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Regulatory Gateway for Development and Marketing Authorization of Biosimilars & Drugs in India

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ABSTRACT

The pharmaceutical sector was valued at US$ 33 billion in 2017. The India's pharmaceutical industry is expected to expand to reach US$ 55 billion. India's pharmaceutical exports stood at US$ 17.27 billion in 2017-18. In 2018-19 these exports are expected to cross US$ 19 billion. Indian companies received 304 Abbreviated New Drug Application (ANDA) approvals from the US Food and Drug Administration (USFDA) in 2017. The country accounts for around 30 per cent (by volume) and about 10 per cent (value) in the US$ 70-80 billion US generics market. India is today one of the top emerging markets in the global pharmaceutical market. The sector is highly knowledge based and its steady growth is positively affecting the Indian economy. The organized nature of the Indian pharmaceutical industry is attracting several companies that are finding it viable to increase their operations in the country. Moreover, India is hub to about 10,500 manufacturing units and over 3,000 pharma companies. India exports all forms of pharmaceuticals from APIs to formulations, both in modern medicine and traditional Indian medicines. India's biotechnology industry is expected grow at an average growth rate of around 30 per cent a year and reach US$ 100 billion by 2025. This article focuses on the current regulatory process for development to commercialization of drugs including biologics and similar biologics.

INTRODUCTION

Indian Pharmaceutical Industry Perspective:

Geographically, India is comprise area of 3.29 million sq. km. (1.27 million sq. mi.); about one-third the size of the USA. Genetically, culturally and socio-economically diverse population base of more than 1.2 billion is a home for a numerous diseases as well as for qualified, English-speaking professionals, Institutions and hub of contract manufacturers and researchers [1, 2]. Today, Indian economy stand as the third largest based on the Purchasing Power Parity (PPP) and in terms of globally eleventh largest by nominal Gross Domestic Product (GDP), due to its rapid growth, especially over the last decade, India is considered an industrialized nation[3]. Apart from being a multi-ethnic, pluralistic society, India is also blessed with a variety of wildlife.

McKinsey & Company a global management and consulting firm, through a major study it has reported that by 2020 India's pharmaceutical sector will touch around US$ 45 billion. The reasons for this optimism are well founded. India is the largest provider of generic drugs globally. Indian pharmaceutical sector industry supplies over 50 per cent of global demand for various vaccines, 40 per cent of generic demand in the US and 25 per cent of all medicine in UK. India enjoys an important position in the global pharmaceuticals sector. The country also has a large pool of scientists and engineers who have the potential to steer the industry ahead to an even higher level. Presently over 80 per cent of the antiretroviral drugs used globally to combat AIDS are supplied by Indian pharmaceutical firms.

Further, as per the Indian government report, the pharmaceutical sector was valued at US$ 33 billion in 2017. The country's pharmaceutical industry is expected to expand at a CAGR of 22.4 per cent over 2015–20 to reach US$ 55 billion. India's pharmaceutical exports stood at US$ 17.27 billion in 2017-18. In 2018-19 these exports are expected to cross US$ 19 billion.

Indian companies received 304 Abbreviated New Drug Application (ANDA) approvals from the US Food and Drug Administration (USFDA) in 2017. The country accounts for around 30 per cent (by volume) and about 10 per cent (value) in the US$ 70-80 billion US generics market.

India's biotechnology industry comprising bio-pharmaceuticals, bio-services, bio-agriculture, bio-industry and bioinformatics is expected grow at an average growth rate of around 30 per

cent a year and reach US$ 100 billion by 2025. The rise of pharmaceutical outsourcing and investments by multinational companies (MNCs), allied with the country's growing economy, committed health insurance segment and improved healthcare facilities, is expected to drive the market's growth. India is today one of the top emerging markets in the global pharmaceutical fraternity.

Figure 1: Advantage India for drugs and biologic medicines hub

The organised nature of the Indian pharmaceutical industry is attracting several companies that are finding it viable to increase their operations in the country. Further, India is home to about 10,500 manufacturing units and over 3,000 pharma companies. India exports all forms of pharmaceuticals from APIs to formulations, both in modern medicine and traditional Indian medicines[4].

