

Central Drugs Standard Control Organization (Import & Registration Division)

Guidance Document

Document No. IMP/REG/200711

Title: Guidance document on Common Submission Format for Import and Registration of bulk drugs and finished formulations in India.



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A. Preface

In India import, manufacturing, sale and distribution of drug is regulated under Drugs and Cosmetics Act 1940 and Drugs and Cosmetic Rules 1945 (hereinafter refer as Act) made there under. At present, bulk drug (Active Pharmaceutical Ingredients) and finished formulations are regulated under the said Act. Any substance falling within the definition of drug (Section 3b of the Act) required to be registered before import into the country. Not only drug but the manufacturing site needs to be registered for import. If the drugs, fall within the definition of New Drug (Rule 122 E of the Act), the new drug approval is the pre-requisite for submission of application for Registration and or import of drug. The application for Registration and import can be made to the Licensing Authority under the Act i.e. to the Drugs Controller General (I) at CDSCO, FDA Bhawan, Kotla Road, Near Bal Bhawan, New Delhi by the Local Authorized Agent of the foreign manufacturer having either manufacturing or sale License or by the foreign manufacturers' having a whole sale License in the country.

The proposed Guidance for applicants for submission of documents for Import of bulk drug(s) and finished formulation(s) are being uploaded for information of all the stakeholders likely to be affected thereby for comments, if any.

All stakeholders are requested to send their comments and or suggestions on this document in writing for consideration of the CDSCO within a period of 20 days from the date of its uploading through post to the Drugs Control General (India), CDSCO, FDA Bhavan, Kotla Road, New Delhi – 110002 and through email at dc@nb.nic.in

The document is intended to provide non-binding guidance for use in the Import & Registration of bulk drug(s) and finished formulation(s) in India.

I. PURPOSE :

To provide guidance for submission of application in Form 40 to CDSCO for Registration Certificate and issuing License for import of drugs into India

with CDSCO authority India, for issuance of import registration certificate for import of drugs into India.

II.SCOPE :

This guidance is applicable to ***those drugs manufactured outside India, and the import registration to be issued***(under Form 41) by the **Central Drugs Standard Control Organization**,(CDSCO) Directorate General of Health Services, Ministry of Health and Family Welfare, Government of India.

III.REFERENCE :

1. Drugs & Cosmetics Act, 1940 and Rules there under.
2. Schedule D(I) (for registration of the manufacturing Premises)
3. Schedule D(II) (for registration of the drugs).

IV.RESPONSIBILITY :

CDSCO: For implementing and to revise the same as notified, from time to time by the authority.

V.Guidance:

1. An application shall be made to the Licencing Authority in Form 40, either by the manufacturer himself, having a valid wholesale License, for sale or distribution of drugs or by his authorized agent in India either having a valid License to manufacture for sale of a drug or having a valid wholesale License for sale or distribution of drugs.

2. DETAILS TO BE CAPTURED IN FORM 40:

The authorized signatory name, designation, department, along with the complete address of the Company.

i) Authorized Signatory:

The person authorized preferably Director approved by the Board of Directors in case of company or by the proprietor in case of proprietorship firm. The application to accompany affidavit in respect of authorized person or the Power of Attorney in the name of the authorized person.

The Form shall detail the Foreign Manufacturer's contact person in the manufacturing site complete address, (i.e. address of the manufacturing premises), with corporate office address, along with the Telephone number, Fax number and E-mail address.

ii) The address of manufacturing premises shall be captured as below:

Undertaking on the document contents by the responsible person at the manufacturing site (contact person in the manufacturing site)

- In respect of import of more than one drug or class of drugs manufactured by the same manufacturer, provided that drug or the classes of drugs, are manufactured at one factory or more than one factory functioning conjointly as a single manufacturing unit.
- In respect of the drugs manufactured in two or more factories situated in different places, for the manufacturing of the same or different drugs the name and address of both the manufacturing site should be included e.g. if the tablets are manufactured at one location and packed at another location, Name and Address of both the locations indicating the activity of each location.
- The Form shall contain the complete and correct Name of the Drugs to be imported in India.

iii) The drug(s) name shall be captured as below:

- The brand name shall be captured.
- Different pack, pack size and/or different strengths of the same brand shall be captured.

Importer's undertaking letter declaring for the information specified in Schedule D (I) and Schedule D (II), provided by the original manufacturer.

The registration Fees amount (Challan number and date) shall be mentioned on Original TR 6 challan having complete name and address of the applicant and details of application to be enclosed.

iv) Fee structure for Import Registration under Form 40:

- Fees and Form(s) and the undertakings as per Schedule D(I) (for registration of the manufacturing premises) and Schedule D(II) (for registration of the drugs):
- Applicant shall make a payment of 1500 USD (or its equivalent to Indian Currency), as registration fee for the Manufacturing premises.
- Applicant shall make an payment of 1000 USD (or its equivalent to Indian Currency), as registration fee for a single drug and additional fee of 1000 USD for each additional drug in case the manufacturing site remains the same. Fees shall be paid through a Challan in the Bank of Baroda, Kasturba Gandhi Marg, New Delhi-110 001 or any other Bank, as notified, from time to time by the authority.

v) Challan and Bank details:

Fees shall be paid through a Challan in the Bank of Baroda, Kasturba Gandhi Marg, New Delhi-110 001 or any other Bank, as notified, from time to time by the authority.

The pay order cheque to be in favour of Pay & Accounts Officer, DGHS, Nirman Bhavan, New Delhi-01

Challan means-the receipt of the Cash paid into the bank, which is attested by the bank with seal and date.

The fee to be credited under the following details

- Head of Account
- 104 – Fees and Fines under the drugs and cosmetic rules 1940. Conversion rate should be mentioned on the Challan.

Electronic Payment: In case of any direct payment of fees by manufacturer in the country of origin through ECS (Electronic Clearance System) from any bank in the country of origin to Bank of Baroda, Kasturba Gandhi Marg, New Delhi-110 001, through the Electronic Code of the Bank in the Head of Account, –104 – Fees and

Finesll and Original receipt of the said transfer can be considered as an equivalent to bank Challan, subjected to approval by Bank of Baroda.

Applicant is liable to pay 5000 USD (or its equivalent to Indian Currency) for Expenditure [Inspection fees + expenditure on inspection to be borned by company] as may be required for Inspection or Visit of manufacturing premises.

The applicant shall be liable for the payment of testing fees directly to a testing laboratory approved by the central government in India or abroad, as required for examination testing and analysis of drugs.

- Applicant has to pay a fee of 300 USD (or its equivalent to Indian Currency) for a duplicate copy of the registration certificate, if the original is defaced, damaged or lost.

Registration time provided further that if the application is complete in all respects and information specified in D (I) & D (II) are in order, the licencing authority shall within 9 months from the date of receipt of application issue such Registration Certificate, and in exceptional circumstances and for the reasons to be recorded in writing, the Registration Certificate may be issued within such extended period not exceeding 3 months as the licencing authority may deemed fit.

- Undertaking for the compliance of the terms and conditions required, by the applicant to obtain the registration certificate and to keep the validity of the registration certificate.
- The data specified in Schedule D (I) and Schedule D (II) shall be enclosed along with the covering letter and Table of content.

VI. Details to be captured in the Covering Letter:

- Information of the drugs to be imported
- Manufacturer information like address and contact details.

- Brief information about the application and List of Documents-
 - Original Challan and the details of the Challan Form 40
 - Schedule D(I) documents as provided by the drug(s) manufacturer (Module 1 of CTD format)
 - Schedule D(II)-documents as provided by the drug(s) manufacturer (Module 2 to 5 of CTD format)
 - Power of Attorney issued by the manufacturer
 - Copy of Whole Sale License of applicant
 - Copy of Authorization letter of Applicant
 - An Undertaking shall be submitted by the proprietor of the firm in case of proprietorship firm and in case of Private limited Company, by the board of Directors.



B. Requirements for Common Submission Format for Registration of bulk drug(s) and finished formulation(s) in India

The following documents are required to be submitted in the following manner and order for the Import & Registration of the bulk drug(s) and finished product(s) in India: -

Applicants are requested to submit application in 3 or more different files as follows: -

- 1. Covering Letter**– The covering letter is an important part of the application and should clearly specify the intent of the application (whether the application for the registration of the manufacturing site is being submitted for the first time, whether the application is for re-registration/renewal or is for the endorsement of additional products to an existing Registration Certificate) the list of documents that are being submitted (Index with page no's) as well as any other important and relevant information may be provided in the covering letter. The covering letter should be duly signed and stamped by the authorized signatory, indicating the name & designation of the authorized signatory along with the name and address of the firm. Any exemption to the submission requirement be clearly specified in the covering letter on the firm/company letter head and justified in the submissions.

A Resolution shall be submitted by the proprietor of the firm in case of proprietorship firm and by the board of Directors in case of Private limited Company/ firm.

- 2. An Authorization letter** in original issued by the Director/Company Secretary/Partner of the Indian Agent firm revealing the name & designation of the person authorized to sign (along with the name and address of the firm) legal documents such as Form 40, Power of Attorney etc. on behalf of the firm should be submitted at the time of submission of the application for registration (Rule122A). It should

have validity period as per company's policies. Duly self-attested photocopies of the Authorization letter may be submitted at the time of submission of subsequent applications.

- 3.** A duly filled **Form 40** as per the proforma prescribed in the Drugs & Cosmetics Rules, signed & stamped by the (Local Authorized Agent/manufacturer) along with name & designation and date. Form - 40 should be signed by the (Local Authorized Agent or manufacturer and should have valid sale or manufacturing License in India. Form 40 proforma is enclosed at **Annexure -I.**

- 4. TR 6 Challan:** In case of any direct payment of fee by the manufacturer in the country of origin, the fee shall be paid through Electronic Clearance System (ECS) from any bank in the Country of Origin to the Bank of Baroda, Kasturba Gandhi Marg, New Delhi, through the electronic code of the bank in the head of Account stated above and the original receipt of the said transfer shall be treated as an equivalent to the Bank Challan, subject to the approval by the Bank of Baroda that they have received the payment.

- 5. Power of Attorney** - The authorization by a manufacturer to his agent in India shall be documented by a Power of Attorney executed and authenticated either in India before a First Class Magistrate, or in the country of origin before such an equivalent authority, The certificate of which is attested by the Indian Embassy of the said country, and the original of the same shall be furnished along with the application for Registration Certificate. Apostille Power of Attorney from Hague convention member countries is also acceptable. Performa for Power of Attorney is enclosed at **Annexure III.** The authorized agent will be responsible for manufacturer's business activity, in India.

While submitting the Power of Attorney, the following points should be kept in mind: -

It should be co-jointly signed and stamped by the manufacturer as well as the Indian Agent indicating the name & designation of the authorized signatories (along with the name and address of the firm).

It should clearly list the names of all the proposed drugs if possible along with their specific Indication and/or intended use. Further, the names of the proposed drug should correlate with those mentioned in the Form 40, Free Sale Certificate or Certificate of pharmaceutical product (COPP) as per WHO-GMP certification scheme.

The names & addresses of the manufacturer (Contract manufacturer name from different sources) as well as the Indian Agent stated in the Power of Attorney should correlate with the Form 40. Multiple sites are in tabular form.

It should be valid for the period of said Registration Certificate. It implies that a fresh POA is to be submitted at the time of revalidation of RC^a.

a) NOTE:

**LEGAL UNDERTAKING BY WAY OF AN AFFIDAVIT
ON HUNDRED RUPEES NON JUDICIAL
STAMP PAPER**

I.....S/o.....R/o.....
aged about.....do hereby solemnly affirm and state as under
that:-

1. I am working for M/s.....in the capacity of.....and as such fully competent and authorized by the M/s.....to swear by way of the present legal undertaking.
 2. I legally undertake to state that the product.....is manufactured by M/s..... at and the documents enclosed with the application Form-40 are true and correct and nothing contained in it is wrong and false.
 3. I legally undertake to state that the Good Manufacturing Practice (GMP) compliance Certificate with respect to the manufacturing site M/s..... and the product.....submitted
-

along with the Form-40 has been issued by the Competent Drugs Regulatory Authority of the country of origin that is.....

DEPONENT

VERIFICATION

Verified on this day of (Month), (Year) that the contents of my above Legal Undertaking are true and correct and that no part of it is false and nothing material concealed there form.

