مجلس الصحة
لدول مجلس التعاون
Gulf Health Council

BYLAWS FOR REGISTRATION OF PHARMACEUTICAL COMPANIES AND THEIR PRODUCTS

FOR THE CENTRAL REGISTRATION SYSTEM

Gulf Central Committee for Drug Registration

2021

GULF HEALTH COUNCIL FOR COOPERATION COUNCIL STATES

Pharmaceutical Companies & Products Thereof Registration Regulation

Of Central Registration Law– 2019

Introduction

Continuing the efforts to develop the Gulf Health Council programs particularly central pharmaceutical registration which is considered as one of the most significant services that the Health Council of ministers is keen to develop since it has an impact on the safety and effectiveness of pharmaceutical products. Through harmonizing the registration process of pharmaceutical manufacturers and their products with competitive and reasonable prices for pharmaceuticals in GCC, to assure that manufacturers are following Good Manufacturing Practices (GMP), Post Marketing Surveillance (PMS) and requirements as well as unifying exporting prices in GCC.

Due to the recent developments in Pharmaceuticals regulatory practices, Gulf Central Committee for Drug Registration felt the importance to update the central pharmaceutical regulations in accordance with the latest global updates in the field. Moreover, developing pharmaceutical guidelines associated with the updated bylaws. updating the pharmaceutical guidelines that related to stability studies, bioequivalent studies and manufacturer company inspection visits.

Pharmaceutical companies and products thereof registration regulation most prominent provisions were the controls of pharmaceutical industry under international companies' license, manufacture of products under contracts for other companies, internal leaflet, pharmaceutical companies and products re-registration requirements, as well as granting GCC-DR the authorization to request any additional documents or conduct central examinations in certain places. Further, companies shall comply therewith. Regarding products approved by some international authorities, availability of raw substance's source shall be required.

Chapter (1)

Definitions

Article (1)

(1-1) **GHC:**

Gulf Health Council for Cooperation Council States

(1-2) **GCC-DR:**

Gulf Central Committee for Drug Registration

(1-3) **Pharmaceutical Company:**

Company possessing single or several pharmaceutical factories that are licensed to operate as per applicable laws in states where they operate.

(1-4) Pharmaceutical Factory:

Facility where drugs are manufactured in accordance with GMP principles.

(1-5) Drugs:

Any substance or formulation prepared for treatment or prevention of disease of humans or animals, or used for diagnosis of medical conditions or restoration, treat or change of physiological functions of humans or animals.

(1-6) State of Origin:

State of manufacturer or the manufacture and/or marketing authorization holder, where the regulatory authorities issue certificate of products free sale or CPP

(1-7) State of Reference:

It is the country that issue CPP, on which product registration approval shall be based.

(1-8) Pharmaceutical Product:

Any drug manufactured in pharmaceutical form.

(1-9) Innovated Products:

Products containing new active substance and are sold in market under trade names.

(1-10) Generic Products:

Pharmaceutical product which is similar to innovative pharmaceutical product in forms of dose, pharmaceutical form, safety, concentration, quality, performance as well as method of use and administration.

(1-11) Raw Substance's Sources:

a. Human

Including blood and derivatives thereof

b. animal

Including microorganisms and animal's body or part thereof as well as secretions and extracts thereof in addition to toxic substances derived therefrom as well as blood and products thereof.

c. Plant

Including microorganisms, the plant body or parts thereof as well as secretions and extracts thereof.

d. Chemical

Whether natural, semi or fully manufactured.

(1-12) Biopharmaceuticals:

Biological substance used in diagnosis or treatment of humans or animals, including blood derivatives, vaccines, serums, and all that is made, contains or extracted from

human or animal origins as well as modified or constructed by using genetic engineering technology.

(1-13) Certificate of Pharmaceutical Product (CPP)

Certificate issued by the country's competent health authority where pharmaceutical product is fully or partly manufactured or marketed, and local (Gulf) factory/company shall be excluded from submission thereof.

(1-14) Marketing Authorization Holder:

Pharmaceutical company that assumes drugs marketing, whether it was manufacturer or marketing covenantor. Furthermore, such company shall be held fully liable for drug's quality, safety, effectiveness and post marketing follow-up as well as all legal procedures related thereto including sale, withdrawal, destruction thereof, or observing the adverse reactions, etc.

