

## **REQUIREMENTS FOR REGISTRATION OF FOREIGN DRUG MANUFACTURING COMPANY**

- 1-Registration form of foreign company.
- 2- Name, address and type of the foreign company.
- 3- Name and address of local licensed local agent
- 4- Copy of agency agreement certified by the Registrar of Companies.
- 5- The manufacturing license ( photocopy) for the company to manufacture pharmaceutical products for use in the country of origin issued by the health authority in the same country .
- 6- Valid Statement of Licensing Status of Pharmaceutical Products ( SLSPP) conforming to the format recommended by the World Health Organization, issued by competent certifying authority in the country of origin authenticated, certified and stamped by Sudan Ministry of Foreign Affairs.
- 7- Valid GMP certificate issued by competent certifying authority in the country of origin authenticated, certified and stamped by Sudan Ministry of Foreign Affairs.
- 8- List of other divisions, subsidiaries...etc. of the Mother Company and their full addresses
- 9- Other countries where the company is registered confirmed by photocopies of the certificates of registration in those countries
- 10- Full information and details about the pharmaceutical plant including at least the following information:
  - 10.1. Name and address of the drug manufacturing plant(s).
  - 10.2. Date of establishment
  - 10.3. Name and address of both Chairman of Board of Directors and the Managing Director of the company.
  - 10.4. Value in US \$ of local sales of products manufactured in the plant during previous 12 months
  - 10.5. Value in US \$ of exported products manufactured in the plant and names of importing countries during previous 12 months
  - 10.6. Products other than pharmaceuticals manufactured in that factory.
  - 10.7. Layout plan of the factory, indicating location and floor area of all buildings and facilities
  - 10.8. List of all technical full-time staff of the factory, their posts and qualifications (name: post: qualifications).
  - 10.9. List of lines and types of production.
  - 10.10. List of major equipment.
11. Evidence of any internationally recognized awards or certifications of excellence or compliance with international standards, e.g. ISO 9000, 9001.

12. List of main research studies performed by the company during the last 5 to 10 years.
13. Pharmaceutical products released to the market based on that research
14. Any other useful information about the company, its manufacturing plants and there products
- 15-The Quality Manual.
- 16- Fill in official forms if any are required

**Dr. Salah edein Abd Elrahman  
Chairman , Committee  
For registration of  
Pharmaceutical Products for  
Human Use**

THE REPUBLIC OF THE SUDAN  
FEDRAL MINISTRY OF HEAL H  
THE BOARD OF PHARMACY  
KHARTOUM

# **General Requirements for the Registration of Pharmaceutical Products**

## **Introduction**

According to the Pharmacy and Poisons Act it is an offence to manufacture, import, sell, offer for sale any pharmaceutical product unless registered under the provisions of the Act, and regulations, and directives issued under the Act. So all applicants for registration of pharmaceutical products should be familiar with all such provisions and requirements issued by the Federal Board of Pharmacy. The Directorate General of Pharmacy in the Federal Ministry of Health is the executive arm of the Board.

Pharmaceutical products submitted for registration should be manufactured in a registered plant.

The criteria for registration of a pharmaceutical product are:

1. Need (health or market need).
2. Efficacy.
3. Safety.
4. Quality.
5. Advantage over similar registered products.

## **I. General Rules to Applicants for Registration of Pharmaceutical Products**

1. The application form for registration of a pharmaceutical available on the web of DGOP.
2. Applications for registration should be submitted to the DGOP according to the time schedule specified by the Directorate.
3. The applicant should be
  - 3.1. Holder of a valid wholesales pharmaceutical license and an agency agreement with the manufacturer.
  - 3.2. A public sector establishment authorized by the Pharmacy and Poisons Act to deal with pharmaceutical products.
4. The applicant should fill the prescribed application form and should not overlook any information required in any part of the form. The prescribed duty stamps should be fixed to the form.

The applicant should also pay the prescribed application and registration fees and attach the receipt to the application form.

