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# BIOSIMILAR REGULATORY REQUIREMENTS IN INDIA

**Sindhuja C*, Dr. Shantha Kumar GS**

Acharya & BM Reddy College of Pharmacy, Soldevanahalli, Acharya Post Office, Hesarghatta Main road, Bangalore-560107

*Corresponding author E-mail: sindujannu2407@gmail.com

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**ABSTRACT**

Many key biologics are scheduled to lose their patent by the year 2020, which will provide the opportunity to other biopharmaceutical companies to develop the similar biologics. Biosimilar or similar biologic used has increased in the recent year following the approval of the first biosimilar in early 2000. India is one of the leading manufacturers of similar biologics. India has developed a new guideline in 2012 for the pre- and post-marketing approval of similar biologics.

## INTRODUCTION

**Regulatory affairs:** It is a practice established by government to keep healthiness of public by improving the wellbeing and ability of medicines in the fields of pharmaceutical company, medical devices, pesticides, complementary medicines, crop protection products and make up products from the company responsible for the detection, research, manufacturing and advertising of medicines to guarantee that they are harmless and effectiveness. [1]

**Biologics:** A biological is a medication manufactured from or containing modules of an individual form of life like fungus, bacterium, and plant. Biologic medicines contain wide-ranging products, using biotechnology, derivative from plant, animal or living organisms.[2] Biologic products that include biomolecules or macromolecules which regulates the purpose of added proteins and cellular procedures, genetic factor regulate essential protein manufacture, improved hormones, or generating cells that trigger immune system mechanisms. Biologicals will alter the normal intracellular and cellular biological activities function.[3]

**Definition:** Biosimilar is a biologic product, which is very similar reference product and has no clinically meaningful differences in term of wellbeing and effectiveness.[4]

### Difference between Biosimilar and Generic drugs[7]:

Generic medicinal products are often confused with the biosimilars. They are all being sold as low-cost alternatives to high price brand names. Both are eligible by drug-makers to expire as exclusive patents on expensive new medicines. And both are designed to exert the same clinical impact in the pricier community as their counterparts. But similar biologics

drugs and generic drugs are different, since even the chemical structure of generic drugs is "very similar" to the original, biosimilar drugs, which is similar enough in replication to produce the same therapeutic and clinical outcome. Difference between generic and biosimilar are copies of original marketed drugs and medicines that use living species as active ingredients, respectively. But many experts hope the two will share a critical commonality and that, like generics, biosimilars will dramatically lower the cost of biologic drugs (Table 1)[8] A biosimilar is a type of biological medicine that is very similar to the 'original medicine'. Similar biologics are approved according to the same pharmaceutical quality, wellbeing and efficacy standards that apply to all biologics. A Biologic Related Product is comparable in consistency, protection and effectiveness to an accepted Biological Reference Product based on comparability. Guideline on Related Biologics will discuss the manufacturing process regulatory pathway. It will also include regulatory requirements for premarket, including comparability for quality, preclinical and clinical studies, and regulatory requirements for similar biologics for postmarkets. Center Drug Standard Control Organization is India's national regulatory body evaluating drug health, effectiveness and efficiency in the country. Biotechnology department through Review Committee Generic Maniplations oversees the production and preclinical evaluation of recombinant DeoxyriboNucleic Acid related products.[9]

**Guidelines and Regulations:** The Related Biologics are governed in compliance with the Drugs and Cosmetics Act, 1940, the Drugs and Cosmetics Laws, 1945 and the Legislation for the production, use, import , export and storage of harmful microorganisms / genetically modified organisms or cells, 1989 notified in the Environment Protection Act , 1986. The following are various Guidelines applicable:

- DNA Safety Guidelines, 1990.
- Guideline for Preclinical and Clinical Data Guidelines Biologicals , 1999.
- CDSCO guidelines, 2008:
  - Clinical Trial Application Submission for Evaluating Safety and Efficacy
  - Permission for NDA
  - Quality, Safety and Efficacy Documents for Post approval changes in Biological products
  - For NDA the Quality information of Drug Submission is Prepared: Biotechnological/Biological Products
    - IBSCs, Handbook and Guidelines, 2011.
    - Similar Biologics Guideline: Regulations Required for Marketing authorization, 2012.