(1-15) Manufacturing License Holder

Pharmaceutical company that manufactures the product or undertakes some of manufacturing phases of pharmaceutical product licensed by health authorities in states thereof as per applicable drugs production and trading rules and laws therein.

Chapter (2)

Pharmaceutical Companies Registration

Article (2)

Pharmaceutical company or its representative shall submit the registration application to GHC. The following documents and information shall be attached: -

(2-1) For the private equity companies, a Company activity type, incorporation date, an overview about the company and owners shall be submitted.

(2-2) Number and addresses of factories possessed by pharmaceutical company.

(2-3) Company's relationship with and its legal and commercial responsibility for each of such factories. (If available)

(2-4) Certificate proving the commercial relationship between authorized agent in any member state and the company. (Certified by competent authorities).

(2-5) Certificate issued by health authorities in factory's state proving compliance with GMP principles, and health authorities' commitment to periodic inspection thereon (Certified by competent authorities).

(2-6) Factory's license issued by health authorities in factory's state allowing the manufacture of pharmaceutical products (indicating production lines) provided that it shall be certified by an embassy of GCC states.

(2-7) Submission of factory's organizational structure indicating various departments and number of employees therein including the qualifications of production, quality control

and research and development departments' managers as well as factory's technical manager.

(2-8) Sketch of factory buildings and workflow therein.

(2-9) List of products produced by factory, whether in its name, for its account (benefit), via contractual manufacturing, or for other companies along with dates of registration and marketing thereof in factory's state and other states.

(2-10) Letter issued by the company confirming that products to be exported to GCC states are conforming in composition to all marketed products in the state of origin.

(2-11) List notarized by company of names of countries where it is registered. Copies of registration certificates shall be attached.

(2-12) A pledge to comply with the Gulf Code of Pharmaceutical Marketing Practices.

(2-13) List of products that company desires to market in region's states.

(2-14) Submission of Site Master File

(2-15) An overview of company's activities in research and development fields

(2-16) Letter stating production lines that company desires to register

(2-17) Submitting a file includes on all statutory justifications for first product(s) that company desires to register and market in Gulf states as indicated in appendix 1.

Article (3)

Registration application of company or establishment distributing, marketing or packaging drugs that does not own independent pharmaceutical factories shall not be accepted. In addition, some companies holding authorization of manufacture or marketing of some of necessary products that do not have registered and marketed substitute or generic products, shall be excluded therefrom.

Article (4)

An inspection team from member of Gulf states shall visit the factory to ensure the implementation of GMP principles approved by GHC after payment of inspection fees as per the ministerial resolutions issued in this regard.

Article (5)

(5-1) If factory's failure to apply approved GMP principles, such factory shall not be registered, and new application for registration thereof may be submitted provided that it shall prove the remedy of observations for which registration application was rejected.

(5-2) Pharmaceutical companies shall respond to the reports produced by the visiting team within a maximum term of (90 days) as from report submission date by GHC. Otherwise, registration application shall be deemed cancelled, and GHC shall inform GCC-DR of the decision on company's registration application cancellation.

(5-3) Company shall be re-visited in the event that GCC-DR considers that inspection committee observations require that, the second visit shall be deemed final.

(5-4) Factory registration certificate will be issued and be valid for five years if the GCC-DR approved the company registration.

Article (6)

Registered company shall inform GCC-DR in writing of any sale, acquisition, merger or any legal or commercial procedure related thereto or to any registered factory thereof within ninety (90) days as from procedure completion, provided that such company shall update its data as per deemed appropriate by GCC-DR.

Article (7)

Centrally registered company shall complete administrative procedures of company registration in all GCC states within six months as from the date of central registration thereof. If the company didn't thereof during such period, it shall be subject to requirements of severally registration in each state.

Article (8)

Company registration shall be canceled or suspended in following events:

If company does not apply to register any of products thereof within one year as from informing the agent of company's registration.

If the submitted documents' forgery or tampering has been proven.

if a decision is issued to ban of company's activity or products thereof

In the event that repetition of violations thereof or products thereof failure to pass analysis, or non-continuation thereof to apply GMP principles is proven.