Biosimilars development pose different challenges when compare to small molecule generics, with additional requirements in terms of:

• Sophisticated technologies

• Clinical development, clinical trial expertise and proving comparative data

• Market access

• Manufacturing in dedicated manufacturing facility

• Sales and marketing capabilities[5]

METHODOLOGY

Description of Biologic and Biosimilars:

Biologic:

A biologic medicine is a large molecule typically derived from living cells and used in the treatment, diagnosis or prevention of disease. These are produced by using biotechnology procedures like r-DNA technology. Biologic medicines include therapeutic proteins, DNA vaccines, monoclonal antibodies and fusion proteins. Biologics are distinct from small molecule drugs in that they are larger, and are far more structurally complex agents. Biologic medicines are often 200 to 1,000 times the size of a small molecule drug. They are also highly sensitive, making them more difficult to characterize and produce. Due to both their size and sensitivity, biologic medicines are almost always injected into a patient's body[6].

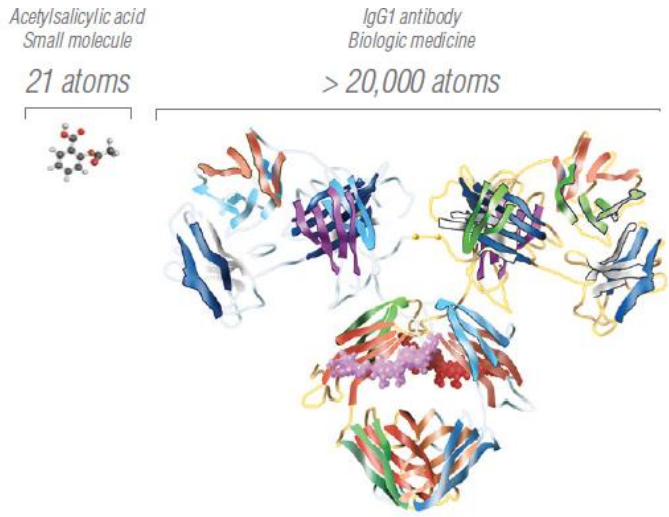

Figure 2: Structural difference between chemical entity drugs and biologic medicines

Reference innovator product for biosimilars:

- Reference innovator product must have same active substance as of the proposed similar biologic.

- The dosage, form and route of administration of the similar biologic should be same as that of reference innovator product.

- Reference innovator product should have been authorized for approval in India to confirm its quality, safety and efficacy. In cases where reference innovator product is not

authorized in India, it should have been approved in countries with well-established regulatory systems such as US FDA, EMA etc. and should have been in use for at least four years.

- Another similar biologic cannot be considered as reference innovator product, as the reference innovator product should be the one that has been licensed based on a full quality, safety and efficacy data.

- Same reference innovator product should be used throughout the development of a similar biologic i.e. manufacturing process, comparability exercise, pre-clinical and clinical evaluation.

- The acceptance of a reference innovator product for evaluation of a similar biologic does not imply approval for use of the reference innovator product in India.

- In case the reference biologic is not marketed in India, the reference biologic should have been licensed and widely marketed for 4 years post approval in innovator jurisdiction in a country with well-established regulatory framework. In case no medicine or only palliative therapy is available or in national healthcare emergency, this period of 4 years may be reduced or waived off[7,8].

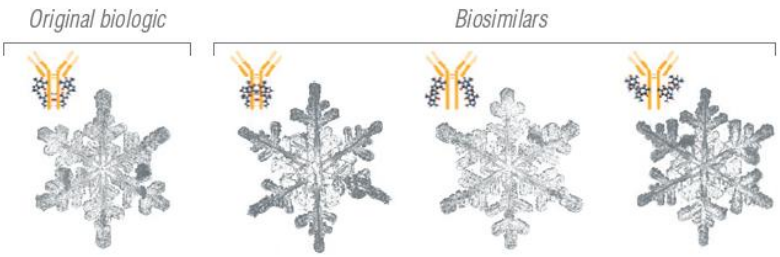

Figure 3: Original biologic and Biosimilars

Biosimilars (similar biologics):

Table 1: Comparative table for definition of biosimilars across global

INDIA	UNITED STATES	EUROPE
As per the Indian Biosimilars guidelines, similar biologic includes: A Similar Biologic product is that which is similar in terms of quality, safety and efficacy to an approved Reference Biological product based on comparability. India[7].	A biological product that is highly similar to a U.S. licensed reference biological product notwithstanding minor differences in clinically inactive components, and for which there are no clinically meaningful differences between the biological product and the reference product in terms of the safety, purity and potency of the product [6].	A biological medicine that is developed to be similar to an existing biological medicine (the 'reference medicine'). When approved, a Biosimilar's variability and any differences between it and its reference medicine will have been shown not to affect safety or effectiveness[6].