DEPONENT

6. A duly attested/notarized (in India) and valid copy of **Wholesale License** for sale or distribution of drugs under Drugs and Cosmetics Rules **in Form 20B & 21B** or its renewal in **Form 21C** issued to the manufacturer (subsidiary office/representative of the parent company) or its agent by the State Licensing Authority in India. If the agent is a manufacturer, a duly attested / notarized (in India) and valid copy of manufacturing License issued by the State licensing Authority.

7. A) Schedule D(I) undertaking as per the proforma prescribed in the Drugs & Cosmetics Act & Rules, signed & stamped by the manufacturer/Authorized agent indicating the name and designation of the authorized signatory is required to be submitted as per proforma for **Schedule D(I)** is enclosed at **Annexure IV** along with CTD module 1 covering the Sch.D(I) requirement.

B) The requirements for **Plant Master File** are enclosed at **Annexure V**.

8. Modules 2-5 covering the schedule D (II) requirements

Standard of drug: Second Schedule of the Act prescribes standards to be complied with by imported drugs and by drugs manufactured for sale / sold stocked or exhibited for sale or

distributed in the country. If the drug is in IP it must meet the standards of identity, purity and strength otherwise USP, BP or EP.

Label submission:

- True copy of label as per Rule 96 of the Act. If the drug is in IP label claim must be as per IP.
- **Testing of drugs** – In case of registration of Bulk (Active Pharmaceutical Ingredient) drugs the consecutive three batches are asked to be submitted to the designated laboratory for testing for which fee is to be paid by the applicant to the Laboratory as per their norms.

The applicant should enclosed adequate samples for reanalysis purpose from each of the three consecutive batches along with specifications, Method of analyses, COA tested in their laboratory, impurity Standards, marker compounds, Reference Standard along with its

COA where ever applicable

9. Duly notarized/Appostilled/Attested (by Indian Embassy the country of origin) and valid copy of **Free Sale Certificate/Certificate to Foreign Government/ Certificate of Marketability**/for each drug issued by the National Drug Regulatory Authority of the country of origin. Free Sale Certificate should state that the proposed drug is freely sold in Country of Origin and can be legally exported.

10. Duly notarized/Appostilled/Attested (by Indian Embassy the country of origin) and valid copy of GMP Certificate of WHO guideline or Certificate of Pharmaceutical Product (COPP) as per WHO GMP Certification Scheme/ Product Registration Certificate issued by NRA and or proof of DMF approval by NRA and / or CEP (EDQM certificate) for each drug issued by the National Drug Regulatory Authority of the country of origin. Format for COPP is enclosed at **Annexure VII.**

11. Duly notarized/Appostilled/Attested (by Indian Embassy the country of origin) and valid copy of the **Manufacturing License and or Market Authorization Certificate** in respect of applied drugs issued by the National Drug Regulatory Authority of the country of origin.). Free sale certificate of other countries if available is also be submitted.

12. Duly notarized/Appostilled/Attested (by Indian Embassy in the country of origin) and valid copy of Product Registration Certificate wherever applicable in respect of the foreign manufacturing sites)

Note:

- a. Soft copy of the Plant Master File and Drugs Master File may also be submitted along with the application.
- b. All certificates submitted should be within the valid period.
- c. All the regulatory and legal documents may be provided as a separate file and Plant Master File and Drug Master File may be provided as separate files.
- d. In case, the item considered as drug as per the definition of section 3 (b) of the Act in India but not registered as drug in the country of origin a legal undertaking from the manufacturer and approval of the item from the competent authority of the country of origin duly notarized and apostled should be submitted.
- e. The application of r-DNA products should be made separately as per the guidance document for submissions for biological.
- f. In case of bulk drug, if the same is approved in EU/USA etc. DMF approval number may mention on the covering letter itself.
- g. In case of toll manufacturer to be registered for a drug, the POA should be signed by the Market Authorization holder (legal manufacturer) in the country of origin. Agreement should be submitted as a proof that the legal manufacturer has agreement with the toll manufacturer to manufacture the products.

h. POA should be supplemented with declarations in respect of sites involved in the manufacturing and testing of the applied drugs as per the format given hereunder:

a. For Bulk Drugs (API)

Name of site intermediates are manufactured	Name of site where API is manufactured	Name of site where API is tested	Name of site where API is packed	Name of dispatch site of API

b. For Finished Formulations (FF)

Name of API source	Name of site where formulation is made	Name of site of Primary Packing	Name of site of Secondary packing	Name of site of testing and Release	Name of dispatch site of FF

14. Renewal of registration or re-registration:

At the time of application for renewal of registration or re-registration, the application is to be made 9 months before the expiry of the Registration Certificate. In addition regulatory documentary compliance like Form 40, POA, GMP / COPP, Registration certificate, DMF (soft copy if no change), License (sale or manufacturing License of drugs of the agent) etc., the following undertaking / information is to be submitted:

- i. Undertakings by the manufacturer or his authorized agent in India in respect of any administrative action taken due to adverse reaction, viz. market withdrawal, regulatory restrictions, or cancellation of authorization, and/or not of standard quality report

of any drug pertaining to this Registration Certificate declared by the Regulatory Authority of the country of origin or by any Regulatory Authority of any other country, where the drug is marketed/sold or distributed.

- ii. Undertaking by the manufacturer or his authorized agent in India in respect of any change in manufacturing process, or in packaging, or in labeling or in testing, or in documentation of any of the drug pertaining to this Registration Certificate
- iii. Undertaking by the manufacturer or his authorized agent in India in respect of any change in the constitution of the firm including name and /or address of the registered office/ factory premises operating under this Registration Certificate.
- iv. Details of drugs imported in India during last three years.
- v. Submission of original RC issued.



C. Requirements for Common Submission Format for Import License in Form 10 of Bulk Drug (s) and Finished Formulation (s) in India.

The following documents are required to be submitted in the following manner and order for issue of the Import License in Form 10 of the drugs for import into India: -

1. Covering Letter- The covering letter is an important part of the application and should clearly specify the intent of the application (whether the application for the Import License in Form 10 of the proposed drug is being submitted for the first time or the application is for renewal). The list of documents that are being submitted (Index with page no's) as well as any other important and relevant information may be provided in the covering letter. The covering letter should be duly signed and stamped by the authorized signatory, indicating the name & designation of the authorized signatory along with the name and address of the firm.

2. An Authorization letter- in original issued by the Director/Company Secretary/Partner of the Indian Agent firm revealing the name & designation of the person authorized to sign (along with the name and address of the firm) legal documents such as Form 8 and Form 9 etc. on behalf of the firm should be submitted at the time of submission of the application for Import License. It should have validity period as per company's policies.

Duly attested photocopies of the Authorization letter may be submitted at the time of submission of subsequent applications.

3. Form 8 - A duly filled (Application for License to import drugs (excluding those specified in Schedule X) to the Drugs and Cosmetic Rules, 1945) as per the Performa prescribed in the Drugs & Cosmetics Rules, duly signed & stamped by the Indian Agent along

with name & designation of the authorized signatory. Form 8 Performa is enclosed at **Annexure – XII**.

4. Form 9- A duly filled and Notarized (Form of undertaking to accompany an application for an Import License)^b as per the Performa prescribed in the Drugs & Cosmetics Rules, signed & stamped by the Authorized Agent or manufacturer with name & designation of the authorized signatory. If the Form -9 is issued by the manufacturer, it should be duly notarized and authenticated from Indian Embassy of the country of origin. Form 9 Performa is enclosed at **Annexure – XIV**.

b) I legally undertake to state that the Form-9 undertaking with respect to the manufacturing site M/s..... and the product submitted along with the Form-8 has been issued by the competent person of the firm M/s.....

DEPONENT

VERIFICATION

Verified on this day of (Month), (Year) that the contents of my above Legal Undertaking are true and correct and that no part of it is false and nothing material concealed there form.

DEPONENT

5. Requisite Fee- As prescribed in the Drugs & Cosmetics Act & Rules viz. Rs.1000 for 1 proposed Drug and Rs.100 for each additional Drug to be imported may be submitted at notified branches of Bank of Baroda under the Head of Account —0210 - Medical and Public Health, 04 - Public Health, 104 - Fees and Finesll adjustable to Pay and Account Officer, DGHS, New Delhi in the form of a Treasury Challan. Performa for Treasury Challan (TR 6) is annexed at Annexure III. The Receipt in original (TR 6) is

required to be submitted along with the application for Import License.

In case of any direct payment of fee by the manufacturer in the country of origin, the fee shall be paid through Electronic Clearance System (ECS) from any bank in the Country of Origin to the Bank of Baroda, Kasturba Gandhi Marg, New Delhi, through the electronic code of the bank in the Head of Account stated above and the original receipt of the said transfer shall be treated as equivalent to the Bank Challan, subject to the approval by the Bank of Baroda that they have received the payment.

6. A duly attested (by gazetted officer)/notarized (in India) and valid copy of wholesale License for sale or distribution of drugs or manufacturing License (should be enclosed with the product permission list), under Drugs and Cosmetics Rules issued by the State Licensing Authority.
7. A Valid copy of Registration Certificate in Form 41 issued by CDSCO with respect to proposed Drug, duly authenticated by Indian Agent.
8. The required documents as per Registration Certificate in Form 41 issued by the CDSCO. (If Applicable)

NOTES:

Name and address of the manufacturer, manufacturing premises, Indian Agent and drug(s) proposed to be imported should correlate with the name mentioned in the Registration Certificate in Form 41.

If an endorsement to an existing License is required, copy/details like License no., date of issue & validity) of the Form 10 License along with its endorsements should be furnished along with the application.

All Form-9 issued by foreign manufacturer will be sent for verification to Indian Agent being responsible for business activities of the foreign manufacturer in the country in all respects.

At the time of application for renewal of registration or re-registration, the application is to be made 3 months before the expiry of the Import License. In addition regulatory documentary compliance like Form 8, Form 9, Copy of Registration certificate, License copy (sale or manufacturing License of drugs of the agent) etc., is to be submitted. In addition, following information is required to be submitted.

- Details of drugs imported in India during last three years.
- Details of sampling of drugs in India and results thereof.
- Submission of original Import License issued.



ANNEXURES:

ANNEXURE-I

FORM 40

(See rule 24-A)

*Application for issue of Registration Certificate for import of drugs into India
under the Drugs and Cosmetics Rules 1945*

I/We* _____

_____ (Name and full address) hereby apply for the grant of Registration Certificate for the manufacturer, M/s. _____ (full address with telephone, fax and E-mail address of the foreign manufacturer) for his premises, and manufactured drugs meant for import into India.

1. Names of drugs for registration.

1 * * *

2. I/We enclose herewith the information and undertakings specified in Schedule D (I) and Schedule D (II) duly signed by the manufacturer for grant of Registration Certificate for the premises stated below.

3. A fee of _____ for registration of premises, the particulars of which are given below, of the manufacturer has been credited to the Government under the Head of Account "0210-Medical and Public Health, 04-Public Health, 104-Fees and Fines" under the Drugs and Cosmetics Rules, 1945-Central vide Challan No. _____ dated _____ (attached in original).

4. A fee of _____ for registration of the drugs for import as specified at Serial No. 2 above has been credited to the Government under the Head of Account "0210-Medical and Public Health, 04-Public Health, 104-Fees and Fines" under the Drugs and Cosmetics Rules, 1945-Central vide Challan No. _____, dated _____. (attached in original).

5. Particulars of premises to be registered where manufacture is carried on:

Address (es) _____

Telephone No. _____ Fax _____

E-mail _____

I/We* undertake to comply with all terms and conditions required to obtain Registration Certificate and to keep it valid during its validity period.

Place: _____

Date: _____

Signature _____

Name _____

Designation _____

Seal/Stamp of manufacturer or his authorised Agent in India.

(Note: In case the applicant is an authorized agent of the manufacturer in India, the Power of Attorney is to be enclosed).

*Delete whichever is not applicable.

ANNEXURE – II
TR6 Challan

T.R. - 6. Civil
 (See Rule 92)
 Challan No.

