Supplement Registration Manual

Under license production -April 2023

Contents

Illustrated and arranged by

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1- Introduction:

The Islamic Republic of Iran requires each importer of pharmaceutical related products to register the brand, supplier and the manufacturer in the Ministry of Commerce (MOC) and Ministry of Health (MOH) of Iran prior to importing any products to the country.

The websites to the chamber of commerce and MoH are as follows:

Iran Chamber of commerce - https://iccima.ir/
Iran Ministry of Health - https://www.fda.gov.ir/

The first step in the registration process is to register the brand name of the parent company in the Ministry of Commerce of Iran. In order to do so, the agent of the parent company requires submitting a true copy of the "Exclusive Distributorship Agreement" between the two companies to the MOC. This document should be signed and approved by the Ministry of Commerce or Chamber of Commerce and the Embassy of Iran in the parent company's country of origin.

After registering the parent company's name and brand in MOC, the agent in Iran has to apply for registering the manufacturing plants of the products in Ministry of Health of Iran. MOH requires a list of documents that has to be given by the parent company and submitted by the agent in order to register the manufacturing plant prior to registration of the products.

Each product that is imported to Iran, requires an IRC Code (Iran Registration Code). This IRC code is a unique code for each and every product. In order to obtain the IRC Code, the distributor has to register each product in MOH and the TTAC - Tracing, Tracking and Authentication Control System (www.ttac.ir).

The registration process is time consuming; it normally takes around 6 to 8 months (depending on the product) to register a manufacturer and its products in the MOC and MOH. Bear in mind that the mentioned time exceeds if the documentation submitted is in complete or have to be revised.

Note: Iran MOH has the right to audit the manufacturing plant before Issuing the IRC.

The current manual is published to help you grasp a better understanding towards the Iranian Ministry of Health registration procedures in detail. The forms and samples of such documents are put within the appendix as a reference for you.

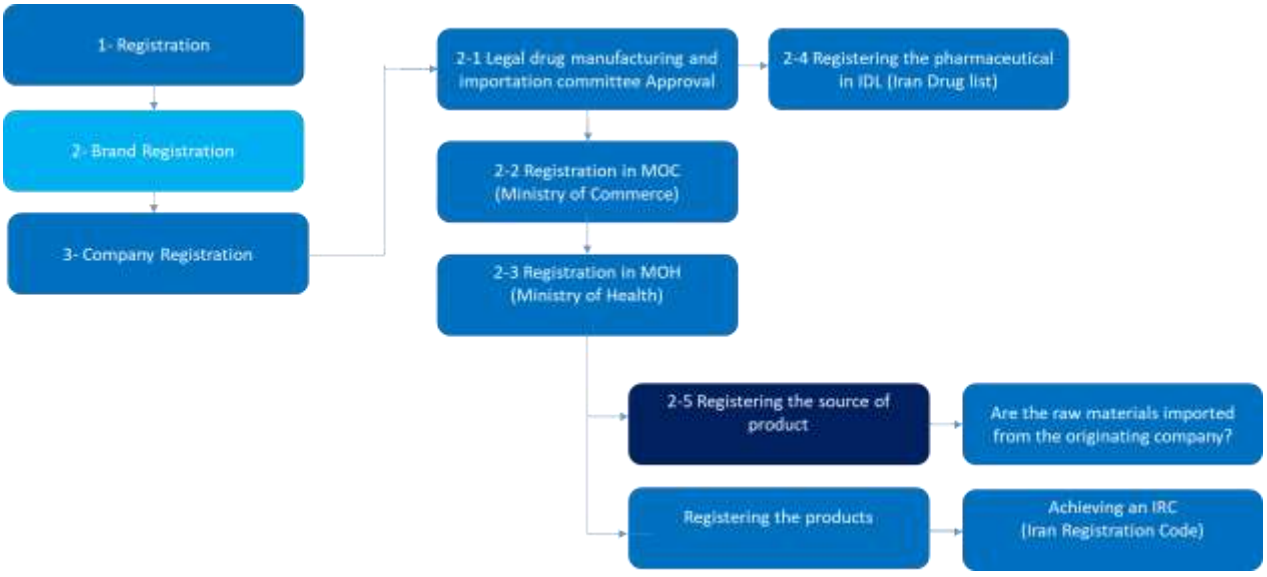
Pharmaceutical under license production refers to a product whose pharmaceutical name, formulation, manufacturing method, all physicochemical properties are in accordance with the Product License Holder's (PLH) file, and all components and packaging, as well as the final product, have the product specifications of the PHL and have been approved