**METHODOLOGY**

**Source of Data:**

- Journals
- INDIA Official website
- Pharma times, Pub med, Science Direct,etc.
- Generic and Biosimilar Initiative (http://gabionline.net/)
- Library: Acharya and BM Reddy College of Pharmacy.
- E-library: Acharya and BM Reddy College of Pharmacy.

**Methods of collection of data:** Each study has some patterns and follows some paths toward achieving the goal. The method to be followed thus plays a significant role in determining the outputs as well as the study's consequences. Work done using the data collected by evaluating the terms of the parameters below:

- Document review
- Case studies
- Internet Sources

**Competent Authorities**

- Institutional Biosafety Committee (IBSC)

Any individual research institutions dealing with microorganisms or any modified organisms shall be required to constitute an IBSC. In addition to initial analysis of applications will be sent to RCGM, and then IBSC is responsible for ensuring biosafety at site. IBSC is also responsible to review and approve the company to trade the

aforementioned species for research purposes.

- Review Committee on Genetic Manipulation (RCGM)

RCGM works at Dept of Biotechnology, Government of India's Ministry of Science and Technology. RCGM is responsible for supporting research and development in the context of unique biologics, exchanging genetically modified cell banks for research and development purposes, and data collection up to preclinical assessment.

- Genetic Engineering Appraisal Committee (GEAC)

Under the MoEF, GEAC serves as a regulatory body to review proposals and approve practices that contain genetically modified organisms / living modified organisms in the final drug product.

- Central Drug Standard Control Organization (CDSCO)

CDSCO, led by Drug Control General of India, is the MoHFW, the Government of India's highest regulatory agency, and is responsible for authorizing all clinical trials and experimental medicines. CDSCO is responsible for approving clinical trials in the form of Similar Biologics (also authorizing the manufacture of medicinal products for clinical trials and the export of clinical samples for biochemical and immunological analysis) and for the manufacturing and marketing authorizations. CDSCO Zonal offices are responsible for approving the import of medicinal products for the assessment, testing and review of research and development.[10]

**Principles for Development of Similar Biologics.**[11]: A sequential procedure is used to create related biologics to demonstrate similarities through detailed characterization studies that reveal molecular and consistency attributes in relation to the biological comparison. Although the scope of the Specific Biologic preclinical and clinical assessment is likely to be less than that required for the Original Biologic, Specific Biologic testing is necessary to ensure that the drug meets adequate standards of protection, efficacy and quality in order to ensure health in accordance with international guidelines. According to the literature, the abbreviated data standards are only suitable for the development plan's preclinical and/or clinical components, but not for the consistency components by product comparability demos. Identifying any significant differences in safety, feasibility, and efficacy studies would involve a more comprehensive preclinical and clinical analysis that would not validate the drug as a biological counterpart. If the Reference Biologic is used for more than one indication, the Specific Biologic will also only apply for additional indication if it is justified and meets the criteria set out in the "Extrapolation of Effectiveness and Safety Data to other indications" section. The rationale for extrapolation of indication shall be based on consistency comparability, preclinical and clinical studies, available lit.

**Reference Product Selection**: Reference Biologic is a drug approved by an innovator that is essential for the development of Similar Biologic after assessment of the dossier compilation. The Reference Biologic must be used in all comparability exercises regarding constancy, preclinical and clinical considerations. The following factors should be considered for Reference Biologic selection:

- In India or ICH countries, the Biologic Comparison should be licensed / approved and be the innovator 's product. The Biologic Comparison will be approved on the basis of full data on fitness, quality and effectiveness. Thus another Biologic Similar can not be considered a Biologic Reference option.
- In any ICH country the Biologic Reference should have been approved in case the Biologic Reference is not sold in India. For consistency, preclinical and clinical comparability the Reference Biologic product may be imported for the production of the Similar Biologic.
- The biologics guide should be used in all study supporting product safety, effectiveness and reliability
- The dosage type, power, and route of administration of Biologic should be similar to that of Reference Biologic.
- The biological comparison active substance (active ingredient) must be identical to that of the biologic.
- Acceptance for evaluation of an innovative drug as a Specific Biological

Reference Biologic does not imply acceptance in India.

