs Administration

License for clinical trial

This license is hereby issued, setting out the following matters, allowing the following person to conduct clinical trial of the following new drug, subject to the Drugs Act, 2035(1978) and the Drugs Registration Rules, 2038(1981).

1. Of the new drug licensed for clinical trial:

Name	System	Group or sub-group	Composition	Type or kind	Active ingredient's		Remarks
					Name	Quantity	

2. Of the disease licensed for clinical trial:
   (a) Name:
   (b) Method of diagnosis:
3. Of the consumption of the new drug to be administered in the course of clinical trial:
   (a) Method:
   (b) Mode:
   (c) Dosage (daily):
   (d) Period:

4. Mode of clinical trial:

5. Place where clinical trial is to be conducted:

6. Of the person allowed to conduct clinical trial:

   (a) Name, surname and address:

   (b) Occupation:

   (c) Qualifications:

7. Validity period of license:

   License receiver's:

   Signature:

   Date:

License issuing officer's: Signature: Name and surname: Designation:

Date:

(The matters to be written on t he reverse side of this license.)

Renewal of the license

Certificate				Department's seal	Remarks
Validity extension period		Renewing officer's signature and date	Renewal fees		
From	To				

Schedule-14

(Relating to Sub-rule (2) of Rule 3, Sub-rule (2) of Rule 4, Sub-rule (2) of Rule 4A, Sub-rule (3) of Rule 4B, Sub-rule (2) of Rule 5, Sub-rule (2) of Rule 6, Sub-rule (2) of Rule 7, Sub-rule (2) of Rule 8, Rule 9, and Sub-rule (2) of Rule 10)

Fees			
SN	**Description**	**Initial fees Rs.**	**Renewal fees Rs.**
1.	For the recommendation letter for the establishment of an industry pursuant to Sub-rule (2) of Rule 3.	200/-	-
2.	For the product license pursuant to Sub-rule (2) of Rule 4 .	200/-	50/-
3.	For the sale and distribution registration certificate pursuant to Sub-rule (2) of Rule 4A.	100/-	50/-
4.	For the import registration certificate pursuant to Sub-rule (2) of Rule 4B.	200/-	100/-
5.	For the export/import recommendation letter pursuant to Sub-rule (2) of Rule 5.	200/-	100/-
6.	For the shop registration certificate pursuant to Sub-rule (2) of Rule 5:		
	(a) Capital not exceeding fifty thousand rupees	200/-	100/-
	(b) Capital from fifty thousand one rupees to one hundred thousand rupees	500/-	250/-
	(c) Capital from one hundred thousand one rupees to five hundred thousand rupees	1000/-	500/-
	(d) Capital exceeding five hundred thousand one rupees	2000/-	1000/-
7.	For the publicity and advertisement license pursuant to Sub-rule (2) of Rule 7:		
	(a) For the license for publicity and advertisement	5000/-	2500/-

Fees			
SN	**Description**	**Initial fees Rs.**	**Renewal fees Rs.**
	through television		
	(b) For the license for publicity and advertisement through printing or other media	2000/-	1000/-
8.	For the clinical trial license pursuant to Sub-rule (2) of Rule 8.	5000/-	-
9.	For duplicate copies of license, certificate and recommendation letter pursuant to Sub-rule (2) of Rule 10.		
	(a) For the first time	50/-	-
	(b) For the second time or each time more than that	100/-	-

Chapter III: Pharmacy registration

3. Procedure

3.1 Application in Schedule-8 (Annex-A)

3.2 Written mutual commitment of owner and pharmacist or pharmacy assistant or Vyabasayi or a) to operate pharmacy only in the physical presence and direct involvement of assigned categories of person(s) mentioned in the section 1 of Schedule-9 (Annex-A) and b) not to engage in any other activities simultaneously in addition to full time engagement in the responsibility mentioned in section 1 of Schedule 9.

3.3 Layout, access sketch of location from certain landmark and complete address including Block no/house no./shop or shutter number, telephone, fax, email/webpage etc.

3.4 Copy of citizen certificate, recognized relevant training/academic/council/committee, certificate of all such person(s) directly involved in sale distribution of medicine from the pharmacy. No one other than named person in section 1 of Schedule-9 can carry out sale distribution of medicine.

3.5 Provision of more than one pharmacist or pharmacy assistant or both in pharmacy operating in 24 hrs basis in hospital set upor as required by directive on hospital pharmacy 2072. Pharmacy cannot be operated in the absence of persons mentioned in the Section-1 of the Schedule-9.

3.6 Fulfillment of all other requirements and conditions as enforced by the Department from time to time for registration or for any variations including change in address, name, personnel in Section 1 or 2 of the Schedule -9 nature of ownership, cancellation, re-registration etc as per Annex-B.

3.7 The applicant is entitled to apply as per above procedure and upload relevant documents into the department's online registration (DAMS) application. The procedure to be followed as instructed on the relevant section of DDA homepage (www.dda.gov.np). Licenses will be issued and delivered as per the procedure and an applicant must submit a hard copy of those documents along with authentic signature and registered fee as prescribed in the Schedule 14 of Drug Registration Regulation

3.8 In a hospital set up pharmacy should be conducted in a manner compliant with the Government's Directive on Hospital Pharmacy 2072.

ANNEX-III

Annex-A

- Schedule-8
- Schedule-9

Schedule-8

(Relating to Sub-rule (1) of Rule 6)

Application for certificate

The Administrator,
Department of Drugs Administration.

Sir,

Whereas, I/we intend to have registered my/our name and the name of the following shop or firm and obtain a certificate for the sale and distribution of the following drug;

Now, therefore, I/we have made this application, setting out the following matters and affixing a stamp of one rupee hereto, to obtain the certificate.

1. The drug selling and distributing pharmacist or entrepreneur and other person's:

Name and Surname	Address	Qualifications		Whether certified copy of qualification is attached or not	Remarks
		Qualification	Experiences		

2. Of the shop or firm selling and distributing the drug:
   (a) Name and address:
   (b) Estimated capital:
   (c) Name, surname and address of the owner:

3.

SN	Of the drug to be sold and distributed						Remarks
	System	Group or sub-group	Composition	Manufacturing company and country	Storage		
					Method	Means	

4. Mode of sale and distribution of the drug: retail/wholesale

5. Whether a certified copy of the document issued by the manufacturer of the drug to be sold and distributed, guaranteeing that such drug is safe for the people, efficacious and of quality standard, is attached or not. If it is not attached, mention that by when it can be submitted.