2- Under license production terms

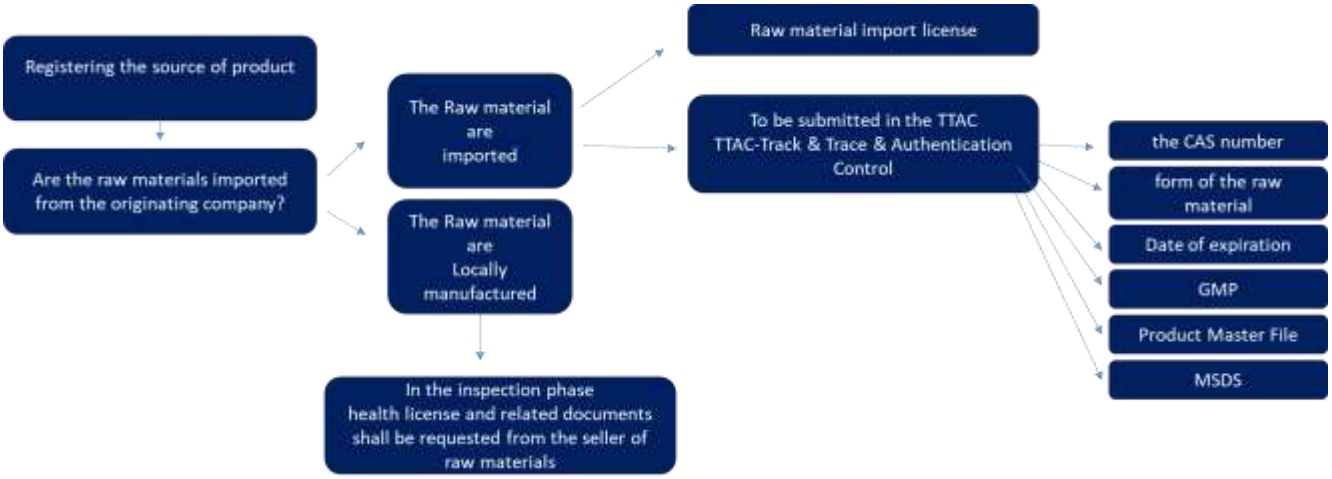
2-1 The pharmaceutical product selected for Under license production must be in-line with the Iranian Drug list

2-2 Should not be stated within the illegal manufacturing or importing pharmaceutical list

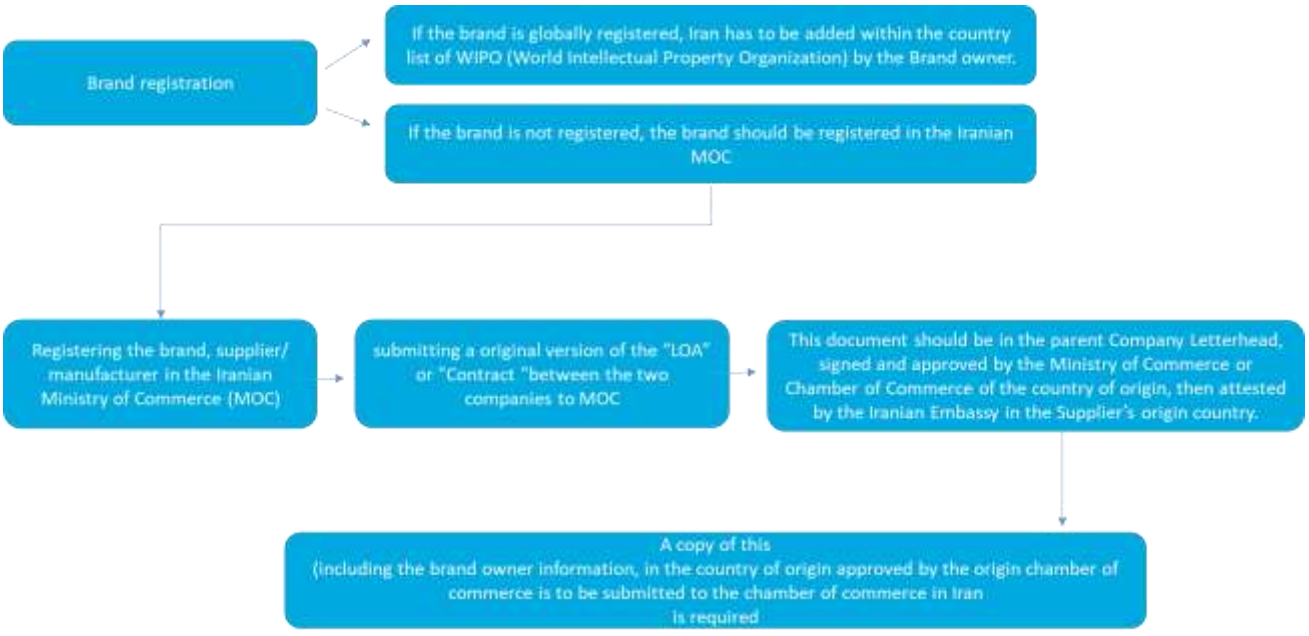
2-3 Must have US FDA (Food and Drug Administration) or European Medicines Agency (EMA) approvals



