Kingdom of Saudi Arabia
Saudi Food & Drug Authority
Drug Sector

المملكة العربية السعودية
الهيئة العامة للغذاء والدواء
قطاع الدواء

DRUG MASTER FILE REQUIREMENTS FOR THE REGISTRATION OF BIOSIMILARS

1st Draft
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This draft is for comments;
Please review and send your comments or suggestions to SFDA
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1. Administrative Information

1.1 Cover letter

1.2 Trade name

1.3 Generic name

1.4 Other trade names of the similar product

1.5 Pharmaceutical form

1.6 Name of manufacturing company

1.6.1 Name of active substance manufacturer (if different from above)

1.7 Status of the company in Saudi Arabia (currently registered or not registered)

1.8 Agent in Saudi Arabia

1.8.1 Name:

1.8.2 Address:

1.9 Marketing status at country of origin and other countries

1.10 Similar products registered in Saudi Arabia

1.11 Reasons for Production

1.12 Advantages over other similar drugs (if any)

1.13 Plant/Site information for the finished product

1.14 Fermentation plant description

1.15 Plant dedication

2. Technical Information

2.1 Name of cell line used

2.2 Active Pharmaceutical Ingredient (API) manufacturing process flow chart

2.3 Equipment used in production

2.4 Fermentation and purification process description

2.5 Quality control process for API and finished product

2.6 Materials used in cell culture (media, trypsin, sera, etc..)

2.7 Materials used in the purification process (buffers and their volumes used in each step)

2.8 Controls of materials :

2.8.1 Host cell description

2.8.2 Gene construct:

2.8.2.1 Methodology of gene isolation

2.8.2.2 Methodology of gene amplification

2.8.3 Vector description:

2.8.3.1 Name

2.8.3.2 Source

2.8.4 Final gene construct

2.8.5 Description of the gene recloning into the vector

2.8.6 Name of the resulting recombinant plasmid

2.8.7 Confirmation of the cloned sequence by sequencing analysis to prove it is identical to the sequence of the original gene

2.8.8 Description of cloning and establishment of the recombinant cell lines

2.8.9 Excipients of human and animals origins

2.8.10 Cell seed lot system: MCB and WCB description

2.8.11 Viral safety of cell seeds.

2.9 In process control tests on the intermediate product (bulk API specifications)

2.10 In process control of the finished product

2.10.1 Manufacturing consistency lots.

2.10.2 Critical production parameters.

2.10.3 Pattern of anticipated heterogenecity (structural or produced during manufacture and/or storage) should be characterized (post-translationally modified forms, e.g., glycoforms).

2.10.4 Possible deleterious effect due to heterogenecity on the safety and efficacy of the desired product. Demonstration of lot-to-lot consistency.

2.10.5 Tests for sterility, endotoxins, microbial limits, volume in container, uniformity of dosage units and particulate matter.

2.10.6 Rationale and justification for including and/or excluding testing for specific quality attributes.

2.11 Type of packaging

2.11.1 Container description: vial, stopper, syringe, Cartridge, ..etc..

2.11.2 Dimensional drawings of the container

2.12 Transporting and storing conditions for the API and finished product

2.13 Package insert description:

2.13.1 Therapeutic indications, dosage, contraindication, warnings and precautions for each indication)

2.13.2 Dosage

2.13.3 Contraindications

2.13.4 Warnings and precautions for each indication

2.13.5 Drug interactions

2.13.6 Pharmacology

2.13.7 Kinetics

2.14 Change reporting:

2.14.1 Pre-, post- or during clinical trial

2.14.2 Description of change

2.14.3 At which stage of the manufacturing process the change was introduced

2.14.4 What is the foreseeable impact of such a change

3. Scientific Information

3.1 Molecular description under the Brand Name

3.2 Active ingredient:

3.2.1 Structure and other characteristics
3.2.2 N-terminal amino acid sequencing
3.2.3 C- terminal amino acid sequencing if required

3.3 Qualitative and quantitative composition of the final preparation

3.4 Strength/Concentration

3.5 Formulation:

3.5.1 Raw material

3.5.2 Excipients

3.6 Specifications (pharmacopeia or non-pharmacopeia)

3.6.1 Release specifications for API and finished product.
3.6.2 Shelf life retest for API.

3.7 Justification of Specifications

3.7 Impurities:

3.7.1 Process product related impurities

3.7.2 Acceptance criteria of impurities

3.8 Manufacturing and expiry dates

3.9 Pharmacotherapeutic group

3.10 Pharmacology and indications

3.11 Kinetics

3.12 Other information:

3.12.1 Contraindications

3.12.2 Adverse reaction events

3.12.3 Precautions

3.13 Comparability:

Reference product: A biotech medicinal product produced by a multinational innovator and approved by U.S FDA or EMEA .

3.13 Comparability studies (comparison with reference product)

3.13.1 Quality (Comparison with reference product)

3.13.1.3 Analytical procedures
3.13.1.4 Validation of Analytical Procedures.
3.13.1.5 Reference analytical standards or materials
3.13.1.6 Batch Analysis
Physico-chemical tests
Bioactivity-Potency assays
Valid biological assays (animal- and cell-culture, ligand binding, and biological activity)
3.13.1.7 Stability studies
- Shelf life for finish product

Validation of analytical procedures. Specifications of acceptable degradation, of drug substance and drug product, during storage. Product specific stability-indicating profile.

3.13.2 Non-Clinical (comparison with reference product)

3.13.2.1 Pharmacology

3.13.2.2 Pharmacokinetics
3.13.2.3 Toxicology

3.13.2.3.1 Single dose toxicity
3.13.2.3.2 Repeat dose toxicity
3.13.2.3.3 Local tolerance

4. Clinical Studies
(comparison with reference product)

4.1 Protocol

4.2 Recruitment details

4.3 Eligibility criteria

4.4 Clinical studies reports:

4.4.1 Reports on biopharmaceutical studies.
4.4.2 Reports of studies pertinent to pharmacokinetics using human Biomaterials.
4.4.3 Reports on pharmacokinetics (PK)
4.4.4 Reports on pharmacodynamics (PD)
4.4.5 Reports on efficacy
4.4.6 Reports on safety

4.5 Statistics *(justification of statistical method used)*

4.6 Literature references.

5. Pharmacovigilance Plan

5.1 Pharmacovigilance plan (track and trace)

5.2 Recall plan

5.3 Plan for ADR reports

5.4 Plan to ensure quality of the product (defect, final formulation package)

5.5 Bar coding method

5.6 Post approval stability protocol and stability commitments

6. Certified Documents

6.1 GMP certificates

6.2 Each raw material

6.3 Product analysis

6.4 Product composition

6.5 Diluents and coloring materials

6.6 Absence of alcohol content in the finished product

6.7 Absence of animal materials in the finished product

6.8 Package insert approval at country of origin

6.9 Registration and marketing at country of origin and other countries

6.10 Pricing at country of origin

6.11 Company from which raw material(s) was obtained

7. Other necessary activities

Site visits to the manufacturing facility, line of production and the raw material source(s) manufacturers (if different from the drug manufacturer) are mandatory.