Article (9)

(9– 1) Company shall be re-registered in any of the following events:

a) In the event of radical change in factory's building, upgrade of production lines, or relocation of manufacture site.

b) If the factory registration certificate issued by executive office is expired, provided that re-registration application shall be submitted at a maximum period of six months prior to shelf life expiry date.

(9-2) Local or foreign pharmaceutical factories (or authorized agents/representatives thereof) shall submit the factory re-registration application to executive office accompanied by following documents and requirements:

1) Factory re-registration application shall be submitted as per factory registration form, which shall be filled, stamped by company's seal and signed by technical manager on each page. Also, such application shall indicate absence of change in company's

previously registered status since five years as from notarized centrally registration thereof.

2) Any amendment to previously registered company's type and activity.
3) Factories and companies contracting with registered factory, addresses thereof, factory's relationship with each thereof, and extent of legal, technical and commercial liability for the same.
4) Certificate issued by regulatory authorities in factory's state proving it's compliance with the recent CGMP principles,which issued and certified by health authorities in manfucterer country.
5) Submission of manufacturing license issued and certified by health authorities.
6) List of products produced by factory, whether in its name, for its benifit or via contractual manufacturing or for other companies, dates of registration and marketing thereof in manfucterer country and other countries.
7) List notarized by company refered to the countries where it is registered. The copies of registration certificates shall be attached.
8) Letter issued by company confirming that products to be exported to GCC states are conforming in forms of quality, composition and manufacture methods to all marketed in the state of origin.
9) A pledge to comply with what is stated in Gulf Code of Pharmaceutical Marketing Practices.
10) An overview of company's activities in research and development fields
11) Submission of SITE MASTER FILE

(9-3) In the event that, as per information stated in previous paragraphs, amendments to manufacturing procedures is proven to GCC-DR, GCC-DR shall have the authorization of assignment of technical team to inspect the factory to ensure GMP principles application.

(9-4) Required fees shall be paid.

Article (10)

GCC-DR shall have the right to request any additional documents or studies, or conduct central examinations in certain places. Further, companies shall comply therewith.

Article (11)

Each manufacturer and/or marketing authorization holder of pharmaceutical product shall appoint QPPV, who shall be responsible for monitoring and performing the follow up of adverse reactions as well as pharmaceutical product's quality. In addition, such QPPV shall assume following duties:

1) create a system to follow up the adverse reactions and pharmaceutical products' quality, as well as monitoring and recording of all cases that are sent to company by

health practitioners, patients or monitored by product marketing representatives in GCC states

2) Conducting continuous assessment of safety and quality of pharmaceutical product marketed in GCC states.

3) Immediate and fully response to any request from GCC-DR to obtain additional information required for assessment of benefits and risks related to pharmaceutical products marketed in the region, including information on sales volume and prescriptions.

4) Preparation and submission of adverse reactions reports to GCC-DR, including reports of adverse reactions resulting from safety studies which conducted by the company upon registration of product, PSURS or ICSR.

Article (12)

Each manufacturer and/or marketing authorization holder of pharmaceutical product shall provide GCC-DR with product monitoring reports as follow:

1) Inform GCC-DR of the name of QPPV appointed by company to monitor the adverse events and pharmaceutical product's quality, as well as substitute in the event of absence thereof. In addition to, all means of twenty-four hours contacts.

2) Inform GCC-DR immediately of any serious adverse reaction, provided that informing period shall not exceed fifteen days as from date of company awareness of such adverse event.

3) Inform GCC-DR of any issue related to pharmaceutical product's safety that is discussed or reached via review or analysis of adverse reactions monitoring information or during reassessment of benefits and risks that related to product.

4) Inform GCC-DR of any resolution issued on product by any pharmaceutical control authority or body as a result of appearance of any information regarding pharmaceutical product's safety in addition to indication of reasons led thereto.

5) Inform GCC-DR of any monitored adverse reaction via the following:

- Medical and pharmaceutical scientific journals
- Clinical Trials
- Websites that interest the company or for which company is responsible
- Pharmaceutical products' post-marketing studies
- Medical Records
- Various means of Media
- Survey studies such as pharmaceutical products' effectiveness and extent of patient's compliance with drug use studies.