Please indicate whether	Civil
	Defence
	Railways
	Posts & Telegraphs

Chellan of cash paid into Treasury/sub- Treasury
Bank of Baroda, K.G Nagar, New Delhi

To be filled by the remitter			To be filled by the department officer or the Treasury		
By whom Tendered	Name (or designation) And address of the person on whose behalf money is paid	Full particulars of the remittance and /of authority(if any)	Head of Account	Accounts officers by Whom adjustable	Order to the Bank
Name		 सत्यमेव जयते			Date Correct, receive and grant receipt (Signature and full Designation of the Officer Ordering the money to be paid in)
Signature		Total			
(in words) Rupees			To be used only in the case of remittance to the Bank through Departmental Officer or the Treasury officer.		

Received payment (in words) Rupees

Treasurer Accountant Date Treasury Officer

Agent or
 Manager

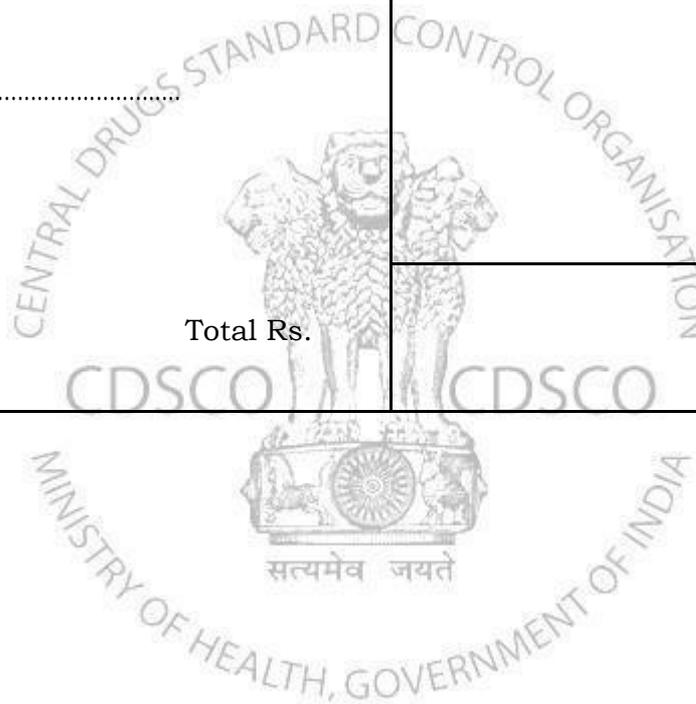
Note: 1. In the case of payment at the treasury, receipts for sums less than Rs 50,000.00 do not require the signature of the Treasury office but only of the accountant and the Treasurer. Receipt for cash and cheques paid for service postage stamps should be given in form T.R.5.

2. Particulars on money tendered should be given below.

Central Drugs Standard Control Organization
Directorate General of Health Services, Ministry of Health and Family Welfare, Government of India

3. In case where direct credit at the bank are permissible the column, Head of Account will be filled in by the Treasury officer or the Accountant General the case may be on receipt of the Bank's Daily Sheet.

Particulars	Amount	
	Rs.	P
Coins.....		
(Notes with details).....		
Cheque (with details).....		
Total Rs.		



ANNEXURE-III

POWER OF ATTORNEY FOR ISSUE OF REGISTRATION CERTIFICATE AND/OR
IMPORT LICENSE FOR IMPORT OF DRUGS IN INDIA

Whereas, M/s....., having Registered Office at at....., (Telephone, Fax ..., email:....) hereinafter to be known as Authorised Agent/Manufacturer of us intends to apply for a Registration Certificate and/or Import License under the Drugs and Cosmetics Rules, 1945, for the import, use and marketing into India, the .. (Product name), Manufactured by (Full address/ telephone no., /e-mail) here after to be known as the Manufacturer, having the factory premises at (Full address/ telephone no., /e-mail), hereby delegate Power of Attorney that for the duration of the said Registration and /or License period:-

- CGS STANDARD CONTROL O.
- (1) The said applicant shall be our Authorized for the Registration Certificate and/or Import License of drugs imported into India, under rule 27-A and 24 of the Drugs and Cosmetics Rules; respectively for purposes of representations and /of signing of the Registration Applications in Form 40, Schedule D(I), Schedule D(II), Form 9 undertaking and /other allied documents.
 - (2) We shall comply with all the conditions imposed on the Registration Certificate and/or Import License, with relevant rules of the Drugs and Cosmetics rules, 1945.
 - (3) We declare that we are carrying on the manufacture of the drugs mentioned in this Schedule, at the premises specified above, and we shall from time to time report 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 Part IX of the Drugs and Cosmetics Rules, 1945:
 - (5) Every drug manufactured by us for import under the Registration Certificate and Import License into India shall be as regard strength, quality and purity conforms with the provisions of Chapter III of Drugs and Cosmetics Act, 1940 and Part IV of the Drugs and Cosmetics Rules, 1945, and their amendments from time to time.

- (6) We shall from time to time report for any change of manufacturing process, or in packaging, or in labeling, or in testing, or in documentation of any of the drugs, pertaining to the Registration Certificate, to be granted to us. Where any change in respect of any of the drugs under the Registration Certificate and Import License has taken place, in respect of any of the above matters, we shall inform the same to the licensing authority, 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 licensing authority, we shall obtain necessary approval within 30 days by submitting a separate application, along with the registration fee as specified in clause (ii) of sub rule (3) of rule 24-A.
- (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 Registration Certificate and/or Import License 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 India also, in consultation with the licensing authority. The licensing authority may direct any further modification to this course of action, including the withdrawal of the drug from Indian market within 48 hours time period.
- (8) We shall comply with such further requirements, if any, as may be specified, by the Government of India, under the Act and the rules, made there under.
- (9) We shall allow the licensing authority 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 Registration Certificate and/or Import License has been made.

- (10) We shall allow the licensing authority 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 licensing authority.
- (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 Licensing authority.

PRODUCT (S) INFORMATION

NAME (S) OF THE PRODUCT:	
Active Ingredients	
Pharmacological Classification	
Dosage Form	

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

Name: ...

Place:

Date: _____

Signature*: _____

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

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

Name:

Place:

Date: _____

Signature: _____

Delete whichever is not applicable.

ANNEXURE-IV

SCHEDULE D (I)

(See rule 21 (d) and rule 24 A)

Information and undertaking required to be submitted by the manufacturer or his authorized agent with the Application Form for a Registration Certificate. The format shall be properly filled in for each application in Form 40. The detailed information, secret in nature, may be furnished on a Computer Floppy.

1. Particulars of the manufacturer and manufacturing premises

1.1 Name and address of the manufacturing premises (Telephone No., Fax No., E-mail address) to be registered.

1.2 Name(s) and address (es) of the Proprietor / Partners / Directors.

1.3 Name and address of the authorized Agent in India, responsible for the business of the manufacturer.

1.4 A brief profile of the manufacturer's business activity, in domestic as well as global market.

1.5 A copy of Plant Master File (duly notarised)

1.6 A copy of Plant Registration / approval Certificate issued by the Ministry of Health/National Regulatory Authority of the foreign country concerned (duly notarised)

1.7 A brief profile of the manufacturer's research activity.

2. Particulars of the manufactured drugs to be registered under Registration Certificate.

2.1 Names of drugs (Bulk/Formulation/Special product) to be registered meant for import into and use in India.

2.2 A copy of the approved list showing the bulk drugs/formulations/special products mentioned in 2.1 above are permitted for manufacturing / marketing in the country of origin (duly notarized).

2.3 A copy of Good Manufacturing Practice (GMP) certificate, as per WHO-GMP guidelines, or Certificate of Pharmaceutical Products (CPP), issued by the National Regulatory Authority of the foreign country concerned, in relation to the bulk drugs or formulations or special products, meant for import into India.

2.4 The domestic prices of the drugs to be registered in India, in the currency of the country of origin.

2.5 The name(s) of the drug(s) which are original research products of the manufacturer.

3. Undertaking to declare that: -

- 3.1. We shall comply with all the conditions imposed on the Registration Certificate, read with rules 74 and 78 of the Drugs and Cosmetics rules, 1945.
- 3.2 We declare that we are carrying on the manufacture of the drugs mentioned in this Schedule, at the premises specified above, and we shall from time to time report 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.
- 3.3 We shall comply with the provisions of Part IX of the Drugs and Cosmetics Rules, 1945.
- 3.4 Every drug manufactured by us for import under the Registration Certificate into India shall be as regard strength, quality and purity conforms to the provisions of Chapter III of Drugs and Cosmetics Act, 1940 and Part IV of the Drugs and Cosmetics Rules 1945, and their amendments from time to time.
- 3.5 We shall from time to time report for any change or manufacturing process, or in packaging, or in labeling, or in testing, or in documentation of any of the drugs, pertaining to the Registration Certificate, to be granted to us. Where any change in respect of any of the drugs under the Registration Certificate has taken place, in respect of any of the above matters, we shall inform the same to the licensing authority 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 licensing authority, we shall obtain necessary approval within 30 days by submitting a separate application, along with the registration fee as specified in clause (ii) of sub rule (3) of rule 24-A.
- 3.6 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 reportll of any drug pertaining to the Registration Certificate 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 India also, in consultation with the licensing authority. The licensing authority may direct any further modification to this course of action, including the withdrawal of the drug from Indian market within 48 hours time period.

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

3.8 We shall allow the licensing authority 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 Registration Certificate has been made.

3.9 We shall allow the licensing authority 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 licensing authority.

Place:

Date:

Signature of the manufacturer

¹ [or his authorized agent] Seal

/ Stamp



Module-1	Contents
1.0	Cover letter
1.1	Comprehensive Table of contents (Modules 1 to 5)
1.2	Application form (Form 40 and TR 6 Challan)
	Coordinates Related to the Application
1.2.1	Name, address, telephone, fax, e-mail of manufacturer of drug substance(API) & drug product(Finished Formulations)
1.2.2	Name, address, telephone, fax, e-mail of the responsible Official
1.2.3	Name, address, telephone, fax, e-mail of the authorized agent in India: (for imported drug products)
1.2.4	Name, designation, address, telephone, fax, e-mail of the official responsible for releasing batches of drug product
1.2.5	Name, address, telephone, fax, e-mail of the manufacturing premises holding Market Authorization of the drug product (for imported drug products)
1.2.6	Name, address, telephone, fax, e-mail of manufacturer of drug substance
1.2.7	Name, address, telephone, fax, e-mail of other manufacturer(s) involved in the production process
1.3	Product Information
A	Proprietary, commercial or trade name of drug product
B	Non-proprietary name or common name of drug product
C	Composition (as per label claim)
D	Dosage form
E	Strength per dosage unit
F	Dispensing requirements
G	Route of administration
H	Commercial presentation
I	Conditions of storage or conservation
1.3.1	Summary of Product Characteristics (SPC),/ Monograph for health professionals
1.3.2	Product Labeling (should conform to the specifications under the Drugs and Cosmetics Rules 1945) a. Primary package label b. Secondary package label c. Package insert (in English)

1.4	A brief profile of the manufacturer's research activity
A	Name of the drug / drug product which are original research product of manufacturer
B	A brief profile of the manufacturer's business activity in domestic as well as global market.
C	Letter of Power of Attorney
D	Letter for Authorized signatory
E	a) A copy of plant registration / approval certificate/ Establishment License issued by the Ministry of Health / National Regulatory Authority of the country of origin. (Notarized Copy)
F	b) A copy of approval, if any, showing the drug is permitted for manufacturing and/or marketing in the country of origin.
G	c) A copy Certificate of Pharmaceutical Product (CPP) as per WHO GMP certification scheme for imported drug products OR Certificate of Good Manufacturing Practices (cGMP) & Free Sale Certificate (FSC) from country of origin for imported Drug Products (Duly Notarized Copy)
H	A copy of market authorization/ permission to manufacture in the country of origin the Bulk Drug/ Drug Product meant for import to India
I	Domestic price of the Drug / Drug product to be registered in India in the currency in the country of origin
J	Registration/ Market authorization of Drug/ Drug Product worldwide along with Registration Certificate(Market Authorization) it should include list of country where import permission or marketing authorization has been granted/ pending or cancelled or withdrawn with date
K	List of countries where drug/ drug product is patented
L	Copy of Plant Master File (Duly Notarized)
1.4.1	Information about the experts
1.4.2	Quality
1.4.3	Non-Clinical
1.4.4	Clinical
1.5	Environmental risk assessment (if applicable)
1.6	Information regarding Pharmacovigilance
1.7	Information relating to Clinical Trials
1.8	Samples from three consecutive batches, quantity sufficient for three analysis
1.9	Undertaking by the manufacturer

ANNEXURE-V

1. Plant Master File. –The Licensee shall prepare a precise document in the form of Site Master File containing specific and factual Good Manufacturing Practices about the production and/or control of pharmaceutical manufacturing preparations carried out at the licensed premises. It shall contain the following: -

1.1 General information:

- (a) Brief information of the firm;
- (b) Pharmaceutical manufacturing activities as permitted by the licensing authority;
- (c) Other manufacturing activities, if any, carried out on the premises;
- (d) Type of products Licensed for manufacture with flow charts mentioning procedure and process flow;
- (e) Number of employees engaged in the production, quality control, storage and distribution;
- (f) Use of outside scientific, analytical or other technical assistance in relation to manufacture and analysis;
- (g) Short description of the Quality Management System of the firm; and
- (h) Products details registered with foreign countries.