Applicant's:

Signature:

Name and surname:

Address:

Date:

Schedule-9

(Relating to Sub-Rule (2) of Rule 6)

Government of Nepal

Ministry of Health

Department of Drugs Administration

Serial number:

Certificate

1. This certificate is hereby issued, setting out the following matters, allowing the following person, shop or firm to sell and distribute the following drug, subject to the Drugs Act, 2035 (1978) and the Drugs Registration Rules, 2038 (1981). Of the pharmacist or entrepreneur and other person allowed to sell and distribute the drug:

Name and Surname	Address	Qualification		Whether certified copy of qualification is attached or not	Remarks
		Qualifications	Experiences		

2. Of the shop or firm allowed to sell and distribute the drug:
   (a) Name and address:
   (b) Estimated capital:
   (c) Name, surname and address of the owner:

3.

SN	Of the drug allowed to be sold and distributed						Remarks
	System	Group or sub-group	Composition	Manufacturing company and country	Storage		
					Method	Means	

4. Mode of allowed sale and distribution of the drug: retail/wholesale

5. Whether, prior to the sale and distribution of any drug as referred to in number 3, a certified copy of the document issued by the manufacturer of that drug, guaranteeing that such drug is safe for the people, efficacious and of quality standard, has been submitted or not.

6. Certificate obtainer's:

   (a) Name and surname:

   (b) Address:

Certificate receiver's:

Signature:

Date:

Certificate issuing officer's:

Signature:

Name and surname:

Designation:

Date:

Note bene: Any person who sells and distributes the drug pursuant to this certificate shall not be entitled to sell and distribute such drug without submitting to the Department a certified copy of the document which that person has obtained from the manufacturer of the drug guaranteeing that such drug is safe for the people, efficacious and of quality standard.

(The matters to be written on the reverse side of this certificate.)

Renewal of the certificate

Certificate					
Validity extension period		Renewing officer's signature and date	Renewal fees	Department's Seal	Remarks
From	To				

Chapter IV: Ayurvedic including Herbal Medicine Registration

4.1: Registration Procedure

Ayurvedic (Herbal) /Homeopatic, Unani Medicine manufacturing Industry

4.1.1 Recommendation letter for establishment of pharmaceutical industry

An applicant requiring establishing a pharmaceutical industry should have recommendation letter (Schedule 2) as per the Drug Registration Regulation 1981. The applicant should submit an application for this purpose with following document:

4.1.1.1 Application as prescribed in Schedule-1 of Drug Registration Regulation (Annex A)

4.1.1.2 A detailed feasibility study report as per given format (Annex B)

4.1.1.3 Land ownership certificate /Agreement paper of the site.

4.1.1.4 Citizenship/registration certificate of the applicant(s) (authorized person from among board of directors)

4.1.1.5 Registration fee as prescribed in the schedule-14 (Annex A) to be paid after departmental approval.

4.1.2 Prerequisites for manufacture of Medicines

An applicant should abide by the following conditions while constructing a pharmaceutical industry

4.1.2.1 Manufacturing plant Layout

The applicant should obtained approval of layout design of the proposed manufacturing premises prior to begin any construction from the Department. Following requirements should be considered for layout & design approval:

I) Manufacturing industry

1. Separate building facility for manufacture of oral herbal medicine with the system of AHU/HVAC grade D or class 100000 facility areas as per need for tablet, capsule and liquid dosage forms. Process area should be demarcated in line with process steps and flow and should be sufficient to carry out the intended process(s).

   However for the Asabarist (Fermentation process), Abaleha, Churna, Bati manufacturing dosage forms no need of AHU/HVAC system as above but change room having sufficient containment facilities, control and uncontrol area should be differentiated to minimize the contamination.
2. Design Parameters of HVAC system likes; temperature, pressure & humidity applicable for different processing & non-processing areas within the manufacturing premises should be depicted and relevant schedule and qualification requirement should support them as per needed
3. External liquid preparation can be manufactured in the separate/dedicated manufacturing area not in oral manufacturing areas.
4. The layout design should clearly show the clean classification of different areas as per the qualification requirement. This should include pressure differential between the interfaces and provisions of appropriate air locks. .
5. Purified/ water purification distribution plant is needed having Reverse Osmosis (RO)/Demineralized water (DM) purification system with sanitization facility.
6. Appropriate service area should be provided to utilities like light, air conduction, water, compressed air, pharmaceutical gases including their repair and maintenance etc.
7. For modern dosage forms (tablets, capsules, liquid, ointment, cream etc) manufacturing company should establish the independent QC laboratory having adequate section for quality control and quality assurance activities.
8. For Churna, Bati and goli manufacturing unit need to establish quality control section with approriate equipments for physical testing parameter (like hardness, weighing machine, bulk density, pH meter) having qualified personnel involvement for testing purpose.

II) Key personnel required to establish and operate manufacturing industry

i. For Churna, Bati and (goli manual preparation) manufacturer

At least one fulltime technical person should supervise the manufacturing and other quality assurance activities with minimum of diploma of Ayurvedic pharmacy or Registered Ayurvedic Kabiraj /BAMS.

ii. Churna (including and/or manufacturing tablet, capsules, liquids, ointment, cream) manufaturer

At least one fulltime technical person should supervise the manufacturing and other quality assurance activities with minimum of Bachelor of pharmacy or Registered Ayurvedic doctor with BAMS degree and other technical personnel are required as per company requirement.

In case of proprietary medicines (modern dosage forms) one full time pharmacist is required. For quality control testing purpose, necessary qualified personnels are also needed as per DDA guidance.

4.1.3. Manufacturing License

4.1.3.1 Prerequisites for manufacturing license

4.1.3.1.1 Compliance with the terms and condition (as appended with Schedule-2)

4.1.3.1.2 Industry registration certificate

4.1.3.1.3 Site visit of the manufacturing premises (optional)

4.1.3.1.4 Approved layout of the concerned Site

4.1.3.1.5 Building work complete certificate or work progress report from registered engineering department for new componies.

4.1.3.2 Application and issue of manufacturing license (Schedule-5)

4.1.3.2.1 Application as prescribed by drug registration regulation in the form of Schedule-3(Active ingredient's quantity mentions in Matric system like mg.gm,mcf and Local and botainical name should be mention in schedule - 3 form.)

4..1.3.2.2 Application should be submitted separately for different strength, and dosage form and pack size of a same active pharmaceutical entity.The category should be mention like classical / proprietory under the colume of brand name .

4.1.3.2.3 An applicant along with the application should submit as per the Annex-3 of the medicine registration regulation. For new or combination product (Proprietary medicine) active ingredient entities in the similar dosage form, rationality/justification/references in the form prescribed by the department should be submitted as per therapeutic purpose.

4.1.3.2.4 Brand name of the products should be proposed by the applicant however the department shall check for its similarity with the other already registered brand. If the proposed Brand name, in any case, registered in the department and is found SALA (sound alike and look alike) with another brand which is already registered in the department, the department shall write off the latest brand and a new brand name shall be given if relevant with the consent of the applicant. For brand naming and other labeling requirement, the applicant is should refer the labeling guidelines issued by the department. Applicant should declare that he proposed name is not used/registered by other companies nationally and internationally to the best of their knowledge and consultation to available international sources.