6) Preparation and submission of PSURs for innovative product immediately at GCC-DR's request. In addition, PSURs shall be routinely submitted every six months during first two years upon product registration. Thereafter, PSURs shall be submitted every year for two years and every three years thereafter.

Article (13)

Company or marketing authorization holder shall be held fully liable for sending of warning messages approved by GCC-DR on product to physicians and pharmacists working in governmental and private health sectors in GCC states at GCC-DR's request.

Article (14)

Company shall have the right of objection to GCC-DR's resolution, and submit their reasons for objection to GHC within two months as from date of being notified of GCC-DR's resolution. In addition, GCC-DR's resolution shall be deemed final after studying of objection.

Article (15)

Canceled companies shall be allowed to apply for re-registration upon GCC-DR's recommendation, when the reasons that led to cancellation thereof are resolved.

Chapter (3)

Registration of Pharmaceutical Products

Article (16)

All pharmaceutical products shall be subject to registration, as per definitions stated herein, and company shall submit an application for registration of its products. In addition, registered pharmaceutical company shall complete administrative and financial procedures for the registration of pharmaceutical products thereof in each member state upon registration of such products centrally within six months as from date of central registration thereof. Company shall be subject to requirements of severally registration in each state if it did not complete all registration procedures.

Article (17)

Pharmaceutical product registration shall require that:

a) All manufacture sites involved in manufacture thereof shall be registered centrally as per approved principles thereof.
b) Biopharmaceuticals shall be registered in states having advanced supervisory authorites. Further, GCC-DR shall have the right to exclude products, if its safety and effectiveness have been proven during their global marketing term.

Article (18)

Registration procedures shall be as follow:

a) Pharmaceutical product registration application shall be submitted to GHC by company or representative thereof accompanied by file including product's chemical, pharmaceutical and biological properties and analysis as per eCTD technical requirements and guidelines published on the website.

b) If the pharmaceutical product submitted for central registration is contractually manufactured, manufactured and marketed under license or cooperatively marketed, the registration applicant shall fulfill requirements stated in Appendix (1), in addition to requirements stated in guidelines that published on the website.

c) If the drug submitted for central registration is manufactured and marketed under license, the registration applicant shall fulfill requirements stated in Appendix (2), in addition to requirements stated in guidelines published on the website.

d) In the event of cooperative/joint marketing, all stated in appendix (3) shall be applied.

e) If the first generic product submitted for central registration, the applicant shall submit document issued by GCC General Secretariat Patent Office stating that inventive product is not protected by patent on condition that innovative product's intellectual property rights shall be considered at severally registration in each GCC state as per local laws thereof.

Article (19)

Applicant shall have the right of objection to GCC-DR's decision on disapproval of pharmaceutical product registration within a maximum period of 60 days as from date of notification thereof.

Article (20)

Pharmaceutical product's registration certificate will be issued by GHC and shall be valid for five years.

Article (21)

In the event of any change to product, companies shall comply with all stated in the approved variation guidelines published on GHC's website.

Article (22)

Companies shall comply with all stated in the package insert, SPC and approved pharmaceutical products' external label on GHC's website.

Article (23)

GCC-DR may exclude some pharmaceutical products from requirements for packages details or internal leaflet, and translation thereof upon studying application submitted by company.

Article (24)

Companies shall respond to GCC-DR's observations within a maximum period of 3 months as from observations notification date, otherwise registration application shall be deemed cancelled.

Article (25)

Clinical, pharmacological, and toxicological studies shall be provided if pharmaceutical products containing known ingredients that have been previously used, but without certain indications (but as enhancers and additives during manufacture) and have been re-used with specific medical claims.

Article (26)

Alcohol and pork derivatives in pharmaceutical products shall be prohibited, companies shall declare and state reasons if they use them. In addition, GCC-DR shall have the right of rejection to register such products.