5. The form certifying the accuracy of documentation and information submitted for registration should be signed by responsible person specified by the applicant.
6. The applicant should present with the application form, the specified documentation and samples (as shown in registration requirements). All documents should be in English and/or Arabic.

7. A general synopsis should be submitted with the application form and it should cover all aspects of the documentation with reference to the actual documents in a reference list. The general synopsis should provide a concise review of the information required by the Board about a pharmaceutical product to enable it to consider the application for registration. The general synopsis should be an accurate precise of the information in the manufacturer full data file. Claimed advantages over registered products should be shown.

8. Application for registration is accepted only for products produced in registered manufacturing plants

9. Any incomplete or incorrect documents will not be accepted .

10. Any documents not properly arranged and filed will not be accepted

**11. Additional requirements for locally manufactured pharmaceutical products:**

Special temporary pre-registration approval is required for locally manufactured products, which enables the manufacturer to start the production of new pharmaceutical product for final registration. The applicant should submit a fully filled pre-approval application forms and should not overlook any information required in any part of the form. The prescribed duty stamps should be fixed to the form.

**II - Registration Requirements**

The registration file submitted should include the following documentation

1- Application form for the registration.

**2. A Certificate of a Pharmaceutical Product (CPP)**

2.1. Provide a WHO type Certificate of a Pharmaceutical Product (CPP) issued under WHO Certification Scheme on the Quality of Pharmaceutical Products moving in International Commerce.

2.2. The Certificate of the Pharmaceutical Product should be issued by the competent authority in the exporting country as notified to WHO, authenticated and stamped by **Sudan Ministry of Foreign Affairs**.

2.3. Date of introduction into the market in country of origin.

2.4. The composition formula in the Certificate of the Pharmaceutical Product should show the active and inactive ingredients.

2.5. The composition formula should be the same in country of origin

**3. Marketing licensing or authorization in other countries**

3.1. Provide a list of the countries in which this product has been granted license for marketing, State for each.

3.2. Photocopy of marketing authorization in each of these countries.

**4. Composition formula**

4.1. Provide complete composition and quantitative formula of the product with justification and purpose of use of each ingredient with mentioning to reference book, which shows allowance for use of this ingredient for that purpose. This should show unit dose formula and batch formula.

4.2. Compatibility of active and inactive ingredients and their effects on the product physicochemical properties should be shown.

**5. Properties of the Active Pharmaceutical Ingredients (API)**

Provide at least the following information

5.1. Active ingredient(s) by international non-proprietary names (INN), or generic or chemical name and their source (s).

5.2 Chemical data on the active ingredient(s) (chemical structure, solubility of active ingredient in water and other solvents such as ether, ethanol, acetone and buffers of different pH, and other relevant physicochemical properties.

5.3. Structural formula (constitutional and empirical), molecular wt. copies of infrared, ultraviolet spectra.

5.4. Active ingredient present in the form of salts or hydrate should be described quantitatively by their total mass and by the mass of the active moiety of the molecules.

5.5. Information on the chemical stability of the active pharmaceutical ingredient and physicochemical stability if relevant.

**6. Manufacturing procedure for the finished product:**

6.1. Provide a detailed method of manufacturing procedure for the finished product, including packaging and showing all materials used in the manufacturing process even if they do not appear in the final product.

6.2. In-process control procedures during manufacturing of the pharmaceutical product.

**7. Description of the finished product:**

Give a detailed visual description of the finished product and its packaging

**8. Method of analysis of the finished product:**

8.1. Provide a detailed method of analysis of the finished product to determine its compliance with quality specifications (identification of active ingredient(s) of the finished product, purity, uniformity, performance, etc.). Differences between the factory method and the latest pharmacopoeial method should be justified.