4.1.3.2.5 A tentative format of the product manufacturing processes in line with requirement of BMR

4.1.3.2.6 The applicant should submit additional evidences of physical as well as technical capability for new dosage forms or products needing specific requirement

4.1.3.2.7 Inspection report (Purpose, observations, remarks, conclusion, date, Signature) DDA/Applicant should also enclosed a copy of current inspection report.

4.1.3.2.8 The applicant should submit spacification of raw materials, standard reference of raw materials with document of raw materials analysis in ayurvedic system.

Note- Qualified full time person like Pharmacist, BAMS/KABIRAJ at least one must be required for the manufacturing.

4.1.4 Marketing authorization (Schedule- 4kha)

An applicant (industry) should submit by fulfilling following requirement to obtain medicine marketing authorization (Schedule- 4Kha) as per Drug Registration Regulation

4.1.4.1 Application in the form of Schedule- 4 (ka) of the Medicine Registration Regulation.

4.1.4.2. Quality test report should be submitted as far as possible at the time of marketing approval of submission as prescribed by DDA. Expiry/Shelf life should be based on the DDA prescribed guidance for -commercial batches.

4.1.4.3 Recent analytical test report for commercial batch from the National Medicines Laboratory or other approved laboratories from DDA microbial test report and Heavy matel containing product like Ayurvedic Ras, Rashyan, Vasma (metelic/non-merelic) should be submitted.

4.1.4.4 Batch manufacturing records of the commercial batch with details of excipients, color, packaging and their Supporting documents if needed.

4.1.4.5 The product specification for the commercial batch of its own laboratory.

4.1.4.6. Clinical study report with safety, efficacy data for propriotory ayurvedic Products.

4.1.4.7. Summary of Product Charactistic for Proprietory medicine should be submitted

4.1.4.8 A copy of valid medicine manufacturing license (Schedule-5)

4.1.4.9 Product samples (of commercial batch)-minimum quantity to be submitted is as follows:

- Strip/blister-one box, bottles/tubes/sachet/pouch/ -3units

Note: The labeling information on or with the product should be as per the Drug Standard Regulation (Annex-5) and as issued by the Department.

4.1.5 Raw Material (starting and packaging material) import recommendation letter (Schedule-7)

The medicine manufacturing industries registered in the department shall apply and receive import recommendation letter for raw material including packaging material as per the Drug Registration Regulation. The documents required for such recommendation letter are as follows:

4.1.5.1 Application as prescribed in the drug registration regulation in the form of Schedule-6

4.1.5.2 Specification and standards (herbal pharmacopoeia reference)

4.1.5.3 Copy of Schedule-5

4.1.5.4 Source (manufacturer/supplier/certificate of origin and release profile of modified R/M, and Vendor qualification)

4.1.6 Renewal of licenses, recommendation letter and certificate of Manufacturing license and marketing license of each product

4.1.6.1 Raw material (Schedule-7)

4.1.6.1.1 Application requesting renewal of Schedule-7

4.1.6.1.2 Original recommendation letter (Schedule-7)

4.1.6.1.3 Consumption and projected requirement (Annex E)

4.1.6.1.4 Fee as applicable after approval.

4.1.6.2 Manufacturing license (Schedule-5)

4.1.6.2.1 Application for renewal of Schedule-5

4.1.6.2.2 Original Schedule-5

4.1.6.2.3 Compliance with terms and condition of Schedule-5

4.1.6.2.4 Fee as applicable after approval.

4.1.6.3 Marketing authorization (Schedule-4 kha)

4.1.6.3.1 Water purification study report with analysis of microbial limit testand other impurities for liquid preparation industries

4.1.6.3.2. Microbiological tests report should be described to demonstrate the absence of pathogenic micro-organisms (eg.E.coli, P.aeroginosa, S aureus and salmenolla spp etc.) for churna production.

4.1.6.3.3. Heavy metals (Mercury, Arsenic, Lead and cadmium) tests report for RAS, VASMA production.

4.1.6.3.4. Price list with product specification.

4.1.6.3.5. Commercial product sample-one unit of market presentation.

4.1.6.3.6. Report of deviation, product withdrawal and any change control made within the period

4.1.6.4 Export recommendation letter (Schedule-7, for finished product)

4.1.6.4.1 Application-schedule-6

4.1.6.4.2 Schedule-5

4.1.6.4.3 Schedule-4 (kha)

4.1.6.4.4 Certificate of pharmaceutical products (Annex F)

4.1.6.4.5 WHO-Good Manufacturing Practices certificate issued from the department

4.1.6.4.6 Site Master File along with copy of approved layout

4.2. Foreign company registration, import recommendation letter and Marketing license

4.2.1 Registration of Manufacturer/ Company

4.2.1.1 Preliminary requirements for registration of manufacturer

As per the Drug Act 1978 (2035) and Drug Registration Regulation, 1981 (2038) a person intending to import the medicine(s) from the licensed manufacturer shall register the product and get the Letter of Recommendation for import before importing the medicine(s).

The following are the requirements for registration of foreign pharmaceutical manufacturer to export their products in Nepal.

1. Compliance to Good Manufacturing Practice as recommended by World Health Organization (WHO-GMP/GMP certificate issued by competent authority)
2. Herbal-based manufacturers (Ayurvedic, Homeopathic, Unani, etc) will be registered if the concerned new company is found to comply with WHO GMP Guideline they have been awarded WHO-GMP certificate and if GMP compliance status is found satisfactory during audit from DDA.
3. Those which can produce valid COPP (in case of homeopathy and Unani) it is exempted)

4.2.1.2 Comapany Approval and its products registration

For company registration

- GMP Certificate issued by the concerned Drug Authority department
- Application by the company.
- Letter of authority to the importer issued by the responsible person of the company.
- Site Master File (guidelines provided by Dept. of Drug Administration.
- Update manufacturing license.
- List of products intended to register.
- Letter of warranty (in format provided by Dept. of Drug Administration).
- Latest GMP internal audit report.
- Photocopy of wholesale registration of Nepalese importer.
- A complete set of documents for at least one product.
- Registration Fee

  a) Audit: $ 1500 for SAARC countries and $ 2500 for non SAARC countries.

  b) Company approval: Rs 50,000 for SAARC countries and Rs 80,000 for non SAARC countries.

4.2.2 Product Registration [Schedule 4D, Certificate, Market authorization (4E)]& Letter of Recommendation for Import (Schedule – 7)

As per the requirements prescribed in the Drug Registration Regulation following documents are needed for product registration and issuance of letter of recommendation for import:

4.2.2.1 Schedule 4 'C' Application form for product registration as per Drug Registration Regulation of Drug Act 1978 (Available in the Department).

4.2.2.2 Schedule 6 Application Form for product recommendation letter as per Drug Registration Regulation of Drug Act, 1978 (Available in the Department).