Article (27)

The following shall be considered in raw substance's sources:

1) Raw substance's source used in pharmaceutical product manufacture as well as methods of production and analysis thereof shall be indicated in addition to statement of pharmacopoeia, if any.
2) Proof that DMF has been approved by reference pharmaceutical authorities, such as pharmaceutical product's certificate of suitability shall be submitted. In addition, letter of access issued by active substance's factory and addressed to company or GHC shall be submitted.
3) Company shall submit an updated DMF and documents stated in clause (2) above upon the change of active raw substance purchase source upon registration of product and obtaining GCC-DR's approval on new source.
4) In the event of substance extracted from humans, animals, plants or blood derivatives, as well as microbiological compounds, company shall provide proof that such substance is free from pathogens like viruses and bacteria. Moreover, it shall specify such substance's sources in detail, as well as methods of collection, transportation and storage thereof, if aviliable
5) If the active substance's chemical and physical characteristics affect bioavailability, detailed image of crystal habit, solubility rates, and substance particle size upon crushing - if any - shall be provided.
6) Copy of GMP certificate of active substances source shall be included in the registration application.

Article (28)

Registration Validity Term:

A centrally registered product shall be granted registration certificate valid for five years as from the date of registration at GCC-DR. In addition, registration renewal application shall be submitted at least three months prior to the registration certificate expiry date.

Article (29)

The central Renewal of Pharmaceutical Products Registration:

All companies which intended to renew their registration license shall submit registration renewal file, upon fulfillment of all requirements as per guidelines published on GHC's website, as well as a pledge on absence of change in specifications in which product is centrally registered, provided that such pledge shall be attached in (1.0 Cover Letter).

Article (30)

Pharmaceutical product registration shall be canceled, suspended or withdrawn from market in following events:

1) If the GCC-DR receives reports proving harmful adverse reactions thereof from competent health authorities.
2) In the event that registration thereof is canceled or production thereof is ceased in the country of origin (exporting state)
3) In the event that incredibility of information related to pharmaceutical product provided in registration files is proven.
4) Manufacturer's non-continuation to apply GMP principles.
5) Any technical reasons estimated by GCC-DR that affect product's quality, efficacy and safety.

Article (31)

(31-1) GCC-DR shall have the right of postpone, rejection and cancellation of any product's registration or renewal thereof upon expressing justifications and reasons.

(31-2) Applicant for registration shall have the right to object to GCC-DR's decision and express reasons for objection thereof to GHC within two months as from date of being notified of GCC-DR's resolution. GCC-DR's decision shall be deemed final upon study of objection. Further, company shall be entitled to resubmit the application upon one year as from GCC-DR decision date.

(-31 -3) Company may submit an application for withdrawal of pharmaceutical file prior to submission to GCC-DR, and it should apply for re-registration at any time.

Article (32)

Pharmaceutical Product Pricing Standardization

Pharmaceutical products pricing shall be standardized as per centrally approved pricing rules.

Article (33)

Pharmaceutical products manufactured by manufacture under license, joint and contractual manufacturing as per approved rules (mentioned in appendices No. 1, 2, 3) shall be registered.

Article (34)

Bioequivalence Centers or representative thereof shall submit an approval application to GHC. The following documents and information shall be attached: -

(34-1) Application form for approval/approval renewal.

(34-2) CRO master file, in accordance with WHO guidelines for preparation of CRO master file's technical report.

(34-3) Copy of registration/renewal license in the country of origin.

(34-4) List of certificates, letters or inspection reports.

(34-5) Payment of all fees that are statuary due and announced on GHC's official website.

(34-6) Inspection process shall be applied to pharmaceutical products as well as medical supplies and devices factories announced on GCC-DR official website for inspection of bioequivalence centers.

(34-7) After having the approval from GCC-DR, bioequivalence centers' list shall be updated on GCC-DR's website.

(34-8) The application for approval renewal shall be made upon lapse of five years as from Bioequivalence Center's approval, provided that it shall fulfill Article 34 requirements.

Chapter (4)

Information approved by GCC-DR shall be stated on pharmaceutical product's inner and outer packaging as well as package internal leaflet, provided that information shall be clearly printed and difficult to remove in accordance with package internal leaflet requirements guidelines, SPC and pharmaceutical products' outer label.

Article (35)

CPP issued by competent health authorities shall include following information:

1) Certificate number and date in country of issue
2) Name of the country issuing certificate.
3) Name of Gulf region or country having authorization to import
4) Pharmaceutical Factory's name and address
5) Product's trade and scientific names. In the event of lack thereof, scientific name in addition to manufacturer's name and trademark shall be considered sufficient.
6) Qualitative and quantitative composition of pharmaceutical product's active and inactive substances in detail.
7) Name and address of manufacturer of pharmaceutical product intended for marketing final form .