1.2 Personnel:

- (a) Organizational chart showing the arrangement for quality assurance including production and quality control;
- (b) Qualification, experience and responsibilities of key personnel;
- (c) Outline for arrangements for basic and in-service training and how the records are maintained;
- (d) Health requirements for personnel engaged in production; and
- (e) Personnel hygiene requirements, including clothing.

1.3 Premises:

- (a) Simple plan or description of manufacturing areas drawn to scale;
- (b) Nature of construction and fixtures/fittings;

- (c) Brief description of ventilation systems. More details should be given for critical areas with potential risk of airborne contamination (schematic drawing of systems). Classification of the rooms used for the manufacture of sterile products should be mentioned;
- (d) Special areas for the handling of the highly toxic, hazardous and sensitizing materials;
- (e) Brief description of water system (schematic drawings of systems), including sanitation;
- (f) Description of planned preventive maintenance programs for premises and of the recording system.

1.4 Equipment:

- (a) Brief description of major equipment used in production and Quality Control Laboratories (a list of equipment required);
- (b) Description of planned preventive maintenance programs for equipment and of the recording system; and
- (c) Qualification and calibration including the recording systems and arrangements for computerized systems validation.

1.5 Sanitation:

- (a) Availability of written specifications and procedures for cleaning manufacturing areas and equipment.

1.6 Documentation. -

- (a) Arrangements for the preparation, revision and distribution of;
- (b) Necessary documentation for the manufacture;
- (c) Any other documentation related to product quality that is not mentioned elsewhere (e.g. microbiological controls about air and water).

1.7 Production:

- (a) Brief description of production operations using, wherever possible, flow sheets and charts specifying important parameters;
- (b) arrangements for the handling of starting materials, packaging materials, bulk and finished products, including sampling, quarantine, release and storage;
- (c) Arrangements for the handling of rejected materials and products;
- (d) Brief description of general policy for process validation.

1.8 Quality Control:

(a) Description of the quality control system and of the activities of the Quality Control Department. Procedures for the release of the finished products.

1.9 Loan License manufacture (Toll manufacturing) and Licensee:

(a) Description of the way in which compliance of Good Manufacturing Practices by the loan Licensee shall be assessed.

1.10 Distribution, complaints and product recall:

- (a) arrangements and recording system for distribution;
- (b) Arrangements for the handling of complaints and product recalls.

1.11 Self inspection. -

(a) Short description of the self-inspection system indicating whether an outside, independent and experienced external expert was involved in evaluating the manufacturer's compliance with Good manufacturing Practices in all aspects of production.

1.12 Export of drugs. -

- (a) Products exported to different countries;
- (b) Complaints and product recall, if any

ANNEXURES:

1. Site plan. Layout (equipment layout, men & material flow lay out, pressure differential lay out)
2. HVAC schematics and details of areas (Where in clearly specify the filtration level & classification of core areas & rooms as required in section 3.3 of SMF)

4. Water system – Schematic diagrams along with the components
5. List of personnel (with designation, qualification & experience)
6. List of primary & secondary Impurity and Reference standards/cultures available with the firm (relevant to the applied products)
7. List of equipments used in production, testing and utilities with their make, model and capacity.



ANNEXURE-VI

SCHEDULE D (II)

[See rule 21 (d) and rule 24 A]

Information required to be submitted by the manufacturer or his authorized agent with the Application Form for the registration of a bulk drug/formulation/special product for its import into India. The format shall be properly filled in and the detailed information, secret in nature, may be furnished on a Computer Floppy

1. GENERAL

- 1.1. Name of the drug/formulation/special product, a brief description and the therapeutic class to which it belongs.
- 1.2 Regulatory status of the drug. Free Sale Certificate and/or Certificate of Pharmaceutical Products (CPP) as per WHO GMP certification Scheme issued by the National Regulatory Authority of the country of origin/ Product Registration Certificate issued by NRA and or proof of DMF approval by NRA and/ or CEP (EDQM certificate).
Free sale approval issued by the Regulatory Authorities of other major countries.
- 1.3 Drugs Master File (DMF) for the drug to be registered (duly notarised).
- 1.4 GMP Certificate in WHO formats or Certificate of Pharmaceutical Products (CPP) issued by
National Regulatory Authority of the country of origin (duly notarised) or Proof of DMF Approval by NRA and or CEP (EDQM certificate).
- 1.5 List of countries where marketing authorization or import permission for the said drug is
granted with date (respective authorisation shall be enclosed).
- 1.6 List of countries where marketing authorisation or import permission for the said drug is Cancelled/withdrawn with date.
- 1.7 List of countries where marketing authorisation or import permission for the said drug is pending since (date).
- 1.8 Domestic price of the drug in the currency followed in the country of origin.
- 1.9 List of countries where the said drug is patented.

2. CHEMICAL AND PHARMACEUTICAL INFORMATION OF DRUGS.

2.1 Chemical name.

Code name or number, if any. Non-proprietary or generic name, if any.

Structure.

Physico-chemical properties.

2.2 Dosage form and its composition.

Qualitative and Quantitative composition in terms of the active substances(s) and excipient(s)

List of active substance(s) separately from the constituent(s) of excipients.

2.3 Specifications of active and inactive ingredient (s) including pharmacopoeial references

2.4 Source of active ingredient(s), name and address.

2.5 Tests for identification of the active ingredient(s), Method of its assays and tests for impurity profile with reference standards for the impurities (Protocol to be submitted along with reference standards for the impurities / relative substances).

2.6 Outline method and flow chart of manufacture of the bulk drug or finished formulation or special product.

2.7 Detailed test protocol for the drug with pharmacopoeial reference or in-house specification as approved by the registration authority, in the country of origin.

2.8 Stability data including accelerated stability and real time stability analysis.

2.9 Documentation on pack size.

2.10 Numerical expression on EAN bar code on the labels and cartons.

2.11 Safety documents on containers and closures.

2.12 Documentation on storage conditions.

2.13 Three samples of medicinal product/drug and outlet packing are to be submitted with batch certificates. Additional samples as well as reference substances with batch certificates including date of manufacture, shelf

life, and storage conditions of reference substance may be required both during registration procedure and during validity of registration decision.

2.14 Batch test reports/certificate of five consecutive production batches in details of the medicinal product are to be submitted for every site of manufacturing premises.

2.15 Manner of labeling as per rule 96 of the Drugs and Cosmetics Rules 1945.

2.16 Package insert.

2.17 Details of safety handling procedure of the drug.

2.18 Details of PMS study report for marketing period not exceeding five years.

3. BIOLOGICAL AND BIOPHARMACEUTICAL INFORMATION OF DRUGS

3.1 Biological control tests applied on the starting material, if applicable.

3.2 Biological control tests applied on the intermediate products, if applicable.

3.3 Biological control tests applied on the finished medical products, if applicable.

3.4 Stability of the finished products in terms of biological potency of the drug, if applicable.

3.5 Sterility tests, if applicable, specification and protocol therein.

3.6 Pyrogen tests, if applicable, specification and protocol therein.

3.7 Acute and sub-acute toxicity tests, if applicable specification and protocol therein.

3.8 Bio-availability studies and bio-equivalence data, if applicable.

3.9 Data relating to the environmental risk assessment for r-DNA products.

3.10 Other information relevant under the section.

4. PHARMACOLOGICAL AND TOXICOLOGICAL INFORMATION OF DRUGS.

Executive summary of the product is to be submitted mentioning the specific and general pharmacological actions of the drug and pharmacokinetic studies on absorption, metabolism, distribution and excretion. A separate note is to be given on acute and sub-acute toxicity studies and long term toxicity studies. Specific studies on reproductive

toxicity, local toxicity and carcinogenic activity of the drug are to be elaborated, as far as possible.

5. CLINICAL DOCUMENTATION

A new drug as defined under rule 122-E of the Drugs and Cosmetics Rules, 1945 is required to be permitted separately by the licensing authority under rule 122-A of the said rules prior to its registration. Such a new drug requires a brief summary and clinical documentation, along with permission under 122-A of the said rules for its Registration Certificate.

6. LABELLING AND PACKAGING INFORMATION OF DRUGS.

6.1 Labels should conform as per the specifications under the Drugs and Cosmetics Rules 1945.

6.2 Package insert should be in English and shall indicate the following therapeutic indications: -

- Posology and method of administration.
- Contra-indications.
- Special warnings and special precautions for use, if any.
- Interaction with other medicaments and other forms of interaction.
- Pregnancy and lactation, if contra-indicated.
- Effects on ability to drive and use machines, if contra-indicated.
- Undesirable effects/side effects.
- Antidote for overdosing.

6.3 Package insert should indicate the following pharmaceutical information: -

- List of excipients.
- Incompatibilities.
- Shelf life in the medical product as packaged for sale.
- Shelf life after dilution or reconstitution according to direction.
- Shelf life after first opening the container.
- Special precautions for storage.
- Nature and specification of the container.

➤ Instructions for use/handling.

7 SPECIFIC INFORMATION REQUIRED FOR THE SPECIAL PRODUCTS

(to be supplied, separately in Annexure, as _A', _B' and _C')

The information submitted above is true to the best of my knowledge and belief.

Place:

Date: Signature of the manufacturer

[or his authorized agent]

Seal/Stamp

NOTE:

1. Any change in the process of manufacture, method of testing, labeling, packaging, designing of the sale pack, medical literature and documentation is to be intimated to the licensing authority forthwith and permission to be obtained from him within 30 days time period.
2. Information relating to Serial No.4 and Serial No.5 are not applicable for drugs figuring in Indian Pharmacopoeia and also for the drugs figuring in United States of Pharmacopoeia, European Pharmacopoeia, and British Pharmacopoeia provided such drugs have already been approved for marketing in India for the applicant under rules 122A, 122B, 122C or 122D of the Drugs and Cosmetics Rules 1945.

ANNEXURE-VII

Certificate of Pharmaceutical Products (COPP)

(Model Certificate of a Pharmaceutical Product (as per WHO GMP guidelines) Certificate of a Pharmaceutical Product ¹)

No. of Certificate: -----

--

Exporting (certifying) country: -----

--

Importing (requesting) country: -----

--

1. Name and dosage form of product: -----

1.1 Active ingredient(s)² and amount(s) per unit dose:³ -----

For complete qualitative composition including excipients, see attached⁴.

1.2 Is this product Licensed to be placed on the market for use in the
exporting country? ⁵

Yes/No (key in as appropriate)

1.2 Is this product actually on the market in the exporting country?
Yes/no/unknown (key in as appropriate)

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

2A.1 Number of product License⁷ and date of issue: -----

-

2A.2 Product-License holder (name and address): -----

2A.3 Status of product-License holder: ⁸ a/b/c (key in appropriate category as defined in note 8)

2A3.1 For categories b and c the name and address of the manufacturer producing the dosage form are: ⁹

2A.4 Is Summary Basis of Approval appended?
¹⁰ Yes/no (key in as appropriate)

2A.5 Is the attached, officially approved product information complete and consonant with the License?

Yes/no/not provided (key in as appropriate)

2A.6 Applicant for certificate, if different from License holder (name and

address):

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

2B.2 Status of applicant: a/b/c (key in appropriate category as defined in note 8)

2B2.1 For categories b and c the name and address of the manufacturer producing the dosage form are: ⁹

2B.3 Why is marketing authorization lacking?