**Manufacturing Process:** The Company who manufactures of Similar Biologics will improve the manufacturing process to yield to the Reference Biologic a comparable quality product with respect to identification, purity and potency. The method of producing Similar Biologics should be checked and proven highly reliable and robust. If the host cell line used for the production of Reference Biologics is released, the same host cell line for the manufacturing of Related Biologics is required. Alternatively, any cell line that is adequately characterized and suitable for intended use may be used to develop a Similar Biologic, with sufficient rationale for minimizing the potential for significant changes in the quality attributes of the product and for avoiding the introduction of certain types of process-related impurities that could affect clinical outcomes and immunogenicity The ICH's recommendations will be deferred for advice on setting up and characterizing the cell banks. The data criteria for the analysis of the manufacturing process at the preclinical submission point provide a full overview of the manufacturing process from the production and characterisation of cell banks, clone stability, cell culture / fermentation, harvest, excipients, composition, purification, key packaging interactions and the impact on product characteristics as indicated below:

- Considerations of Molecular Biology
- Development of Upstream Process
- Development of Downstream Process
- Consider the Quality Aspects for Similar Biologics
  - Analytical tests
  - Product Characteristic
  - Specifications
  - Stability
- Compare Quality Study

**Preclinical Data Requirements**

**Precondition before preclinical studies:** The applicant must meet the RCGM requirements, such as process and product consistency presentation, product description and product specifications. The applicant should send the produced data along with the following basic clinical details and preclinical research protocols to RCGM to obtain permission. The toxicology tests will be performed after RCGM acceptance. The basic Biological and Related Biologic reference knowledge can include the following:

**Information about the Reference Biologic**

- Drug Information
- Bioequivalence range, if available.
- Tissue-specific localization, if available.
- Available toxicity data on Reference Biologic.
- Mode of action.

**Information about the Similar Biologics**

- Known / proposed clinical use
- Population for whom drug has been made (Age, sex, pregnancy, lactating, children etc.)
- Type of dosage
- Type of Administration
- Complete formulation + adjuvants
- Diluents
- Shape of Product

The RCGM application should be followed by IBSC approval by the developer, and IAEC approval where appropriate. In addition, the applicant will include information on the proposed site for carrying out toxicity testing and including staff such as the director of the study, the principal investigator, the pathologist, other investigators and the quality control officer on site. It should also have GLP certification status for the proposed plant.

**Non clinical Studies (Pharmacodynamic and Toxicity Studies)**[12]**:** Non clinical research will carry out until any clinical studies are started. Such studies should be comparable in nature, and should be designed in order to identify

difference between the Related Biologic & Biologic Comparison. Preclinical study design will differ when depended upon the criteria applied, as that of therapeutic index, form and indications. Method followed, in the preclinical summary, should be thoroughly explained. Preclinical experiments with the confirmed formulation of Similar Biologic used clinically and Reference Biologic should be performed, unless otherwise stated. The Specific Biologic dosage type, dose, power, and route of administration will be similar to the reference product, it should be justified by the event in following parameters. The following are required for Non Clinical evaluation:

**Pharmacodynamic Studies**

- *In vitro* studies: the comparability of Specific Biologic and Reference Biologic will be identified through bioassays based on in vitro cells.
- *In vivo* studies: *In vivo* evaluation of biological / pharmacodynamic activity may be dispensable if there are *in vitro* tests available that reliably demonstrate Reference Biologic's clinically important pharmacodynamic activity. In cases where in-vitro assays do not suit the pharmacodynamics, In vivo studies should be conducted as appropriate.

**Toxicity Studies:** During the *in vivo* toxicology, minimum one repeat dose study with an expected route of administration in a pharmacologically appropriate species is needed. The applicant should provide the scientific rationale for choosing the animal model(s) based on the evidence available in the literature with respect to the animal models to be used. Nevertheless, if the pharmacologically relevant animal species are not eligible and have been adequately validated, toxicity tests shall be carried out with the permission of RCGM as in rodent or non-rodent species as per the requirements of Schedule Y.