8.2. Provide the results of validation of the assay method for product formulation. For pharmacopoeial method provide data which demonstrate that the method is applicable to this formulation

**9. Containers/closure system(s) and other packaging:**

9.1. Give a detailed description of the container/closure system(s), including any liner or wadding.

9.2. Provide details of the composition of each component

9.3. Describe other (e.g. outer) packaging, and state what material they are made from

9.4. Provide the specifications for any part of the container/ closure system(s),

which comes into contact with the product, or its protective, cover .

9.5. For parenteral products, packing components that will at any stage come into contact with any part of the product must comply with requirements specified by the BP, USP, or EuPh.

9.6. Provide information and data about the stability of the container and packaging materials to the product storage conditions.

**10. Certificate of analysis of the finished product:**

10.1. Provide original certificate of analysis with batch number, manufacturing and expiry date signed and stamped by the quality control laboratory of the factory (on a headed paper).

**11. Describe package size**

**12. Stability data (according to WHO protocol)**

12.1. Provide the results of stability testing of the formulation in each of the proposed marketing pack. Results should include physical as well as chemical tests.

12.2. Data should also provided on the product's stability during any processing prior to use that may be recommended on the label or in product information, such as reconstitution of a powder, dilution of an injection, or dispersion of a tablet.

12.3. State the proposed shelf life with justification in terms of the results of stability testing, and the difference between release and expiry specifications

12.4. State storage conditions for the finished product.

12.5. Stability indicating method should be used in testing the stability of the product

12.6. Complete data and information about degradation products should be submitted

12.7. With respect to both locally manufactured or imported products additional stability studies are required whenever major modifications are made to formulation, manufacturing process, packaging or method of preparation.

12.8. Conditions used for accelerated and ongoing stability studies will be as follows

<b>Type of stability</b>	<b>Storage temperature C°</b>	<b>Relative humidity</b>	<b>Duration of studies (months)</b>
accelerated stability studies	40± 2	75± 5	6
Real time stability studies	30± 2	65± 5	Minimum 24

12.9 Batches to be tested minimum 3 batches.

### **13. Product package insert**

13.1. The package insert must be written in clear and understandable terms for both prescriber and patient.

13.2. The package insert should be at least written in an English and/ or Arabic language(s).

### **14. General information about the pharmaceutical product on package insert:**

This should include at least the following

14.1. Name of the pharmaceutical product, generic and scientific name

14.2. Different dosage forms and strength available for this pharmaceutical product

14.3. Number of doses of the medicinal product in case of more than one pharmaceutical dosage form or strength

14.4. Route of administration.

14.5. Pharmacology of the pharmaceutical product .

14.6. Main therapeutic group.

14.7. Indications and dosage regimen.

14.8. Contraindications, warnings, precautions and drug interactions.

14.9. Use in pregnancy and other special group of patients.

14.10. Adverse effects.

14.11. Overdose, signs, symptoms and treatment.

### **15. Sample and label:**

#### **15.1. Labeling of the outer pack should include at least the following information:**

15.1.1. The name of the pharmaceutical product.

15.1.2. Name of active ingredient(s) showing the amount of each present in a dosage unit.

15.1.3. Specification of active ingredient (s).

15.1.4. Package size for retail sale (number of dosage units, volume or weight and description of unit).

15.1.5. Registration number of the pharmaceutical products in Sudan, (if registered )

15.1.6. Pharmaceutical dosage form.

15.1.7. Storage conditions and precautions.

15.1.8. Manufacturing and expiry date and batch number (expiry date should be in an uncoded form).

15.1.9. Warnings or precautions that may be necessary.

15.1.10. Others (measuring unit, ...).

15.1.11. The name, country and address of the manufacturer

15.1.12 Legal status for distribution purposes (e.g. to be dispensed on prescription only)

15.1.13. Package insert

15.1.14. Method of administration and the route of administration, if not for oral use.

15.1.15. Name of excipients to be of a safety concern for some patients or known to have a recognized action or effect.

**15.2. Labeling of the inner (primary) pack should include at least the following information:**

15.2.1. The trade name of the pharmaceutical product and dosage form.

15.2.2. Name of active ingredient(s) showing the amount of each present in a dosage unit.

15.2.3. Specification of the active ingredient(s).

15.2.4. Manufacturing and expiry date and batch number.

15.2.5. The name and country of the manufacturer

15.2.6. Route of administration, (if not for oral use) .

15.2.7. Package size for retail sale, (number of dosage units, e.g. volume or weight

per pack) except for tablets, capsules, lozenges, powder for injection and suppositories (rectal and vaginal).