Table 2: Different terminolgy used for the word biosimilars across Global

COUNTRY/AUTHORITY	TERM
WHO	Similar biotherapeutic products
USFDA, Japan	Follow on protein products/Follow on biologics
Canada	Subsequent entry biologics
EMA, Korea, China, Australia	Biosimilars
India	Similar Biologics

COMPARISON BETWEEN BIOSIMILARS & BIOLOGICS:

A biosimilar medicine is analogous to a biological medicine that has already been approved (the 'biologic reference medicine') and they are the genetic versions of biologics. The active ingredient of a biosimilar medicine is analogous to the biological reference medicine. Biosimilar and biological reference medicines are given in general at the same dose to treat the same disease.

Based on these different definitions, there are three determinants in the definition of the biosimilar product:

i. It should be a biologic product;

ii. The reference product should be a previously licensed biologic product;

iii. The demonstration of high similarity in safety, quality, and efficacy is obligatory[9].

Table 3: Differences between Generic, Biologics and Biosimilars

GENERIC	BIOLOGICS	BIOSIMILARS
Chemical and therapeutic equivalent of original low molecular weight drug whose patent has expired.	Biological medicinal products developed through biopharmaceutical techniques such as: • Recombinant DNA technology • Cell fusion	Biological product referring, but not identical to an existing product, submitted for separate marketing approval following patent expiration.

Similar biologics are not expected to be direct copies of biologic medicines and are therefore not the same as generic drugs. Due to the complex structure of biologic medicines and the processes involved in production, biosimilars must be shown on the basis of analytical, non-clinical and clinical data to be similar to an original biologic in terms of structural characteristics, and safety and efficacy. Minor differences with the active ingredient are expected and permitted so long as any such differences are demonstrated not to be clinically meaningful[6].

Table 4: Comparison of Generics and Biosimilars

	GENERICS	BIOSIMILARS
Definition	A generic drug is the same as a brand name drug in dosage, safety, strength, how it is taken, quality, performance, and intended use. A generic drug product must contain the identical amounts of the same active ingredient(s) as the brand name product.	A biological product or drug produced by genetic engineering techniques and claimed to be "similar" in terms of quality, safety, efficacy to a reference innovator product
Product related differences	• Produced by chemical synthesis • these are far smaller (<500 Da), i.e., mol.wt,1000, self-contained, organic molecules • Well-defined physiochemical properties • Usually Stable • Single entity, high chemical purity, purity standards well established • Identical copy can be made • Administered through different routes of administration. • Rapidly enters systemic circulation	• Biotechnologically produced by host cell lines • 100 to 1000 times larger in size(5000-3,00,000 Da), having several hundred amino acids (average molecular weight of 150 per amino acid), biochemically joined together in a defined sequence by peptide bonds to form a polypeptide. • Complex physiochemical properties • Often unstable, Sensitive to heat and shear (aggregation), may require specific formulation • Heterogeneous nature, broad

	through blood capillaries. • Distribution to any combination of organ/tissue • Often specific toxicity • Often non-antigenic	specifications which may change during development, difficult to standardize • Impossible to ensure identical copy. • Usually administered parenterally • Larger molecule primarily reach circulation via lymphatic system, subject to proteolysis during interstitial and lymphatic transit • Distribution usually limited to plasma and/or extracellular fluid • Mostly receptor mediated toxicity • Usually antigenic
Manufacturing differences	• Completely characterized by analytical methods • Easy to purify, costs cheap • Contamination can be generally avoided, easily detectable and removable • Not affected by slight changes in production process and environment • Reproducibility easy to establish	• Difficult to characterize • Lengthy and complex purification process & isolation, expensive • High possibility of contamination, detection is harder and removal is often impossible • Highly susceptible to slight changes in production process and environment • Reproducibility difficult to establish
Clinical development	• Limited clinical activities, often only phase 1 PK/PD studies • Short timeline for approval • Development costs upto 5 m$ • Enrolment of around 20-100 subjects	• Extensive clinical trial activities, including phase 1 & 3 studies. • Pharmacovigilance and periodic safety updates after launch needed • Development costs around 350-800m$ • Timeline of 6-15 years • Enrolment of >1000 patients/subjects
Marketing	• Large price discounts • No or limited detailing to physicians • Key role of wholesalers and payers • Special delivery device not usually necessary • Automatic substitution is possible in some pharmacies • Simple to distribute	• Smaller price discounts; price sensitivity is product-specific • Detailing to specialist physicians required • Method of delivery can be a key differentiator • No automatic substitution • Specialist distribution often required
Regulation	• Must be identical to reference product • Substitutable/interchangeable • Abbreviated procedure is applicable to all drugs	• Must be highly similar to reference product • Not automatically substitutable • Abbreviated approval requirements vary depending on the drug