Not required/not requested/under consideration/refused (key is as appropriate)

2B.4 Remark: ¹³

3. Does the certifying authority arrange for periodic inspection of the manufacturing plant in which the dosage form is produced? Yes/no/not applicable¹⁴ (key in as appropriate)

If no or not applicable proceed to question

3.1 Periodicity of routine inspections (years):-----

3.2 Has the manufacture of this type of dosage form been inspected? Yes/no (key in as appropriate)

3.3 Do the facilities and operations conform to GMP as recommended by the World Health Organization? ¹⁵
Yes/no (key in as appropriate)

4. Does the information submitted by the applicant satisfy the certifying authority on all aspects of the manufacture of the product? ¹⁶

Yes/no (key in as appropriate)

If no, explain: -----

Address of certifying authority: -----

Telephone number: ----- Fax number: -----

--

Name of authorized person: -----

Signature: -----

Stamp and date: -----

General Instructions

Please refer to the guidelines for full instructions on how to complete this form and information on the implementation of the Scheme. The forms are suitable for generation by computer. They should always be submitted as hard copy, with responses printed in type rather than handwritten. Additional sheets should be appended, as necessary, to accommodate remarks and

Explanatory notes

1. This certificate, which is in the format recommended by WHO, establishes the status of the pharmaceutical product and of the applicant for the certificate in the exporting country. It is for a single product only since manufacturing arrangements and approved information for different dosage forms and different strengths can vary.
2. Use, whenever possible, International Non-proprietary Name (INNs) or national non-proprietary name.
3. The formula (complete composition) of the dosage form should be given on the certificate or be appended.
4. Details of quantitative composition are preferred, but their provision is subject to the agreement of the product-License holder.
5. When applicable, append details of any restriction applied to the sale, distribution or administration of the product that is specified in the product License.
6. Section 2A and 2B are mutually exclusive.
7. Indicate, when applicable, if the License is provisional, or the product has not yet been approved. 8. Specify whether the person responsible for placing the product on the market: (a) manufactures the dosage form; (b) Packages and/or labels a dosage form manufactured by an independent company; or (c) Is involved is none of the above.
8. This information can be provided only with the consent of the product-License holder or, in the case of non-registered products, the applicant. Non-completion of this section indicates that the party concerned has not agreed to inclusion of this information. It should be noted that information concerning the site of production is part of the product License. If the production site is changed, the License must be updated or it will cease to be valid.
9. This refers to the document, prepared by some national regulatory authorities, that summarizes the technical basis on which the product has been licensed.
10. This refers to product information approved by the competent national regulatory authority, such as a Summary of Product Characteristics (SPC).

11. In this circumstance, permission for issuing the certificate is required from the product- License holder. This permission must be provided to the authority by the applicant.
12. Please indicate the reason that the applicant has provided for not requesting registration: (a) the product has been developed exclusively for the treatment of conditions- particularly tropical diseases-not endemic in the country of export; (b) the product has been reformulated with a view to improving its stability under tropical conditions; (c) the product has been reformulated to exclude excipients not approved for use in pharmaceutical products in the country of import; (d) the product has been reformulated to meet a different maximum dosage limit for an active ingredient; (e) any other reason, please specify.
13. Not applicable means that the manufacture is taking place in a country other than that issuing the product certificate and inspection is conducted under the aegis of the country of manufacture.
14. The requirements for good practices in the manufacture and quality control of drugs referred to in the certificate are those included in the thirty-second report of the Expert Committee on Specifications for Pharmaceutical Preparations (WHO Technical Report Series, No. 823, 1992, Annex 1). Recommendations specifically applicable to biological products have been formulated by the WHO Expert Committee on biological Standardization (WHO Technical Report Series, No. 822, 1992, Annex 1).
15. This Section is to be completed when the product-License holder or applicant conforms to status (b) or (c) as described in note 7 above.
It is of particular importance when foreign contractors are involved in the manufacture of the product. In these circumstances the applicant should supply the certifying authority with information to identify the contracting parties responsible for each stage of manufacture of the finished dosage form, and the extent and nature of any controls exercised over each of these parties.

The Layout for this Model Certificate is available on WordPerfect from the Division of Drug Management and Policies, World Health Organization, 1211 Geneva 27, Switzerland

ANNEXURE VIII

MODULE 3: QUALITY

3.1.	<p>TABLE OF CONTENTS OF MODULE 3</p> <p>A Table of Contents for the filed application should be provided.</p>
3.2	<p>BODY OF DATA</p>
3.2. S	<p>DRUG SUBSTANCE(S) (NAME, MANUFACTURER)</p> <p><u>NOTE:</u> For a drug product containing more than one drug substance, the information requested for part —SII should be provided in its entirety for each drug substance.</p> <p>If the applicant has a manufacturing permission for bulk drug(s)/Drug substance / API, please provide a copy of the same and further details under drug substance can be concise as the same would have already submitted in great details to this office at the time of request for approval of drug substance. Otherwise, provide complete details below.</p> <p style="text-align: center;">WHO GMP Certification/ CPP as per WHO GMP Certification Scheme or Product License (product registration certificate issued by NRA or the Proof of DMF approval by NRA and or CEP (EDQM) certificate) shall be submitted.</p>
3.2. S.1	<p>General Information (name manufacturer)</p>
3.2. S.1.1	<p>Nomenclature (name manufacturer)</p> <p>Information on the nomenclature of the drug substance should be provided.</p> <p>For example:</p> <ul style="list-style-type: none"> • Recommended International Nonproprietary Name (INN);

3.2. S.1.2	<ul style="list-style-type: none"> • Compendial name if relevant • Chemical name(s) • Company or laboratory code; • Other non-proprietary name(s), e.g., national name, United States Adopted Name (USAN), Japanese Accepted Name (JAN); British Approved Name (BAN), etc. • Chemical Abstracts Service (CAS) registry number. <p>Structure (name, manufacturer)</p> <p>The structural formula, including relative and absolute stereochemistry, the molecular formula, and the relative molecular mass should be provided (As applicable).</p>
3.2. S.1.3	<p>General Properties (name manufacturer)</p> <p>A list should be provided of physicochemical and other relevant properties of the drug substance.</p>
3.2. S.2	<p>Manufacture of drug substance (name, manufacturer)</p>
3.2. S.2.1	<p>Manufacturer(s) (name, manufacturer)</p> <p>The name, address, and responsibility of each manufacturer, including contractors, and each proposed production site or facility involved in manufacturing and testing should be provided.</p>
3.2. S.2.2	<p>Description of Manufacturing Process and Process Controls (name, manufacturer)</p> <p>The description of the drug substance manufacturing process represents the applicant's commitment for the manufacture of the drug substance. Information should be provided to adequately describe the manufacturing process and process</p>

controls.

For example:

A sequential procedural narrative of the manufacturing process should be submitted. The narrative should include, for example, quantities of raw materials, solvents, catalysts and reagents reflecting the representative batch scale for commercial manufacture, identification of critical steps, process controls, equipment and operating conditions (e.g., temperature, pressure, pH, and time).

A flow diagram of the synthetic process(es) should be provided that includes molecular formulae, weights, yield ranges, chemical structures of starting materials, intermediates, reagents and drug substance reflecting stereochemistry, and identifies operating conditions and solvents.

Alternate processes should be explained and described with the same level of detail as the primary process. Reprocessing steps should be identified and justified. Any data to support this justification should be either referenced or filed in 3.2.S.2.5.

Fermentation products:

Information should be provided on the manufacturing process, which typically starts with a vial(s) of the cell bank, and includes cell culture, harvest(s), purification and modification reactions, filling, storage and shipping conditions.

Batch (es) and scale definition:

An explanation of the batch numbering system, including information regarding any pooling of harvests or intermediates and batch size or scale should be provided.

Cell culture and harvest:

A flow diagram should be provided that illustrates the

manufacturing route from the original inoculums (e.g. cells contained in one or more vials(s) of the Working Cell Bank up to the last harvesting operation. The diagram should include all steps (i.e., unit operations) and intermediates. Relevant information for each stage, such as population doubling levels, cell concentration, volumes, pH, cultivation times, holding times, and temperature, should be included. Critical steps and critical intermediates for which specifications are established (as mentioned in 3.2.S.2.4) should be identified.

A description of each process step in the flow diagram should be provided. Information should be included on, for example, scale; culture media and other additives (details provided in 3.2.S.2.3); major equipment (details provided in 3.2.A.1); and process controls, including in-process tests and operational parameters, process steps, equipment and intermediates with acceptance criteria (details provided in 3.2.S.2.4). Information on procedures used to transfer material between steps, equipment, areas, and buildings, as appropriate, and shipping and storage conditions should be provided. (Details on shipping and storage provided in 3.2.S.2.4.).

Purification and modification reactions:

A flow diagram should be provided that illustrates the purification steps (i.e., unit operations) from the crude harvest(s) up to the step preceding filling of the drug substance. All steps and intermediates and relevant information for each stage (e.g., volumes, pH, critical processing time, holding times, temperatures and elution profiles and selection of fraction, storage of intermediate, if applicable) should be included. Critical steps for which specifications are established as mentioned in 3.2.S.2.4 should be identified.

A description of each process step (as identified in the flow

	<p>diagram) should be provided. The description should include information on, for example, scale, buffers and other reagents (details provided in 3.2.S.2.3, major equipment (details provided in 3.2.A.1), and materials. For materials such as membranes and chromatography resins, information for conditions of use and reuse also should be provided. (Equipment details in 3.2.A.1; validation studies for the reuse and regeneration of columns and membranes in 3.2.S.2.5.) The description should include process controls (including in-process tests and operational parameters) with acceptance criteria for process steps, equipment and intermediates. (Details in 3.2.S.2.4.).</p> <p>Reprocessing procedures with criteria for reprocessing of any intermediate or the drug substance should be described. (Details should be given in 3.2.S.2.5.).</p> <p>Information on procedures used to transfer material between steps, equipment, areas, and buildings, as appropriate, and shipping and storage conditions should be provided (details on shipping and storage provided in 3.2.S.2.4.).</p> <p>Filling, storage and transportation (shipping):</p> <p>A description of the filling procedure for the drug substance, process controls (including in-process tests and operational parameters), and acceptance criteria should be provided. (Details in 3.2.S.2.4.) The container closure system(s) used for storage of the drug substance (details in 3.2.S.6.) and storage and shipping conditions for the drug substance should be described.</p>
3.2. S.2.3	<p>Control of Materials (name, manufacturer):</p> <p>Materials used in the manufacture of the drug substance (e.g., raw materials, starting materials, solvents, reagents, catalysts)</p>

	<p>should be listed identifying where each material is used in the process. Information on the quality and control of these materials should be provided. Information demonstrating that materials (including biologically-sourced materials, e.g., media components, monoclonal antibodies, enzymes) meet standards appropriate for their intended use (including the clearance or control of adventitious agents) should be provided, as appropriate. For biologically-sourced materials, this can include information regarding the source, manufacture, and characterization. (Details in 3.2.A.2 for both NCE and fermentation based products).</p>
3.2. S.2.4	<p>Controls of Critical Steps and Intermediates (name manufacturer):</p> <p>Critical Steps:</p> <p>Tests and acceptance criteria (with justification including experimental data) performed at critical steps identified in 3.2.S.2.2 of the manufacturing process to ensure that the process is controlled should be provided.</p> <p>Intermediates:</p> <p>Information on the quality and control of intermediates isolated during the process should be provided.</p> <p>Additionally for Fermentation products:</p> <p>Stability data supporting storage conditions should be provided.</p>
3.2. S.2.5	<p>Process Validation and/or Evaluation (name, manufacturer)</p> <p>Process validation and/or evaluation studies for aseptic processing and sterilization should be included.</p> <p>Fermentation products:</p>