- Regarding route of administration in animal models that are either pharmacologically relevant or pharmacologically irrelevant, the route of administration should cover only the intended route as provided for in Schedule Y.
- In general, the length of the analysis will not be less than 28 days with a 14-day recovery period. However the duration can differ based on the dosage and other factors on a case-by - case basis.
- Dosage will be measured on the basis of the Reference Biologic therapeutic dose. Pilot batch response test will be performed before the toxicity studies are started if necessary. In animal toxicology research, three ranges of dosing corresponding to human equivalent dose or other study dose will be used for repeated toxicity dosing research. During the toxicology study the Biologic product will be compared at least 1X of the HED with Reference Biologic. Other disparity is dosage rates should be explained and accepted before test.

Local tolerance can be evaluated when it is depended on the administration of drug. The evaluation are performed by toxicity study.

The repeat dose toxicity consist of the following

i. Historical Control (Optional)

ii. Vehicle Control

iii. Vehicle Control for recovery group

iv. Formulation without protein (for vaccines) if multiple adjuvants - each to be checked independently

v. 1X Similar Biologic for study duration (lowest dose)

vi. 1X Reference Biologic for study duration

vii. 2X Medium dose Similar Biologic

viii. 5X High dose Similar Biologic

The protocols and the study reports should provide the full details of the various toxicity testing steps as shown below:

- Pre-euthanasia procedures e.g. blood draw, body weight, etc.
- Events immediately following euthanasia, necropsy, gross-description, organ weights and histopathologically sampled organs.
- Biochemical parameters-Equipment and methods used-measuring and expression units.
- Hematology procedures and parameters-method (automated or manual) to be used.
- Methods used in statistics.
- Bone marrow either examined as an aspirate /smear or on histopathology section.

The applicants will consider the following points in terms of histopathological observations:

- Any findings that are regarded as variations from the defined standard histology must be reported and the frequency of each of these in the various groups should be denoted.
- Whether such a feature is significant or not, a review of statistical significance or a dose response can be decided, or whether it is within or outside the normal range of values for biochemical and hematological observations
- It should be documented if not all organs of all animals have been examined.
- The proposed course of action is to be included in the protocol in the event of premature death or morbidity.
- The toxicity studies are not required for evaluation of similar biologics unless until there is requirement of results from repeated dose toxicology study.
- The final report should have all the aspects in the protocol and also the following documents:
  - Regulatory Approval for test center
  - Institution Approval Report
  - Animal Ethical Committee approval letter
  - Quality Assurance Department statement
  - People who all involved in study there details and their Signatures
  - Analytical Reports
  - Animal Health Certification from Ethical Committee.

Deviation in Protocol if any

- Result Discussion.
- Output of data

➢ **Responses in Animals**

The antibody response to the Particular Biologic should be contrasted with that generated by the reference Biologic in an acceptable animal model. The serum research samples should be compared against host protein in the cells for reaction. The tolerance will be evaluated to determine the toxicity of immunity in the similar biologic analysis. Therefore, when designing the protocols, immune study will be included in the repeat dose analysis. Criteria for immunotoxicity which include complexity in targeted tissues when evaluation of cells. After the Non Clinical Study the data collected will be submitted to RCGM for review. Toxicology data, includes pharmacology, mutagenicity, reproductive toxicity,and carcinogenicity research, which is not required to test a Similar Biologic unless the findings of repeated toxicological tests are necessary. Based on the positive assessment of preclinical research reports including method and product quality analysis, product classification, product characteristics and biological reference comparison, RCGM would prescribe the

DCG(I) to allow the sponsor to undertake the appropriate phase of clinical trials in compliance with the CDSCO requirements. The patient may apply to RCGM and the DCGI office, requesting approval for clinical testing, for a concurrent application. However, only after getting recommendation from RCGM can the DCG (I) office complete client review and problem authorisation.