Table 5: Comparision in Development Stages of Generics, Biosimilars &Originators

Activities	Generics	Biosimilars	Reference biologics(originators)
No.of patients in various phases of development	20-50 patients	~500 patients	~1000-2000 patients
Time to market	2-3 years	7-8 years	8-12 years
Development costs	USD 2 million-3 million	USD 100 million-150 million	USD 500 million-1 billion
Success probability	90-99%	50%	5%

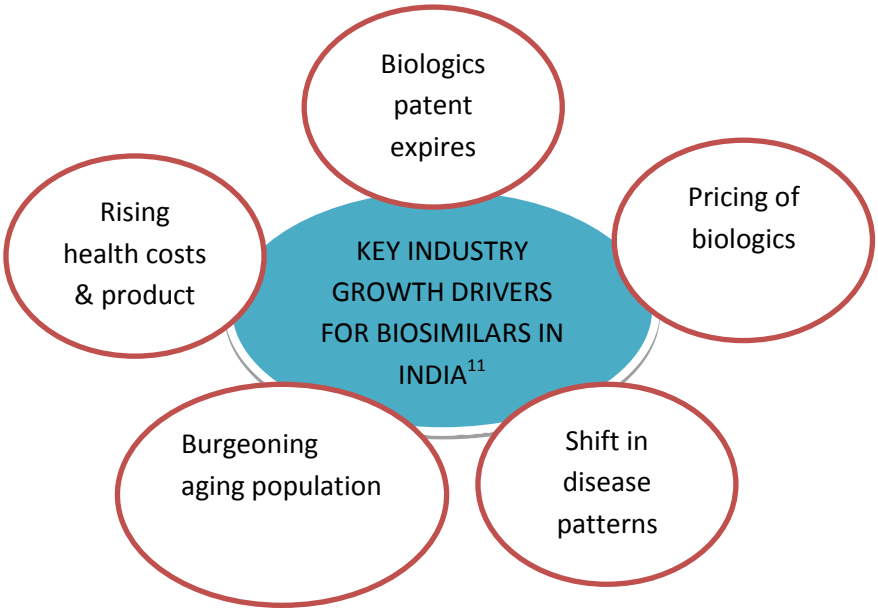

Figure 4: Industry Growth Drivers

Table 6: Application Forms and Corresponding licenses for Indian Regulatory Authorities to carry out development stage of products

Application types	Application Form No.	License Form No.	Regulatory body	Validity	Timelines in Days
Import of drugs for the purpose of examination, test or analysis	Form 12	Form 11	CDSCO	3 Year	15
NOC for manufacture for the purpose of examination, test or analysis (Form 29)	-	NOC	CDSCO	-	60#
Manufacture for the purpose of examination, test or analysis	Form 30	Form 29	SLA	3 Year	30

Table 7: The list of various application to CDSCO/ state licensing authorities (SLA) for drug import, site registration, manufacture and marketing authorization

Application types	Application Form No.	License Form No.	Regulatory body	Validity	Timelines in Days
Import of a new drug (DP)/ (DS)	Form 44	Form 45/ Form 45 A	CDSCO	-	180
Manufacture of New Drug (DP)/ (DS)	Form 44	Form 46/ Form 46 A	CDSCO	-	180
Permission to undertake clinical trial	Form 44	NOC	CDSCO		180
Registration certificate for import of Drugs into India	Form 40	Form 41	CDSCO	3 Years	180
Import license for drugs for commercial use	Form 8	Form 10	CDSCO	3 Years	45
Manufacture for sale or distribution (Mfr.)	Form 24	Form 25 (Fresh) Form 26 (Renewal)	SLA	5 Years	30
Mfr. of Drugs specified in schedule C & C(1) and not in schedule X	Form 27	Form 28 (Fresh) Form 26 (Renewal)		5 Years	30
Mfr. of LVP/Sera and Vaccines excluding those specified in Schedule X	Form 27 D	Form 28 D		5 Years	60
Mfr. of Loan licenses except schedule C & C(1) and X	Form 24 A	Form 25A (Fresh) Form 26A (Renewal)	Concerned SLA	5 Years	30*
Sale licence to sell, stock or exhibit or offer for sale or distribution of drugs(Drugs other than and X)	Form 19	Form 20 (Retail) Form 20 B (Wholesale)		5 Years	30*
Sale license rugs specified in schedule X and not in schedule C & C(1)	Form 19 C	Form 20F (Retail) Form 20 G (Wholesale)		5 Years	30*
[#]If inspection of premises involved, the timelines will be consider from the date of receipt of the inspection report *Timelines vary state to state licensing authority					