Registering the source of the product:



Brand registration procedure:



3- General requirements for initially applying for import/under license manufacturing

3-1 Distribution agreement for under license production

3-2 A timetable for each of the under license manufacturing phase in addition to stating the place of the production facility and packaging

3-3 Certificate of Pharmaceutical Product (CPP) or Free Sale Certificate

3-4 International approvals if necessary

3-5 An original version of the GMP

Please note the following:

All documentation stated in the above, must be issued by a legal authority of the country of origin (parent company) on the parent company letter head, approved by the ministry of commerce or the chamber of commerce in the country of origin then attested by the Iranian embassy in the country of origin.

A document containing the registration information of the brand owning company in the country of origin, which has been approved by the Chamber of Commerce, must be submitted to the Chamber of Commerce.

Once the stated documents are reviewed, the case shall be mentioned in the legal committee for drug manufacturing and importation.

After the the approval for importing or under license manufacturing is achieved, all documents requested in clause 3 have to be legalized and shared with the Iranian MoH in order to proceed.

4- Under license manufacturing phases

Based on the importing/supplying company's request and achieving the approval for production from the legal committee for drug manufacturing and importation, under license manufacturing shall cover a part or all of the stages below:

4-1 Importing the finished dosage form (FDF) specifically for a certain time period

4-2 Importing the pharmaceutical as bulk* and primary packaging

The definition of bulk means, the formulated product in the desired drug form before packaging

4-3 Manufacturing the first production series from the granule phase ready to be pressed (tablet) or to be filled (capsules)

4-4 Manufacturing the first production series from the API (Active pharmaceutical Ingredient) phase and pharmaceutical formulation

Please note that depending on the timetable and business model agreed between the two companies, each model requires different set of documentation.

5- Requested documents for each under license manufacturing collaboration method

The requirements to be presented to the MOH:

- Initial under license application request to be presented to the MOH
- Mutual under license manufacturing contract between the two companies presented to the MOH
- Free sale certificate (FSC)
- Certificate of Pharmaceutical product (CPP)
- PMF- Product master file
- Filling in the questionnaire
- A sample of the product for stability testing
- And any additional approvals COA of product and etc.,

If the product is registered in the Iranian supplement/drug list (IDL)

Once the positive confirmation from committee is given, along with editing the comments given by the committee, and submitting the source, the IRC is issued.

After the first semi-batch is manufactured, the pricing procedure is started

5-1 – Manufacturing the first production series from the granule phase

- GMP
- PMF- Plant master file
- All documentation related to the using granule

5-2 – Manufacturing the first production series from the API phase

- GMP
- PMF- Plant master file
- All artworks having the how to use/instructions section and the ingredients part written in in English and Persian

Source registration

At first, source of origin must be separately registered in IFDA for every product.

Needed documents:

- The COA of premix issued by the manufacturing site and COA of raw materials.
- Manufacturing site GMP.

NOTE: All RM's sources must be registered in Iran, usually most raw material sources have been registered before by other companies. In case some sources have not been registered by now, we must register them by ourselves. For this, we need COA of raw materials.