8) The commitment of the health authorities that signed such certificate to inspect the manufacturer to ensure its compliance with the principles of good pharmaceutical manufacturing, and the period during which the periodic inspection is carried out.
9) In the event that package insert is not attached to CPP, certification thereof by health authorities located at the state of issue shall be deemed sufficient.
10) Statement of whether pharmaceutical product is marketed in certificate issuance state (or not).
11) Pharmaceutical product registration number and date in certificate issuance state, if any. Reasons shall be stated if such infromation are not avilable.
12) Pharmaceutical product marketing authorization holder's name and address
13) Marketing Authorization Holder
14) Name and address of authority attesting the certificate and seal thereof. Further, certificates issued by Gulf health authorities shall be excluded from certification.

Article (36)

- Child resistant cap shall be complied with and used in all liquid bottles.
- Package shall be equipped with tamper proof for all packages.
- Tablets should be labeld with Identification code.
- Registered products' outer package shall be labeled with safety tape so that they are neither easily counterfeited nor opened.

Article (38)

For registration of blood products, vaccines and biosimilar products, requirements for such products shall be fulfilled as per innovative products eCTD requirements and guidelines published on website.

Appendix (1)

Registration of contractually or cooperatively manufactured drugs (contractual or cooperative manufacture):

Registered pharmaceutical company holding authorization to manufacture or market or patent of product shall conclude contract with another pharmaceutical company for product's manufacture fully or partly.

Contract awardee for contractually manufactured product shall comply with the following:

First: If the company executing the contract is registered in the Gulf:

1) Specification of manufacture process basic procedures and site in which each procedure shall be performed.
2) Copy signed by contract awardee and executor stated in technical contract that includes following clauses:

a) Contract awardee shall inspect production, control and storage areas, as well as manufacture and analysis methods in addition to batches records and all technical capabilities.

b) Both contract's awardee and executor's liability with regard to manufacture and control procedures. In addition to specification of party liable for product's final release, whether contract awardee or executor.

c) Specifications of name, job and signature of party responsible for batches authorization, provided that GCC-DR shall be informed of substitute in the event of change thereof.

d) Specification of contract's effectiveness term.

3) Letter from company awarding the contract stating liability thereof for drug's quality and safety .

4) Pledge of contract awarding company's technical manager to inform GCC-DR of any change to information stated in clauses 1 and 2 prior to commencement of change.

5) Submission of statement of states names and copy of product's marketing certificates under same manufacturing conditions stated above, in addition to statement of marketing date in each state.

6) Manufacture by third parties shall not be limited to GCC states only, unless it is related to national companies.

Second: If the company executing the contract is not registered in the Gulf:

1) Fulfillment of all stated in paragraph (first).

2) Submission of drug manufacturing license certificate for company executing the contract issued by relevant authorities in country of manufacture.

3) Submission of GMP principles application certificate for executing company, issued by concerned authorities in country of manufacture. In addition, factory shall be subject to periodic inspection.

4) Companies authorized to manufacture for third parties shall be subject to periodic visits by technical committees nominated by GCC-DR to ensure the application of GMP principles.

Third: Secondary Packaging

1) Centrally registered companies may perform secondary packaging for products thereof registered at national pharmaceutical factories without any change to the product.

2) Such products shall remain to be treated as registered product of company which awarding the contract.

Fourth: Generic products that are submitted for registration from national factories and manufactured outside of KSA:

Generic products that are submitted for registration from national factories, and are manufactured in a country other than GCC states, and only filling or secondary packaging is made shall require the following:

1) Company shall be one of the leading companies.
2) GMP principles implementation shall be verified.
3) Product should require a manufacture technique that cannot be manufactured locally.