**Data Requirements for Clinical Trail Application:**[13] Along with the submitted data in the Non – clinical study, as per CDSCO guidance for industry, 2008, the applicant must submit an NDA to conduct the clinical trials. The quality data submitted should indicate that Essential Quality Attributes do not vary, and that all Main Quality Attributes are well regulated to allow the initiation of clinical evaluations.

**Pharmacokinetic (PK) studies:** PK results will give subsequent clinical study of Phase III provided that the suspected Identical Biologic is close to that of the Reference Biologic. After extensive characterization comparability on quality attributes has been completed, a PK study of the Similar Biologic in comparison with the Reference Biologic product may be carried out in an appropriate number of:

- Healthy Participants and / or
- Patients

Consider the following factory for Comparative PK stud.

- T½ - Half life
- PK parameter - Linearity
- Endogenous levels and diurnal variations (where applicable) of Similar Biologic under study
- Diseased Condition which is to be treated
- Type of Administration and
- Drug indications

Considerations for product design:

- If the dosing is Single dose then it will be comparative and PK study
- Parallel study will be carried out
- Cross over design study
- Multiple dose, comparative parallel arm steady state PK studies

**Pharmacodynamic Studies:** The pharmacodynamic (PD) studies, as required for the PK studies in the Similar Biologic clinical development program, should also be comparative in nature. In order to detect differences between Similar Biologic and Reference Biologic in the most important population (patients or healthy volunteers), comparative, parallel arm, or cross-over, PD study is required. When a PD predictor is available in healthy volunteers, PD should be conducted in healthy volunteers, unless considered inappropriate due to possible side effects and toxicity e.g. oncology medications.

**Safety and Efficacy Confirmatory study:** Establishing in-vitro, pre-clinical and PK / PD similarity as described in the previous section is important as robust, high-quality processes, comprehensive quality comparison and pre-clinical and PK / PD comparative studies help to demonstrate the similarity of similar biologics in these settings. In order to eliminate any residual risk, a comparative phase III clinical trial may also be required to establish the comparability with respect to clinical safety and efficacy. Only in exceptional cases i.e. if there are no residual uncertainties left after comparing Similar Biologic and Reference Biologic at the analytical, non-clinical and PK/PD level, an additional comparative safety and efficacy trial is not needed. Only in exceptional cases , i.e. where there are no residual uncertainties left after comparing Similar Biologic and Reference Biologic at the analytical, non-clinical and PK / PD levels, there is no need for an additional comparative safety and efficacy test.

**Data for MAA:** The applicant will apply business authorisation application as per Industry Guidelines Paper CDSCO, 2008.

**Classification of Biologics:**

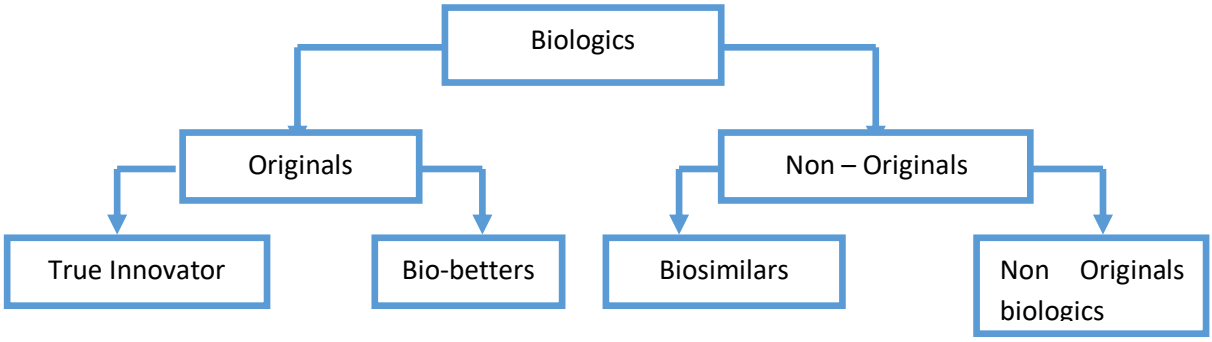


**Figure 1 : Classification of Biologics** [5]

**Table 1: India country profile**

| | |
|---|---|
| Capital of India | **New Delhi** |
| Biggest city | Bombay or Mumbai |
| Language | Hindi (Primary Official Language) |
| Governing Society | Parliamentary System |
| Currency | Indian rupee |
| Biosimilar Market | The Indian biosimilar market in 2015 was around 300 million US Dollars. |
| Regulatory Authority | Central Drug Standards and Control Organization (CDSCO) |