4.2.2.3 Up-to-date manufacturing license issued by the concerned Drug Regulatory Authority (Drug License)

4.2.2.4 Attested copy of valid Certificate of Pharmaceutical Product (CPP) as recommended by WHO (Attested by Drug Regulatory Authority or Notary Public).

4.2.2.5 COPP certificate as recommended by WHO.

4.2.2.6 Detail formulation including API excipients, color, flavor, packaging and/presentation.

4.2.2.7 Product specification.

4.2.2.8 Latest analytical test report for commercial batch from the National Medicines Laboratory or other approved laboratories from DDA, including microbial test report should be submitted for oral dosage forms. Heavy metal test should be conducted for those products as needed.

4.2.2.9 Samples of label, duplex box catch cover and cartoon.

4.2.2.10 Sample of the product (2 unit pack).

4.2.2.11 Analytical report from National Medicine Laboratory or any other DDA approved laboratory.

4.2.2.12 Photocopy of wholesale registration of Nepalese importer.

4.2.3 Renewal of letter of recommendation for importation and market authorization

The certificate issued by the Department should be renewed within 35 days after the validity period. The license holder (importer) should submit the following document for renewal purpose:

4.2.3.1 Application

4.2.3.2 Original certificates of Schedule- 4 D and Schedule- 7

4.2.3.3 Update Manufacturing License of the manufacturer along with the product list.

4.2.3.4 Notarized copy of valid Certificate of Pharmaceutical Product (CPP)

4.2.3.5 Paying voucher for renewal

4.2.3.6 Sample of the product(s).

4.2.3.7 Report of deviation, change control, revised SMF where relevant.

4.2.3.8. Microbial tesrt report should be described to demonstrated the abscence of pathogenic micro-organisms(eg.E.coli,P.aeroginosa,S aureus and salmenolla spp etc.) for churna, and Heavy metals(Mercury,Arsenic,Lead and cadmium) tests report for Ras,Vasma from the NML.

4.2.4 Re-registration of the product

The products which are registered in the Department but the importer failed to renew within 125 days after the validity period can get re-registration. For this the manufacturer must have other products renewed up to date. If the manufacturer has not renewed its products for last two years, the company will not be considered for renewal of its products. The following are the documents required for re-registration of the product:

4.2.4.1 Update manufacturing license of the manufacturer.

4.2.4.2 Notarized copy of valid Certificate of Pharmaceutical Product (CPP).

4.2.4.3 Finished Product Specification.

4.2.4.4 Method of Analysis

4.2.4.5 Supporting document (s) justifying rationality for re -registration.

4.2.5 License for publicity and advertisement Schedule-11

4.2.5.1 Application in Schedule-10

4.2.5.2 Copy of manufacturing license

4.2.5.3 Copy of marketing authorization

4.2.5.4 Material (audio-visual)suitable for TV, Radio, Printed media etc consistent with the provision of clause 19 of Drug Act and WHO Ethical criteria for medicinal drug promotion,1988

4.2.5.5 Independent reference (s) supporting the claim(s)

4.2.6 License to conduct clinical trial (Schedule-13)

4.2.6.1 Application in Schedule-12

4.2.6.2 Approval of Nepal Health Research Council (NHRC)/ Nepal Ayurveda Research and Tranning Centre (NART) and other government approved agencies.

4.2.6.3 Clinical trial protocol

4.2.6.4 Independent reference(s) supporting the objectives and hypothesis of the clinical trial.

Note;- Approval of clinical study report only in government approved Ayurvedic hospital and rescarch centre with In- Patient bad and Laboratory service available.

4.2. 7 Certificate of Pharmacy registration (Schedule-9)

4.2.7.1 Application in Schedule-8

4.2.7.2 Written mutual commitment of owner and pharmacist or pharmacy assistant or Vyabasayi involved in the conduct of the pharmacy a) to operate pharmacy only in the physical presence and direct involvement of assigned categories of person(s) mentioned in the section 1 of Schedule-9 and b) not to engage in any other activities simultaneously in addition to full time engagement in the responsibility mentioned in section 1 of Schedule 9

4.2.7.3 Layout, access sketch of location from certain landmark and complete address including Block no/house no./shop or shutter number, telephone, fax, email/webpage etc.

4.2.7.4 Copy of citizen certificate, recognized relevant training/academic/council/committee, certificate of all such person(s) directly involved in sale distribution of medicine from the pharmacy. No one other than named person in section 1 of Schedule-9 can carry out sale distribution of medicine.

4.2.7.5 Provision of more than one pharmacist or pharmacy assistant or both in pharmacy operating in 24 hrs basis in hospital set up or in the vicinity of hospital. Pharmacy cannot be operated in the absence of persons mentioned in the Section-1 of the Schedule-9.

4.2.7.6 Fulfillment of all other requirements and conditions as enforced by the Department from time to time for registration or for any variations including change in address, name, personnel in Section 1 or 2 of the Schedule -9 nature of ownership, cancellation, reregistration etc.

4.3. Sample to be submitted to DDA

4.3.1 Sizes (e.g. Liquids in different volume, tablets in 1x10x10's, 15x10x10's, and 20x10x10's) may be done with application and sample of the packing size(s). These changes or addition shall be recorded in the drug manufacturing license.

4.3.2 Variation like brand name, pharmacopoeial standard and other statements mistakenly recorded during registration shall be made if requested so from the industry with necessary explanation.

4.3.3 Variation of Name of the industry and address shall be made if application for such variation along with evidences of changes made at company registrar's office, department of industry and department of cottage industry are submitted at the department.

Note: Variation like one dosage form to another consisting of same active pharmaceutical ingredient cannot made. Addition or deletion of active pharmaceutical ingredient(s) shall be allowed but the stability requirement for marketing authorization are applied and such changes in the drug marketing authorization certificate shall be allowed.

ANNEX-I

Annex-A:

- Application for recommendation letter for establishment of drug industry (Schedule-1)
- Recommendation letter for establishment of drug industry (Schedule-2)
- Application for product license (Schedule-3)
- Registration book (Schedule-4)
- Application for drug sale and distribution registration certificate (Schedule-$4A^{+}$)
- Drug sale and distribution registration certificate (Schedule-$4B^{+}$)
- Application for drug import registration certificate (Schedule-$4C^{+}$)
- Registration import book (Schedule-$4D^{+}$)
- Drug import registration certificate (Schedule-4E)
- Product license (Schedule-5)
- Application for drug export/import recommendation letter (Schedule-6)
- Drug export/import recommendation letter (Schedule-7)
- Application for Pharmacy registration certificate (Schedule-8)
- Pharmacy registration Certificate (Schedule-9)
- Application for license to have publicity and advertisement of drug (Schedule-10)
- License for publicity and advertisement of drug (Schedule-11)
- Application for license to conduct clinical trial (Schedule-12)
- License for clinical trial (Schedule-13)

Annex B: Essential contents of feasibility study report

Annex-C: Registration and renewal fees (Schedule 14)

Annex D: Summary of product characteristics (SPC)

Annex E: Raw Material consumption report

Schedule-1

(Relating to Sub-rule (1) of Rule 3)

Application for recommendation letter of establishment of drug industry

The Administrator,

Department of Drugs Administration.