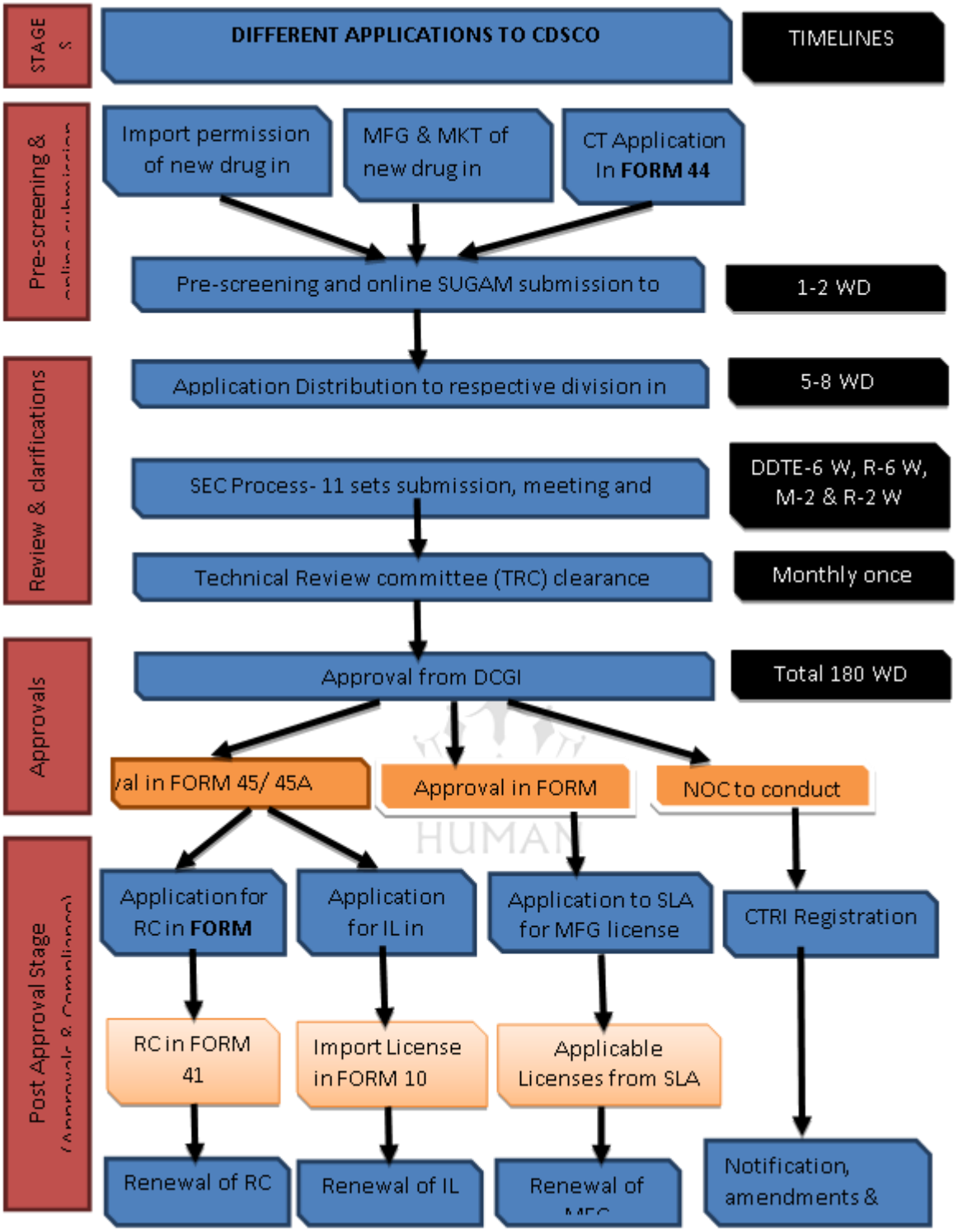

Figure 5: REGULATORY PATHWAY FOR NEW DRUGS (CT, MAA, RC and Import) APPLICATIONS AT CDSCO

Stepwise Procedures for the Development of r-DNA Biosimilars Products

Constitution of Institutional Biosafety committee (IBSC):