**16. Price**

Provide the following information:

16.1. Proposed C& F price for registration in Sudan. The specified port of entry should be indicated.

16.2. Whole sale and retail price in country of origin ( certified , authenticated and stamped from the competent authority in country of origin).

16.3. Whole sale price in other countries including neighboring countries to Sudan and African countries(certified ,authenticated &stamped from the competent authorities in those countries.

16.4. Proposed retail price for registration in Sudan

**17. Dispensing category**

17.1. Indicate dispensing category (proposed method for dispensing) in the country

of origin with justification of that categorization, OTC (Over The Counter), pharmacy only, hospital only or prescription only

**18. Withdrawal of product from markets**

Provide a list of all countries where the product has been withdrawn from the market or where the application for marketing has been rejected or withdrawn by the applicant, state the reason in each case

**19. Efficacy report:**

19.1 For pharmaceutical specialists submit detailed report on all efficacy studies carried out on the product .

19.2. For generic product submit detailed documentations of equivalence studies on the product in accordance to WHO recommendations , stamped and authenticated from the competent certifying authority in country of origin . This is required only for attached list .

**20. Claimed advantage:**

Claimed advantage over the registered products should be shown and supported by reference to randomized, controlled, comparative trials. Details of these trials should be given in an appendix.

**21. Samples of actual product and/or Reference Standard**

**Substance:**

21.1. The Registration Department will request sample of the actual Products with document for **committee** only . The remaining **samples** and **Reference Standard** will be requested with first imported consignment .

21.2. The number of samples required for each dosage form is shown on Table (1) for committee( column 4) and for analysis(column 3) samples should be accompanied by the certificate of analysis.

21.3. A quantity of Reference Standard Substance, which is sufficient for testing at least TEN samples, should be submitted in an air tight, light resisting container and clearly labeled with the name, concentration, manufacturing date , and expiry date, batch number and storage conditions. An extra quantity should be supplied , if needed.

21.4. Samples of any other ingredient, that can be expected to be of importance in the quality control of the specialty, should also be submitted in sufficient amount for testing at least TEN samples.

**Note** If special requirements must be imposed on the storage of samples or Reference Standard are needed, their storage conditions should be written on the label of the inner and outer container

**III. Special requirements for specific dosage forms**

**1/ Tablets :**

- appearance, colour, shape, friability, hardness, uniformity of weight with its specification, uniformity of thickness and diameter with specification, moisture and dissolution in full details.

**2/ Capsules :**

appearance, moisture, colour, shape, brittleness, dissolution, description of appearance and the colour of the filled material, uniformity of weight with its specification.

**3/ Emulsions :**

- appearance, colour, odour, pH, viscosity

It is recommended that a heating-cooling cycle to be employed between 4 - 45°C

**4/ Solutions :**

- appearance, colour, odour, clarity of solution, pH

**5/ Suspensions and powder for suspension**

- appearance, precipitate and sedimentation rate, colour, odour, taste, cloudiness, particle size, dispersability, redispersibility, suspendibility, particle size ,colouring matters, flavour used and pH

- strength through the recommended storage period before and after reconstitution for powder of suspension.

**6/ Syrups and Elixirs**

- description of colour, odour, taste and appearance .etc, pH with specifications, refractive index with its specification, specific gravity, viscosity with specification, coloring matters, flavour and preservatives used.

**7/ Dry powder for external use :**

appearance, colour, odour, and moisture content

**8/ Ophthalmic , Otical and Nasal preparations**

- description, appearance, colour, clarity viscosity, uniformity of volume, particle size specification and pH

- preservative on label (for ophthalmic preparations).