**Table 2: Biosimilar versus Generic**

| | **Biosimilar** | **Generic** |
|---|---|---|
| Source | Living Organism | Chemical synthesis |
| Size | Large molecule | Small molecule |
| Structure | Complex, heterogeneous | Well defined |
| Manufacturing Process | Difficult | Relatively simple |
| Stability | Unstable and sensitive to outside conditions | Stable |
| Immunogens | Immunogenes | Usually Non- Immunogenic |
| Bio- equivalence with reference product | No | Yes |
| Interchangeable with reference product | No | Yes |
| Cost | High | Low |

**Table 3 –** Forms for submission process

| Phases | Governament | Forms for Application purpose | Forms for Approval |
|---|---|---|---|
| Manufacturing License (After CDSCO NOC) for testing, analysis and examination | FDA – Food and Drug Administration | Form 30 | Form 29 |
| License to import for testing, analysis and review | CDSCO – Center Drug Standard Control Organization | Form 12 | Form 11 |
| Import / export/ transfer/ received by cell bank | RCGM – Review Committee of Generic Manupulation | Form B1/B3/ B5/B7 | |

| | | | |
|---|---|---|---|
| Investigation and Development | RCGM - Review Committee of Generic Manupulation | Form C1 | |
| Permission to preclinical study | RCGM - Review Committee of Generic Manupulation | Form C3a | |
| Reporting on preclinical data | RCGM - Review Committee of Generic Manupulation | Form C5a | |
| Study on Human Participants | CDSCO - Center Drug Standard Control Organization | Form 44 | CT Permission Letter |

**BIOLOGICAL PRODUCTS: PHASE-I & PHASE- II CLINICAL TRIAL**

**Table 5: Table of content**

| TABLE OF CONTENTS | |
|---|---|
| **SECTION A** | General Information |
| **SECTION B** | Chemistry manufacturing Control |
| **SECTION C** | Non clinical Data |
| **SECTION D** | Proposed Phase I/II |

For situations where industrial processing is performed on a different size and/or with a different method similar to those used for the manufacture of phase III clinical trial samples, so product comparability knowledge has to be balanced with sufficient evidence and must be treated on a case-by - case basis.

- **Forms for Application**

The forms are submitted for regulatory body are as follows in table 3.

General Information:

1. Company Introduction
   Brief description about company
2. Administrative Information
   Provide address of company Headquarters
3. Site plan and Manufacturing Facility
   Provide address of company Headquarters
4. Approval from Regulatory

a. NOC that is No Objection Certificate issued by the Central License Approving Authority for Form 29.
b. State Licensing Authority issuing Form 29.
c. Grant of Permission for conducting toxicology study

5. Status of Intellectual Property rights countries.

a. Detailed information of original drug from where it is,
   - IND approved
   - NDA approved
   - Approval for marketing
   - If product withdrawed then its details

b. Patent details

**CMC - Chemistry Manufacturing Control:**

1. Product Information

Details of drug and the class of product for which it belongs.

1.1 Product name
1.2 Product's INN name
1.3 Administration of Product
1.4 Dosage Form and Strength
1.5 Composition

2. Development of Product

2.1 Strain information
Name of Product

If the product is derived from Deoxynitronucleic Acid (DNA) then the following will be included,

2.1.1 Development of Clone

- Source details
  Nucleic acid Nucleic acid sequence
- Details about Vector that is about the vector gene
- The target gene which carries vector

2.2 Name and source of Substrate

2.3 Details of Master and Substrate Details

3. Drug Substance

3.1 Drug substance Production

3.1.1 Raw materials

- List
- Raw material test procedure
- The origin and its compliance with TSE / BSE compliance