Submission of required documents to IFDA

Filled PMF: PMF is a formal questionnaire which must be filled for every product separately (its responsibility is with us) and must include: formulation (active and inactive ingredients), dosage form, directions, side effects, caution and warning, storage condition, detailed manufacturing procedure for finished product, method of analysis for assay of all active ingredients, art work (Label, Leaflet, Box) (as bilingual), the name of original company, license holder and the manufacturing plant where filling will be done.

Some of them will be written according to origin company's COA, COC and PMF/PIAF such as formulation, dosage form, …, and others be written according the international references such as side effects, caution and warning.

The acceptable references by Iran FDA are US Pharmacopoeia, Natural Medicines, Health Canada, British Pharmacopoeia.

List of documents needed for under license production in Iran:

1- GMP
2- Free Sale Certificate (FSC)
3- Letter of Authorization (LOA)
4- COA of premix powder or liquid
5- COA of API & excipient
6- COA of finished product
7- PIAF (Product Importation Application Form)
8- Method of analysis
9- MSDS
10- Detailed manufacturing procedure for finished product.
11- Master formula/Batch sheet (list of ingredients, API/EXCIPIENT & their Qty.)
12- Stability tests
13- Packaging material specification. (Foil/Blister/Bottle)
14- Art work files (Label, Leaflet, Box)

Good Manufacturing Practice (GMP)

The GMP certificate has to be issued by one of recognized authorities and has to clearly mention the phrase of "Good Manufacturing Practice" in their letter.

Free Sale Certificate (FSC)

You can find the Template of Free sale certificate in the Appendix. The authorized body can issue this certificate for you and you have just to get it signed and approved by the Iran Embassy.

Here are some points which should be noted in Free Sales Certificate:

1. Please make sure that you state the full address and phone number of the manufacturer.
2. The Certificate has to be on a letter head of the authorized body.
3. Please make sure that all pages of the certificate are signed, stamped and bundled together.
4. Please note that you have to submit a Free Sales Certificate per Manufacturing Plant. For example,if you have part of your product manufactured in a factory in Italy and you have some products manufactured in France, you will require 2 separate Free Sale Certificates, one for the manufacturing plant in Italy and one for the manufacturing plant in France.

5. Please make sure that you indicate the Brand name in front of each product in the Product Table.

Letter of Authorization(LOA)

One of the most important step is to submit a true copy of a legalized “LOA”. We need to receive an authorization letter based on we will be authorized for registration, manufacturing under license, marketing, distribution and sales your products as your business partner. You can find the sample of LOA in the Appendix.

Appendix 1-GMP

Appendix 2-Free Sales Certificate

Date:

Name of Licensee:	Name of Manufacturer:
Address:	Address:
Tel:	Tel:
Fax:	Fax:
Website:	Website:

Free Sales Certificate

This is to certify that the products of company *(Please name your company)*, under ……Brand *(Name your Brand)* are freely sold in large scale in …… *(Countries names)*, and are freely and in large scale exported to other countries.

Products: *(List your products in details; please insert a table for this part)*

..

..

Appendix 3- Letter of Authorization

We ……, located

…….

……. and represented by ……. as an authorized signatory to the title of Managing Director Tel: ……., Email …… **confirm that** ……. having office at ……, Postal Code: ……., Phone: ……. Fax: ……., Email: …….. website: ……, Registration number: …… is our Exclusive

Distributor for Manufacturing under license from premix /API, Marketing, Distribution and Sales of the following products with the following brands in Iran territory.

Row	Product name/ consumable item	Description	Net wt
1.			
2.			
3.			
4.			
5.			

Brand name: …….

Termination: It will be after the expiry of the LOA and / or should the other party put an end to its business or its main interests, each party notifies the other party by giving written notice at least 6 months' calendar days before the effective date.

Dispute Resolution: Any difference, dispute, controversy and/or claim should be settled in accordance with the Arbitration Rules of the International Chamber of Commerce in ……..

We also undertake to inform Iran health ministry/ FDO of any changes of this agreement or our new distributor in Iran territory for distributing our items in case of any nullification of this contract.

This agreement is valid for 5 years after the date of issue.

Sincerely yours,

Name: …..

Title: ….

Address: ….

Ph: ….