**9/ Injectable preparations**

- type of container and sealing

- appearance, colour, clarity of solution, uniformity of weight, preservative (if applicable) and pH.

- description of solution on reconstitution of powder for injection

- stability and strength through the recommended storage period before and after reconstitution of powder for injection

**10/ Suppositories**

- appearance, shape, colour, uniformity of weight, disintegration time or melting

time with specification.

**11/ Ointment , Creams and Gels :**

- appearance, colour, odour, consistency, viscosity, homogeneity, uniformity of weight, uniformity of content and water content determination.

**12/ Antiseptic and Disinfectants :**

- appearance, colour, clarity of solution and pH.

- the concentration and recommended dilution for optimal action.

- microbial spectrum

- evaluation of bactericidal, fungicidal and bacteriostatic actions.

**13/ Aerosol pharmaceutical :**

- uniformity of content (with limitation).

- propellant used.

- active ingredient / propellant ratio.
- spray testing.
- leaking testing.
- pressure measurement.

#### **IV. Additional requirements for pharmaceutical products containing new entities application**

**1-** New entities should be registered in countries that have an advanced system for

registration of new drug entities. Provide a list of these countries and photocopy of registration certificate in each of these countries.

**2-** Reports on all pre-clinical and clinical studies should be submitted to the Registration Department ; including:-

##### **2.1. Toxicological data:**

- Single dose toxicity, species used and route(s) of administration
- Repeated dose toxicity, species, dose, duration, numbers and methods of evaluation
- Reproduction toxicity, dose, species and numbers of animal used in studies of teratogenic and embryotoxic effects.
- Pharmacokinetic information to validate interspecies comparison of toxicity

##### **2.2. Animal Pharmacology:**

- Primary action relevant to the proposed therapeutic use
- General pharmacology on vital body systems.
- Dose/concentration effect relationship of primary or general pharmacological action.
- Absorption, distribution, biotransformation and main routes of elimination

##### **2.3. Clinical documentation Synopsis:**

###### **2.3.1. Clinical pharmacological studies**

Pharmacological action(s) of the drug in man.

Time course of effect of single and multiple doses

Dose-response relationship and concentration effect relationship

Absorption, route of biotransformation, (if of pharmacology or toxicological significance), routes of elimination

- Systemic bioavailability of products intended to have a systemic effect.

###### **2.3.2. Therapeutic efficacy:**

Controlled trials carried out to support each claimed indication

Dose range use, modification of dosage in special group, e.g. children, the elderly or malnourished individual, patients with renal or other irreversible effects.

Interactions with other drugs likely to be given concurrently

Interaction with specific foods

Evidence concerning dependency potential

Has the drug been used in pregnancy? Is it excreted in breast milk?

Specific contraindications.

Recommendations concerning treatment of overdose or intoxication (antidotes .

**2.4. Any other relevant scientific information .**

**VI Table (1): Size of samples to be submitted for registration**

NO	DOSAGE FORM	NUMBER OF SAMPLE (UNIT) FOR QC LAB	NUMBER OF SAMPLE (UNIT) FOR COMMITTEE
1.	Tablets, capsules, lozenges, for dispensing in original pack to individual patient course of treatment .	100 tablets , capsules or lozenges in original packs	15 packs
2.	Tablets, capsules, lozenges large pack (100 tablets , capsules or more )	100 tablets , capsules or lozenges + 3 empty packages	150 tablets , capsules or lozenges + 3 empty packages
3.	Syrups, oral suspension, emulsions, elixir, aerosols	10 bottles	15 bottles
4.	Dry powder or granules in sachets	20 sachets	15 sachets
5.	Injectable ampoules and individual dose vial	50 ampoules + 3 empty packages	15 ampoules + 3 empty packages
6.	Multidose vials	50 vials + 3 empty packages	15 vials + 3 empty packages
7.	Ointments , creams , eye drops (topical or ophthalmic)	10 tubes	15 tubes
8.	Suppositories or vaginal tablets	100 suppositories or vaginal tablets	150 suppositories or vaginal tablets