Subject: Request for recommendation letter for establishment of drug industry.

Sir,

Whereas, I/we intend to establish the following drug industry; Now, therefore, I/we make this application, affixing a stamp of one rupee hereto, and setting out the following details, to obtain a recommendation letter for the same.

1. Proposed drug industry's:
   (a) Name:
   (b) Place where it is established: (Also mention the name and ward number of the District and Municipality or Village Development Committee)
   (c) Estimated capital and source of that capital:
   (d) Where a preliminary study report carried out on the establishment is attached or not:
   (e) Whether a sketch and map of the plan also showing the area where the industry is to be established is attached or not:

S.N.	**Of the drug to be manufactured by the proposed**				**Remarks**
	Name	System (et out whether it is Allopathic , Homeopathic, *Ayurvedic,* Unani etc.	Group or sub-group	Composition (set out whether it is a tablet, injection, capsule etc.)	

2. For the manufacturing of drug by proposed industry:

(a) Description of required raw materials and source thereof:

(b) Whether a machine is required or not, if so required, possible details thereof:

(c) Of the required house or building:

(1) Whether sketch and map is attached or not:

(2) What will be its composition:

(3) Whether outside environment will be polluted, neat and clean or otherwise, mention it:

(4) Whether the air can pass through the room or not: Mention why and for what reasons such room has to be so built that the air can or cannot so pass through it:

(5) Whether the sun or light can enter the room or not: Mention why and for what reasons such room has to be so built that the sun or light can or cannot so enter it:

Applicant's:

Signature:

Name, surname:

Address:

Date:

Schedule-2

(Relating to Sub-rule (2) of Rule 3)

Government of Nepal

Ministry of Health Department of Drugs Administration

Recommendation letter for establishment of drug industry

This recommendation letter is hereby issued, setting out the following matters, for the establishment of the following drug industry, subject to the Drugs Act, 2035 (1978) and the Drugs Registration Rules, 2038 (1981).

1. Of the drug industry recommended for establishment:
   (a) Name:
   (b) Place where it is established:
   (c) Estimated capital:
2. Of the drug that can be manufactured by the drug industry after having obtained the product license:

Of the drug				Remarks
Name	System	Group of sub-group	Composition	

3. Recommendation letter receiving person's:
   (a) Name and surname:
   (b) Address:
4. Validity period of recommendation letter:

   Signature of the recommendation letter receiving person:

Date:

Recommendation letter issuing officer's:

Signature:

Name and surname:

Designation:

Date:

(The matters to be written on the back side of this recommendation letter)

Renewal of the recommendation letter

Recommendation letter				Department's Seal	Remarks
Validity extension period		Renewing Officer's signature and date	Renewal fees		
From	To				

Schedule-3

(Relating to Sub-rule (1) of Rule 4)

Application for product license

The Administrator,

Department of Drugs Administration.

Sir,

Whereas, in order to manufacture the following drugs by the following drug industry already established after having obtained the following recommendation letter and license, I/we intend to obtain the product license by having the drugs registered;

Now, therefore, I/we have made this application, affixing a stamp of one rupee hereto, to obtain the product license. The duplicate copies of the recommendation letter and license are attached herewith.

1. Serial number of the recommendation letter of that Department and date thereof:
2. Date of license obtained from-----Department:
3. Drug industry:
   (a) Name:
   (b) Place of establishment: (Also mention the name and ward number of the district, Municipality and Village Development Committee.)

Drug to be manufactured										
S.N.	**Name**	**System**	**Group or sub-group**	**Composition**	**Type of kind**	**Colour**	**Weight per unit**	**Active ingredient**		**Disease to be cured from consumption**
								Name	**Quantity**	

5. Whether the required materials related with the manufacture of drugs are available in an adequate quantity or not:

Applicant's:
Signature:
Name and surname:
Address:

Date:

Schedule-4

(Relating to Sub-rule (2) of Rule 4-----)

Registration book

The following drug has been registered as follows for its manufacture,subject to the Drugs Act, 2035(1978) and the Drugs Registration Regulation, 2038(1981).

Registration No	Of the drug										
	Name	System	Group or sub-group	Composition	Type or kind	Colour	Active ingredient		Disease to be cured from its consumption	Name manufacturing company and country	Registering officer's signature and date
							Name	Quantity			

Deleted by the First Amendment.
Inserted by the First Amendment.

Schedule-4A

(Relating to Sub-rule (1) of Rule 4)

Application for drug sale and distribution registration certificate

The Administrator,
Department of Drugs Administration.

Dear sir,

Whereas, the drug as referred to in the product license, bearing number....., issued by that Department is appropriate for sale and distribution; Now, therefore, I/we have made this application, setting out the following details and affixing a stamp of five rupees hereto, to obtain the sale registration certificate, pursuant to Sub-rule (2) of Rule 4A. of the Drugs Registration Rules, 2038(1981).

1. Drug of which sale registration certificate is intended to be obtained:
   (a) Name:
   (b) System:
   (c) Group or sub-group:
   (d) Composition:
   (e) Active ingredient and quantity (per unit):
   (f) Expiry date:
   (g) Pharmacopoeia standard:
   (h) Retail price:
   (i) Laboratory having conducted analysis and test, and the analysis and test report issued by that laboratory and date thereof:

Inserted by the First Amendment.

2. Other details:

(a) Whether the product specification setting down the size, color, measurement or weight, taste and flavor of drug, method of packing and details mentioned in its label is attached or not:

(b) Whether the method of analyzing and testing the drug is attached or not:

(c) Whether the label, cartoon and sample of drug is attached or not:

Applicant's:

Signature:

Name and surname:

Address:

Date:

Schedule-4B
(Relating to Sub-rule (2) of Rule 4A.)

Government of Nepal

Ministry of Health Department of Drugs Administration

Drug sale and distribution registration certificate

Sale and distribution registration certificate number:

Sir,

The sale and distribution registration certificate has been issued for the following drug, pursuant to Sub-section (1) of section 8A of the Drugs Act, 2035(1978) and Sub-rule (2) of Rule 4A of the Drugs Registration Rules, 2038 (1981).

1. Of the drug:
   (a) Name:
   (b) System:
   (c) Group and sub-group:
   (d) Composition:
   (e) Active ingredient and quantity (per unit):
   (f) Expiry date:
2. Product specification (certified copy is attached):
3. Fees received for the sale registration certificate: Rs.---
4. Validity period of certificate:

Certificate receiver's:
Name and surname:
Address:
Signature:
Date:

Certificate issuing officer's:

Signature:

Name and surname:

Designation:

Date:

Inserted by the First Amendment.