Appendix (2) Registration of medicines that are manufactured and marketed under a license

First: Drug local manufacture under license issued by international companies:

a) In the event that licensing company and drug to be manufactured and marketed are centrally registered. The following shall be followed:

1) Licensing Company shall hold patent or authorization to manufacture.
2) Written approval shall be submitted by licensing company to allow local factory or company to manufacture and market product thereof within GCC states.
3) Upon approval of registration of product manufactured under a license, licensing company registered product's registration and pricing shall be suspended upon lapse of six months as from national company's product registering date and informing its agent thereof.
4) Licensing and local companies shall inform GCC-DR at least six months as from manufacture licensing agreement expiry in the event of non-renewal of manufacturing agreement concluded with licensing company.
5) Licensing company innovative product registration suspension shall be lifted (renewal of registration thereof) and local company product registration shall be canceled in the event of expiry of manufacture license agreement concluded with local factory/company.
6) Active substances, sources thereof, inactive substances included in product composition, manufacture method, pharmaceutical formula, concentration, package, label and all product's specifications shall be as manufactured by licensing company.
7) Local factory/company shall be held liable before GCC-DR for product's quality and post marketing issues.
8) Local factory/company shall have all required capabilities and equipment to manfucture and analyze the licensed product.

9) Trade name of product manufactured under central license shall be as trade name of centrally registered product that manufactured by licensing company, provided that made by local factory under license issued by licensing company shall be written on the package .
10) Local factory/company may agree with licensing company to manufacture another brand product under trade name related to local factory in addition to company's innovative product, provided that registration requirements shall be similar to generic products registration requirements.
11) Product which manufactured under license issued by local factory/company shall pass registration and analysis phases required by GCC-DR.
12) Registered products that require bioequivalence studies shall be excluded from such studies if they are manufactured thereof by local factory/company under license issued by an international company, provided that:
    a) Product shall be registered by a licensing company, and that parent company shall provide all required bioavailability or bioequivalence studies.
    b) Product locally manufactured shall have the same specifications and manufacture methods applicable by licensing company.
    c) Active substances and additives source shall be from a licensing company or a source approved thereby and under the responsibility thereof regarding bioequivalence.
    d) Product shall not be a sustained release pharmaceutical form.
    e) Provision of Comparative Dissolution Study
13) Product manufactured under a license issued by local factory/company shall have shelf life based on stability studies provided by the licensing company, provided that local factory/company shall submit accelerated stability and stability studies under storage conditions which specified in stability studies guidelines. Also, submission of study for 12 months shall be deemed sufficient provided that entire study shall be submitted upon completion thereof. In addition, submission of CPP shall not be required in the event of non-registration thereof in the country of origin. Central registration certificate shall only be issued upon referring to the country of origin company to issue CPP, and GHC to issue central registration certificate and complete administrative procedures in member states.
14) Manufacturer shall perform all required control analysis conducted by the licensing company on product to ensure product's quality in all manufactured batches.
15) Licensing company shall perform all required control analysis on product that manufactured under a license issued by local factory/company to ensure conformity

thereof to manufacture specifications approved thereby, on at least first three batches produced by local factory/company of product manufactured under a license issued thereby, provided that such analysis results shall be sent to GCC-DR, in addition to such batches analysis results that were conducted by local factory/company.

b) If the licensing company shall be centrally registered and drug to be manufactured is not centrally registered, the following shall be considered:

1) Product shall be registered as per approved registration principles.

2) Fulfillment of all stated in paragraph (First)

c) If the licensing company is not centrally registered, the following shall be considered:

1) Licensing company shall be registered as per companies registration law in GHC.

2) Fulfillment of all stated in paragraph (Second)

Second: Drug foreign manufacture under a license issued by innovative or generic companies:

Products manufactured under a license issued by innovative or generic companies shall not be registered by generic companies outside GCC states. Further, GCC-DR shall have the right to consider the exclusion of some products as per following conditions:

1) Fulfillment of all conditions stated in paragraph (First)
2) Can not be locally manufactured.
3) Manufacture thereof shall not be limited to gulf market.

Third: Local manufacture of drug under other tradenames for the same registered product:

Only local company/factory shall be allowed to manufacture other generic products for the same product that registered under other tradenames of local factories, provided that:

1) File shall be submitted by the marketing authorization holder company.
2) Technical and legal liability shall be shared between two factories as per agreement contract.
3) It shall be priced as per pricing rules.

Fourth: Local manufacture of drug for export purpose:

Local company/factory shall be allowed to manufacture and register pharmaceutical product for export purpose only, provided that it shall be priced at export price only.