## **REQUIREMENT FOR REGISTRATION AND RE- REGISTRATION FOR MINOR CHANGES REGARDING COMPANIES AND THEIR DRUGS**

### **I - CHANGE OF THE PACK / PACK SIZE AND / OR ADDITIONAL PACK**

- 1- Request for minor change.
- 2- Prescribed form should be filled correctly by type writing.
- 3- Five samples from each old and new pack.
- 4- Photocopy of Certificate of Registration in Sudan.
- 5- Proposed price for the new pack (retail & whole) sale.

### **2. CHANGE IN THE INNER PACK**

1. Request for minor change
2. Prescribed form should be filled correctly by type writing
3. Five samples from each old and new pack
4. Photocopy of Certificate of Registration in Sudan.
5. Stability study for the pharmaceutical product in the new pack
6. Approval from health authorities in the country of origin for the new pack
7. Batch Certificate of Analysis
8. Proposed price for the new pack

### **3. EXTENSION OR CHANGE OF SHELF LIFE OR STORAGE CONDITIONS**

- 1- Request for changing shelf life or storage conditions.
- 2- Prescribed application form should be filled correctly by type writing.
- 3- New stability study confirming the new shelf life or storage conditions.
- 4- Five samples labeled with the new and old shelf life or storage conditions.
- 5- Batch Certificate of Analysis.
- 6- Approval of health authorities in the country of origin for the new shelf life.

### **4. CHANGE IN PACKAGE INSERT**

- 1- Covering letter with explanations for changes in the information and supporting references.
- 2- 10 copies from old insert.
- 3- 10 copies from new insert.
- 4- Approval of health authorities in the country of origin for the new package insert.

### **5. CHANGE OF SOURCE**

- 1- Addition of new source(s) for the same pharmaceutical product is not allowed.
- 2- New registration of new source and product is required.

3- In addition to registration form, the prescribed application form for change of source should be filled correctly by type writer.

**6. CHANGE OF COMPOSITION (ACTIVE AND/ OR INACTIVE INGREDIENTS)**

1- New registration is required

**7. CHANGE OF PHARMACEUTICAL TRADE NAME**

1- Covering letter

2- Certificate of Pharmaceutical Product for the new pharmaceutical trade name issued by the health authorities in country of origin as notified to WHO), certified by Ministry of Foreign Affairs, authenticated and stamped by Sudan Embassy in country of origin.

3- Five samples from each, old and new names, labeled.

4- Batch certificate of analysis

**8. CHANGE OF COMPANY NAME**

1- Covering letter with explanations

2- Approval of health authorities in the country of origin for the new company name authenticated and stamped by Sudan Embassy in country of origin.

3- New Certificate of Pharmaceutical Product for the new company name issued by the health authorities in country of origin (as notified to WHO), certified by Ministry of Foreign Affairs, authenticated and stamped by Sudan Embassy in country of origin.

4- Five samples from each, labeled with the new and old company name.

5- Batch Certificate of Analysis.

**9. CHANGE OF PRICE OF PHARMACEUTICAL PRODUCT**

1- Request for changing price.

2- Prescribed application form should be filled correctly .

3- Justification for change of price should be explained.

4- Wholesale price in the country of origin and other countries as required.

5- Photocopy of certificate of registration in Sudan

**7. CHANGE OF LOCAL AGENT OF A FOREIGN MANUFACTURER:**

1- New agency agreement with the new local agent

2- Termination of the previous agency agreement.

**12. RENEWAL OF REGISTRATION OF PHARMACEUTICAL PRODUCT**

1- Specified application form should be filled correctly.

2- Payment of renewal fees.

3- Photocopy of Certificate of Registration in Sudan.

4- Photocopy of last importation invoice.

**N.B** If there is no Sudan Embassy in country of origin, the Registration Department will suggest an alternative

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