Note bene: Prior approval has to be obtained from the Department if any alteration is to be made in the product specification and label submitted to the department and in the above-mentioned details:

Amendment to the certificate

Date	Details o Amendment

Renewal

Period of extension of validity		Fees	Officer's signature	Remarks
From	To			

Schedule-4C

(Relating to Sub-rule (1) of Rule 4B)

Application for drug import registration certificate

The Administrator,
Department of Drugs Administration.

Sir,

I/we have made this application, setting out the following details and affixing a stamp of five rupees hereto, to obtain the drug import registration certificate, pursuant to Sub-section (2) of Section 8A. of the Drugs Act, 2035(1978) and Sub-rule (1) of Rule 4B of the Drugs Registration Rules, 2038 (1981).

1. Drug of which import registration certificate is intended to be obtained:
   (a) Name:
   (b) System:
   (c) Group and sub-group:
   (d) Composition:
   (e) Active ingredient and quantity (per unit):
   (f) Expiry date:
   (g) Pharmacopoeia standard:
   (h) Retail price:
   (i) Laboratory having conducted analysis and test, and the analysis and test report issued by that laboratory and date thereof:

Inserted by the First Amendment.

2. Other details:

(a) Whether the product specification setting down the size, color, measurement or weight, taste and flavor of drug, method of packing and details mentioned in its label is attached or not:

(b) Whether the method of analyzing and testing the drug is attached or not:

(c) Whether the label, cartoon and sample of drug are attached or not:

Applicant's:

Signature:

Name and surname:

Address:

Date:

Schedule-4D

(Relating to Sub-rule (3) of Rule 4B)

Registration book

The following drug has been registered as follows for its import, subject to the Drugs Act, 2035(1978) and the Drugs Registration Rules, 2038(1981).

Registration No	Of the drug											
	Name	System	Group or sub-group	Composition	Type or kind	Colour	Active ingredient		Disease to be cured from its consumption	Name manufacturing company and country	Registering officer's signature and date	Remarks
							Name	Quantity				

Inserted by the First Amendment.

Schedule-4E

(Relating to Sub-rule (3) of Rule 4B)

Government of Nepal

Ministry of Health

Department of Drugs Administration

Drug import registration certificate

Import registration certificate number:

Sir,

The drug import registration certificate has bee issued, setting out the following details, pursuant to Sub-section (2) of Section 8A of the Drugs Act, 2035(1978) and Sub-rule (3) of Rule 4B. of the Drugs Registration Rules, 2038(1981).

1. Of the drug:
   - (a) Name:
   - (b) System:
   - (c) Group and sub-group:
   - (d) Composition:
   - (e) Active ingredient and quantity (per unit):
   - (f) Expiry date:
2. Manufacturer's:
   - (a) Name:
   - (b) Address and country:
3. Fees received for the import registration certificate: Rs.---
4. Validity period of certificate:

Import registration certificate obtainer's:

Name and surname:

Address:

Import registration certificate receiver's:

Signature:

Name and surname:

Address:

Date:

Certificate issuing officer's:

Signature:

Name and surname:

Designation: Date:

Note bene: Prior approval has to be obtained from the Department if any alteration is to be made in the product specification and label submitted to the department and in the above-mentioned details:

Amendment to the certificate

Date	Details of Amendment

Renewal

Period of extension of validity		Fees	Officer's signature	Remarks
From	To			

Inserted by the First Amendment.

Schedule-5

(Relating to Sub-rules (2) and (3) of Rule 4)

Government of Nepal

Ministry of Health

Department of Drugs Administration

Serial number:

Product license

This product license is hereby issued setting out the following matters, allowing the-------industry already established in -------, based on the following recommendation letter and the license, subject to the Drugs Act, 2035(1978) and the Drugs Registration Rules, 2038(1981).

1. Serial number of the recommendation letter of this Department and date thereof:
2. Date of license obtained from-----Department:
3. Drug industry:
   (a) Name:
   (b) Place of establishment: (Also mention the name and ward number of the district, Municipality and Village Development Committee.)

S.N.	Drug licensed for Manufacture									Remarks
	Registration No	System	Group or sub-group	Composition	Type or kind	Colour	Weight and measurement per unit	Active ingredient		
								Name	Quantity	

4. Product license obtainer's:
   (a) Name and surname:
   (b) Address:
5. Fees received for the issuance of product license: Rs.---
6. Validity period of product license:

Product license receiver's:

Signature:

Date:

Product license issuing officer's:

Signature:

Name and surname:

Designation:

Date:

(The matters to be written on the reverse side of this product license)

Renewal of the product license

Products license				Department's Seal	Remarks
Validity extension period		Renewing officer's signature and date	Renewal fees		
From	To				

Schedule-6

(Relating to Sub-rule (1) of Rule 5)

Application for drug export/import recommendation letter

The Administrator,
Department of Drugs Administration.

Sir,

Whereas, I/we intend to obtain a recommendation letter to export/import the following drug;

Now, therefore, I/we have made this application, setting out the following matters and affixing a stamp of one rupee hereto, to obtain the recommendation letter.

Drug to be exported/imported							
S.N.	Name	System	Group or sub-group	StandardComposition	Active ingredient's		Name of manufacturing company and country
					Name	Quantity	

Applicant's:

Signature:

Name and surname:

Address:

Date:

Schedule-7

(Relating to Sub-rule (2) of rule 5)

Government of Nepal

Ministry of Health

Department of Drugs Administration

Drug export/import recommendation letter

This recommendation letter is hereby issued, setting out the following matters, to export/import the following drug, subject to the Drugs Act, 2035(1978) and the Drugs Registration Rules, 2038 (1981).

1.

Drug recommended to be exported/imported							
S.N.	Name	System	Group or sub-group	StandardComposition	Active ingredient's		Name of manufacturing company and country
					Name	Quantity	

2. Recommendation letter obtainer's:

   (a) Name and surname:

   (b) Address:

3. Validity period of recommendation letter:

4. Recommendation letter receiver's:

Signature:

Date:

Recommendation letter issuing officer's:

Signature:

Name and surname:

Designation:

Date:

(The matters to be written on the reverse side of this recommendation letter.)

Renewal of the recommendation letter

Recommendation letter		Renewing officer's signature and date	Renewal fees	Department's Seal	Remarks
Validity extension period					
From	To				

Schedule-8

(Relating to Sub-rule (1) of Rule 6)

Application for certificate

The Administrator,
Department of Drugs Administration.

Sir,

Whereas, I/we intend to have registered my/our name and the name of the following shop or firm and obtain a certificate for the sale and distribution of the following drug;

Now, therefore, I/we have made this application, setting out the following matters and affixing a stamp of one rupee hereto, to obtain the certificate.

1. The drug selling and distributing pharmacist or entrepreneur and other person's:

Name and Surname	Address	Qualifications		Whether certified copy of qualification is attached or not	Remarks
		Qualification	Experiences		

2. Of the shop or firm selling and distributing the drug:
   (a) Name and address:
   (b) Estimated capital:
   (c) Name, surname and address of the owner:

3.