	<p>Sufficient information should be provided on validation and evaluation studies to demonstrate that the manufacturing process (including reprocessing steps) is suitable for its intended purpose and to substantiate selection of critical process controls (operational parameters and in-process tests) and their limits for critical manufacturing steps (e.g., cell culture, harvesting, purification, and modification).</p> <p>The plan for conducting the study should be described and the results, analysis and conclusions from the executed study (ies) should be provided. The analytical procedures and corresponding validation should be cross-referenced (e.g., 3.2.S.2.4, 3.2.S.4.3) or provided as part of justifying the selection of critical process controls and acceptance criteria.</p> <p>For manufacturing steps intended to remove or inactivate viral contaminants, the information from evaluation studies should be provided in 3.2.A.2.</p>
3.2. S.2.6	<p>Manufacturing Process Development (name, manufacturer)</p> <p>A description and write up should be provided of the significant changes made to the manufacturing process and/or manufacturing site of the drug substance used in producing nonclinical, clinical, scale-up, pilot, and, if available, production scale batches.</p> <p>Reference should be made to the drug substance data provided in section 3.2.S.4.4.</p> <p>Fermentation products:</p> <p>The developmental history of the manufacturing process, as described in 3.2.S.2.2, should be provided. The description of change(s) made to the manufacture of drug substance batches used in support of the marketing application (e.g., nonclinical or clinical studies) should include, for example, changes to the</p>

	<p>process or to critical equipment. The reason for the change should be explained. Relevant information on drug substance batches manufactured during development, such as the batch number, manufacturing scale, and use (e.g., stability, nonclinical, reference material) in relation to the change, should be provided.</p> <p>The significance of the change should be assessed by evaluating its potential to impact the quality of the drug substance (and/or intermediate, if appropriate). For manufacturing changes that are considered significant, data from comparative analytical testing on relevant drug substance batches should be provided to determine the impact on quality of the drug substance (may refer Q6B of ICH guidelines for additional guidance). A discussion of the data, including a justification for selection of the tests and assessment of results, should be included.</p> <p>Testing used to assess the impact of manufacturing changes on the drug substance(s) and the corresponding drug product(s) can also include nonclinical and clinical studies. Cross-reference to the location of these studies in other modules of the submission should be included.</p> <p>Reference should be made to the drug substance data provided in section 3.2.S.4.4.</p>
3.2. S.3	Characterization of Drug Substances (name, manufacturer)
3.2. S.3.1	<p>Elucidation of Structure and other Characteristics (name, manufacturer)</p> <p>Confirmation of structure based on e.g., synthetic route and spectral analyses should be provided. Information such as the potential for isomerism, the identification of stereochemistry, or the potential for forming polymorphs should also be included.</p>

3.2.S.3.2	<p>Impurities (name, manufacturer)</p> <p>Details information on impurities should be provided.</p>
3.2. S.4	<p>Quality control of Drug Substance (name, manufacturer)</p>
3.2. S.4.1	<p>Specification and Justification of Specification (name, manufacturer)</p> <p>An In House specification for the drug substance and the justification for the drug substance In House specification should be provided if not in any of the official pharmacopieas.</p>
3.2. S.4.2	<p>Analytical Procedures (name, manufacturer)</p> <p>The analytical procedures used for testing the drug substance should be provided.</p>
3.2. S.4.3	<p>Validation of Analytical Procedures (name manufacturer)</p> <p>Analytical validation information, including experimental data for the analytical procedures used for testing the drug substance, should be provided.</p>
3.2. S.4.4	<p>Batch Analyses (name, manufacturer)</p> <p>Description of batches and results of batch analyses should be provided.</p>
3.2.S.5	<p>Reference Standards or Materials (name, manufacturer)</p> <p>Information on the reference standards or reference materials used for testing of the drug substance should be provided.</p>
3.2. S.6	<p>Container Closure System (name manufacturer)</p> <p>A description of the container closure system(s) should be provided, including the identity of materials of construction of each primary packaging component, and their specifications. The specifications should include description and identification (and critical dimensions with drawings, where appropriate). Non-compendial methods (with validation) should be included, where appropriate. For non-functional secondary packaging</p>

	<p>components (e.g., those that do not provide additional protection), only a brief description should be provided. For functional secondary packaging components, additional information should be provided.</p> <p>The suitability should be discussed with respect to, for example, choice of materials, protection from moisture and light, compatibility of the materials of construction with the drug substance, including sorption to container and leaching, and/or safety of materials of construction.</p>
3.2. S.7	Stability (name, manufacturer)
3.2.S.7.1	<p>Stability Summary and Conclusions (name manufacturer)</p> <p>The types of studies conducted, protocols used, and the results of the studies should be summarized. The summary should include results, for example, from forced degradation studies and stress conditions, as well as conclusions with respect to storage conditions and retest date or shelf-life, as appropriate.</p>
3.2. S.7.2	<p>Post approval Stability Protocol and Stability Commitment (name, manufacturer)</p> <p>The post-approval stability protocol and stability commitment should be provided.</p>
3.2. S.7.3	<p>Stability Data (name of the manufacturer)</p> <p>Results of the stability studies (e.g., forced degradation studies and stress conditions) should be presented in an appropriate format such as tabular, graphical, or narrative. Information on the analytical procedures used to generate the data and validation of these procedures should be included.</p>
3.2. P	DRUG PRODUCT (NAME, DOSAGE FORM)
3.2. P.1	Description and Composition of the Drug Product dosage

	<p>form)</p> <p>A description of the drug product and its composition should be provided. The information provided should include.</p> <p>for example:</p> <ul style="list-style-type: none">• Description of the dosage form. For a drug product supplied with reconstitution diluents(s), the information on the diluents should also be provided.• Composition, i.e., list of all components of the dosage form, and their amount on a per-unit basis (including overages, if any) the function of the components, and a reference to their quality standards (e.g., compendial monographs or manufacturer's specifications)• Description of accompanying reconstitution diluents (s); if any and• Type of container and closure used for the dosage form and accompanying reconstitution diluents, if applicable.• For a drug product supplied with reconstitution diluent(s), the information on the diluent(s) should be provided in a separate part —P11, as appropriate.
3.2. P.2	<p>Pharmaceutical Development (name dosage form)</p> <p>The Pharmaceutical Development section should contain information on the development studies conducted to establish that the dosage form, the formulation, manufacturing process, container closure system, microbiological attributes and usage instructions are appropriate for the purpose specified in the application. The studies described here are distinguished from routine control tests conducted according to specifications.</p> <p>Additionally, this section should identify and describe the</p>

	<p>formulation and process attributes (critical parameters) that can influence batch reproducibility, product performance and drug product quality. Supportive data and results from specific studies or published literature can be included within or attached to the Pharmaceutical Development section. Additional supportive data can be referenced to the relevant nonclinical or clinical sections of the application.</p>
3.2. P.2.1	Components of the Drug Product (name, dosage form)
3.2. P.2.1.1	<p>Drug Substance (name, dosage form)</p> <p>The compatibility of the drug substance with excipients listed in 3.2.P.1 should be discussed. Additionally, key physicochemical characteristics (e.g., water content, solubility, and particle size distribution, polymorphic or solid state form) of the drug substance that can influence the performance of the drug product should be discussed.</p> <p>For combination products, the compatibility of drug substances with each other should be discussed.</p> <p>WHO GMP Certification/COPP as per WHO GMP Certification Scheme or Product License (product registration certificate issued by NRA or the Proof of DMF approval by NRA and or CEP (EDQM) certificate) shall be submitted.</p>
3.2. P.2.1.2	<p>Excipients (name dosage form)</p> <p>The choice of excipients listed in 3.2.P.1, their concentration, and their characteristics that can influence the drug product performance should be discussed relative to their respective functions.</p>
3.2. P.2.2	Drug Product (name, dosage form)
3.2.P.2.2.1	<p>Formulation Development (name dosage form)</p> <p>A brief summary describing the development of the drug</p>

	<p>product should be provided, taking into consideration the proposed route of administration and usage. The differences between clinical formulations and the formulation (i.e. composition) described in 3.2.P.1 should be discussed. Results from comparative in vitro studies (e.g., dissolution) or comparative in vivo studies (e.g., bioequivalence) should be discussed when appropriate.</p>
3.2. P.2.2.2	<p>Overages (name, dosage form)</p> <p>Any overages in the formulation(s) described in 3.2.P.1 should be justified.</p>
3.2. P.2.2.3	<p>Physicochemical and Biological Properties (name dosage form)</p> <p>Parameters relevant to the performance of the drug product, such as pH, ionic strength, dissolution, redispersion, reconstitution, particle size distribution, aggregation, polymorphism, rheological properties, biological activity or potency, and/or immunological activity, should be addressed.</p>
3.2. P.2.3	<p>Manufacturing Process Development (name dosage form)</p> <p>The selection and optimization of the manufacturing process described in 3.2.P.3.3, in particular its critical aspects, should be explained. Where relevant, the method of sterilization should be explained and justified. Differences between the manufacturing process(es) used to produce pivotal clinical batches and the process described in 3.2.P.3.3 that can influence the performance of the product should be discussed.</p>
3.2. P.2.4	<p>Container Closure System (name dosage form)</p> <p>The suitability of the container closure system (described in 3.2.P.7) used for the storage, transportation (shipping) and use of the drug product should be discussed. This discussion should consider, e.g., choice of materials, protection from</p>

	moisture and light, compatibility of the materials of construction with the dosage form (including sorption to container and leaching) safety of materials of construction, and performance (such as reproducibility of the dose delivery from the device when presented as part of the drug product).
3.2. P.2.5	<p>Microbiological Attributes (name, dosage form)</p> <p>Where appropriate, the microbiological attributes of the dosage form should be discussed, including, for example, the rationale for not performing microbial limits testing for non-sterile products and the selection and effectiveness of preservative systems in products containing antimicrobial preservatives. For sterile products, the integrity of the container closure system to prevent microbial contamination should be addressed.</p>
3.2. P.2.6	<p>Compatibility (name dosage form)</p> <p>The compatibility of the drug product with reconstitution diluent(s) or dosage devices (e.g., precipitation of drug substance in solution, sorption on injection vessels, stability) should be addressed to provide appropriate and supportive information for the labeling.</p>
3.2. P.3	<p>Manufacture of Drug Product (name dosage form)</p>
3.2. P.3.1	<p>Manufacturer(s) (name dosage form)</p> <p>The name, address, and responsibility of each manufacturer, including contractors, and each proposed production site or facility involved in manufacturing and testing should be provided.</p>
3.2. P.3.2	<p>Batch Formula (name dosage form)</p> <p>A batch formula should be provided that includes a list of all components of the dosage form to be used in the manufacturing process, their amounts on a per batch basis,</p>

	including overages, and a reference to their quality standards.
3.2. P.3.3	<p>Description of Manufacturing Process and Process Controls (name dosage form)</p> <p>A flow diagram should be presented giving the steps of the process and showing where materials enter the process. The critical steps and points at which process controls, intermediate tests or final product controls are conducted should be identified.</p> <p>A narrative description of the manufacturing process, including packaging, that represents the sequence of steps undertaken and the scale of production, should also be provided. Novel processes or technologies and packaging operations that directly affect product quality should be described with a greater level of detail. Equipment should, at least, be identified by type (e.g., tumble blender, in-line homogenizer) and working capacity, where relevant.</p> <p>Steps in the process should have the appropriate process parameters identified, such as time, temperature, or pH. Associated numeric values can be presented as an expected range. Numeric ranges for critical steps should be justified in Section 3.2.P.3.4. In certain cases, environmental conditions (e.g., low humidity for an effervescent product) should be stated.</p> <p>Proposals for the reprocessing of materials should be justified. Any data to support this justification should be either referenced or filed in this section (3.2.P.3.3).</p>
3.2. P.3.4	<p>Controls of Critical Steps and Intermediates (name dosage form)</p> <p>Critical Steps:</p> <p>Tests and acceptance criteria should be provided (with</p>