Appendix 4-PIAF

Product Importing Application Form (PIAF)

1. Product Information

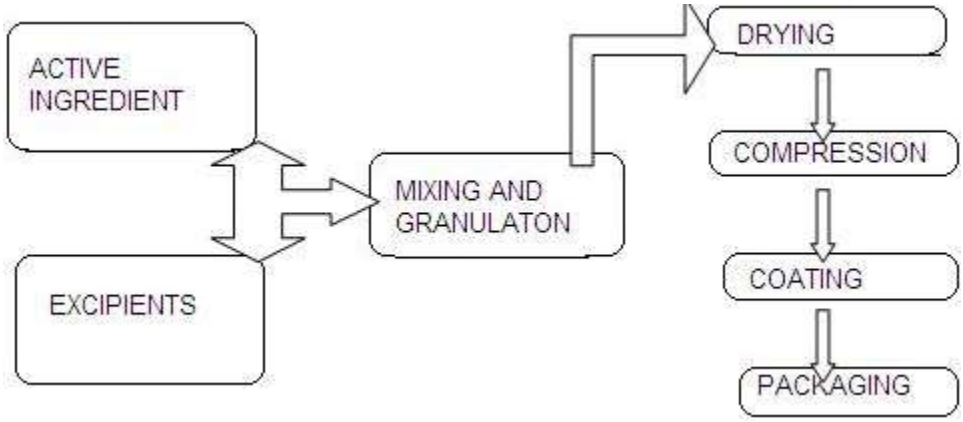
Product (Trade) name (as used in the country of origin)	
Active Substance(s)	
Strength	
Dosage form	
Route of Administration	
Container, closure and administrative device	E.g. :Carton box (96x43x132 mm) containing 4 blisters (85x125 mm) by 10 tablets.
Pack size	
Pack size and strengths used in the country of origin	
Shelf life period	
Shelf life (after reconstitution of dilution)	-
Storage condition	

2. Manufacturer

License/ Marketing authorization holder (name, address & country)	
Number and date of first marketing authorization/renewal	
Manufacturer of finished product (name, address & country)	

Flow chart indicating the different sites involved in the manufacturing process, packaging & release of the medicinal product:

E.g.:



Manufacturer of active substance(s) (name, address & country)	

3. Licensee in Iran

Name & address	

4. Qualitative and quantitative composition

4.1. Qualitative end Qualitative composition in terms of active substance(s) and excipient(s).

List the active substance(s) separately from the excipient(s).

Name of active substance(s)*	Quantity	Unit

Name of active excipient(s)	Function	Quantity	Unit

Note: the active substance should be declared by its recommended INN/Scientific name

4.2. a. List of materials of animal and/or human origin contained or used in the manufacturing process of the medicinal product

NONE	YES

Name	Function			Human	Animal (to be prescribed)	Animal origin Susceptible to TSE
	*AS	*EX	*R			

*AS=active substance, *EX= excipient (including starting materials used in the manufacture of the active substance/excipient), *R= reagent/culture medium

4.2. b. List of constituents from other origins

CONSTITUENTS	**Function**	**ORIGIN**

4.3. Coloring, flavoring and perfume compounds

4.4. A specimen of the label and leaflet

5. Clinical Particulars

5.1. Therapeutic indicators

5.2. Pharmacological action(s)

5.3. Contra-indications

5.4. Warnings and precautions

5.5. Interaction with other Medicinal Products and other forms of interaction

5.6. Uses in Pregnancy and Lactation

5.7. Effects on Ability to Drive and Use Machines

5.8. Undesirable Effects

5.9. Overdose

6. Names and titles of official signatories of PMF / signature

This is to certify that the information contained herein is true and correct.