Application to RCGM for constitution of IBSC

↓

RCGM approves & appoints a Govt. nominee in IBSC

↓

Formation of IBSC

↓

IBSC meetings

Ref: Guidelines & Handbook for IBSC;
2nd revised version May 2011

New product development

↓

Submit application in Form B1 to RCGM

Requirements for import license:
1. Applicant name
2. Description of GMO
3. Quantity of GMO
4. Source of GMO
5. Objective of the proposal
6. Mode of shipment
7. Information on containment facilities installed at R& D & production premises (whichever is applicable)
8. SOP on decontamination, disposable mechanisms & risk management

Copies: 23

↓

Clearance in Form B2 from RCGM

↓

Submit application Form 12 with RCGM recommendation to DCGI

Requirements for import license:
1. Form 12 (application) clearly indicate the name of country, manufacturer, generic name, composition of drug & therapeutic class
2. Mfg-form 29: Purpose of import and detailed utilization indicating nature of tests and quantity required for test
3. An undertaking that drugs imported under test license would be used for test & analysis
4. Detailed information regarding import of same drug during last 3 years along with certificate destruction of unused drug

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Form 11 from DCGI (License to import drugs/strains/kit for the purposes of examination, test or analysis

Development phase

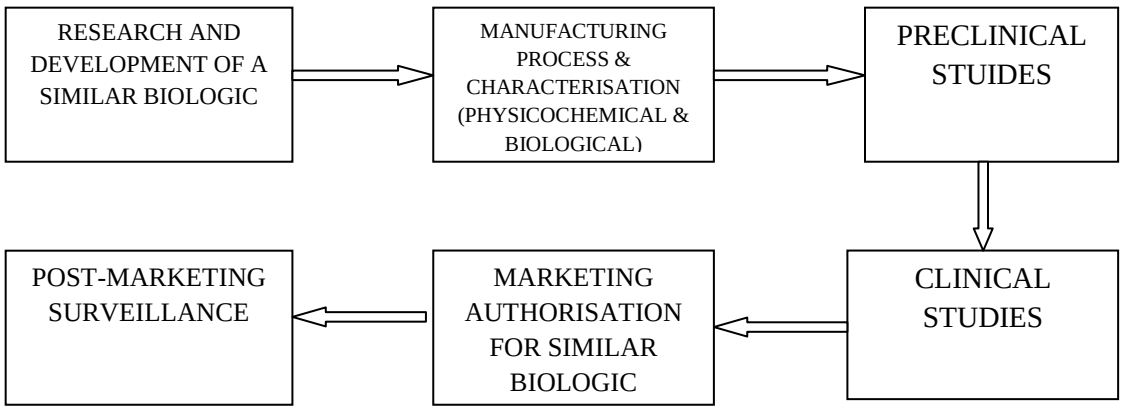

Figure 6: Steps involved in the Development and Marketing of a Biosimilar

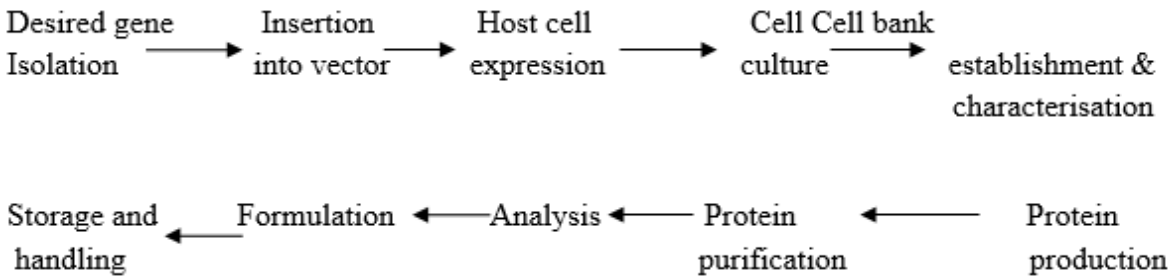

Figure 7: Typical steps in the Manufacture of a biological product

In India, an applicant is required to file application in Form 44 along with prescribed fees in the form of treasury challan and all relevant data as per Schedule Y of Drugs and Cosmetics Rules, for seeking permission to import or manufacture of new drug substances and its formulations for marketing in the country or conduct of clinical trials in India through SUGAM portal a recent initiative of e-governance by Government of India. The documents include chemical and pharmaceutical information, animal pharmacological and toxicological data, clinical data of safety and efficacy, regulatory status in other countries etc., and results of clinical trials on local population.