	<p>justification, including experimental data) performed at the critical steps identified in 3.2.P.3.3 of the manufacturing process, to ensure that the process is controlled.</p> <p>Intermediates:</p> <p>Information on the quality and control of intermediates isolated during the process should be provided.</p>
3.2. P.3.5	<p>Process Validation and/or Evaluation (name dosage form)</p> <p>Description, documentation, and results of the validation and/or evaluation studies should be provided for critical steps or critical assays used in the manufacturing process (e.g., validation of the sterilization process or aseptic processing or filling). Viral safety evaluation should be provided in 3.2.A.2, if necessary.</p>
3.2. P.4	<p>Control of Excipients (name dosage form)</p>
3.2. P.4.1	<p>Specifications and justification of Specifications (name dosage form)</p> <p>The specifications for excipients and justifications or the proposed specifications should be provided.</p>
3.2. P.4.2	<p>Analytical Procedures (name dosage form)</p> <p>The analytical procedures used for testing the excipients should be provided, where appropriate.</p>
3.2. P.4.3	<p>Validation of Analytical Procedures (name dosage form)</p> <p>Analytical validation information, including experimental data, for the analytical procedures used for testing the excipients should be provided, where appropriate.</p>
3.2. P.4.4	<p>Excipients of Human or Animal Origin (name dosage form)</p> <p>For excipients of human or animal origin, information should</p>

	be provided regarding adventitious agents (e.g., sources, specifications; description of the testing performed; viral safety data). (Details in 3.2.A.2).
3.2. P.4.5	Excipient(s) used for the first time Novel Excipients (name, dosage form) For excipient(s) used for the first time in a drug product or by a new route of administration, full details of manufacture, characterization, and controls, with cross references to supporting safety data (nonclinical and/or clinical) should be provided according to the drug substance format. (Details in 3.2.A.3).
3.2. P.5	Control of Drug Product (name dosage form)
3.2. P.5.1	Specification(s) (name dosage form) The specification(s) for the drug product should be provided.
3.2. P.5.2	Analytical Procedures (name, dosage form) The analytical procedures used for testing the drug product should be provided.
3.2. P.5.3	Validation of Analytical Procedures (name dosage form) Analytical validation information, including experimental data, for the analytical procedures used for testing the drug product, should be provided.
3.2. P.5.4	Batch Analyses (name, dosage form) A description of batches and results of batch analyses should be provided.
3.2. P.5.5	Characterization of Impurities (name dosage form) Information on the characterization of impurities should be provided, if not previously provided in "3.2.S.3.2 Impurities".
3.2. P.5.6	Justification of Specification(s) (name, dosage form)

	Justification for the proposed drug product specification(s) should be provided.
3.2. P.6	Reference Standards or Materials (name dosage form)
	Information on the reference standards or reference materials used for testing of the drug product should be provided, if not previously provided in "3.2.S.5 Reference Standards or Materials".
3.2. P.7	Container Closure System (name dosage form) A description of the container closure systems should be provided, including the identity of materials of construction of each primary packaging component and its specification. The specifications should include description and identification (and critical dimensions, with drawings where appropriate). Non-compendial methods (with validation) should be included where appropriate. on-functional secondary packaging components (e.g., those that neither provide additional protection nor serve to deliver the product), only a brief description should be provided. For functional secondary packaging components, additional information should be provided. Suitability information should be located in 3.2.P.2.
3.2. P.8	Stability (name dosage form)
3.2. P.8.1	Stability Summary and Conclusion (name dosage form) The types of studies conducted, protocols used, and the results of the studies should be summarized. The summary should include, for example, conclusions with respect to storage conditions and shelf-life, and, if applicable, in-use storage conditions and shelf-life.
3.2. P.8.2	Post approval Stability Protocol and Stability Commitment

	<p>(name, dosage form)</p> <p>The post-approval stability protocol and stability commitment should be provided.</p>
3.2. P.8.3	<p>Stability Data (name dosage form)</p> <p>Results of the stability studies should be presented in an appropriate format (e.g. tabular, graphical, and narrative). Information on the analytical procedures used to generate the data and validation of these procedures should be included.</p> <p>Information on characterization of impurities is located in 3.2.P.5.5.</p>
3.2. A	<p>APPENDICES</p>
3.2. A.1	<p>Facilities and Equipment (name manufacturer)</p> <p>A diagram should be provided illustrating the manufacturing flow including movement of raw materials, personnel, waste, and intermediate(s) in and out of the manufacturing areas. Information should be presented with respect to adjacent areas or rooms that may be of concern for maintaining integrity of the product.</p> <p>Information on all developmental or approved products manufactured or manipulated in the same areas as the applicant's product should be included.</p> <p>A summary description of product-contact equipment and its use (dedicated or multi-use) should be provided. Information on preparation, cleaning, sterilization, and storage of specified equipment and materials should be included, as appropriate.</p> <p>Information should be included on procedures (e.g., cleaning and production scheduling) and design features of the facility (e.g., area classifications) to prevent contamination or cross-contamination of areas and equipment, where operations for</p>

	<p>the preparation of cell banks and product manufacturing are performed.</p>
3.2. A.2	<p>Adventitious Agents Safety Evaluation (name dosage form)</p> <p>Information assessing the risk with respect to potential contamination with adventitious agents should be provided in this section.</p> <p>For non-viral adventitious agents:</p> <p>Detailed information should be provided on the avoidance and control of non-viral adventitious agents (e.g., transmissible spongiform encephalopathy agents, bacteria, mycoplasma, fungi). This information can include, for example, certification and/or testing of raw materials and excipients, and control of the production process, as appropriate for the material, process and agent.</p> <p>For viral adventitious agents:</p> <p>Detailed information from viral safety evaluation studies should be provided in this section. Viral evaluation studies should demonstrate that the materials used in production are considered safe, and that the approaches used to test, evaluate, and eliminate the potential risks during manufacturing are suitable. The applicant should refer to Q5A, Q5D, and Q6B for further guidance.</p>
3.2. A.3	<p>Excipients:</p> <p>Any documents/ appendices of excipients should be provided.</p>

S. No	Name of the product	Number of batches produced in last two years (with scale R&D/Pilot/Commercial)		Stability studies (maximum period completed) in months Accelerated / Real time		Process Validation	Analytical Method Validation	Cleaning Validation/verification	Annual Product Review	If permitted for marketing / sale in the country of origin Y/N/NA
						Completed/Not completed	Completed/Not completed	Completed/Not completed	Completed/Not completed	
				<u>Acc</u> <u>6M</u>	<u>RT</u> <u>36M</u>					
1	Example Tablet	20	(Commercial)			<u>Completed</u>	<u>Completed</u>	<u>Completed</u>	<u>Not completed</u>	<u>Y</u>
2										
3										

Key points to consider

1. All critical and key performance parameters for each process step should be reviewed in the APR. This should include process consistency parameters (step recoveries, potency, final batch size etc.), product quality parameters (product related impurities, product related substances, impurities, etc.) and environmental controls (bioburden,

	<p>endotoxin, etc.)</p> <ol style="list-style-type: none">2. Data analysis should include statistically significant number of lots. If the number of lots manufactured in the year is too few, data from earlier lots should be included in the analysis.3. Appropriate statistical tools should be used for data analysis. Selection of tools should be consistent and appropriate for the analysis performed.4. Appropriate form of data trending should be performed (e.g. Nelson rules). Any violation should be clearly presented along with the corrective and preventive action taken. <p>c) Where validation is still to be completed, a summary of the studies intended to be conducted should be provided.</p>
3.3	<p>LITERATURE REFERENCES</p> <p>Key literature referenced should be provided, if applicable</p> <p>Further Clarification:</p> <ul style="list-style-type: none">• There can be a number of instances of where repeated sections can be considered appropriate. Whenever a section is repeated, it should be made clear what the section refers to by creating a distinguishing title in parentheses following the CTD-Q heading for example, 2.3.S Drug Substance (Name, Manufacturer A).• In some cases, information at Drug Product section has to be presented separately meaning complete Drug Product section followed by other complete Drug Product sections. <p>Example:</p> <p>A drug product supplied with a reconstitution diluents</p>

should be presented in separate Drug Product sections and it could be titled 3.2.P (Drug Product) and (Diluents').

- If both drug substance and drug product information is included in the appendices, then the preferred presentation is drug substance first and then drug product within each section, for example, 3.2.A.1 (Drug Substance, then Drug Product), then 3.2.A.2 (Drug Substance, then Drug Product), then 3.2.A.3 (Drug Substance, if applicable, then Drug Product).



ANNEXURE -IX

Form 41 (See rule 27-A) Registration Certificate

Registration Certificate to be issued for import of drugs into India under Drugs and Cosmetics Rules, 1945.

Registration Certificate No. _____ Date _____

M/s _____ (Name and full Address of registered office)
_____ having factory
premises at _____ (full address) has been registered
under rule 27-A as a manufacturer and is hereby issued this Registration
Certificate.

2. Name (s) of drugs, which may be imported under this
Registration Certificate.

(1)

(2)

(3)

3. This Registration Certificate shall be in force from _____
to _____
_____ unless it is sooner suspended or cancelled under the
rules.

4. This Registration Certificate is issued through the office of the
manufacturer or his authorised agent in India M/s (name and full
address)

_____ who
will be responsible for the business activities of the manufacturer, in
India in all respects.

5. This Registration Certificate is subject to the conditions, stated
below and to such other conditions as may be specified in the Act
and the rules, from time to time.

Place _____

Date: _____

Licensing Authority

Seal/Stamp

Conditions of the Registration Certificate

1. The Registration Certificate shall be displayed at a prominent place by the authorised agent.
2. No drug shall be registered unless it has a free sale approval in the country of origin, and/or in other major countries.
3. The manufacturer or his authorised agent in India shall comply with the conditions of the import License issued under the Drugs and Cosmetics Rules, 1945.
4. The manufacturer or his authorised agent in India shall inform the licensing authority forthwith in the event of any administrative action taken due to adverse reaction, viz. market withdrawal, regulatory restrictions, or cancellation of authorisation, and/or not of standard quality report of any drug pertaining to this Registration Certificate declared by the Regulatory Authority of the country of origin or by any Regulatory Authority of any other country, where the drug is marketed/sold or distributed.

The despatch 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 such stopped marketing of drug shall be followed as per the direction of the licensing authority. In such cases, action equivalent to that taken with reference to the concerned drug in the country of origin or in the country of marketing shall be followed in India also, in consultation with the licensing authority. The licensing authority may, however, direct any further modification to this course of action, including the withdrawal of the drug from Indian market within 48 hours time period.

5. The manufacturer or his authorised agent in India shall inform the licensing authority within 30 days in writing in the event of any change in manufacturing process, or in packaging, or in labelling or

in testing, or in documentation of any of the drug pertaining to this Registration Certificate.

In such cases, where there shall 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 licensing authority, the manufacturer or his authorised agent in India shall obtain necessary approval within 30 days by submitting a separate application along with the registration fee, as specified in clause (ii) of sub rule (3) of rule 24-A.

6. The manufacturer or his authorised agent in India shall inform the licensing authority immediately in writing in the event of any change in the constitution of the firm and /or address of the registered office/ factory premises operating under this Registration Certificate. Where any such change in the constitution of the firm and/or address takes place, the current Registration Certificate shall be deemed to be valid for a maximum period of three months from the date on which the change has taken place unless, in the meantime, a fresh Registration Certificate has been taken from the licensing authority in the name of the firm with the changed constitution of the firm and/or changed address of the registered office or factory premises.]•.

ANNEXURE -X

FORM 10

(See rules 23 and 27)

License to import drugs (excluding those specified in Schedule X) to the Drugs and Cosmetic Rules, 1945

License Number..... Date.....

..... (Name and full address of the importer)

is hereby Licensed to import into India during the period for which the License is in force, the

drugs specified below, manufactured by M/s.....
(name and full

address) and any other drugs manufactured by the said manufacturer as may from time to time be endorsed on this License.

2. This License shall be in force from to unless it is sooner suspended or cancelled under the said rules.

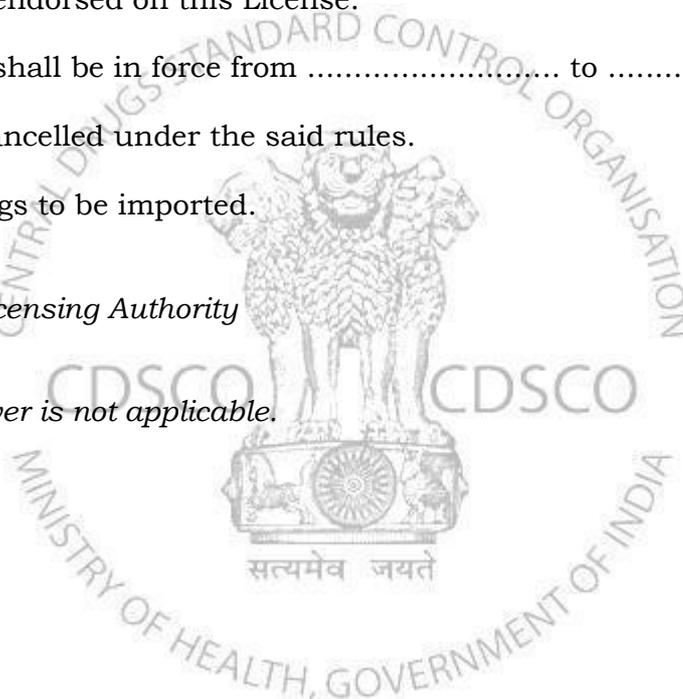
3. Names of drugs to be imported.