SN	Of the drug to be sold and distributed						Remarks
	System	Group or sub-group	Composition	Manufacturing company and country	Storage		
					Method	Means	

4. Mode of sale and distribution of the drug: retail/wholesale

5. Whether a certified copy of the document issued by the manufacturer of the drug to be sold and distributed, guaranteeing that such drug is safe for the people, efficacious and of quality standard, is attached or not. If it is not attached, mention that by when it can be submitted.

Applicant's:

Signature:

Name and surname:

Address:

Date:

Schedule-9

(Relating to Sub-Rule (2) of Rule 6)

Government of Nepal

Ministry of Health

Department of Drugs Administration

Serial number:

Certificate

1. This certificate is hereby issued, setting out the following matters, allowing the following person, shop or firm to sell and distribute the following drug, subject to the Drugs Act, 2035 (1978) and the Drugs Registration Rules, 2038 (1981). Of the pharmacist or entrepreneur and other person allowed to sell and distribute the drug:

Name and Surname	Address	Qualification		Whether certified copy of qualification is attached or not	Remarks
		Qualifications	Experiences		

2. Of the shop or firm allowed to sell and distribute the drug:
   (a) Name and address:
   (b) Estimated capital:
   (c) Name, surname and address of the owner:

3.

SN	Of the drug allowed to be sold and distributed						Remarks
	System	Group or sub-group	Composition	Manufacturing company and country	Storage		
					Method	Means	

4. Mode of allowed sale and distribution of the drug: retail/wholesale

5. Whether, prior to the sale and distribution of any drug as referred to in number 3, a certified copy of the document issued by the manufacturer of that drug, guaranteeing that such drug is safe for the people, efficacious and of quality standard, has been submitted or not.

6. Certificate obtainer's:

   (a) Name and surname:

   (b) Address:

Certificate receiver's:

Signature:

Date:

Certificate issuing officer's:

Signature:

Name and surname:

Designation:

Date:

Note bene: Any person who sells and distributes the drug pursuant to this certificate shall not be entitled to sell and distribute such drug without submitting to the Department a certified copy of the document which that person has obtained from the manufacturer of the drug guaranteeing that such drug is safe for the people, efficacious and of quality standard.

(The matters to be written on the reverse side of this certificate.)

Renewal of the certificate

Certificate					
Validity extension period		Renewing officer's signature and date	Renewal fees	Department's Seal	Remarks
From	To				

Schedule-10

(Relating to Sub-rule (1) of rule 7)

Application for license to have publicity and advertisement of drug

The Administrator,
Department of Drugs Administration.

Sir,

Whereas, I/we intend to publicize or advertise the following drug; Now, therefore, I/we have made this application, setting out the following matters and affixing a stamp of one rupee hereto, to obtain the license for the same.

1.

S N	Of the drug to be publicized or advertised									Remarks
	Name	System	Group or sub-group	Composition	Type or kind	Active ingredient's		Name of manufacturing company and country	Disease to be cured by consumption	
						Name	Quantity			

2. Means of publicity or advertisement of drug:

(a) In which language:

(b) By which means: (poster, motion picture, newspapers, mobile demonstration etc.)----------

3. Description relating to the words or symbols to be used for publicity and advertisement of drug:
4. Area where the drug is publicized or advertised:

Applicant's:

Signature:

Name and surname:

Address:

Date:

Schedule-11

(Relating to Sub-rules (2) and (3) of Rule 7)

Government of Nepal

Ministry of Health

Department of Drugs Administration

License for publicity and advertisement of drug

This license is hereby issued, setting out the following matters, allowing the following person to publicize and advertise the following drug, subject to the Drugs Act, 2035(1978) and the Drugs Registration Rules, 2038(1981).

S N	Of the drug licensed for publication or advertisement									Remarks
	Name	System	Group or sub-group	Composition	Type or kind	Active ingredient's		Name of manufacturing company and country	Disease to be cured by consumption	
						Name	Quantity			

2. Allowed for publicity and advertisement of drug:
   (a) Means:
   (b) Words or symbols:
   (c) Area:
3. Licensee's:
   (a) Name and surname:
   (b) Address:
   (c) Occupation:
4. Fees received for the issuance of license: Rs.

5. Validity period of the license:

License receiver's: Signature:

Date:

License issuing officer's:

Signature:

Name and surname:

Designation:

Date:

(The matters to be written on the reverse side of this license.)

Renewal of the license

Certificate				Department's Seal	Remarks
Validity extension period		Renewing officer's signature and date	Renewal fees		
From	To				

Schedule-12

(Relating to Sub-rule (1) of Rule 8)

Application for license to conduct clinical trial

The Administrator,
Department of Drugs Administration.

Sir,

Whereas, I/we intend to conduct the clinical trial of the following drug; Now, therefore, I/we have made this application, setting out the following matters and affixing a stamp of one rupee hereto, to obtain the license for the same.

1. Of the new drug of which clinical trial is to be conducted:

Name	System	Group or sub-group	Composition	Type or kind	Active ingredient's		Remarks
					Name	Quantity	

2. Of the disease to be suffered by a patient or person on whom clinical trial is conducted:
   (a) Name:
   (b) Method of diagnosis:

3. Of the consumption of the new drug to be administered in the course of clinical trial:
   (a) Method:
   (b) Mode:
   (c) Dosage (daily):
   (d) Period:
4. Mode of clinical trial:--
5. Place where clinical trial is or intended to be conducted:
   (a) Name and address of hospital:
   (b) Name and address of other doctor:
6. Of the person on whom clinical trial is intended to be conducted:
   (a) Name and surname:
   (b) Address:
   (c) Occupation:
   (d) Qualifications:
7. Mention whether the following details of the new drug are attached or not:
   (a) Toxicological report:
   (b) Quality control method:
   (c) Other necessary matters:

Applicant's:
Signature:
Name and surname:
Address:

Date:

Schedule-13

(Relating to Sub-rule (2) of Rule 8)

Government of Nepal

Ministry of Health

Department of Drugs Administration

License for clinical trial

This license is hereby issued, setting out the following matters, allowing the following person to conduct clinical trial of the following new drug, subject to the Drugs Act, 2035(1978) and the Drugs Registration Rules, 2038(1981).

1. Of the new drug licensed for clinical trial:

Name	System	Group or sub-group	Composition	Type or kind	Active ingredient's		Remarks
					Name	Quantity	

2. Of the disease licensed for clinical trial:
   (a) Name:
   (b) Method of diagnosis:
3. Of the consumption of the new drug to be administered in the course of clinical trial:
   (a) Method:
   (b) Mode:
   (c) Dosage (daily):
   (d) Period:

4. Mode of clinical trial:

5. Place where clinical trial is to be conducted:

6. Of the person allowed to conduct clinical trial:

   (a) Name, surname and address:

   (b) Occupation:

   (c) Qualifications:

7. Validity period of license:

   License receiver's:

   Signature:

   Date:

License issuing officer's: Signature: Name and surname: Designation:

Date:

(The matters to be written on t he reverse side of this license.)