Import of drugs for examination, test or analysis in Form 11[16, 17]

Test license or Form 11 license is obtained for the import of small quantities of drugs, which is otherwise prohibited under section 10 of the Drugs and Cosmetics Act and Rules, 1945, for the purpose of examination, test or analysis

The application to be submitted in Form 12, requisite fee Rs. 5000/- for single drug Rs. 2000 for each additional drugs along with the supporting documents to CDSCO SUGAM portal for approval in Form 11 having validity of 3 years.

The following conditions to be considered by the applicant as laid down in the D&C act and Rules:

(a) No drug shall be imported for such purpose except under a license in Form 11.

(b) The licensee shall use the substances imported under the license exclusively for purposes of examination, test or analysis and shall carry on such examination, test or analysis in the place specified in the license, or in such other places as the licensing authority may from time to time authorise;

(c) The licensee shall allow Drug Inspector authorized by the licensing authority in this behalf to enter, with or without prior notice, the premises where the substances are kept, and to inspect the premises, and investigate the manner in which the substances are being used and to take samples thereof;

(d) The licensee shall keep a record of, and shall report to the licensing authority, the substances imported under the license, together with the quantities imported, the date of importation and the name of the manufacturer;

(e) The licensee shall comply with such further requirements, if any, applicable to the holders of license for examination, test or analysis as may be specified in any rules subsequently made under Chapter III of the Act and of which the licensing authority has given to him not less than one month's notice.

Manufacture of drugs for examination, test or analysis in Form 29[16, 17]:

For development of any new drug the applicant is required to obtain license in Form-29 from State Licensing Authority based on NOC obtained from CDSCO. No objection certificate (NOC) to be sought from the CDSCO by submitting the application in prescribed format which comprise of product general information, manufacturing facility details, technical staff. On January 19, 2018, the Central Drug Standard Control Organization (CDSCO) has published clarification regarding issuance of No Objection Certificate (NOC) for issuing Form 29 License used to manufacture drugs for the purposes of examination, test or analysis of biological products (Vaccines 86 r-DNA products).

Form 29 is a license to manufacture drugs for the purpose of Examination Testing and Analysis. An application for a Form 29 license shall be made to the Licensing Authority appointed by the State Government for the purpose of this Part (hereafter in this Part referred to as the Licensing Authority) in Form 30 and shall be made by or countersigned by the head of the institution in which, or a director of the firm or company by which, the substance will be manufactured. A license in Form 29 shall, unless sooner cancelled, be in force for a period of one year from the date of issue, and may thereafter be renewed for periods of three year at a time.

Also, the CDSCO on its previous notification has also clarified that "the product manufactured under Form 29 license can be exported only for the purpose of examination, test or analysis including clinical evaluation involving human subjects and not meant for commercial purposes as per Drug and Cosmetic Rules".

CDSCO's further discussion with stakeholders has streamlined the application process as:

The applicants shall submit application for obtaining Form 29 license to the concerned State Licensing Authority (SLA).

Applicant shall simultaneously apply to CDSCO, HQ for issuance of NOC to obtain Form 29 with the documents as mentioned in the checklist along with undertaking, with a copy to concerned CDSCO, Zonal office by hard copy as well as soft copy through e-mail.

NOC for issuance of Form 29 will be issued by this Directorate (CDSCO) within 7 working days.

The joint inspection will be carried out based on risk based approach as per following criteria:

- If the seed/strain falls under BSL - III & IV, joint inspection shall be conducted in such cases. The applicant shall also inform about the BSL of the microorganisms/ strains with supporting documents while submitting the application.

- If seed/stain falls under BSL I & II, joint inspection may not be required, provided that the manufacturing facility is already jointly inspected earlier.

- The joint inspection shall be conducted for all new facilities which have never been licensed/incorporated.

The joint inspection shall be conducted within 15 working days from the date of receipt of application wherever required.

In all cases, if the NOC from CDSCO, HQ is not granted within 7 working days after receipt of application, NOC will be deemed as granted.

The SLA days from the date of receipt of NOC from CDSCO-HQ.

In case of non-compliances observed during the joint inspection, the firm is required to submit the Corrective and Preventive action (CAPA) along with supported documents within 30 days to CDSCO, HQ for review. In case of unsatisfactory reply and/or compliance, Form 29/NOC so granted may be cancelled/ suspended. However, in current practice application in Form 30 along with prescribed fee Rs. 250/- for single product to be submitted to SLA will grant of form 29, upon receipt of NOC from CDSCO.