Appendix (3) **Collaborative/joint pharmaceutical marketing**

Registered pharmaceutical company holding manufacture and/or market authorization of centrally registered or unregistered innovative product shall agree with another centrally registered pharmaceutical company to market or participate in marketing thereof.

Collaborative/Joint Pharmaceutical Marketing Requirements for Centrally Registered Product:

1) Submission of certificate issued by the company that authorized to market the product in GCC states which ensures product's quality and liability thereof for all technical/financial and legal aspects, and certified by competent authorities in state of marketing company
2) Submission of pharmaceutical product or product's free sale certificates issued by state of marketing pharmaceutical company indicating manufacturer and marketing company names.
3) Submission of statement of countries names and copy of product's marketing certificates under same manufacturing conditions stated above, in addition to statement of marketing date in each country.
4) If the product is registered in agency contract between manufacturer and agent in GCC member states, approval letter on product shall be submitted by pharmaceutical manufacturer's agent to marketing pharmaceutical company's agent, or proof that product is not registered in agency contract shall be submitted by the company that own the manufacturing authorization .
5) If the product is not registered, the following requirements shall be fulfilled:
    a) Submission of full justification for product registration file by pharmaceutical company that will market the product via company or official agent thereof.
    b) Submission of letter certified by competent authorities in the country of origin that clarifies the relationship between the company which holding the authorization to manufacture and/or market and pharmaceutical company which market or participat in the marketing as well as the term of the contract concluded therebetween.
    c) Submission of product patent ownership certificate issued by the state of origin.
    d) In the event that company holding patent desires to protect its patency in any Gulf state, it shall submit an application to GCC General Secretariat Patent Office to register the patent of products thereof.
    e) Manufacturer's name shall be written on outer and inner package as well as package insert.

General Provisions

1) Manufacturer and marketing company shall immediately inform GCC-DR of marketing and/or manufacturing contract termination or expiry.
2) Joint marketing or manufacture by third parties shall not be limited to GCC states only, unless it is related to national companies.

Appendix (4) **Relocation of registered drug manufacturing site to same company**

Requirements: ـ

a) An application for relocation of drug manufacturing site registered by company or agent thereof shall be submitted, and attached to the following:

1) Manufacture process basic procedures and site in which each procedure shall be performed.
2) Identification of specifications, composition and sources of raw substance for registered product whose manufacturing site shall be relocated.
3) Company's declaration of absence of change to specifications, composition and method of manufacture of registered product or clarification of any change that will occur to product's manufacture in new site.
4) A pledge to provide authentic stability studies of drug at new site as per instructions issued for such purpose.
5) Pharmaceutical product registration certificate or free sale certificate issued by company or new manufacturing site's state.
6) Provide an accelerated drug stability studies from the new site as per instructions issued in this regard.
7) A pledge to provide authentic stability studies covering product's shelf life as per instructions issued for such purpose.
8) Submission of comparative solubility studies as per applicable instructions in this regard. In addition, serum, vaccines, and biopharmaceuticals shall be excluded therefrom.
9) GCC-DR have the right to suspend the drug trade or import in the event of non-submission of studies stated in clause (7).
10) If the product contains plasma products, product's plasma master file as well as manufacturer's declaration stating non-change of approved plasma source shall be submitted.
11) Serums, vaccines and biopharmaceuticals form approved by company awarding or executing the contract shall be filled. In addition, each page thereof shall be sealed and signed by responsible personal.

12) Clarification of reasons for moving manufacturing site.

b) GCC-DR may allow company's agent to import quantity of registered drug from another source if required prior to registration of new site.

c) Technical committee shall inspect new product's manufacture site to ensure application of GMP principles thereby in the event of non-registration thereof.

General Provisions:

1) Manufacturer and marketing company shall immediately inform GCC-DR of marketing and/or manufacturing contract termination or expiry.

2) Joint marketing or manufacture by third parties shall not be limited to GCC states only, unless it is related to national companies.

Abbreviations Explanation:

cGMP: Good Manufacturing Practice

PMS: Post Marketing Surveillance

DMF: Drug Master File

CPP: Certificate of Pharmaceutical Product

PSUR: Periodic Safety Update Report

eCTD: Electronic Common Technical Document

SPC: Summary Of Product Characteristics

ICSR: Individual Case Safety Reports

QPPV: Qualified Person Responsible For Pharmacovigilance