Place :

Date : Licensing Authority

Seal/Stamp

* Delete whichever is not applicable.



ANNEXURE - XI

FORM 10A

(See rules 23 and 27)

License to import drugs specified in Schedule X to the Drugs and Cosmetics Rules, 1945

License Number..... Date.....
.....(Name and full address of the importer) is hereby Licensed to import into India during the period for which the License is in force, the drugs specified below, manufactured by M/s..... (name and full address) and any other drugs manufactured by the said manufacturer as may from time to time be endorsed on this License.

2. This License shall be in force from..... to..... unless it is sooner suspended or cancelled under the said rules.

3. Names of drugs to be imported.

Place:.....

Date:

**Delete whichever is not applicable.*

Licensing Authority
Seal/ Stamp.

ANNEXURE -XII

FORM 8

(See rule 24)

Application for License to import drugs (excluding those specified in Schedule X)
to the Drugs
and Cosmetics Rules, 1945

I/We* (full address with telephone number,
fax number and e-mail address) hereby apply for a License to import drugs
specified below manufactured by M/s(full address
with telephone no, fax and e- mail no.).

2. Names of the drugs to be imported:

- (1)
- (2)
- (3)

3. I/We*
Form 9

enclose herewith an
undertaking in

dated signed by the manufacturer as required by rule 24 of the Drugs
and Cosmetics
Rules, 1945.

4. I/We* enclose herewith a copy of Registration
Certificate
concerning the drugs to be imported in India, issued under Form 41 of the rules,
vide Registration
Certificate No dated issued through
M/s (name and full
address) valid up to

5. I/We* hold a valid wholesale License for sale or
distribution of
drugs or valid License to manufacture drugs, under the provisions of the Act and
rules made
thereunder. A copy of the said License is enclosed.

6. A fee of has been credited to Government under the Head of
Account "0210- Medical
and Public Health, 04-Public Health, 104-Fees and Fines" under the Drugs and
Cosmetics Rules, 1945 - Central vide Challan No
dated (attached in original)

Signature

Name

Designation

Seal/ Stamp of Manufacturer's agent in India.

Place:

Date:

*Delete whichever is not applicable.]

ANNEXURE -XIII

FORM 8A

(See rule 24)

Application for License to import drugs specified in Schedule X to the Drugs
and Cosmetics
Rules, 1945

I/We*(full address with telephone number, fax number and e-mail address)

hereby apply for a License to import drugs specified below manufactured by
M/s..... (full address with telephone no, fax and e-mail no.)

2. Name of the drugs to be imported:

- (1)
- (2)
- (3)

3. I/We*enclose herewith an undertaking in Form 9 dated.....signed
by the manufacturer as required by rule 24 of the Drugs and Cosmetics Rules, 1945.

4. I/We*enclose herewith a copy of Registration Certificate concerning the
drugs to be imported in India, issued under Form 41 of the rules, vide Registration Certificate No
dated issued through M/s.(name and full address)
..... valid upto.....

5. I/We*hold a valid wholesale License for sale or distribution of drug or License to
manufacture drugs, under the provisions of the Act and rules made thereunder. A copy of the said
License is enclosed.

6. A fee of..... has been credited to Government under the Head of Account
"0210 - Medical and Public Health, 04- Public Health, 104- Fees and Fines"
under the Drugs and
Cosmetics Rules 1945 - Central vide Challan No..... dated
..... (attached in
original).

Signature.....

Name.....

Designation.....

Seal/ Stamp of Manufacturer's agent in India.]

Place:

Date:

*Delete whichever is not applicable.

ANNEXURE -XIV

FORM 9

(See rule 24)

Form of undertaking to accompany an application for an import License

Whereas of..... intends to apply for a License under the Drugs and Cosmetics Rules, 1945, for the import into India, of the drugs specified below manufactured by us, we...of..hereby give this undertaking that for the duration of the said License—

- (1) the said applicant shall be our agent for the import of drugs into India;
- (2) we shall comply with the conditions imposed on a License by ¹[rules 74 and 78] of the Drugs and Cosmetics Rules, 1945;
- (3) we declare that we are carrying on the manufacture of the drugs mentioned in this undertaking at
the premises specified below, and we shall from time to time report 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 Part IX of the Drugs and Cosmetics Rules, 1945;
- (5) every drug manufactured by us for import under License into India shall as regards strength,
quality and purity conform with the provisions of Chapter III of the Drugs and Cosmetics Act,
1940, and the Drugs and Cosmetics Rules, 1945;
- (6) we shall comply with such further requirements, if any, as may be specified by Rules, by the
Central Government under the Act and of which the licensing authority has given to the Licensee
not less than four months' notice.

Names of drugs and classes of drugs

Particulars of premises where manufacture is carried on.

Date.....

²[Signature, Name, Designation Seal/Stamp
of manufacturer or on behalf of the manufacturer.]

E. Rules Related to Import and Registration of bulk drug(s) and finished formulation(s) in India.

24. Form and Manner of Application for Import License.–

(1) An application for an import License shall be made to the licensing authority in Form 8 for drugs excluding those specified in Schedule X, and in Form 8-A for drugs specified in Schedule X, either by the manufacturer himself having a valid wholesale License for sale or distribution of drugs under these Rules, or by the manufacturer's agent in India either having a valid License under the Rules to manufacture for sale of a drug or having a valid wholesale License for sale or distribution of drugs under these Rules, and shall be accompanied by a License fee of one thousand rupees for a single drug and an additional fee at the rate of one hundred rupees for each additional drug and by an undertaking in Form 9 duly signed by or on behalf of the manufacturer:

Provided that in the case of any subsequent application made by the same importer for import License for drugs manufactured by the same manufacturer, the fee to accompany each such application shall be one hundred rupees for each drug:

(2) Any application for import License in Form 8 or Form 8-A, as the case may be, shall be accompanied by a copy of Registration Certificate issued in Form 41 under Rule 27-A:

Provided that in case of emergencies the licensing authority may, with the approval of the Central Government, issue an import License in Form 10 or 10-A, as the case may be, without the issuance of Registration Certificate under Rule 27-A, for reasons to be recorded in writing.

Provided further that Registration certificate shall not be required to be accompanied with an application for an import License under the Rules for the import of in-vitro diagnostic kits and reagents, except for the diagnostic kits notified from time to time under sub-clause (iv) of clause (b) of section 3.]

(3) A fee of two hundred and fifty rupees shall be paid for a duplicate copy of the License issued under this Rule, if the original is defaced, damaged or lost.]

24-A. Form and Manner of Application for Registration Certificate.—

- (1) An application for issue of a Registration Certificate shall be made to the licensing authority in Form 40, either by the manufacturer himself, having a valid wholesale License for sale or distribution of drugs under these rules, or by his authorised agent in India, either having a valid License under the rules to manufacture for sale of a drug or having a valid whole ale License for sale or distribution of drugs under these rules, and shall be accompanied by the fee specified in sub-rule (3) and the information's and undertakings specified in Schedules D-I and D-II duly signed by or on behalf of the manufacturer.
- (2) The authorisation by a manufacturer to his agent in India shall be documented by a power of attorney executed and authenticated either in India before a First Class Magistrate, or in the country of origin before such an equivalent authority, the certificate of which is attested by the Indian Embassy of the said country, and the original of the same shall be furnished along with the application for Registration Certificate.
- (3)
 - (i) A fee of one thousand and five hundred US dollars [or its equivalent in Indian rupees] shall be paid along with the application in Form 40 as registration fee for his premises meant for manufacturing of drugs for import into and use in India.
 - (ii) A fee of one thousand US dollars [or its equivalent in Indian rupees] shall be paid along with the application in Form 40 for the registration of a single drug meant for import into and use in India and an addition fee at the rate of one thousand US dollars for each additional drug:

Provided that in the case of any subsequent application for registration of additional drugs by the same manufacturer, the fee to

company shall be one thousand US dollars [or its equivalent in Indian rupees] for each drug.

- (4) The fees shall be paid through a Challan in the Bank of Baroda, Kasturba Gandhi Marg, New Delhi-110001 or any other branch or branches of Bank of Baroda, or any other bank, as notified, from time to time, by the Central Government, to be credited under the Head of Account —0210-Medical and Public Health, 04-Public Health, 104-Fees and Fines. Provided that in the case of any direct payment of fees by a manufacturer in the country of origin, the fees shall be paid through Electronic Clearance System (ECS) from any bank in the country of origin to the Bank of Baroda, Kasturba Gandhi Marg, New Delhi, through the Electronic Code of the bank in the Head of Account —0210-Medical and Public Health, 04- Public Health, 104-Fee and Fines, and the original receipt of the said transfer shall be treated as an equivalent to the bank challan, subject to the approval to the Bank of Baroda that they have received the payment.
- (5) The applicant shall be liable for the payment of a fee of five thousand US dollars [or its equivalent in Indian rupees] for expenditure as may be required for inspection or visit of the manufacturing premises or drugs, by the licensing authority or by any other persons to whom powers have been delegated in this behalf by the licensing authority under Rule 22.
- (6) The applicant shall be liable for the payment of testing fees directly to a testing laboratory approved by the Central Government India or abroad, as may be required for examination, tests and analysis of drug.
- (7) A fee of three hundred US dollars [or its equivalent in Indian rupees] shall be paid for a duplicate copy of the Registration Certificate, if the original is defaced, damaged or lost.

- (8) No Registration Certificate shall be required under these Rules in respect of an inactive bulk substance to be used for a drug formulation, with or without pharmacopoeial conformity.

25B Registration Certificate for Import of Drugs Manufactured by One

Manufacturer:—

- (1) A single application may be made, and a single Registration Drugs and *Cosmetics Rules, 1945*

Certificate in Form 41 may be issued in respect of the import of more than one drug or class of drugs, manufactured by the same manufacturer:

Provided that the drug or classes of drugs, are manufactured at one factory or more than one factory functioning conjointly as a single manufacturing unit: Provided further that if a single manufacturer has two or more factories situated in different places manufacturing the same or different drugs, separate Registration Certificates shall be required in respect of the drugs manufactured by each such factory.

27-A Grant of Registration Certificate-

- (1) On receipt of an application for Registration Certificate in the Form and manner specified in Rule 24-A, the licensing authority shall, on being satisfied, that, if granted, the conditions of the Registration Certificate will be observed, issue a Registration Certificate in Form 41:

Provided further that if the application is complete in all respects and informations specified in Schedules D-I and D-II are in order, the licensing authority shall, within nine months from the date of receipt of an application, issue such Registration Certificate, and in exceptional circumstances and for reasons to be recorded in writing, the Registration Certificate may be issued within such extended period, not exceeding three month as the licensing authority may deem fit.

(2) If the applicant does not receive the Registration Certificate within the period as specified in the proviso to sub-rule (1), he may appeal to the Central Government and the Central Government may after such enquiry into the matter, as it considers necessary, may pass such orders in relation thereto as it thinks fit.]

28-A Duration of Registration Certificate.—

A Registration Certificate, unless, it is sooner suspended or cancelled, shall be for a period of three years from the date of its issue:

Provided that if the application for a fresh Registration Certificate is made nine months before the expiry of the existing certificate, the current Registration Certificate shall be deemed to continue in force until orders are passed on the application.

29-A Suspension and cancellation of Registration Certificate. —

If the manufacturer fails to comply with any of the conditions of the Registration Certificate, the licensing authority may after giving an opportunity to show cause why such an order should not be passed, by an order in writing stating the reasons therefore, suspend or cancel the Registration Certificate for such period as it thinks fit either wholly or in respect of some of the substances to which it relates:

Provided that a person, who is aggrieved by the order passed by the licensing authority under this rule may, within thirty days of the receipt of the order, appeal to the Central Government, and the Central Government may, after such enquiry into the matter as it considers necessary and after give the appellant an opportunity for representing his views in the matter, pass such orders in relation thereto as it thinks fit.