Name and title of responsible official in the company:

Signature of responsible official in the company:

Date and Stamp:

Full Address:

Appendix 5- Certificate of Analysis (CoA)

Header:
Logo of the laboratory or company issuing the certificate (if applicable) Identification no. of the CoA

Name and address of the laboratory issuing the CoA: _____

Identification no. of the CoA: _____ Name, address and contact person representing the originator of the request for analysis: _____

Registration no. of the sample: __ Date received: _____ Quantity received: _____ Name of the product (International Nonproprietary Name (INN), brand name, etc.): _____

Dosage form, strength, package size (if applicable): _____ Type and material of the primary packaging: _____

Batch number: _____ Date of manufacture (if available): _____ Expiry date/retest date: _____ Name and address of the original manufacturer: _____

Phone: _____ Email: _____ Name and address of the repacker and/or trader (if applicable): _____

Phone: _____ Email: _____ Specifications for testing: _____

Test	Method reference[1]	Acceptance criteria	Result[2,3]	Compliance statement

Additional information, if requested by the customer:

Comments:

Conclusion on compliance of the sample with the specifications:

Name of the head of laboratory or person authorized to approve the certificate:

Phone: _____ Email: _____ Signature:
Date:

Appendix 6-MSDS (Material safety Data Sheet)

SAFTY DATA SHEET

SECTION 1 - IDENTIFICATION OF THE SUBSTANCE/MIXTUREAND OF THE COMPANY/UNDERTAKING

Contact information
General

Product identifier	
Synonyms	
Trade names	
Chemical family	
Relevant identified uses of the substance or mixture and uses advised against	

SECTION 2 - HAZARDS IDENTIFICATION

Classification of the substance or mixture	
Other/Supplemental	
GHS hazard pictogram	
GHS signal word	
GHS hazard statements	
GHS precautionary statements	
Other hazards	
Note	

SECTION 3 - COMPOSITION/INFORMATION ON INGREDIENTS

Ingredient	CAS Number	EU	GHS Classification	%

		EINECS/ELINCS List		

SECTION 4 - FIRST AID MEASURES

SECTION 5 - FIREFIGHTING MEASURES

SECTION 6 - ACCIDENTAL RELEASE MEASURES

SECTION 7 - HANDLING AND STORAGE

SECTION 8 - EXPOSURE CONTROLS/PERSONAL PROTECTION

SECTION 9 - PHYSICAL AND CHEMICAL PROPERTIES

Information on basic physical and chemical properties

Appearance	
Color	
Odor	
Odor threshold	
pH	
Melting point/ freezing point	
Initial boiling point and boiling range	
Flash point	
Evaporation rate	
Flammability (solid,gas)	
Upper/lower flammability or explosive limits	
Vapor pressure	
Vapor density	
Relative density	
Water solubility	
Partition coefficient (n-octanol/water)	
Auto-ignition temperature	
Decomposition temperature	
Viscosity	
Molecular formula	
Molecular weight	

SECTION 10 - STABILITY AND REACTIVITY

Reactivity	
Chemical stability	

Possibility of hazardous reactions	
Conditions to avoid	
Incompatible materials	
Hazardous decomposition products	

SECTION 11 - TOXICOLOGICAL INFORMATION

The information included in this section describes the potential hazards of the individual ingredients.

Irritation/Corrosion	
Sensitization	
STOT-single exposure	
STOT-repeated exposure/Repeatdose toxicity	
Reproductive toxicity	
Carcinogenicity	
Aspiration hazard	

SECTION 12 - ECOLOGICAL INFORMATION

Persistence and Degradability	
Bioaccumulative potential	
Mobility in soil	
Results of PBT and vPvB assessment	
Other adverse effects	

SECTION 13 - DISPOSAL CONSIDERATIONS

SECTION 14 - TRANSPORT INFORMATION

SECTION 15 - REGULATORY INFORMATION

SECTION 16 - OTHER INFORMATION

Full text of H phrases and GHS classifications	
Sources of data	
Abbreviations	
Issue Date	
Revisions	
Disclaimer	

Appendix 7-Stability Test

STABILITY STUDY

Studying time:

Experimental conditions to which the product was subjected:

The product was stored at controlled temperature and humidity at 30 +/- 2◦C temperature and 65% +/- 5% Relative Humidity, preserving the product in its original container, protect from light.

Formula product:

Packing material:

Description of the lots studied:

lots studied Batch type Date elaboration Date expiration Start date analysis Finish date

Test and analytical methods:

Product specification:

Storage Condition: 30±2◦C temperature and 65%±5% Relative Humidity

Reference: Packaging:

Mfg.Date: Exp.Date:

Parameters Initial

3 Months

6 Months

9 Months

12 Months

18 Months

24 Months

Standard Limit

Comments:

Analyst Approved

 Rejected QC manager Authorized Person

CONCLUSIONS OF THE STUDY OF STABILITY