3.1.2 Details of Manufacturing Flow

3.1.3 Flow chart of Drug Substance Process Operations flow path

3.1.4 In process steps
Includes process at every stage of Drug substance

3.2. Drug substance Characteristic

3.2.1 Biological

3.2.2 Physicochemical

3.3 Drug substance Control

3.3.1 Specification

3.3.2 Analytical Test and Standardized Studies

3.3.3 COA

3.4 Standard Reference Material

3.5 Container closure network

3.5.1 Specification and test procedure of Packing

3.5.2 Drug Substance Label

a. Stability study

i. Write-up Program for stability study
ii. Specification and Research Methods: The study of Stability
iii. Accelerated batches Stability Data (3 months)
iv. Stability Details on pilot batches in real time(3 months)

2. Drug Product Information

a. Composition & Description
b. Drug product Components
c. Process of manufacturing describe the facility where the clinical trial material will be produced.
d. Flow chart of Manufacturing
e. Control of intermediates & Critical steps
f. Equipment and Premises
g. Excipients Control
   i. Requirements
   ii. Analytical tests
   iii. Excipients of human or animal origin and which compliance with TSE / BSE
h. Drug Product Control
   i. Final product specifications with reference to the respective compendia should be included in detail. Also to include Non-pharmacopeial tests.
   ii. Analytical test will describe the research methodology adopted in the final product analysis in detail. Contain, where applicable ,detailed references to pharmacopeia. However, Data expected for recombinant products should not be submitted for biological products like Vaccines.
   iii. COA (Pilot batches Scale)
i. Standards of Reference
j. Container Closure network
   i. Packaging Materials: Research procedures and requirements
   ii. Art work – Packaging material (label, primary cardboard, secondary cardboard and insert pack.
   iii. Packaging Specials
k. Stability study

i. Write-up Program for stability study
ii. Specification and Research Methods: The study of Stability
iii. Accelerated batches Stability Data (3 months)
iv. Stability Details on pilot batches in real time(3 months)

**Non-clinical Data**

Drug and Cosmetic Act, 1945, Schedule – Y.

**Clinical Data**

Drug and Cosmetic Act, 1945, Schedule – Y.

CDSCO, DCGI and Government of India published GCP guideline.

Indian Council of Medical Research, New Delhi gave Ethical Guidelines for Biomedical Research on Human Subjects.

**Recommendations for Applicants Seeking Licensure of a Biosimilar Or Interchangeable Biosimilar:**

**Support Draft Labeling for a Biosimilar to the product license:** Submission- Original or Supplement BLA 351(k)

- Submission of an Original 351(k) BLA for Licensure for Support Draft Labeling for a Biosimilar to the product license.
- Submission of a Supplement to a 351(k) BLA
- Development of Draft Labeling for a Proposed Biosimilar or Interchangeable Product Support Draft Labeling for a Biosimilar to the product license.
- Draft Labeling Content
- Information to Support Draft Labeling for a Biosimilar to the product license.

- Timing Considerations for Submission of a BLA 351(k) or Supplement to a BLA 351(k)
  - Targeted Timelines for Review
  - Unexpired Exclusivity
  - Circumstances Other Than Exclusivity, Including Patents

**DISCUSSION**

Biosimilars are expected to be a vital component in reducing health care costs and enhancing patient access to special, often lifesaving medications. It is hoped that the India will soon finalize these regulatory guidelines, clarify unanswered questions, and establish a biosimilars pathway that's based upon sound scientific principles. In doing so, the agency will must find the correct balance between rigorous data and testing requirements and providing a cost-efficient, expedited pathway for biosimilar approval. Robust evidence is critical to confirm drug efficacy and safety, but so as to encourage the provision of biosimilars, it can't be too burdensome to dissuade company sponsors from developing and introducing biosimilars to the market.

**CONCLUSION**

Biosimilar don't seem to be generic; biologics are larger and more complicated than chemical drugs, because of the complexity of biological/biotechnology derived products the generic approach is scientifically not appropriate for biosimilar products. there's must use well-designed clinical trials to determine biosimilarity. The challenge with biosimilars is to understand the differences which matter clinically. the precise product given to the patient should be clearly identified.

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