Approval Mechanism for Clinical Trials in India[16, 17]

For Clinical trials application, the data should be submitted online in form 44 along with pre-requisite fee and supportive details such as chemical and pharmaceutical data; generic & chemical name; dosage form; composition; animal pharmacology & toxicity data; animal toxicology and clinical data; as well as phase I, II, III & IV data to the DCGI. The protocol of the clinical trial with a consent form is also submitted. The authority also needs to know about the regulatory status of the drug in other countries, including names of countries where the drug is approved, and international package insert or the place where Investigational New

Drug (IND) application is filed. Applicants have to report any Suspected or Unexpected Serious Adverse Reaction (SUSAR) from other participating countries, if any. Further, it is necessary to submit an affidavit from the sponsor stating that the study has not been discontinued in any country. In case of discontinuation, reasons for the same must be communicated to the DCGI. Furthermore, a letter of undertaking for compensation as per appendix XII of schedule Y and marketing authorization application submission to CSDCO once approved in country of origin.

For comprehensive details applicant can refer Schedule Y of the Drugs and Cosmetics Act 1940, and the rules therein, pre-screening checklist displayed on CDSCO website (https://cdsco.gov.in/opencms/opencms/en/Clinical-Trial/clinical-trials/).

Post submission the application shall be reviewed by CDSCO and experts, before issuance of approval, the detail steps have been mentioned in Figure 5.

Clinical trials can be initiated only upon receipt of approval from both CDSCO and concerned ethics committee.

All the trials have to be registered prior to the initiation of clinical trials in Indian Council of Medical Research (ICMR) clinical trial registry which is mandatory since June 2009 onwards.

New Drug Approval Process[16, 17]

Schedule Y deals with regulations pertaining to clinical trial requirements for import, manufacture and obtaining marketing approval for a new drug in India.

Demonstration of safety and efficacy of the drug product for use in humans is essential before the drug product can be approved for import or manufacturing and marketing in the country. For new drug application, the dossier is to be submitted online in Form 44,treasury challan of Rs. 50,000/- for manufacturing permission whereas 2,50,000/- for import permission application and information should be submitted as per Schedule Y format, D &C act and subsequent amendment of D & C rules basic dosage and indication data, active and inactive data, patents information, regulatory status in other countries, and marketing information. Post review by CDSCO officials and SEC, DCGI will issue approval as follows, if approval sought for permission to manufacture than DCGI will issue Form 46A for API,

Form 46 for drug product for permission to manufacture of new drugs, accordingly applicant needs to seek manufacturing license from SLA. If the approval sought for import permission than in Form 45A for API, Form 45 for Drug product for import permission, after approval import and registration process to be initiated.

Registration of Site and Products and import licence[16, 17]

The drugs which are being imported must have to register with CDSCO before importation into India. Foreign manufacturers must apply for registration certification for their manufacturing premises and for the individual drugs proposed to be imported.

Applications can be submitted by authorized agents of foreign firms in India through SUGAM portal. According to recent new legislation, import license will be required for all types of drugs, rather than the existing import license requirements for Schedule C and C (1) and Schedule X drugs only.

Import license applications should be applied in Form 40, treasury challan of 10,000/- USD for site registration and 5000/- USD for each product registration along with information and undertakings specified in Schedule D(I) and Schedule D(II) should duly signed by the manufacturer. Schedule D(I) and D(II) should comprise actual plant and drug data, such as the plant master file; the manufacturing license in country of origin; a GMP certificate; a Certificate of Pharmaceutical Products (CPP) issued by the regulatory authority of the country of origin; drug substance information; finished formulation information; clinical documentation, and packaging and labelling information. Import registration is valid for three years for a drug. Based on this, applicant can apply commercial import license Form 8 or Form 8A along with fee of Rs. 10000/ for single drug and 1000/- for each additional drugs. Based on this approval product can be import into Indian Territory for marketing.

CONCLUSION

In the present scenario, India has stringent and at par regulatory requirements for approval of a new drug. The single regulatory approach for Marketing Authorization Application (MAA) of a new drug product belonging to various categories of drugs (NCE, Biologicals, Controlled Drugs etc.) is utmost difficult. Therefore, the knowledge of precise and detailed regulatory requirements for MAA of different categories of drugs should be known to establish a suitable regulatory strategy for advancing of the commercial launch.

Pharmaceutical product approval process should be seen as a critical milestone in ensuring access to safe and effective drugs. In order to protect the public health and facilitate healthy growth of pharmaceutical firms.

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