Renewal of the license

Certificate				Department's seal	Remarks
Validity extension period		Renewing officer's signature and date	Renewal fees		
From	To				

Annex B

Essential contents of feasibility study report

- The name of the person/firm responsible for carrying the feasibility studies both technical and financial part should be provided along with their qualification, experience and expertise (full CV) and the references used in the report.
- Physical infrastructure including land, road accessibility, electricity, building, equipment, and utilities of the proposed venture as per the type and nature of dosage form. The standards of building material and equipment, plant layout and finishes should be inconsistent with WHO-GMP requirement
- Financial analysis including, BEP, IRR. Sensitivity analysis, NPV, payback period, loan repayment , working capital required, fixed asset investment financial analysis shall be presented with 10 years projected period with relevant assumption
- Technical aspects including, list of finished products/presentation/price/reference personnel (category, qualification, experience/skill, required number), process flow diagram, material specification/source and vendor requirement GACP/GSP/GDP etc, quality management system including chemical reference material, QA, QC, and environment consistent with WHO GMP Guideline.
- In case of traditional medicines the following should be provided:
  i) API name (Scientific and Vernacular), reference and sources: collection/procurement/transportation/strategy; identification and QC testing parameters; supplier/vendor qualification; reference specimen/marker compound; approval/rejection criteria; storage requirement and method etc.
  ii) Reference test for classical formulations/products and clinical trial report/ reference document/ reference product in case of proprietary product/formulation and patent registration certificate in case of patent product, marketed products of similar nature and market size.
  iii) Labeling sample consistent with the requirement of Drug Act 2035.

- A Tentative format for the report is as follows:

  Front page

  Project Highlight

  1. Introduction
  2. Objectives
  3. Market Analysis
  4. Existing market Structure
  5. Market Strategies
  6. Technical Aspects
  7. Quality Assurance and Quality control
  8. Engineering and maintenance
  9. Project Management
  10. Land Building and infrastructure
  11. Financial Explanation
  12. Conclusion on feasibility status based on technical and financial sensitivity analysis.

  Annexures

  I. Financial Structure

  II. Fixed Assets Investment

  III. Annual Operating Cost

  IV. Break Even Point Calculation

  V. Working Capital Estimation

  VI. Sales Revenue

  VII. Long Term Loan Repayment

  VIII. Annual Production Cost

  IX. Profit and Loss Statement

  X. Cash Flow Projection

  XI. Balance Sheet

  XII. Calculation of Payback Period

  XIII. Financial Ratio

XIV. Cash Flow for Discounting

XV. Net Present Value

XVI. Sensitivity Analysis

XVII. List of Equipments-Utilities, manufacturing, quality control purposes

XVIII. Raw Materials & Packaging Materials with applicable pharmacopoeial standards XIX. Process flow diagram, QC specification and relevant references

XX. List of documents referred and consulted with details for verification.

Annex-C Registration Renewal and fees (Schedule 14)

Annex C: Schedule 14

Annex C (1): Sample required for submission of application for analytical services to National Medicines Laboratory (NML)

Annex C (2) Medicine analysis fee structure of National Medicine Laboratory

Schedule-14

(Relating to Sub-rule (2) of Rule 3, Sub-rule (2) of Rule 4, Sub-rule (2) of Rule 4A, Sub-rule (3) of Rule 4B, Sub-rule (2) of Rule 5, Sub-rule (2) of Rule 6, Sub-rule (2) of Rule 7, Sub-rule (2) of Rule 8, Rule 9, and Sub-rule (2) of Rule 10)

Fees			
SN	**Description**	**Initial fees Rs.**	**Renewal fees Rs.**
1.	For the recommendation letter for the establishment of an industry pursuant to Sub-rule (2) of Rule 3.	200/-	-
2.	For the product license pursuant to Sub-rule (2) of Rule 4 .	200/-	50/-
3.	For the sale and distribution registration certificate pursuant to Sub-rule (2) of Rule 4A.	100/-	50/-
4.	For the import registration certificate pursuant to Sub-rule (2) of Rule 4B.	200/-	100/-
5.	For the export/import recommendation letter pursuant to Sub-rule (2) of Rule 5.	200/-	100/-
6.	For the shop registration certificate pursuant to Sub-rule (2) of Rule 5:		
	(a) Capital not exceeding fifty thousand rupees	200/-	100/-
	(b) Capital from fifty thousand one rupees to one hundred thousand rupees	500/-	250/-
	(c) Capital from one hundred thousand one rupees to five hundred thousand rupees	1000/-	500/-
	(d) Capital exceeding five hundred thousand one rupees	2000/-	1000/-
7.	For the publicity and advertisement license pursuant to Sub-rule (2) of Rule 7:		
	(a) For the license for publicity and advertisement	5000/-	2500/-

Fees			
SN	**Description**	**Initial fees Rs.**	**Renewal fees Rs.**
	through television		
	(b) For the license for publicity and advertisement through printing or other media	2000/-	1000/-
8.	For the clinical trial license pursuant to Sub-rule (2) of Rule 8.	5000/-	-
9.	For duplicate copies of license, certificate and recommendation letter pursuant to Sub-rule (2) of Rule 10.		
	(a) For the first time	50/-	-
	(b) For the second time or each time more than that	100/-	-

Annex C (1)

Sample required for submission of application for analytical services

to

National Medicines Laboratory (NML)

A. Quantity of samples required

S. No.	Particular	Quantity
1.	Powder (Oral)	5 Pkt

B. Documents Required

1. Product Specification/Protocol
2. Analytical Report (In-house)
3. Method of Analysis

Annex D

SUMMARY OF PRODUCT CHARACTERISTICS

The following summary of product characteristics shall be submitted for every application: -

1. Trade name and dosage form of the product
2. Physical description of the product
3. Botanical name or any other name, family of the plant(s) from which the drug(s) has been extracted including plants part(s) used. Synonym if available should be given. The English name if available shall be provided. For locally produced products the local name and geographical distribution shall be provided.
4. Plant used whether wild or cultivated
5. Brief pharmacology of the medicines
6. Therapeutical indications
7. Dosage regimen and route of administration
8. Brief toxicological information of the medicine
9. Contra-indications
10. Warnings and precautions
11. Drug Interactions
12. Adverse reactions
13. Side Effects
14. Shelf-life and storage conditions
15. Presentation or pack size

Annex E

Consumption report

Fiscal year:

Name and pharmacopoeial reference of raw material

……
……

Import			**Used in**			**Total consumption Kg**	**Balance quantity Kg**
Date	**Source**	**Quantity (Kg)**	**Product**	**Batch Number**	**Quantity (Kg)**		

Name of applicant:

Signature:

Stamp:

Date: